Studies of the Hydrogen Held by Solids. XII. Hydroxyapatite Catalysts

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Abstract: A series of hydroxyapatite catalysts of varying Ca/P ratios were prepared and characterized by a number of physical methods. All of these catalysts were nonporous crystalline solids whose BET N_2 surface areas were in fair agreement with areas calculated from their electron micrographs. It was shown that most of this area stemmed from edges of the *ab* planes stacked along the *c* axis. Direct assay of catalyst hydrogen, when compared with the known variations in Ca/P ratio, made it possible to discriminate among the several possible ways by which the stoichiometry can be maintained. It was concluded that for each Ca^{2+} removed, two protons were introduced into the solid; these probably resided (temporarily) on phosphate groups. On mild heating to remove H_2O, about half of the phosphate hydrogen was removed by reaction with structural OH groups; on heating to 500°, most of the remainder was lost through formation of intracrystalline pyrophosphate; and on heating above 800°, this reacted with the residual structural OH groups as the structure rearranged to β-tricalcium phosphate. Studies of the reaction of hydroxyapatites with triphenylcarbinol, tritolylcarbinol, and trianisylcarbinol showed that surface acidity was developed as the preparations were made calcium deficient, and that the acidity was much higher with catalysts after mild heating than with those heated to 500°. In no case, however, was the surface carbonium ion concentration as high as the residual phosphate hydrogen calculated to be in unit cells adjacent to the surface. Rates of alcohol dehydration correlated with increasing acidity and with increasing calcium deficiency.

Because it is the mineral phase in bone, the structure and properties of the hydroxyapatites have been the subject of many investigations. The unit cell of the parent compound, stoichiometric hydroxyapatite, $3[Ca_3(PO_4)_2]\cdot Ca(OH)_2$, has been established by both X-ray[1-3] and neutron diffraction,[2a] but the calcium-deficient hydroxyapatites are of greater biological interest because the Ca/P ratio in bone is nearer to 1.5 than to 1.67. (Some carbonate is always present.) Because of this flexibility of stoichiometry, bone hydroxyapatite acts as a buffer to the composition of blood.

Controversy has centered about the hypothesis[4,5] that caicium phosphates form an isostructural series from stoichiometric hydroxyapatite (Ca/P = 1.67) to tricalcium phosphate (Ca/P = 1.5). An alternative (adsorption) theory, which proposed that calcium-deficient compounds were formed by the adsorption of biphosphate ions on the surface of hydroxyapatite, had been advanced,[3] but this was rejected by Posner[4] on the basis that the available surface area is insufficient in some calcium-deficient preparations to explain the over-all composition. Posner preferred a statistical model in which Ca^{2+} ions were removed from column positions of hydroxyapatite, the deficiency being balanced by the addition of two protons per calcium removed. Infrared identification of both structural hydroxyls and acid phosphate groups in calcium-deficient hydroxyapatites has been claimed by two groups,[5,6] but the workers did not agree on the location of the bands used to identify phosphate hydrogen (POH). This identification, together with the quantitative determination of $P_2O_7^{4-}$, led Winand, *et al.*,[5] to suggest that the charge balance was maintained in nonstoichiometric preparations by the net addition of one proton and removal of one structural OH per missing Ca^{2+}. However, Posner, *et al.*,[6] pointed out that the available data do not justify this hypothesis and opined that missing hydroxyl ions would allow collapse of the hydroxyapatite structure. It is shown herein that Winand's hypothesis nevertheless approximates the real situation more closely than any other simple model.

Recently, Brown and co-workers[7] have suggested a further possibility, *viz.*, that calcium-deficient hydroxyapatites are epitaxial intergrowths of octacalcium phosphate, Ca/P = 1.33, and stoichiometric hydroxyapatite, Ca/P = 1.67, to give the observed low Ca/P ratio. Berry[8] has shown that both Winand's hypothesis and the lamellar structure of Brown will explain the formation of $P_2O_7^{4-}$ and the weight loss at 800° associated with loss of H_2O, but that neither infrared data nor thermal analyses give any indication of octacalcium phosphate in calcium-deficient hydroxyapatites.

Our principal interest in the hydroxyapatite system has been in its potential as a model heterogeneous catalyst in which the stoichiometry could be changed without altering the crystal structure. Bowman and Piasecky[9] have shown that basic calcium phosphates effect the dehydrogenation and dehydration of alcohols, and that the selectivity for these reactions is controlled by the composition. However, their work did not provide a basis for understanding the origin of the selectivity. Data on the influence of the stoichiometry of hydroxyapatite on dehydration are given herein,

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(1) W. F. Neuman and M. W. Neuman, *Chem. Rev.*, **53**, 1045 (1953).

(2) (a) M. I. Kay, R. A. Young, and A. S. Posner, *Nature*, **204**, 1050 (1964); (b) A. S. Posner, A. Perloff, and A. F. Dorio, *Acta Cryst.*, **11**, 308 (1958).

(3) (a) F. K. Cameron and J. M. Bell, *J. Am. Chem. Soc.*, **27**, 1512 (1905); (b) S. B. Hendricks and W. L. Hill, *Proc. Natl. Acad. Sci. U. S.*, **36**, 731 (1950).

(4) A. S. Posner and A. Perloff, *J. Res. Natl. Bur. Std.*, **58**, 279 (1957); A. S. Posner and S. R. Stephenson, *J. Dental Res.*, **31**, 371 (1952).

(5) (a) L. Winand and G. Duyckaerts, *Bull. Soc. Chim. Belges*, **71**, 142 (1962); (b) see also L. Winand, *Anal. Chim.*, **6**, 62 (1961).

(6) A. S. Posner, J. M. Stutman, and E. R. Lippincott, *Nature*, **188**, 486 (1960); **193**, 368 (1962).

(7) W. Brown, J. P. Smith, J. R. Lehr, and A. W. Frazier, *ibid.*, **196**, 1048 (1962).

(8) E. E. Berry, *J. Inorg. Nucl. Chem.*, **29**, 317 (1967).

(9) R. S. Bowman and L. J. Piasecky, U. S. Patent 3,149,082 (1964).

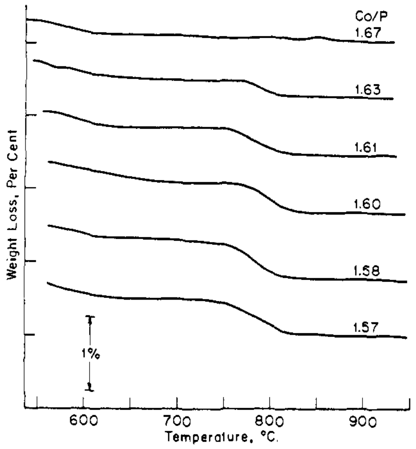

Figure 1. Thermogravimetric analysis of calcium-deficient hydroxyapatites.

and the effects of composition on the selectivity will be the subject of a later paper.

Experimental Section

Preparation and Characterization of Catalysts. Preparation. The hydroxyapatites were made by titrating concentrated H_3PO_4 into saturated $Ca(OH)_2$. From the volume and concentration of the latter, the volume of H_3PO_4 required to give a desired Ca/P ratio was slowly stirred into the $Ca(OH)_2$ at room temperature. Pyrex vessels were used and the reagents were mixed under N_2. A fine gel-like precipitate appeared immediately, and this suspension was reduced to dryness during 15 hr over a hot plate. The pH of the solution fell from 12.6 to 11.6 during titration for hydroxyapatite and to somewhat lower values for calcium-deficient preparations. The products, white crystalline solids, were sieved for catalytic studies to 30–60 mesh.

In a typical preparation (stoichiometric hydroxyapatite), 59.8 ml of 0.769 M H_3PO_4 was added dropwise in 1 hr to 3.67 l. of saturated (0.0211 M) $Ca(OH)_2$. The large volume of the $Ca(OH)_2$ solution prevented the temperature from rising perceptibly from room temperature (22°) during titration.

In order to reduce minor impurities, CaO was prepared by calcining Fisher certified $CaCO_3$ in a quartz vessel at 900°. The resulting oxide was dissolved in deionized H_2O and stored in a plastic container. Fisher certified orthophosphoric acid was purified by passage through an ion-exchange column of Amberlite IR-120 in the acid form. Spark spectra showed the total cationic impurities (except Si) in the final catalysts to be less than 500 ppm, principally Na and Al; Si occurred in some samples up to 0.1%. These impurities undoubtedly stemmed from the Pyrex containers used in the preparations.

Characterization. Because of the rather small changes in stoichiometry and properties of the calcium-deficient hydroxyapatites, a variety of chemical and physical measurements were made. The results of these diverse measurements, which are given below, are consistent with a description of our preparations as a series of hydroxyapatites of constant structure and similar morphology, but with stoichiometry varying from Ca/P = 1.67 to 1.57.

Analytical Methods. Calcium was determined by standard EDTA titration techniques and phosphate by the differential spectrophotometric technique of Gee and Dietz.[10] The calcium to phosphorus ratios were found to correspond to the ratios expected from the starting materials to within ±0.01. Analyses of aliquots of the same samples, in our laboratory and in Posner's, agreed within the same limits. Some representative data are recorded in Table I.

X-Ray Diffraction. In accord with the frequently recorded observation[1,2b] that both hydroxyapatite and calcium-deficient hydroxyapatites yield closely similar X-ray diffraction patterns, all preparations between Ca/P = 1.67 and 1.57 (our most calcium-deficient preparation) gave fairly well-resolved patterns similar to hydroxyapatite, both when dried over a hot plate at 175° and when heated to 600°. Preparations with different Ca/P ratios could be identified, however, by their behavior on heating above 780°. While stoichiometric hydroxyapatite maintained its structure virtually intact to 1000°, increasing calcium deficiency was indicated by the appearance of increasing amounts of β-tricalcium phosphate. The intensity of the strongest lines of each phase are given in arbitrary units in Table II (as peak height above background). The ratio of these peaks reflects qualitatively the increase in the β-tricalcium phosphate phase.

Table I. Chemical Analyses of Representative Hydroxyapatite Preparations[a]

Ca/P atom ratio	
Initial solution	Chemical analysis
1.67	1.68 ± 0.008
1.61	1.62 ± 0.008
1.58	1.60 ± 0.008

[a] The authors wish to express their gratitude to Dr. A. S. Posner in whose laboratory these analyses were performed.

Table II. Formation of β-Tricalcium Phosphate in Hydroxyapatites Heated to 1000°

Ca/P	Intensity, 311 reflection,[a] hydroxyapatite	Intensity, 2·0·10, 217[b] reflections, β-tricalcium phosphate	100 × $I_{\beta TCP}/I_{HA}$
1.67	84	2	~2
1.60	43	21	49
1.58	52	39	75

[a] Not completely resolved from 112. [b] Coincident.

Thermogravimetric Analysis. The curves of Figure 1 are consistent with those of other workers,[5b,11] as well as with the X-ray data. Brasseur[11] reported an inflection in the weight loss curve near 800°, corresponding to the loss of about half a molecule of water per calcium deficiency in a sample with Ca/P = 1.5, while the inflection was absent in stoichiometric hydroxyapatite. Winand[5b] identified this loss with that accompanying the removal of structural OH in the transition to β-tricalcium phosphate. The data in Figure 1 showed an increasing weight loss with calcium deficiency corresponding to approximately 0.5 mole of water per calcium deficiency (Table III).

Table III. Thermogravimetric Analyses of Hydroxyapatites[a]

	From each mole of $3[Ca_3(PO_4)_2]Ca(OH)_2$		
Ca/P	Ca^{2+} deficiency, moles	Loss at 780°, moles of H_2O	Ratio, $H_2O/\Delta Ca^{2+}$
1.67	0	0	...
1.63	0.23	0.14	0.61
1.61	0.34	0.22	0.64
1.60	0.40	0.24	0.60
1.58	0.52	0.29	0.56
1.57	0.57	0.29	0.51

[a] Weight loss at 780°. Water is lost mainly by the reaction $P_2O_7^{4-} + 2OH^- \rightarrow H_2O + 2PO_4^{3-}$ as hydroxyapatite is converted to β-tricalcium phosphate; see ref 5.

Infrared Spectroscopy. An attempt was made to identify two types of OH bands: the structural OH groups and the acidic POH presumed to be present in the nonstoichiometric preparations. Spectra from preparations pressed into KBr disks agreed well with those of Winand and Duyckaerts,[5] taken in the same way. The strong band due to the structural OH in the 3550-cm^{-1} region was readily identified and confirmed by deuteration. The weak bands

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(10) A. Gee and V. R. Dietz, *J. Am. Chem. Soc.*, **77**, 2961 (1955).

(11) H. Brasseur, *Bull. Soc. Chim. Belges*, **62**, 383 (1953).

Table IV. Behavior of the Band at 875 Cm^{-1} (POH) Deformation as a Function of Calcium Deficiency

Ca/P	Relative POH intensity[a]
1.67	0.15
1.60	0.42
1.58	0.53

[a] Band at 875 cm^{-1} normalized to the PO_4^{3-} harmonic at 2000 cm^{-1} to correct for sample concentration in KBr disk.

at 875 and 2400 cm^{-1}, which they assigned to POH, were evident but poorly resolved. The area of the former, normalized to the area of the PO_4^{3-} harmonic at 2000 cm^{-1}, paralleled the degree of nonstoichiometry (Table IV). However, it was impossible to confirm that these were OH vibrations by deuteration, even though attempts were made in Nujol and halocarbon mulls, as well as with pressed disks of pure catalyst under high-vacuum conditions. Possibly this was because exchange of these intracrystalline hydrogens did not occur with either D_2O or D_2 at temperatures where condensation of orthophosphate to pyrophosphate groups was not rapid. Nevertheless, we must agree with Posner, *et al.*,[6] that these band assignments do not establish the presence of POH. However, our work does not support the conclusions drawn by Posner[6] from his published data, that the POH bands occur at 3330–3400 cm^{-1}. We see these bands but find that they disappear *in vacuo* at temperatures ($\leqslant 300°$) where other measurements indicate POH should be stable (*vide infra*).

Electron Microscopy and Diffraction from Selected Single Crystals. The morphology of our samples was established by transmission electron microscopy and electron diffraction to be predominantly well-crystallized prisms of average dimensions, $0.02 \times 0.02 \times 0.07\ \mu$. The size distributions were in all cases fairly narrow. The crystals were assumed to be hexagonal prisms, and electron diffraction showed that most of the exposed area was from the edges of the *ab* planes stacked along the *c* direction (Figure 2b). This crystal habit corresponds closely to that described by Frank, *et al.*,[12] for apatite crystals in human enamel, rather than the hexagonal platelets described by Neuman and Neuman[1] for bone apatite. Values from conventional BET surface area measurements are listed in Table V, where they are compared with values calculated from the electron micrographs. The areas were calculated by summing the surface area per particle and the weight per particle over the distribution shown on the electron micrographs, assuming a hexagonal prism geometry. The agreement with BET data could only be achieved with a solid made up of microscopic single crystals. Thus, all the pores are large and intercrystalline; indeed, the shape of the BET isotherms indicated that most of the pores had radii greater than 100 A. The higher area of the stoichiometric sample reflected its slightly smaller crystallite size.

Table V. Surface Areas of Hydroxyapatites

Ca/P	BET area, m^2/g	Electron micrograph area,[a] m^2/g
1.67	75	80
1.60	60	63
1.58	46	67

[a] Calculated from micrographs using $\Sigma_i A_i / \Sigma_i W_i$, where A_i and W_i are the area and weight of crystals of size *i*. The sums are made over the observable distribution.

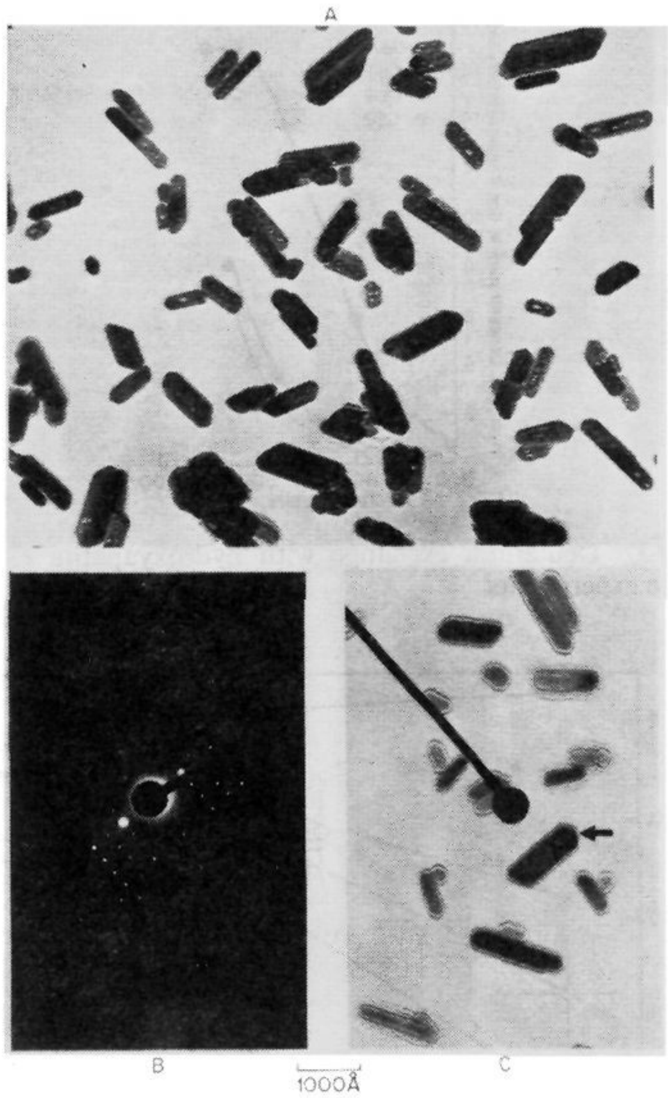

Figure 2. Electron micrographs and electron diffraction pattern of hydroxyapatite catalyst: (A and C) magnification of 125,000, (B) diffraction pattern typical of single crystal shown in C.

Hydrogen-Content Measurements. The hydrogen contents of the hydroxyapatites were determined using the rising temperature D_2-exchange method described previously.[13,14] Samples were evacuated at 550° for 5 hr prior to each experiment. A measured quantity of D_2 was circulated over the catalyst as its temperature was raised at a rate of about 2°/min. The concentration of hydrogen in the gas phase (mole fraction $H_2 + 0.5$ HD) was continuously monitored with thermal conductivity cells. Initial experiments showed that stoichiometric hydroxyapatite reached equilibrium at about 500° while calcium-deficient samples required nearly 600°. The hydrogen assay could be calculated from the isotope dilution of the D_2 at equilibrium.[14]

Measurements of Carbonium Ion Concentrations. Techniques were used whereby both the strength and concentration of acid protons on solid surfaces could be estimated[15,16] from the spectra of suitable adsorbed indicators. The concentration of carbonium ions formed from (substituted) triphenylcarbinols was determined, using the method of Porter and Hall.[16]

Catalyst plates were prepared by pressing powdered catalyst at 15,000 psi between Teflon disks which prevented sticking. Quartz spectrophotometric cells were the same as used previously; these had an arrangement for addition of benzene solutions of the indicators and for removal of solvent under high-vacuum conditions. Absorption spectra were determined using a Cary Model 14 spectrophotometer. Extinction coefficients were taken to be the same as those in solution,[17] an assumption shown to be justified with triphenylcarbinol.[15,16]

Catalytic Measurements. These were carried out in a semiautomatic microcatalytic reactor[18] which operated at a temperature where the vapor pressure of 2-butanol exceeded 1 atm; it will be described in detail elsewhere.

Each catalyst sample was heated to 530° in a stream of dry helium for 15 hr prior to reaction. For comparison of the catalytic activities of members of the series of hydroxyapatites, 2-butanol was introduced into the stream and the products of dehydrogenation (methyl ethyl ketone) and dehydration (isomeric butenes) were determined by glpc.

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(12) R. M. Frank, R. F. Sognnaes, and R. Keon in "Calcification of Biological Systems," R. F. Sognnaes, Ed., American Association for the Advancement of Science, 1960.

(13) W. K. Hall, H. P. Leftin, F. J. Cheselske, and D. E. O'Reilly, *J. Catalysis*, **2**, 506 (1963).

(14) W. K. Hall, F. J. Cheselske, and W. E. Wallace, *J. Phys. Chem.*, **65**, 128 (1961).

(15) A. E. Hirschler, *J. Catalysis*, **2**, 428 (1963).

(16) R. P. Porter and W. K. Hall, *ibid.*, **5**, 366 (1966).

(17) N. C. Deno, J. J. Jaruzelski, and A. Schreisheim, *J. Am. Chem. Soc.*, **77**, 3044 (1955).

(18) W. K. Hall, D. S. MacIver, and H. P. Weber, *Ind. Eng. Chem.*, **52**, 421 (1960).

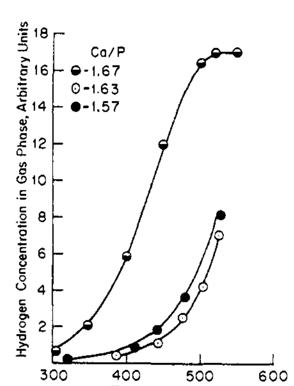

Figure 3. Deuterium exchange with hydroxyapatite rising-temperature experiments.

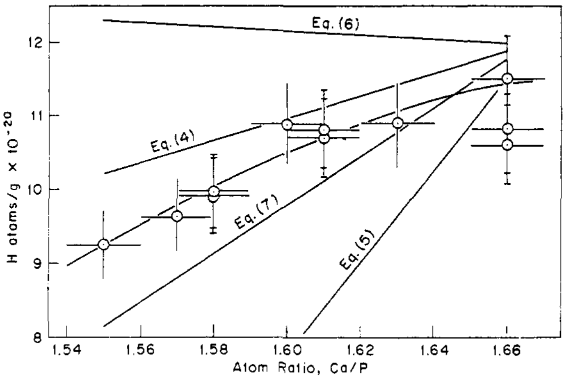

Figure 4. Hydrogen content of hydroxyapatites after heating *in vacuo* at 500 to 550°.

Results

Hydrogen Content of Hydroxyapatites. Rising-temperature experiments showed that the hydrogen of stoichiometric hydroxyapatite exchanged with D_2 at lower temperatures than with calcium-deficient samples (Figure 3). With the latter, exchange did not become significant until temperatures were reached where Winand, *et al.*,[5,12] reported that the condensation of orthophosphate to pyrophosphate was already considerable. Thus, values of hydrogen content, measured after pretreatment at 550°, were nearly free of acid orthophosphate; *i.e.*, they were close to the values of the free structural hydroxyl groups. In Figure 4 the hydrogen contents of the hydroxyapatites are plotted (points) against the Ca/P atom ratio. The formula value (12×10^{22}[H]/g) was approached for the stoichiometric hydroxyapatite, but the hydrogen content fell continuously as the Ca/P ratio was lowered. In the course of these experiments, an attempt was made to measure the acid orthophosphate initially present by trapping the water evolved by condensation to form pyrophosphate, while heating the sample to 500°. The results were in qualitative agreement with 1POH ($0.5H_2O$) per ΔCa^{2+}, but were erratic due to the difficulty in distinguishing between condensation and the desorption of adsorbed water. A better estimate was obtained from the H_2O evolved near 780° (Table III) which resulted from the reaction

$$P_2O_7^{4-} + 2OH^- \longrightarrow 2PO_4^{3-} + H_2O \qquad (1)$$

the OH^- being in excess. These results indicated that

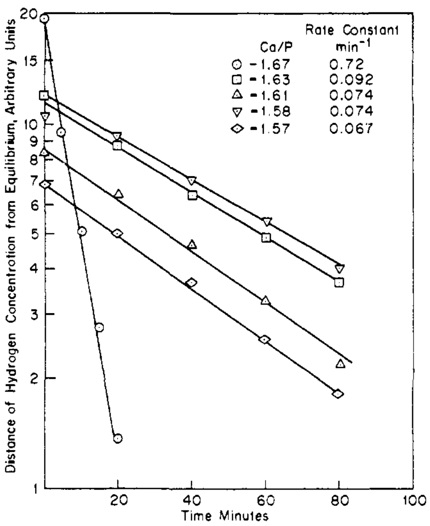

Figure 5. Rates of exchange of deuterium with the OH^- of hydroxyapatite at 500°.

pyrophosphate formation was nearly complete. The X-ray data demonstrated changes consistent with eq 1; in all nonstoichiometric samples heated above 750°, the $Ca_3(PO_4)_2$ phase appeared.

The rate of exchange of deuterium could be measured at 500° and, when plotted as first order in the distance from equilibrium, gave good straight lines (Figure 5), suggesting that only one exchanging species (OH) was present.[13,14] The rate for stoichiometric hydroxyapatite was very much faster than for the calcium-deficient samples given a comparable pretreatment, but was dependent on the temperature of pretreatment.

Acidity of Hydroxyapatite Surfaces. When triphenylcarbinol was added to a pellet of calcium-deficient hydroxyapatite, a yellow color developed. The spectrum had an absorption with twin peaks at 404 and 430 mμ, confirming the formation of the triphenylcarbonium ion, presumably by the reaction

$$ROH + H^+ \rightleftharpoons R^+ + H_2O \qquad (2)$$

Excess triphenylcarbinol (three to five monolayers) was used in all measurements, and the samples were evacuated after equilibration to remove solvent and H_2O of reaction. Hence, the carbonium ion density should have measured the density of acid sites as eq 2 was driven to the right. This was the reason carbonium ion formation was readily detectable despite the fact that it can be estimated from literature data[17,19] that in 85% H_3PO_4 the ratio of $(C_6H_5)_3C^+$ to $(C_6H_5)_3$ should be less than 0.1; 50% H_2SO_4 corresponds to a ratio of unity.[15]

The concentration of carbonium ions on the surface was calculated[16] using the expression

$$\sigma = (ANL \times 10^{-3})/EW \qquad (3)$$

where σ is the number of carbonium ions per gram of solid, A the absorbance, N Avogadro's number, L the geometric area of the catalyst platelet (cm²), E the extinction coefficient (l. mole^{-1} cm^{-1}), and W the weight of the catalyst pellet (g). The surface concentrations on several hydroxyapatite catalysts after different pretreatments are shown in Table VI. The

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[19] M. A. Paul and F. A. Long, *Chem. Rev.*, **57**, 1 (1957).

Table VI. Concentration of Triphenylcarbonium Ions Formed on Calcium-Deficient Hydroxyapatites

Ca/P	Triphenylcarbonium ions, (ions/g) × 10^{17}, pretreatment 180°	290°	500°
1.67	. . .	≤0.2	0
1.63	. . .	0.5	. . .
1.60	6.0 3.9[a]	3.4	0
1.58	8.1[a]	7.2 4.4[a]	0
1.57	. . .	6.7	0

[a] Regenerated by heating at 350° with 20 mm of water vapor for 15 hr.

carbonium ion concentration fell as the Ca/P ratio approached 1.67 where it became too low to measure (colorless). Moreover, the carbonium ion concentration fell as the temperature of pretreatment was raised until, after evacuating at 500°, it was no longer detectable with this reagent on any of the catalysts. After the platelets had been burned in O_2 at 530° to remove the adsorbed organic matter, the acidity could be partially restored by exposing the calcium-deficient hydroxyapatite to 20 mm of H_2O at 350° for several hours.

Similar experiments were made using trianisylcarbinol, which is a much stronger base ($pK_a = +0.82$ *vs.* $pK_a = -6.6$), instead of triphenylcarbinol. The results differed in quantitative aspects only (compare Tables VI and VII), and the differences were surprisingly small. The surface density of carbonium ions was higher in all cases, but the concentration still increased with calcium deficiency. In fact, measurable carbonium ion concentrations were found even after pretreatment at 500° where none was detectable with triphenylcarbinol. Maximum ion concentration was obtained for the catalyst whose Ca/P was 1.58 after evacuation at 160°. Interestingly, nearly identical results were obtained for tritolylcarbinol ($pK_a = -4.1$) and trianisylcarbinol (18×10^{17} and 19×10^{17}/g, respectively) with this catalyst under these conditions. This result suggests that base strength is not limiting the ion concentration in this case.

Table VII. Formation of Trianisylcarbonium Ions on Calcium-Deficient Hydroxyapatites

Ca/P	Trianisylcarbonium ions, (ions/g) × 10^{17}, pretreatment 290°	500°
1.67	3.6	0.66
1.63	13	3.2
1.61	10	3.9
1.58	13	4.9

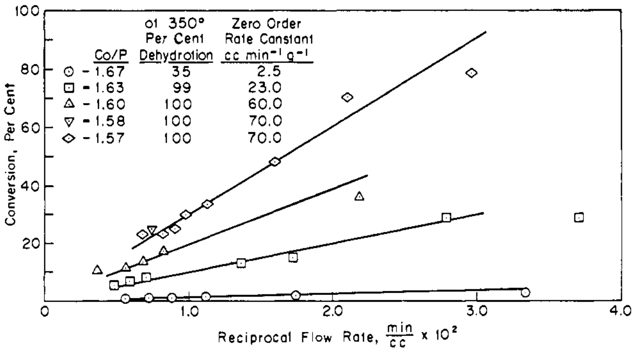

Figure 6. Dehydration rates of 2-butanol over hydroxyapatites.

Decomposition of 2-Butanol. The dehydration rates of 2-butanol for the series of calcium-deficient and stoichiometric hydroxyapatites are given in Figure 6, where the data are treated according to zero-order kinetics. Since in each experiment the catalyst weight and surface area were very similar, these also constitute a comparison on an equal surface area basis. The zero-order rate constants are given and demonstrate that the rate of dehydration increased as the Ca/P ratio decreased. The activation energies did not vary appreciably over the compositional range; 39 ± 1 kcal/mole were derived for each catalyst. Dehydrogenation and dehydration occurred to about an equal extent when the Ca/P ratio was 1.67, but the former dropped to less than 1% when the Ca/P ratio was 1.63 or less.

Discussion

Three possible explanations have been advanced for the existence of calcium phosphates which have the X-ray pattern of hydroxyapatite but which have Ca/P ratios less than 1.67, *viz.* (1) calcium-deficient hydroxyapatites are in fact formed by the adsorption of acid phosphate on the surface of crystals of stoichiometric hydroxyapatite,[3,20-22] *e.g.*, as $CaHPO_4$ or $Ca(H_2PO_4)_2$; (2) calcium-deficient hydroxyapatites truly have the hydroxyapatite structure, but calcium ions are missing statistically from the lattice;[4,23] (3) calcium-deficient hydroxyapatites are epitaxial intergrowths of octacalcium phosphate, $Ca_4H(PO_4)_3$, and hydroxyapatite.[7]

Posner[4] showed that the X-ray diffraction and index of refraction data from Pb^{2+} and Ca^{2+} hydroxyapatites were consistent with a model in which cations are missing statistically from the "columnar" positions of the lattice and argued that the adsorption theory was inadmissible because calcium-deficient hydroxyapatites exist with such low surface areas that it would be impossible to adsorb sufficient biphosphate ions to give low Ca/P ratios. However, this question has not been conclusively settled.

There are several possible ways of maintaining charge neutrality in the calcium-deficient hydroxyapatites. Two hydroxyl groups could be missing from the lattice to balance each calcium deficiency. Posner[4] argued, however, that the lattice would be unstable under these circumstances and suggested that instead two protons were added. Winand and Duyckaerts interpreted their data[5] to mean that one proton was added and one hydroxyl removed, a circumstance which could result from neutralization of one proton with one OH^- group. Each of these conditions leads to a different dependence of the hydrogen content on Ca/P ratio and to the formation of different amounts of pyrophosphate on heating to 550°. Specifically, if two hydroxyl groups were

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(20) H. Hodge, M. Lejeune, and W. Bale, *Ind. Eng. Chem.*, 10, 156 (1938).

(21) A. Schleede, W. Schmidt, and A. Kindt, *Z. Elektrochem.*, 38, 633 (1932).

(22) G. Tromel and H. Moller, *Z. Anorg. Allgem. Chem.*, 206, 227 (1932).

(23) A. S. Posner, C. Fabray, and M. J. Dallemagne, *Biochim. Biophys. Acta*, 15, 304 (1954).

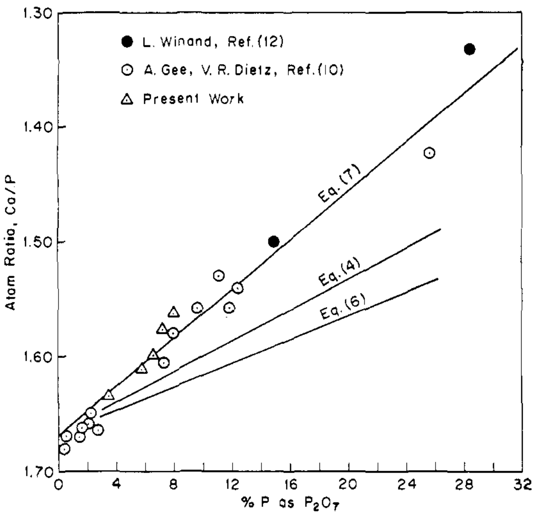


Figure 7. Pyrophosphate formation as a function of Ca/P ratio.

removed (the first suggestion), the hydrogen content would *decrease* from 12×10^{20}/g for Ca/P = 1.67 to zero for Ca/P = 1.5, and no pyrophosphate would be formed. The addition of two protons per calcium deficiency would effect an increase in hydrogen content, but in the limit where pyrophosphate formation is complete, no net change would be observed. The removal of one hydroxyl and the addition of one proton would cause no change in hydrogen content prior to pyrophosphate formation, but, on heating to 550° to eliminate POH, the hydrogen content would fall to 6×10^{20}/g. These different possibilities are embodied in the following equations.

(a) Adsorption theory

$$Ca_{10}(PO_4)_6(OH)_2 \cdot nCaHPO_4 \xrightarrow[550°]{\Delta} Ca_{10}(PO_4)_6(OH)_2 \cdot Ca_n(P_2O_7)_{n/2} + n/2H_2O\uparrow \quad (4)$$

(b) Removal of two hydroxyl groups

$$Ca_{10-n}(PO_4)_6(OH)_{2-2n} \xrightarrow[550°]{\Delta} Ca_{10-n}(PO_4)_6(OH)_{2-2n} \quad (5)$$

(c) Addition of two protons

$$Ca_{10-n}(PO_4)_{6-2n}(HPO_4)_{2n}(OH)_2 \xrightarrow[550°]{\Delta} Ca_{10-n}(PO_4)_{6-2n}(P_2O_7)_n(OH)_2 + nH_2O\uparrow \quad (6)$$

(d) Addition of one proton and removal of one hydroxyl

$$Ca_{10-n}(PO_4)_{6-n}(HPO_4)_n(OH)_{2-n} \xrightarrow[550°]{\Delta} Ca_{10-n}(PO_4)_{6-n}(P_2O_7)_{n/2}(OH)_{2-n} + n/2H_2O\uparrow \quad (7)$$

It can be shown[7] that an interlamellar compound of octacalcium phosphate and hydroxyapatite would also be described by eq 7. Hence, it is not possible to distinguish between the two structures on a chemical basis, but since the X-ray and infrared spectra[8] of calcium-deficient hydroxyapatites do not show the presence of octacalcium phosphate, the postulate that the calcium defects are uniformly distributed throughout the lattice appears more reasonable.

The validity of the above equations can be tested in several ways: (1) by the quantitative determination of $P_2O_7^{4-}$ formation; (2) by comparing the residual hydrogen contents of the solids after heating to 550° with the formulas predictions; and (3) by evaluating the amount of water lost at 780° according to eq 1. The last two tests can be made with our data.

The data of Figure 4 do not conform accurately to any of these possibilities. The simple situations represented by eq 5 and 6 are obviously not operative. This means that a second form of hydrogen must have been introduced to maintain the charge balance (eq 5) and that some structural OH^- must have been removed by "neutralization," if two protons were added (eq 6). The data do not distinguish between the adsorption theory (eq 4) and the suggestion of Winand and Duyckaerts[5a] that one H^+ is added and one OH^- removed (eq 7). Since it is easier to get a high result than a low one (dehydration incomplete), the latter postulate is favored. It should be noted that the adsorption of $Ca(H_2PO_4)_2$ would be described by an equation similar to eq 4, but higher values of catalyst hydrogen would be predicted. Hence, the deviation from the experimental data would be still greater.

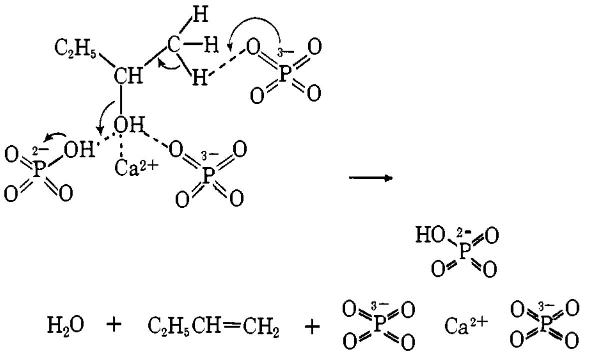
There is no apparent reason why exactly one H^+ must be added and one OH^- be removed in the real system. It seems more likely to the present authors that $2H^+$ were added for each Ca^{2+} deficiency in the wet preparation, but that, on drying, both "self-neutralization" and pyrophosphate formation occurred in amounts governed by statistical and energetic factors. The data of Figure 4 conform more closely to about one-third "self-neutralization" and two-thirds reaction to pyrophosphate. The high $H_2O/\Delta Ca^{2+}$ ratios of Table III also favor this view. An $H_2O/\Delta Ca^{2+}$ ratio of 0.5 is predicted by the model of eq 7; the corresponding value is 0.67 for the one-third, two-thirds partition. The data could also be explained, however, by assuming that the split was more nearly equal but that one or both of the dehydration processes was incomplete. These conclusions are in agreement with the finding of Gee and Dietz[10] that the amounts of $P_2O_7^{4-}$ present in calcined hydroxyapatites of varying Ca/P ratios were insufficient to account for their calcium deficiencies on the basis of the adsorption theory.

Gee and Dietz did not consider the process of eq 7. Berry[8] has recently replotted their data, together with that of Winand,[5b] and shown that all the data fit eq 7 within experimental error. We have included these data with our own in Figure 7, which confirms this finding. It is concluded, therefore, that this picture is essentially correct and that eq 7 semiquantitatively describes the system.

The infrared studies were made to establish that two forms of hydrogen (aside from H_2O) were present in nonstoichiometric samples. The results were inconclusive. Although the H content data indicated considerable orthophosphate hydrogen to be present after heating to 300°, bands due to this species could not be positively identified. Evidence of weakly acidic hydrogen was found, however, with the phenylated alcohols. The surface density of carbonium ions (Tables VI and VII) qualitatively reflected changes derived from the H-content data. The concentrations correlated with the calcium deficiency of preparations; those catalysts treated at 300° or lower were more "acidic" than those evacuated at 500°. Higher values could be effected on catalysts heated to the higher temperature, by exposing to H_2O at lower temperature. Somewhat higher values were also found for more basic carbinols, but not to the extent indicated by their pK_a's. This was at least partly due to the leveling effect of the experimental method, but the latter could not have been totally responsible because identical values were not found for all indicators. Leveling was evident, however, in that nearly identical values ($\sim 2 \times 10^{18}$/g) were obtained with tritolylcarbinol and trianisylcarbinol under conditions of maximum acidity. Quantitatively, this "site density" was at least 20-fold lower than the phosphate hydrogen calculated to be present from the model, assuming the unit cells at the surface contained the same average amount of hydrogen as distributed "uniformly" throughout the solid. It is perhaps significant that on a unit surface area basis, the maximum observed concentration (2×10^{12}/cm^2) was close to that reported by Leftin and Hall[24] for triphenylcarbinol on silica–alumina (5×10^{12}/cm^2). It may be that the ion concentration is limited by a barrier potential as the surface is "charged up" like a condenser plate. Alternatively, some other factor may be controlling.

Both the carbonium ion measurement and the catalytic measurements demonstrated the acidity of the orthophosphate hydrogen. The morphology of the hydroxyapatite preparations was ideally suited for catalytic studies, because the total surface areas were comprised of the sums of the exposed areas of single crystals of nearly uniform size. Hence, a valid activity comparison could be made of the series and the mechanism discussed in terms of a clearly defined surface structure. In this way, the system is analogous to the zeolites.

The catalytic activity of the hydroxyapatites for the dehydration of 2-butanol is shown in Figure 6 to increase with increasing calcium deficiency, as would be expected if the reaction were catalyzed by acid protons. The dehydration of alcohols in solution is acid-catalyzed[25] and takes place at measurable rates in solutions of low acid strength. It is apparent from the carbonium ion measurements described above that under the conditions of reaction, *i.e.*, after pretreatment at 530°, only a very small number of protons remained on the surface; however, more acid protons may have been regenerated by hydrolysis of pyrophosphate by the H_2O of reaction. Thus, trianisylcarbinol must have been protonated by the orthophosphate hydrogen atoms which catalyzed the dehydration, and these were present in increasing concentrations as the Ca/P ratio fell. A mechanism which is consistent with the surface chemistry and geometry is given in eq 8.



(8)

In conclusion, a number of different measurements of the behavior of hydrogen in stoichiometric and calcium-deficient hydroxyapatites have demonstrated qualitatively the presence of two kinds of hydrogen, *viz.*, acidic phosphate hydrogen and the structural hydroxyls of the parent unit cell. The hydrogen assays are consistent with the model proposed by Winand and Duyckaerts for charge balance of the calcium defects in apatites of low Ca/P ratios. Measurements with adsorbed carbonium ions indicate that there are fewer acid phosphate groups at the surface of the hydroxyapatites than would be expected from a uniform distribution of calcium "defects" with associated protons, throughout the crystal lattice, or else there is another limitation on ion formation.

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