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STUDY OF CALCIUM ORTHOPHOSPHATES

I. A NEW METHOD FOR THE PREPARATION OF DICALCIM PHOSPHATE DIHYDATE

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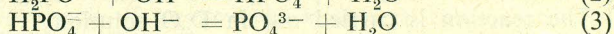
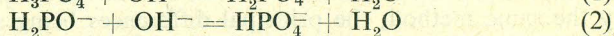
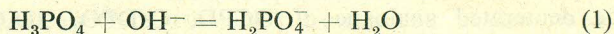
INTRODUCTION

In our investigation of the infrared spectra of calcium orthophosphates [1,2] we encountered a need for well-formed crystals of certain calcium orthophosphates, namely anhydrous dicalcium phosphate (DCP), dicalcium phosphate dihydrate (DCPD), octacalcium phosphate (OCP) and hydroxyapatite (HA) and also of their deuterated analogues.

Several methods for the preparation of these compounds have been described in the literature, but whilst the procedures given for the preparation of OCP [3,4] and of HA [5,6] yield products of high purity which are suitable for spectroscopic work, this is not the case with the methods given for DCPA and DCPD. Moreover, to the best of our knowledge, no method has so far been published for the preparation of the deuterated analogues for either DCPA or DCPD. The commercial products have also been tested and found unsuitable for our purposes.

Inasmuch as samples of DCPA can easily be prepared by dehydration of DCPD, our task was to find a method which would not be time-consuming and which would yield well-formed crystals of DCPD of high purity. The method described below seems to be satisfactory in both respects.

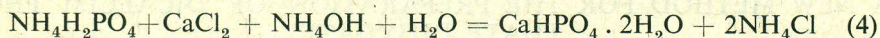
This method, as are some of those already published [7, 8, *cf.* also 9], is based on the precipitation reaction of the HPO_4^{2-} ion with the ion of calcium. It is well-established that the reactions leading to the formation of calcium orthophosphates are reversible and extremely pH dependent. This is to be expected in view of the ionization behavior of phosphoric acid, which may form H_2PO_4^- , HPO_4^{2-} and/or PO_4^{3-} ions. These same ions are also formed in the course of the neutralization of phosphoric acid:



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It is obvious that the reaction proceeds according to Eq. (2) not only in the case of phosphoric acid itself, but also in the case of alkaline dihydrogen phosphates. In order to ensure precipitation of dicalcium phosphate and to avoid contamination by other calcium orthophosphates, the reaction mixture should be slightly acidic (between, approximately, pH 4 and pH 6). The pH value of the medium is not, however, the only variable which should be taken into account, since it has been shown [9—13] that the constitution and the properties of the precipitated calcium orthophosphates are greatly influenced by the temperature of the medium, the concentration of the reactants and the method by which they are mixed, as well as by the impurities which may be present, etc.

In the procedure given below, equal volumes of equimolar solutions of $\text{NH}_4\text{H}_2\text{PO}_4$ and CaCl_2 are mixed and the solution is slowly neutralized by the addition of an ammonia solution of the same concentration:



PROCEDURE

Equal volumes of 0.05 M $\text{NH}_4\text{H}_2\text{PO}_4$ and CaCl_2 are mixed in an Erlenmeyer flask and a solution of ammonia, of the same concentration, is added to this mixture from a microburette, while constantly and vigorously stirring. Such stirring is essential since it eliminates the possibility of locally high OH^- concentrations and thus prevents precipitation of octacalcium phosphate (which precipitates at approximately pH 7) and/or hydroxyapatite (precipitating at still higher pH values). An amorphous precipitate of calcium orthophosphates which are more basic than DCPD is formed initially, and care must be taken not to add the next drop before this precipitate has been completely dissolved. The supernatant liquor is at first slightly opalescent, but it becomes clear almost immediately.

Initially the reaction mixture has a pH value of about 3.9, and precipitation of shiny crystals of dicalcium phosphate dihydrate begins when the pH value has risen to about 4.1. The addition of ammonia is discontinued when the pH value of the reaction mixture reaches 6. At that point the amount of ammonia which has been added is only about 80 percent of the equivalent quantity which would be expected on the basis of Eq. (2). The reaction is terminated at this point, since by then the precipitation of DCPD has been completed to a great extent and since the primary purpose of this method is a high degree of purity and the crystalline state of the product, rather than high yield.

The crystals are filtered by suction and washed rapidly several times with distilled water until there is no reaction with AgNO_3 . The crystals are then washed once with acetone and dried in air.

The yield is about 65 percent of the theoretical value. Such a low yield is apparently due to incomplete precipitation and to a partial dissolving of the crystals during the washing process.

When the temperature is maintained between 18°C and 20°C, well-formed crystals of pure $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ are produced.

The deuterated analogue of DCPD, $\text{CaDPO}_4 \cdot 2\text{D}_2\text{O}$, is prepared using essentially the same method, the principal differences being as follows:

- (1) The reaction is carried out in D_2O solution;
- (2) The ammonia solution must be prepared by passing NH_3 gas through D_2O ;

(3) The Erlenmeyer flask should be stoppered with a two-hole rubber stopper. A dropping funnel containing the D_2O solution of NH_3 is inserted through one of the holes and a glass tube, connected to a desiccating battery, is inserted through the other;

(4) A magnetic stirrer is used to stir the reaction mixture;

(5) The crystals are washed with D_2O and dried by suction in atmosphere free of water vapor.

The degree of deuteration thus achieved is quite high, as seen from the infrared spectrum (Ref. 1, Fig. 2).

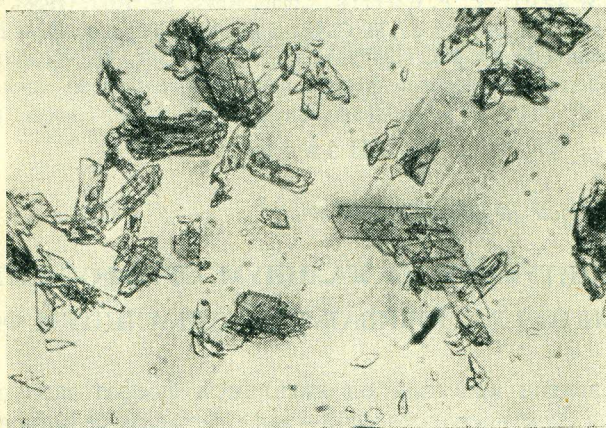


Figure 1 — Crystals of Dicalcium Phosphate Dihydrate

PROPERTIES

The crystals of DCPD are white monoclinic plates (Fig. 1). The refractive indices of DCPD are: $n_\gamma = 1.551$, $n_\beta = 1.545$ and $n_d = 1.540$ [14]. The infrared spectra of DCPD and DCPD- d_3 are given in Ref. 1, Fig. 2.

By dehydration at 180 – $200^\circ C$, DCPD forms DCPA. The crystals thus obtained are more suitable for spectroscopic work than any of those prepared by the methods so far published (for a rather extensive list of such methods *cf.* Ref. 8).

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И з в о д

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ИСПИТУВАЊЕ НА КАЛЦИУМ ОРТОФОСФАТИ

I. НОВ МЕТОД ЗА ДОБИВАЊЕ НА ДИКАЛЦИУМ ФОСФАТ

Убаво развиени кристали од дикалциум фосфат дихидрат, $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$, погодни за спектроскопско испитување, може да се добијат по следнава постапка:

Се мешаат еднакви волумени од 0,05 М раствори од CaCl_2 и $\text{NH}_4\text{H}_2\text{PO}_4$ и во ерленмаерот во кој се наоѓа реакционата смеша полека, од микробирета, се додава раствор од NH_4OH со истата концентрација. Растворот треба постојано енергично да се меша за да се избегнат локално високи OH^- концентрации и така да се спречи таложeње на калциумови ортофосфати побазични од дикалциум фосфатот.

Реакционата смеша во почетокот има рН околу 3,9. Таложeње на сјајни кристали од $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ (Сл. 1) започнува при вредности на рН од околу 4,1. Додавањето на амонијачен раствор се прекинува кога рН на реакционата смеша ќе достигне 6.

Составот и својствата на талогот зависат, покрај од рН вредноста на средината, и од концентрацијата на растворите на реактитите, од начинот, на нивното мешање, од температурата итн.

Образуваните кристали се филтрираат на вакуум, се испираат со дестилирана вода до негативна реакција на хлориди, потоа уште еднаш со ацетон и се сушат на воздух.

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Приносот е околу 65% од теоретскиот, но тоа и не е од особена важност, затоа што целта на методот е да се добијат убаво развиени и чисти кристали, а не голем принос.

Употребувајќи ја принципиелно истата метода, само работејќи во раствори од D_2O и преземајќи претпазни мерки за да се спречи изотопската измена на деутериумот со водород, може да се добие и деутерираниот аналог на дикалциум фосфат дихидратот, $CaDPO_4 \cdot 2D_2O$. Степенот на деутерирање е многу висок, како што може да се види од инфрацрвениот спектар Сл. 2. во Реф. 1.

Кристалите од дикалциум фосфат дихидрат се бели моноклински плочки (Сл. 1). Инфрацрвените спектри на $CaHPO_4 \cdot 2H_2O$ и $CaDPO_4 \cdot 2D_2O$ се дадени на Сл. 2. Во Реф. 1.

Со дехидрација на $180-200^\circ C$, $CaHPO_4 \cdot 2H_2O$ образува $CaHPO_4$ и кристалите кои вака се добиени се попогодни за спектроскопско испитување од оние добиени според досега објавените методи.