Thermochimica Acta, 131 (1988) 47–55
Elsevier Science Publishers B V , Amsterdam – Printed in The Netherlands

CALORIMETRIC INVESTIGATIONS OF CALCIUM PHOSPHATE PRECIPITATION IN RELATION TO SOLUTION COMPOSITION AND TEMPERATURE

W KIBALCZYC

Institute of Physics, Technical University of Łódź, Wólczańska 219, 93-005 Łódź (Poland)

A ZIELENKIEWICZ and W ZIELENKIEWICZ

Institute of Physical Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw (Poland)

(Received 4 November 1987)

ABSTRACT

The kinetics of formation and conversion of calcium phosphate under different initial solution compositions and temperature have been studied by calorimetric methods Experimental values of enthalpy of calcium phosphate formation at various Ca P molar ratios, initial pH of solution and temperatures are given It is found that in the initial pH range $5\ 8 < \text{pH} < 11\ 79$ the formation of calcium phosphate from relatively high supersaturated solutions is associated with a strong endothermic effect Under a wide range of Ca P ratios (0 33–2 79) and with an initial pH of 7 40 the formation of calcium phosphate is associated with the repeated heat effect This effect, which is connected with the transformation of the first precipitated phase, is revealed clearly and occurs in two stages This transformation may be explained by considering that a mixture of $Ca_4H(PO_4)_3$ 2 $5H_2O$-like and $Ca_5(PO_4)_3OH$-like phases is formed during the amorphous-to-crystalline transition

INTRODUCTION

The formation of calcium phosphates from supersaturated aqueous solutions has been studied extensively, largely because of their occurrence in dental enamel, bones and phathological (e.g. phosphatic renal stones) calcifications Although calcium phosphate precipitate is usually referred to as hydroxyapatite [$Ca_5(PO_4)_3OH$, HAP], there is still considerable uncertainty as to the nature of the phases which form in the early stages of the reaction [1] It is now well established that the initially formed phase does not correspond to that of the final crystalline, thermodynamically stable HAP The stoichiometric calcium phosphate molar ratio of the initially precipitated phase does not correspond to the required values of 1.67 for the thermodynamically favored HAP. In order to reach the HAP composition,

0040-6031/88/$03 50

extended solid–solution equilibration is required, and several theories have been put forward in an attempt to account for this phenomenon Recently the phase formed initially at high supersaturations has been attributed to amorphous calcium phosphate (ACP) particles which are composed of randomly packed $Ca_9(PO_4)_6$ clusters [2] According to this model, the autocatalytic transformation of ACP to the thermodynamically more stable HAP can take place quite rapidly [3] The transformation from the amorphous to the crystalline form depends on the pH, temperature, concentration and composition of the solution It has been observed that, in the presence of water, ACP is converted into apatite [4]. This change depends on the solid solution ratio. At a low ratio, the apatite formation is accompanied by an increase in the solid Ca P ratio This evolution is interpreted as ACP dissolution/apatite reprecipitation [5,6]. A simultaneous increase in the Ca P ratio and crystallinity accompanies this phenomenon The ACP–HAP conversion process has been visualized to occure in three steps (a) the dissolution of ACP to give a saturated solution of ions or ion clusters, (b) the formation of the first HAP nuclei from these ions, and (c) the autocatalytic proliferation of HAP by secondary nucleation It has been shown [6] that Mg effects the transformation by reducing the ACP solubility At very high solid solution ratios the conversion of ACP into calcium phosphate with a Ca . P ratio similar to tricalcium phosphate [$Ca_3(PO_4)_2 \cdot xH_2O$, TCP] but a structure resembling apatite has also been observed [5]

An alternative explanation for the formation of solid phases with low molar Ca P ratios (Ca P < 1.67) and apparent non-stoichiometry involves the formation of octacalcium phosphate [$Ca_4H(PO_4)_3$ 2 5 H_2O, OCP] [7] There is now good evidence for the formation of this phase as a precursor phase both from seeded growth experiments [1] and during the maturation of spontaneously precipitated solids [8] Recently, it has been shown [9] that the solubility of OCP is lower than that reported previously making this phase an even more important potential precursor to HAP precipitation. However, in order to elucidate the mechanism that occurs during calcium phosphate formation, it is necessary to investigate this process using different techniques under a wide range of experimental conditions

The aim of the present study was to investigate the heat effects which occur during calcium phosphate precipitation under different initial concentrations of the reacting components, initial pH of the mixed solutions and temperature

METHODS

The precipitation experiments were carried out in an LKB batch microcalorimeter (Model 10700-2) by mixing equal volumes of 0 02 M $CaCl_2$ solution and K_2HPO_4 solution of various concentrations and pH Both solutions were prepared from reagent-grade chemicals and triply distilled carbon dioxide free water. The changes in the initial pH of the mixed solution were obtained by adding suitable amounts of KOH or HCl to K_2HPO_4 solution The initial pH was calculated by following the procedure described by Lundager Madsen and Thorvardarson [10] and Feenstra [11] The calorimetric measurements were made in the following way 2 + 2 cm^3 of distilled water were inserted into the reference calorimetric cell, whereas $CaCl_2$ and K_2HPO_4 solutions (2 cm^3 each) were inserted into the measurement cell.

After initiation of the reaction, the temperature changes were recorded every 2 s. The measurements were made until the calorimetric system reached the temperature $\theta(t_f)$ equal to the initial temperature of measurement $\theta(t_0) = \theta(t_f)$ On the basis of the dependence of temperature, θ, on time, t, observed from the experiments, the total heat effect of the studied reaction was determined from the relation

$$Q = -\Delta H = \alpha \int_{t_0}^{t_f} \theta(t)\,\mathrm{d}t \tag{1}$$

where α is the heat loss coefficient, and t_0 and t_f are the times corresponding to the initial $\theta(t_0)$ and the final temperature $\theta(t_f)$, respectively

Calorimetric measurements also allow for the determination of the thermokinetics of the studied chemical precipitation, i e the changes in heat power, W, with time, t, [12]

$$W(t) = \frac{\mathrm{d}Q(t)}{\mathrm{d}t} = c\frac{\mathrm{d}\theta(t)}{\mathrm{d}t} + \alpha\theta(t) \tag{2}$$

where c is the heat capacity of the calorimeter. The value of α was obtained from the electrical calibrations which were performed after each individual experiment The values of c were determined from the relation

$$c = \alpha T \tag{3}$$

where T is the time constant of the calorimeter, which was calculated on the basis of the cooling curve of a thermally inert object [13]

Apart from the calorimetric measurements, the pH of the precipitating solution during calcium phosphate formation was measured with an OP-211-type pH meter (Hungary) The pH was measured with an OP-0808 combination electrode, which was calibrated before and after each experiment with Radelkis standard buffer solutions of pH 7 10 and 9.30 The change in pH with time for a precipitating solution was registered under the conditions used for calorimetric measurements In these experiments the measurement cell and the initial solutions were kept at the same temperature before mixing

RESULTS

Calcium phosphate was formed in experiments by spontaneous precipitation at various initial pH values of the mixtures, various Ca P molar ratios and at temperatures 303, 310 and 315 K From the investigations, it follows that the total heat of calcium phosphate formation has a negative value which depends on the Ca P ratio and on the initial pH of the mixture Figure 1 shows the plot of the time dependence of the heat power change, W, per mole of phosphorus for precipitating solutions at initial pH 7 40 and temperature 310 K corresponding to Ca $P = 1$ 67 and Ca $P = 1$ 33, as required for HAP and OCP, respectively After the violent energy change (effect A) lasting about 50 s (Fig 1), the next characteristic changes (effect B) appear in the time interval between 100 and 300 s after mixing the reagents These B changes are connected with the conversions of calcium phosphate particles

In Table 1 the values of the total heat of calcium phosphate formation $(\Delta H > 0)$ calculated per mole of phosphorus introduced to the reaction at different initial composition and pH are presented These results show that for a given Ca P value, the dependence of ΔH on initial pH has a maximum at pH in the range $8 < \text{pH} < 10$.

Heat effects connected with the conversion of calcium phosphate for the precipitating solution of Ca $P = 1$ 67 at temperature 303 K and at different values of the initial pH are presented in Fig 2 From the nature of the curves of Fig 2, it may be noted that there is a strong influence of the initial pH of the mixture on the character of the heat conversion taking place between 200 and 500 s after mixing the reagents

The dependence of the heat power (W) per mole P on time for B effects taking place in the precipitating solution with Ca $P = 1$ 33 (required value

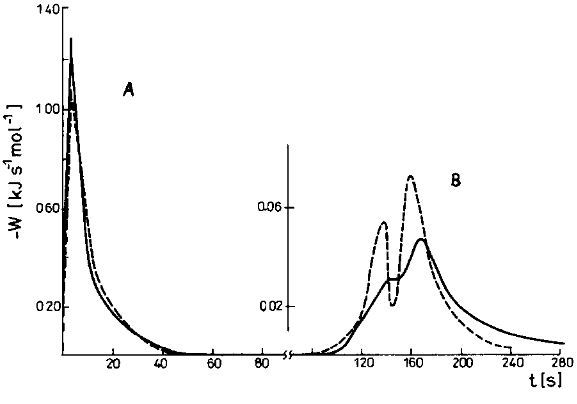

Fig 1 Dependence of the heat power (W) per mole P on time at the initial pH 7 40 and at temperature 310 K for the precipitating solution of different Ca P molar ratio (———) Ca $P = 1$ 67, (- - - - - -) Ca $P = 1$ 33

TABLE 1

Enthalpies of calcium phosphate formation at different Ca P ratios, initial pH of mixture and temperature

Ca P	pH	T (K)	ΔH (kJ mol^{-1})
3 33	7 40	303	12 5
	8 63	303	18 1
2 79	7 40	310	14 7
		315	15 8
	8 60	310	19 5
		315	21 2
	10 38	303	18 5
		310	20 6
		315	22 6
1 67	5 80	303	0 1
	7 40	303	13 6
		310	16 2
	8 62	303	18 2
	9 50	303	18 7
		310	20 8
		315	22 2
	10 70	303	19 1
		310	21 2
		315	0 0
	11 03	303	18 6
	11 74	303	12 8
	11 79	303	0 0
		310	0 0
		315	0 0
1 33	7 40	303	14 9
		310	15 9
		315	17 1
0 33	6 04	303	3 0
	6 50	303	5 9
	7 40	303	8 6
		310	8 9
	8 71	303	8 2
	9 70	303	8 3
	10 53	303	7 7
	11 04	303	6 2
0 17	6 00	303	2 7
	7 40	303	4 2
	8 68	303	4 2
	9 50	303	4 1
	11 00	303	2 6

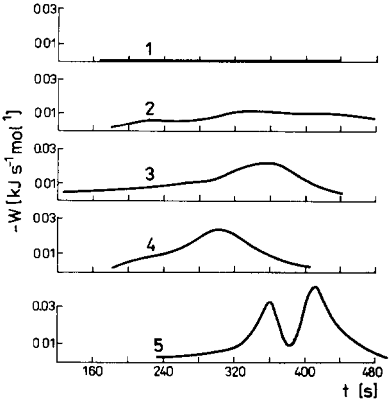

Fig 2 Dependence of the heat power (W) per mole P on time for the B effect at Ca P = 1 67 and temperature 303 K at different values of the initial pH (1) pH 11 79 ($\Delta H^{\star} = 0$ kJ mol^{-1}), (2) pH 10 70 ($\Delta H^{\star} = 3$ 3 kJ mol^{-1}), (3) pH 9 50 ($\Delta H^{\star} = 3$ 9 kJ mol^{-1}), (4) pH 8 60 ($\Delta H^{\star} = 2$ 5 kJ mol^{-1}), (5) pH 7 40 ($\Delta H^{\star} = 3$ 5 kJ mol^{-1}) $\Delta H^{\star}$ is the enthalpy value of the B effect

for OCP) and 1 67 (required value for HAP) at pH 7 40 and pH 9 50, respectively, at different temperatures, are presented in Fig 3 From the curves presented in Fig 3, it may be inferred that, at the stoichiometric composition of OCP in the solution (Ca P = 1.33), the transformation of initially forming particles of the solid phase takes place in two stages The time interval during which there is the B heat effect, connected with the

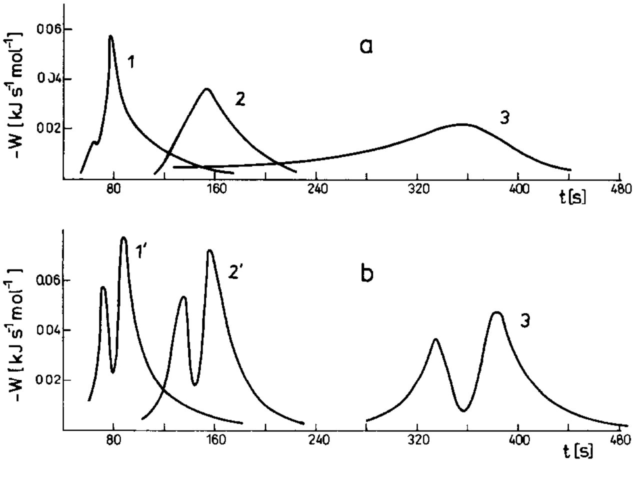

Fig 3 Dependence of the heat power (W) per mole P on time for the B effect at pH 9 50, at (a) Ca P = 1 67 and pH 7 40, and (b) at Ca P = 1 33 at different values of temperature (1) $T = 315$ K ($\Delta H^{\star} = 2$ 0 kJ mol^{-1}), (2) $T = 310$ K ($\Delta H^{\star} = 3$ 5 kJ mol^{-1}), (3) $T = 303$ K ($\Delta H^{\star} = 4$ 2 kJ mol^{-1}), (1′) $T = 315$ K ($\Delta H^{\star} = 2$ 7 kJ mol^{-1}), (2′) $T = 310$ K ($\Delta H^{\star} = 3$ 5 kJ mol^{-1}), (3′) $T = 303$ K ($\Delta H^{\star} = 4$ 2 kJ mol^{-1})

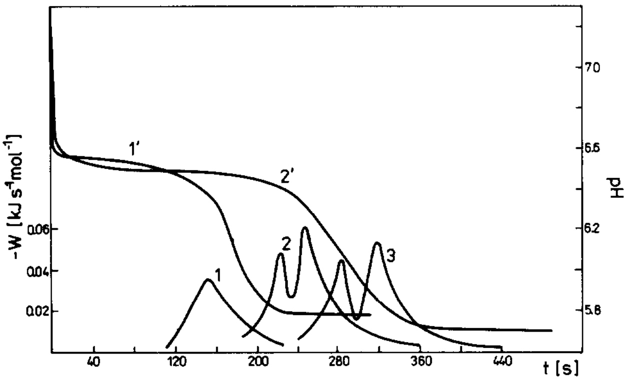

Fig 4 Dependence of (1,2,3) the heat power *W* (B effect) per mole P and (1', 2') pH of the mixture on time for the same experimental condition at 310 K (1, 1') Ca P = 1 67, initial pH 9 50, (2, 2') Ca P = 2 79, initial pH 7 40, (3) Ca P = 2 79, initial pH 7 40 and Mg Ca = 0 04

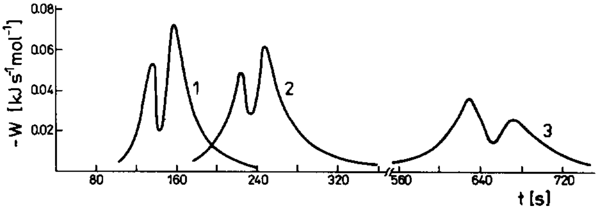

Fig 5 Dependence of the heat power *W* (B effect) per mole P on time at the initial pH 7 40 and at temperature 310 K for the precipitating solution at molar ratios (1) Ca P = 1 33 ($\Delta H^{\star}$ = 3 5 kJ mol^{-1}), (2) Ca P = 2 79 ($\Delta H^{\star}$ = 2 5 kJ mol^{-1}), (3) Ca P = 0 33 ($\Delta H^{\star}$ = 3 5 kJ mol^{-1})

formation of intermediate phase, corresponds to a period of decreasing pH of the mixed solution as shown in Fig 4 This heat effect for a precipitating solution obtained at the same initial conditions, but in the presence of Mg^{2+} ions, is also shown in Fig 4 for comparison. This process occurs under a wide range of experimental conditions Figure 5 shows the plot of the change in heat power, *W*, for B effect with time of this process for a precipitating solution with different values of the Ca P molar ratio at pH 7 40 and temperatures 310 K From Fig 5 it is seen that the B heat effects for different Ca P ratios appear at different times

DISCUSSION

Our earlier studies [14,15] showed that HAP crystals are formed without intermediate phases in the high initial pH range and at molar ratio Ca P = 1 67 At very high values of pH in solution there exists a high concentration of PO_4^{3-} and OH^- ions At a Ca P molar ratio in solution such as that required for HAP crystals at the time of mixing of the initial solutions, these ions give the appropriate conditions for HAP crystallization Experimental data in this study show that at an initial pH > 11 74 there are no measured heat effects connected with HAP crystallization

From Table 1 it follows that in the pH range 9–10 at Ca P = 1 67 the formation of calcium phosphate is associated with the strongest endothermic heat effect In this pH range the conditions are appropriate for the formation of amorphous calcium phosphate [4] When the value of the initial pH decreases, the value of total heat endothermic effect, ΔH, of calcium phosphate formation also decreases This decrease in ΔH may be attributed to the formation of phases with higher crystallinity This view is also consistent with Heughebaert's concept [4] that endothermic effects of calcium phosphate formation are connected with the interaction of water with ACP and exothermic effects associated with the crystallization process From Fig 2 it follows that at the initial pH 7 40 and Ca P = 1 67, B effects connected with the transformation of the first precipitated phase are revealed clearly and occur in two stages The value of the B effect is highest when the pH of the initial mixture is 7 40, Ca P = 1 33 (stoichiometric Ca P ratio for OCP) and the process is carried out at 303 K (Table 1, and Fig 3, curve 2)

The experimental data presented in this work show that the formation of calcium phosphate from highly supersaturated solution is associated with the repeated heat effect (B effect) connected with the conversion process under a wide range of Ca P ratios (0 33–2 79) when the initial pH is 7 40 The induction period for this conversion decreases with an increase in temperature (Fig 3) This transformation may be explained from a consideration that a mixture of OCP-like and HAP-like phase is formed during the amorphous to crystalline transition It seems unlikely that the initial transformation is simply ACP to stoichiometric OCP because a balanced reaction, such as

$$7\,Ca_3(PO_4)_2 + HPO_4^{2-} + 4\,H^+ \rightarrow 5\,Ca_4H(PO_4)_3 + Ca^{2+} \tag{4}$$

proposed by Meyer and Eanes [16] requires an uptake of hydrogen ions, which is contrary to the observed facts shown in Fig 4 Additional evidence, which supports our view, is provided by Feenstra and de Bruyn [17] who found that OCP is present as an intermediate in the conversion of ACP to an apatitic calcium phosphate. The curves of heat power versus time for the B effect at different Ca P ratios (Fig 5) show that the induction period is the shortest for Ca P = 1 33 and Ca P = 1 67, i e at the stoichiometric composition of OCP and HAP in the solution, respectively

We observed that magnesium inhibits insignificantly the induction period of the B effect when the Mg Ca ratio in solution is higher then 0 04. Lundager Madsen et al [18] and Boskey and Posner [6] also observed that the effect of Mg^{2+} is to stabilize ACP, once it is formed

Details of our results on the influence of magnesium on calcium phosphate formation will be reported in a subsequent publication

ACKNOWLEDGMENTS

The authors thank Dr M Żółkiewski and Dr E Margas for their help with the computer program and calculations This work was carried out under Research Projects RPBP 01 3 and CPBP 01.06, 6 04

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