Solubility and Crystallization-controlled Synthesis of Lamellar Mesostructured Calcium Phosphate in the Ethanol/Water System

Nobuaki Ikawa,[1] Yasunori Oumi,[1] Tatsuo Kimura,[2] Takuji Ikeda,[3] and Tsuneji Sano*[1]
[1]*Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University, Higashi-Hiroshima 739-8527*
[2]*National Institute of Advanced Industrial Science and Technology (AIST), Shimoshidami, Moriyama-ku, Nagoya 463-8560*
[3]*AIST, Tohoku, Nigatake, Miyagino-ku, Sendai 983-8551*

(Received May 10, 2006; CL-060556; E-mail: tsano@hiroshima-u.ac.jp)

A novel lamellar mesostructured calcium phosphate was synthesized at room temperature by using *n*-hexadecylamine in the EtOH/H_2O system, which controlled the solubility of calcium source and the preferential formation of crystalline calcium phosphate species.

There are a lot of articles concerning the synthesis of non-silica-based mesostructured and mesoporous materials composed of transition-metal oxides and metal phosphates because of their potential applications in the fields of catalysts, adsorbents, optics, electrics, and so on.[1–4] In those non-silica-based materials, metal species in the frameworks are connected by oxygen atoms through covalent bonds. Although calcium phosphate has been extensively studied as biocompatible materials,[5] there have been few reports on mesostructural control of calcium phosphates by using surfactants as structure-directing agents.[6,7] This is due to the preferential formation of crystalline calcium phosphates because of the strong interaction between Ca^{2+} and PO_4^{3-} ions. Once the charge of framework is extinguished by strong interaction between the inorganic species, surfactant molecules are difficult to be interacted with the inorganic framework and then such mesostructured materials have never been obtained so far. Therefore, the most important point to succeed in the synthesis of mesostructured calcium phosphates is how to suppress crystallization of calcium phosphate species with keeping interaction with surfactant molecules. In this communication, we provide a new "solubility and crystallization-controlled synthesis" to obtain mesostructured materials whose inorganic frameworks are built up by ionic bonds. According to the synthetic strategy, a lamellar mesostructured calcium phosphate is successfully synthesized at room temperature using *n*-hexadecylamine as a structure-directing agent in the ethanol/water (EtOH/H_2O) system.

In a typical synthesis, a lamellar mesostructured calcium phosphate was prepared as follows: *n*-Hexadecylamine ($C_{16}H_{33}NH_2$) and phosphoric acid (85% H_3PO_4) were added into a mixed solvent of EtOH and H_2O, and the mixture was kept at room temperature for 1 h under stirring. Calcium acetate monohydrate ($Ca(CH_3COO)_2 \cdot H_2O$) and an aqueous solution of ammonia (25% NH_3 aq) were then introduced into the above mixture. After vigorous stirring for 15 min, the mixture with a chemical composition of $Ca(CH_3COO)_2$:H_3PO_4:$C_{16}H_{33}NH_2$:0.5NH_3:0–40EtOH:2–40H_2O was kept at room temperature for 120 h statically. The solid product was filtered off, washed with ethanol, and dried at room temperature.

On the basis of preliminary experiments, both Ca/P and $C_{16}H_{33}NH_2/H_3PO_4$ molar ratios were fixed at 1/1. As listed in Table 1, brushite ($CaHPO_4 \cdot 2H_2O$) known as one of crystalline calcium phosphates was mainly obtained (Sample 1) when water was only used as solvent. However, the formation of brushite was suppressed with an increase in the EtOH/H_2O ratio, and a lamellar mesostructured calcium phosphate was obtained without by-products at the EtOH/H_2O ratio of 50/50 mol % (Sample 3). At a further increase in the EtOH/H_2O ratio, both unreacted Ca source and lamellar hexadecylammonium phosphate salt ($[C_{16}H_{33}NH_3^+][H_2PO_4^-]$) were recovered (Samples 4 and 5), indicating a change in the solubility of Ca species. The results strongly indicate that complete crystallization of calcium phosphate species would not be proceeded by using the mixed solvent of EtOH and H_2O, leading to the successful preparation of the lamellar mesostructured calcium phosphate by using the self-assembling ability of the surfactant. Yuan et al. reported the possibility to synthesize lamellar mesostructured calcium phosphate. However, they cannot show the direct evidence for the formation of a lamellar phase; striped patterns were not observed in the TEM image though they claimed that the material is unstable under electron-beam irradiation.[6]

The XRD pattern of the mesostructured calcium phosphate obtained is shown in Figure 1.[8] Three well-resolved peaks were observed in the region of $2\theta = 1.5$–6.0°, which are indexed to the (001), (002), and (003) reflections of a lamellar phase. As can be also seen in Figure 1, the clear striped patterns were observed in the TEM image and the repeat distance of the striped patterns was ca. 4.1 nm. The value was slightly smaller than the d_{001} spacing (4.4 nm) from XRD, probably owing to the slight shrinkage of the layer distance under vacuum for TEM observation.[9] It is also found that the d_{001} spacing was slightly larger than that expected from the chain length of the surfactant. It is considered that calcium phosphate layers would be thicker than

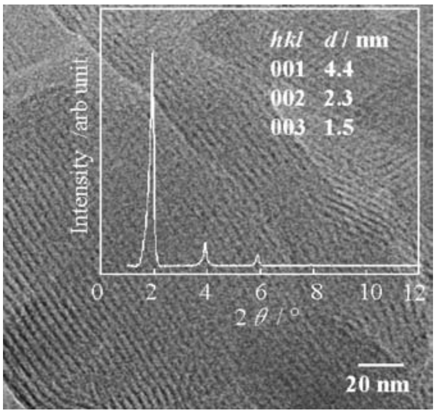

Figure 1. XRD pattern and TEM image of the lamellar mesostructured calcium phosphate (Sample 6).

Table 1. Effect of synthetic conditions on the formation of lamellar mesostructured calcium phosphate

Sample no.	Starting gel[a]			Product
	EtOH/H_2O molar ratio	Solvent/H_3PO_4 molar ratio	Surfactant	Phase
1	0/100	40	$C_{16}H_{33}NH_2$	Bru,[b] Salt[c]
2	25/75	40	$C_{16}H_{33}NH_2$	Bru, MCP
3	50/50	40	$C_{16}H_{33}NH_2$	MCP
4	75/25	40	$C_{16}H_{33}NH_2$	MCP, (Ca[d])
5	96/4	40	$C_{16}H_{33}NH_2$	(Ca), Salt
6	50/50	80	$C_{16}H_{33}NH_2$	MCP
7	50/50	120	$C_{16}H_{33}NH_2$	MCP, Bru
8	0/100	40	Non	Bru
9	25/75	40	Non	Bru, Mon[e]
10	50/50	40	Non	Mon, Bru
11	75/25	40	Non	Mon, Bru

[a] Synthetic conditions: Ca/P = 1, $C_{16}H_{33}NH_2/H_3PO_4 = 1$, NH_3 aq/$H_3PO_4 = 0.5$, Time = 120 h, Temp. = room temperature. [b] Bru: Brushite. [c] Salt: Hexadecylammonium phosphate with d_{001} spacing of 3.8 nm. [d] Ca: Calcium source. [e] Mon: Monetite.

those observed for conventional mesostructured materials.

The chemical state and content of the surfactant in the lamellar mesostructured calcium phosphate were investigated by thermal analysis (TG/DTA) and ^{13}C CP/MAS NMR. The major mass loss in the TG/DTA curve occurred below 150 °C and between 150 and 500 °C. It seems that the mass loss between 150 and 500 °C is due to the surfactant, whereas the mass loss below 150 °C is ascribed to adsorbed H_2O. The mass loss between 150 and 500 °C was ca. 48.5 mass %. The ^{13}C CP/MAS NMR spectrum exhibited two broad peaks at around 15 and 33 ppm. The chemical shifts were consistent with those of a lamellar hexadecylammonium phosphate salt, being related to the presence of protonated surfactant molecules ($C_{16}H_{33}NH_3^+$) in the lamellar mesostructured calcium phosphate. Considering the fact that the Ca/P molar ratio of the framework determined by ICP was 1.0, the framework is negatively charged like $CaPO_4^-$ which can be interacted with $C_{16}H_{33}NH_3^+$. If it is assumed that the lamellar mesostructured calcium phosphate is only composed of $CaPO_4^-$ and $C_{16}H_{33}NH_3^+$, the $(CaPO_4^-)/(C_{16}H_{33}NH_3^+)$ ratio must be 1. The organic content of the product checked by CHN analysis was 36.1 mass % of carbon atoms, 7.9 mass % of hydrogen atoms and 2.6 mass % of nitrogen atoms. The $(CaPO_4^-)/(C_{16}H_{33}NH_3^+)$ ratio was calculated to be ca. 2. The composition of the product is represented as $2\ CaO{\cdot}P_2O_5{\cdot}C_{16}H_{33}NH_2$. Consequently, we must consider the presence of another calcium phosphate species in addition to the $CaPO_4^-$ species.

The ^{31}P MAS NMR spectra were applied to get further information on the framework of the lamellar mesostructured calcium phosphate. The ^{31}P MAS NMR spectra were measured with and without ^1H–^{31}P cross-polarization (CP). The ^{31}P MAS NMR spectrum showed two peaks at −0.5 and 3.4 ppm (not shown here). The peaks were different from the peak at around 1.4 ppm which is observed for hexadecylammonium phosphate salt. On the other hand, in the ^{31}P CP/MAS NMR spectrum, an increase in the intensity of the peak at −0.5 ppm was observed, indicating the presence of proton atoms nearby to the P atoms in the corresponding PO_4 units. The assignment of these peaks is now in progress.

Synthetic parameters such as EtOH/H_2O and solvent/H_3PO_4 ratios in the starting mixtures as well as the synthesis temperature were found to be also important for controlling crystallization of calcium phosphate species. Influences of solvent/H_3PO_4 (solvent = EtOH + H_2O) ratio in the starting mixtures on the synthesis of the lamellar mesostructured calcium phosphate were investigated further using the starting mixture with the EtOH/H_2O ratio of 50/50 mol % (Table 1). The crystallinity of the lamellar mesostructured calcium phosphate increased with the solvent/H_3PO_4 ratio, and the highest crystalline mesostructured calcium phosphate was obtained at the solvent/H_3PO_4 ratio of 80 without impurities (Sample 6). At the solvent/H_3PO_4 ratio of more than 120, however, cocrystallization of brushite occurred (Sample 7). No mesostructured calcium phosphate can be obtained without H_2O. In this case, Ca species are hardly reacted with phosphate species because of lower solubility of the Ca source. The synthesis of mesostructured calcium phosphate was also carried out at higher temperatures (50–100 °C). However, cocrystallization of a crystalline calcium phosphate monetite ($CaHPO_4$) occurred. The formation of monetite is more preferential at higher temperature than that of brushite. For reference, the synthesis without the surfactant was also carried out at room temperature (Samples 8–11). Both brushite and monetite were obtained. With an increase in the EtOH/H_2O ratio, the formation of brushite was suppressed, whereas the formation of monetite was enhanced. From these results, it was strongly indicated that the strong interaction exists between inorganic species and surfactant molecules in the EtOH/H_2O system.

In conclusion, a lamellar mesostructured calcium phosphate was prepared by using *n*-hexadecylamine as a surfactant through controlling solubility of Ca source and crystallization of calcium phosphate species in the EtOH/H_2O system. This is the first example of the synthesis of mesostructured calcium phosphates constructed by ionic bonds, being very important as model systems for biomimetic materials design such as bone and teeth. This synthetic method would also have the high potential for preparing a variety of mesostructured and mesoporous materials whose inorganic frameworks are built up by ionic bonds.

The authors would like to thank Dr. J. Ashida at Varian Technologies Japan Ltd. for ^{31}P MAS NMR measurement.

References and Notes

1 F. Schüth, *Chem. Mater.* **2001**, *13*, 3184.
2 G. J. de A. A. Soler-Illia, C. Sanchez, B. Lebeau, J. Patarin, *Chem. Rev.* **2002**, *102*, 4093.
3 C. Yu, B. Tian, D. Zhao, *Curr. Opin. Solid State Mater. Sci.* **2003**, *7*, 191.
4 T. Kimura, *Microporous Mesoporous Mater.* **2005**, *77*, 97.
5 J. Anderson, S. Areva, B. Spliethoff, M. Lindén, *Biomaterials* **2005**, *26*, 6827.
6 Z. Y. Yuan, J. Q. Liu, L. M. Peng, B. L. Su, *Langmuir* **2002**, *18*, 2450.
7 G. A. Ozin, N. Varaksa, N. Coombs, J. E. Davies, D. D. Perovic, M. Ziliox, *J. Mater. Chem.* **1997**, *7*, 1601.

8 X-ray powder diffraction data of the sample were collected at room temperature on a Bruker D8 ADVANCE (Vario-1) powder diffractometer with a modified Debye–Scherrer geometry and a high-speed 1D-PSD VÅNTEC-1 detector. The sample was packed into a borosilicate capillary tube with an inside diameter of 0.7 mm. Conditions of the XRD experiment were as follows: Cu Kα_1 radiation provided by a Ge(111) primary monochromator; output: 40 kV and 50 mA; scan range: $1.0° < 2\theta < 50°$; step width: 0.017473°.
9 TEM observation was carried out by uisng a Hitachi H-9000 NAR microscope with an accelerating voltage of 300 kV.

Published on the web (Advance View) July 22, 2006; doi:10.1246/cl.2006.948