Preparation and luminescence characteristics of lanthanide phosphors crystallized in phase separated glass

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Borosilicate glass crystallized into the borate phases GdBO3:Tm3⁺ and GdF3:Tm3⁺ was successfully prepared using the phase separation phenomenon. By optimizing its composition, the glass was ‘binodal’ phase separated into borate droplets inside a silica matrix. The lanthanide oxide and fluoride phosphors were restrictively created in the borate phase and an emission attributable to 1D2→3H4 transition of Tm3⁺ was observed at 458 nm. Furthermore, the luminescent intensity of lanthanide trifluoride crystallized glass at low vibrational energy was 25% larger than that of oxide glass. Based on these results, glass phosphor appears to be a promising candidate for use as a new Gadolinium Neutron Capture Therapy material in cancerous tissue imaging.

Key-words : Borosilicate glass, Phase separation, Luminescence, Binodal, Crystallization

1. Introduction

Recently, direct physical attacks on cancer cells using α-rays emitted from an organic boron complex (Boron Neutron Capture Therapy; BNCT) have steadily progressed from the research phase to application at clinical sites.1–4 In this technique, the targeted ranges of tumor tissues for α particles and 7Li nuclei, generated from 10B with a thermal neutron, are 7.3 and 4.0 μm, respectively, with linear energy transfer (LET) of a similar order of magnitude to the cell dimensions.5 For this reason, organic boron complexes can be used for BNCT by introducing them into cancer cells, allowing α particles generated from 10B (thermal neutron cross section; 3800 b) to attack the cancer cell nuclei directly.6–9 This condition greatly increases the difficulty of practical treatment of BNCT.10 Gd3+(thermal neutron cross section; 254 000 b) can emit γ-rays through capture of thermal neutrons and is a promising candidate for the process of generating compounds for NCT.7 In addition to use in Gadolinium Neutron Capture Therapy (GdNCT), the material can serve as a contrast agent for MRI and a cancer tissue and/or cell imaging agent through its luminescent properties. On the other hand, blood vessels close to tumor tissue often have pore sizes of less than 200 nm and are known to be easier to pass through and to introduce more nanoparticles than in the case of the normal tissue (enhanced permeation and retention effect; EPR effect).9–10 As shown in Illustration I, an antibody-modified inorganic nanoparticle able to perform as a strong radiation source to penetrate cell walls and attack cell nuclei from outside the cell membrane can be a promising new candidate for drug delivery systems (DDS). Although such inorganic materials are attractive for DDS, it is difficult to modify an inorganic surface by attaching organic compounds and/or antibodies to tumor tissue. The authors have so far studied the preparation of several functional glass materials by phase separation under high temperature using borosilicate glass.11–17 Most notably, we have succeeded in the synthesis of red luminescent phosphors including lanthanide ions such as Y3+, Gd3+ and Eu3+ crystallized glass using the phase separation phenomenon.18 Unfortunately, this glass was prepared as a ‘spinodal’ phase separated glass, but the borate phase (polar phase) can be easily dissolved into an acid solution with fine crystals, indicating that stable glass phosphors in air and/or aqueous (acid) solution can be synthesized as a ‘binodal’ phase separated glass as shown in Illustration II. Although boron and rare earth atoms possess high toxicity, the exposure to these species in the human body can be suppressed in high-durability glass, since these species can be introduced into the phase separated glass as droplets of the borate phase present in silica phase. Furthermore, the borosilicate glass host material for the functional species can be chosen by simply changing the mixing ratio of the three components in the SiO2–B2O3–Na2O, in contrast to the case of organic hosts.

In this study, the preparation of binodal phase separated glass through incorporation of fluorescent Tm3+ and B atoms in borosilicate glass as well as the structural and luminescent properties
of fine crystals in the glass were investigated.

2. Experimental section

For our study, SiO2 and Na2CO3 were purchased from Kishida Chemical Co., Ltd, H3BO3 from Kanto Chemical Co., Ltd and TmF3, MgF2, CaF2, SrF2, and BaF2 from Kojundo Chemical Laboratory Co., Ltd, and used without further purification.

The raw materials for the synthesis of the glass had chemical compositions of 65.2SiO2−25.4B2O3−9.4Na2O−2.75Gd2O3−0.2Tm2O3 for the lanthanide borate crystallized glass and 54.6SiO2−11.1B2O3−15.8NaF−18.5Al2O3−5.5Gd2O3−0.2Tm2O3 (TmF3) for the lanthanide fluoride crystallized one. The chemicals were mixed, placed into an alumina crucible and molten in an electric furnace (Motoyama Rh-2025D, SUPER-BURN) at a heating rate of 500°C/h. They were then kept at 1350°C for 1 h until the raw materials were completely molten. After the melting process, the molten glass solution was poured into a 1.5 cm graphite mold. Next, the glass sample was gradually cooled from 600°C to room temperature in a desktop muffle furnace (DENKEN Co., Ltd, KDF P90). The resulting glass sample was cut to a thickness of 2.65 mm by diamond cutter (Refine Tec Co., RCA-005). Heating of untreated glass under high temperature to achieve phase separation produces an ‘as-prepared’ sample.

The glass was embedded in fine alumina powder (Kanto Chemical Co., alpha-type, 99%) in an alumina crucible and heated at 800°C for 48 h in a small desktop furnace (Nitto Kagaku, NHK1-170) at a heating rate of 200°C/h for phase separation of the glass followed by crystallization of the phosphor. The glass treated under the conditions was defined as the ‘crystallized’ sample.

The crystalline phase was determined by an X-ray diffraction apparatus (XRD, Rigaku Ltd., Ultima IV) using Cu Ka1 line (λ = 1.541Å). The sample was used as the bulk and measured using a tube voltage of 40 kV, tube current of 40 mA and scanning speed of 2.00°/min. The measurement angles 2θ ranged from 10 to 80°. Using the diffraction profile obtained by XRD measurement, the identification of crystalline in the glass was performed with ‘Jade 7’ X-ray analysis software.

The surface of the obtained sample was polished with waterproof SiC abrasive paper (IMT Co., Ltd, S31SR-2232000-DN), and the polished sample was measured by spectrophotometer (HITACHI, Ltd., F-2500) with a 150 W Xe lamp as the light source. The luminescent spectra were measured at an excitation wavelength of 355 nm and a measurement range 420 to 480 nm.

Fourier Transform Infrared Spectroscopy (FT-IR) measurement was carried out using a JASCO Corporation FT/IR-480 plus by the KBr method under the following measurement conditions: accumulated runs: 64; resolution: 4 cm⁻¹; gain: 8; scanning speed: 2 mm/sec; measurement range: 400–4000 cm⁻¹.

3. Results and discussion

The glass was transparent when obtained but turned white after heating at 800°C for turning phase separation. This contributed to light scattering by fine crystals in the borate phase of the phase separation glass. The XRD measurement results before and after crystallization process of the borate glass are shown in Fig. 1. Although a broad peak attributed to the amorphous phase was observed in the as-prepared sample, crystalline GdBO3 and a small SiO2 impurity peak at 800° were observed.

Figure 2 shows the fluorescence spectra at an excitation wavelength of 355 nm before and after the crystallization process of the glass. In the spectra, a peak assigned to the 1D2 ground state of Gd3+ was observed in the as-prepared sample, crystalline GdBO3 and a small SiO2 impurity peak at 800° were observed. The excitation wavelength was 355 nm before and after heat treatment for phase separation.
lization are shown in Fig. 3. Although a broad peak attributed to the as-prepared glass sample was observed, GdF₃ was predominantly formed after crystallization, leading to orthorhombic dominant crystal structure and a limited number of hexagonal structures.

In order to prevent elution of boron and gadolinium from the glass due to toxicity, it is necessary to form binodal phase separation in the glass. As spherical shapes in the silica phase form when the glass separates, the borate phases are not eluted for separation, even if the glass is treated in acid solution. Therefore, in order to examine the elution of the borate phase in acid solutions, we conducted acid solution leaching treatment of the glass.

Figure 4 shows the XRD results before and after acid treatment. This suggested the formation of bimodal phase separation but not spinodal in the glass.

Figure 5 indicates the luminescent spectra of the glass sample excited at 355 nm before and after the crystallization process. An emission peak corresponding to the 1D²→3H₄ transition can be observed at 458 nm similarly to the case of borosilicate glass. As for the fluoride phosphor crystallization in borosilicate glass, the luminescent intensity was slightly higher than in the case of lanthanide borate phosphor.

It is well known that F⁻ in crystal is easily volatilized when reacting with O²⁻ in air due to the lower melting point of the fluorine compound. Since the melting point of GdF₃ is 1231°C, it is possible that the formation of GdF₃ crystal in the phase separated glass was suppressed owing to the volatilization of fluorine during the melting process of the raw materials of the glass. First, the possibility of fluorine volatilization under various melting conditions was studied. Figure 6 shows the XRD results after crystallization under melting conditions of 40 min, 1 and 2 h retention times when melting the raw materials in air. Since there are no observed oxide peaks such as GdOF and Gd₂O₃, the influence of fluorine volatilization is considered to be very small. In comparison to other peak intensities, the 40 min retention time peak intensity was lower overall, however the intensity of hexagonal GdF₃ with increase in retention time was confirmed. Orthorhombic GdF₃ (space group Pnma) is thermodynamically stable at room temperature, but there are very few studies on unstable hexagonal GdF₃. GdF₃ easily undergoes phase transition to the hexagonal form at higher temperatures, because the ionic radius of Gd³⁺ is smaller than that of F⁻ and the repulsion between the F⁻ ions increases.

The luminescent spectra of glass treated under the conditions described above are shown in Fig. 7. Since the luminescent intensities increase with increasing retention time, the intensity is considered to be dependent on the amount of GdF₃ precipitation in the phase separation glass. In addition, the reason for the higher fluorescence intensity for the 2 h retention time is due to the larger amount of precipitation of the hexagonal GdF₃ as compared with the orthorhombic one.

To determine the fluorine volatilization from the glass and the Gd atoms bonded to either the O atom and/or F atom in the glass, FT-IR measurements of the sample were made for a 1h retention time as shown in Fig. 8. It is difficult to distinguish Gd₂O₃ from GdF₃ because a peak is present near 450 cm⁻¹ in both materials. Although no Gd–O peak is observed at 542 cm⁻¹ in the glass.
sample, one can be seen in the Gd₂O₃ reference sample. Hence the Gd in the glass is considered to be present as a fluoride. Based on these results, the volatile amount of fluoride emitted from the glass during the heating process is estimated to be very low.

XRD profiles of the glass with Tm₂O₃ compositions ranging from 0.2 to 0.6 mol% at 2θ angles of 27.5 to 30.0 are shown in Fig. 9. By increasing the doping amount, the diffraction peak assigned to (0, 0, 2) was shifted to a lower angle. Since the ion radii of Tm³⁺ and Gd³⁺ are 1.10 and 1.05 Å, respectively, the diffraction peak should shift to a lower angle with increases in the substituted amount of Tm³⁺. As the peak position of GdF₃ in the XRD profile did not shift to a lower angle, however, we concluded that no Tm³⁺ was substituted for Gd³⁺ sites in the glass.

We next changed the additional source of Tm³⁺ in the glass from Tm₂O₃ to TmF₃. The XRD results for the glass after phase separation treatment using Tm₂O₃ and TmF₃ as Tm³⁺ sources are shown in Fig. 10. These profiles showed no difference among the additional chemicals, and the precipitation of TmF₃ in the glass was confirmed in both samples. On the other hand, as seen in the results of the emission spectra in Fig. 11, the luminescent intensity of the TmF₃-added glass was higher than that of the Tm₂O₃-added glass. This fact reveals that Tm³⁺ derived from TmF₃ is easier to substitute in the Gd³⁺ sites in GdF₃. In addition, the melting points were 2425 and 1158°C for Tm₂O₃ and TmF₃, respectively. The reason why it was easy to substitute Tm³⁺ in TmF₃ for Gd³⁺ in GdF₃ is that TmF₃ and GdF₃ have the same orthorhombic crystal structure and the melting point of TmF₃ is lower than that of Tm₂O₃. To decide the optimum doping amount of TmF₃, the added amount was varied from 0.4 to 2.0 mol% in the phase separation glass. Figure 12 shows the fluorescence spectrum results for changes in the TmF₃ composition, where the fluorescence intensity was significantly changed by the amount of doping. Figure 13 indicates the relationship between the fluorescence intensity at 458 nm and the amount of TmF₃ amount in the glass. The maximum strength occurred at 0.8 mol%, decreasing in intensity with increases in the TmF₃ composition. This was due to the concentration of quenching, and thus, the optimum doping amount in the glass was found to be 0.8 mol%.

The luminescence intensity of the fluoride crystallized glass was stronger than that of the lanthanide borate glass. As shown in Table 1, the vibrational energy of the fluoride crystallization glass was 30 to 50% smaller than that of the lanthanide borate glass. Thus, the excitation energy was prevented from diffusing into the glass phase, and we observe an increase in emission intensity.

![Fig. 8. FT-IR spectra of borosilicate glass doped with lanthanide fluoride with GdF₃ and Gd₂O₃ as a reference sample.](image)

![Fig. 9. Partial enlargement of XRD patterns of borosilicate glass doped with lanthanide fluoride in the 2θ range from 27.5 to 30.0 at various compositions of Tm₂O₃.](image)

![Fig. 10. XRD patterns of borosilicate glass doped with lanthanide fluoride on additional source differences between Tm₂O₃ and TmF₃.](image)

![Fig. 11. Fluorescence properties of Tm₂O₃ and TmF₃ sources.](image)

![Fig. 12. Fluorescence properties of fluoride glass at various compositions of TmF₃.](image)

![Fig. 13. Relationship between the fluorescence intensity and amount of TmF₃.](image)
Table 1. Vibrational energy of glass composition

| Glass composition  | $\nu$ (cm$^{-1}$) |
|--------------------|------------------|
| Borate glass (B−O) | 1400             |
| Silicate glass (Si−O) | 1200         |
| Fluoride glass (M−F) | 500            |

4. Conclusion

Crystallized GdBO$_3$:Tm$^{3+}$ and GdF$_3$:Tm$^{3+}$ in glass suitable for such roles as MRI contrast agents, bio-imaging and GdNCT was successfully synthesized using the phase separation phenomena. In this study, we were able to deduce the following:

1. In glass crystallized GdF$_3$:Tm$^{3+}$, it was confirmed that there are two types of crystal structure; orthorhombic and hexagonal.

2. Since dissolution of crystals was not observed after acid leaching treatment, the phase separation glass was formed in the binodal phase, and it was shown that GdF$_3$ crystals were precipitated in B$_2$O$_3$ spherical phases.

3. There were no impurity peaks such as GdOF and Gd$_2$O$_3$ in the glass with lanthanide fluoride XRD profiles, and there was a Gd−O peak in FT-IR. Hence, the volatility of fluorine emitted from the phase separated glass was confirmed to be very small.

4. The luminescent intensity of the lanthanide trifluoride crystallized glass was higher than that of borate glass. From this result, the fluoride glass was found to be suitable as a material for bio-imaging and GdNCT due to the high Gd concentration in the glass.

Acknowledgment A part of this study was supported by a JSPS Grant-in-Aid for Scientific Research (B) (KAKENHI) Grant Number JP24350098.

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