Chem. Pharm. Bull. 42(3) 727—729 (1994)

META-STABLE COMPLEX FORMATION BETWEEN 2,6-DI-*O*-METHYL-β-CYCLODEXTRIN AND NAPHTHALENE DURING SEALED-HEATING PROCESS

Hiroyuki KAWASHIMA, Etsuo YONEMOCHI, Toshio OGUCHI, and Keiji YAMAMOTO*

Faculty of Pharmaceutical Sciences, Chiba University, 1-33 Yayoicho, Inage-ku, Chiba 263, Japan

When a physical mixture of naphthalene and amorphized 2,6-di-*O*-methyl-β-cyclodextrin was heated in a sealed container, a meta-stable complex was crystallized under a mild condition of heating, which showed excimer fluorescence emission of naphthalene. On the other hand, heating of the mixture at high temperature caused the crystallization of stable inclusion complex which showed monomer fluorescence emission.

KEYWORDS naphthalene; 2,6-di-*O*-methyl-β-cyclodextrin; sealed-heating; solid-state fluorescence spectrum; excimer; meta-stable complex

A new methodology has been developed for preparing a solid inclusion complex of cyclodextrin. 1) Inclusion complex was formed by heating a physical mixture of cyclodextrins and guest compounds in a sealed container. The sealed heating method appears to be superior to the other conventional methods for preparing cyclodextrin inclusion complex in term of simplicity of the procedure and no requirement of any solvent.

2,6-Di-*O*-methyl-β-cyclodextrin (DMβCD) was amorphized by means of grinding with a vibrational mill. An equimolar physical mixture of crystalline naphthalene and amorphous DMβCD was heated in a 2 ml glass ampule at various temperatures. Figure 1 shows the powder X-ray diffractograms of the physical mixture before and after heating for 24 h. The physical mixture showed a halo diffraction pattern, characteristic of amorphous state. After heating above 60°C, the diffraction patterns changed to crystalline patterns, which were obviously different from those of DMβCD crystal and the

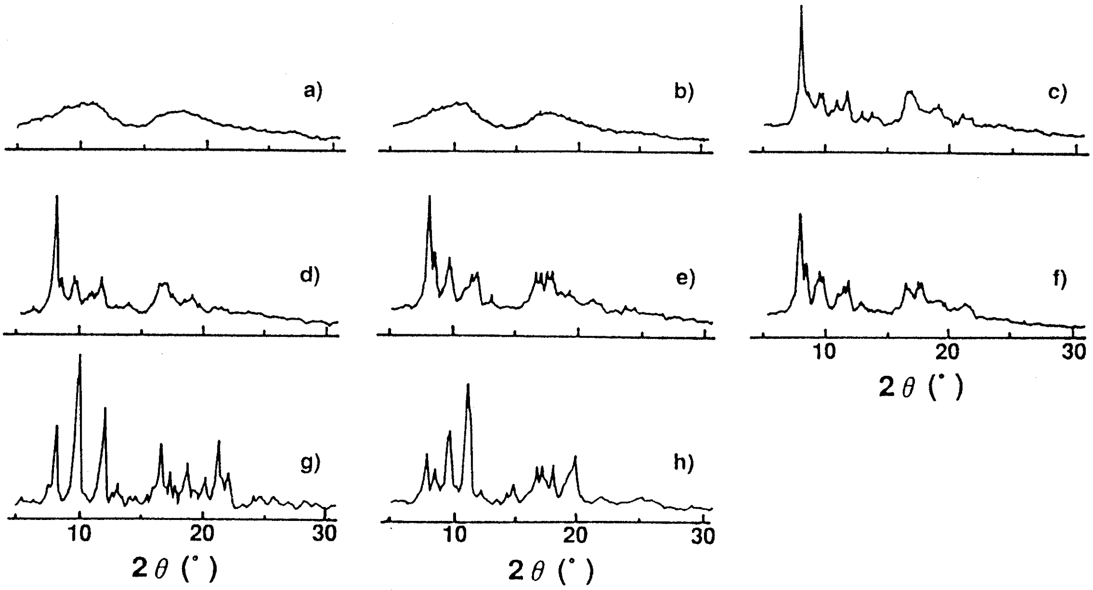

Fig. 1 Changes in the Powder X-Ray Diffraction Pattern of an Equimolar Physical Mixture of DMβCD and Naphthalene by Sealed-Heating at Various Temperature for 24 h
(a), Physical mixture; after sealed-heating at : (b), 50 °C; (c), 60 °C; (d), 70 °C ; (e), 90 °C; (f), 100 °C; (g), DMβCD crystals; (h), Coprecipitate.

coprecipitate.2) This suggests that a DMβCD - naphthalene complex which differed from the coprecipitate was formed during the sealed-heating process. By careful observation of the diffraction patterns around $2\theta = 11$ ° and 18 °, differences were observed among the samples heated at 60 - 70 °C and 90 - 110 °C.

Solid-state fluorescence spectroscopy 3,4) was carried out for the sealed-heated samples at an excitation wavelength of 256 nm (Fig. 2) by using an FP-770E spectrofluorometer (Japan Spectroscopic Co., Ltd.). The samples heated at 60 and 70 °C showed a fluorescence emission peak of naphthalene at 390 nm, while the samples heated at 90 - 110 °C showed a fluorescence emission peak at 341 nm. The sample heated at 80 °C showed an intermediate pattern. It was reported that naphthalene in *n*-heptane solution showed monomer fluorescence emission at 312 nm, and excimer fluorescence was observed at 391 nm at a high concentration. 5) Chandross and Dempster demonstrated that the excimer configuration of naphthalene was the symmetrical (long and short axis parallel) sandwich arrangement. 6) Hamai reported that naphthalene and β-cyclodextrin formed the 1:1 and 2:2 inclusion complexes in aqueous solution to show monomer fluorescence at 330 nm and excimer fluorescence at 410 nm, respectively. 7) It was assumed that the peaks at 341 and 390 nm corresponded to the fluorescence of monomer and excimer states of naphthalene in the sealed-heated samples, respectively. Two types of complexes were also found to be distinctive from differential thermal analysis, as the sublimation of naphthalene was inhibited distinctively between the samples heated at lower and higher temperatures. Consequently, two different kinds of complexes of DMβCD and naphthalene were obtained by the sealed-heating dependent on heating temperature.

Figure 3 shows the changes in fluorescence emission spectrum of the equimolar physical mixture of DMβCD - naphthalene during the process of sealed-heating at 90 °C. As shown in Fig. 3, the monomer fluorescence emission was observed after 24 h heating. The sample heated for 15 min, however, indicated excimer emission, and had the same powder X-ray diffraction pattern as shown in Fig. 1-(c) and (d). A structural stabilization should take place during the process of sealed-heating at

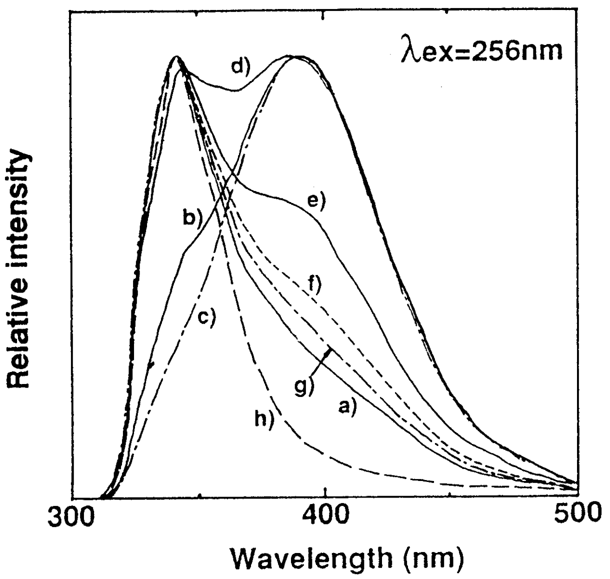

Fig. 2 Solid-State Fluorescence Emission Spectra of the Sealed-Heated Samples Prepared at Various Temperatures for 24 h (λ_{ex}= 256 nm)
Sealed-heating temperature : (a), 50 °C ; (b), 60 °C ; (c), 70 °C ; (d), 80 °C ; (e), 90 °C ; (f), 100 °C ; (g), 110 °C ; (h), Coprecipitate.

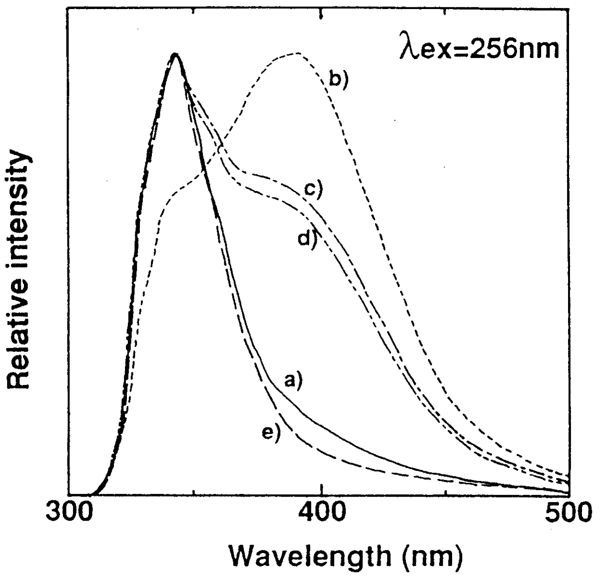

Fig. 3 Changes in the Solid-State Fluorescence Emission Spectrum of an Equimolar Physical Mixture of DMβCD and Naphthalene during Sealed-Heating at 90 °C (λ_{ex}= 256 nm)
(a), Physical mixture; after sealed-heating for : (b), 15 min ; (c), 4 h ; (d), 24 h ; (e), Coprecipitate.

90 °C. The complex showing excimer emission was formed immediately after crystallization, and then the naphthalene molecules changed gradually from the dimeric state to the monomeric state without drastic changes in the crystal structure of the complex. We may say, from these results, that the complex showing excimer was in a meta-stable state and should be transitive to the stable state showing the monomer emission. It was concluded that a meta-stable complex between DMβCD and naphthalene was formed by sealed-heating under a mild condition, which showed excimer fluorescence emission.

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(Received January 5, 1994; accepted January 31, 1994)