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Kazunori Nakano [a], Yukio Hishikawa [b], Kazuki Sada [b], Mikiji Miyata [b] & Kenji Hanabusa [c]

[a] Nagoya Municipal Industrial Research Institute, Atsuta-ku, Nagoya, Aichi, 456-0058

[b] Material and Life Science, Graduate School of Engineering, Osaka University, Yamadaoka, Suita, Osaka, 565-0871

[c] Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano, 386-8567

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PHYSICAL GELATION OF A BILE ACID FOR ORGANIC SOLVENTS

Kazunori Nakano
Nagoya Municipal Industrial Research Institute, Atsuta-ku, Nagoya, Aichi 456-0058

Yukio Hishikawa, Kazuki Sada, and Mikiji Miyata
Material and Life Science, Graduate School of Engineering, Osaka University, Yamadaoka, Suita, Osaka 565-0871

Kenji Hanabusa
Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano 386-8567

Chenodeoxycholic acid (1) was found to induce physical gelation for some organic fluids, while the other derivatives have no gelation ability. A TEM image revealed a three-dimensional gathering of interlocked fibers that encircle solvent molecules. X-ray diffraction and FT-IR measurements showed that the molecular aggregation of the gel was different from that of the crystal ever reported.

Keywords: chenodeoxycholic acid; physical gelation; organic solvent; fibrous aggregate; hydrogen bond; chiral

INTRODUCTION

Low molecular-weight organogelators, which can solidify organic liquids, have received much attention [1]. In the gel state, gelator molecules form intertwining fibrous aggregates that can be observed by TEM and SEM. Since the molecular aggregates are constructed by noncovalent intermolecular interactions, such as hydrogen-bonding and van der Waals interaction, it is still difficult, as the case of crystals, to predict and control the molecular packing and the resulting morphology [2]. In fact, most

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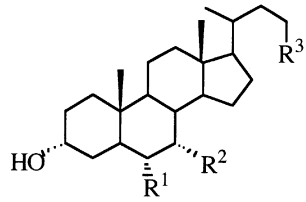

R^1	R^2	R^3	
H	OH	CO_2H	**1**
OH	H	CO_2H	**2**
H	OH	$CONH_2$	**3**
H	OH	CO_2CH_3	**4**
H	OH	CH_2OH	**5**

organogelators have been discovered by chance or trial and error. Recently, many efforts have been made to design the gelators on the basis of characteristic features of molecular structures and molecular aggregates of gelling agents ever found [3–5]. For further development of organogelators, it is expected to find novel agents and to reveal the mechanism of physical gelation.

It has been known that bile acids, cholic acid, deoxycholic acid chenodeoxycholic acid **1**, and hyodeoxycholic acid **2**, form crystals, in which some organic substances are included [6]. Recently, we have reported that the bile acid derivatives having long alkyl chains, alkylcholamides and salts of bile acids with alkylamines, can induce physical gelation for many organic liquids [7]. On the other hand, Hofmann reported that **1** can form gel as well for ethyl acetate [8], indicating that the bile acid without long alkyl units can induce physical gelation. We found that the physical gelation of **1** occurred in other organic fluids, thereby forming the numerous intertwined aggregates. Here, we report the gelation of **1** and the molecular aggregate of the resulting gel.

EXPERIMENTAL

A Typical Procedure for Gelation

Bile acids (**1** and **2**) were commercially available, and were used without any purification. The derivatives (**3**, **4** and **5**) were prepared by the method in the literature [9]. A weighted compound was placed in a screw-capped test tube holding an organic liquid and the mixture was heated until the

compound was dissolved. When a compound were incompletely soluble in the liquid, a good solvent was used. The resulting solution was cooled by holding at room temperature for five hours and then gelation was checked visually. A test tube filled with gelled sample could be turned upside down without causing significant flow.

Instruments

Infrared spectra (IR) spectroscopy, X-ray powder diffraction (XRD) analysis, and transmission electron micrograph (TEM) were carried out by using a JASCO FT/IR-5M, a Rigaku RINT-1100, and a Hitachi H-700, respectively.

RESULTS AND DISCUSSION

Formation of Gels

A part of the results of the gelation tests of **1**–**5** at 25°C is shown in Table I. A compound **1** forms gels for ester, ether, and ketone at the concentration range of 30–100 $g \cdot dm^{-3}$. The resulting gels were transparent irrespective of the solvents. However, the gels were not so stable that they transform to needle-like crystals in a month. Other compounds (**2**–**5**) had no gelation ability, indicating that the intermolecular hydrogen-bondings involving hydroxy and carboxy groups of the bile acid play an important role in the physical gelation of **1**.

TABLE I Gelation Tests[a)] of Bile Acids and the Derivatives

Solvent	**1**	**2**	**3**	**4**	**5**
Acetic acid	S	S	S	S	S
Oleic acid	G	I	I	S	S
Ethanol	S	I	S	P	S
2-Butanone	G	C	S	S	C
Acetophenone	S	I	I	S	C
Ethyl acetate	G	C	S	S	S
Methyl benzoate	G	I	I	S	C
Diisopropyl ether	G[b)]	S	S	S	S
Anisole	G	I	I	S	P
Benzene	I	I	I	S	P
Cotton Seed Oil	G[b)]	I	I	C	P
Silicone Oil	G[b)]	I	I	S	P

[a)]G = gel, S = solution, C = crystal, I = insoluble, P = precipitation.
[b)]Acetic acid was used as a good solvent for dissolving.

Molecular Aggregation of 1

Figure 1 shows a TEM image of a gel formed by **1** in 2-butanone, which is negatively strained by osmic acid. Numerous fibers with 50 to 100 nm diameter gather and interlock to form a huge intertwined aggregate, which would be responsible for immobilization of organic fluids.

Next, the molecular aggregates of the gel from 2-butanone and the transformed crystal of **1** were investigated by means of FT-IR spectrum and XRD patterns. The transformed crystal was obtained by permitting the gel from 2-butanone to stand for a month at room temperature. Since the resulting crystal involved 2-butanone as well as the gel, the solvent in both media was evaporated under vacuum. The IR spectrum of the dried gel and the dried crystal had strong absorption band at 1709.1 and 1703.4 cm^{-1} corresponding to carbonyl groups, respectively. This indicates that the molecular aggregate of the gel has weaker hydrogen-bonding networks than that of the crystal. Considering that the hydrogen-bond is the main interaction for the both molecular aggregates, the difference of the networks would result in the decisive difference in molecular aggregates. This was confirmed by XRD patterns. The XRD pattern of the dried gel of **1** shows broad peaks at $2\theta = 6.9$, 9.1, 14.5, 16.5, 18.6 and 20.0°, as shown in Figure 2. This pattern was different from that of the dried crystal transformed from the gel. The XRD pattern of the crystal shows the sharp peaks

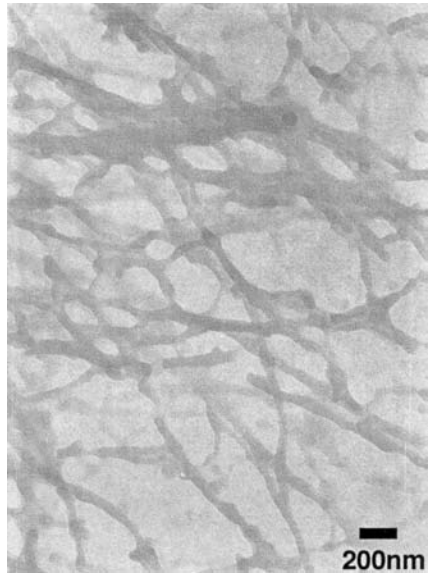

FIGURE 1 TEM image of loose gel from **1** in 2-butanone

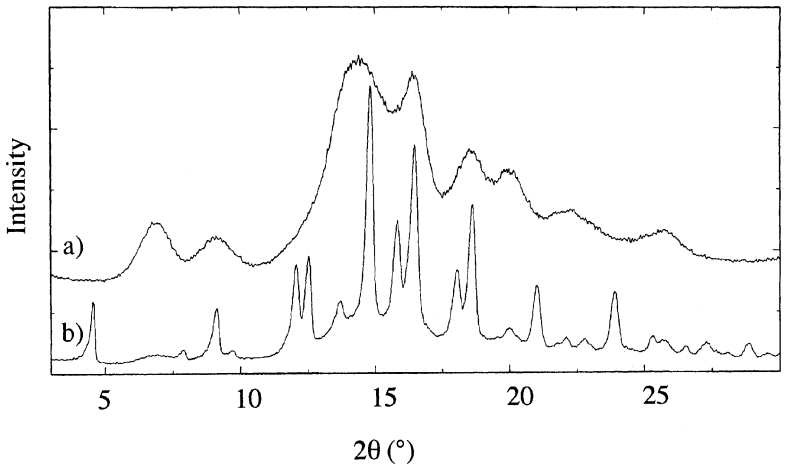

FIGURE 2 X-Ray diffraction patterns of a) dried gel, b) dried crystals.

at $2\theta = 4.6$, 9.1, 12.1, 12.5, 14.9, 15.8, 16.5, 18.1, and 18.6°, indicating that the crystal is hexagonal packing ever reported [10].

CONCLUSION

We demonstrate that **1** can form gel, in which intertwining fibrous aggregate can be observed by TEM. The molecule of **1** has a rare molecular structure for low molecular-weight organogelators because many gelators have long aliphatic chains. This result and recent reports of physical gelation by sugar-integrated compounds [11] and a β-hydroxy-α-amino acid derivative [12] suggest that chiral and multi-functional molecules without long aliphatic chains can induce physical gelation in organic solutions.

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