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Molecular organogel-forming porphyrin derivative with hydrophobic L-glutamide

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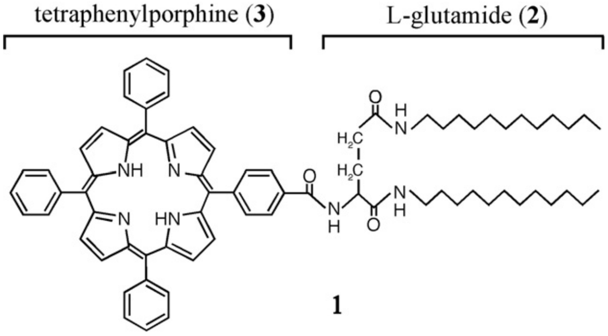
Abstract

An L-glutamide-functionalized tetraphenylporphyrin derivative has been newly synthesized. This can dissolve in various organic solvents to form nanofibrillar aggregates with both right-handed and left-handed chiral stacking structures among the porphyrin rings. It is also discussed on thermotropic and lyotropic phase transitions between gel and sol states.

1. Introduction

Molecular assemblies of porphyrin derivatives such as bacteriochlorophylls are key components for light-harvesting and energy migration in photosynthesis.[1] Synthetic porphyrins such as tetraazaporphyrin have been utilized as essential compounds for plasma-display filters.[2] Therefore, highly ordered assemblies of synthetic porphyrins such as molecular wires would be widely applicable and promising for electronic devices as light-harvesting molecular wires. For this purpose, many porphyrin-containing derivatives have been reported. Some successes can be seen in sugar-immobilized[3] and polypeptide-supported[4] porphyrins. In this article, we introduce a novel porphyrin derivative (**1**) to form highly ordered structures by self-assembling in organic media. The chemical structure can be characterized by the fact that a long chain-alkylated L-glutamide (**2**) is combined as a driving force for chirally molecular ordering into tetraphenylporphine (**3**). **2** is a very useful tool for promoting the intermolecular hydrogen bonding to lead to superstructural fabrication both in aqueous[5] and organic[6] media, and thus would induce chirally-stacking interaction among the porphyrin rings to develop to one-dimensional aggregates.



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1 was prepared by coupling of 5-(4-carboxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphine (**3**) with *N*,*N*′-didodecyl L-glutamide (**2**) according to the previously reported procedures[6] with slight modification.

1 dissolved in various organic solvents such as methanol, ethanol, acetonitrile, DMF, THF, benzene, pyridine, and chloroform which were good solvents. However, when a solvent system was adjusted by mixing with a poor solvent such as cyclohexane, the **1** solution changed to a

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gel state. A typical example can be obtained as follows: when **1** (0.5 mM) dissolved in a mixture of cyclohexane and THF (20:1) at 60 °C to a solution state and cooled down to 20 °C, a sol-to-gel transition happened immediately as shown in Figure 1a. A TEM observation in the cast film from the **1** cyclohexane–THF (20:1) gel showed well-developed fibrous aggregates with the minimum thickness of around 3 nm (Fig. 1b and c) although some parts were larger as twisted ribbon-like and bundled aggregates.[7] The minimum thickness is nearly close to the molecular length (3.75 nm) of **1** estimated by HyperChem-MM2. Therefore, it is preliminarily concluded that the **1** aggregates are based on molecular layered structures similar to aqueous lipid membranes and the gel formation can be brought about through the three-dimensional network formation with the **1**-nanofibrillar aggregates. This phenomenon can be recognized as molecular gelation.[8]

The Soret band of a porphyrin moiety (**3**) is very useful for evaluating the dispersion state of **1** in organic media. Figure 2a includes a UV–visible spectrum in a cyclohexane–THF (20:1) mixture containing 0.1 mM of **1** at 10 °C. The λ_{max} at 417 nm corresponds to that in the Soret band when **3** is in a monomeric dispersion state. However, a drastic spectral change was observed by slight change of the concentration of **1**. For example, when the concentration increased from 0.1 mM to 0.2 mM, the solution not only changed to a fragile gel but also the Soret band split into two peaks with λ_{max}s of 399 and 428 nm. A similar split pattern was reported in a protoporphyrin IX derivative with bis(glycosamides) in an aqueous solution[9] and a bis(imidazolyl)porphyrinato–cobalt(III) complex in chloroform[10] although their detailed mechanisms are different from our observation.

The further important information was obtained by CD spectroscopy. As shown in Figure 2b, an extremely strong Cotton effect was observed in 0.2 mM. The maximum molecular ellipticity ($[\theta]_{max}$) reaches 1.5×10^6 deg cm^2 dmol^{-1} at 420 nm and -1.45×10^6 deg cm^2 dmol^{-1} at 398 nm, and the CD pattern was almost constant in the concentration above 0.2 mM. Since a porphyrin moiety is achiral, the strong CD strength with the λ_{max} shift can be explained only by the induction of chiral ordering of the achiral porphyrin moiety through the formation of highly ordered structures with the chiral L-glutamide moiety. Similar induction of chirality was observed by isoquinoline[5]- and pyrene[11]-containing L-glutamide derivatives in organic media. On the other hand, the concentration dependency of $[\theta]_{max}$ (Fig. 3) showed a distinct bending point at

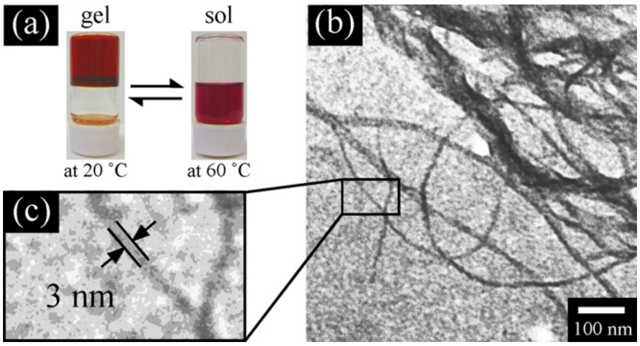

Fig. 1. Temperature-dependent sol-to-gel transition of **1** (0.5 mM) in a cyclohexane–THF (20:1) mixture (a) and TEM images of **1** aggregates in the cast film prepared from 0.2 mM (b and c). Stained by 2.0 wt % ammonium molybdate after casting and drying.

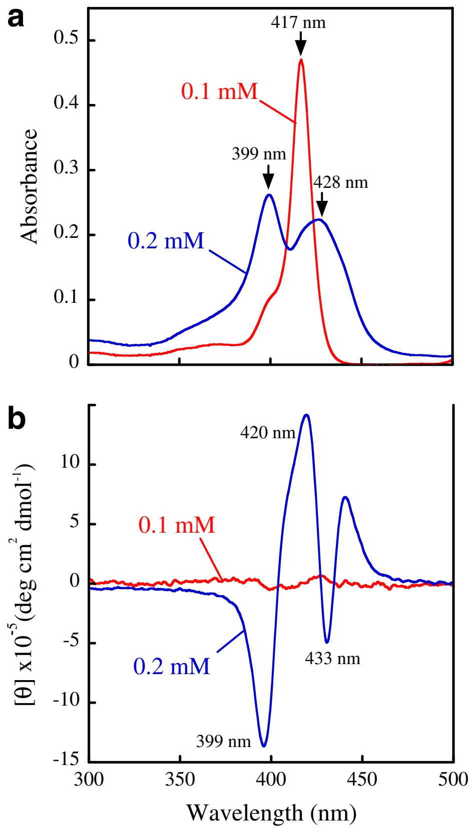

Fig. 2. UV–visible (a) and CD (b) spectra of **1** in a cyclohexane–THF (20:1) mixture at 10 °C.

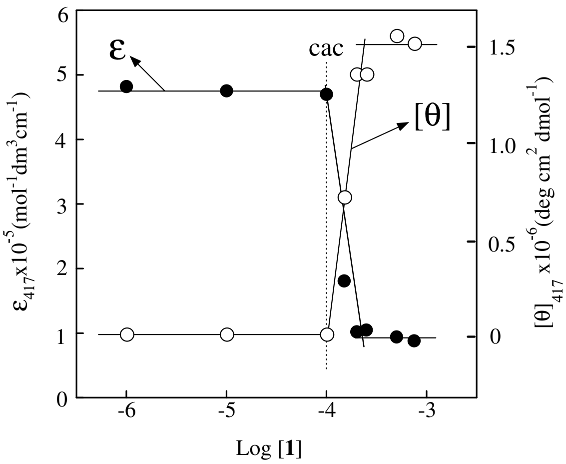

Fig. 3. Concentration-dependent molecular coefficient (ε) (a) and molecular ellipticity [θ] (b) at 417 nm on Log[**1**] in a cyclohexane–THF (20:1) mixed system at 10 °C.

0.1 mM. The $[\theta]_{417}$ value is very small in the concentration below 0.1 mM and almost constant in the concentration above 0.2 mM. Therefore, it is estimated that the critical aggregation concentration (cac) of **1** is around 0.1 mM in a cyclohexane–THF (20:1) mixed system at 10 °C.

The detailed investigation of the CD pattern enables us to clarify the chirally ordered structures of the **1** aggregate. Firstly, there is almost no CD signal around the absorption band on a porphyrin moiety in the concentrations below cac. The induction of CD is only observed in the concentration above cac. Secondly, the complicated CD pattern in Figure 2b can be segmented into two kinds of CD spectra as shown in Figure 4a and b. The two $\lambda_{\max}$s of the split UV–visible spectrum (Fig. 2a) agree with those in the CD spectra, respectively. Thirdly, a thermotropic sol-to-gel transition was also observed. For example, the cyclohexane–THF (20:1) mixed system containing 0.25 mM of **1** showed a remarkable temperature-dependent spectral change in both their UV–visible and CD spectroscopies.[12] In this case, two isosbestic points were observed at 405 nm and 426 nm in this temperature dependency. These observations support the following proposed structures on the chiral **1** aggregates: the split pattern in Figure 2a can be explained by two species composed of right-handed (*R*-chiral) H-like aggregates with a hypsochromical shift and left-handed (*S*-chiral) J-like aggregates with a bathochromical shift according to the Simonyi's explanation.[13] An FT-IR spectrum of the **1** aggregates in a cyclohexane–THF (20:1) mixture showed typical amide I absorptions corresponding to the parallel and antiparallel hydrogen bonding[14,15] at 1637 and 1678 cm^{-1}, respectively. This spectrum is similar to that in a solid state with an absorption peak at 1639 cm^{-1} but different from that in a chloroform solution state with an absorption peak at 1652 cm^{-1}. The schematic illustration shown in Figure 5 satisfies this assumption. Figure 5 shows that fibrous networks were consisted of chirally ordered structure. One-dimensional aggregation of **1** can be derived from a long-range face-to-face stacking (H-like aggregation) and an edge-to-edge interaction (J-like aggregation) can be almost simultaneously formed to lead to a ribbon-like morphology.[7]

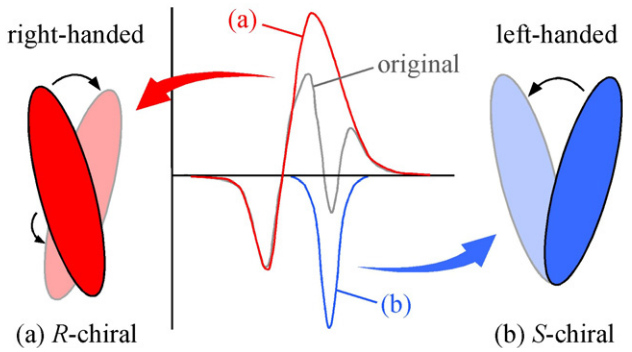

Fig. 4. Resolution of CD spectrum of the 0.2 mM gel in a cyclohexane–THF (20:1) mixture at 10 °C.

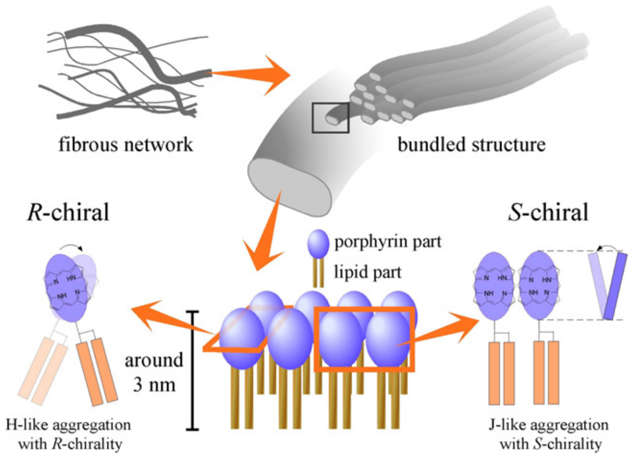

Fig. 5. Schematic proposal on the ordered structure in the **1** aggregates.

In conclusion, an L-glutamide-functionalized tetraphenyl-porphyrin derivative **1** can form a molecular gel in organic media through three-dimensional network formation with chirally self-assembled nanofibrillar aggregates. It should be also emphasized that a unique chiral microenvironment is produced by both *R*-chiral H-aggregation and *S*-chiral J-aggregation among the porphyrin moieties. In addition, these phenomena are reversible (viz. switchable) by changing the temperature, solvent-combination, concentration, and so on. Further investigation on singlet–singlet energy migration using a **1** system will be reported later.

2. Experimental

^{1}H NMR (400 MHz) spectra were recorded in CDCl$_3$, SiMe$_4$ as an internal standard with JNM-EX400 (JEOL). IR spectra were measured in a KBr method with FT/IR-4100 (JASCO). TEM images were observed with JEM-2000X (JEOL). UV–visible and CD spectra were measured with UV–vis Spectrophotometer V-560 (JASCO) and Spectropolarimeter J725 (JASCO), respectively.

A solution of 1 N NaOH 3.75 mL was added dropwise to 5-(4-methoxycarbonylphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphine (0.25 g, 0.4 mmol) in DMF (100 mL) at room temperature for 30 min. After the reaction mixture was stirred at room temperature for 3 h, it was acidified with aqueous 2.0 wt % HCl to pH 2.0. The precipitates were filtered and dried in vacuo, to give 5-(4-carboxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphine (0.23 g, 92%). 0.40 g (0.6 mmol) of 5-(4-carboxyphenyl)-10,15,20-triphenyl-21*H*,23*H*-porphine and 0.35 g (0.7 mmol) of *N*,*N*′-didodecyl-L-glutamide, which was obtained by the previously reported procedure[6] with slight modification, were dissolved in THF (150 mL) in the presence of triethylamine (1.2 mL, 0.9 mmol) and diethyl cyanophosphate (1.5 mL, 0.9 mmol). After being stirred for 1 day at room temperature, the solution was concentrated in vacuo.

The residue was redissolved in chloroform, and the organic layer was washed three times with 0.2 N HCl and 0.2 N NaOH, then washed with water, and dried with sodium sulfate. The solution was concentrated in vacuo, and the residue was reprecipitated from chloroform–*n*-hexane and then dried in vacuo to give a purple solid: 0.50 g (80%). Mp 229.5–233.0 °C. IR (KBr): 3316, 2925, 2853, 1639, 1542 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ −2.78 (s, 2H, –N*H*), 0.80–0.87 (m, 6H, –CH_3), 1.17–1.35 (br, 40H, –(CH_2)$_{10}$–), 2.32 (q, 2H, $J = 5.2$ Hz, –CH_2–), 2.45–2.75 (br, 2H, –CH_2CO–), 3.30–3.38 (m, 4H, –NCH_2–), 4.74 (q, 1H, $J = 6.0$ Hz, –C*H*–), 6.03–6.06 (br, 1H, N*H*), 7.04–7.07 (br, 1H, N*H*), 7.73–7.79 (m, 9H, Ar*H*), 8.20–8.33 (m, 10H, Ar*H*), 8.42–8.44 (br, 1H, N*H*), 8.79–8.87 (m, 8H, Ar*H*). Anal. Calcd for $C_{74}H_{87}N_7O_3$: C, 79.01; H, 7.81; N, 8.72. Found: C, 78.88; H, 8.09; N, 8.61.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.04.103.

References and notes

1. (a) McDermott, G.; Prince, S. M.; Freer, A. A.; Hawthornthwaite-Lawless, A. M.; Papiz, M. Z.; Cogdell, R. J.; Isaaca, N. W. *Nature* **1995**, *374*, 517–521; (b) Melkozernov, A. N.; Barber, J.; Blankenship, R. E. *Biochemistry* **2006**, *45*, 331–345; (c) Egawa, A.; Fujiwara, T.; Mizoguchi, T.; Kakitani, Y.; Koyama, Y.; Akutsu, H. *Proc. Natl. Acad. Sci. U.S.A.* **2007**, *104*, 790–795.
2. Davies, C.; Petty, D. M.; Willis, M. R. *Synth. Met.* **1989**, *28*, 775–780.
3. Tamaru, S.; Nakamura, M.; Takeuchi, M.; Shinkai, S. *Org. Lett.* **2001**, *3*, 3631–3634.
4. Hasobe, T.; Kamat, P. V.; Troiani, V.; Solladie, N.; Ahn, T. K.; Kim, S. K.; Kim, D.; Kongkanand, A.; Kuwabata, S.; Fukuzumi, S. *J. Phys. Chem. B* **2005**, *109*, 19–23.
5. (a) Yamada, K.; Ihara, H.; Ide, T.; Fukumoto, T.; Hirayama, C. *Chem. Lett.* **1984**, 1713–1716; (b) Ihara, H.; Hachisako, H.; Hirayama, C.; Yamada, K. *Liq. Cryst.* **1987**, *2*, 215–221.
6. (a) Ihara, H.; Hachisako, H.; Hirayama, C.; Yamada, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1244–1245; (b) Ihara, H.; Yoshitake, M.; Takafuji, M.; Yamada, T.; Sagawa, T.; Hirayama, C.; Hachisako, H. *Liq. Cryst.* **1999**, *26*, 1021–1027.
7. Supplementary data regarding the ribbon-like and bundled aggregates.
8. (a) Terech, P.; Weiss, R. G. *Chem. Rev.* **1997**, *97*, 3133–3159; (b) Van Esch, J. H.; Feringa, B. L. *Angew. Chem., Int. Ed.* **2000**, *39*, 2263–2266; (c) Ihara, H.; Takafuji, M.; Sakurai, T. *Encycl. Nanosci. Nanotechnol.* **2004**, *9*, 473–495; (d) Shimizu, T.; Masuda, M.; Minamikawa, H. *Chem. Rev.* **2005**, *105*, 1401–1443; (e) Oda, R. *Materials with Self-assembled Fibrillar Networks* **2006**, 577–612; (f) Ariga, K.; Nakanishi, T.; Hill, J. P. *Curr. Opin. Colloid Interface Sci.* **2007**, *12*, 106–120.
9. Fuhrhop, J.-H.; Demoulin, C.; Boettcher, C.; Koning, J.; Siggel, U. *J. Am. Chem. Soc.* **1992**, *114*, 4159–4165.
10. Ikeda, C.; Fujiwara, E.; Satake, A.; Kobuke, Y. *Chem. Commun.* **2003**, 616–617.
11. (a) Ihara, H.; Sakurai, T.; Yamada, T.; Hashimoto, T.; Takafuji, M.; Sagawa, T.; Hachisako, H. *Langmuir* **2002**, *18*, 7120–7228; (b) Takafuji, M.; Ishiodori, A.; Yamada, T.; Sakurai, T.; Ihara, H. *Chem. Commun.* **2004**, 1122–1123.
12. Supplementary data regarding the temperature-dependent spectral change in both their UV–visible and CD spectroscopies.
13. Symonyi, M.; Bikadi, Z.; Zsila, F.; Deli, J. *Chirality* **2003**, *15*, 680–698.
14. Yamada, N.; Ariga, K.; Naito, M.; Matsubara, K.; Koyama, E. *J. Am. Chem. Soc.* **1998**, *120*, 12192–12199.
15. Suzuki, M.; Setoguchi, C.; Shirai, H.; Hanabusa, K. *Chem. Eur. J.* **2007**, *13*, 8193–8200.