ORGANIC LETTERS

2001
Vol. 3, No. 23
3631−3634

Rational Design of a Sugar-Appended Porphyrin Gelator That Is Forced To Assemble into a One-Dimensional Aggregate

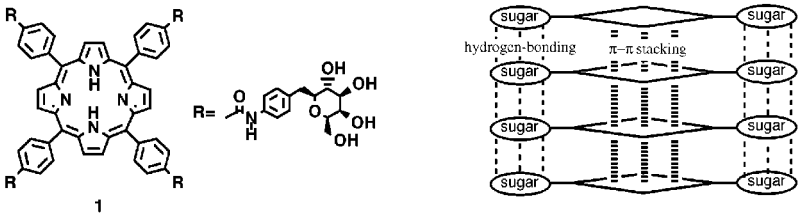
Shun-ichi Tamaru, Michihiko Nakamura, Masayuki Takeuchi, and Seiji Shinkai*

Department of Chemistry and Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka 812-8581, Japan

seijitcm@mbox.nc.kyushu-u.ac.jp

Received August 9, 2001

ABSTRACT



As an attempt to rationally design organogelators, an amphiphilic porphyrin bearing four β-D-galactopyranoside groups at its periphery was synthesized. This compound tends to aggregate in a one-dimensional direction, resulting in very robust gels in DMF/alcohol mixed solvents. Spectroscopic studies and electron-micrographic observations support the view that the π–π stacking interaction among porphyrin moieties and the hydrogen-bonding interaction among sugar moieties operate synergistically to give rise to a stable one-dimensional aggregate structure indispensable for gel formation.

One-dimensional alignment of porphyrins and phthalocyanines is of much concern in relation to the creation of novel supramolecular architectures such as nanowires, discotic liquid crystals, helical ribbon structures, etc.[1−5] The major driving force in these architectures is considered to be a π−π stacking interaction. More recently, other supramolecular architectures constructed in organogels have attracted the widespread attention of supramolecular chemists: the origin of organogel formation is considered to be one-dimensional alignment of gelator molecules supported by a van der Waals interaction and/or a hydrogen-bonding interaction.[6,7] This situation has offered a new idea that porphyrins and phthalocyanines, which a priori tend to assemble into the one-dimensional supramolecular architecture, would act as powerful building blocks for the design

(1) (a) van Nostrum, C. F.; Picken, S. J.; Schouten, A.-J.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1995**, *117*, 9957−9965. (b) Schenning, A. P. H.; Benneker, F. B. G.; Geurts, H. P. M.; Liu, X. Y.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1996**, *118*, 8549−8552. (c) van Nostrum, C. F.; Nolte, R. J. M. *Chem. Commun.* **1996**, 2385−2392. (d) Engelkamp, H.; van Nostrum, C. F.; Picken, S. J.; Nolte, R. J. M. *Chem. Commun.* **1998**, 979−980. (e) Engelkamp, H.; Middelbeek, S.; Nolte, R. J. M. *Science* **1999**, *284*, 785−788. (f) Samorí, S.; Engelkamp, H.; de Witte, P.; Rowan, A. E.; Nolte, R. J. M.; Rabe, J. P. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 2348−2350 and references therein.

(2) (a) Fuhrhop, J.-H.; Demoulin, C.; Boettcher, C.; Köning, J.; Siffel, U. *J. Am. Chem. Soc.* **1992**, *114*, 4159−4165. (b) Fuhrhop, J.-H.; Bindig, U.; Siggel, U. *J. Am. Chem. Soc.* **1993**, *115*, 11036−11037. (c) Bindig, U.; Schulz, A.; Fuhrhop, J.-H. *New J. Chem.* **1995**, *19*, 427−435 and references therein.

(3) (a) Smolenyak, P.; Peterson, R.; Nebesny, K.; Torker, M.; O'Brien, D. F.; Armstrong, N. R. *J. Am. Chem. Soc.* **1999**, *121*, 8628−8636. (b) Drager, S. A.; Zangmeister, R. A. P.; Armstrong, N. R.; O'Brien, D. F. *J. Am. Chem. Soc.* **2001**, *123*, 3595−3596.

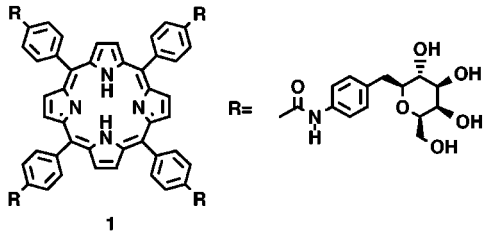
(4) (a) Kimura, M.; Kitamura, T.; Muto, T.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *Chem. Lett.* **2000**, 1088−1089. (b) Kimura, M.; Muto, T.; Takimoto, H.; Wada, K,; Ohta, K.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *Langmuir* **2000**, *16*, 2078−2082. (c) Kimura, M.; Wada, K.; Ohta, K.; Hanabusa, K.; Shirai, H.; Kobayashi, N. *J. Am. Chem. Soc.* **2001**, *123*, 2438−2439.

(5) (a) Imada, T.; Murakami, H.; Shinkai, S. *Chem. Commun.* **1994**, 1557−1558. (b) Arimori, S.; Takeuchi, M.; Shinkai, S. *J. Am. Chem. Soc.* **1996**, *118*, 245−246. (c) Arimori, S.; Takeuchi, M.; Shinkai, S. *Supramol. Sci.* **1998**, *5*, 1−8.

(6) Luboradzki, R.; Gronwald, O.; Ikeda, M.; Shinkai, S.; Reinhoudt, D. N. *Tetrahedron* **2000**, *56*, 9595−9599.

10.1021/ol0165544 CCC: $20.00
Published on Web 10/24/2001

of new gelators. In addition, we found that many new hydrogen-bond-based gelators can be developed utilizing a natural library of carbohydrate molecules.[8,9] In a few cases, the solvents were gelated by only 0.03−0.05 g mL^{-1} sugar-based gelators.[10] The finding suggests that one-dimensional aggregates composed of porphyrins or phthalocyanines would be "reinforced" by the hydrogen-bonding interaction among saccharide groups covalently appended to the central porphyrin (or phthalocyanine) column. However, this idea has never been utilized for the design of a robust organogel system.[11] It thus occurred to us that porphyrin molecules, the periphery of which is modified with saccharide groups, would form a one-dimensional aggregate as a result of the synergistic effect of porphyrin−porphyrin $\pi-\pi$ stacking and saccharide−saccharide hydrogen bonding and eventually result in stable organogels.[12] With these objects in mind we synthesized porphyrin **1** bearing four peripheral β-D-galactopyranoside groups. We have found that **1** results in stable organogels showing both thermotropic and lyotropic behaviors. The aggregation mode was estimated by various spectroscopic methods and scanning electron micrograph (SEM) and transmission electron micrograph (TEM) observations.



1

Compound **1** was synthesized from 5,10,15,20-tetrakis-(4-carboxyl-1-phenyl)porphyrin (**2**) and *p*-aminophenyl-2,3,4,6-tetra-*O*-acetyl β-D-galactopyranoside (**3**).[13] Compound **2** was converted to its acid chloride, which was treated with **3** in THF in the presence of triethylamine. The product was deacetylated by treatment with MeONa in a mixed solvent of MeOH/THF 80:20 (v/v). The product (**1**, mp 271 °C (dec)) was identified by ^{1}H NMR and MALDI-TOF-MS ($[M + H]^+$ 1804.28) spectral evidence and elemental analysis.

The gelation test was carried out as follows. Compound **1** was dispersed in solvent (3.0 wt %, 16.6 mM), and the mixture was heated in a septum-capped test tube. The solution was cooled to room temperature and left for 1 day in the dark. By this treatment, **1** was insoluble in most solvents (water, *i*-PrOH, *n*-BuOH, chloroform, dichloromethane, *n*-hexane, cyclohexane, benzene, toluene, THF, MeCN, anisole, ethyl acetate, etc.). It swelled in MeOH, EtOH, and benzyl alcohol (BzlOH) but was not dissolved into these solvents even at reflux temperature. In contrast, it was well dissolved in DMF. Thus, we evaluated the gelation ability in 1:4 (v/v) DMF/solvent mixtures. Compound **1** was again insoluble in DMF mixed solvents with benzene and chloroform. In DMF mixed solvents with *n*-BuOH and BzlOH, it was dissolved at reflux temperature but when cooled just precipitated without forming the organogel. Interestingly, the gelation was observed for DMF mixed solvents with MeOH, EtOH, and *i*-PrOH. In mixed solvent with BzlOH, **1** was precipitated at 1:4 (v/v) DMF/BzlOH, whereas the gelation was observed at 1:2 (v/v) DMF/BzlOH. These findings indicate that, despite extensive gelation tests, the gel is formed only in DMF/alcohol mixtures. We thus consider that porphyrin groups primarily constitute a one-dimensional column and saccharide groups surround this central column. In aprotic solvents these columns tend to aggregate with each other owing to the intercolumnar saccharide−saccharide interaction, so that they cannot disperse into these solvents. In alcoholic solvents, on the other hand, these columns should be "moderately" solvated to maintain the one-dimensional structure suitable for gel formation and to protect each columnar structure from aggregation and precipitation. Hereafter, we used this 1:2 (v/v) DMF/BzlOH solvent, having a higher bp than others, as a standard solvent.

The "stability" of organogels is usually evaluated with two factors, viz., critical gelation concentration (CGC) where the sol phase changes into the gel phase and sol−gel phase transfer temperature (T_{gel}) where the gel melts into the sol solution.[7] The T_{gel} values were determined in various DMF/BzlOH mixed solvents as a function of gelator concentration (Table 1). It is seen from Table 1 that the CGC for **1** is very low (ca. 2 wt % in 1:2 (v/v) DMF/BzlOH and ca. 0.4 wt % in 1:3 (v/v) DMF/BzlOH) and the T_{gel} values at [**1**] > 1.3

Table 1. Gelation Test and T_{gel} Values in DMF/BzlOH[a]

	DM/:BzlOH (v/v)					
[**1**] (wt %)	1:19	1:6	1:5	1:4	1:3	1:2
0.1	G (32)	HVS	HVS	HVS	S	S
0.7					G (78)	
0.8					G (90)	
0.9					G (102)	
1.3					G (127)	
1.4	P	G (136)	G (153)	G (148)	G (140)	S
1.8					G (149)	
2.2					G (163)	
2.5					G (167)	
3.0	P	P	P	P	P	G (175)

[a] G = gel; P = precipitation; HVS = highly viscous solution; °C in the parentheses.

(7) For comprehensive reviews for organogels, see: (a) van Esch, J.; Schoonbeek, F.; de Loos, M.; Kooijman, H.; Veen, E. M.; Kellogg, R. M.; Feringa, B. L. In *Supramolecular Science: Where It Is and Where It Is Going*; Ungaro, R., Dalcanale, E., Eds,; Kluwar: The Netherlands, 1999; pp 233−259. (b) Melendez, R. E.; Carr, A. J.; Linton, B. R.; Hamilton, A. D. *Struct. Bond.* **2000**, 31−61. (c) Shinkai, S.; Murata, K. *J. Mater. Chem.* **1998**, *8*, 485−495.

(8) (a) Yoza, K.; Ono, Y.; Yoshihara, K.; Akao, T.; Shinmori, H.; Takeuchi, M.; Shinkai, S.; Reinhoudt, D. N. *Chem. Commun.* **1998**, 907−908. (b) Yoza, K.; Amanokura, N.; Ono, Y.; Akao, T.; Shinmori, H.; Shinkai, S.; Reinhoudt, D. N. *Chem. Eur. J.* **1999**, *5*, 2722−2729. (c) Amanokura, N.; Yoza, K.; Shinmori, H.; Shinkai, S.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 2* **1998**, 2585−2591. (d) Gronwald, O.; Sakurai, K.; Luboradzki, R.; Kimura, T.; Shinkai, S. *Carbohydr. Res.* **2001**, *331*, 307−318.

(9) For a comprehensive review for sugar-based gelators, see: Gronwald, O.; Shinkai, S. *Chem. Eur. J.* **2001**, *7*, 4328−4334.

(10) Luboradzki, R.; Gronwald, O.; Ikeda, A.; Shinkai, S. *Chem. Lett.* **2000**, 1148−1149.

wt % are higher than 130 °C. The T_{gel} values can be further enhanced at high gelator concentrations, e.g., 167 °C at 2.5 wt % in 1:3 (v/v) DMF/BzlOH and 175 °C at 3.0 wt % in 1:2 (v/v) DMF/BzlOH. The CGC decreases with the increase in the BzlOH concentration. At 1:19 (v/v) DMF/BzlOH, the solution can be gelated even at [**1**] = 0.1 wt %, although the T_{gel} is relatively low (32 °C). The results indicate that **1**, which is rationally designed for the formation of one-dimensional supramolecular architectures, can act as an excellent gelater showing both thermotropic and lyotropic transition phenomena.

Table 1 also shows that when compared at [**1**] = 1.4 wt %, the gel formation is possible only between 1/6 (14 vol % DMF) and 1/3 (25 vol % DMF). Below 14 vol % DMF **1** was insoluble, whereas above 30 vol % DMF it was dissolved. The most stable organogel with T_{gel} = 153 °C was obtained at 1:5 (v/v) DMF/BzlOH. One may regard, therefore, that the gel is formed on the basis of a subtle balance between porphyrin−porphyrin $\pi-\pi$ stacking and saccharide−saccharide vs saccharide−solvent hydrogen bonding interactions.

Direct evidence for the porphyrin−porphyrin stacking was obtained from absorption and CD spectral examinations. As shown in Figure 1A, **1** in homogeneous solution gave the Soret band at 422.5 nm and the Q-bands at 516.0, 551.0, 592.5, and 648.0 nm. In the gel phase, the Soret band shifted to shorter wavelength (401.0 nm) with the appearance of a shoulder at 420.0 nm. This blue-shift implies that the porphyrin moieties form a stacked aggregate,[14] but a significant amount of **1** still remains as a monomer in bulk solution. The Q-bands in the gel phase appeared at 522.5, 558.0, 599.0, and 654.0 nm, which were all red-shifted compared with those in homogeneous solution. The red shift is also compatible with the formation of porphyrin−porphyrin stacked aggregates.[14] The CD spectra are shown in Figure 1B. It is seen from Figure 1B that the CD band assignable to the positive exciton coupling is observable only in the gel phase.[15] This indicates that, as already observed for cholesterol-appended porphyrin gelators,[12] the one-dimensional porphyrin column is helically twisted by the chirality of peripheral saccharide groups.

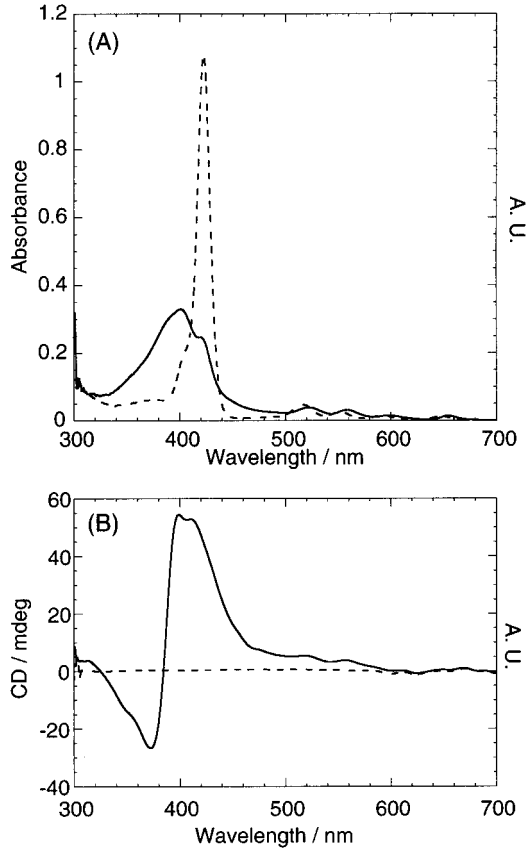


Figure 1. (A) UV/vis absorption spectra of **1** at 25 °C in 1:2 (v/v) DMF/BzlOH: (- - -) homogeneous solution ([**1**] = 2.3 × 10^{-6} M); (——) gel phase ([**1**] = 3.0 wt % (16.6 × 10^{-3} M)). (B) CD spectra of **1** at 25 °C: (- - -) homogeneous solution ([**1**] = 2.3 × 10^{-6} M, 1:2 (v/v) DMF/BzlOH); (——) gel phase ([**1**] = 0.1 wt % (5.5 × 10^{-4} M), 1:19 (v/v) DMF/BzlOH.

If this "microscopic" helicity is reflected by the "macroscopic" bundle structure, one may be able to recognize the one-dimensional helical structure by electron micrograph. As shown in Figure 2A, the SEM picture of the xerogel (prepared from [**1**] = 3.0 wt %, 1:2 (v/v) DMF/BzlOH gel) shows a network consisting of fibrous structures with 200−300 nm diameters. The close-up picture (Figure 2B) shows that all fibers are twisted into a left-handed helical direction. One may thus consider that molecular design of one-dimensionally stacked chiral structure eventually leads to the "macroscopic" helical aggregate observable with SEM. Comparing the fiber diameter with the size of **1** (ca. 4.0 nm), one may consider that these bundles are composed of about 60 incipient, one-dimensionally stacked porphyrin columns. The growing process of incipient fibers into a large bundle can be seen by a TEM picture (Figure 2C): it is clearly seen that small fibers are twined together into a ropelike large fiber.

In conclusion, the present paper has demonstrated that a sugar-appended porphyrin derivative, which is rationally

(11) The tetrakis(*O*-tetraacetyl) derivative of compound **1** was very soluble in most organic solvents and did not act as a gelator. The similar porphyrin derivatives were synthesized by Fuhrhop's group,[2] but they were not applied to the organogel system. More recently, Stoddart et al. synthesized sugar-coated discotic liquid crystals bearing a triphenylene core. The gelation properties were not examined therein: Barbera, J.; Garces, A. C.; Jayaraman, N.; Omenat, A.; Serrano, J. L.; Stoddart, J. F. *Adv. Mater.* **2001**, *13*, 175−180.

(12) More recently, we found that certain cholesterol-appended porphyrins act as gelators of organic solvent: Ishi-i, T.; Jung, J. H.; Shinkai, S. *J. Mater. Chem.* **2000**, *10*, 2238−2240. Tian, H. J.; Inoue, K.; Yoza, K.; Ishi-i, T.; Shinkai, S. *Chem. Lett.* **1998**, 871−872. In these organogels, however, it is considered that porphyrin moieties are located around a helical central colmun of cholesterol moieties, like a spiral staircase.

(13) Amaike, M.; Kobayashi, H.; Shinkai, S. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 2553−2558.

(14) Kano, K.; Fukada, K.; Wakami, H., Nishiyabu, R.; Pasternack, R. F. *J. Am. Chem. Soc.* **2000**, *122*, 7494−7502.

(15) Although a weak band arising from linear dichroism exists in the Soret band region, the intensity is negligibly small compared with this CD band.

(16) (a) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *J. Am. Chem. Soc.* **1997**, *119*, 8492−8502. (b) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *Supramol. Chem.* **1998**, *9*, 169−174. (c) Tanaka, T.; Endo, K.; Aoyama, Y. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 907−916.

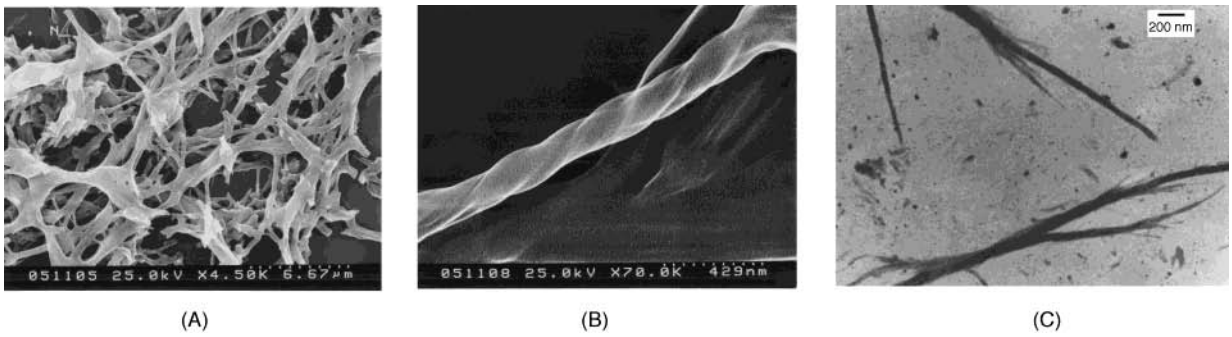


Figure 2. (A) (B) SEM pictures of the xerogel prepared from [**1**] = 3.0 wt %, 1:2 (v/v) DMF/BzlOH gel. To remove involatile solvent the gel was washed with a small amount of benzene and dried under reduced pressure. (C) TEM picture of the same xerogel (stained with 2.0 wt % phosphomolybdic acid).

designed toward construction of one-dimensional architectures, acts as an excellent gelator for very specific solvent mixtures. Although one-dimensional alignment of porphyrins has been attained in liquid crystal systems[1] and crystal systems,[2,16] no such precedent exists in an organogel system. The organogel system, being different from the liquid crystal and crystal systems, can feature both thermotropic and lyotropic characters, which are conveniently used to append the switch function and the self-assembling function to the one-dimensional porphyrin stack. In addition, the helical pitch will be finely tuned by combinatorial displacement of saccharide groups available from a natural library of carbohydrate molecules. We thus believe that these structural variations possible in the organogel phase are useful to control the catalytic and photochemical functions of porphyrins existing as a core of the one-dimensional array.

OL0165544