A photo-responsive hydrogelator having gluconamides at its peripheral branches†

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A newly designed anthracene derivative having gluconamides at its peripheral branches formed a photo-responsive hydrogel. SEM observation of the xerogel showed a network structure consisting of fibrils. Upon photoirradiation ($\lambda > 300$ nm) of the hydrogel, regioselective photodimerization of the anthracene moiety occurred to give head-to-tail photodimers and the physical state changed from the gel to the sol.

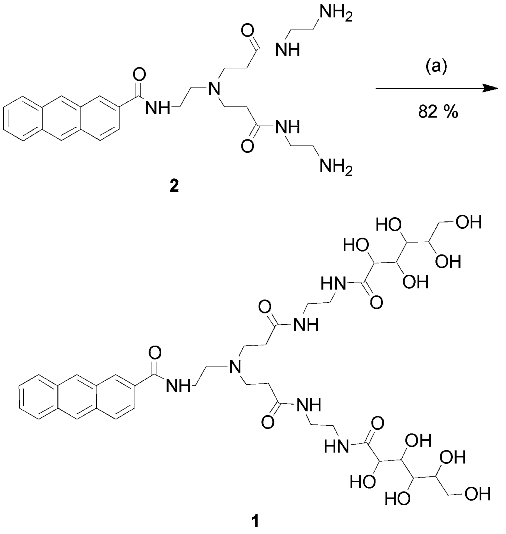
Introduction

Photo-responsive hydrogels are regarded as some of the most intriguing biomaterials applicable to the biological and medical fields. This is because light is an ideal stimulus for fabricating and manipulating the various properties of semi-wet materials due to its clean, fast, and spatio- and temporally-controllable nature.[1] It is now crucial to explore the capability and limitations of photo-responsive hydrogels as potential biomaterials.[2] On the other hand, dendritic gelators, whose structures are between low molecular weight gelators and polymer gelators, have received particular attention because dendritic molecules possess some of the advantages of both low molecular weight and polymeric gelators.[3] However, a photo-responsive dendritic gelator has never been reported. Meanwhile, we have described syntheses of several anthryl dendrons that formed self-organized liquid crystals, whose molecular arrangements were reflected in the regioselectivity of the photodimerization reaction of the anthracene moiety.[4] For example, an anthracene derivative having a poly(amidoamine) dendritic substituent at the 9-position self-assembled to form a smectic E phase, in which the alternative orientation of the dendron molecules caused a regioselective and quantitative photoreaction affording only the *anti*-photodimer. In this context, we expected that anthryl dendrons could be candidate material for a new class of photo-responsive hydrogelator. During our studies on the synthesis and photoreactivity of anthryl dendrons, we have found that a tiny anthryl dendron having only one branching unit forms a photo-responsive hydrogel. This paper describes the synthesis, characterization, and photoreactivity of this anthryl dendron having gluconamides at its peripheral branches, along with its hydrogel properties. To our knowledge, this is the first example of a photo-responsive hydrogelator having an anthracene moiety acting as the photo-responsive switch.

Results and discussion

Synthesis and gel formation of dendritic hydrogelator 1

The dendritic hydrogelator **1** having gluconamides at its peripheral branches was prepared from a first-generation poly(amidoamine) dendron **2**[5] as shown in Scheme 1. The gluconamide arms were introduced by the aminolysis in methanol of D-glucono-1,5-lactone with the NH_2 groups of dendron **2**. The structure of hydrogelator **1** was confirmed by ^1H and ^{13}C NMR spectroscopy, FT-IR, and MALDI-TOF mass spectroscopic analysis. The MALDI-TOF mass spectrum of hydrogelator **1** clearly showed the parent peak at *m*/*z* 849.545 (see ESI†), which is consistent with the molecular weight of **1** ([MH$^+$], calcd 849.388).



Scheme 1 Synthesis of hydrogelator **1**. *Reagents and conditions*: (a) D-glucono-1,5-lactone, MeOH, 50 °C, 3 h.

Dendritic hydrogelator **1** was studied with regard to its gelation behavior in water. A hydrogel was formed by heating **1** at 60 °C in water and cooling to room temperature. The critical gelation concentration, the minimum concentration at which gelation is

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† Electronic supplementary information (ESI) available: ^1H and ^{13}C NMR spectra, and MALDI-TOF MS, of hydrogelator **1** before and after irradiation. See DOI: 10.1039/b810900a

induced, was 3.5×10^{-2} mol dm^{-3}. The gel-to-sol phase transition temperature,[6] denoted as T_{gel}, for the hydrogel of **1** (3.5×10^{-2} mol dm^{-3}) was 46 °C.

SEM observation

To obtain visual images of the conformation in the hydrogel, we took pictures of the xerogel with a scanning electron microscope (SEM). The SEM picture obtained from the hydrogel of **1** shows a network structure consisting of fibres (Fig. 1(a)). The diameter of the bundled fibres was evaluated to be approximately 100–500 nm. Of further interest is the fact that each fibre consists of a bundle of much thinner fibrils with a diameter of approximately 50 nm (Fig. 1(b)).

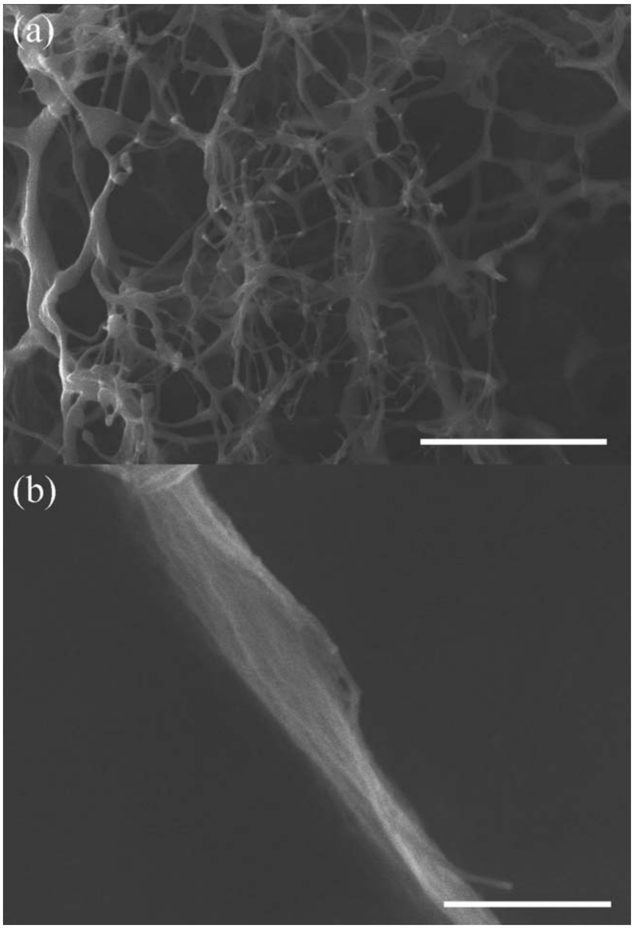


Fig. 1 SEM images of the xerogel of **1** [(a) scale bar is 5 μm, (b) scale bar is 1 μm].

Photo-responsive functions

The hydrogel containing **1** (3.5×10^{-2} mol dm^{-3}) was subjected to photoirradiation with a high-pressure Hg lamp at less than 15 °C. Interestingly, the photodimerization of the anthracene moiety of gelator **1** proceeded quite smoothly to give the corresponding photodimer in quantitative yield (>99% conversion), which was confirmed by UV–vis spectroscopy, fluorescence spectroscopy, and ^{1}H NMR spectrometry. The UV–vis absorption bands characteristic of the anthracene moiety disappeared with photoirradiation time (Fig. 2) and the physical state changed from the gel to the sol (Fig. 3). As the gel-to-sol phase transition temperature for the hydrogel of **1** (3.5×10^{-2} mol dm^{-3}) was 46 °C, the phase transition induced below 15 °C is ascribed to a photo-induced structural change (photodimerization) in the anthracene moiety. The fluorescence characteristics of the anthracene moiety also disappeared with photoirradiation time (Fig. 4). Furthermore, the anthracene proton signals [δ 7.53–7.59 (m, 2H), 7.91–7.93 (m, 3H), 8.11–8.17 (m, 3H), 8.71 (s, 1H)] of **1**, which were observed in the ^{1}H NMR spectrum in DMSO-d_6, disappeared and new peaks appeared at 6.78–7.50 ppm (Fig. 5). The methyne proton signals

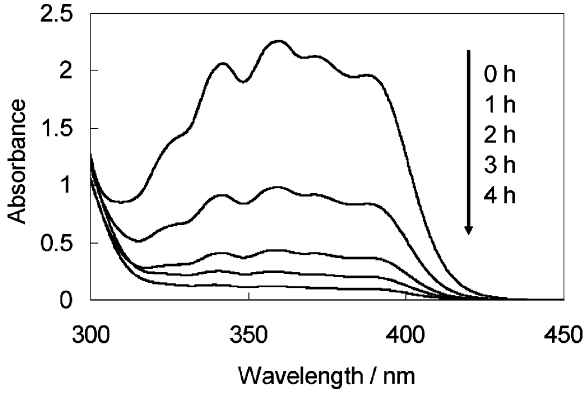


Fig. 2 Absorption spectra of **1** after photoirradiation (>300 nm) for different periods. The concentration for the photoirradiation experiments was 3.5×10^{-2} mol dm^{-3} in water, whereas for the absorption spectral measurements the solution was diluted to 7×10^{-4} M in water.

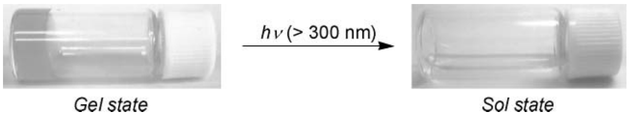


Fig. 3 Photograph of the hydrogel of **1** before and after photoirradiation.

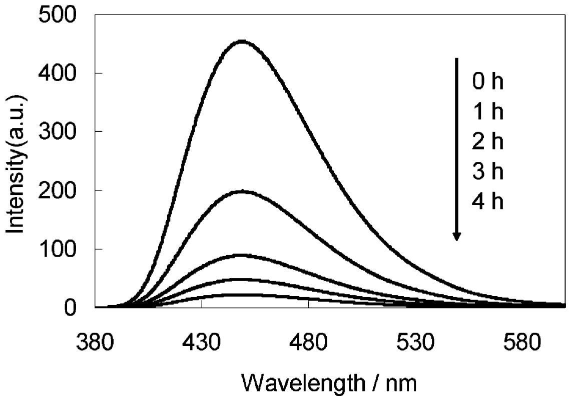


Fig. 4 Fluorescence spectra of **1** after photoirradiation (>300 nm) for different periods. The concentration for the photoirradiation experiments was 3.5×10^{-2} mol dm^{-3} in water, whereas for the absorption spectral measurements the solution was diluted to 7×10^{-4} M in water.

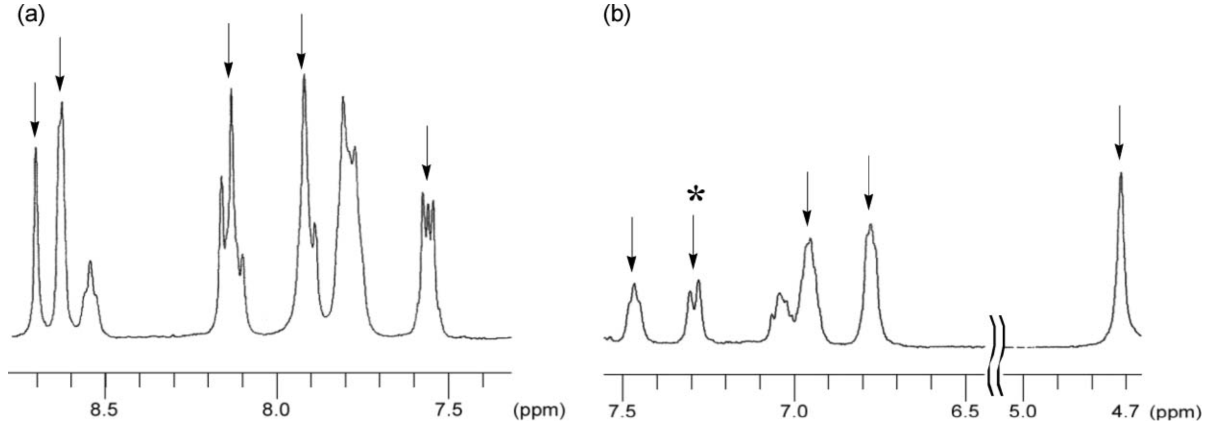


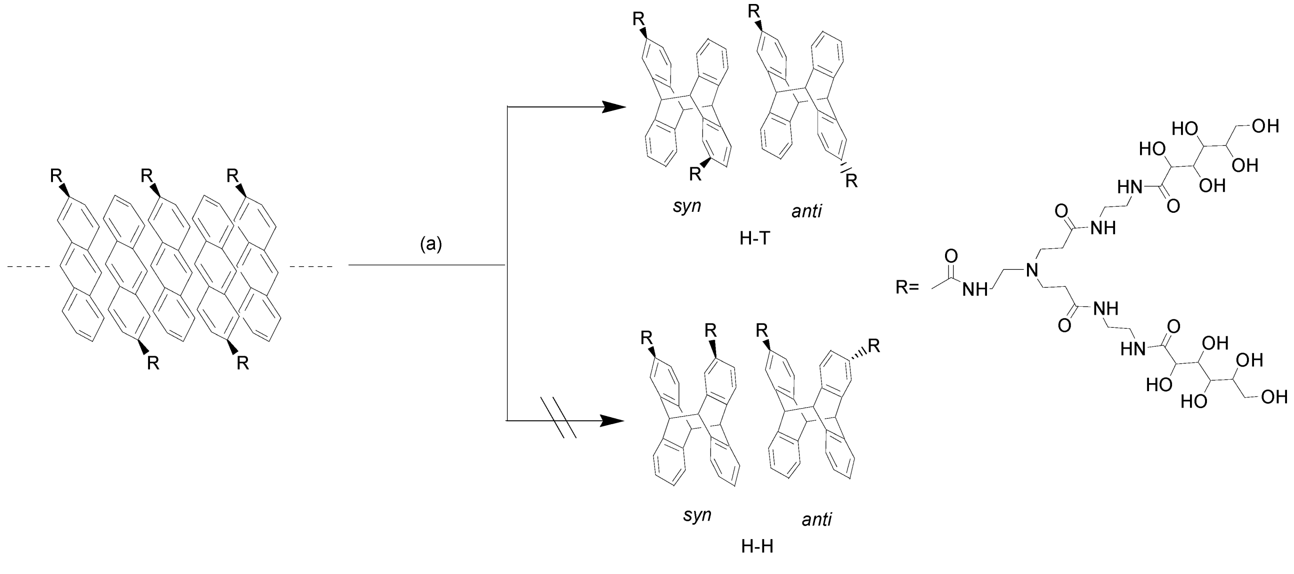
Fig. 5 Partial ^{1}H NMR spectra of **1** (a) before irradiation (arrows: anthracene moiety), (b) after irradiation (arrows: photodimer of anthracene moiety, *: characteristic signal of H–T regioisomer).

[δ 8.63 (s, 1H), 8.65 (s, 1H)] of the 9- and 10-positions of the anthracene moiety in **1** disappeared and a new peak appeared at δ 4.73. This result is consistent with dimer formation.

The structures of the photodimer were confirmed by ^{1}H and ^{13}C NMR spectroscopy. The photodimerization of 2-substituted anthracene gives four regioisomers [*anti* or *syn* head-to-tail (H–T), *anti* or *syn* head-to-head (H–H)] as shown in Scheme 2. Especially in viscous media, the pairs have insufficient time to reorient themselves during the singlet state of the anthryl groups, from which the photodimerization reaction emanates.[7,8] Therefore, the ratio of H–H : H–T should reflect, at least indirectly, the ground state distribution of parallel and anti-parallel pairs of 2-substituted anthracene derivatives.[8] According to the previous report,[4f,8] the ratios of H–H : H–T were estimated by ^{1}H NMR. The diagnostic signal of the photodimer due to anthracene's 3-position appeared as only one doublet at 7.30 ppm, which is characteristic of the H–T photodimer, although the H–H photodimer shows partially overlapped double doublets in the same region. This result indicated that the neighbouring anthracene moieties are aligned in an *anti*-parallel orientation in the gel phase. The photoinduced gel-to-sol phase transition might arise from collapse of the network constructed with the anthryl dendrons *via* π–π interactions, due to the structural change in the anthracene moiety upon photoirradiation.

Conclusion

In this paper we have presented the first example of a photo-responsive hydrogelator having an anthracene moiety as the photo-responsive switch. Although the anthryl dendron described has only one branching unit, it is the progenitor of photo-responsive dendritic hydrogelators. Absorption, fluorescence, and NMR spectra showed that the gel-to-sol transition of the hydrogel was caused by the regioselective photodimerization of the anthracene moiety of dendron **1**. Since only the H–T photodimer was



Scheme 2 Regioselective dimerization of dendron **1** upon photoirradiation of its hydrogel. *Conditions*: (a) photoirradiation (>300 nm), below 15 °C, 4 h.

observed after the photodimerization reaction, anthryl dendrons might be arranged in an anti-parallel orientation to form a network structure consisting of fibres. We are currently exploring the applications of these photo-responsive dendritic hydrogelators, such as biomedical materials.

Experimental

General

NMR spectra were measured using a JEOL AL-300 spectrometer and a Bruker AVANCE400 spectrometer. Matrix-assisted laser desorption ionization time-of-flight mass spectroscopy (MALDI-TOF mass spectroscopy) was performed using a Bruker autoflex mass spectrometer using dithranol (1,8-dihydroxy-9[10*H*]-anthracenone) as the matrix. Photoirradiation was carried out in a Pyrex reactor. A 500 W high-pressure mercury lamp was used as the light source. Absorption spectra were measured using a Shimadzu UV-3150 spectrophotometer. Fluorescence measurements were carried out with a JASCO FP-6600 spectrofluorometer. SEM pictures were taken using a HITACHI S-3500N scanning electron microscope.

The reagents were obtained from Wako Pure Chemical Industries Ltd., Tokyo Kasei Co. Ltd., Kanto Kagaku Co., Ltd., or Aldrich Chemical Co. The methanol and D-glucono-1,5-lactone used in reactions were further purified by general methods. Other solvents and reagents were used as received without further purification. The first-generation poly(amidoamine) dendron **2** was synthesized according to the previously reported method.[5]

Synthesis of hydrogelator 1

A solution of **2** (0.226 g, 0.459 mmol) in dry methanol (4 mL) was slowly added to a solution of D-glucono-1,5-lactone (0.818 g, 4.59 mmol) in dry methanol (46 mL) at 50 °C, and the solution was stirred for 3 h under a nitrogen atmosphere. The solution was left overnight at 4 °C then the precipitate was filtered, washed with methanol and acetone, and dried to afford hydrogelator **1** (0.320 g, 0.376 mmol) in 82% yield, mp 168–171 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.27 (t, 4H, $J = 6.8$ Hz), 2.65 (t, 2H, $J = 6.8$ Hz), 2.76 (t, 4H, $J = 6.8$ Hz), 3.15–3.19 (m, 8H), 3.39–3.45 (m, 4H), 3.50 (brs, 4H), 3.58–3.61 (m, 2H), 3.94 (brs, 2H), 3.99–4.02 (m, 2H), 4.40–4.55 (m, 8H), 5.37 (d, 2H, $J = 4.4$ Hz), 7.53–7.59 (m, 2H), 7.77–7.81 (m, 2H), 7.91–7.93 (m, 3H), 8.11–8.17 (m, 3H), 8.54 (t, 1H, $J = 5.2$ Hz), 8.63 (s, 1H), 8.65 (s, 1H), 8.71 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 33.2, 38.2, 38.3, 39.1, 49.4, 58.5, 63.3, 70.11, 70.13, 71.5, 72.2, 73.4, 73.5, 123.5, 125.88, 125.94, 126.3, 127.7, 127.98, 128.04, 128.17, 128.23, 130.1, 131.3, 131.5, 131.6, 132.1, 166.1, 171.7, 172.8; MALDI-TOF mass for $C_{39}H_{57}N_6O_{15}$: *m/z* calcd, 849.388 [MH$^+$]; found, 849.545; IR (ATR, cm^{-1}): ν 3302, 2945, 1642, 1540.

Gel formation and determination of T_{gel}

In a typical gelation experiment, a weighed amount of **1** and 5.0 mL of the water were placed in a test tube, which was sealed and then heated at 60 °C until the compound dissolved. The solution was then cooled to room temperature. The sol-to-gel temperature was determined according to a method described in the literature.[6] A glass ball was placed on top of the gel and the test tube was subsequently placed in a thermostated waterbath and heated at 1 °C min^{-1}. The temperature at which the ball started to fall through the gel was denoted as T_{gel}.

Photoirradiation

The hydrogel (3.5×10^{-2} mol dm^{-3}) was irradiated with a high-pressure mercury lamp through a Pyrex filter for 4 h at less than 15 °C. After removal of the solvent under vacuum, the residue was characterized by ^{1}H and ^{13}C NMR spectroscopy in DMSO-d_6 and MALDI-TOF mass spectroscopic analysis.

Photodimer; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.10 (t, 8H, $J =$ 6.4 Hz), 2.50–2.53 (m, 4H), 2.70 (t, 8H, $J = 5.6$ Hz), 3.13–3.26 (m, 16H), 3.27 (brs, 4H), 3.38–3.41 (m, 8H), 3.50 (brs, 8H), 3.58–3.60 (m, 4H), 3.93 (brs, 4H), 4.01 (m, 4H), 4.34 (brs, 4H), 4.40–4.55 (m, 12H), 4.73 (brs, 4H), 5.37 (d, 4H, $J = 3.2$ Hz), 6.78–6.80 (m, 4H), 6.95–7.00 (m, 4H), 7.03–7.08 (m, 2H), 7.30–7.32 (m, 2H), 7.47–7.50 (m, 2H), 7.75–7.81 (brs, 6H), 7.86–7.90 (m, 4H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 33.3, 37.5, 38.8, 49.8, 52.6, 52.8, 63.7, 70.7, 71.0, 71.9, 72.7, 72.9, 74.0, 126.09, 126.13, 126.2, 127.4, 127.5, 131.4, 143.3, 143.4, 144.40, 144.43, 147.8, 147.9, 167.0, 172.9, 173.8; MALDI-TOF mass for $C_{78}H_{113}N_{12}O_{30}$: *m/z* calcd, 1697.769 [MH$^+$]; found, 1697.879.

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