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Water-soluble azobenzene dendrimers ☆

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Abstract—Water-soluble azobenzene-cored dendrimers **4**–**6** were synthesized as potential photoresponsive micelles to which the aggregation is triggered by photoirradiation. In the absorption spectra, the π–π* absorption band of the dendrimers largely blue-shifted with increasing the generation due to the shielding effect of surrounding dendron on the interaction between the core azobenzene and solvent water. Not only the surrounding dendron groups suppressed the *E*-to-*Z* photoisomerization, but also the rate of thermal *Z*-to-*E* isomerization depended on the generation of the dendrimer. Furthermore, we have observed a novel temperature dependence of the rate constant of the thermal isomerization.

The azobenzene has been widely used as a photoresponsive chromophore to regulate the molecular structure by *E*–*Z* isomerization with light and heat.[1–3] As a basic approach of the photochemical and thermal isomerization of azobenzene we have prepared some azobenzene dendrimers soluble in organic solvents to determine the relative efficiencies and the activation parameters such as activation energy and frequency factors in the ground state depending on the molecular size of the dendrimers.[4] The dendron groups as large and congested substituents decreased the photochemical *E*-to-*Z* isomerization efficiencies and the activation entropy of the thermal *Z*-to-*E* isomerization. Thus, the surrounding dendron groups in the azobenzene dendrimers may affect the isomerization behavior of the core azobenzene.

In order to improve the effect of dendron groups on the dynamic behaviors of the isomerizable azobenzene core, we now come to explore the photochemical and thermal behavior of water-soluble azobenzene dendrimers. In this respect we have synthesized azobenzene dendrimers bearing water-soluble dendron groups at the *ortho* position of the azobenzene core. Our aims of this study are twofold: First, water-soluble azobenzene dendrimers may exhibit unique photochemical as well as thermal isomerization properties. In the course of our study, the explore of dendrimer effects on the isomerization behaviors of azobenzene are of interest. Second, development of photoresponsive micelles. As shown in Figure 1, *trans*-isomer of azobenzene dendrimer with

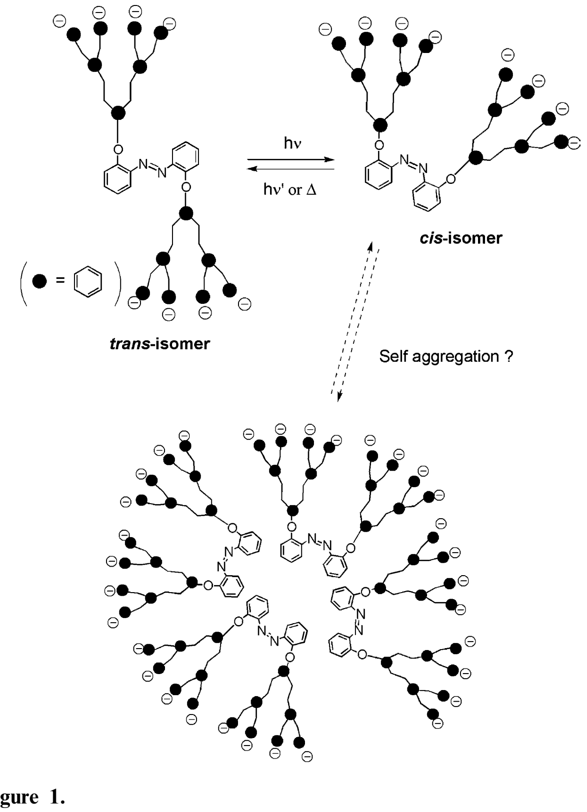

Figure 1.

Keywords: Dendrimers; Azobenzenes; Photoisomerization; Thermal-isomerization.

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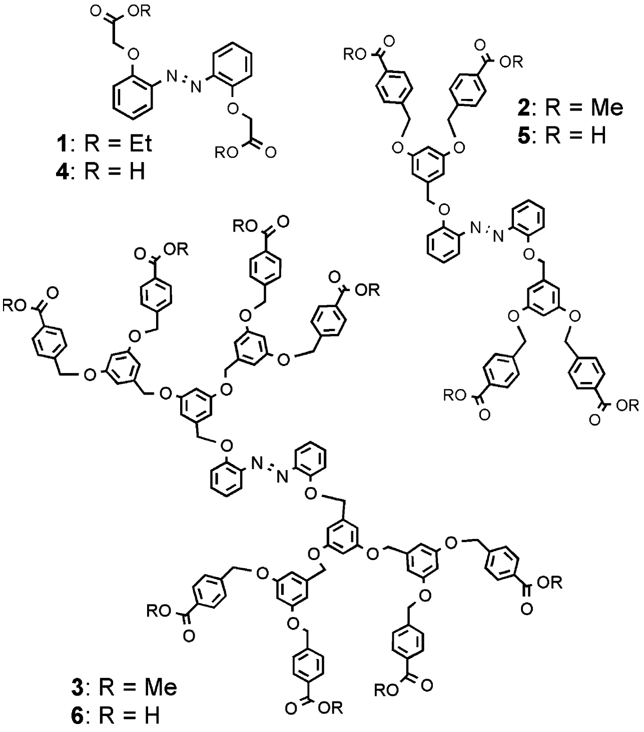

Figure 2. Structures of water-soluble azobenzene dendrimers.

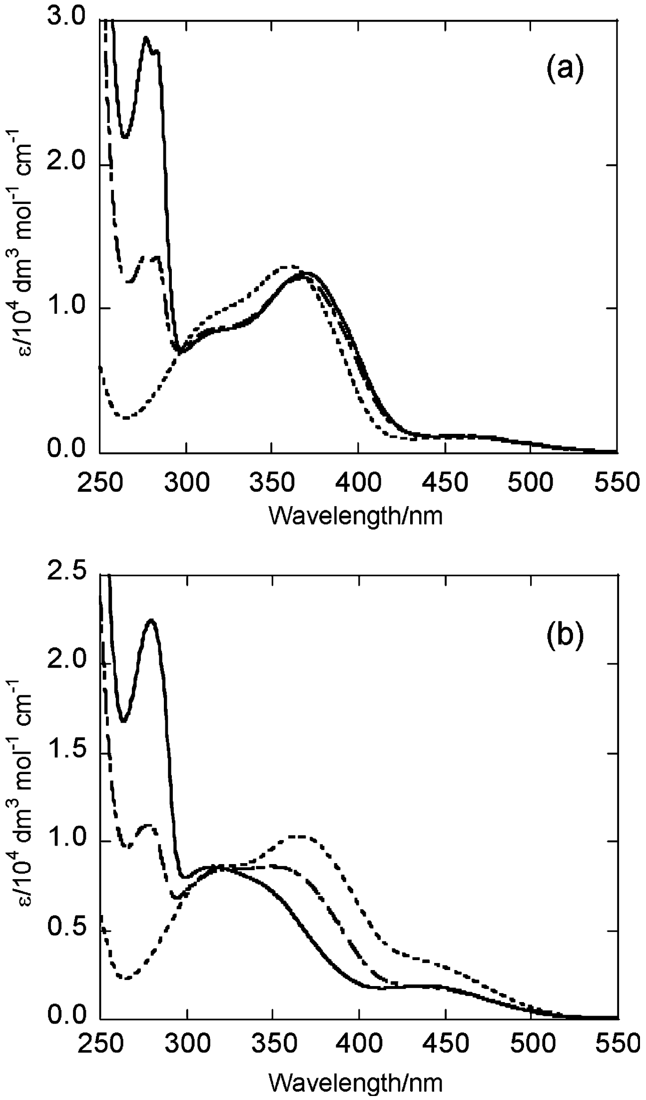

Figure 3. UV absorption spectra of **1** (...), **2** (—.—), and **3** (—) in $CHCl_3$ (a) and **4** (...), **5** (—.—), and **6** (—) in 1.0 mM KOH aqueous solution (b).

water-soluble dendrons probably exist as a monomer. On irradiation, the *trans*-isomer isomerize to the *cis*-form, which may aggregate to give the association form due to hydrophobic interaction. Therefore, water-soluble azobenzene dendrimers, which have hydrophobic interior in the higher generations, may have a character of drug delivery material regulated by light. We wish to report here the first synthesis and some photochemical and thermal properties of water-soluble azobenzene-centered dendrimers.

Zeros, second, and third generation dendrimers **1**, **2**, and **3** were prepared by coupling reaction of 2,2′-dihydroxy azobenzene with ethylbromoacetate for **1**, and corresponding dendritic bromide[5,6] for **2** and **3**, respectively, in the presence of K_2CO_3 and 18-crown-6 ether in refluxing acetone. Following hydrolysis with KOH in ethanol gave water-soluble azobenzene dendrimers **4**–**6** as *E*-isomers (Fig. 2). Dendrimers **4**–**6** were characterized by ^{1}H NMR, elemental analysis, UV absorption spectra, and ESI-TOF MS for **4** and MALDI-TOF MS for **5** and **6**, respectively.[†]

Figure 3a shows the absorption spectra for **1**–**3** in $CHCl_3$. The peaks at 280 nm in **2** and **3** are due to the dendron groups. The π–π* and n–π* absorption band of azobenzene moiety appeared in almost the same region among **1**–**3**. On the other hand, the absorption bands of **4**–**6** in the range of 300–500 nm, attributed to azobenzene moiety, largely blue-shifted in higher generation dendrimers in 1.0 mM KOH aqueous solution, as shown in Figure 3b. This spectral differences of azobenzene moiety in **4**–**6** in KOH aqueous solution may be explained by two different functions of dendrons: (1) Shield effect: It is clear effect of the surrounding dendrons on shielding the core azobenzene from the solvent water. In general, π–π* absorption band of aromatic compounds red shifts in polar solvents. The π–π* absorption band appeared at 350–430 nm in **4** in water actually red-shifted compared to that in **1** in $CHCl_3$, and is the typical example of the stabilized π–π* excited state by polar solvent. In G3 dendrimer **6**, however, π–π* absorption band largely blue-shifted from that of **3** in $CHCl_3$, which is appeared almost the same region as in azobenzene in organic solvents.[6] In addition, the π–π* absorption band in **5** appeared in the region between **4** and **6**. The result indicates that the core azobenzene in **5** is partially isolated from water and the core in **6** is in hydrophobic environment in the dendrimer molecule. (2) Hydrophobic interaction: the azobenzene moiety in **5** and **6** is possibly wrenched, or in the difficult conditions

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[†] Electronic supplementary information (ESI) available: experimental data for **1**–**6**.

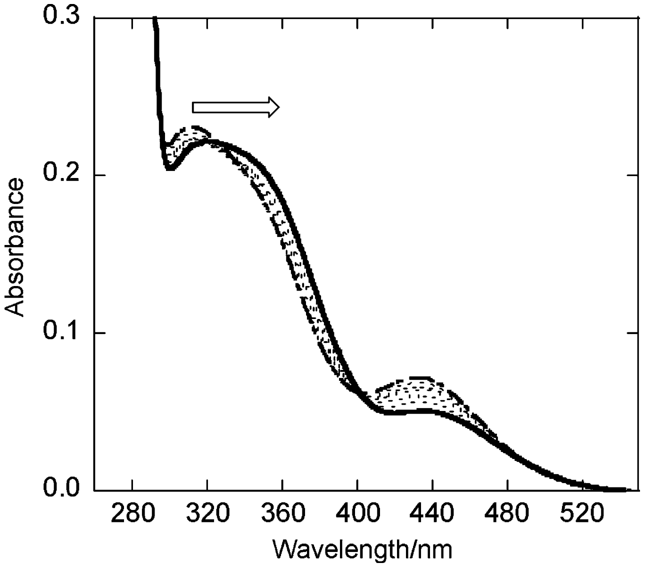

Figure 4. Change of the absorption spectra of **6** with increasing temperature in 1.0 mM KOH aqueous solution: at 15 °C (—.—) and at 75 °C (—).

to keep the planar conformation, probably due to the shrinkage of the dendron groups by hydrophilic interaction of the branching units. Figure 4 shows the change in the absorption spectra of **6** upon increasing the temperature. The π–π* absorption band of azobenzene moiety in **6** red-shifted with increasing temperature, indicates that the interaction of azobenzene core with solvent water increased at higher temperature, or the wrenched azobenzene core in **6** can take more planar conformation at higher temperature.

Since the environment of core azobenzene among **4**–**6** is different depending on the generation due to the remarkable effect of dendron groups, the dendron effect on photochemical and thermal isomerization of azobenzene core is of interest. All the azobenzene dendrimers underwent photochemical *E*–*Z* isomerization in $CHCl_3$ for **1**–**3** and in 1.0 mM KOH aqueous solution for **4**–**6**, respectively. The change of the absorption spectra of **6** on irradiation with 350 nm light was shown in Figure 5 as a typical example. The photostationary state isomer composition $([E]/[Z])_{pss}$ was determined by ^{1}H NMR to be 28/72, 46/54, and 56/44, respectively, for **4**, **5**, and **6**. The relative rate of photoisomerization was compared among **4**–**6** (Inset in Fig. 5); the initial rate of decrease of the *E*-azobenzene absorbance at 350 nm is smaller for higher generation than lower generation. These results indicate that the dendron group may suppress the photochemical *E*-to-*Z* isomerization of the azobenzene chromophore in **5** and **6**.

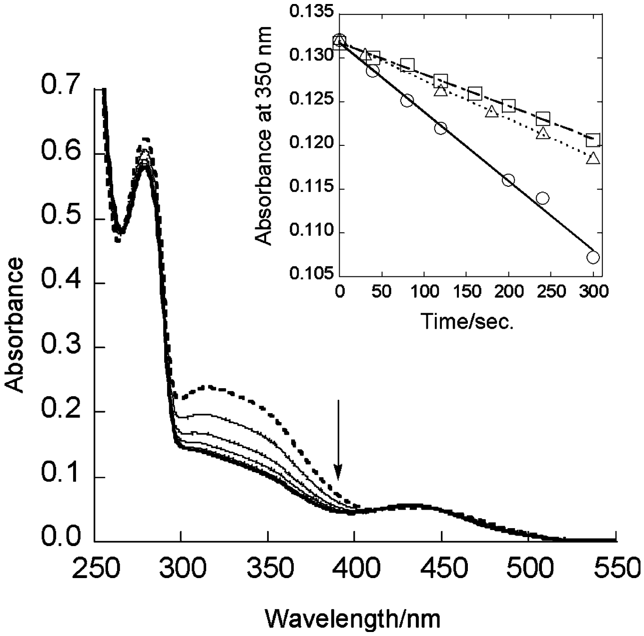

Figure 5. Change of the absorption spectra of **6** in 1.0 mM KOH aqueous solution upon the irradiation at 350 nm light. Inset shows the initial absorbance change of **4** (○), **5** (△), and **6** (□) upon 350 nm light irradiation. The concentrations of **4**–**6** were normalized at 350 nm.

In the dark, thermal *Z*-to-*E* isomerization for all dendrimers in $CHCl_3$ for **1**–**3** and in 1.0 mM KOH aqueous solution for **4**–**6**, respectively, took place. Very interestingly, the rate of thermal *Z*-to-*E* isomerization depended on the generation of the dendrimer among water-soluble dendrimers **4**–**6**.

Furthermore, we have observed a novel temperature dependence of the *Z*-to-*E* isomerization and the rate constant of the thermal isomerization were shown in Table 1. The Arrhenius plot exhibited straight line for all the azobenzene dendrimers. While the activation parameters are very similar among **1**–**3**, those of **6** are considerably different from those of **4** and **5**. Thus the activation energy and frequency factor for *Z*-to-*E* thermal isomerization were estimated to be 23.0 kcal mol^{-1} and 2.1×10^{13} s^{-1}, respectively, for **4**, and 23.3 kcal mol^{-1} and 0.96×10^{13} s^{-1}, respectively, for **5**, and 29.7 kcal mol^{-1} and 8.61×10^{16} s^{-1}, respectively, for **6** (Table 1). Both the frequency factor and activation energy for **4** and **5** are almost the same with those for

Table 1. The rate constants, activation energy, frequency factor, activation enthalpy, and activation entropy of thermal *Z*-to-*E* isomerization of **1**–**6**

Entry	k (75 °C)/s^{-1}	k (65 °C)/s^{-1}	k (60 °C)/s^{-1}	k (50 °C)/s^{-1}	k (40 °C)/s^{-1}	E_a/kcal mol^{-1}	$A/10^{12}$ s^{-1}	$\Delta H^{\neq}$/ kcal mol^{-1}	$\Delta S^{\neq}$/ cal mol^{-1} K^{-1}
1			4.88×10^{-3}	1.74×10^{-3}	5.78×10^{-4}	22.1	1.54	21.4	−12.1
2			6.97×10^{-3}	2.32×10^{-3}	8.07×10^{-4}	22.3	3.03	21.7	−10.7
3			6.24×10^{-3}	2.28×10^{-3}	7.64×10^{-4}	21.8	1.18	21.1	−12.6
4	7.90×10^{-2}	2.81×10^{-2}		5.67×10^{-3}		23.0	20.7	22.3	−7.0
5	2.15×10^{-2}	8.45×10^{-3}		1.77×10^{-3}		23.3	9.64	22.6	−8.5
6	1.91×10^{-2}	5.25×10^{-3}		7.19×10^{-4}		29.7	86,000	29.0	9.6

azobenzene dendrimers without carboxylate group at the surrounding dendron groups in organic solvent.[4] These results indicate a different molecular environment of **6** in water compared to that of **4** and **5**. We could propose the formation of the molecular aggregates by irradiation of photon to form *Z*-isomers. Thus, the molecular structure of **6** favors to form aggregates of several molecules to form some kind of micellar structure, which has rather rigid structure to reduce the conformational change of the *Z*-isomer to *E*-isomer by thermal process. At higher temperature, the rate constant of the formation and the dissociation of molecular aggregates may be faster and the thermal isomerization may take place by two steps; dissociation to the molecule and the thermal *Z*-to-*E* isomerization. Otherwise, the *Z*-to-*E* thermal isomerization in the aggregates may take place by a quite different mechanism from that taking place as a monomer. The isomerization in the aggregates need large structural change of the aggregates and may take place by the mechanism with higher activation energy and frequency factor.

The activation enthalpies ($\Delta H^{\neq}$) and activation entropies ($\Delta S^{\neq}$) for the *Z*-to-*E* isomerization of **1**–**6** were obtained from Eyring plots. In order to explore the reaction mechanism of the thermal *Z*-to-*E* isomerization, a liner relationship between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ has been used for various azobenzene and its derivatives.[4,7–11] When we combined our data with those of others, the points for **1**–**6** all fell on the line for the inversion mechanism. Thus, the inversion mechanism might be operative in the *Z*-to-*E* thermal isomerization processes for **1**–**3** in $CHCl_3$ and **4**–**6** in water.

In summary, we have prepared water-soluble azobenzene dendrimers **4**–**6** and studied their photochemical and thermal isomerization. In absorption spectra, the π–π^* absorption band largely blue-shifted with increasing the generation, indicating the clear effect of dendron to give the different environment for the azobenzene core depended on the generations. In the photochemical reaction, the surrounding dendron groups suppress the *E*-to-*Z* photoisomerization. Interestingly, the rate of thermal *Z*-to-*E* isomerization depended on the generation of the dendrimer. Furthermore, we have observed a novel temperature dependance of the *Z*-to-*E* isomerization and the rate constant of the thermal isomerization. To the best of our knowledge, this is the first clear report of the synthesis of water-soluble azobenzene dendrimers with the considerably large change of the absorption spectra depending on the generation. Further study on the aggregation of the water-soluble azobenzene dendrimers, controlling by light and heat, is on going.

Acknowledgements

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