

Bis(PheOH) Maleic Acid Amide–Fumaric Acid Amide Photoisomerization Induces Microsphere-to-Gel Fiber Morphological Transition: The Photoinduced Gelation System

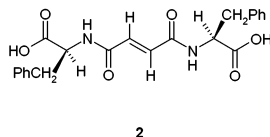
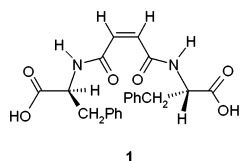
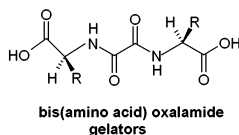
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In recent years, a wide variety of low-molecular weight organic compounds have been found to form gels with organic liquids or, in some more rare cases, also with water.¹ To understand gelation induced by small organic molecules, it is of the utmost importance to reveal the relationship between the gelator structure, gelled solvent properties, and the organization in fibrous supramolecular aggregates constituting the three-dimensional gel network.² Precise knowledge of this relationship would allow a reliable design of a specific gelator for a liquid with selected properties as well as preparation of gels suitable for various applications.³ Even more challenging, it would be possible to design controlled gelation systems based on configurational or conformational changes of a gelator molecule induced by external stimuli.⁴ Such “smart” gels might find further application as sensors or controlled-release systems for biomedical purposes.

Here, we report on the preparation⁵ of bis(phenylalanine) maleic acid (1) and fumaric acid (2) amides and show that in water they constitute an irreversible photoinduced gelation system that works on photochemical isomerization of nongelling maleic acid amide (1) to gelling fumaric acid amide (2). This represents the first example of gelation induced by configurational isomerization and one of the very few examples of gelation systems controlled by external stimuli.⁶ In addition, we present the evidence that the photoisomerization at the molecular level induces a morphological transition at the supramolecular level comprising transformation of the microspheres formed by 1⁷ into fibrous gel network of 2 and that the gel is formed under supramolecular kinetic control.



Gelation of water by 2 can be predicted on the basis of its structural and conformational similarity to the previously studied bis(amino acid) oxalamide gelators.⁸ That type of gelator molecules were found to readily self-assemble into gel fibers in water, primarily by intermolecular lipophilic (van der Waals, aromatic π - π stacking and edge-to-face) interactions followed by cooperative

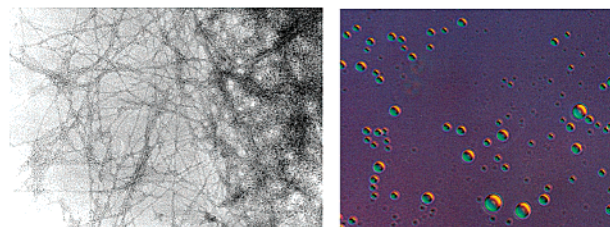


Figure 1. TEM of 2-hydrogel (left, fiber diameters in the 10–20 nm range) and the light microscope image of the microspheres (right, diameters in the 2–10 μm range) formed by 1.

hydrogen bonding between self-complementary oxalamide groups.⁸ In contrast, the maleinamide unit with *cis*-configuration is nonself-complementary so that intermolecular hydrogen bonding is prevented and lack of gelation can be predicted for 1. We considered the preparation of an irreversible photoinduced gelation system based on the photochemical maleic amide 1 to fumaric amide 2 isomerization in water, catalyzed by bromine radicals. It was found that 1 dissolves in water and that the solution, upon addition of trace amounts of bromine and irradiation with a 400-W high-pressure Hg lamp (UV; $\lambda > 330$ nm; glass filter), almost instantaneously (<30 s) turns to gel. To the best of our knowledge, this represents the first example of gel preparation by photochemical isomerization of a nongelling (soluble) compound. The TEM micrograph of the gel shows a typical picture of a gel network consisting of entangled fibers with diameters in the 10–20 nm range (Figure 1, left). We observed, however, that addition of bromine (added by spilling a small amount of bromine vapors onto the surface of the solution) to the fully transparent aqueous solution of 1 turns it into a turbid one and lowers the pH from 5 to 2–3 due to formation of HBr. Light microscopy of the sample (Figure 1, right) reveals the presence of tiny spheres with diameters in 2–10 μm range; lightening edges of the microspheres observed under crossed polarizers (Figure 1, Supporting Information) show the organization with optical anisotropy. Recently, Bergeron⁷ has reported that 1 also self-assembles into microcapsules upon citric acid acidification of the aqueous solution of 1-dilithium salt. We have repeated the latter procedure, and the light microscopic comparison of both samples shows formation of similar microspheres. However, in our case we were not able to observe formation of hollow spheres (capsules) by SEM (Figure 1, Supporting Information). The TEM micrograph of the gel formed by 1 to 2 photoisomerization shows only the presence of fibrous network and not the microspheres. This clearly shows that the morphological transition also took place. The ¹H NMR spectrum of the microsphere-containing system shows only the presence of the maleic amide 1 (D₂O; δ of *cis*-double bond H's 6.01 ppm;

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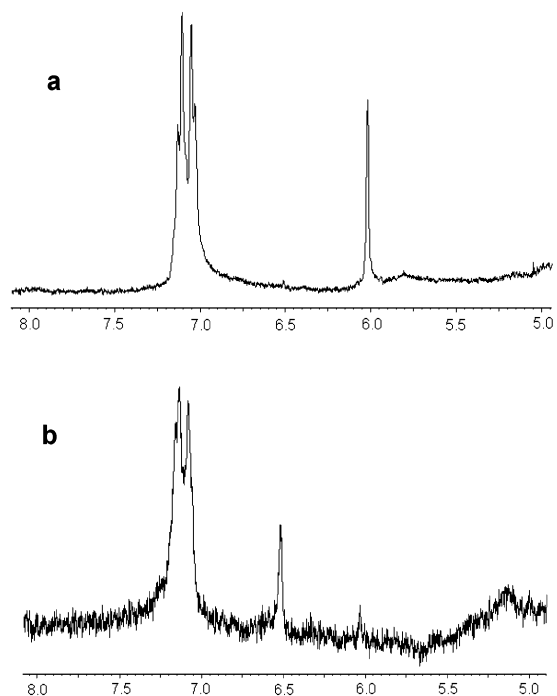


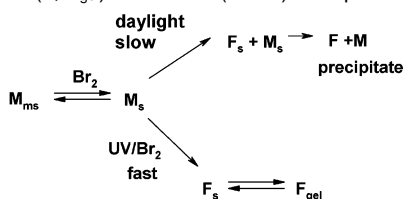
Figure 2. ^1H NMR spectra (δ 5–8 ppm region shown; D_2O ; $\mathbf{1}$, 7×10^{-3} mol dm^{-3} ; dioxane as the internal standard 0.1 mL) of (a) microsphere containing system of $\mathbf{1}$; (b) the solution at 80°C obtained by heating of the gel sample.

Figure 2a). In the ^1H NMR spectrum of the gel formed after UV irradiation (D_2O , 20°C), only two very broad signals of low intensity and the solvent signals could be observed (Figure 2, Supporting Information). The latter shows that most of the gelator molecules are organized in a rigid network and consequently their signals are broadened, close to the point of nonobservability, due to long correlation times.^{8,9} Heating of the same gel sample to 80°C results in the network dissolution, and the spectrum shows the presence of the fumaric amide derivative $\mathbf{2}$ (D_2O ; δ of *trans*-double bond H's 6.5 ppm; Figure 2b), and only a trace of $\mathbf{1}$.

If the microsphere-containing system of $\mathbf{1}$ is left to stand at room temperature for several hours, a precipitate is formed. The ^1H NMR spectrum of the precipitate collected by filtration and dissolved in $\text{DMSO}-d_6$ (Figure 3, Supporting Information) shows a 3:1 mixture of $\mathbf{2}$ and $\mathbf{1}$, respectively.

Both processes can be described as outlined in Scheme 1. Dissolved maleic amide $\mathbf{1}$ (M_s) self-assembles into microspheres (M_{ms}) after addition of bromine. UV irradiation of this system leads to a fast and irreversible isomerization of M_s to fumaramide $\mathbf{1}$ (F_s). This shifts the M_{ms}/M_s equilibrium toward M_s .

Scheme 1. Processes Describing Photoinduced Maleic Acid Amide $\mathbf{1}$ to Fumaric Acid Amide $\mathbf{2}$ Molecular Isomerization Induced by UV and Daylight Exposure and Conversion of Microspheres ($\mathbf{1}$; M_{ms}) to Gel ($\mathbf{2}$; F_{gel}) and Mixed (F + M) Precipitate



Since $\mathbf{1}$ is only slightly soluble in water and evolves in a fast process, the crystallization centers cannot be formed and the system stabilizes by fast aggregation into fibers, which entangle into a gel

network. In contrast, the slow partial photoisomerization of M_s into F_s in daylight provides sufficient time for the formation of crystallization centers; the optical micrograph taken soon after bromine addition to the solution of $\mathbf{1}$ revealed the simultaneous existence of the microspheres ($\mathbf{1}$) and microcrystals ($\mathbf{2}$) (Figure 4, Supporting Information). Once the microcrystals are present, the process is directed toward crystallization of less soluble $\mathbf{2}$ with partial inclusion of unreacted $\mathbf{1}$.

In summary, we have described the aqueous photoinduced gelation system based on the molecular maleic acid amide ($\mathbf{1}$) to fumaric acid amide ($\mathbf{2}$) photoisomerization and presented the evidence that the configurational isomerization induced the morphological transformation at the supramolecular level, exemplified by the conversion of microspheres to gel fibers. The microscopy and ^1H NMR monitoring of these processes sheds new light on the gelation phenomenon. It provides the clear-cut evidence that formation of the gel depends on the configurational properties of a molecule and that the gel forms in the conditions where the self-assembly into fibrous aggregates is a process faster than the concurrent process of crystallization.

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Supporting Information Available: Light microscope (crossed polarizers) and SEM micrographs of microspheres (Figure 1), ^1H NMR spectrum of $\mathbf{2}$ -gel (Figure 2), ^1H NMR spectrum of $\mathbf{1}$ and $\mathbf{2}$ coprecipitate (Figure 3), light microscopic image of microspheres and microcrystals and SEM of the $\mathbf{1}$ and $\mathbf{2}$ coprecipitate (Figure 4) (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (5) Fumaramide $\mathbf{2}$ (60% yield) was prepared by condensation of fumaroyl chloride with PheOH (biphasic $\text{CH}_2\text{Cl}_2/\text{aqueous NaOH}$ system); The maleinamide $\mathbf{1}$ was prepared according to ref. (7). The compounds have been characterized by FTIR, ^1H , and ^{13}C NMR spectra and elemental analysis.
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