

Oligoamide Duplexes as Organogelators

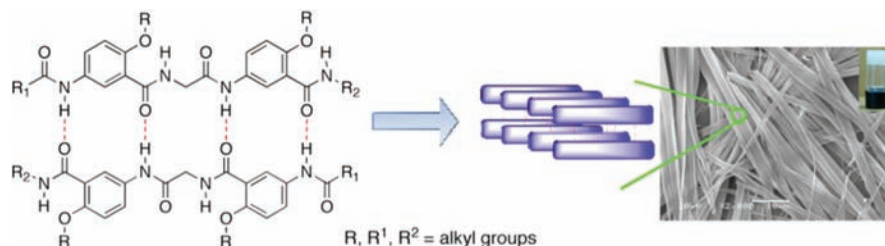
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ABSTRACT



Oligoamide duplexes carrying multiple alkyl side chains were found to serve as gelators for aromatic solvents. The double-stranded backbone was essential for the hierarchical self-assembly of the molecular duplex into fibers of high aspect ratios. The demonstrated gelating abilities may be extended to a large family of analogous H-bonded duplexes having different H-bonding sequences, leading to a unique platform for developing a diverse variety of potential gelators based on a supramolecular and/or a dynamic covalent approach.

Gelation, as a phenomenon frequently observed in nature, has attracted wide attention due to its fundamental significance and potential applications.^{1,2} Gelators associate into three-dimensional networks that immobilize the flow of liquid by trapping solvent molecules. Interest in organic gelators derives not only from the motivation of developing materials with applications in fields such as membrane and separation technology, catalysis, nanotechnology, light-harvesting materials, dye-sensitized solar cells, etc. but also from the desire to understand how noncovalent interactions function cooperatively to bring about such unique properties. Many

synthetic molecules that assemble into supramolecular networks via hydrogen bonding, π - π stacking, and solvo-

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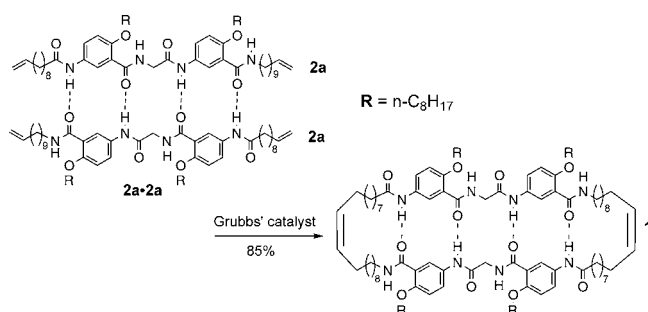
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phobic effects have been reported as gelators.³ Organic gelators are developed as “smart” or responsive gel systems that respond to stimuli such as photoirradiation, electrochemistry, solvent polarity and/or pH change. Nevertheless, the mechanism behind gelation remains elusive.^{1d} Molecules allowing ready structural modification could afford new gelators capable of interacting with different solvents. The availability of new gelators may also lead to valuable insights into the mechanism of gelation. Herein we report the gelation of several organic solvents by a series of double-stranded oligoamides. These duplexes not only offer convenient structural tunability, but more importantly, can be formed based on simple mixing of strands having complementary H-bonding sequences.

During our study on H-bond-mediated reactions, it was found that the metathesis of H-bonded duplex **2a** led to the efficient formation of **1** (Scheme 1). Compound **1** was

Scheme 1. Covalent Cross-Linking of Hydrogen-Bonded **2a**·**2a**



then observed to gelate benzene and toluene (Table 1). Unlike benzene and toluene, *o*-xylene formed a partial gel, i.e., a flowing, viscous but gel-like solution, with **1**.

Table 1. Gelation Properties and Values of CGCs^a

solvent	1	2a	2b	2c	2d	2e	2f
CH ₂ Cl ₂	I	S	S	S	G _{19.1, tr}	S	S
benzene	G _{6.1, o}	pG	P	pG	G _{8.1, o}	G _{11.1, tr}	G _{13.5, tr}
toluene	G _{5.4, o}	pG	pG	pG	G _{7.3, o}	G _{11.9, tr}	G _{16.5, tr}
<i>o</i> -xylene	pG	pG	I	pG	G _{7.4, o}	G _{17.8, tr}	G _{22.0, tr}
mesitylene	I	pG	I	pG	P	G _{12.5, o}	G _{12.6, o}
nitrobenzene	I	P	I	pG	P	pG	G _{16.7, o}
diphenyl ether	I	P	I	pG	P	G _{9.8, o}	G _{12.2, o}

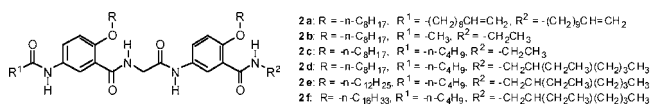
^a Critical gelation concentrations (CGCs) at room temperature (25 °C) are given in mM. Abbreviations: G = gel, pG = partial gel, I = insoluble, S = soluble, P = precipitation, tr = transparent, o = opaque.

Such an observation led to additional questions. For example, could **1** gelate other solvents? Could **2a** or its

H-bonded dimer (duplex) **2a**·**2a** serve as a gelator? Dimer **2a**·**2a** belongs to a family of duplexes consisting of complementary strands that associate sequence-specifically via interstrand H-bonds, which have been developed by us as reliable association units for directing intermolecular assembly.⁴

A H-bonded duplex like **2a**·**2a** offers three sets of sites that may allow the tuning of gelating property. For example, the four interstrand H-bonds ensure the sequence-specific pairing of two oligoamide strands into a duplex. Compared to individual strands, a H-bonded duplex is significantly rigidified, leading to a well-defined, largely flat surface that should promote further intermolecular association via π - π stacking interactions. In addition, adjusting the alkyl side chains and end groups attached to the oligoamide strands allows properties such as solubility, precipitation, crystallization, and packing of the corresponding molecules and supermolecules to be varied, which provides a platform for the systematic exploration of the influence of structures on gelating ability. It would thus be very attractive if **2a** could gelate solvents since such ability may also be shared by analogous oligoamides and their H-bonded duplexes, which may lead to many new gelators.

Simple screening indicated that **2a** was able to form partial gels with benzene, toluene, and *o*-xylene, the same solvents gelled or partially gelled by **1**. In mesitylene, in which **1** was insoluble, partial gelation was induced by **2a**. The modest gelating ability demonstrated by **2a** prompted us to design and prepare strands **2b**–**f** that share the same backbone with **2a** but differ in their side (R) chains and end (R¹ and R²) groups.



To probe the effects of end groups, the gelation of several aromatic solvents by **2b**, **2c**, and **2d** were examined (Table 1). Oligoamide **2b**, which can be regarded as being derived from **2a** by shortening the end groups, could form a partial gel only with toluene while being insoluble in the other aromatic solvents. Replacing the end methyl group of **2b** with *n*-butyl group led to **2c** that partially gelled all of the aromatic solvents tested. Replacing the ethyl group of **2c** with 2-ethylhexyl group resulted in **2d** that showed a significantly expanded gelating ability. In contrast to the partial gels formed with **2a**–**c**, compound **2d** gelled benzene and toluene, with CGC values of 8.1 and 7.3 mM, respectively. In addition, compound **2d** gelled *o*-xylene with which **1** could only formed a partial gel. Methylene chloride, in which **1** was insoluble and compounds **2a**–**c** readily dissolved, was also gelled by **2d**.

The influence of side (R) chains was then explored by comparing **2e** and **2f** with **2d** (Table 1). With its *n*-dodecyl side chains, compound **2e** not only gelled the same solvents that formed gels with **2d** but also resulted in the gelation of mesitylene and diphenyl ether in which **2d** precipitated out upon cooling. Further increasing the length of the side chains

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led to **2f** that turned out to be a “broad-spectrum” gelator capable of gelling all the aromatic solvents examined. Comparing the CGC values of **2d** (8.1 mM), **2e** (11.1 mM), and **2f** (13.5 mM) in benzene indicates that the gelling efficiencies are inversely related to the length of the side chains.⁶ This phenomenon had been observed before.⁵ Extending the length of side chains probably enhanced the solubility of the gelators, which weakened intermolecular aggregation and resulted in higher CGC values.

The reliance of gelation on the presence of the double-stranded backbone was demonstrated by comparing the different behavior of **1** and **2d** in a mixed solvent containing CHCl₃ and CH₃OH (9/1, v/v). It was found that **2d** was soluble in this solvent, while **1** acted as a gelator.⁶ The inability of **2d** to gelate this mixed solvent can be explained by the reduced ratio of its H-bonded duplex in a solvent of enhanced polarity. On the basis of ¹H NMR dilution experiments (25 °C), the dimerization constant of **2d** in CDCl₃ was found to be $1.9 \times 10^4 \text{ M}^{-1}$ and that in CDCl₃/CD₃OD (100/1, v/v) to be $1.7 \times 10^3 \text{ M}^{-1}$, a difference of more than 1 order of magnitude.⁶ It was thus concluded that the population of H-bonded duplex **2d**·**2d** was significantly diminished in CHCl₃/CH₃OH (9/1), a solvent of much higher polarity than the one used in the ¹H NMR titration experiments.

Gelation is contingent upon the aggregation of gelator molecules into supramolecular networks. In CDCl₃, the ¹H NMR spectra of **2d** (15 mM) showed well-resolved peaks, whereas in benzene-*d*₆ (15 mM), poorly resolved signals were observed.⁶ The variable-temperature ¹H NMR spectra of **2d** in benzene-*d*₆ provided additional evidence for the self-assembly process.⁶ At 10 °C, the ¹H NMR signals of **2d** nearly disappeared, suggesting strong intermolecular aggregation. Above temperatures above 25 °C, the signals of aromatic protons became increasingly resolved. At 70 °C, the otherwise weak and broad signals characteristic of **2d** became well dispersed. Further heating led to no additional change. These results indicate that the aggregation of **2d** is weakened at elevated temperatures and eventually disrupted. At room temperature, compound **1** also gave distinct ¹H NMR signals in CDCl₃ but had low solubility in benzene-*d*₆, which again suggested strong intermolecular aggregation. These observations demonstrate that **1** and **2d** aggregate in benzene with which they form gels.

A large shift of 89 nm was observed in the emission maxima of the fluorescence spectra of the solution (0.1 mM) and the gel of **2d** in CH₂Cl₂.⁶ This observation is consistent with the parallel, face-to-face packing of the duplexes in the gel state via π - π stacking interaction. In addition, the UV-vis spectra of **2d** in benzene (10⁻⁵ M) contained a broad peak around 318 nm at 15 °C. As the temperature was raised from 15 to 70 °C, a new peak appeared at 276 nm with increasing intensity. This was accompanied by a slight decrease in the intensity of the peak at 318 nm.^{6,7} These

observations imply that **2d** undergoes aggregation at a concentration far below its CGC for benzene.

Xerogels obtained by freeze-drying the gels of **1** and **2d** with benzene were examined using scanning electron microscopy (SEM). Rigid fibers were observed for the gel of **1** (Figure 1a). The SEM image of the xerogel of **2d** revealed

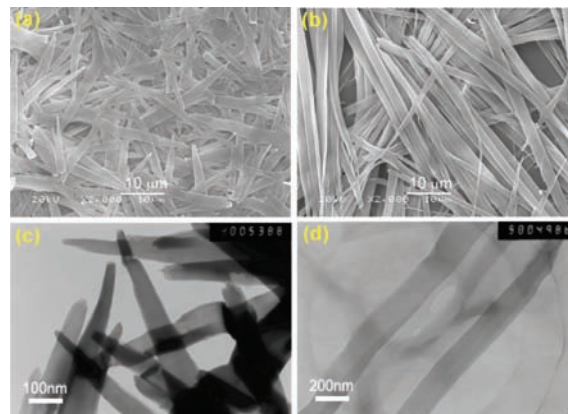


Figure 1. SEM images of the free-dried benzene gel formed by (a) **1** (average width of fibers $\sim 3.5 \mu\text{m}$, length ~ 10 – $25 \mu\text{m}$) and (b) **2d** (average width of fibers $\sim 2 \mu\text{m}$, length $> 100 \mu\text{m}$). TEM image of the gel from benzene with (c) **1** (average width of fibers $\sim 60 \text{ nm}$, length $> 0.6 \mu\text{m}$) and (d) **2d** (average width of fibers $\sim 190 \text{ nm}$, length $> 1.5 \mu\text{m}$).

long fibers (Figure 1b). The formation of fibers suggests that both **1** and **2d** indeed formed extended networks, which is consistent with and explains the observed gelation of benzene by these compounds. The formation of long fibers was also revealed by transmission electron microscopy (TEM) images (Figure 1c, d). The high aspect ratio of the fibers from SEM and TME images indicates the highly anisotropic interactions, which is in line with π - π aromatic stacking interactions among these molecules and supermolecules.⁶ Additional evidence for the presence of a 3D network was provided by atomic force microscopy (AFM), which revealed bundles of fibers formed by **2d** in benzene.⁶

The xerogels of **1** and **2d** from benzene were also examined by X-ray diffraction (XRD), which provided additional insights into the packing of these molecules.⁶ The diffraction patterns revealed low angle reflections at 26.7 and 13.0 Å, respectively, for **1** and 28.7 and 15.2 Å for **2d**. Given the different sizes of the end groups of **1** and **2d**, these distances are within the length ($\sim 20 \text{ Å}$) and width ($\sim 12 \text{ Å}$) revealed by the crystal structure of an H-bonded duplex having the same backbone.^{4a} The diffractograms of both **1** and **2d** contain a peak at 4.1 Å that is within the range of documented π - π stacking distance.⁸ These XRD data confirmed that the H-bonded or covalently cross-linked duplexes indeed serve as the basic units for assembling into supramolecular networks. With their large surface areas, the

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duplexes associate into 1D networks via π - π stacking interaction. The 1D networks pack further into fibers via van der Waals interaction between the alkyl side chains and end groups of the duplexes, which leads to the formation, further association and entanglement of the fibers, and therefore the observed gelation of solvent molecules.⁶

Having demonstrated the correlation between the double-stranded backbone and the gelation of organic solvents, it was reasoned that gelators with altered capabilities might be obtained by pairing two different strands. Such a duplex may consist of two different strands that (1) have the same H-bonding sequence but differ in their side chains and end group; or (2) consist of two strands having different, complementary H-bonding sequences and the same or different side chains and end groups. In this work, the first possibility was probed by mixing **2b**, which is insoluble in benzene at room temperature, and **2f**, which forms a transparent gel with benzene with a CGC of 13.5 mM (Figure 2). It was found that the presence of both **2b** and **2f** in

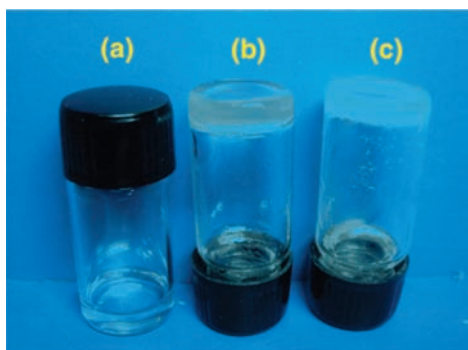


Figure 2. Photos of (a) a solution of compound **2f** in benzene at 9.3 mM, (b) a transparent gel formed by **2f** in benzene at 13.5 mM, and (c) an opaque gel formed by a 1:1 mixture of **2b** and **2f** in benzene at 9.3 mM, at room temperature.

benzene led to significant changes of gelation properties for both strands. Specifically, heating a 1:1 mixture of **2b** and **2f** in benzene led to a clear solution that turned into a stable gel upon cooling to room temperature. The resultant gel, being opaque, had no similarity to the transparent gel induced by **2f** alone in benzene. Besides, in the presence of 1 equiv

of **2b**, the CGC value of **2f** changed to 9.3 mM, a concentration that is too low for pure **2f** to gelate benzene. Although additional details remain to be elucidated, this example serves to demonstrate an encouraging first step for developing duplex gelators by pairing different strands.

In summary, oligoamide duplexes have been observed to serve as organogelators. Varying the side chains and end groups of the oligoamides has resulted in gelators with expanded and altered gelating abilities. Evidence from NMR, SEM, TEM, AFM, fluorescence, UV-vis, and XRD demonstrated the aggregation of the duplexes into fibrous networks. Noncovalent forces such as π - π stacking and van der Waals interactions should be the cause of the formation of fibrillar aggregates that lead to gelation.⁶ These duplexes offer multiple levels of tunability including convenient structural modification as well as rapid, straightforward recombination based on the simple mixing of complementary strands.⁴ Therefore, such a double-stranded system represents a platform allowing the diversity of potential gelators to be systematically expanded. Furthermore, duplexes cross-linked via dynamic covalent bonds⁹ may lead to gelators for polar solvents including water. The dynamic formation of the duplexes foretells the prospect of identifying gelators of desired properties based on a supramolecular and/or dynamic covalent combinatorial approach. The corresponding studies are being carried out, results from which will be reported in due course.

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Supporting Information Available: Synthesis, analytical data, gelation procedures, NMR and mass spectra, TEM and additional SEM images, XRD results, AFM, fluorescence, UV-vis spectra, and a model of the assemblies of the duplexes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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