lyzed reaction. Table 1 shows that **5** is indeed an active catalyst for this reaction. Although the initial activity of **5** expressed in TOF per Pd site per h is somewhat lower than that of **6b**, the total turnover number (TTN)/Pd site for both **6b** and **5** are similar.

In summary, we have established a general route to nanosize, hyperbranched-polycarbosilane compounds that are functionalized with aryldiamine metal complexes using a lithiation/transmetalation procedure. The Pd^{II} centers in the soluble, macromolecular catalyst **5** function as independent catalytic sites in a standard aldol condensation reaction and their activity is similar to that of the single-site Pd catalyst **6b**. To our knowledge, this is the first example of the use of hyperbranched polymers as soluble macromolecular supports for homogeneous catalysis. Moreover, the catalyst support properties of hyperbranched polymers are very similar to those of analogous dendrimers; thus, structural perfection is not always required. Purification of the polymers **3** and **4** by means of dialysis shows that **5** is suitable for continuous membrane applications.

Experimental Section

Standard protocol for the catalytic aldol condensation reaction: 1 mol% of Pd catalyst was added to a mixture of benzaldehyde (2.4 mmol), methyl isocyanoacetate (1.6 mmol), mesitylene (1.6 mmol, internal standard), and $EtN(iPr)_2$ (10 mol%) in CH_2Cl_2 (10 mL). Samples were taken from the reaction mixture at regular time intervals, after careful removal of the solvent ^{1}H NMR spectra of these samples were recorded.

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Effective Gelation of Water Using a Series of Bis-urea Dicarboxylic Acids[**]

Lara A. Estroff and Andrew D. Hamilton[*]

A wide range of small organic molecules has been found, either through design or serendipity, to gel a variety of organic solvents.[1] The property of gelation is thought to arise from the self-assembly of these small molecules into fibers, which, like polymer gels, become entangled and trap solvent.[2] The formation of fibers requires a stabilizing intermolecular interaction and represents a balance between the tendency of the molecules to dissolve or to aggregate in a given solvent.

Organogelators often have hydrogen-bond donors and acceptors that promote aggregation and subsequent fiber formation. The attachment of long alkyl chains onto the hydrogen-bonded core enhances its solubility in organic solvents but also promotes association among the fibers, through van der Waals forces, and eventual gel formation. One effective class of organogelators exploits bis-urea derivatives to form a central, hydrogen-bonded stack to which long chain alkyl groups are attached. We[3] and others have shown that bis-ureas such as **1** are able to gel a variety of nonpolar organic solvents (including supercritical carbon dioxide)[3d] at concentrations less than 4 wt%. Recent crystal structures of these derivatives[3b,c] have confirmed the importance of

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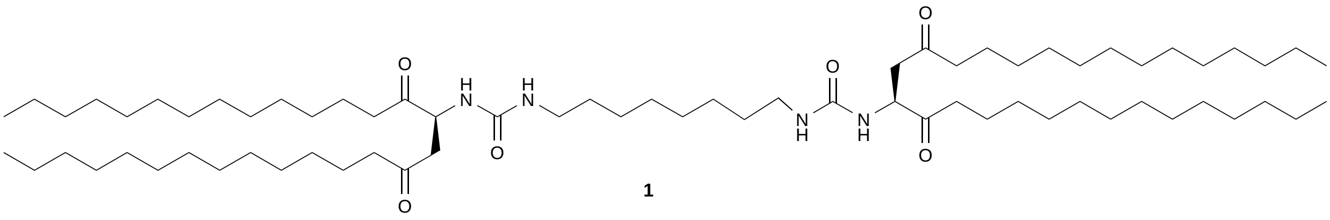

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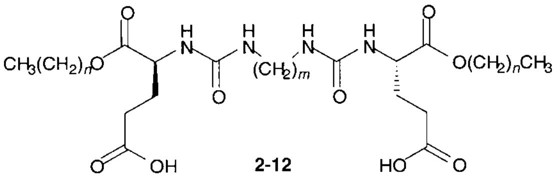
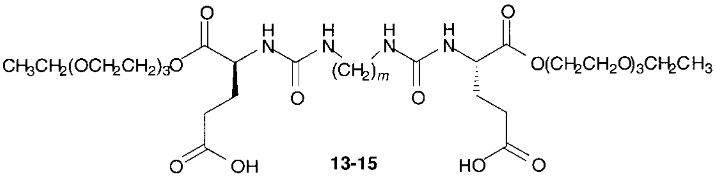
bidentate hydrogen-bonding interactions between urea groups in neighboring molecules and an intertwining of alkyl groups.

As part of an effort to use these aggregates as porous reaction vessels we were interested in extending the gelation properties into hydroxylic solvents, such as water. The design challenge was to modify the character of **1** to cause an already proven self-aggregating subunit to function in more polar solvent systems. Fiber formation by amphiphilic organic molecules in water is well documented,[4] however, these fibers generally precipitate without forming a gel or display viscoelastic behavior at concentrations above the critical micelle concentration.[5] There are only a few examples of nonpolymeric hydrogels formed by the self-assembly of small molecules.[6]

Here we report the rational design of a novel family of hydrogelators (**2**–**15**) and the characterization of their aggregation properties in water. In the design, the self-assembling bis-urea motif of **1** was retained and free carboxylic acids were added for both solubility in water and pH control. We also anticipated that the long alkyl chains would promote aggregation in an aqueous environment. This series of compounds shows aggregation in aqueous bases that displays a strong pH and ionic strength dependence. Of particular interest is the gelation of water by these molecules at concentrations less than 0.3 wt% (>17000 molecules of water per gelator molecule) over a narrow pH range that varies depending on the total number of carbon atoms (M) in the spacer and alkyl esters ($M = 2n + m + 2$; see Table 1).



2-12



13-15

2 $n = 0, m = 8$
3 $n = 3, m = 8$
4 $n = 5, m = 8$
5 $n = 3, m = 12$
6 $n = 7, m = 8$
7 $n = 11, m = 4$
8 $n = 7, m = 12$
9 $n = 11, m = 6$
10 $n = 11, m = 8$
11 $n = 11, m = 12$
12 $n = 14, m = 8$
13 $m = 4$
14 $m = 6$
15 $m = 8$

To test gelation ability, compounds **2**–**15** were dissolved in a series of hot phosphate buffers (0.2 M; pH 5.2, 5.9, 6.7, 7.9, and 10.7) with high ionic strength ($I = 1$ mol kg^{-1} from added NaCl). Upon cooling, one of several types of aggregates (gel, vesicles, sheets, fibers, or crystallites) was formed depending on the chemical characteristics of the molecule and the pH of the solution (Table 1). These aggregates were examined by both polarizing light microscopy and scanning electron microscopy (SEM).

Giant vesicles (10–150 μm in diameter) were observed at pH values below the gelation pH by polarizing light microscopy (Figure 1a). Often these vesicles were weakly birefringent and cracked when gentle pressure was applied. Fibers

Table 1. Aggregation of 0.3 wt% (2 mg in 0.75 mL of water) of bis-urea dicarboxylic acids **2**–**12**.[a]

	M[b]	Water	pH 5.2[c]	pH 5.9[c]	pH 6.7[c]	pH 7.9[c]	pH 7.9[d]	pH 10.7[c]
2	10	C	S	S	S	S	S	N/A
3	16	F	V	V	AP	AP	S	N/A
4	20	Sh	V	OPG	C	F	S	S
5	20	Sh	V	LG	G	S	S	N/A
6	24	I	I	V	G	S	S	N/A
7	28	I	BP	V	LG	F	N/A	Sh
8	28	I	N/A	V	G	F	F	S/F[e]
9	30	I	I	V	G	OPG	S	Sh
10	32	I	I	V	V	G	LG	F
11	36	I	N/A	N/A	V	OPG	G	C
12	38	I	N/A	N/A	V	G	LG	F

[a] I: insoluble, AP: precipitate with no definite structure under the microscope, LG: loose gel that forms AP upon mechanical disruption (shaking), BP: strongly birefringent precipitate, F: fibrous aggregates, weakly birefringent, Sh: sheets, V: giant vesicles (10–150 μm), G: clear gel, S: homogeneous solution, OPG: opaque gel, C: fibrous crystallites, strongly birefringent. [b] $M = 2n + m + 2$. [c] 0.2 M phosphate buffer, $I = 1$ mol kg^{-1} from NaCl. [d] 0.2 M phosphate buffer, $I = 0.4$ mol kg^{-1}. [e] **8** gave a turbid solution at pH 10.7 with no visible precipitate, however, small bundles of fibers were observed at 220X magnification. The solid line outlines the conditions under which gelation is observed.

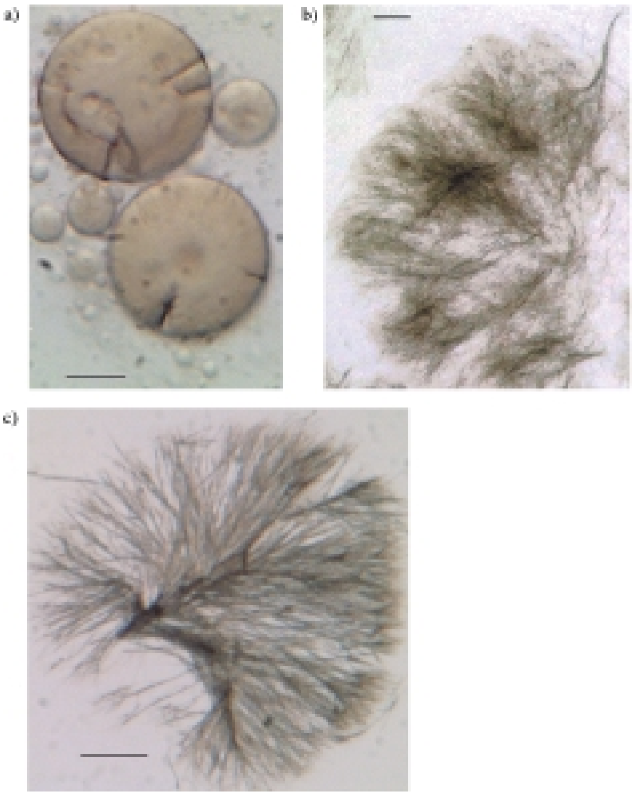


Figure 1. Optical micrographs of the precipitate formed by a) **12** in pH 6.7 phosphate buffer, b) **4** in pH 7.9 phosphate buffer and c) **3** in water. Scale bars: 50 μm.

were the predominant aggregate at higher pH values, as observed by both light microscopy (Figure 1 b, c) and electron microscopy. These fibers precipitated above the gelation pH and were birefringent as observed by polarizing light microscopy. The SEM images further revealed that the fibers themselves were composed of tightly intertwined and thinner fibers (ca. 500 nm in diameter; Figure 2 a). Although the gels appeared amorphous when viewed by polarizing light microscopy, observation by SEM showed them to be composed of fibers (Figure 2 c, d). In contrast to the fibrous aggregates of **3** and **4**, these fibers are entangled and less densely packed, which is in agreement with their formation of a gel.[7]

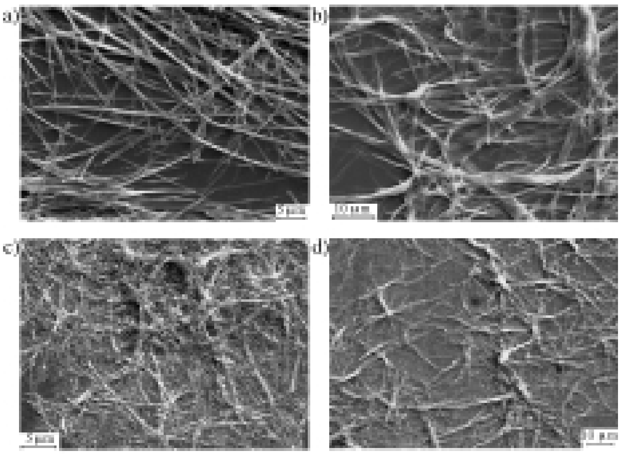


Figure 2. Scanning electron micrographs of a) the precipitate formed by **3** in water, b) the precipitate formed by **4** in pH 7.9 phosphate buffer, c) the dried hydrogel formed by **10** in pH 7.9 phosphate buffer, and d) the dried hydrogel formed by **7** in pH 6.7 phosphate buffer.

The circular dichroism spectra of **4**–**12** and the water-soluble derivatives **13**–**15** have minima at wavelengths similar to that observed for the corresponding organogelator **1** in hexanes (Figure 3). The similarity between the CD spectra of the alkyl and dicarboxylic acid derivatives suggests a related mode of aggregation (hydrogen-bonded stacks of bis-ureas)[3c] for the two families of gelators. Therefore, it appears that the carboxylic acids do not significantly influence the structure of the aggregates formed by **2**–**15**.

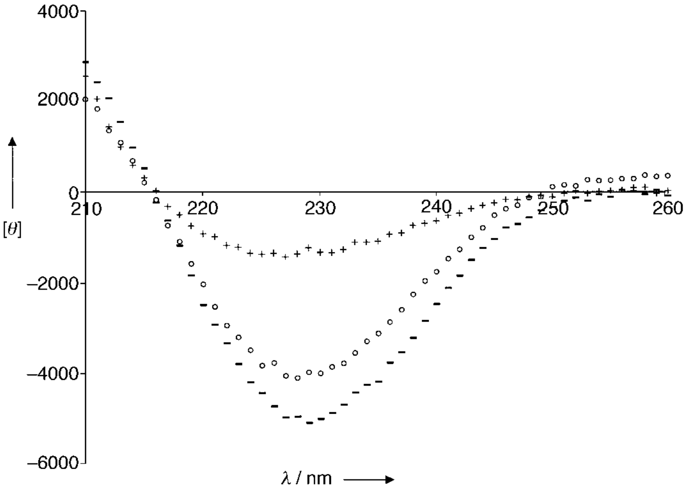


Figure 3. Circular dichroism spectra of **1** in hexanes (+), **15** in 0.2 M (I = 1.0 mol kg^{-1}) pH 7.9 phosphate buffer (−), and **10** in 0.2 M (I = 1.0 mol kg^{-1}) pH 7.9 phosphate buffer (○). All spectra were recorded at 55 °C.[8]

Potentiometric titrations of water-soluble derivatives **13**–**15** were performed to further investigate the dependence of gelation on the pH of the solution.[4b–d, 6c, 9] Bis-ureas **13**–**15** displayed pK_a values in the expected range for free carboxylic acids (p$K_a \approx 4.3$) and the pK_a values did not vary significantly with the linker length. This result suggests that the carboxylic acids do not play a vital role in the aggregation of this family of hydrogelators.

The relationship between the number of methylene units (molecular weight) and the pH value at which gelation occurs (Table 1), indicates that a) hydrophobic interactions play an important role in promoting gelation and b) the primary function of the carboxylic acids is to modulate the solubility in water.[6d] By controlling both the degree of ionization of the carboxylic acids and the hydrophobic surface area (molecular weight) of the molecule, control over the pH of gelation can be exercised. At lower pH values, where the carboxylates are partially protonated, the bolaform molecules assemble into vesicles.[4c, 6c,d, 10, 11] As the pH is raised the solubility increases as a result of the increasing negative charge on the molecules. Aggregation now leads to the formation of fibers that can become entangled through the hydrophobic alkyl esters, thus trapping solvent and forming a gel. Above the pH of gelation, the bis-ureas precipitate from solution as either fibers or sheets. As the molecular weight decreases, the pH at which each of the aggregates forms is lowered until the aggregates

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become too soluble and gelation does not occur at any pH. This trend can be explained by the reduction in the hydrophobic surface area and the accompanying increase in the solubility of the compounds and their aggregates in aqueous environments.[6d, 12]

The dependence of aggregation on the ionic strength was shown to be directly related to the length of the alkyl linker (Table 1). Bis-ureas **9**, **10**, and **12** require 0.2 M phosphate buffers with $I = 1\,\mathrm{mol\,kg^{-1}}$ to form a stable gel or other aggregate. However, bis-ureas **8** and **11**, which have the longest linkers (12 methylene groups), form stable aggregates in 25 mM phosphate buffer ($I = 0.2\,\mathrm{mol\,kg^{-1}}$). This result suggests that the role of the cation is primarily to reduce the electrostatic repulsion between the carboxylate groups, which allows the molecule to assume the conformation required to form gelating fibers. As the linker length increases the distance between carboxylates increases, which decreases the concentration of the cation required to shield them from each other.

In summary, we have developed a novel series of molecules that can gel water. The presence of carboxylate groups in the design imparts a pH and ionic-strength dependence on the gelation process. We are currently investigating the use of these hydrogels to control reactions and crystal growth within the matrix.

Experimental Section

Synthesis: The bis-urea dicarboxylic acids (**2**–**15**) were accessible by a four step synthesis (45–70% overall yields). The commercially available *N*-*t*Boc-glutamic acid γ-benzyl ester (*t*Boc = *tert*-butoxycarbonyl) was first coupled (3-(3-dimethylaminopropyl)-1-ethylcarbodiimide (EDCI), 4-dimethylaminopyridine (DMAP)) to the long-chain alcohol. Treatment with trifluoroacetic acid (TFA) removed the Boc group. The bis-ureas were synthesized by the reaction of the TFA salts with bisisocyanates in the presence of triethylamine. Finally, the benzyl ester was cleaved by hydrogenation (1 atm) using palladium on carbon.

Gelation: A weighed amount (ca. 1–2 $\mathrm{mg\,mL^{-1}}$) of the bis-urea dicarboxylic acid (**2**–**13**) was dissolved in hot buffer and cooled to room temperature in a test tube fitted with a septum. The aggregation state was observed every ten minutes. The test tube was inverted to check for gelation. If no flow was observed and the resulting substance was homogeneous, the compound was said to have successfully gelled the solution. The solutions were allowed to set and the resulting gels/aggregates were transferred to glass slides, covered, and observed by a polarizing light microscope (Olympus SZH12, 7X-225X).

Electron microscopy: Samples were prepared by evaporation onto glass slides followed by multiple rinses with water to remove excess salts. The surfaces of the slides were then coated with carbon and imaged by a JEOL JXA-8600 electron microprobe with an accelerating voltage of 15 kV and an emission current of 2–10 nA.

pH titrations: Aqueous solutions of **13**–**15** (10 mM) were prepared and stirred overnight to allow equilibration to occur. They were then titrated with 0.1 M NaOH using a Corning semi-micro combo pH probe. The degree of ionization (α) was calculated by using Equation (1), where $C_{\mathrm{H^+,\,total}}$ and $C_{\mathrm{H^+,\,free}}$ are the total and free molar amounts of protons, respectively, and C is the molar concentration of bis-urea. The pK_a value was determined from a graph of α versus pH as the pH value at $\alpha = 0.5$.[6c]

$$\alpha = 1 - \frac{C_{\mathrm{H^+,\,total}} - C_{\mathrm{H^+,\,free}}}{2C} \qquad (1)$$

CD spectroscopy: A hot solution of gelator was prepared as described above and transferred to a quartz CD cell (0.1-cm path length). The solutions were then equilibrated at 55 °C for 30 minutes after which time wavelength scans from 210–260 nm were recorded on a Model 202 Aviv CD spectrometer equipped with a temperature control unit.

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[7] The large dimensions and high degree of entanglement of these fibers are in contrast to rodlike micelles that are normally smaller (in terms of molecular dimensions).[5]

[8] Compounds **10** and **1** (but not **15**) exhibit linear dichroism at temperatures below 40 °C and 50 °C, respectively. This effect leads to a bathochromic shift and an increase in intensity in the circular dichroism spectra. These changes are presumably the result of further aggregation of the fibers upon gel formation.

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