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# The Design of Organic Gelators: Solution and Solid State Properties of a Family of Bis-Ureas

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***Abstract:*** *A family of bis-urea derivatives has been synthesized and shown to function as effective gelators in certain organic solvents. The X-ray structure of one bis-urea shows a cylindrical hydrogen bonding network with extensive interdigitation of the alkyl esters which project from the central rod.* 

In recent years there has been intense interest in the design of porous organic materials that might possess the properties of molecular sieving and catalysis more commonly associated with inorganic zeolites.[1] Most attention has focused on controlling the packing arrangements in crystals to create well defined voids or channels.[2] To this end, extensive use has been made of intermolecular interactions, such as hydrogen bonding[3] or metal-ligand[4] motifs, that persist despite changes in the molecular components or the extent of included solvent. We have exploited the bidentate interactions between two carboxylic acid,[5] carboxylic acid-acylaminopyridine,[6] and urea-carboxylate[7] groups to form ordered and, in some cases,[5] porous solid state structures. An alternative approach to porous materials involves the design of small molecules that form three-dimensional networks and encapsulate solvent within a gel matrix.[8] Such gelling agents are frequently based on molecular self-complementarity and the subsequent formation of extended and interacting fibers within an organic solvent. Recently, we[5a] and others[9] have investigated the use of different hydrogen bonding motifs to stabilize gel formation in a range of organic solvents. In particular, bis-urea derivatives represent versatile components that can interact with complementary guests to form 1:1 complexes (Figure 1A)[10] or with each other to form hydrogen bonded networks that can gel organic liquids (Figure 1B).[9] In the present paper we report the design of a new family of bis-urea gelling agents and the investigation of their aggregation structure by X-ray crystallography.

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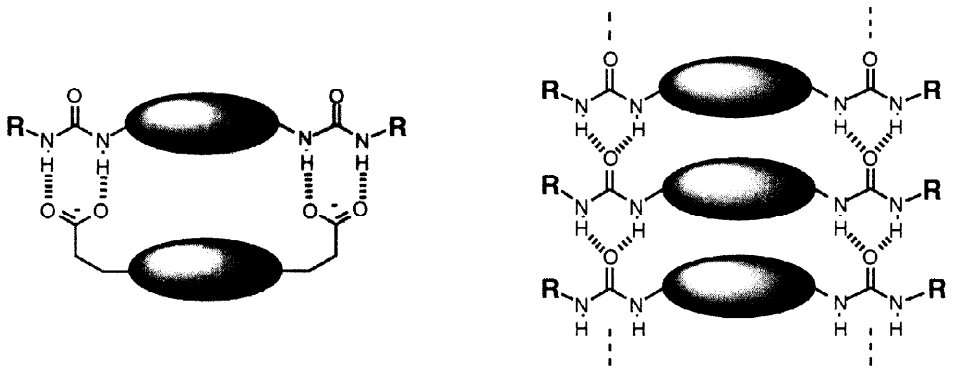
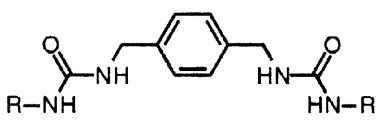
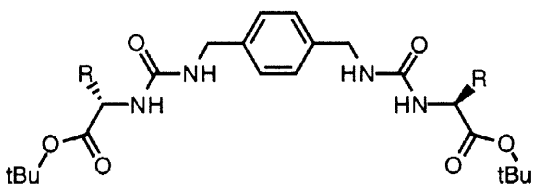


**Figure 1**. A) 1:1 complex formation and B) aggregation behavior of bis-ureas.

We have previously shown that bis-urea derivatives such as **1** form strong complexes with bis-carboxylates (as in Figure 1A) in polar organic solvents.[10] However, the poor solubility of bis-ureas in less polar solvents suggested that in the solid state significant intermolecular interactions (as in Figure 1B) are present.[11] Since gelation depends upon initial dissolution followed by aggregation and network formation, we reasoned that a modest increase in the solubility of the bis-ureas might lead to a new family of gelling agents. The use of different amino acid esters gave us access to a range of solubilizing and potentially interacting functionalities. These self-complementary components were prepared by reaction of xylylene-1,4-bis-isocyanate with the tert. butyl esters of L-alanine, L-phenylalanine and L-valine to give **2a**, **2b**, and **2c**, respectively.



**1** (R = nButyl)



**2a** (R = -$CH_3$), **2b** (R = -$CH_2Ph$), **2c** (R = -$CH(CH_3)_2$)

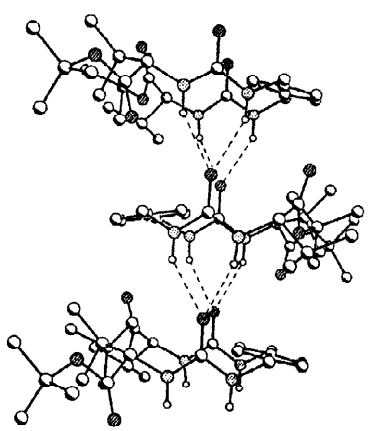
The gelation properties of the tert-butyl ester bis-urea derivatives were measured in a range of organic solvents. In all cases (unless otherwise noted) the compound was dissolved in a solvent at a concentration of 56 mM. The solution was then cooled to 5°C for thirty minutes and the presence of a gel was assessed by inverting the vial and observing the flow of the sample.[12] Bis-alanine derivative **2a** was able to gel THF and acetone at 5°C but the gel melted on warming to room temperature. The bis-phenylalanine analog **2b** showed enhanced solubility but without improved network formation and no gelation properties were observed in any solvent. The best gelling agent in this series of bis-ureas was bis-valine **2c** which appears to combine good solubility with side chain functionality that can interact effectively to form the gel matrix. A particularly stable gel was formed by **2c** in ethyl acetate which retained its form at room temperature for hours. The compound also gels mixed solvents of hexanes with acetone and ethyl acetate. But these gels are less stable than those in ethyl acetate, either melting or crystallizing upon standing at room temperature. Concentrations and conditions for gel formation and stability are shown in Table 1.

**Table 1**. Gelation properties of bis-urea derivatives in various solvents.

| Solvent | 2a | 2b | 2c |
|---|---|---|---|
| $CHCl_3$ | Sol. | Sol. | Sol.-Cryst |
| $CH_2Cl_2$ | Sol. Cryst. | Sol. | Sol. |
| DMSO | Sol. | Sol. | Sol. |
| Ether | Insol. | Insol. | Insol. |
| Hexanes | Insol. | Insol. | Insol. |
| Hexanes/ 25% Acetone | Insol. | Insol. | Gel 5°C (10 mM) Cryst. (56 mM) |
| Hexanes/ 50% Ethyl Acetate | Cryst. | Cryst. | Gel 5°C (10 mM) |
| Ethyl Acetate | Sol | Gel 5°C (98mM) | Gel -stable at RT |
| Acetone | Gel 5°C | Sol. | Sol. |
| Tetrahydrofuran | Gel 5°C | Sol. | Sol. |
| Ethanol | Sol. | Sol. | Sol. |
| Acetonitrile | Sol. | Insol. | |

Sol.- Soluble with no gel formation. Insol.- Insoluble.
Gel 5°C- gel formed when solution of compound was cooled to 5°C for 30 min.

Crystals of **2c** were grown from $CHCl_3$ and methanol. The structure (Figure 2) was determined by X-ray crystallography and confirms the formation of an extensive hydrogen bond network in the crystal. Each molecule forms four hydrogen bonds from its urea-NH groups to the carbonyl-CO groups of an adjacent monomer (NH...OC, 2.18, 2.23Å). The resulting stacked structure is cylindrical in shape with opposite urea strands forming the ends (CO...CO, 7.87Å) and the phenyl groups the sides of the aggregate. A key feature of the structure is the sandwiching of one tert. butyl ester group from each molecule between the π-faces of the phenyl rings (plane-plane distance, 9.47Å) from the flanking bis-ureas in the stack. This projects a methyl group close to the face of the phenyl ring (C-methyl...ring center, 3.69Å), presumably stabilizing the structure via π-alkyl interactions.[13] The structure also provides an insight into the gelating network arrangement in



A

**Figure 2**. X-ray structure of **2c**.

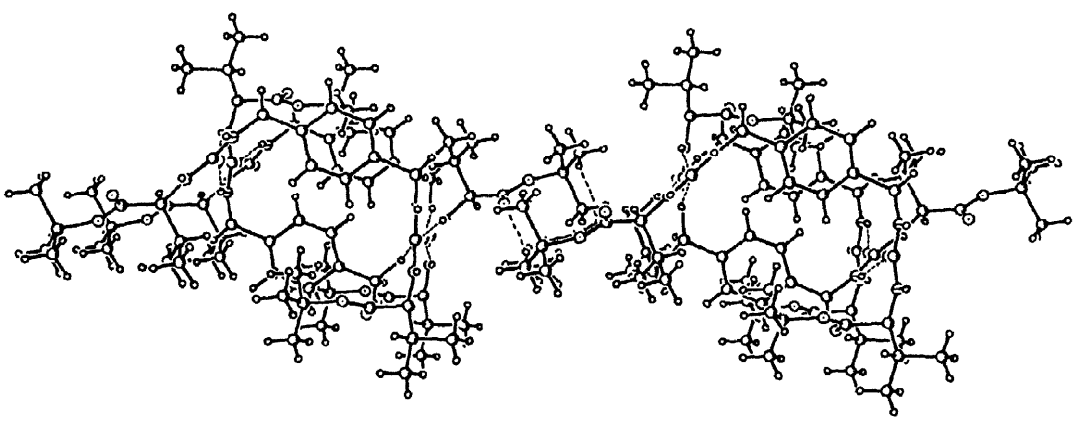


**Figure 3**. Top view of the structure of **2c** showing interacting alkyl chains.

solution. Projecting from the hydrogen bonded cylinders are the second of the tert. butyl esters from each component which form a van der Waal's contact with the corresponding groups on adjacent and parallel stacks (closest $CH_{stack1}....OC_{stack2}$, 2.49Å). The overall result is a series of parallel hydrogen bonded cylinders that form an extended network through the interaction of othogonally projecting alkyl chain. The molecules in the hydrogen bonded cylinders are related to each other through $2_1$ screw symmetry. Surprisingly, adjacent cylinders are oriented in the same direction expanding polarity to the whole crystal.

In summary, we have developed a new type of gelling agent based on the hydrogen bonding and network forming properties of bis-ureas. A crystal structure of one derivative provides important insights into the intermolecular interactions and the basis for design of new gelling agents. The attraction of self-assembled gel matrices of this type lies in their ease of formation, their potential for functionalization and the presence of large pores throughout the network.

**Acknowledgments.**

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