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Di-urea Compounds as Gelators for Organic Solvents

Jan van Esch, Richard M. Kellogg*, Ben L. Feringa*

Department of Organic and Molecular Inorganic Chemistry,
Groningen Centre for Catalysis and Synthesis, University of Groningen,
Nijenborgh 4, 9747 AG Groningen, The Netherlands
Feringa@Chem.rug.nl

***Abstract*:** Simple diurea compounds form thermoreversible gels with several organic solvents. These gels are stable up to temperatures of 100°C, and can be stored for months. Electron microscopy reveals that in these solvents the gelation agents assemble into very thin rectangular sheets which are several tens of micrometers long. Copyright © 1996 Elsevier Science Ltd

In recent years a number of low molecular weight organic compounds have been reported to be effective gelators for several organic solvents[1,2]. Most of the gelating molecules known so far have in common that they possess at least one moiety which can participate in highly directional non-covalent interactions with other gelator molecules. Aggregation of these molecules can for instance lead to extended one dimensional arrays of hydrogen bonds.[3] These strands of gelator molecules subsequently assemble into fiber like structures, which in turn form an extended three dimensional network in the liquid. Another class of compounds particularly able to form extended one dimensional arrays of hydrogen bonds are the ureas.[4] This feature of substituted ureas has been used elegantly in the design and synthesis of layered crystals.[5] Even in dilute solution, urea compounds are known to form one dimensional aggregates through intermolecular hydrogen bonding.[6] We have designed a series of urea compounds in which additional groups are incorporated to enforce non-covalent interactions and have studied their ability to gelate organic solvents (Chart 1). In order to favor association of one dimensional aggregates of these substituted ureas into fiber like structures the benzyl group was included. A highly successful approach to reach this goal is by the introduction of a second urea group.

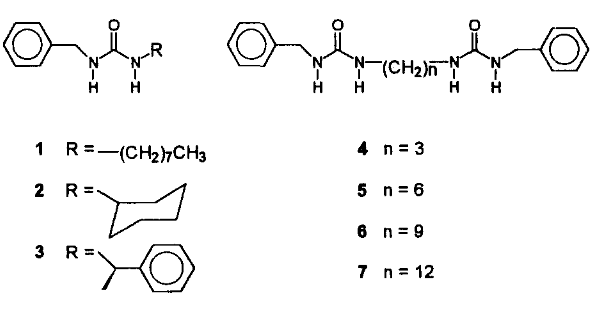

Chart 1

Urea compounds **1-7** were synthesized by addition of the requisite amines to benzyl isocyanate.[7] All compounds were isolated as white solids.[8] The mono ureas **1-3** were moderately soluble in solvents like ethyl acetate and dichloromethane and highly soluble in solvents like dimethyl sulfoxide, dimethyl formamide, and aliphatic alcohols (see Table 1). Compounds **1**-**3** dissolve in aliphatic or aromatic hydrocarbons only on heating to 70°C - 90 °C. Only in the case of **1** in hexadecane a gel was formed upon cooling.[9] Typically $\leq$ 1 % of gelating agent was required. This gel was very turbid and was found to be stable for at least weeks. In all other cases the compounds simply precipitate after the solutions have been cooled to room temperature, or even crystallize slowly upon standing (Table 1).

Table 1. Gelation of Solvents by Compound **1**-**7**[1)]

	Compound						
Solvent	**1**	**2**	**3**	**4**	**5**	**6**	**7**
1-Octanol	s	s	s	p	p	<10	<10
2-Octanol	s	s	s	p	p	9	<10
Toluene	c	p	c	i	<10	p	p
p-Xylene	-	-	-	p	<10	p	p
Tetralin	p	p	c	7	4	7	6
Hexadecane	<10	c	p	i	i	i	i
Olive oil	p	p	p	i	i	s	<10

1) Minimum amount (mg/mL) of compound required for gelation of 1 mL of solvent; c: crystallization; i: no gelation, compound was not completely soluble upon heating; p : no gelation, precipitation of compound occurred; s: no gelation, soluble at RT.

As one would expect, the diurea compounds **4**-**7** were much less soluble. In fact, at room temperature they did not dissolve in any of the solvents investigated (Table 1), but upon heating to temperatures of 100°C to 150°C they gradually dissolve. For this reason we chose some high boiling solvents for testing the gelation capability of these compounds(Table 1). We found that the diurea compounds **4**-**7** are potent gelators for several organic solvents, *e.g.* 1- and 2-octanol and tetralin. Only very low amounts of **4**-**7** were needed for gelation, usually $\leq$ 1%. Similar low critical gelation concentrations have been reported for a number of other low molecular weight organic compounds.[1] For the diurea compounds, we found that below these concentrations a gel-like precipitate formed on cooling. Similarly, when the solubility at elevated temperatures became too low, as was the case with **4**-**7** in hexadecane, the non-dissolved material simply solidified whereas the dissolved material flocculates upon cooling. Apparently, in these cases aggregates were formed upon cooling, but the concentrations of these aggregates are too low to form an extended three dimensional network. From Table 1 it is clear that compounds **6** and **7** behave very similarly. Decreasing the length of the spacer between the two urea groups as with **4** and **5**, makes solutions of these compounds less susceptible to gelation.

The gels mentioned in Table 1 are stable for at least several weeks when stored at room temperature, but upon heating they melt; it should be noted that gel formation is completely reversible. The thermotropic behavior of the gels was studied by melting point measurements[10] and DSC (Table 2). Melting of a gel of **1** in hexadecane starts at 78°C and occurs over a rather small temperature range. The enthalpy of melting is within the range one would expect for the breaking of an urea hydrogen bond in an apolar solvent.[6,11] The gels formed by the diurea compounds **6** and **7**, on the other hand, display a much higher thermal stability. The tetralin gels of these compounds are even stable up to a temperature of 150°C. This increased thermal stability is also reflected in the enthalpies of melting, which are significantly higher than one would expect for the breaking of the two urea hydrogen bonds.[6] On the other hand, melting of these gels occurs over a broad temperature range pointing to a less cooperative phase transition. This results indicate that other intermolecular interactions, such as Van der Waals and dipole-dipole interactions, also contribute to the stability of the aggregates, but that the packing of the molecules within the aggregates is much less ordered than within crystals. The lower melting temperatures and enthalpies of melting observed for gels of **6** and **7** in 1-octanol are in line with the observation that in more polar solvents the enthalpy contribution to hydrogen bonding decreases in favor of the entropy contribution.

Table 2 Thermotropic behaviour of gels[1)]

Compound	*Solvent*	T_m / °C	T_{on} / °C	T_{max} / °C	ΔH / kJ.mol^{-1}
1	hexadecane		78	81	31
6	tetralin	148	151	162	80
7	tetralin	150	152	162	87
6	1-octanol	104	107	123	56
7	1-octanol	103	114	129	62

1) For all measurements gels were freshly prepared using 10 mg compound / mL solvent.[9] T_m is the melting temperature as measured by the dropping ball method; T_{on}, T_{max}, ΔH refer to the DSC measurements. T_{on} is the onset of the phase transition of the first heating run (10°C/min) and T_{max} is the temperature where the transition has its maximum heat flow.

All the gels formed are highly turbid. Light microscopy revealed that the gels are birefringent, but did not show significant structural features, in contrast to the information obtained by electron microscopy (EM) of gels of 6 in tetralin (fig. 1). As is evident from the micrographs, the diurea compound forms large planar sheet like structures, up to several tens of μm long. The transparency of these platelets indicates that they are very thin. Their thickness, however, could not be determined from the micrographs. All platelets are rectangular shaped, with their length exceeding at least 5 to 10 times their width. This indicates that the rate of growth of the various faces is clearly anisotropic, which is most likely the result of a preferred orientation of the molecules within the sheets. This is remarkable, since due to the presence of a flexible spacer between the two urea groups, these molecules have a large degree of conformational freedom, and hence should be highly susceptible to polymorphism. The sheets are sometimes folded and tend to stack. Furthermore, the present micrographs do not show any splitted sheets or any junction zones. Although the present micrographs do not reveal how the sheets are arranged in the gels, the sheets most likely form an extended three dimensional network throughout the liquid. Agitation of the gels causes an irreversible destruction of the network. Apparently, these networks of sheets are in a metastable state. The long term kinetic and thermal stability arises most likely form the inertness of the mechanical construct, rather than specific interactions between sheets.[12] Electron micrographs of gels of 7 in 1-octanol or tetralin revealed the presence of similar rectangular shaped platelets. On the other hand, electron micrographs of a gel of 1 in hexadecane did not show the presence of such platelets. Instead, fiber-like structures were observed.

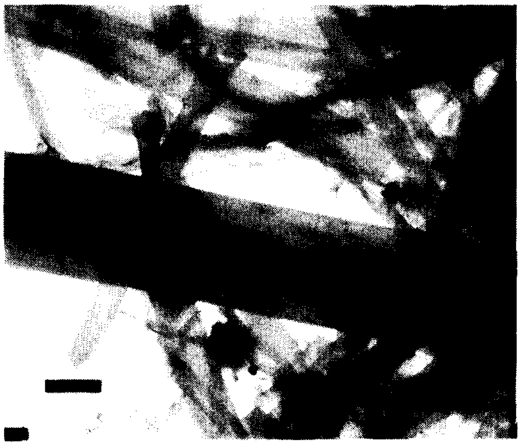

Figure 1 Transmission electron micrographs of gels of 10 mg of 6 in tetralin. The gels were negatively stained using osmium tetroxide. The bars indicates 2.3 μm.

In conclusion, we have shown that simple diurea compounds form thermoreversible gels with several organic solvents. The facile access to these new gelating agents from cheap starting materials and the samll amounts required to form highly stable gels are attractive features. The gels consist of a network of large planar sheet like structures. Since these structures are very different from the entangled fiber networks more commonly observed in gels of low molecular weight organic gelators, these diurea compounds represent a new class of organic gelators. The very regular appearance of the sheets, and their high thermal stability indicate that the molecules within these sheets are well ordered. Allthough we do not know the arrangement of the molecules within the sheets, it is tempting to propose that the flexible alkyl chains form the core of the lamella,whereas the benzyl moieties are exposed to the solvent. This structure is stabilized by formation of extended arrays of hydrogen bonded urea groups. Such an arrangement would offer excellent possibilities to tune the surface properties of the sheets, which should be an important factor for gelation.[1,2] Research in this direction is in progress.

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References and Notes

1. (a) Twieg, R.J., Russell, T.P., Siemens, R.S., Rabolt, J.F. *Macromolecules*, **1985**, 18, 1361-1362, (b) Lin, Y.-C., Weiss, R.G. *Macromolecules*, **1987**, 20, 414-417, (c) de Vries, E.J., Kellogg, R. M. *J. Chem. Soc. Chem. Comm.*, **1993**, 238-240, (d) Hanabusa, K., Matsumoto, Y., Miki, T., Koyama, T., Shirai, H. *J. Chem. Soc. Chem. Comm.*, **1994**, 1401-1402, (e) Snijder, C.S., de Jong, J.C., Meetsma, A., van Bolhuis, F., Feringa, B.L. *Chem. Eur. J.*, **1995**, 1, 594-597.
2. Fuhrhop, J.H., Koenig, J., *Membranes and molecular assemblies: the synkinetic approach*, Royal Society of Chemistry, Cambridge, **1994**.
3. Hanabusa, K., Miki, T., Taguchi, Y., Koyama, T., Shirai, H. *J. Chem. Soc. Chem. Comm.*, **1993**, 1382-1384.
4. Desiraju, G. R., *Crystal Engineering: The Design of Organic Solids*, Elsevier, Amsterdam, **1989**.
5. (a) Chang, Y.-L., West, M.-A., Fowler, F.W., Lauher, J.W. *J. Am. Chem. Soc.*, **1993**, 115, 5991-6000 (b) Kane, J.J., Liao, R.F., Fowler, F.W., *J. Am. Chem. Soc.*, **1995**, *117*, 12003-12004 .
6. Jadzyn, J., Stockhausen, M., Zywucki, B. *J. Phys. Chem.*, **1987**, *91*, 754-757.
7. Arnold, R.G., Nelson, J.A., Verbanc, J.J. *Chem. Rev.*, **1957**, 57, 47.
8. Compounds 1-7 showed spectroscopic and analytical data in accordance with the structures.
9. In a typical gelation experiment 10 mg of the urea compound and 1 mL of the solvent were placed in a sealed test tube and were heated untill a homogeneous solution was obtained. The solution was then allowed to cool to room temperature after which it was inspected. Gelation was considered to have occurred when a homogeneous substance was obtained, which exhibited no gravitational flow. Separate DSC and ^{1}H nmr experiments revealed that none of the compounds showed any sign of detoration up to temperatures of 180°C.
10. Takahashi, A., Sakai, M., Kato, T. *Polym. J.* , **1980**, 12, 335.
11. Doig, A.J., Williams, D.H. , *J. Am. Chem. Soc.*, **1992**, 114, 338-343.
12. Philipse, A.J. *Langmuir*, **1996**, 12, 1127-1133.

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