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# Tripodal Tris-Urea Derivatives as Gelators for Organic Solvents

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**Keywords:** Self-assembly / Hydrogen bonds / Gels / Solvent effects

Several new tripodal tris-urea derivatives are prepared and found to be efficient gelling agents for organic solvents. The structure and thermotropic properties of the gels are studied by electron microscopy, differential scanning calorimetry (DSC) and FT-IR spectroscopy. Remarkably, the range of solvents to be gelled can be tuned by the peripheral substituents.

## Introduction

The gelation of organic solvents by low-molecular weight compounds in recent years has progressed from discovery by chance to reasonably well-defined guidelines.[1,2] Recently, our group[3] and the groups of Hanabusa[4] and Hamilton[5] have developed organogelators based on the self-assembling properties of urea moieties. Bis-urea compounds in particular were found to be highly effective gelators for a variety of organic solvents. Moreover, due to the highly specific and directional hydrogen bonding between the urea groups it was possible to introduce a variety of functional groups without interfering with the intermolecular hydrogen bond formation.[3,6]

Urea groups are known not only for their self-assembling properties, but also as complexing agents for anions and metals.[7] Especially interesting are multidentate urea compounds in which two or more urea-containing chains are connected at a central amine. For example, tripodal tris-urea compounds have been reported as complexing agents for phosphate[8] and metal[9] ions. Compared to the bis-urea organogelators,[3] these types of compounds are interesting for several reasons. First, introduction of an additional urea group is expected to alter the strength and morphology of the hydrogen bonded aggregates and thus the properties of the gel. Furthermore, the potential complexing capability of these compounds offers possibilities in controlling the morphology of the gel.[10] Finally, the polarity of the compounds can be altered by protonation or alkylation of the central amine, which might extend their scope to more polar solvents like water. Here we wish to report the first results in the application of these tripodal tris-urea compounds as efficient gelators for organic solvents.

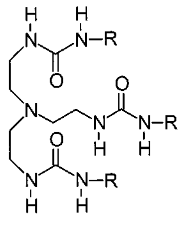
## Results and Discussion

The tripodal tris-urea compounds **1−7**[11] were easily prepared by addition of the corresponding isocyanate to tris(2-aminoethyl)amine. All compounds were isolated as white powders and characterized by $^1$H and $^{13}$C NMR spectroscopy. At room temperature the compounds were found to be sparingly soluble in common organic solvents like ethanol, acetone and chloroform. Upon extensive heating the solid slowly dissolved and upon cooling, the formation of a gel was observed for several of the solid-solvent combinations. These results are summarized in Table 1.

Table 1. Gelation properties of tripodal tris-urea derivatives[a]

| Solvent | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| hexane | i | i | i | sw | 2 | 10 | p |
| cyclohexane | i | i | i | sw | 15 | 15 | 2 (t) |
| *n*-hexadecane | i | i | i | p | p | 10 | p |
| *p*-xylene | i | i | 10 | 5 | 2 | p | 10 |
| benzene | i | i | 2 | 15 | 5 | p | 20 |
| toluene | i | i | 5 | 5 | 2 | p | 10 (t) |
| tetralin | p | i | 5 | 10 | 10 | p | p |
| *n*-butyl acetate | p | i | p | 10 | p | p | 10 (t) |
| ethyl acetate | p | i | p | 15 | p | p | 10 |
| cyclohexanone | s | i | s | s | s | p | s |
| olive oil | p | i | p | p | 15 | vs | 10 |
| $CH_2Cl_2$ | p | i | 5 | s | g/p | p | s |
| 1,2-dichloroethane | p | i | 2 | g | g/p | p | 20 (t) |
| DMSO | s | s | s | s | p | 15 | s |
| 1-octanol | s | i | p | s | s | p | s |
| ethanol | p | i | p | s | s | p | s |
| $H_2O$ | i | i | i | i | i | i | i |

[a] Abbreviations used: g: gelation concentration (concentration in mg/mL); i: insoluble at solvent reflux temperature; p: precipitates; s: soluble at room temperature (solubility > 20 mg/mL); vs: viscous solution; sw: swells in solvent; g/p: gel-like precipitate; t: thixotropic



**1** R= −Ph
**2** $-p\text{-PhNO}_2$
**3** $-CH_2Ph$
**4** $-(CH_2)_3CH_3$
**5** $-(CH_2)_7CH_3$
**6** $-(CH_2)_{11}CH_3$
**7** $-CH(C_2H_5)CH_2CH_2CH_2CH_3$

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Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/eurjoc or from the author.

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From Table 1 it can be seen that compounds **1** and **2**, which have phenyl moieties attached directly to the urea groups, are highly insoluble ($c < 2$ mg/mL) even at elevated temperatures. If a homogenous solution was obtained at reflux temperatures, in most cases precipitation occurred upon cooling. However, introduction of only one $CH_2$ segment between the urea and phenyl group, as in compound **3**, increased the solubility at reflux temperatures to levels above 10 mg/mL. Upon cooling, opaque gels were formed with both aromatic and chlorinated solvents. The substitution of the aromatic groups for aliphatic chains as in compounds **4**−**6**, improved the solubility of these tripodal tris-urea compounds even more, and upon cooling gels were obtained with a variety of aromatic and aliphatic solvents. The gels formed with the aromatic solvents were optically transparent, but with the other solvents the gels were opaque.

It was found that the length of the alkyl chains has a pronounced effect on the gelation properties of these compounds. Compound **4**, for instance, which contains only short butyl chains, gelates a variety of solvents, including aromatic solvents and esters. Elongation of the side chain length to 8 (**5**) or 12 (**6**) carbon atoms resulted in a shift of the gelation abilities towards more apolar, aliphatic solvents. Apparently, for these tripodal tris-urea derivatives an increase in the chain length of the R group does not result in improvement of the gelation capability, but in a shift in the range of gelated solvents. This contrasts with the cyclohexane bis-urea[4] and tris-amide[12] compounds, for which introduction of longer alkyl chains mainly results in an improvement of the gelation capability.

Remarkably, **6** was also found to gelate DMSO, which is a solvent that strongly competes for hydrogen bond formation. Most likely, in very polar solvents solvophobic effects due to the presence of the dodecyl chains become important in the stabilization of the gel. This effect is also observed for gels of bis-dodecylurea cyclohexane in polar solvents.[3c]

Compound **7**, which contains branched alkyl chain substituents, was found to be the gelator with the broadest scope, covering almost the entire range of solvents. On the other hand, the critical gelation concentrations are substantially higher for this compound, and all gels obtained were opaque. Some gels of **7** have the distinct feature that they are thixotropic, i.e. mechanical agitation or vortexing turns the gel into a viscous liquid, from which the gel state is regained upon standing for some time.[13] Furthermore, gelation of organic solvents by **7** takes, in most cases, up to several weeks, whereas for **3**−**6** gelation occurs within a few hours. This might be due to the fact that **7** consists of a mixture of stereoisomers. However, the kinetics and mechanism of gelation have not been studied in more detail.

The morphologies of the gels were studied by electron microscopy.[14] Micrographs of *p*-xylene gels of **3** and **4** show a clear difference in morphology between both gels (Figure 1). For compound **4**, the gel structure consists of very thin and irregularly twisted fibers, with a diameter of <20 nm for the smallest entities (Figure 1b). The thicker fibers clearly consist of bundles of these very thin fibers. The fibers in turn fuse and intertwine to form an entangled network. A similar morphology is observed for *p*-xylene gels of **5**.

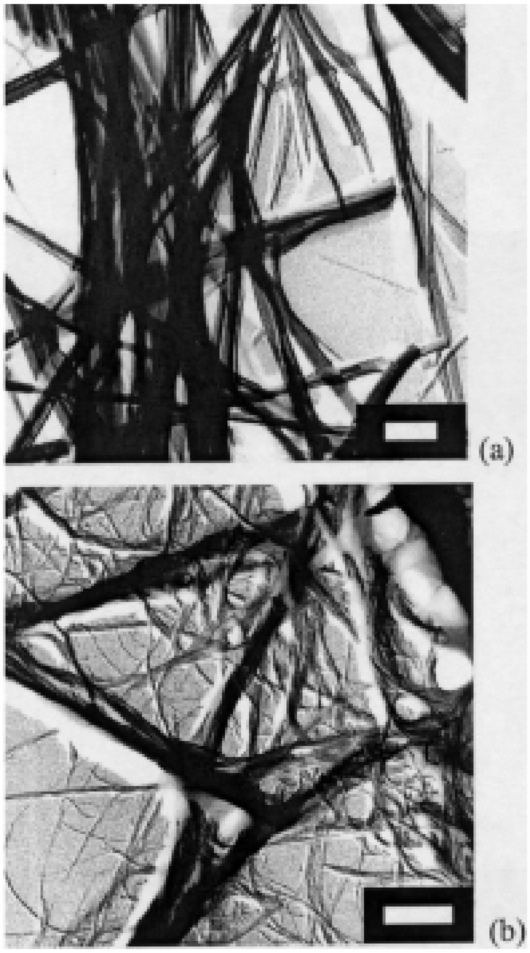


Figure 1. Electron micrographs of *p*-xylene gels of **3** (a) and **4** (b) (10 mg/mL, Pt shadow 45°, bar = 1 μm)

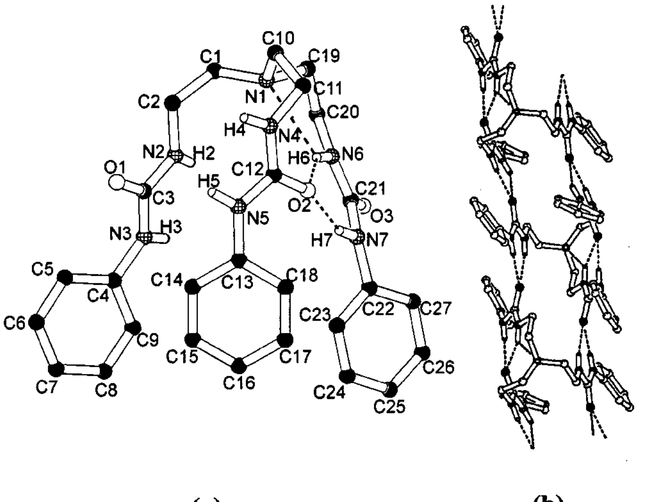
In contrast, compound **3** forms elongated flat fibers, which are neither twisted nor intertwined with each other (Figure 1a). The fibers exhibit some fine structure and appear to be multi-layered. Occasionally, the fibers split or fuse, which might contribute to the formation of a stable gel. Thus, as for bis-urea gelators,[3] structural differences between the compounds have a large effect on the morphology of the gel.

The thermal stability and reversibility of the gel was investigated by DSC measurements.[15] Heating of a freshly prepared gel of **5** (43 mg/ml; *p*-xylene) resulted in a single endothermic peak at $T = 89$ °C with an enthalpy of 49 kJ/mol. This value is significantly lower than expected for the breaking of hydrogen bonds between three urea moieties in apolar solvents.[3c,16] Subsequent cooling resulted in one exothermic peak at 55 °C with an enthalpy of −43 kJ/mol. Independent melting point measurements[17] on a *p*-xylene gel of **5** (50 mg/mL) showed that, at 90 °C, the gel is completely transformed into a homogeneous liquid. Therefore the peak in the heating curve was assigned as the melting point of the gel and the corresponding peak in the cooling curve was assigned as the gelation point. A subsequent second DSC run gave almost identical heating and cooling curves, showing that the gelation process is completely thermoreversible. Increasing the period between two successive scans to several days, however, resulted in a slight but significant increase in the melting enthalpy (55 kJ/mol), indicating that some structural reorganization takes place upon aging.

The role of hydrogen bonding for the stability of the gel was studied by FT-IR spectroscopy on compounds **3** and **4**. In solution (10 mM, CHCl$_3$) maxima are observed for **3** at 3365 cm$^{-1}$ for the NH stretch and 1646 and 1568 cm$^{-1}$ for the NH-I and NH-II bands (for **4**: 3369 cm$^{-1}$, 1646, and 1568 cm$^{-1}$ respectively). Measurements on gels (10 mg/mL, 1,2-dichloroethane) revealed a shift to 3330 cm$^{-1}$ for the NH stretch and 1620 and 1586 cm$^{-1}$ for the NH-I and NH-II bands (for **4**: 3336 cm$^{-1}$, 1630 and 1583 cm$^{-1}$ respectively). These spectral changes indicate that gel formation is accompanied by the formation of hydrogen bonds between the urea groups.[18]

As shown in Table 1, compound **1** did not gelate any of the solvents investigated. However, we were able to isolate crystals from 1-octanol, suitable for X-ray analysis (Figure 2).[19] Evaluation of the data revealed that, within the molecule, two of the urea groups are involved in intramolecular hydrogen bonds, one as donor, donating both N−H groups, and one as acceptor (Figure 2a). These two ureas are tilted towards each other and positioned anti-parallel with respect to the remaining urea group. Furthermore, one of the protons of the intramolecular donor forms a bifurcated bond with the central amine, forcing the unpaired electron pair of the amine to point into the interior of the molecule. The individual molecules are linked by intermolecular hydrogen bonds into infinite one-dimensional chains of alternating molecules in the [101] direction (Figure 2b). These crystallographic data, together with the FT-IR data might point to the formation of hydrogen-bonded stacks of alternating molecules in the gel. Previously, it was found that formation of gels might be accompanied by polymorphism.[3c] Therefore, further spectroscopic measurements should reveal whether this hydrogen bonding pattern is also present in gels formed by **3**−**7**.

In summary, we have prepared several new tripodal tris-urea derivatives and have studied the gelation ability for a variety of organic solvents. The range of gelated solvents as well as the morphology of the gel is dependent on the structure of the side chains. X-ray crystallography together with FT-IR provided evidence for the formation of hydrogen bonded stacks of alternating molecules. The formation of these hydrogen bonds accounts for the high thermal stability of the gel. However, the introduction of the additional urea group did not significantly increase the stability of the gels, compared to the gelators containing two urea groups. This can be explained by the intramolecular hydrogen bond, which reduces the number of hydrogen bonds available for intermolecular aggregation, as observed in the X-ray structure. Studies on the effect of complexation of anions or protonation of the amine on the properties of these compounds and their gels are in progress.



**(a)** **(b)**

Figure 2. (a) PLUTON plot of the molecular structure of **1**, as obtained from the X-ray crystal structure determination; (b) Hydrogen-bonded chain of alternating molecules, running in the [101] direction; hydrogen atoms, not involved in hydrogen bonding, are omitted for clarity

## Acknowledgments

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[19] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-144891. Copies can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) +44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

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