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# Gels with exceptional thermal stability formed by bis(amino acid) oxalamide gelators and solvents of low polarity

**Janja Makarević, Milan Jokić, Leo Frkanec, Darinka Katalenić and Mladen Žinić***
*Laboratory of Supramolecular Chemistry, Rudjer Boškovic Institute, Bijenicka 54, Zagreb, Croatia.*
*E-mail: zinic@rudjer.irb.hr; Fax: 385 1 46 80 195; Tel: 385 1 46 80 217*

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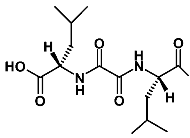
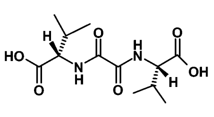
**Some bis (amino acid) oxalamide gelators form common thermo-reversible gels with various organic solvents but also gels of exceptional thermal stability with some solvents of medium and low polarity; the latter gels can be heated up to 50 °C higher temperatures than the bp of the solvent without apparent gel-to-sol transition.**

The gelation phenomenon exhibited by low molecular weight organic compounds has recently attracted much attention.[1] Gels form by entanglement of many fibres into a network, which entraps the solvent in the network compartments. The supramolecular nature of the phenomenon has been recognized; gel fibres, typically of micrometer scale lengths and nanometer scale diameters, are formed in solution predominantly by the unidirectional self-assembly of gelator molecules.[2] The supramolecular gels represent new "soft" materials with numerous potential applications, such as slow drug delivery systems,[3] sensing devices responding to internal or external stimuli (pH, temperature, light, solute),[4] and as hardeners of liquid waste materials.[5] Additional applications, *e.g.* in the safer transport of gelled dangerous liquids or as compartmental reaction or crystallization vessels, may be envisioned.



**1**



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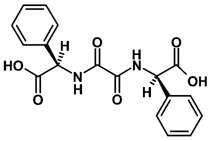

**3**

The main characteristic of gels formed by small organic compounds is their thermo-reversible gel-to-sol transition that occures by self-assembly and dis-assembly processes, respectively. However, in the course of our studies of bis(amino acid) oxalamide gelators,[6] we have found that, besides the common thermo-reversible gels, gels with exceptional thermal stability can also be formed. Such thermo-stable gels can be heated to temperatures exceeding the bp of the solvent present without gel-to-sol transition. Due to the very low solubility of bis(amino acid) oxalamides in the majority of solvents, except alcohols and DMSO, the gelation experiments were performed using a minimal volume of DMSO as the solubilizing component and a large excess of another solvent tested for gelation. The bis(LeuOH) oxalamide **1** forms thermo-reversible gels with solvents of high polarity such as water, EtOH and other alcohols but also gels of exceptional thermostability with some solvents of medium (acetone, butan-2-one, EtOAc, THF) and low ($CCl_4$) polarity (Table 1). The bis(ValOH) derivative **2** was found to form a thermo-stable gel only with $CCl_4$. Interestingly, the related aromatic (*R*-phenylglycine) amino acid derivative **3** does not form gels with any of the examined solvents, giving the precipitate in most cases. Heating of thermo-stable gel samples (stoppered NMR tube, temp. increase 3 °C min$^{-1}$, oil bath temperature measured) produced no apparent change of gel consistency until a sufficiently high temperature was reached which caused violent solvent evaporation and decomposition of the gel (gel decomposition temperature, $T_d$). Impressively, some such thermo-stable gels could be heated at up to 50 °C higher oil bath temperatures than the boiling point of the predominating solvent (Table 1). The effect remains also for much lower gelator concentrations (gelator; $c_g$; solvent system; $T_d$: **1**; 0.015 (0.5 wt %); $CCl_4$/DMSO 17 : 1; 127 °C; **1**, 0.03 (1 wt %); $CCl_4$/DMSO 17 : 1; 129 °C; **2**, 0.03 (1.1 wt %); $CCl_4$; 127 °C). The latter results show that the $T_d$ values are not appreciably concentration dependent. The effect can be explained by the less efficient heat transfer through the bulk gel and increased pressure in the micro-compartments filled with solvent molecules. To shed more light on the formation of thermo-reversible and thermo-stable gels by bis(LeuOH)-**1**, $^1$H-NMR and FTIR studies of both gel types were performed. As described earlier, in the $^1$H-NMR spectra of gels, only the gelator molecules (free or weakly aggregated) dissolved in the entrapped solvent could be observed;[6] the signals of molecules assembled in the rigid gel network can not be observed due to strong broadening induced by long correlation times.[1d,7] As a consequence, the gelator signals in the $^1$H-NMR spectra of thermo-reversible gels increase with increasing temperature due to network disassembly giving dissolved, NMR observable aggregates (Fig. 1; **2**–$CDCl_3/CD_3CN$ and **1** EtOD gels); for these types of gel, slopes of $6 \times 10^{-3}$ and $2 \times 10^{-3}$ mol dm$^{-3}$°C corresponding to their solubility increase per °C were obtained.[6] In contrast, the thermostable gels of **1**–acetone-d$_6$, and **1**–$CCl_4$/DMSO-d$_6$ showed 10–30 times lower solubility increase per °C (slopes around $2 \times 10^{-4}$ mol dm$^{-3}$ °C) (Fig. 1). Thus, the observed thermal stability of the latter gels may be explained by the very low gelator solubility in these solvents, preventing network disassembly even at higher temperatures. To additionally prove this conclusion, we examined the thermal stabilities of the bis(LeuOH) oxalamide gels formed with $CCl_4$/DMSO mixtures of different compositions. At a $CCl_4$/DMSO ratio lower than 1.75, solution was obtained. The gels formed at 1.75, 2 and 2.5 solvent ratios were fully thermo-reversible, giving gel melting temperatures ($T_g$/°C, tube inversion method, oil bath, heating rate 3 °C min$^{-1}$) of 49, 53, and 60 °C, respectively. Apparently, in solvent mixtures with a higher

**Table 1** Solvent mixtures (bp/°C; v/v) and gel decomposition temperatures ($T_d$/°C) of the thermo-stable bis(LeuOH) (**1**) and bis(ValOH) (**2**) oxalamide gels[a] ($c_g$ = 0.12–0.14 mol dm$^{-3}$)

| Gelator | Solvent composition | $T_d$ |
|---|---|---|
| **1** | Acetone (55)/DMSO, 17 : 1 | 100 |
| **1** | Butan-2-one (80)/DMSO, 16 : 1 | 125 |
| **1** | THF (67)/DMSO, 12 : 1 | 120 |
| **1** | $CCl_4$ (77)/DMSO, 7 : 1 | 128 |
| **1** | EtOAc(77)/ DMSO, 10 : 1 | 120 |
| **1** | EtOAc (77)/ MeOH, 10 : 1 | 128 |
| **2** | $CCl_4$ (77) | 127 |

[a] All prepared gels were fully transparent.

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**Table 2** Selected FTIR bands ($v$; cm$^{-1}$) of bis(LeuOH) oxalamide in thermo-stable EtOH gel and thermo-irreversible CCl$_4$/DMSO17 : 1 gel

| Gel solvent | $T$/°C | NH | COOH | Amide I | Amide II |
|---|---|---|---|---|---|
| EtOH | 24 | [a] | 1716 | 1673; 1657 | 1513 |
| | 44 | [a] | 1717 | 1673; [b]dis. | 1508 |
| CCl$_4$/DMSO 17 : 1 | 24 | 3295 | 1714 | [b]—; 1658 | 1513 |
| | 104 | 3298 | [b]dis. | [b]—; 1658 | 1513 |

[a] Overlapped by solvent OH band. [b] —, Absent; dis., disappears upon heating.

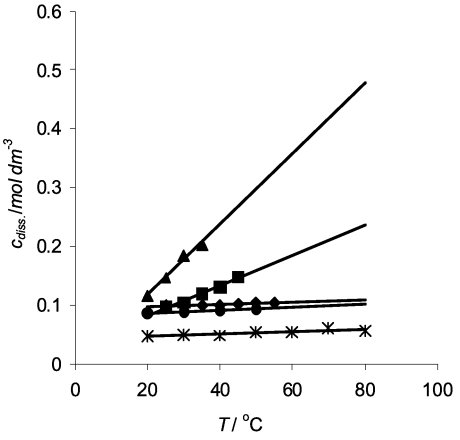

**Fig. 1** Temperature dependent concentration change of dissolved gelator ($c_{\text{diss.}}$) in thermo-stable **1**–EtOD (■) and **2**–CDCl$_3$/CD$_3$CN (▲) gels and in the thermostable **1**–acetone-d$_6$/DMSO-d$_6$ 17 : 1 (◆); –CCl$_4$/DMSO-d$_6$ 3 : 1 (●) and –CCl$_4$/DMSO-d$_6$ 7 : 1 (⁎).

DMSO content, **1** is more soluble, which results in easy network dissolution and gel-to-sol transition at increased temperatures. However, at a solvent ratio of 3 : 1, a thermo-stable gel was formed giving the gel decomposition temperature $T_d$ of 124 °C. Further increase of the CCl$_4$/DMSO ratio to 5 : 1 ($T_d$ 127 °C) and 7 : 1 ($T_d$ 128 °C) also gave thermo-stable gels with very slightly increased $T_d$ temperatures; the gel sample with extreme 17 : 1 CCl$_4$/DMSO ratio gave a similar $T_d$ value. It is important to note that the dependence of gel thermal stability on CCl$_4$/DMSO solvent composition shows a sharp transition from a thermo-reversible to a thermo-stable gel and a strong increase of thermal stability in the relatively narrow range of solvent ratios between 2.5 and 3 (Fig. 2). This observation clearly shows that the thermal properties of gels can be altered by relatively small changes of solvent composition and polarity. At solvent ratios below 1.75 a solution was obtained showing that gelation can be totally suppressed by higher DMSO content.

The effects in the temperature dependent FTIR spectra of the thermo-reversible **1**–EtOH and the thermo-stable **1**–CCl$_4$/DMSO 17 : 1 gels lead to the same conclusions as those reached on the basis of the temperature dependent $^1$H-NMR spectra. The spectrum of the thermo-reversible **1**–EtOH gel at room temperature exhibits the carboxylic C = O band at 1716 cm$^{-1}$, two amide I bands at 1673 and 1657 cm$^{-1}$ of approximately equal intensity originating from free and hydrogen bonded oxalamide units,[6] respectively, and an amide II band at 1513 cm$^{-1}$. At the gel melting temperature of 44 °C ($T_g$ determined by tube inversion), only the higher frequency amide I band (1673 cm$^{-1}$) remains. This clearly shows that the lower frequency amide I band belongs to the network assembled gelator molecules. In sharp contrast, the room temperature spectrum of the thermo-stable CCl$_4$ /DMSO 17 : 1 gel shows only the lower frequency amide I band at 1658 cm$^{-1}$ and one NH stretching band (3295 cm$^{-1}$) corresponding to hydrogen bonded NHs (Table 2). The fact that the bands corresponding to non-hydrogen bonded NHs and amide carbonyls[6] at around 3400 and 1680 cm$^{-1}$, respectively, can not be observed suggests quantitative self-assembly. The spectrum does not change upon temperature increase up to 104 °C, showing lack of any appreciable network dis-assembly to dissolved, free or weakly aggregated gelator molecules.

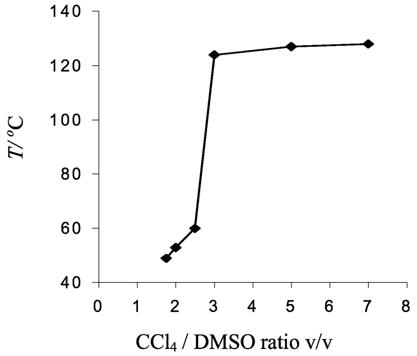

**Fig. 2** $T_g$ values of the thermo-stable **1**–CCl$_4$/DMSO gels at solvent ratios of 1.75, 2 and 2.5 and $T_d$ values of the thermostable gels at solvent ratios of 3, 5 and 7.

In conclusion, we present evidence that small organic gelators are capable of forming not only thermo-reversible gels but also thermo-stable gels and that formation of such gels is solvent dependent. We have also shown that the gel thermal properties can be substantially altered by a slight change in solvent composition and polarity. The most exciting property of the thermo-stable gels is the fact that they remain stable in heating medium at temperatures of 40–50 °C above the boiling point of the gelled solvent. The latter opens an interesting possibility of using such gels as reaction or crystallization vessels. Experiments in this direction are in progress.

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