

An Insight Into the Gelation Properties in Multi-Component Gels

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ABSTRACT

The self-assembly process in multi-component supramolecular gels depends on the nature of various non-covalent interactions. The molecular assembly is also influenced by the geometry and spatial arrangement of the functional groups, making it challenging to understand the nature of self-assembly in multi-component supramolecular gels. We have previously reported the self-assembly modes in enantiomers based on bis-terephthalic amides of valine methyl ester. In this work, we are analyzing the role of alkyl side chain in the self-assembly process of multi-component gels by changing the amino acid into alanine derivative. The gelation experiments performed in the aqueous solvent mixtures proved that mixing enantiomers based on terephthalic amide of alanine methyl ester resulted in weaker gels in comparison with the individual enantiomeric gels. Analyzing the thermal strength using sol-gel transition temperature and mechanical strength using rheological measurements revealed the individual enantiomeric gels were more robust than the mixed gel. The morphologies of the individual and the mixed gels were analyzed by using scanning electron microscopy (SEM), which revealed that there was no change in morphology. These results indicated that the self-assembly mode in multi-component supramolecular gels depends on the substituents of the building blocks.

INTRODUCTION

Multi-component systems are an excellent class of smart materials with a wide range of applications such as high tunability of properties, robust mechanical properties, high stability, and resistance to high yield strain.¹ Multi-component gels are often made up of two or more components mixed together in a precise ratio, as well as the addition of foreign particles containing organic or inorganic moieties to the individual system.²⁻⁴ This can be achieved by mixing individual gels, gelator with a non-gelator, or two non-gelators, which form gels when mixed together.⁵ Multi-component gels based on mixing two gelators result in self-recognition at the molecular level, and the individual gelator molecules can form independent fibers (self-sorting), or self-assemble in a specific (specific co-assembly) or random way (random co-assembly).⁶ We are interested in multi-component gels based on enantiomeric low molecular mass gelators (LMWGs) with structural similarity because of their tunable gel-state properties.⁷ Moreover, enantiomeric gelators favor co-assembled fibers rather than self-sorting,⁸ but structurally non-similar gelators tend to self-sort.⁹

In recent years, multi-component systems based on enantiomeric gelators have emerged as a prolific field in LMWGs due to their intriguing potential applications and tunable

properties.¹⁰⁻¹² Although chirality is not an essential factor for gelation, the majority of the gels are based on chiral compounds resulting in LMWGs with favorable properties. The self-recognition in multi-component gels based on enantiomers occurs at the molecular level, and these individual enantiomers interact with one another to produce gels with better packing and favorable properties.^{10, 13} We have shown that the mixed enantiomeric gels displayed enhanced thermal and mechanical stabilities compared to the individual enantiomeric gels,^{8, 14} and have proved that specific co-assembly was obtained in multicomponent gels based on terephthalic amide of methyl valinate (**TAV**) using single crystal X-ray diffraction.⁸ However, predicting the formation of co-assembled or self-sorted multi-component gels is a challenging task since it depends upon various parameters such as the gelation condition, nature of functional groups, mutual interaction, pH, and temperature.¹⁵

In this work, we are analyzing the nature of the alkyl side chain in the self-assembly modes of multi-component gels based on terephthalic amide of methyl alaninate (**TAA**). The mechanical strength of these gels will be studied by rheology, which will enable us to analyze the self-assembly modes in multi-component supramolecular gels.

EXPERIMENTAL SECTION

The starting materials and solvents were commercially purchased from Sigma-Aldrich and TCI-Europe and were used as supplied. The gelation experiments were performed using deionized water. Enantiomeric (*S* or *R*)-alanine methyl ester was purchased as a hydrochloride salt. ¹H and ¹³C NMR spectra were recorded on a Bruker AVANCE 400 spectrometer. Rheological experiments were performed on an Anton Paar MCR 302 rheometer and the morphology of the xerogel was analyzed by scanning electron microscopy (SEM) on a Leo Supra 25 Microscope.

Synthesis: The **RR-TAA** and **SS-TAA** were synthesized following a reported procedure from our group.¹⁶ The mixed form (**RR+SS**)-**TAA** was prepared by mixing equimolar ratio of individual **RR-TAA** and **SS-TAA** compounds.

Gelation test: In a standard 7.0 mL vial with an inner diameter of 1.5 cm, an appropriate amount of the compound was taken, and 1.0 mL of solvent/solvent mixture was added. An equimolar ratio of individual **RR**- and **SS**- compounds were added to prepare the (**RR+SS**), followed by the addition of the solvent/solvent mixture. The vial was closed, gently shaken, and heated to get a clear solution, and then left undisturbed for gelation. After 24.0 h, an inversion test was performed to confirm the gel formation.

Sol-gel transition temperature (T_{gel}): T_{gel} measurements were performed with the **TAA** gels obtained in various aqueous mixtures. After 24 h since the gelation test, a tiny spherical glass ball (106.0 mg) was gently placed on top of the gel. The vial was immersed in an oil bath fitted with a thermosensor and magnetic stirrer. The temperature of the oil bath was steadily increased by 10.0 °C per minute. The glass ball gradually immersed into the gel upon heating, and the temperature at which the glass ball touches the bottom of the vial was noted as the T_{gel} .

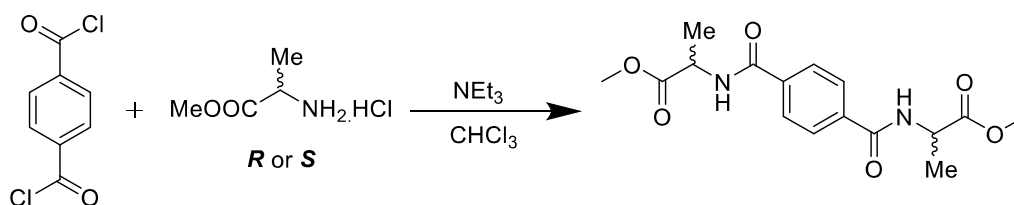
Rheology: The mechanical strengths of the gels prepared in ethanol/water and DMF/water (1:1, v/v) were measured in an Anton Paar MCR 102 modular compact rheometer utilizing a stainless-steel parallel plate geometry design with a diameter of 25.0 mm. Gels of **RR-TAA** and **SS-TAA** were prepared at 50.0 mg of the corresponding gelator in 1.0 mL of the solvent mixture, while the (**RR+SS**)-**TAA** gel was prepared by dissolving a mixture of 25.0 mg of **RR-TAA** and 25.0 mg of **SS-TAA** in 1.0 mL of the solvent mixture. Experiments were carried out by scoping a ~1.0 mL portion of the gel on the plate. The viscoelastic properties were evaluated by oscillatory measurements at a constant temperature of 20.0 °C.

Amplitude sweeps were performed with a constant frequency of 1.0 Hz and log ramp strain (γ) = 0.01–100%, while the frequency sweeps were carried out between 0.1 and 10.0 Hz within the linear viscoelasticity domain (0.02% strain). For frequency and amplitude sweeps, a Peltier temperature control hood was employed to avoid evaporation and maintain a temperature of 20.0 °C.

Scanning Electron Microscopy (SEM): The mixed gel of **TAA** gelators was prepared at 5.0 wt/v% in DMF/water (1:1, v/v). Gel obtained was filtered after a span of 24.0 h. It was then dried in air to obtain the xerogel, and a small portion of the xerogel was placed on a pin mount with the carbon tab on top and was coated with gold for 2.0-3.0 min. On a Leo Supra 25 microscope with an in-lens detector at an operating voltage of 3.0 kV, and with a working distance of 3.0-4.0 mm, the morphology of the dried gel was examined.

RESULTS AND DISCUSSION

Chiral LMWGs has been utilized as a viable candidate in many domains, including asymmetric catalysis, chiral nanomaterials, and chiral identification.¹⁷ We have selected terephthalic amide of amino acid derivatives due to its ability to generate C_2 -symmetric chiral LMWGs.⁸ The amino ester-based terephthalic amides are known to be excellent candidates for the enantiomeric multi-component gels, as the starting materials are available in both enantiomeric forms, and are inexpensive, and ease of modification.⁷ The diamides are known to exhibit β -tape type self-assembly to form a well-defined fibrous network, both in enantiomeric and mixed forms. The conversion of the carboxylic acid group to ester derivative prevents the hydrogen bonding interaction between the carboxylate and amide functionalities to retain the one-dimensional self-assembly mode of the amide moiety.¹⁸ Thus, we have synthesized (Scheme 1) and characterized enantiomeric forms of terephthalic amide of methyl alaninate compounds (**TAA**), and the analytical data matched with our reported data.¹⁶ The gel-state properties were compared with the valine derivatives (**TAV**) to analyze the role of substituents in the gelator structure.



Scheme 1: Synthesis of **RR-TAA** and **SS-TAA**.

The gelation experiments were performed (1.0 - 5.0 wt/v%) with the enantiomeric and mixed forms in aromatic solvents such as *p*-xylene and mesitylene. The individual enantiomers formed gel in these solvents, but gelation was not observed for mixed form, presumably due to the destructive co-assembly in comparison with the constructive co-assembly in **TAV** compounds. The enantiomeric and the mixed forms were not soluble in water, which made us use aqueous mixtures to evaluate the gelation properties in the mixed solvents. We have performed the experiments in the aqueous mixtures (1:1, v/v) of DMF, DMSO, and ethanol. The compounds were dissolved in polar solvents (DMF, DMSO, and ethanol) followed by the addition of water, and the resulting aqueous mixture was heated to get a clear solution. The solution was then cooled and left undisturbed, and gels were formed in all cases (Figure 1).

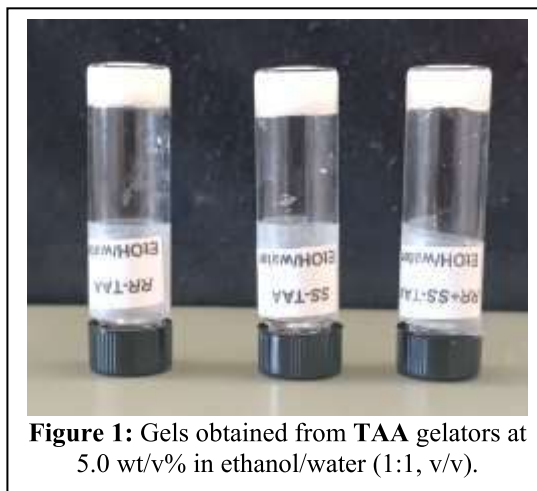


Figure 1: Gels obtained from TAA gelators at 5.0 wt/v% in ethanol/water (1:1, v/v).

The thermal stability of the gel network was measured by recording the sol to gel transition temperature (T_{gel}) using the ‘dropping ball’ method. The gels were prepared at 5.0 wt/v% in aqueous mixture (1:1, v/v) of DMSO, DMF, and ethanol. Analysis of T_{gel} values indicated that ***RR*-TAA** and ***SS*-TAA** had similar thermal stability (Table 1), but the mixed gel (***RR+SS*-TAA**) displayed lower T_{gel} values compared to the enantiomeric gels (***RR*-TAA** and ***SS*-TAA**) (Table 1). These results indicated that the mixed gels may have a different self-assembly mode with lower thermal strength compared to individual gels.

Table 1. Sol–Gel Transition Temperature (T_{gel})

Solvent (1:1, v/v)	T_{gel} (°C)		
	<i>RR</i>-TAA	<i>SS</i>-TAA	<i>(RR+SS)</i>-TAA
Ethanol/water	75.6	77.2	64.5
DMSO/water	86.3	87.4	76.9
DMF/water	73.0	71.8	49.0

Rheology was performed to study the semi-solid properties of the **TAA** gels. Rheological measurements were performed at 5.0 wt/v% in aqueous mixture of DMF and ethanol (1:1, v/v). The linear viscoelastic region (LVR) was obtained from the strain sweep experiments. The LVR ensured that the gels underwent reversible deformation during the trials, which will enable us to examine the exact mechanical strength of the gels. The amplitude sweep measurement revealed that all the enantiomeric and the mixed gels displayed lower storage modulus (G') from 0.02% of strain (Figure 2). Around 0.5 - 3.0% of strain was observed to be the crossover point where the gel network collapsed to the liquid phase (Figure 2). Frequency sweep experiments showed that all the gels have higher storage modulus (G') than loss modulus (G'') under varying frequency, corroborating gel-like behavior (Figure 3). Analysis of the frequency sweep revealed that enantiomeric gels (**RR-TAA** and **SS-TAA**) were stiffer than the mixed gel (**RR+SS**)-TAA in DMF/water (~10 times) and ethanol/water (~20 times) at 1:1 v/v (Figure 3). This supports the fact of an altered self-assembly mode upon mixing the enantiomers, which resulted in decreased mechanical strength in the mixed gels in comparison with the enantiomeric gels. As mentioned above, this is due to the change in self-assembly modes in mixed gels (co-assembly) and the comparison of the thermal (ethanol/water) and mechanical stabilities (ethanol/water and DMF/water) of individual and mixed gels of valine⁸ and alanine derivatives supported this hypothesis. Thus, the addition of two carbon atoms to the alanine-based gels resulted in enhanced thermal and mechanical stabilities for mixed valine derivatives prepared by mixing **TAV** enantiomers (crystallized from ethanol/water) which indicate the role of substituents in tuning the gel state properties.

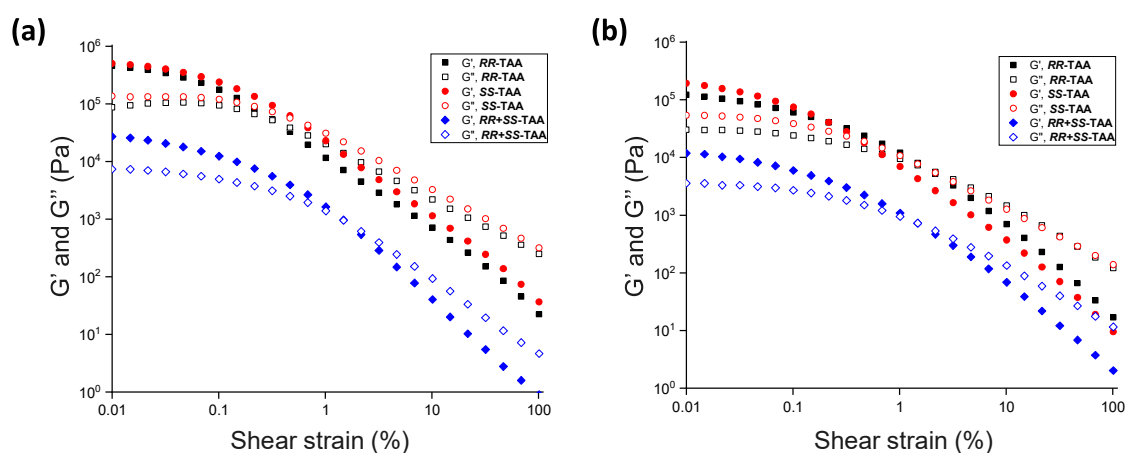


FIGURE 2. Strain sweep experiments with **TAA** gels (5.0 wt/v%) in (a) DMF/water (1:1, v/v), (b) ethanol/water (1:1, v/v) at 20.0 °C measured at a constant frequency of 1.0 Hz.

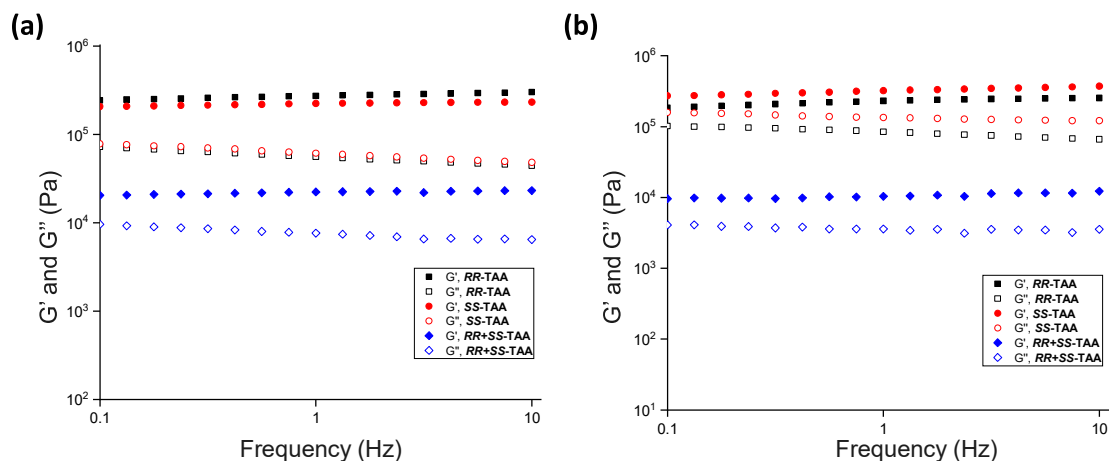


FIGURE 3. Frequency sweep experiments with **TAA** gels (5.0 wt/v%) in (a) DMF/water (1:1, v/v), (b) ethanol/water (1:1, v/v) at 20.0 °C measured at a constant strain of 0.02%.

SEM is an efficient tool to visualize the morphology and the nature of the self-assembled fibrous network in LMWGs.^{19,20} For instance, fibers with comparable morphologies as individual components will predominantly be found in self-sorted systems, but fibers with distinct morphologies are visible in co-assembled systems. The SEM images of the **RR-TAA** and **SS-TAA** in DMF/water (1:1, v/v) were previously reported, which formed thicker fibers with fiber width ranging 0.5 to 15.0 μm .¹⁶ The dried gel of the mixed form (**RR+SS**)-**TAA**, displayed similar morphology with identical fiber width. Hence, the mixing of enantiomers did not affect the morphology of the fibers in the selected solvents. Similar morphologies were observed for valine-based gelators in ethanol/water (1:1, v/v).⁸

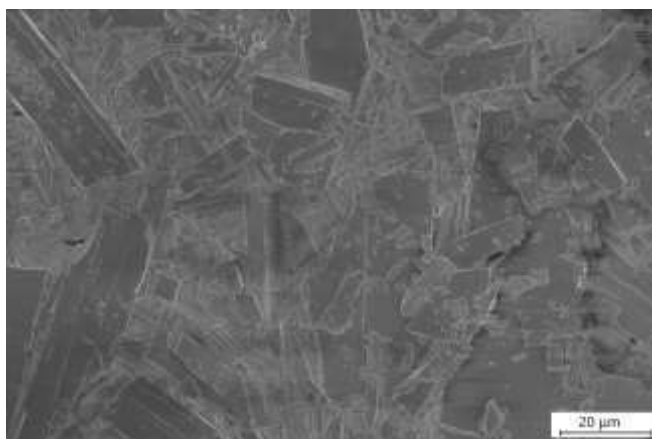


FIGURE 4. SEM image of the dried gel obtained from (**RR+SS**)-**TAA** in DMF/water (1:1, v/v) at 5.0 wt/v%.

CONCLUSION

The self-assembly in multi-component system based on terephthalic amide of methyl alaninate (**RR+SS**)-**TAA** was studied using T_{gel} and rheological experiments. The enantiopure compounds and the mixture formed gel in the aqueous mixture (1:1, v/v) of ethanol, DMSO,

and DMF, respectively. The mixed gel displayed lower thermal stability in comparison with the enantiomeric gels. Oscillatory amplitude- and frequency-sweep experiments revealed that the mixed gel displayed lower mechanical strength compared to the enantiopure gels. These results indicate that the self-assembly mode in the mixed gel is different from individual enantiomers, presumably due to the co-assembly (specific or random) rather than self-sorting. The effect of the substituents in gel network formation was analyzed by comparing the results with the next analogous **TAV** gels, and the results indicated that adding two carbon atoms enhanced the thermal and mechanical strength of the multi-component gels. These results indicate that the length of the substituents is crucial in designing multi-component LMWGs with tunable properties.

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