Robust gels created using a self-assembly and covalent capture strategy†

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The self-assembly of dendritic building blocks containing multiple terminal alkenes on their surfaces yields soft gel-phase materials – subsequent Grubbs' metathesis leads to covalent cross-linking between the alkenes and the formation of robust swellable gels.

The self-assembly of individual molecules allows the creation of complex supramolecular nanomaterials.[1] Recently, significant interest has developed in the covalent capture of self-assembled architectures *via* a subsequent chemical reaction step. In 1995, Ghadiri and co-workers reported the use of Grubbs' ring-closing metathesis reaction to trap self-assembled peptide cylinders.[2] Indeed, since this initial report, cross-linking has been used for the covalent capture of self-assembled peptides and proteins, with the synthetic strategies including olefin metathesis, disulfide bond formation and lysine cross-linking.[3] Covalent capture has also been of use in synthetic systems, with Reinhoudt and co-workers demonstrating how complex assemblies of hydrogen bonded calix[4]arenes can be effectively trapped.[4] Zimmerman and co-workers pioneered the use of dendritic architectures with peripheral alkene groups for the covalent fixation of non-covalent assemblies, for example hollow nanotubes.[5] The multiple alkene groups on the dendritic surface provide many points of reaction for effective cross-linking and this is therefore a good strategy for the capture of structural information. A similar dendritic strategy has been applied to cross-linking the surfaces of metal nanoparticles by the groups of Feldheim and Peng.[6]

Gels composed of low molecular weight gelators are nanostructured materials in which individual molecular scale building blocks self-assemble into nanoscale morphologies (often fibres).[7] However, gels assembled in this way generally have little materials strength as a consequence of being held together solely by non-covalent interactions. A number of attempts have therefore been made to 'capture' the self-assembled architectures in a more robust form. Shinkai and co-workers have led the development of inorganic–organic hybrid materials – templating silica growth on the nanoscale organic fibres.[8] Recently, the self-assembled structures underpinning gels have been captured in a more direct manner. Weiss and George synthesised organogelators containing diacetylene units.[9] Diacetylenes polymerise in the solid state *via* 1,4-addition reactions if the monomer units are appropriately aligned. On UV irradiation of the gels, polymerisation occurred within the ordered gel fibres to yield an insoluble covalently linked polymer. Similarly, the groups of Kim and Shinkai have used the same approach to achieve post polymerisation of gel fibres.[10] Indeed, Kim and co-workers used UV irradiation to cross-link the surfaces of dendritic gelators functionalised with diacetylene units.

We have recently developed a versatile dendritic system which self-assembles to yield gel-phase materials.[11] We reasoned that the presence of multiple surface groups on the branched architecture of this type of molecule provided excellent prospects for effective cross-linking within the self-assembly. We were interested in making our system as general as possible, and therefore decided to use cross-linking between simple alkene groups (*via* Grubbs' ring-closing metathesis)[12] in order to achieve covalent capture of our self-assembled architectures. As such, this paper is one of the first examples in which a soft gel is converted into a robust gel *via* chemical (rather than photochemical) methods.

Compound **1** (Fig. 1) was synthesised (see supp. info.) in a 3-step process. Firstly, 1-undecanoic acid was coupled to the free amine groups of lysine methyl ester in excellent yield (81%). The ester group was then saponified using sodium hydroxide (89% yield) and the resultant material was coupled twice to cystamine dihydrochloride to yield the desired product in good yield (46%). The intermediates and product were fully characterised using all appropriate methods (see supp. info.).

Compound **1** formed gels in non-hydrogen bonding, apolar, organic solvents such as toluene, dichloromethane and chloroform. Measurement of T_{gel} values *via* the tube inversion method indicated that, in toluene, this gelator formed a gel which was thermally stable up to 107 °C (concentration $\geqslant$ 9 mM). Differential scanning calorimetry exhibited an endothermic peak, with a peak maximum in agreement with the T_{gel} value determined by tube inversion.

Variable temperature NMR experiments were performed on compound **1** in d_8-toluene. From 20–60 °C, no peaks corresponding to the amide N–H peaks could be identified – consistent with these peaks being broadened due to their immobilisation through hydrogen bond interactions. These specific intermolecular hydrogen bond interactions are primarily responsible for the self-assembly of compound **1** into gel-phase materials. Interestingly, in

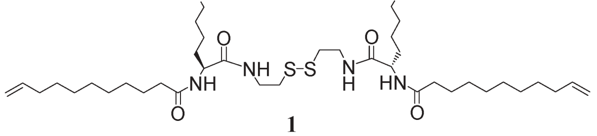

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Fig. 1 Branched gelator **1**.

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the same temperature range, broad NMR signals *could* be observed for the alkene protons – indicating that the peripheral groups retain some mobility within the gel-phase network.

Scanning electron microscopy (SEM) was performed on a sample dried from a low concentration of compound **1** (4 mM in toluene). Inter-tangled fibre bundles (longer than 1 μm) were observed, each consisting of several individual smaller fibres (Fig. 2). The diameter of a single fibre was measured as *ca.* 20 nm.

In spite of being thermally stable, these supramolecular gels were, as is usually the case for this type of material, relatively weak. Indeed, vigorous shaking of the sample was sufficient to break down the gel into an isotropic solution. We were therefore interested in using a covalent fixing step to generate a gel which may exhibit more robust materials properties. The aim was to use ring-closing metathesis to cross-link the multiple surface groups of the self-assembled gelator molecules.

Initially, as a control experiment, ring-closing metathesis was performed on compound **1** in dichloromethane/methanol at a concentration of 10 mM. Methanol is a competitive hydrogen bonding solvent, which inhibits the self-assembly of compound **1**. Treatment of **1** with Grubbs' second generation catalyst[13] led to 73% consumption of starting material to yield a soluble product. By electrospray mass spectrometry (ESMS) the only observed products were determined to be single and double *intramolecular* ring-closed products (*e.g.* **2** and **3**, Fig. 3). There are various possible isomeric forms of these compounds (not illustrated), but the formation of these was not characterised. No *intermolecular* ring-closed products were observed by mass spectrometry.

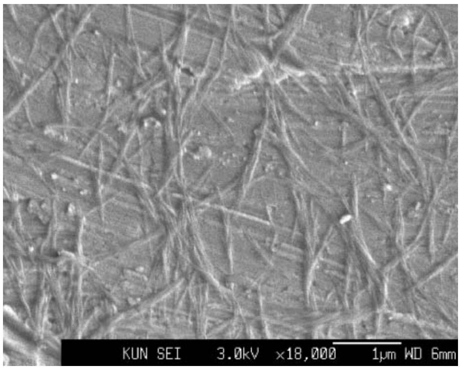

Fig. 2 SEM image of gel formed from dendrimer **1** in toluene (4 mM).

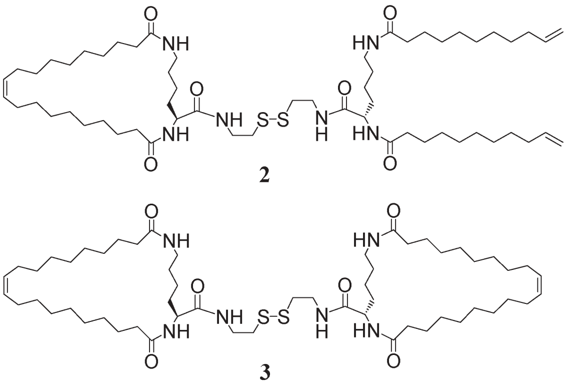

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Fig. 3 Intramolecular ring-closed products **2** and **3** formed from ring-closing metathesis of **1** in methanol solution. The different possible isomeric forms of these compounds are not illustrated.

The reaction was then performed using toluene as solvent, as compound **1** is known to self-assemble in these conditions (see above). A concentration of compound **1** of 0.5 mM was chosen for the reaction. This is below the minimum concentration at which the gel is completely immobile, ensuring effective mixing of the gelator and catalyst. A very viscous solution was obtained – indicative of self-assembly of the individual molecules into a network, but which cannot quite achieve macroscopic gelation. On the addition of Grubbs' second generation catalyst, the progress of the reaction was different to that observed in methanol solution. On removal of the solvent, a solid material was obtained. Of this solid, 65% was insoluble in toluene, whilst the remaining 35% was soluble. We characterised these two materials separately.

The soluble portion (35%) was examined by analytical gel permeation chromatography (GPC, Fig. 4). The peak at 26.4 min corresponds to a species with similar molecular weight to compound **1**, whilst GPC calibration (using a variety of dendritic systems made within our laboratory) indicated that the peaks at 24.9, 23.9 and 23.3 correspond (approximately) to *intermolecular* cross-linked dimers, trimers and tetramers of **1** respectively. The presence of dimer and trimer in the soluble fraction was confirmed by MALDI-TOF mass spectrometry (Fig. 5). This method showed

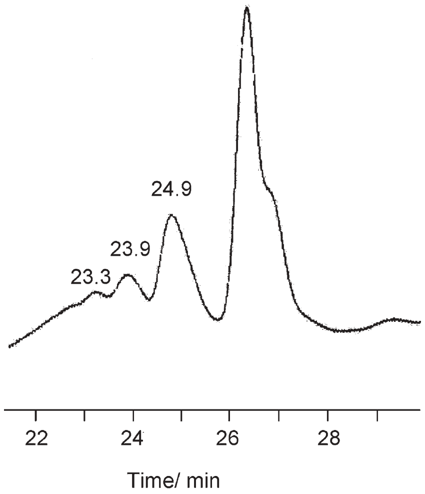

Fig. 4 GPC traces of soluble portion (35%) from ring-closing metathesis reaction of compound **1** in toluene solution.

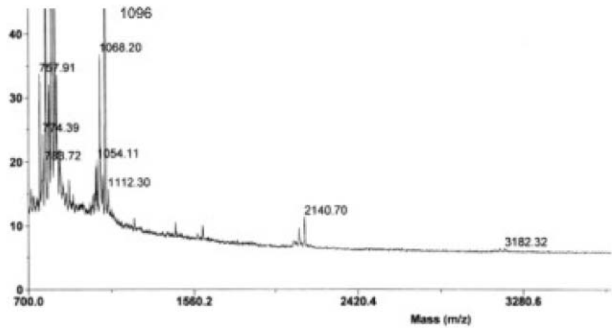

Fig. 5 MALDI-TOF mass spectrum of the soluble portion (35%) from ring-closing metathesis reaction of compound **1** in toluene solution.

a peak with *m*/*z* 1096, corresponding to unreacted starting material. A peak at 1068 was also observed, corresponding to an intramolecularly cross-linked species such as **2**. Interestingly, peaks at 2140 and 2112 were observed, corresponding to singly and doubly cross-linked *intermolecular* dimers respectively. In addition a small peak at *m*/*z* 3182 was noted, which corresponds to a doubly cross-linked *intermolecular* trimer. It is worth noting that in MALDI-MS, the peak heights do not necessarily correspond to the relative quantities of material present in the sample.

The insoluble fraction (65%) was then examined. The solid-phase FT-IR spectrum of the insoluble material was effectively identical to the spectrum obtained for the starting material, indicating that no dramatic changes (*e.g.* degradation) had occurred during the reaction. However, the insoluble product did not melt or decompose, even up to temperatures of 210 °C, whereas the melting point of compound **1** was 159–161 °C. This provides clear evidence of a chemical transformation within the structure. The insoluble material remained insoluble, even on extended boiling in dimethylformamide or dimethylsulfoxide. Taken together, these results indicate the likelihood of this material corresponding to a permanently captured, cross-linked material.

The insoluble material was sheet-like in nature (Fig. 6), whereas compound **1** was a powder. The dried material was brittle and its shape could not readily be altered. Most interestingly, however, the solid could be re-swollen on the addition of further amounts of toluene to the sample. This was a relatively rapid process. The resolvated material was far more pliable and robust, indeed it could be readily folded or flattened. Preliminary attempts to quantify the amount of solvent taken up by the material indicated that the material could absorb up to approximately ten times its own weight in toluene. The drying/resolvation process could be repeated many times. This behaviour is analogous to hydrogels used in applications such as contact lenses, which are typically composed of *ca.* 30% polymer and 70% water. Interestingly, with our material, the addition of a solvent which had *not been able to form gels* with compound **1** (*e.g.*, methanol) *did not cause re-swelling of the sample*. We therefore believe that re-swelling is due to solvation of the cross-linked network giving rise to its expansion. Clearly the covalently fixed material has a degree of 'memory' of its previous properties and behaviour (*i.e.*, solvent compatibility).

Preliminary scanning and transmission electron microscopy (SEM and TEM) imaging experiments were performed on the insoluble material. The images (see supp. info.) supported the possible presence of some one-dimensional structures, although the objects observed by SEM did not have the same dimensions as the initial fibres – this could be a consequence of a degree of fibre–fibre cross-linking or could be an artefact of sample preparation. More conclusive morphological imaging is the subject of further work.

Fig. 6 Photograph of the sheet-like insoluble material recovered from the ring-closing metathesis reaction of compound **1** performed in toluene.

Overall, these results are consistent with the hypothesis that the self-assembly of **1** in toluene has a direct impact on the outcome of the ring-closing metathesis reaction, enabling the formation of oligomeric species and robust gels. As such the *intermolecular* products can be considered to be the result of an *intrasupramolecular* reaction.

In summary, this study has demonstrated that ring-closing metathesis is a plausible method for the covalent capture of gel-phase materials. The broad compatibility of this reaction, and the simple requirements for multiple alkene groups in the gelator molecules, means that this approach may be of general utility for the simple fabrication of more robust gels from soft self-assembled nanoscale materials. In future work we intend to identify and characterise the morphologies which underpin these robust gels and perform a more detailed investigation of their materials behaviour.

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