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PROPERTIES OF MOLECULAR GELS WITH CRYSTALLINE
NETWORKS**

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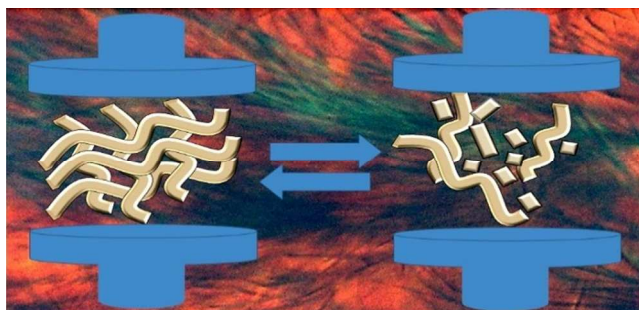
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Abstract:

This review focuses on correlations between the thixotropic and structural properties of molecular gels having crystalline fibrillar networks (**SAFINs**). Formation of thixotropic molecular gels and their recovery after the application of destructive strain depends on the strength and type of intermolecular interactions in the **SAFINs** of the gelator molecules. Here, we limit our discussion to gelator molecules with simple structures in order to dissect more easily the important contributors to the thixotropic behaviors. Possible mechanisms to explain the thixotropic phenomena, involving the transformation of the **SAFINs** into unattached objects, and their reassembly into 3-dimensional networks, are advanced. The data are analyzed to provide insights into the rational design of thixotropic molecular gelators.

Introduction:

Self-assembled materials change their mechanical properties, sometimes reversibly, when disturbed by an external stimulus, such as temperature, electromagnetic radiation, electric field, pH, mechanical stress, etc.^{1,2,3} The probability of reversibility is linked to morphological changes on the microscopic distance scale that are manifested macroscopically. Molecular organogels, one type of self-assembled ‘soft matter’, are comprised of low molecular-mass organogelators (**LMOGs**) that organize into 3-dimensional (3D) fibrillar or other networks (i.e., self-assembled fibrillar networks, **SAFINs**) that entrap macroscopically the liquid in which they reside.⁴⁻⁹ They have become an important subclass of soft matter because of the insights they provide to how molecules aggregate as well as their potential and realized applications.^{10,11}

Thixotropy can be defined as the “...reversible reduction and recovery of elastic modulus, yield stress and viscosity isothermally upon the application and removal of a destructive shear strain.”¹² Examples of thixotropic materials range from paints and foods to biological materials such as actomyosin¹³ and tooth enamel.¹⁴ The reversible mechanotropic properties occur as a consequence of structural reorganizations of self-assembled aggregates on the microscopic distance scale. In many cases, the source of the microscopic changes can be traced to the loss or gain of weak, intermolecular interactions, such as H-bonding, electrostatic forces, π - π stacking, and London dispersion forces.^{15,16,17} Molecular gels which are thixotropic regain a large part of their viscoelasticity after cessation of destructive mechanical strain. They are still relatively rare, and there are no design criteria for new types of **LMOGs** that lead to such gels.¹⁸ A recent, excellent review has described the properties of different types of molecular gels formed by sonication and mechanical stress, including some thixotropic molecular gels, without delving into the specific structural characteristics of the gelators and why they are thixotropic.¹⁹

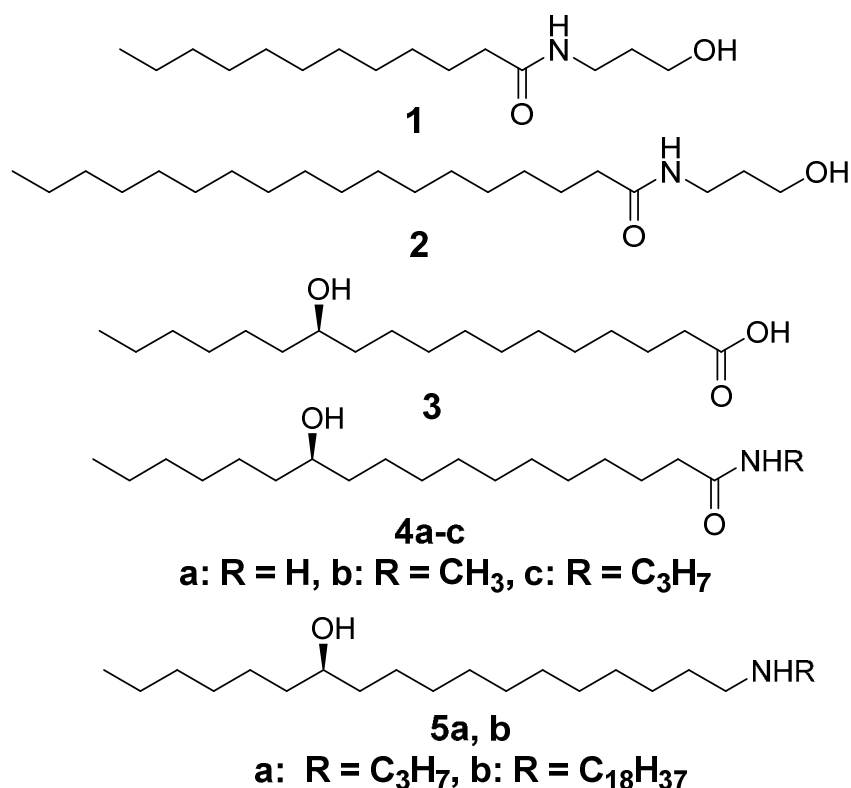
Most of the known thixotropic molecular gels have **SAFINs** that are not crystalline in nature. Many of these have organometallic **LMOGs**, so that their organization into a **SAFIN** (or its mechano-destruction) depends on the formation (or loss) of relatively weak metal-ligand bonds. An example is thixotropic hydrogels with a Cu(II)-pyridyl terminated oligophenylenevinylene as the gelator.²⁰ The **SAFINs** of many (but not all!) of these organometallic gels are non-crystalline²¹ or liquid-crystalline.²²

Examples of thixotropic molecular gels with crystalline **SAFINs** are even rarer, and their discovery remains primarily a matter of serendipity.²³ Also, most of them are only weakly thixotropic; they are able to regain only a small fraction of their initial viscoelasticity after cessation of destructive strain. To regain their original level of viscoelasticity, the mixtures of most of these gels must be heated to their sol/solution states and re-cooled to below the gel melting temperatures.

In this review, we summarize the efforts to employ structurally-simple molecular gelators which form crystalline, self-assembled fibrillar networks (**SAFINs**) to make thixotropic gels with substantial or complete recovery of their viscoelasticity after their mechanical transformation into sols. The distinction between thixotropic gels with non-crystalline and crystalline **SAFINs** is very important because the manner in which the gels regain their viscoelasticity can be completely different: whereas those with non-crystalline **SAFINs** can be transformed from 3D to 1D and back to 3D networks without disruption of fundamental intermolecular interactions, those with crystalline **SAFINs** must undergo a different set of intermolecular changes, some of which may be manifested at very different distance scales and involve much less disorganization. In order to understand these differences, we focus on examples where sufficient data are available to correlate the gel morphologies and characteristics

with the thixotropic properties and recovery kinetics of the gels after cessation of destructive mechanical stress. Here, the gelators leading are organized on the basis of molecular structure. Examples where degrees of recovery or recovery times have not been reported in the original articles will be noted. In addition, the manner by which the gels are formed from their sol phases (e.g., slow- or fast-cooled) can be a very important parameter in determining the thixotropic properties; except where noted, all of the gels discussed here were formed via a fast-cooling process in which the hot sol phases were placed in the air or in a cold water bath.

Aliphatic molecular gelators:



Scheme 1. Aliphatic molecular gelators based on *n*-alkanes with 2 hetero-functionalities.

The structurally simplest thixotropic molecular gelator that has been reported to date is *N*-(3-hydroxypropyl)dodecanamide (**1**).²⁴ The spherulite-like texture of the toluene gel of **1** that is seen by polarizing optical microscopy (POM) demonstrates that this **SAFIN** is comprised of crystalline objects (Figure 1).

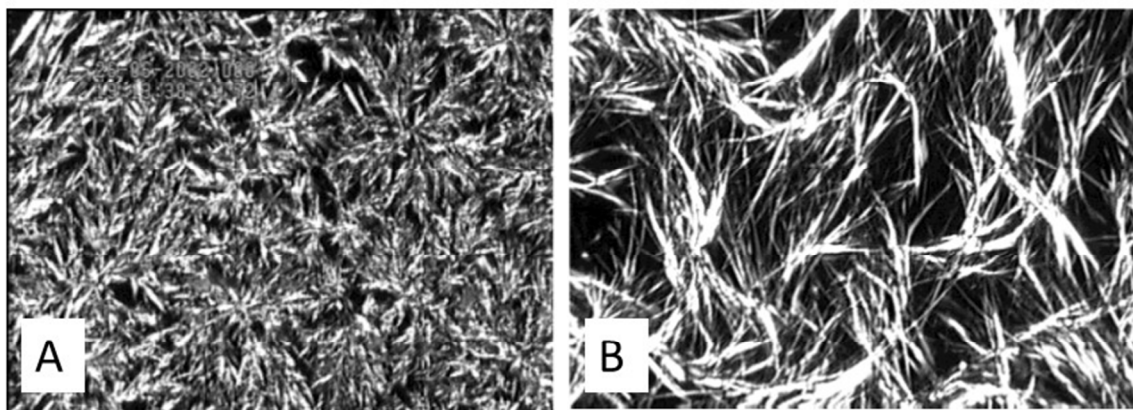


Figure 1. POM images of ~ 1 wt % **1** in toluene gels at 15 °C (A) 10 s after being quenched from the sol phase at 20 °C/min (full scale, 400 microns \times 280 microns) and (B) 1 h after being quenched from the sol phase 1 °C/min (full scale, 250 microns \times 175 microns). Adapted with permission from ref 24. Copyright (2004) American Chemical Society.

Upon application of a constant shear of 20 Pa for 1 min, the viscoelastic properties of the 1 wt % **1** in toluene gel (fast-cooled) were completely lost. The destruction of the gel was evidenced by the fact that the value of the loss modulus, G'' , became higher than that of the storage modulus, G' . Ca. 1000 s after removal of the destructive strain, the gel was completely reformed; G' returned to its initial value (i.e., before application of the destructive strain).²⁴

The mechanism of this thixotropy was hypothesized based upon results obtained from a rheometer equipped with an optical microscope (Figure 2).²⁴ A ‘jammed phase’ with inhomogeneous flow that is characteristic of a gel (Figure 2A) was observed for a ~ 2 wt % **1** in toluene gel at a shear rate within the linear viscoelastic region, 10 s⁻¹ (Figure 2A). Upon application of destructive strain, the **SAFIN** underwent a phase transition from the ‘jammed’ to another phase in which many of the fibers become disconnected and aligned (Figure 2B); the fibrillar objects are no longer connected at their junction zones. If the elements of the **SAFIN** are connected by H-bonding interactions along their surfaces, the force (i.e., destructive strain)

needed to break the junction zones will not be very large, and the cessation of destructive strain allows the aligned fibers to diffuse rotationally and to reform a **SAFIN**.²⁴

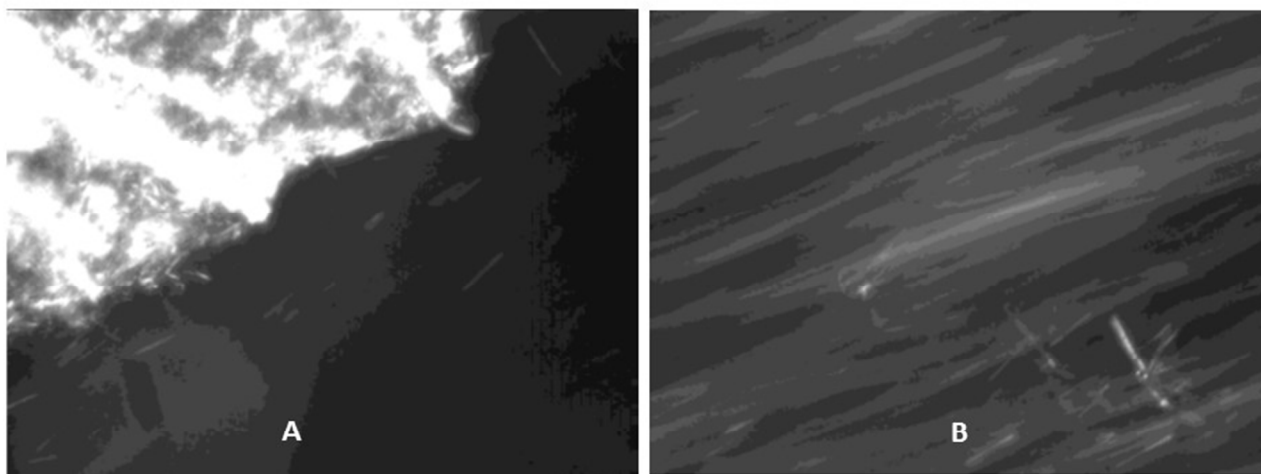


Figure 2. Rheo-optic images of fast-cooled **1** in toluene (~2wt %) showing inhomogeneous flow (A, shear rate 10 s^{-1}) and aligned aggregates (B, shear rate 500 s^{-1}). Full scale: 400×280 microns. Adapted with permission from ref 24. Copyright (2004) American Chemical Society.

The 1 wt % **1** in toluene gel prepared from the sol phase by fast cooling (i.e., at a rate of $20 \text{ }^{\circ}\text{C}/\text{min}$) and slow cooling (i.e., at a rate of $1 \text{ }^{\circ}\text{C}/\text{min}$) have different **SAFINs** on the micrometer distance scale (Figure 1). Thixotropic studies of the slow-cooled toluene gels of **1** were not reported.

Interestingly, an octadecanamide homologue of **1**, *N*-(3-hydroxypropyl)octadecanamide (**2**), does not gelate toluene.²⁵ Increasing the alkyl chain length from 12 carbon atoms in **1** to 18 carbon atoms in **2** increases the London dispersive interactions in the aggregates, and we conjecture that this increase is the cause of the precipitation of **2** without gel formation. The fast-cooled sols of 2 wt % **2** in isostearyl alcohol yielded gels, but they did not recover their viscoelasticity after cessation of the application of destructive strain.²⁵

The absence of thixotropy in the isostearyl alcohol gel of **2** may be related to the lack of a ‘lubrication’ effect from hydroxyl groups. In somewhat related research, liquid crystallinity has been induced by addition of 1 molar equivalent of methanol to several solid methyl-tri-*n*-alkylphosphonium salts or placement of an ω -hydroxyl group on a short alkyl group of a phosphonium salt having 3 long alkyl chains.^{26,27,28} We hypothesize that hydroxyl groups added to the terminal carbon atoms of the alkyl groups of **6a** enhance the thixotropic behavior of their crystalline gels by an analogous type of ‘lubrication’ within their **SAFINs**.²⁵

Organogels with many derivatives of (*R*)-12-hydroxystearic acid as the **LMOGs** exhibit thixotropic properties.²⁵⁻²⁹ For example, a 2 wt % fast-cooled silicone oil gel of **3** is thixotropic, and ~70 % of its *G'* value was recovered after cessation of the application of destructive strain.²⁹ Thus, 50 % strain disrupted the extensive H-bonding interactions of the ribbon-like **SAFINs** (Figure 3) in a manner similar to that reported for the **1** in toluene gels. Upon the cessation of the destructive strain, the **SAFINs** are reformed by a process thought to involve H-bonding interactions among the hydroxyl groups on the chiral carbon atoms of **3** (Figure 3).²⁴ Spherulitic textures observed for the organogels of **3** confirm that its **SAFINs** are crystalline.^{29,30} In addition, these organogels exhibit enhanced circular dichroic signals resulting from the helical arrangements of the molecules in its **SAFINs**.^{31,32}

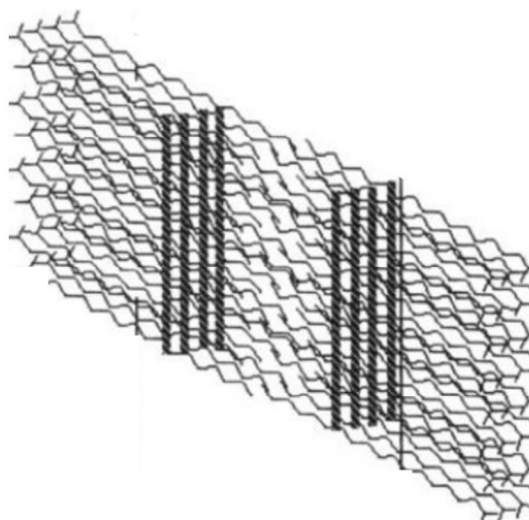


Figure 3. Structural model of the **3** fibrillar or ribbon-like aggregates in organic solvents with the parallel vertical lines representing the direction of the H-bonding network. Adapted with permission from ref 30. Copyright (1994) American Chemical Society.

As with the gels of **3**, the spherulite-like textures observed for ~ 2 wt % **4a** (Figure 4) and **4c** (Figure 5) in silicone oil confirm that its SAFINs are crystalline. The objects were larger when the gels were prepared from the sol phases by the fast-cooling protocol (20 °C/min).²⁹ Super-saturation and the greater driving force for phase separation of a sol in the fast-cooling protocol for sols resulted in smaller and more crystals.^{33, 34}

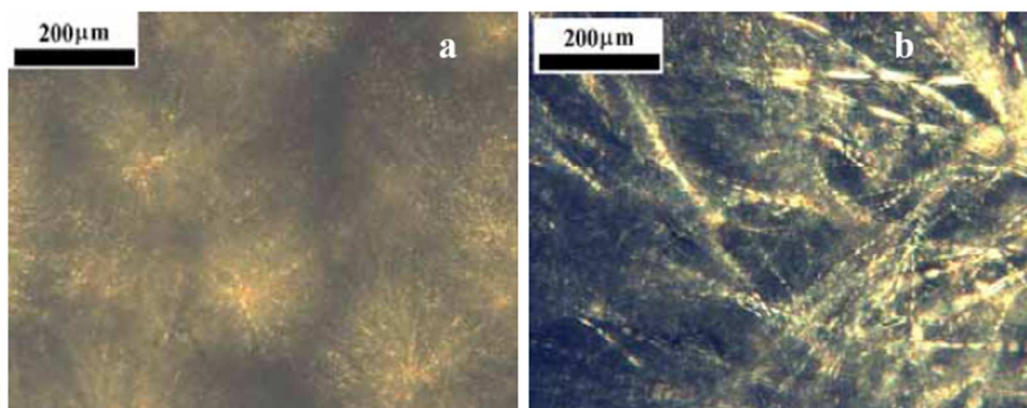


Figure 4. Polarizing optical micrographs at 24 °C of 2 wt % **4a** in silicone oil prepared by (a) fast-cooling and (b) slow-cooling protocols. Adapted with permission from ref 29. Copyright (2009) American Chemical Society.

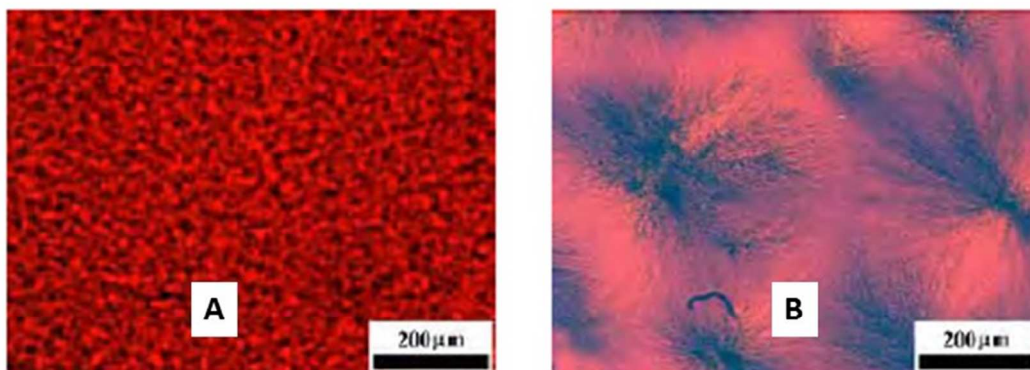


Figure 5. Polarizing optical micrographs at 24 °C of gels of 2 wt % **4c** in silicone oil prepared by (a) fast-cooling and (b) slow-cooling protocols. The images were taken with a full-wave plate. Adapted with permission from ref 29. Copyright (2009) American Chemical Society.

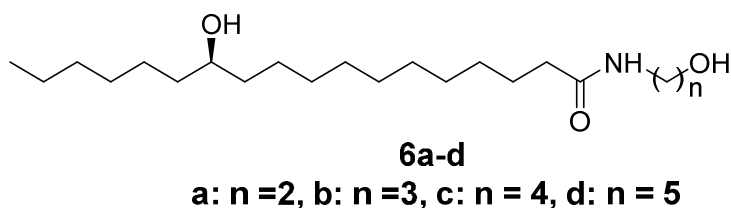
Table 1. Percentage of thixotropic recovery after application of destructive strain to fast-cooled gels of ~2 wt % **3-5** in silicone oil. In all cases, the recovery times were <10 s.²⁹

Gelator	% of recovery
3	~70 %
4a	90 %
4b	50 %
4c	50 %
5a	<10 %
5b	<10 %

The results in Table 1 show that the degree of recovery correlates qualitatively with the strength of potential hydrogen-bonding interactions among the hetero-functional groups on the LMOGs: 1° amide (**4a**) > acid (**3**) > 2° amide (**4b**) > 2° amine (**5a-b**). In fast-cooled silicone oil gels with 2 wt % **4a** (primary amide), ~90 % of the original G' value was recovered less than 10 s after cessation of destructive strain,²⁹ whereas the corresponding gels with 2 wt % of a 12-

hydroxy-*N*-alkyloctadecanamide (secondary amide, **4b** or **4c**) or 18-(alkylamino)octadecan-7-ols (secondary amine, **5a** or **5b**) recovered only ~50 % and ~10 %, respectively, of their initial G' values. Note that the thixotropic recovery for the parent molecule **3**, ~70 %, was less than that of the primary amide **4a** but significantly higher than the recovery when **LMOGs** with the less efficient H-bonding groups, secondary amides (**4b** or **4c**), were employed.

Correlations between the molecular structures and **SAFINS** can be explored for gelators containing 3 hetero-functional groups as well: an amide group, an ω -hydroxyl group on an *N*-alkyl chain, and a hydroxyl group at C12 of the octadecanamide backbone (**6a-d**).²⁵ POM images of gels consisting of 2 wt % **6a-d** in isostearyl alcohol and 2 wt % **2** in isostearyl alcohol are similar, showing spherulite-like **SAFINS**.²⁵



Scheme 2. Aliphatic thixotropic molecular gelators having 3 hetero-functional groups.

Only 38 % of the original G' value was recovered for a 2 wt % **6a** in isostearyl alcohol gel after cessation of the application of destructive strain.²⁵ However, subsequent destruction-recovery cycles resulted in > 99 % recovery of the immediately previous value, and the recovery time was calculated to be ~ 0.4 s.³⁵ The evolution and thixotropic recovery were analyzed using a stretched exponential model (eq 1)³⁶ in which τ represents the recovery time and m is a dimensionless constant.

$$\ln\left[-\ln\frac{G'(\infty)-G'(t)}{G'(\infty)-G'(0)}\right]=m\ln t-m\ln\tau \quad (1)$$

By contrast, a fast-cooled 2 wt % **6b** in isostearyl alcohol gel at 25 °C recovered ~99 % of its initial G' value after cessation of the application of 30 % destructive strain, and this level

of recovery was found over several additional cycles (Figure 6). The recovery time was calculated to be ~ 0.6 s. Differences in the morphology of the two isostearyl alcohol gels are indicated by comparisons of their solvent-subtracted X-ray diffraction patterns (Figures 7a,b). Note also that the neat solid and SAFIN diffraction patterns for **6b** differ as well.²⁵

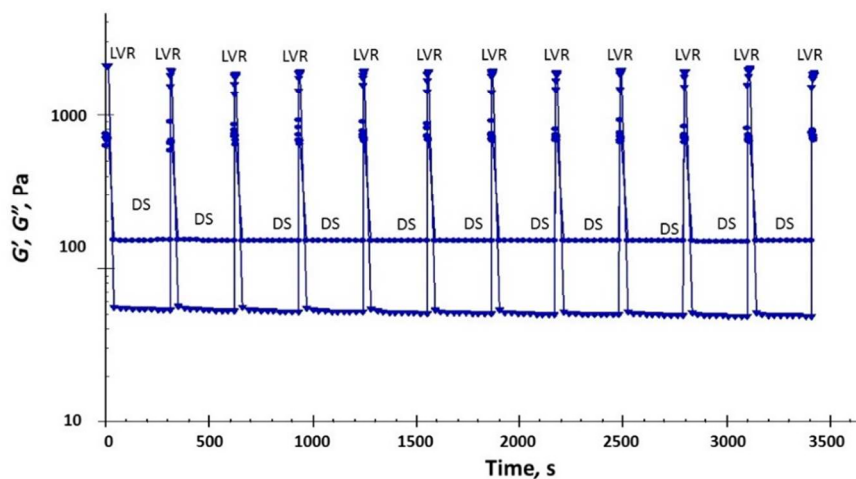


Figure 6. G' (\blacktriangledown) and G'' (\blacksquare) at 25 °C as a function of time and application of different strains and frequencies to a fast-cooled 2.0 wt % **6b** in isostearyl alcohol gel. Linear viscoelastic region (LVR): $\gamma = 0.05$ %, $\omega = 100$ rad/s. Destructive strain (DS): $\gamma = 30$ %, $\omega = 1$ rad/s. Rotational strain was kept at 0 % for 0.05 s before changing from DS to LVR conditions. Reproduced from ref 25 with the permission from the Royal Society of Chemistry.

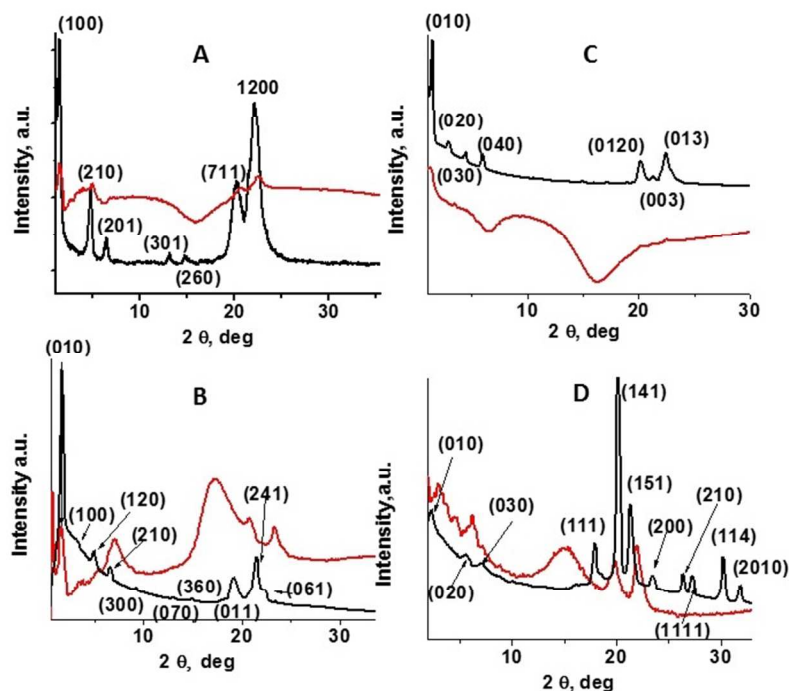


Figure 7. Vertically offset XRD patterns at 22 °C of neat **6a-d** (black; crystallized from ethyl acetate) and their ~ 5 wt % isostearyl alcohol gels (red) after empirical subtraction of the liquid components: (A) **6a**; (B) **6b**; (C) **6c**; (D) **6d**. Reproduced from ref 25 with the permission from the Royal Society of Chemistry.

The recoveries of G' for 2 wt % isostearyl alcohol gels of **6c** and **6d** were ~99 % during the initial and subsequent destruction-recovery cycles, but the τ values were ~1000 and ~150 s, respectively. These results demonstrate that addition or subtraction of one methylene unit of **6a-d** has no significant effect on the eventual recovery of viscoelasticity after application of destructive strain, but has a very large effect on the rates of recovery. Again, the differences between the thixotropic behaviors of the isostearyl alcohol gels of **6c** and **6d** may be due to the differing morphologies of their SAFINs (Figures 7c,d).

A possible general model to explain the thixotropic properties of the **6a-d** in isostearyl alcohol gels is shown in Figure 8.²⁵ As with many molecular gel systems, above their gel melting temperatures (T_{gel}), **6a-d** exist as 0D objects (or as small aggregates if sols), and below T_{gel} they aggregate into 1D fibers joined at “junction zones” to form 3D SAFINs that immobilize the liquid. The gel networks are stabilized by intermolecular H-bonding interactions involving the

C12 hydroxyl groups of the octadecanoyl chains, the terminal ω -hydroxyl moieties on the *N*-alkyl chains, and the amide groups. The Bragg spacings derived from powder XRD diffractograms of gels of **6a-d** in isostearyl alcohol are consistent with a 'head-to-tail' bilayer packing arrangements in the SAFINs (Figure 7). The calculated extended length of a molecule of **6a** is 27.2 Å. That is half of the distance calculated from Bragg's law for the lowest reflection in the diffractogram, 54.6 Å. In 'head to tail' a packing arrangement of **6a** the H-bonding interactions of two C12 hydroxyl groups and of two amide groups on adjacent molecules can help to stabilize the crystalline lattice. In this model, application of destructive strain weakens the H-bonding interactions among the ω -hydroxyl groups at or near junction zones and disrupts the SAFIN without disassembling the individual fibers. These changes lead to macroscopic fluidity of the sample, and cessation of destructive strain allows the fiber networks to reassemble.

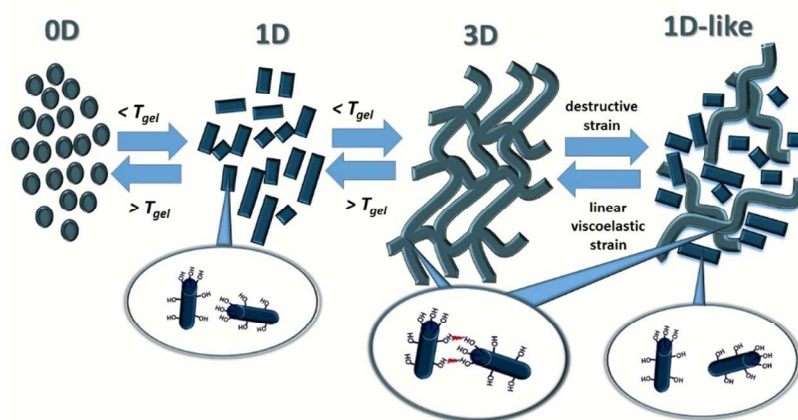
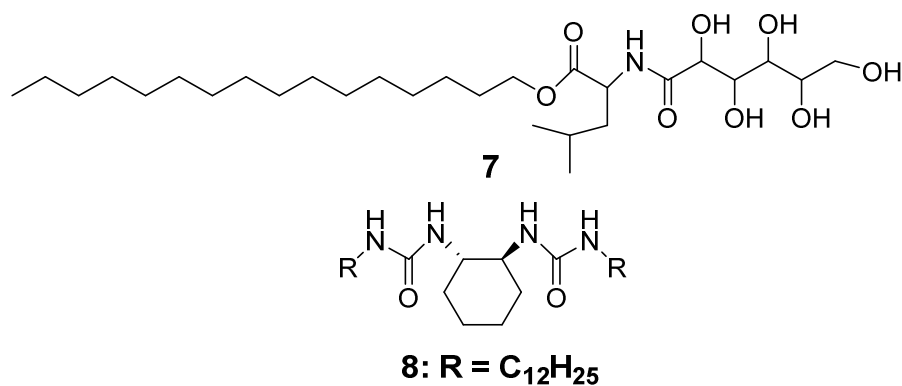


Figure 8. Cartoon representation of a possible mechanism for mechanotropic destruction and reformation of SAFINs in **6a-d** gels. Reproduced from ref 25 with the permission from the Royal Society of Chemistry.



Scheme 3. Aliphatic thixotropic molecular gelators having more than 3 hetero-functional groups.

7 and **8** are examples of thixotropic gelators having more than 3 hetero-functional groups. In principle and without consideration of packing constraints in the **SAFINs**, it seems reasonable to assume that the large number of hydroxyl groups in **7** and the strongly associating urea groups in **8** will increase H-bonding interactions and perhaps ‘lubricate’ their **SAFINs**, resulting in faster and more efficient thixotropic recovery. Unfortunately, only qualitative data concerning the organogels of **7** have been reported. Thus, rapid shaking of a 3 wt % **7** in liquid paraffin gel led to a sol phase which, upon being left at rest, became a gel again.³⁷

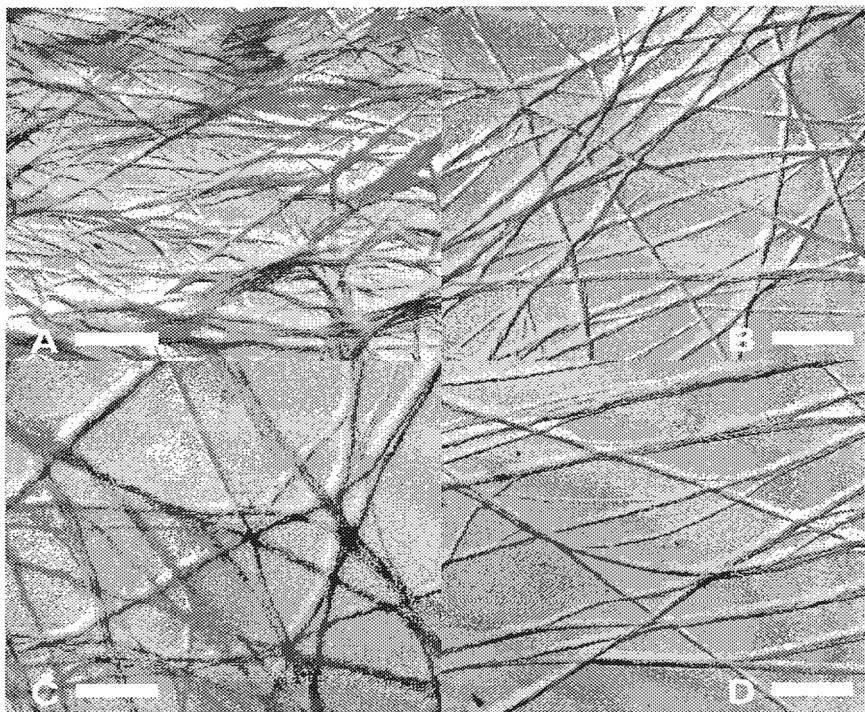
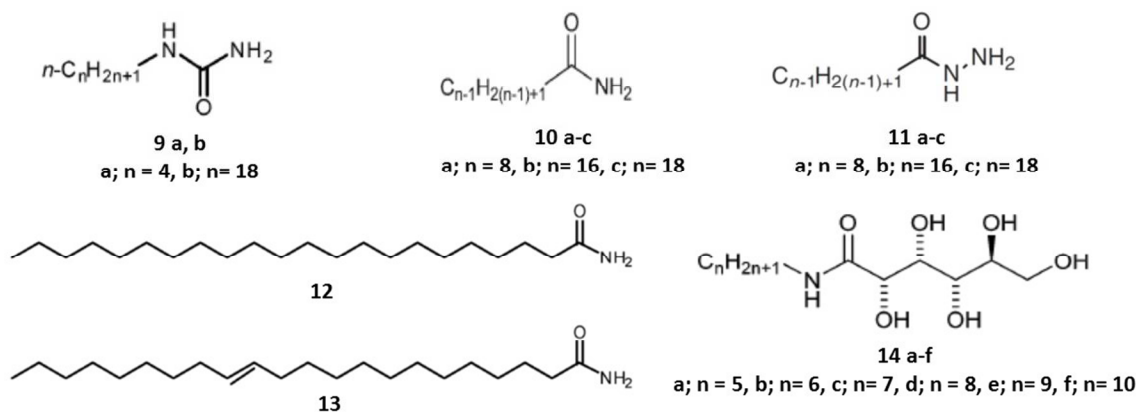


Figure 9. Transmission electron micrographs of xerogels of **8** in 1-propanol (A), 1-butanol (B), 1-hexanol (C), and 1-octanol (D). The concentration of **8** is in all cases was 9 mM, and the gels had been aged for 16 h at 20 °C prior to their preparation for TEM analyses. The bars are 500 nm. Adapted with permission from ref 38. Copyright (2000) American Chemical Society.

Gels of enantiomerically pure *trans*-1,2-*bis*(3-dodecylureido)cyclohexane (**8**) in an alcohol (1-propanol, 1-butanol, 1-hexanol, and 1-octanol) were disrupted by stirring with a spatula until a pourable dispersion of sub-millimeter particles was obtained.³⁸ The dispersions of **8** in 1.3 wt % 1-hexanol were placed in a rheometer, and G' was measured as a function of time within the linear viscoelastic region. Eventually, the G' value reached that of the mechanically undisturbed organogels.³⁸ Transmission electron micrographs (Figure 9) of the xerogels of **8** show elongated fibers with diameters up to 100 nm and left-handed helical pitches that are formed from thinner fibers of ~15-20 nm.³⁸

Mixtures of aliphatic molecular gelators:



Scheme 4. Aliphatic, acyclic molecular gelators exhibiting thixotropic properties in binary mixtures.

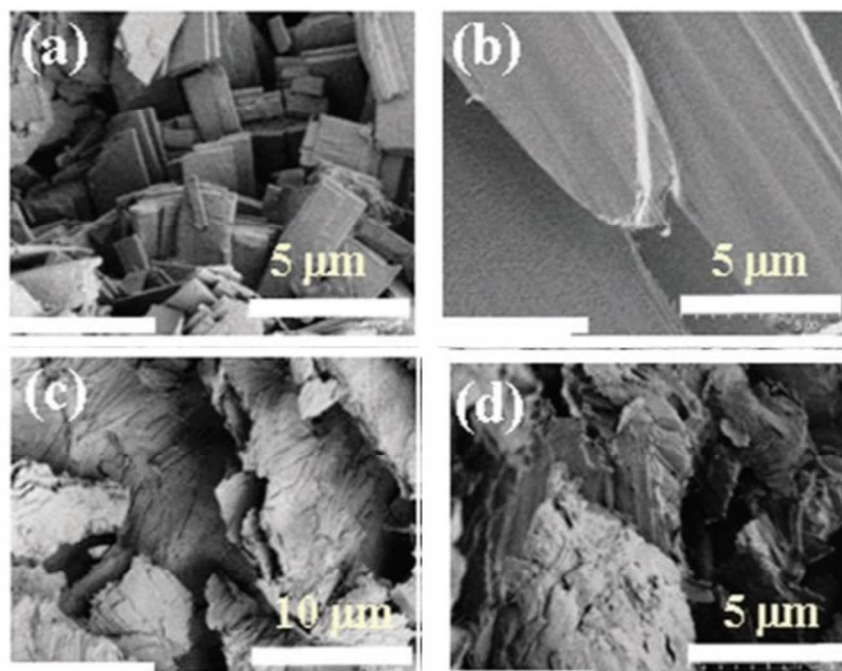


Figure 10. SEM images of xerogels (dried under vacuum and coated with a 10 nm layer of Pt) from toluene for **9a** and **9b** and their mixtures: (a) **9b** (2 wt %), (b) **9a** (6 wt %), (c) 1:1 **9a:9b** (3 wt %), and (d) 2:1 **9a:9b** (3 wt %). The values in parentheses denote the concentrations of the gelators in toluene before converting the gels to xerogels. Reproduced from ref 39 with permission from the Centre National de la Recherche Scientifique (CNRS) and the Royal Society of Chemistry.

The SEM images of xerogels from **9a** and **9b** in toluene showed sheet-like, crystalline networks (Figure 10). The SEM image of the xerogel from two component (**9a:9b**) toluene gels exhibit higher fibrillar network densities than the gels from the individual gelators (Figures 10 d). The authors interpreted this difference as indicative of greater crystallinity in the two component gel.³⁹ Also, XRD diffractograms of xerogels of 3 wt % 10:1 (wt:wt) **9a:9b** indicated different crystalline packing arrangements from those of the single-component gelators. Qualitatively (by the inverted tube test), gels of 3 wt % 1:1, 1:2, 1:4 (wt:wt) mixtures of **9a:9b** in toluene were thixotropic.³⁹ The measurements also showed that the G' recovery, after cessation of a destructive shear rate of 3000 s^{-1} for 0.1 s, was complete after 30 min, and higher (recovery % was not reported) for the 3 wt % 1:10 (wt:wt) **9a:9b** in toluene gel than that of either of the corresponding single component gels.³⁹ In addition, the two-component gel systems with **9a** and **9b** exhibited lower critical gelator concentrations than of those of each of the single alkyl ureas.

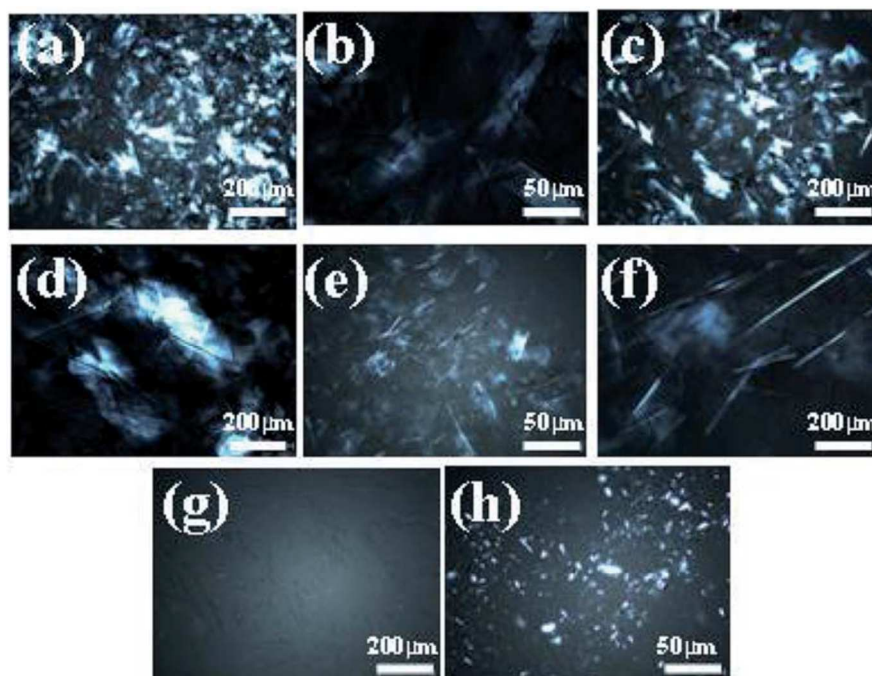


Figure 11. POM images 2 wt% **10c** in squalene gel (a and b), 2 wt% **10b** in squalene gel (c and d), 2 wt% **10a** in squalene gel (e and f), and squalene gel containing 1 wt% 1:1:10 (wt:wt:wt)

10c: 10b: 10a (g and h). Reproduced from ref 40 with permission from the Royal Society of Chemistry.

Multicomponent mixtures of simple alkyl amides (**10a-c**) as LMOGs in olive oil or squalene gels exhibit thixotropic properties as well, although their individual component gels do not.⁴⁰ POM images of squalene gels of 2 wt % **10 a-c**, showed tape-like crystal networks, whereas a 2 wt% 1:1:10 (wt:wt:wt) **10a:10b:10c** in squalene gel exhibited a 'broken crystallites'-like texture (Figure 11). A gel-sol phase transition was achieved by manually shaking gels of 1 wt % 1:1:10 (wt:wt:wt) **10a:10b:10c** in olive oil gel or 2 wt % in squalene. Upon cessation of destructive shearing, both the olive oil gel and squalene gel phases were recovered qualitatively (i.e., by the inverted tube test).⁴⁰ In the mixed component gels, cross linking of the fibrillar networks may be improved and they may also experience a lubrication effect.⁴⁰

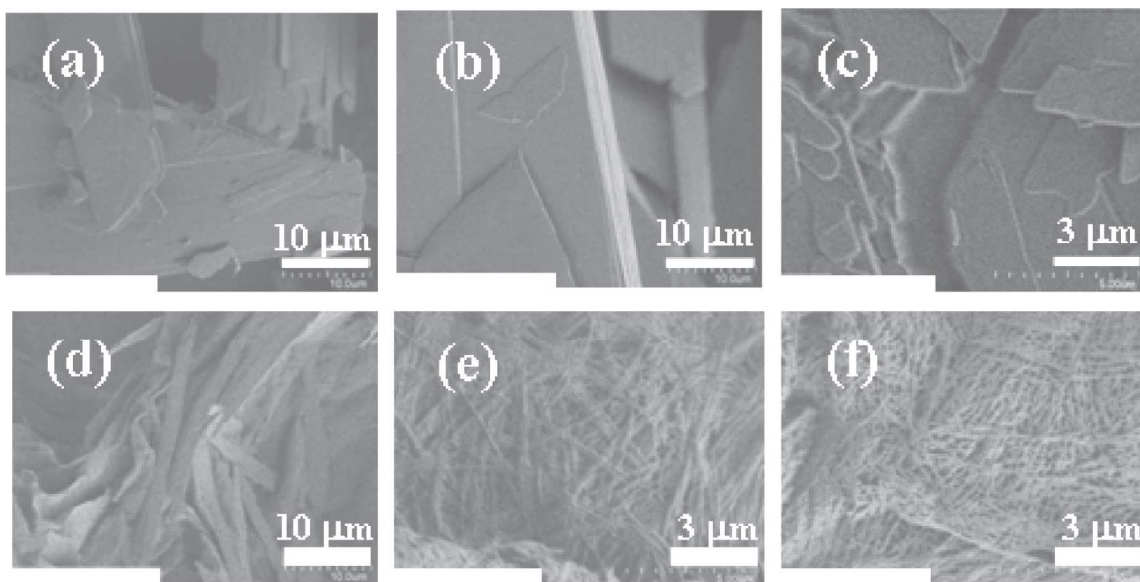


Figure 12. SEM images of xerogels (samples prepared by drying the gels and placing them on 10-nm thick Pt conductive tape) from 2 wt % toluene gels of (a) **11c**, (b) **11b**, (c) **11a**, (d) 1:1:2

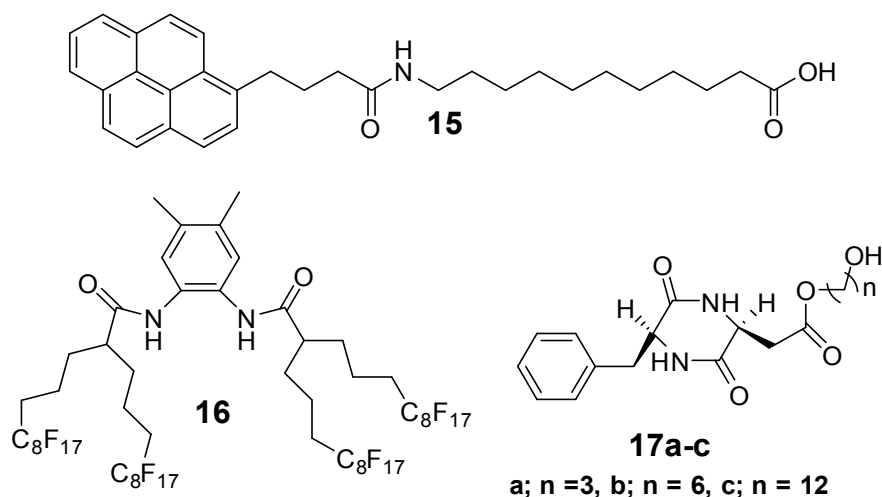
(wt:wt:wt) **11c:11b:11a**, (e) 1:1:4 (wt:wt:wt) **11c:11b:11a**, and (f) 1:1:6 (wt:wt:wt) **11c:11b:11a**. Reproduced from ref 41 with permission from Chemical Society of Japan.

Toluene gels with 2 wt % 10:1:1 (wt:wt:wt) **11a:11b:11c** show higher degrees of thixotropy than the corresponding gels with the individual components.⁴¹ SEM images of the xerogels from 2 wt % of the individual components in toluene showed tape-like crystal networks. The SEM images show that the fiber network density increased on increasing the concentration of **11a** in the mixture of **11c:11b:11a** (Figure 12), and XRD diffractograms show different reflection peaks for xerogels from the **11c:11b:11a** mixture and from the individual alkyl hydrazide; again, the mixtures lead to a change in the packing arrangements within the **SAFINs**.

From qualitative analyses of the rheological data, a 2 wt % 1:1 mixture of **12** and **13** in squalene gel was found to be thixotropic,⁴² although squalene gels of 2 wt % **12** or **13** did not recover their viscoelasticity after application of destructive shear.⁴² Optical micrographs of 1 wt % squalene gels of **12** and **13** exhibit strand-like crystalline networks and broken gel networks, respectively. SEM images of the xerogels and POMs from the one component toluene gels of **12** and **13** show sheet-like crystals, whereas xerogels of their mixture exhibit dense, tape-like structures.

G' recovery after mechanical destruction of hydrogels from 1:1 (wt:wt) mixtures of two homologues of *N*-alkyl-*D*-glucamides **14b:14d** is twice as large as from the comparable hydrogels of **14b** and **14d**,⁴³ and the phase transition temperatures of the mixture gels are higher (indicative of higher thermal stability). Furthermore, a hydrogel of 5 wt% 1:1 (wt:wt) **14b:14d** recovered its initial G' value after application of destructive strain in the first and subsequent cycles.⁴³

Gelators containing one aromatic moiety:



Scheme 5. Thixotropic molecular gelators containing one aromatic moiety.

The hydrogel of 1 wt % 11-(4-(pyrene-1-yl)butanamido)undecanoic acid (**15**) is thixotropic.⁴⁴ A TEM image of the xerogel (Figure 13A) shows nanofibers whose widths are 15–40 nm. Interestingly, fibers in the 2–4 nm range are present in the AFM image of the same xerogel (Figure 13B).

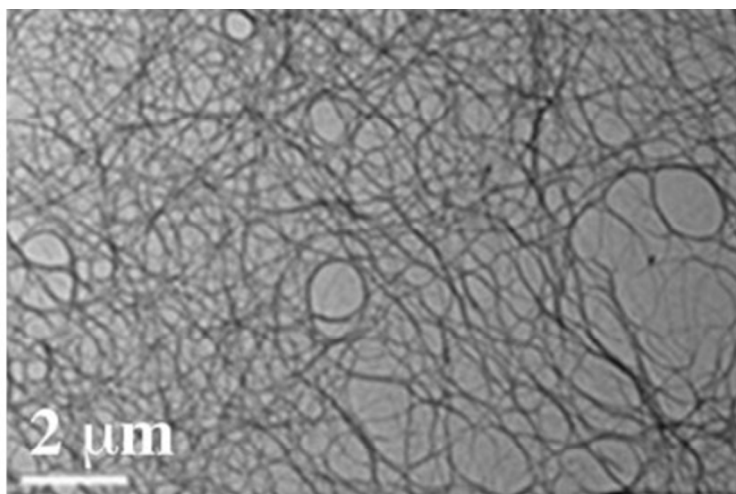


Figure 13. TEM image of the xerogel made from 1 wt % hydrogel of **15**. Reproduced from ref 44 with permission from John Wiley and Sons.

A simple step-strain experiment at constant angular frequency of 1 rad/s was performed on a 1 wt % **15** hydrogel.⁴⁴ First, a strain of 0.1% (in the linear viscoelastic regime) was applied.

Then, the strain was increased to a destructive level, 10%; in this regime, the sol-like nature was indicated by $G'' > G'$. Finally, strain was decreased to 0.1% and kept there to observe the gel-recovery. Ca. 93 % of the initial G' value was recovered in 3 min.⁴⁴ The XRD of the xerogel showed a sharp peak corresponding to d values of 4.42Å and 3.48 Å, indicative of hydrogen bonding and π - π stacking interactions within the pyrenyl moieties. Although the mechanism of thixotropic recovery was not reported, we conjecture that it may be similar to that described in Figure 8. Upon application of destructive strain, the π - π interactions among the pyrenyl groups at or near junction zones become weakened or disrupted preferentially, without disassembling the individual fibers.

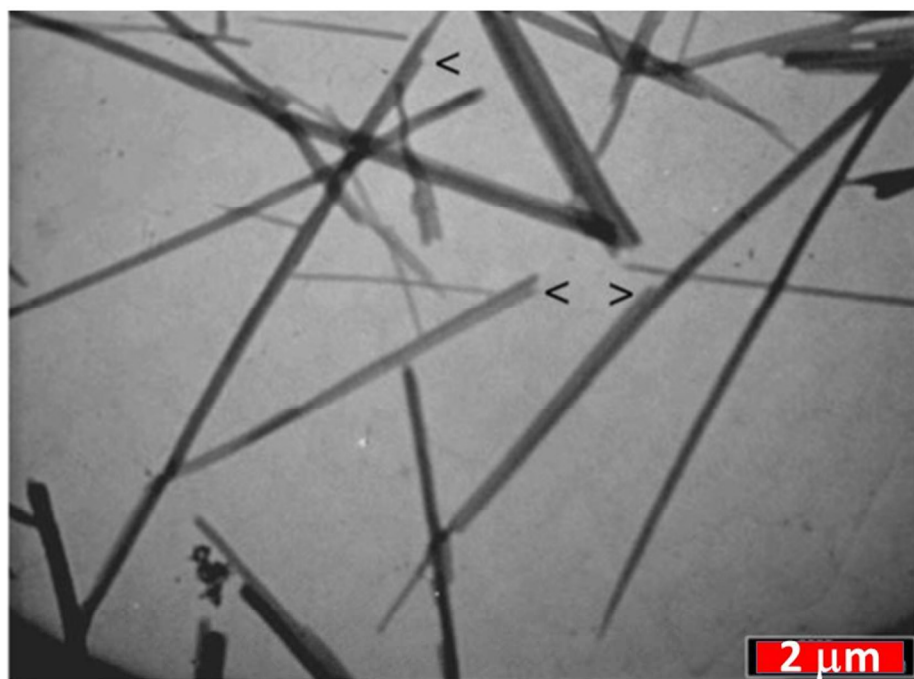


Figure 14. TEM images of the xerogel from 5 wt % **16** in isopropyl alcohol. Adapted from ref 45. Copyright (2002) Elsevier.

The TEM images of the xerogel from 5 wt % **16** in isopropyl alcohol show a **SAFIN** network consisting of fibrillar bundles having lengths of 5-15 μ m and diameters of 0.05-0.25 μ m

(Figure 14).⁴⁵ Upon application of mechanical strain, the gel became a sol, and it recovered its initial G' value several minutes after being returned to the linear viscoelastic region.⁴⁵

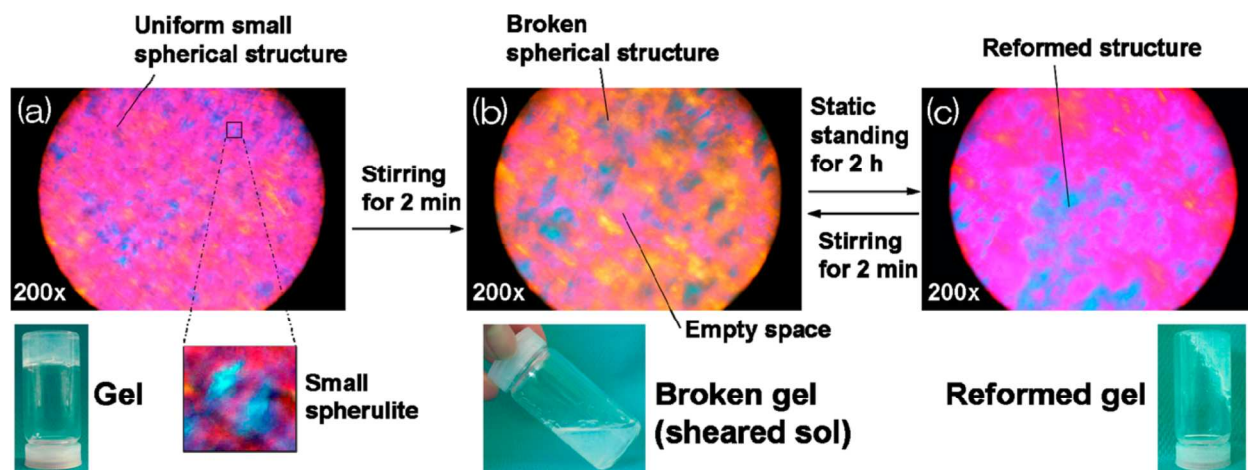


Figure 15. POM images of the gel, sol, and reformed gel prepared from 5 wt % **17a** in a 1:4 (v:v) ethanol:water mixture. Adapted from ref 46. Copyright (2013) American Chemical Society.

Molecular gels of cyclo(*L*-*O*-hydroxyalkylasparaginyll-*L*-phenylalanyl) (**17a-c**) in alcohols and water exhibit thixotropic properties.⁴⁶ As shown in Figure 15, 5 wt % **17a** or (~2.6 wt % **17b**) in an ethanol:water (1:4 (v:v)) gel became a sol under vigorous shaking and returned to a gel after cessation of the mechanical perturbation.⁴⁶ The small small spherulitic structures in the gel (Figure 15a), which confirm the crystalline nature of the SAFIN, disappeared upon stirring the gel (Figure 15b). A POM image taken 2 h after cessation of the destructive strain and reformation of the gel (Figure 15c) indicates that the destroyed spherulites had been transformed into a lamella-like, higher-order structure. For the ~2.6 wt % **17b** in ethanol/water (1:4 v:v) gel, G' changed from 8000 to 3000 Pa upon application of destructive strain and rose again to 8000 Pa within 3 h after removal of the destructive strain.

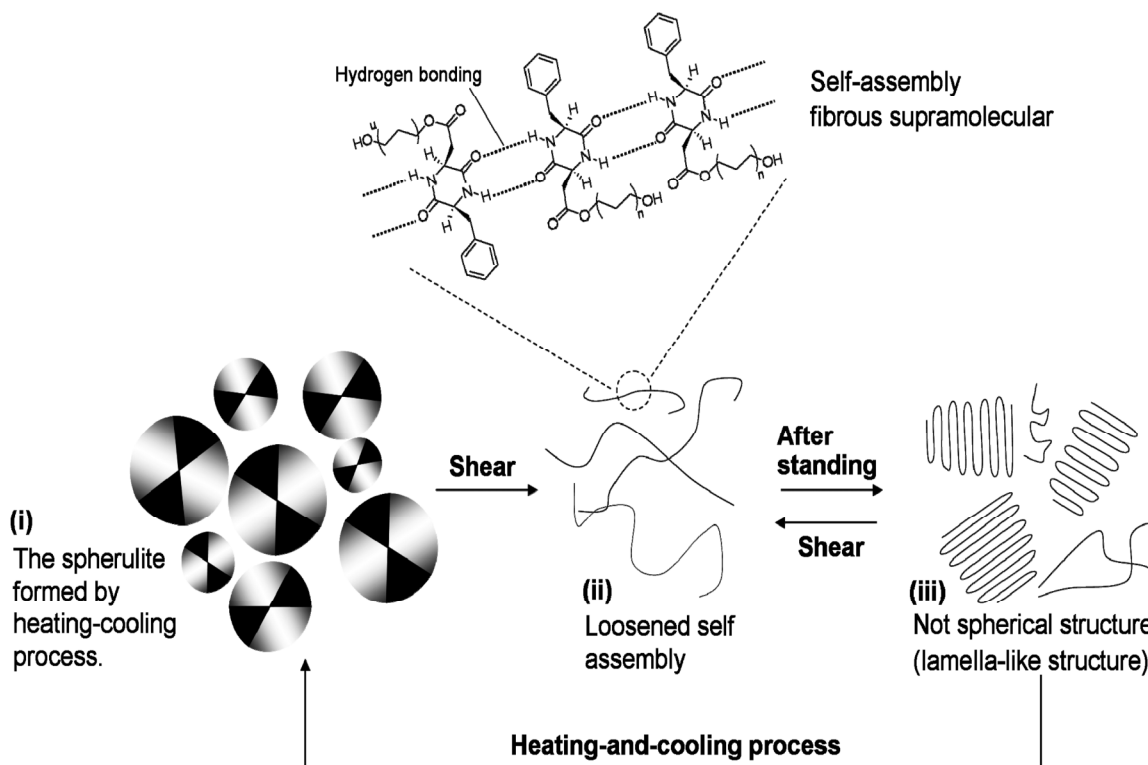
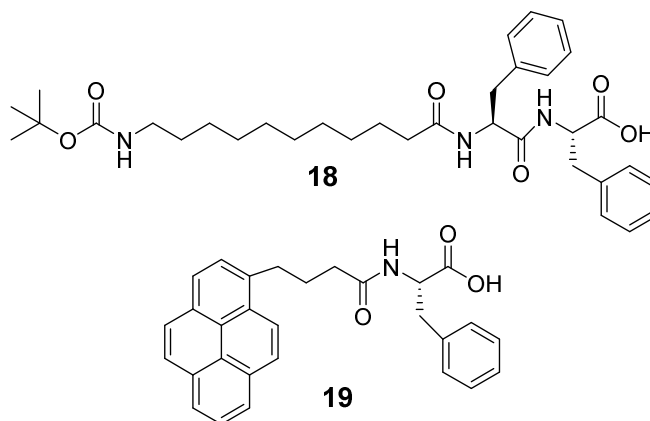


Figure 16. Schematic of a model for thixotropic behavior in gel–sol–gel transitions of the **17b** gels. Adapted from ref 46. Copyright (2013) American Chemical Society.

The C=O stretching band in FT-IR spectra of **17b** in chloroform solution was at 1681 cm^{-1} (i.e., a frequency where no hydrogen bonding is expected). However, the frequency for the C=O stretch in D_2O , 1646 cm^{-1} , is consistent with the presence of H-bonding, and these interactions seem to occur in both the unsheared and sheared gels. Based on this and other infrared spectral evidence, a model for the thixotropic behavior in the gel–sol–gel transformations of **17b** in water-ethanol mixtures has been proposed (Figure 16).

Gelators containing more than one aromatic group:



Scheme 6. Thixotropic molecular gelators containing more than one aromatic group.

The entangled fibrillar network of a tripeptide (**18**) hydrogel provides a cage-like environment which entraps water molecules.⁴⁷ Electron microscopy images of a xerogel (Figure 17) formed from a 0.8 wt % **18** hydrogel showed nano-fibrillar objects having widths of 25-45 nm.⁴⁷ Upon application of 40 % strain, the hydrogel became a sol. When returned to a strain of 0.1 % (i.e., within the linear viscoelastic regime), the initial G' value was restored in 6 min.⁴⁷ These hydrogel networks can be stabilized by both π - π and intermolecular H-bonding interactions involving the amide groups. Again, it appears that destructive strain breaks intermolecular interactions near junction zones of the **SAFIN** without disassembling the individual fibers.

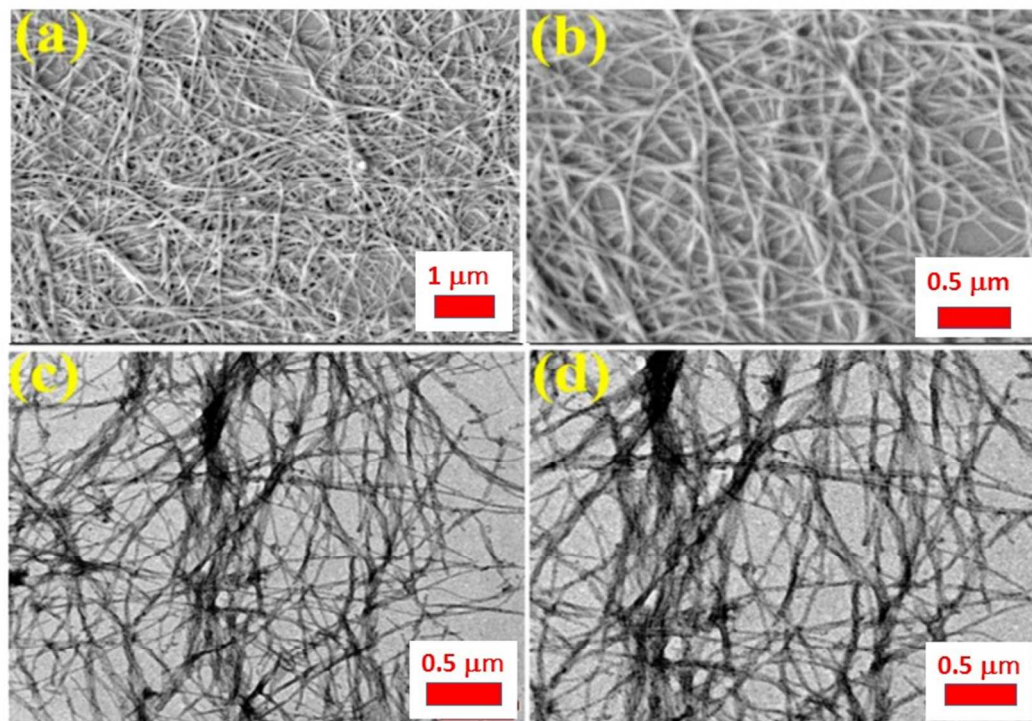


Figure 17. (a) Field emission scanning electron microscope (FE-SEM), (b) high-resolution field emission scanning electron microscope (HR-FE-SEM), (c) TEM and (d) high-resolution transmission electron microscope (HR-TEM) images of dried hydrogels (i.e., xerogels) of **18**. Reproduced from ref 48 with permission from the Royal Society of Chemistry.

Although the pyrenyl-containing single amino acid **LMOG (19)** forms hydrogels over a wide pH range, their appearance does depend on the acidity of the medium.⁴⁸ The minimum gelator concentration of **19** in phosphate buffered solution (pH 7.46) is 0.037 % (wt:v).⁴⁸ FESEM images of dried hydrogels indicate left-handed, helically-twisted fibers having widths of 30 -55 nm (Figure 18). At pH 14, the xerogels have tape-like network structures with 80-210 nm widths.⁴⁸

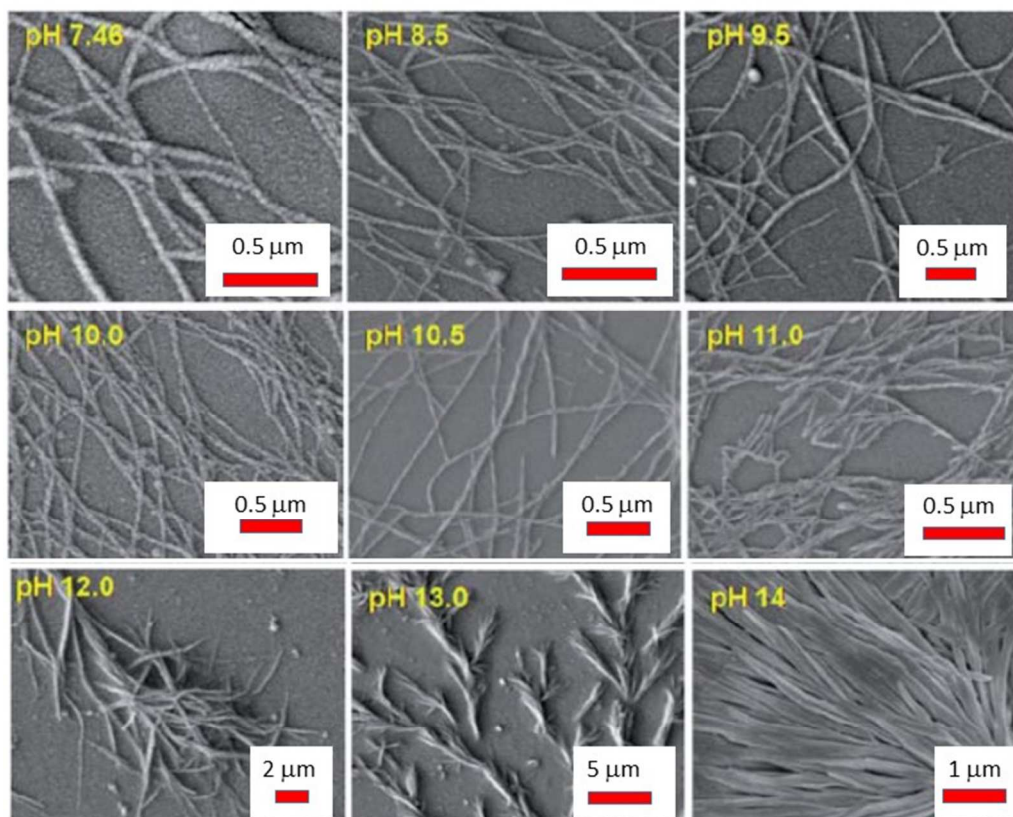
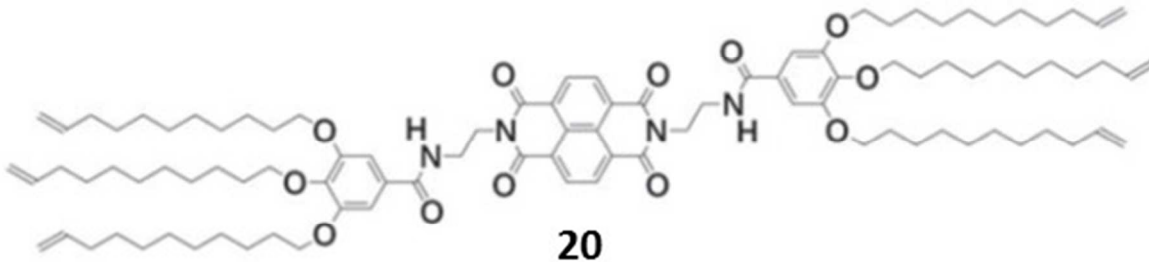


Figure 18. FE-SEM images of the xerogels from hydrogels of **19** prepared at different pH values. Reproduced from ref 48 with permission from the Royal Society of Chemistry.

Hydrogels of **19** within the pH range 7.46-10.5 are thixotropic and recovered fully their viscoelasticity within 10 min after removal of destructive strain. At pH >7.46, the viscoelastic properties of the hydrogels of **19** were not completely recovered after the cessation of destructive strain.⁴⁸ At basic pH values, the carboxylic acid group of the gelator is deprotonated so that the H-bonding interactions between amides, as well as ionic interactions among carboxylic acid groups, are disturbed. We speculate that junction zones of the **SAFIN** may be weakened and not able to reassemble at basic pH values as do those in the acidic range.



Upon application of destructive force using a mechanized vibrator operating at 60 Hz and 2600 rpm, a gel of 0.075 wt % **20** in cyclohexane was transformed into a sol, and then back to a gel upon cessation of the external mechanical force.⁴⁹ From UV/Vis and IR spectroscopic data, it was concluded that a combination of π - π stacking, hydrogen-bonding, and van der Waals interactions is responsible for stabilization of the SAFIN.⁴⁹ 1D fibers of several tens of micrometers in length and 10-150 nm in diameter were found for the xerogel from a 0.3 wt % **20** in cyclohexane gel (Figures 19a, b). Immediately after application destructive force (by vortexing), the objects became numerous smaller fibers with \sim 4 mm lengths and in bundles of maximum width \sim 75 nm (Figures 19b, c). After removal of the destructive force, the SAFINs reformed; complete recovery to fibers of 8-10 mm length required \sim 24 h. Of the original G' value of 9.7 Pa for the gel, ca. 70 % ($G' = 6.6$ Pa) was recovered eventually from the disintegrated gel when it was kept in its linear viscoelastic region.

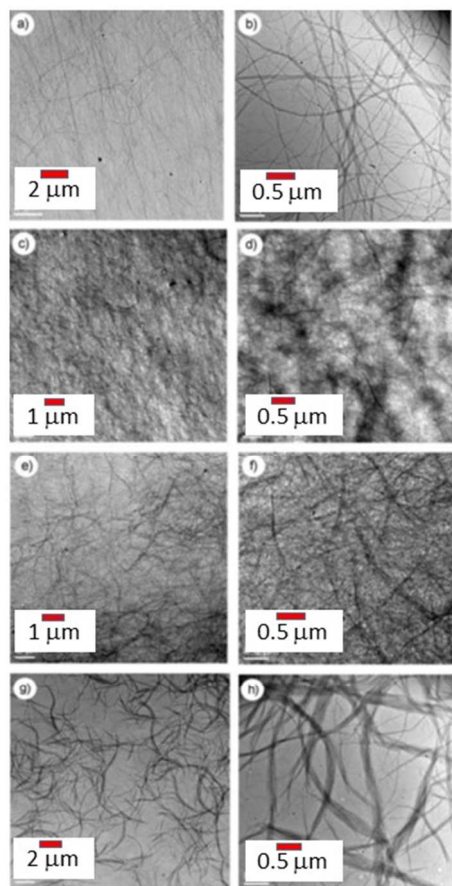


Figure 19. TEM images (at low and high magnifications) of xerogels from (a, b) the gel of 0.3 wt % **20** in cyclohexane with extremely long (several tens of mm) fibers in large bundles of 10-100 nm diameter; (c, d) images recorded within 60 s after application of destructive strain, showing small fibers and clusters of many small fibers (black regions); (e, f) images taken 6 h after cessation of destructive strain, showing the regeneration of the long fibers (up to 5 mm in length) and bundles of them; (g, h) images 40 h after, showing the complete regeneration of the fiber and bundle sizes found in the original gel. Samples were prepared by casting the gels or their sols from vortexed gels on carbon coated Cu grids. Adapted from ref 49. Copyright John Wiley and Sons.

Conclusions and perspectives for the future:

The structural and thixotropic properties of molecular gels with crystalline **SAFINs** comprised of simply structured gelators have been correlated. Those correlations indicate that a structural requirement for a gelator of this type to form thixotropic gels is the presence of at least two hetero-functionalities that involve in H-bonding interactions (e. g., **1**). Thus, in all of the gels examined in this review, the **SAFINs** are stabilized by intermolecular H-bonding interactions. Upon application of destructive strain, those interactions at or near junction zones are weakened, broken or disrupted preferentially, without disassembling the individual fibers. However, this pattern may not apply to other molecular gelators with more complex structures.

Regardless, it appears that the degree of thixotropic recovery of the silicone oil gels of **3**, **4a-c**, and **5a-b** correlate qualitatively with the strength of potential H-bonding interactions among the hetero-functional groups on the **LMOGs**. Increasing H-bonding interactions in the crystalline **SAFIN** networks of molecular gels of **7** and **8** also increased thixotropic behavior. In addition, the enhanced thixotropy and fast recovery observed for gels of **6a** in isostearyl alcohol may be attributed, at least in part, to a ‘lubrication’ effect of terminal hydroxyl moieties.

However, only binary mixtures of the aliphatic, acyclic molecular gelators, **9-14**, produce thixotropic gels. This observation may be related to the greater crystallinity and higher fibrillar network densities in the mixtures than in the corresponding gels from single gelator components. Also, gels made from multicomponent mixtures of simple alkyl amides, **10a-c**, and olive oil or squalene as the liquid exhibit thixotropic properties, although their individual component gels do not.

What should the future bring? The authors hope that this review will stimulate others to design new gelators that will yield additional insights into the requirements for making thixotropic gels that are capable of new, important applications. The field covered by this review

is in an embryonic stage, one reminiscent of our understanding of molecular gels 30 years ago— patterns are beginning to emerge, but their specific origins are largely conjectural. “Scratching the surface” in this context has more than one meaning, but without such “scratching”, it will not be possible to make *a priori* designations about which molecular gelators will and which will not form thixotropic gels in a designated liquid. Gaining that predictability will be necessary if the many potential applications for molecular gels are to be realized.

This new frontier in gel chemistry and physics awaits new investigations and new investigators.

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