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**Systematic Modifications of Alkane-Based Molecular Gelators and the Consequences to the Structures and Properties of their Gels**

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## PERSPECTIVE

# Systematic Modifications of Alkane-Based Molecular Gelators and the Consequences to the Structures and Properties of their Gels

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A systematic structural development of molecular gelators based on *n*-alkanes is presented. The properties of the resultant molecular gels with a wide range of liquids can, in some cases, be correlated with the structural modifications to the gelators and the natures of their self-assembled fibrillar networks as analyzed at different distance scales. A special emphasis is placed on 12-hydroxystearic acid and its derivatives in which the chirality, placement, and functionality of the hydroxyl group center have been varied and the carboxylic head group has been modified systematically. The resulting correlations between molecular gelator structure and the various properties of their gels provide a basis for the design of structurally more complex gelators. However, the nuances of the systems explored demonstrate that additional factors, some of which are currently not well studied, must be considered before *a priori* design of molecular gelators with specific gelating abilities will be possible.

## Introduction

This Perspective will not attempt to cover the many types of known gels. It will focus on ‘molecular gels’, materials formed when low concentrations (usually <5 wt%) of a molecule (i.e. a ‘gelator’), whose molecular weight is usually  $\leq 3000$  Daltons, is able to aggregate and self-assemble in a liquid component so that the eventual phase does not flow perceptibly over periods of minutes. Many reviews, both recent<sup>1,2</sup> and within the last 2 decades,<sup>3-5</sup> have examined different aspects of this subject. Despite the current attention that research in this field is receiving (N.B., more than 4000 citations in the Web of Science during 2013), many of the true advances in designing truly new classes of molecular gelators still occur serendipitously. Much remains to be understood before it will be possible to predict with confidence whether newly designed molecules will be capable of gelating a particular liquid, and to predict the properties of the resultant gel!<sup>1</sup>

Computational approaches to the design of efficient molecular gelators, although important in principle, have not gained much traction in practice. Such calculations can analyze *a posteriori* the interactions of a self-assembled fibrillar network (SAFiN) with a known structure; they cannot (at this stage of our understanding) identify the nature of the structure-determining aggregates that precede full SAFiN formation. Empirical design and testing remain for now the best method to find new, efficient gelators.

The very crude definitions of a molecular gelator and a molecular gel presented above will be refined within the body of the Perspective, and much more comprehensive information can be found elsewhere.<sup>3,6</sup> In fact, the Perspective will be limited to a critical discussion of gelators in which relatively small substituents have been inserted at an end (X) and/or along (Y) an *n*-alkane chain ( $XmYo$ , where  $m + o = n$ ). These molecules, ‘organogelators’, afford a convenient ‘platform’ to investigate how minor structural changes affect the nature of aggregation and efficiency of gelators. Factors such as the length of the alkyl chain, and the location and type of substituent(s) will be correlated with the nature of the aggregates that are produced in a wide range of liquid types. It will be shown how such correlations can be used to glean basic information about what constitutes a good (or bad!) gelator, at least within this class of molecules. Also, challenges to the extension of the conclusions derived here to other classes of molecular gelators will be discussed.



One approach to gain *a priori* knowledge of molecular gelators and their gels has been to correlate the influence of small structural changes in the chemical makeup of a known gelator on the properties of its gels. We describe here how such studies have been used to dissect the factors responsible for gelation of a very simple class of molecular gelators by starting with the simplest organogelators possible, *n*-alkanes, and progressing to more complex molecules by sequentially adding functional groups, X and Y. This Perspective demonstrates that even within this class of

molecular gelators, small structural changes sometimes lead to unexpected consequences; the link between the molecular structure of a gelator and its gels must proceed through several steps, including aggregation and nucleation, time-dependent interactions between the gelator and the liquid component along the path leading to a SAFiN, and the protocol by which the solution/sol phases are transformed into their gel phases.

A major focus of this presentation is on 12-hydroxystearic acid (12HSA;  $X = \text{HO}_2\text{C}$ ,  $Y = \text{CHOH}$ ,  $m = 10$ , and  $o = 6$ ) and molecules derived from it. 12HSA is an efficient gelator of many liquids and the properties of its gels have been well characterized.<sup>7–18</sup> Equally important for the purposes of this Perspective, it is another convenient platform to perform many systematic structural changes.

## *n*-Alkanes as gelators

The structurally simplest class of organogelators is *n*-alkanes ( $X = \text{H}$  and  $Y = \text{no atom}$ ), and the simplest organogels consist of short-chained *n*-alkanes gelated by long-chained *n*-alkanes. Discovery of these gels occurred as a consequence of a long-term research project to simplify the structures of gelators and the associated liquids; our initial gelators were very complex molecules. Thus, rings, unsaturated groups, and heteroatoms were eliminated systematically to arrive at the alkane systems. Long *n*-alkanes are sparingly soluble in short *n*-alkanes at ambient temperatures; the degree of solubility decreases as the disparity between the ‘long’ and ‘short’ chain lengths increases. When sols/solutions of these mixtures are cooled to below their saturation limits, the long *n*-alkanes tend to separate in the form of interlocking platelets (i.e., 2-dimensional (2D) objects) in the micrometer size range.<sup>19</sup> The resultant materials are weak gels according to rheological and other criteria.<sup>20</sup> In a few cases, the long *n*-alkane gelator molecules have been shown to be in essentially *all-transoid* conformations and packed in layered, orthorhombic ( $B_0$ ) arrangements<sup>20</sup> (i.e., with their long molecular axes orthogonal to the platelet planes).<sup>21</sup>

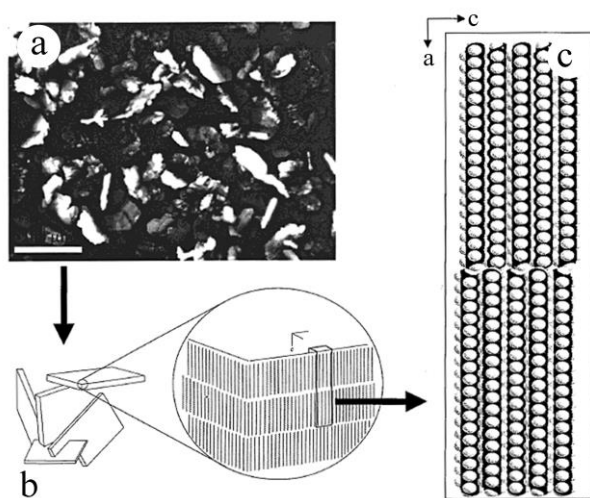


Figure 1: Optical micrograph of a 4 wt % **C36** in 1-octanol gel viewed through crossed polars (a), a cartoon representation of the microplatelets in (a) showing the orientations of the long molecular axes of **C36** molecules (b), and the molecular packing of **C36** in its  $B_0$  phase viewed from the *b*-axis (c). The distance bar in (a) is 100  $\mu\text{m}$ . Reprinted with permission from ref 19. Copyright 2000, the American Chemical Society.

Long *n*-alkanes are able to gelate a variety of other liquids in addition to short-chained *n*-alkanes (Figure 1).<sup>22, 23</sup> The likelihood to form a gel with any liquid, decreases with decreasing length of the *n*-alkane gelator. In the several hexatriacontane (**C36**;  $XmYo$  where  $X = \text{H}$ ,  $Y = \text{no atom}$  and  $m+o = 36$ ) gels examined, the polymorphic units are again organized in lamellae with predominantly  $B_0$  configurations and with platelet shapes at the micrometer distance scale.<sup>21</sup> However, traces of monoclinic packing ( $B_M$ )<sup>24</sup> are evident in the gels with some liquids. Given that four morphs of neat crystalline **C36** are known,<sup>25, 26</sup> it is somewhat surprising that the  $B_0$  form predominates in a wide variety of liquids; both the  $B_0$  and  $B_M$  morphs can be obtained by crystallizing **C36** from decane under different experimental conditions.<sup>27</sup>

Modification of *n*-alkane structures, starting with very simple substituents, while progressing to more complicated ones, and their consequences to gel formation

By inserting a functional group at various positions along the chain (N.B., inserted at an end methyl ( $\text{CH}_3$ ) or interior methylene ( $\text{CH}_2$ ) group) of a long *n*-alkane, it has been possible to explore the influence of inter-molecular interactions other than London dispersion forces—the most important attractive interactions available to *n*-alkanes—on the ability of structurally simple molecules to act as gelators.<sup>28</sup> The groups explored have been as simple as an oxygen atom (resulting in an alcohol or an ether when the insertion occurs at a terminal carbon or between two carbon atoms, respectively), a sulfur atom,  $\text{NH}$ , carbonyl, and carboxylic groups, etc. Each of these permits, *in principle*, one or more additional inter-molecular interactions, such as dipole-dipole and H-bonding forces, to come into play during the aggregation steps leading in some cases to SAFiNs and ultimately to gels. At the same time, these groups have ancillary effects on intermolecular packing because they impose structural constraints that affect the ability of the chain to adopt a completely linear conformation and occupy a different amount of van der Waals space than a methylene group, as well as altering the energy needed for rotations along the molecular chain. As a result, some or all of the energetic advantages of including a heterogroup in stabilizing packing arrangements conducive to SAFiN formation may be offset by reductions in attractive London dispersion forces. Thus, insertion of a functional group may aid or inhibit the gelating ability of an *n*-alkane.

Many structurally simple alkanols and alkanic acids are known to act as surfactants, making emulsions, micelles, etc; this is not the subject of our Perspective, and, for that reason, these types of aggregates (and the various alkanols and alkanic acids which are components of them) have not been included. More complex alkanol and alkanic acid structures (e.g., steroidal and terpenoid species and saccharides), do act as gelators; they too are not included here. In addition, a study of the gelating properties of relatively low concentrations of long 1-alkanols ( $X = \text{OH}$  and  $Y = \text{no atom}$ ) and alkanic acids ( $X = \text{HO}_2\text{C}$  and  $Y = \text{no atom}$ ) in vegetable oils indicates that neither is a very efficient gelator.<sup>29, 30</sup> In a similar fashion to the *n*-alkanes, they also form platelet units. However, some compositions of their mixtures yield fibers and stronger gels (Figure 2). For example, a maximum hardness was measured by the elastic modulus ( $G'$ ) at a 7:3 1-octadecanol:octadecanoic acid ratio.<sup>29</sup> When the long-chained acids are converted to their salts with any of the alkaline metal counterions, a plethora of different self-assembled materials can be formed in water.<sup>31–33</sup> Of special interest here are hydrogel phases. For

example, at room temperature and 50 wt% of potassium octadecanoate or potassium hexadecanoate, the surfactant molecules are arranged in interdigitated bilayers with their long axes orthogonal to the layer planes and packed hexagonally, as observed in smectic B liquid crystals.<sup>31</sup> By contrast, 50 wt% 1:1 1-octadecanol:potassium octadecanoate hydrogels have non-interdigitated, hexagonally-packed bilayers in which the alcohol and carboxylate head groups alternate at each layer interface with water.<sup>33</sup> At other concentrations, compositions, chain lengths, and temperatures, different types of gel phases can be formed.<sup>32</sup>

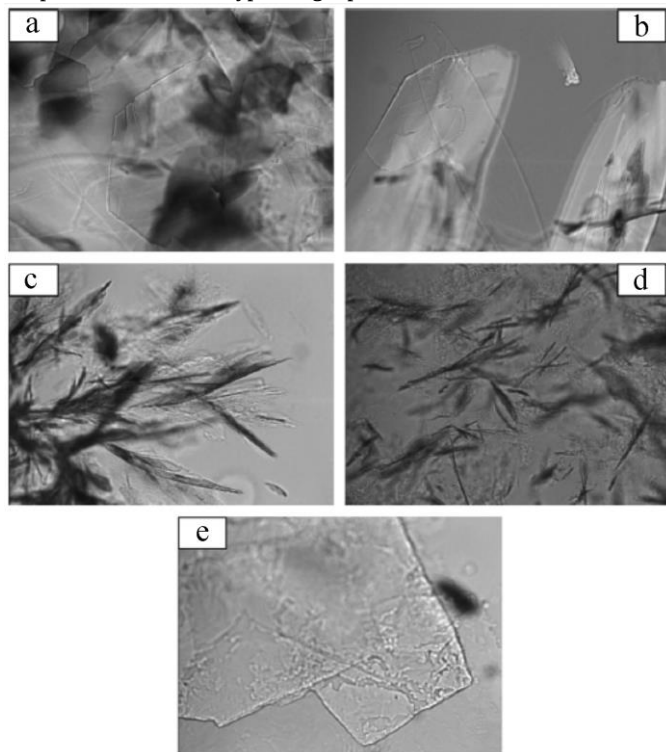


Figure 2: Optical micrographs obtained by cooling solutions/sols of different ratios of octadecanoic acid and 1-octadecanol in a vegetable oil. Acid:alcohol ratios: 1:0 (a); 7:3 (b); 1:1 (c); 3:7 (d); 0:1 (e); the size of each image is 0.577 x 0.770 mm. Reprinted from ref 29. Copyright 2007, with permission from Elsevier.

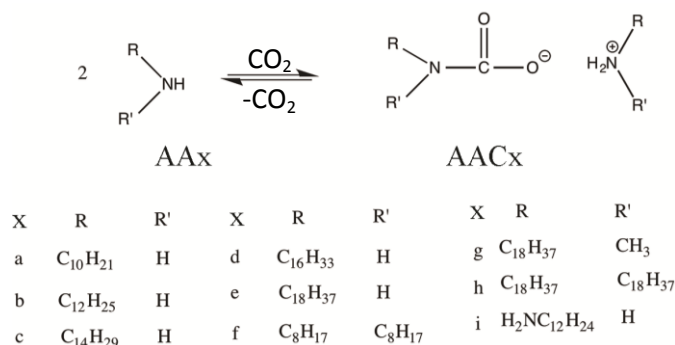
As alluded to above, *n*-alkanes in which a heteroatom or small group has been inserted along the chain, also can act as gelators. Although long-chained ethers examined were not gelators under the limited conditions explored,<sup>34</sup> 3 wt% of a thioether, dithetradecylsulfide (X = H, Y = S, and m = o = 7) was capable of gelating some alkanols,<sup>35</sup> presumably as a result of the higher polarizability and London force interactions between sulfur atoms than oxygen atoms.

At 2 wt%, 1-octadecylamine (X = H<sub>2</sub>N, Y = no atom, and m+o = 18; having two H-atoms for donation per head group) was able to gelate 1-pentanol partially, and at 5 wt%, it gelated DMSO and silicone oil completely.<sup>35</sup> The rheological properties of the silicone oil gel were investigated in detail.<sup>36</sup> The storage modulus (*G'*) remained higher than the loss modulus (*G''*) in the 1–8 wt% concentration range and over a very wide range of frequencies within the linear viscoelastic region—these are true gels. Furthermore, changes in the value of *G'* versus temperature allowed the dependence of the SAFiN melting temperature, *T<sub>g</sub>*, on gelator concentration to be measured much more precisely than by the classical ‘falling drop’<sup>37</sup> and the inverted tube methods.<sup>38</sup> The more

lipophilic secondary amine, dioctadecylamine (X = H, Y = NH, and m = o = 18), having only one H-atom per molecule for donation and the most efficient gelator of the amines investigated, was able to gelate a variety of alkanes, aromatic liquids, dichloromethane, and alcohols at 3 wt% concentrations; the gels were stable in closed vessels for more than 7 months. The gelating properties of two tertiary amines, dioctadecylmethylamine and trioctadecylamine (X = H, Y = NCH<sub>3</sub> and N(CH<sub>2</sub>)<sub>18</sub>H, respectively, and m = o = 18), were examined as well. From IR spectral investigations, the SAFiNs of 1-octadecylamine have extensive H-bonding. However, they have less London dispersive interactions than found in dioctadecylamine, which also acts as an H-bond donor and acceptor. In the two tertiary amines, only H-bond acceptance is possible, and no donor groups exist within several of the liquids gelated by them. On that basis, their ability to gel is attributed primarily to London dispersive interactions within their SAFiNs. The effect of increasing the molecular lipophilicity on gelating ability is clear, even with the limited number of molecules in the series.

Bubbling CO<sub>2</sub> through dilute solutions (in a wide variety of liquids) of primary and (to a lesser extent) secondary alkylamines (AAx),<sup>39, 40</sup> resulted in gels that are thermally reversible. Adding other triatomic molecules, CS<sub>2</sub> and SO<sub>2</sub> (the adducts with NO<sub>2</sub> yielded no gels in a wide range of liquids and concentrations, and their structures were not investigated) as liquids or gases, also yielded gels.<sup>41</sup> even at room temperature. The chemistry of the addition by CO<sub>2</sub>, resulting in the formation of alkylammonium alkylcarbamates (AACx), and the different amines examined are shown in Scheme 1.<sup>40</sup> Each of the triatomic molecules employed successfully has a central atom flanked by two more electronegative ones. As a result, the central atom has a partial positive charge and is susceptible to nucleophilic attack by the lone pair of electrons on the nitrogen atom of the amine. The enhanced likelihood of gelation in these cases is attributed to the electrostatic attraction of the ion pairs in the alkylammonium alkylcarbamates, an interaction energy that is higher than that of the intermolecular H-bonding available to the amine groups before the introduction of CO<sub>2</sub>. X-ray diffraction studies indicated that the SAFiNs of many of the systems investigated consist of salts arranged in bilayers. When CO<sub>2</sub> was the added triatomic molecule, the gels were chemically reversible simply by bubbling through a displacing gas, such as N<sub>2</sub> (Figure 3). Although macroscopically stable indefinitely at room temperature in closed vessels under one atmosphere of CO<sub>2</sub>, the gels could be returned to their amine/liquid solution states in this way because the carbamate C—N bonds are weak, and they break and reform rapidly even within the sol states.<sup>42</sup> However, it is likely that even these gels undergo Ostwald ripening and other aging phenomena.

Scheme 1. Reversible formation of ammonium carbamate gelators from amines and carbon dioxide.



Results from differential scanning calorimetry (DSC) and thermal gravimetric analyses (TGA) indicated that heating the adducts causes the loss of a molecule of  $\text{CO}_2$  by the ammonium carbamates, loss of a molecule of water by the  $\text{SO}_2$  adducts (diammonium  $\text{S}_2\text{O}_5^{2-}$  salts), and loss of a molecule of  $\text{H}_2\text{S}$  by the  $\text{CS}_2$  adducts (ammonium dithiocarbamates), yielding thioureas.<sup>41</sup> The difference between the fates of the alkylammonium alkylcarbamates and the alkylammonium alkyldithiocarbamates can be explained on the basis of the much stronger C—N bonds of the dithiocarbamates which results from basic thermodynamic considerations: the heat of formation of  $\text{CO}_2$  is very negative whereas that of  $\text{CS}_2$  is positive; once  $\text{CS}_2$  adds to an amine, the thermodynamic driving force for it to return to its independent state is much smaller than for  $\text{CO}_2$ . Regardless, adducts of both  $\text{CO}_2$  and  $\text{CS}_2$  to 5 wt% 1-octadecylamine (**AAe**) proved to be exceedingly diverse and efficient gelators; the  $\text{SO}_2$  adduct was somewhat less efficient but was still able to gelate several liquids.

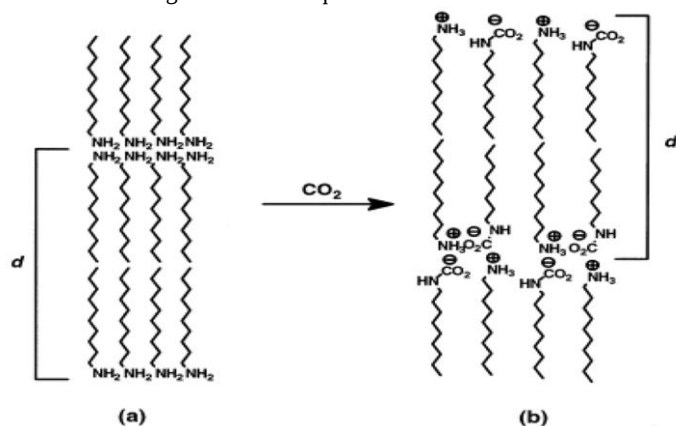
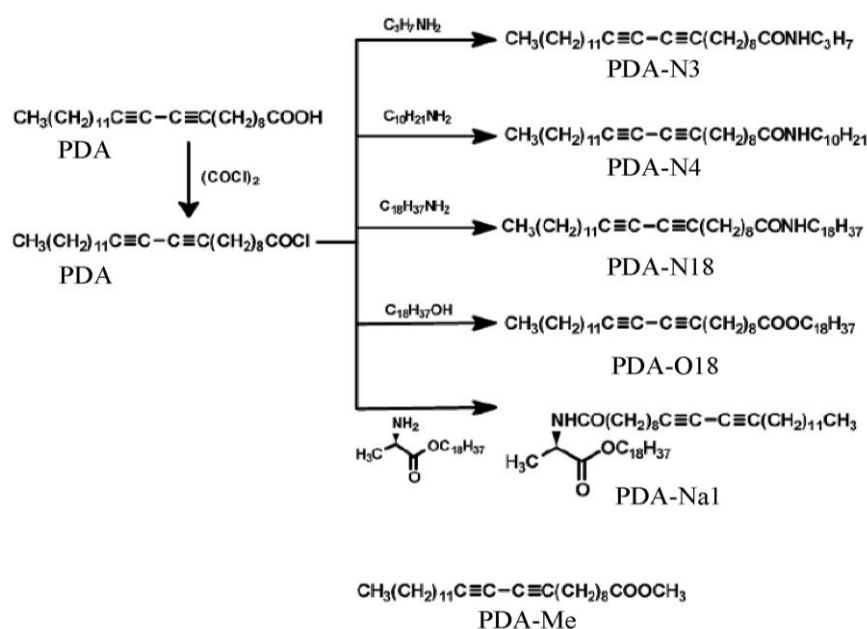


Figure 3: Packing arrangement of **AAx** and **AACx** in gels and distances  $d$  associated with low-angle X-ray diffractions of the gels:

(a) **AA(a-e)**, (b) **AAC(a-e)**, (Scheme 1). The proposed packing arrangements of the secondary amines, **AA(f-h)**, and their corresponding ammonium carbamates, **AAC(f-h)**, are somewhat analogous to those in (a) and (b). Reprinted with permission from ref 40. Copyright 2002, the American Chemical Society.

If a urea or thiourea group (i.e., both a very strong H-bond donor and acceptor), is added to the end ( $\text{X} = \text{H}_2\text{N}(\text{CO})\text{NH}$ ,  $\text{Y} = \text{no atom}$ , and  $m+o = n$ ) or middle of an alkane chain ( $\text{X} = \text{H}$ ,  $\text{Y} = \text{HN}(\text{CO})\text{NH}$ , and  $m = o$ ), fair-to-excellent gelators result, even when the alkane is short.<sup>43</sup> The molecular packing of some of the  $N,N'$ -dialkylureas in their SAFiNs of silicone oil gels and in their neat solid phases have been found to be the same by X-ray diffraction methods. These data and those from IR spectroscopic investigations indicated that the ureas and thioureas form extensive 1-D H-bonding networks with the alkyl groups placed at the sides. Urea and thiourea, the parent molecules for these series, construct 3-D H-bonding networks and clathrate channels when precipitated in the presence of  $n$ -alkanes.<sup>44</sup> The difference in these morphologies can be attributed to removing one of the N—H groups and, thereby, truncating the ability of the ureas or thioureas to form the 3-D networks. The shortest of the alkanes into which a urea group has been inserted is ethane, and its urea insertion product,  $N,N'$ -dimethylurea, is the lowest molecular weight (88 Daltons) organogelator known to date. Based on the limited data reported, elongating the  $n$ -alkane chain does improve the gelating ability of the  $N,N'$ -dialkylureas significantly, and insertion of the urea group at the end of an alkane chain (i.e.,  $N$ -alkylureas) or in the middle yields gelators of comparable efficiency, as does adding the urea group 'end-on' (i.e., making an  $N,N'$ -dialkylurea). At the same concentrations, the long-chained thioureas are able to gelate a range of liquids like that of the corresponding ureas.

Scheme 2. Gelators derived from 10,12-pentacosadiynoic acid.



## Introduction of a second group along the alkane chain and the consequences to gelation

The consequences to gelator efficiency of inserting both a 1,3-diyne and a carboxylic acid group within cosane (**C20**) have been examined.<sup>44</sup> The resulting molecule, 10,12-pentacosadiynoic acid (**PDA**;  $X = \text{HO}_2\text{C}$ ,  $Y = \text{C}\equiv\text{C}-\text{C}\equiv\text{C}$ ,  $m = 0$ ,  $n = 8$ ), contains two groups that can potentially act intermolecularly to alter the ability of an *n*-alkane to be a gelator. It was hypothesized that the carboxylic acid groups might interact to form cyclic dimers, as they do in structurally simpler alkanolic acids, while the dispersive interactions and stiffness of the diyne units might aid in organizing chain-chain orientations. Also, if the diyne groups were appropriately aligned within the SAFiN units, they might undergo photo-induced polymerizations, further stabilizing thermally their gels. Finally, the acid group can be changed easily into a number of derivatives, each of which might exhibit somewhat different gelating abilities (Scheme 2).<sup>44</sup> Among the derivatives synthesized was the optically active amide from the octadecyl ester of L-alanine (**PDA-Nal**).

As expected, the organogels of the parent acid and its derivatives were thermally reversible before photo-polymerization. Some of the gelators were very efficient even before irradiation. For example, ca. 1 wt% of amide **PDA-N18** was able to form gels at room temperature in alcohols, nitrobenzene and silicone oil. However, the parent acid, **PDA**, was able to gel silicone oil only and the methyl ester of **PDA**, **PDA-Me**, was soluble in all of the liquids examined; gelation by the derivatives does depend upon the type and degree of head group interactions. The longer chained derivatives were much better gelators: at 2 wt%, both **PDA-N18** and **PDA-Nal** formed gels in a wide variety of liquids, and many of them were stable for months at room temperature in closed vessels. After irradiation, the SAFiNs became insoluble and colored polymers that, with the exception of **PDA-O18** in silicone oil and **PDA-Nal** in nitrobenzene, were able to retain their gel properties when heated to ca. 70 °C (where further structural modifications occurred) and then cooled to room temperature. In general, the gelation efficiencies of the derivatives in Scheme 2 were similar before and after irradiation. Very minor changes were observed in the H-bonding peaks of the gelators in the SAFiNs before and after irradiation and post-heating treatment of the polymerized gels.

A 1 wt% chloroform solution of the optically active **PDA-Nal** did not display a Cotton effect in the UV or visible regions; the chiral molecules are dispersed throughout the liquid (Figure 4). A **PDA-Nal** silicone oil gel, before irradiation, displayed a strong circular dichroism (CD) band before irradiation that tailed into the visible region. After irradiation, it contained two Cotton effects at 611 nm and 563 nm (in the region of the excitonic transition); both were increased in intensity after heating the polymerized gel and cooling it to room temperature. These results demonstrate that the fibrillar organization of the molecules in their SAFiNs is helical.

Partially fluorinated *n*-alkanes are another type of gelator. The immiscibility of the perfluoroalkyl and non-fluorinated alkyl parts—fluorocarbons and hydrocarbons are immiscible below a certain temperature, and the cross-sectional area of the  $(\text{CH}_2)_n$  and  $(\text{CF}_2)_n$  segments are 18.5 and 28.3 Å<sup>2</sup>, respectively<sup>45</sup>—can force supramolecular aggregation that is based upon segregation. Also, perfluorinated *n*-alkanes capitalize on the very strong covalent C—F bonds, very weak intermolecular interactions, and very low surface free energies.<sup>46, 47</sup> Thus, relatively high concentrations of relatively long partially fluorinated *n*-alkanes, (perfluoroalkyl)alkanes, are

known to gelate several liquids,<sup>48</sup> including hydrocarbons,<sup>49</sup> perfluorodecalin,<sup>50</sup> and mixtures of perfluorooctane and isooctane.<sup>51</sup> These are interesting systems because they demonstrate the utility of repulsive as well as attractive interactions in effecting SAFiN formation and gelation.

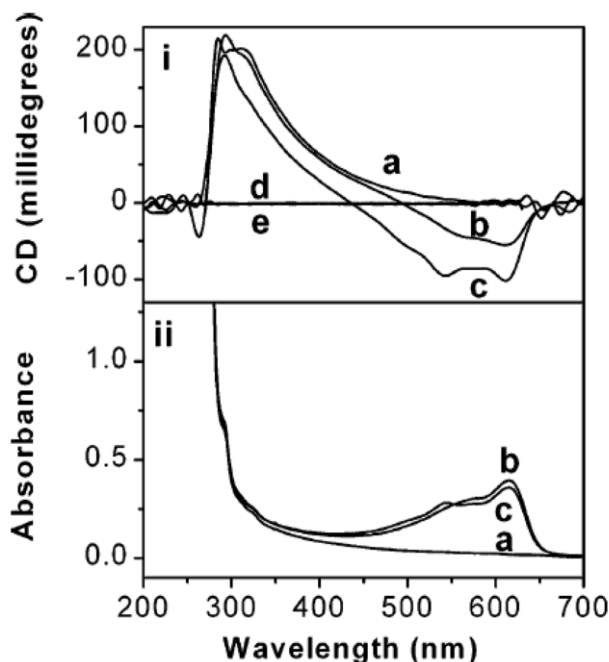


Figure 4: CD (i) and absorption (ii) spectra of 1 wt % **PDA-Nal** in a silicone oil gel (a) before irradiation, (b) after irradiation for 1 min, and (c) after heating the irradiated gel to ca. 70 °C for ca. 2 min. CD spectra of a solution of 1 wt % **PDA-Nal** in chloroform (d) and of neat silicone oil (e) are also included in (i). Note that the CD data in (i) below ca. 300 nm have no meaning because of the very high optical densities at these wavelengths. Reprinted with permission from ref 44. Copyright 2003 American Chemical Society.

Derivatives of (perfluoroalkyl)alkanes, in which an ester or amide group has been inserted, overcome some of the difficulties in attaining gelation at low concentrations of the gelator molecules.<sup>44</sup> Especially the gelators containing amide groups ( $\text{F}(\text{CF}_2)_m\text{CONH}(\text{CH}_2)_n\text{H}$ , where  $m = 7$ , and  $n = 18$  or  $m = 11$  and  $n = 3, 4$ , or  $6$ ), with their ability to form intermolecular H-bonds, are exceedingly efficient gelators of a wide range of liquids, including some perfluorinated ones,<sup>52</sup> including at low concentrations (i.e., < 2 wt%), and their gels were stable in closed containers for more than one year. The analogous esters ( $\text{F}(\text{CF}_2)_m\text{CO}_2(\text{CH}_2)_n\text{H}$ , where  $m = 11$  and  $n = 3$  or  $18$ ) do have enhanced dipolar interactions (with respect to (perfluoroalkyl)alkanes), but ester groups do not contribute as much as the amides to the stabilization of aggregates; the variety of liquids that they gelated was limited. Results from IR investigations confirmed that the amide groups do undergo extensive H-bonding within the SAFiN networks. XRD studies indicated that the gelator molecules pack in the same fashion within the neat solid as in some of the gel phases, and analyses of small angle neutron scattering (SANS) data on the gels were consistent with lamellar arrangements in the fibrils (which tend to bundle to extents that depend on the specific structure of the gelator and of the liquid and the gelator concentration).

With the exception of **PDA-Nal**, all of the gelators discussed thus far have been achiral, and their SAFiNs consist of spherulites, rods, or platelets. It is widely recognized that SAFiNs and gelator efficiency can be influenced greatly by judicious placement of centers of chirality into a gelator structure. A pertinent example, employing 12HSA and its derivatives, is discussed below.

Structures of gels from a gelator with 2 functional groups, racemic (DL) and optically pure (D) 12HSA ( $X = \text{HO}_2\text{C}$ ,  $Y = \text{CHOH}$ ,  $m = 10$ , and  $o = 6$ ), and its salts

From analyses of SANS data, Terech et al. found that the SAFiN of a 2 wt% gel of DL-12HSA in cyclohexane- $d_{12}$  consisted of ribbons whose cross-sectional dimensions are ca.  $150 \times 300 \text{ \AA}$ .<sup>53</sup> The cross-sectional dimensions were calculated to be ca.  $200 \times 200 \text{ \AA}$  in toluene- $d_8$  (assuming squares) and  $300 \text{ \AA}$  nitrobenzene- $d_5$  (assuming cylinders).<sup>54</sup> Unfortunately, the packing arrangement of molecules even within neat solid DL-12HSA is not well-defined—both triclinic<sup>55</sup> and monoclinic arrangements<sup>8</sup> have been suggested, and ‘powder’ X-ray diffraction analyses of a DL-12HSA aerogel (i.e., an organogel in which the liquid has been removed but the SAFiN is not destroyed) (cross-sections of ca.  $190 \text{ \AA}$ ), prepared from supercritical  $\text{CO}_2$ , are consistent with the coexistence of two lamellar phases.<sup>56</sup> The molecular packing and fiber structures of the aerogel differ in subtle but important ways from the SAFiN structures found in the toluene and cyclohexane gels.<sup>57</sup>

The SANS curves of SAFiNs of DL-12HSA and its optically pure (R) form, D-12HSA, are very different,<sup>17</sup> as are the shapes of the aggregates in the micrometer distance scale. However, both rely on interactions between carboxylic acid groups of pairs of molecules. Using the intensity of scattered neutrons as an indicator of the degree of aggregation, the kinetics of gelation for a 2 wt% sol of DL-12HSA in cyclohexane- $d_{12}$ , after cooling rapidly to room temperature, was found to have a rapid aggregation component, followed by a much slower one associated with equilibration of the initially formed SAFiN.<sup>58</sup>

D-12HSA gels in low polarity liquids, such as alkanes and thiols, have a hexagonal sub-cell spacing ( $\sim 4.1 \text{ \AA}$  between chains) and are multi-lamellar, with a long spacing greater than the sum of the lengths of two extended molecules ( $\sim 54 \text{ \AA}$ ). This polymorph has a CGC  $< 1 \text{ wt\%}$  and a fibrillar morphology.<sup>59</sup> 12HSA gels in nitriles, aldehydes and ketones, have a triclinic parallel sub-cell ( $\sim 4.6$ ,  $3.9$ , and  $3.8 \text{ \AA}$ ) and interdigitated lamellar structures ( $38$  to  $44 \text{ \AA}$ ). In these more polar liquids, the polymorph is less effective at immobilizing liquids due to the spherulitic micro-morphology that results. It has been suggested that the fiber cross-sections may be tuned from square to rectangular in specific liquids.<sup>7</sup>

Also, D- and L-12HSA and their alkali metal soaps (12HSA-M, where M is a metal ion) have been dissolved in numerous liquids, including Nujol,  $\text{C}_6\text{H}_6$ ,  $\text{CCl}_4$ ,  $\text{CHCl}_3$ ,  $\text{Me}_2\text{CO}$ , and ethanol for the acid and Nujol and ethanol for the soaps.<sup>13</sup> Isothermal crystallization resulted in fibers that transposed the molecular chirality for D-12HSA, D-12HSA-Na, D-12HSA-Li, D-12HSA-K, D-12HSA-Rb, and D-12HSA-Cs to a supramolecular sense of twist, irrespective of the liquid studied. The magnitude of the twist was independent of the absolute configuration of the gelator; as expected, the sign of the optical rotation was inverted by changing between enantiomers of 12HSA, and the magnitude of the rotation (and thus, the degree of twisting) depended on the cation.<sup>13</sup>

At concentrations between 0.1 and 4 wt%, D-12HSA-Na in soybean oil<sup>60</sup> and in ethanol, benzene, tetrahydrofuran, and dimethyl sulfoxide,<sup>61</sup> was an extremely effective gelator, and the sense of the helical twist of its SAFiN units was unaffected by the nature of the monovalent metal employed as a counterion.<sup>60</sup> These salts have led to the development of some interesting porous nanomaterials.<sup>61</sup> They may be useful as membranes.

Kinetic and thermodynamic aspects of gelation of D-12HSA and its isomers and derivatives

The consequences of the presence of chiral centers on the aggregation of molecules such as 12HSA in aqueous and organic media have been discussed from both experimental and theoretical standpoints.<sup>62</sup> In addition, a very provocative investigation of the influence of chiral and racemic hydroxyalkanoic acids (with various chain lengths and hydroxyl positions) on the thermodynamic stability of dimyristoylphosphatidylcholine membranes has been conducted.<sup>63</sup> Both studies demonstrate the importance of chirality in affecting the detailed nature of self-assembled structures like the SAFiNs being emphasized here.

Molecules of D-12HSA aggregate in non-aqueous media when their solutions/sols are cooled. The energies of the sol and aggregated/precipitated phases correspond to the activation energy for nucleation.<sup>11, 64-69</sup> Applying a statistical approach, the activation energy of nucleation for D-12HSA was calculated to be  $5.4 \text{ kJ/mol}$ .<sup>67</sup> Similar analyses were applied to molecules of similar shape that did not form gels (e.g., octadecanoic acid ( $\sim 2.12 \text{ kJ/mol}$ ) and trihydroxystearin ( $\sim 7.87 \text{ kJ/mol}$ ). Thus, the activation energies differ for molecules that form SAFiN fibers without a large number of branches and platelets (e.g., octadecanoic acid) or spherulites (e.g., trihydroxystearin) as a result of how the molecules orient themselves to exclude the polar regions from a low polarity liquid; this is primarily a result of the entropy of demixing.<sup>67</sup>

D-12HSA crystallizes via a two-step process in dodecane, toluene and xylene. Using time-resolved synchrotron SAXS, a large increase in the scattering intensity, without the appearance of crystalline peaks (Figure 5A,C) was observed.<sup>70</sup> During the first stage of assembly, the thickness of the cross-section of the fibers increased without development of long-range crystalline order.<sup>70</sup> Following the first stage of assembly, a 001 peak was observed, corresponding to a lamellar, highly-ordered crystal (Figure 5B,D).<sup>70</sup> During the second stage of crystallization, the fiber width,  $\sim 100 \text{ \AA}$ , remained unchanged in opaque D-12HSA gels in dodecane and  $\sim 82 \text{ \AA}$  in transparent 12HSA toluene/xylene gels. These results suggest that the second stage of crystal growth involves fiber elongation and fiber-fiber interactions.<sup>70</sup> Others have also observed a two-step gelation process for D-12HSA, where a main network is formed, followed by a minor contraction that is postulated to correspond to fiber aggregation into bundles.<sup>54</sup> From light scattering data of the isothermally cooled sols, the kinetics of self-assembly of D-12HSA was found to be very fast, and the half-time needed for complete crystallization,  $t_{1/2}$ , ranged from 0.8 to 4.6 min, depending on the liquid. In the same study,  $t_{1/2}$  values determined rheologically were found to be  $\sim 200 \text{ s}$ . The order of the  $t_{1/2}$  values was hexafluorobenzene  $<$  dodecane  $<$  toluene  $<$  nitrobenzene.<sup>54</sup>

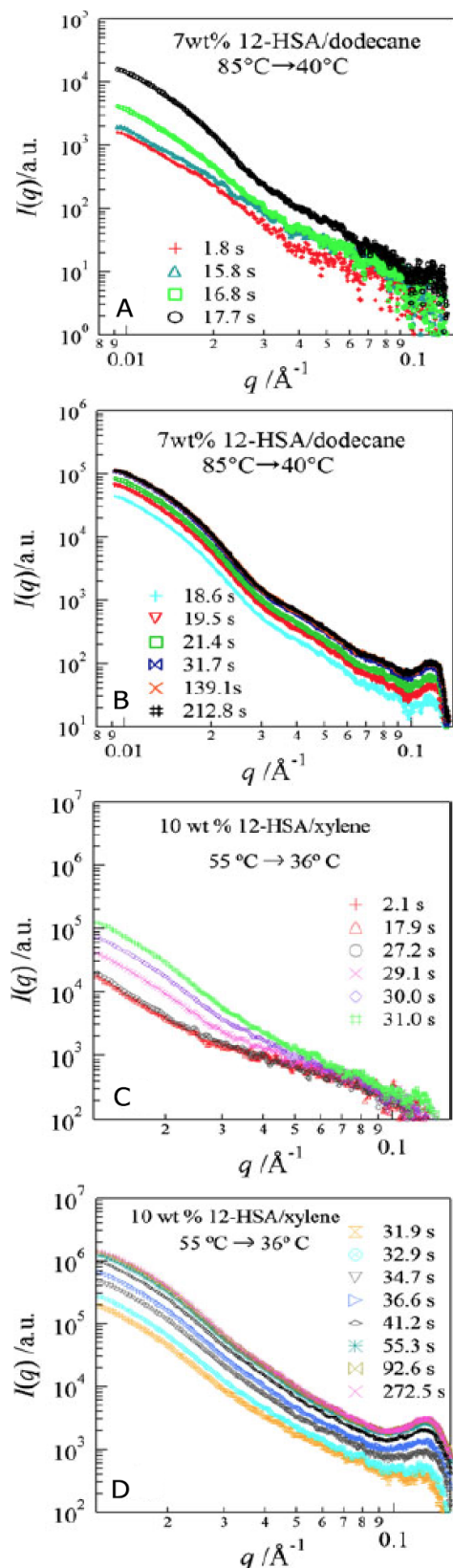


Figure 5: Time evolution of SAXS profiles for D-12HSA/dodecane (A,B) and D-12HSA/xylene (C,D) gels at 40 °C in the regime before crystalline nucleation (A,C) and after the nucleation (B,D). Figures 1 and 2 in ref 70. With kind permission from Springer Science and Business Media.

In crystalline DL-12HSA, molecules interact via a hydrogen-bonding sequence of the 12-hydroxyl groups, resulting in a zig-zag (*all-transoid*) conformation for the long alkyl chains, and a distance between adjacent 12-hydroxyl groups of 2.87 Å (Figure 6, black straight lines).<sup>8</sup> The angle of the hydrogen bonds for C12-O3—O'3 (i.e., of two hydroxyl groups between adjacent 12HSA molecules) is 117°. Furthermore, the dihedral angles of C4-C5-C6-C7 and C15-C16-C17-C18 are 180°, while C10-C11-C12-C13 has an angle of 173°. The deviation from 180° to 173° for DL-12HSA is thought to be partially responsible for the twisted helical structure observed in enantiomers of 12HSA. DL-12HSA dimerizes between the carboxylic acid groups and the distance between the adjacent O2--O3 atoms was found to be 2.62 Å.<sup>8</sup> Epitaxial growth patterns in SAFiNs are largely dependent on the presence of at least one stereocenter.<sup>71-73</sup> Chirality is observed not only on a molecular level, but is often expressed at much larger length scales, and, as noted above, has been observed in the supramolecular SAFiN assemblies of D-12HSA.<sup>12-16, 74, 75</sup> The sense of supramolecular twist of optically pure 12HSA can be correlated with the chirality of the enantiomer (i.e., D-12HSA forms left-handed helices).<sup>13</sup> There have been conflicting reports on the importance of chirality on the nature of the 12HSA aggregates (i.e., fibers versus platelets).<sup>12, 15, 17, 74-76</sup> The controversy arises over the fact that both optically active and racemic mixtures form molecule gels, but the SAFiNs consist of fiber units with D-12HSA and platelet units with DL-HSA (Figure 7).<sup>74</sup>

At the molecular level, DL-12HSA formed single, in-plane, hydrogen-bonded acyclic dimers in mineral oil that prevented longitudinal growth and attenuated the ability of the polar groups to phase-separate during nucleation.<sup>74</sup> This molecular arrangement is responsible for the appearance of platelets at the micrometer distance scale and for a percolation threshold above 2 wt%. Highly enantio-enriched and enantio-pure 12HSA had a percolation threshold < 1 wt% in mineral oil because the primary SAFiN units were fibers with high aspect ratios. Enantio-pure 12HSA dimerized in a head-to-head fashion, and the 12-hydroxyl groups formed an H-bonding network along the axis transverse to the longitudinal growth. Molecular chirality also affected the crystal growth kinetics and activation energies of aggregation. The kinetics of assembly were studied using data from synchrotron FTIR spectroscopy, integrating the area of the evolving hydrogen bonding peak between 3000 and 3200 cm<sup>-1</sup>, and were analyzed by the Avrami model.<sup>11, 64, 67, 77-79</sup> At enantio-enrichments ≥90 wt%, the Avrami exponent ( $n_A$ ) was 2, while at <90 wt% enrichments, it was 3.<sup>74</sup> The Avrami exponents, coupled with structural observations that showed fibers and platelets, respectively, for the two regimes of enantiomeric enrichment, suggest sporadic nucleation as the growth mechanism. Over the range of crystallization temperatures studied,  $n_A$  remained constant. Therefore, the rate constants for aggregation,  $k_a$ , could be used to calculate the activation energies of nucleation and growth using the Arrhenius model: ~42 kJ/mol for DL-12HSA and ~12 kJ/mol for D-12HSA.<sup>74</sup> Cyclic dimerization of the carboxylic acid groups and the necessity for the 12-hydroxyl groups to form H-bonds with other immediately adjacent 12-hydroxyls within the SAFiNs of >90 wt% optically pure D-12HSA shields the polar groups from the low polarity mineral oil liquid and, consequently, leads to a large reduction in the chemical potential and activation energy. The acyclic dimer, prevalent in the <90 wt% optically enriched SAFiNs, does not shield the polar head groups from the liquid as effectively; consequently, the chemical potential and activation energy are higher.<sup>74</sup>

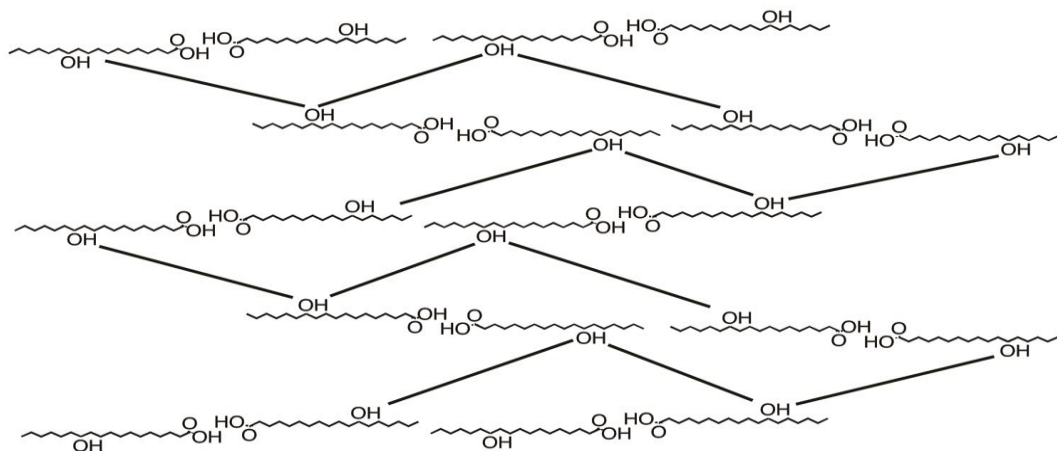


Figure 6: Hydrogen bond sequences along the a-axis of DL-12HSA. Thick black lines represent 2.87 Å; the zig-zag lines are not to scale.

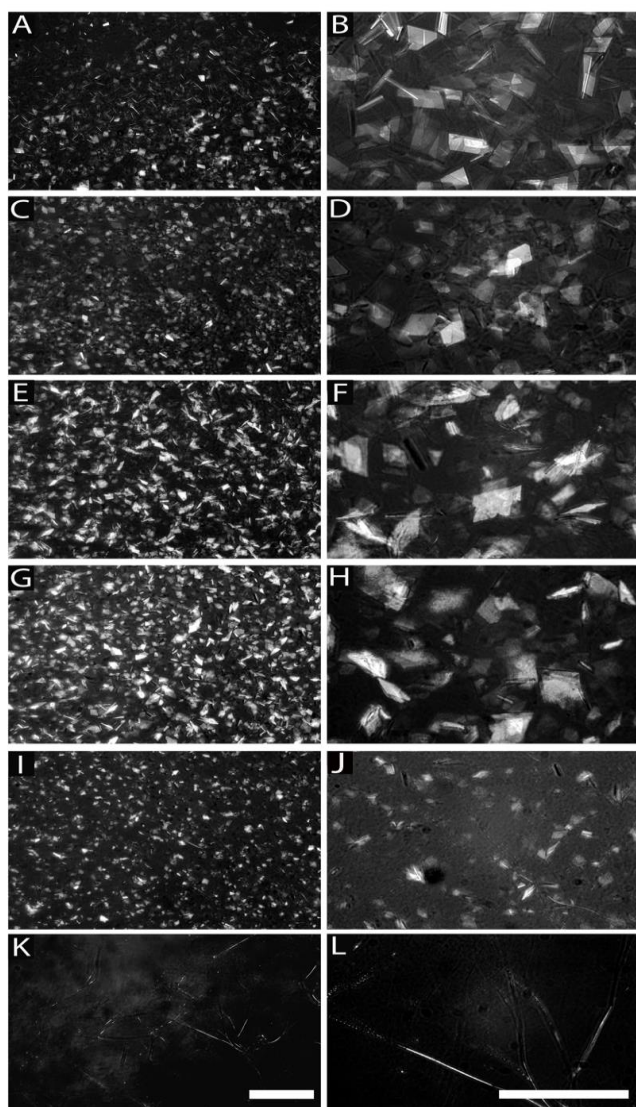


Figure 7: Polarized optical micrographs of (A,B) 50:50, (C,D) 60:40, (E,F) 70:30, (G,H) 80:20, (I,J) and 90:10 D:L-12HSA, and (K,L) D-12HSA. Magnification at 10X (A,C,E,G,I,K) and 40X (B,D,F,H,J,L) (Magnification bar = 20 μm).

### Positional isomers of DL-12HSA (nHSA)

Varying the position of hydroxyl groups added to the alkyl chain of stearic acid (i.e., leading to nHSA, where *n* refers to the position of the hydroxyl group in the racemic isomers) between  $C_{(2)}$  and  $C_{(14)}$  promoted either gelation or the formation of viscous solutions.<sup>80</sup> 2HSA and 3HSA (of unknown enantiomeric enrichment) formed viscous solutions at 2 wt% in mineral oil, while racemic mixtures of 6HSA, 8HSA, 10HSA, 12HSA and 14HSA formed molecular gels under the same conditions. The supramolecular assemblies differed depending on the position of the hydroxyl group. In the dispersions with 2HSA and 3HSA, few nuclei were present and crystal growth appeared as fibers growing in a radial fashion from nucleating centers. Domains of the separate crystals did not interpenetrate (i.e., form a continuous crystal network and an organogel) (Figure 8). Orthorhombic crystal platelets and fibers resulted when the hydroxyl group was at or beyond position  $C_{(6)}$  on the fatty acid backbone. Many more crystalline centers were present than observed in the 2HSA or 3HSA assemblies; more nucleating sites formed during the initial stages and less subsequent crystallization occurred when the hydroxyl position was at  $C_{(6)}$  or beyond.<sup>80</sup> The large number of small platelets and fibers interpenetrated, forming a 3-D network capable of entrapping the liquid component and leading to gels.

SAXS patterns of 2HSA and 3HSA show peaks corresponding to shorter 001 spacings, ~41–42 Å, than those of 6HSA, 8HSA, 10HSA, 12HSA and 14HSA (~43–45 Å).<sup>80</sup> 2HSA and 3HSA lack wide angle peaks and the other nHSA have peaks corresponding to a ~4.1 Å spacing, consistent with hexagonal packing of the fatty acid chains.<sup>81</sup> FTIR spectra indicated major differences in the chemical environments of the carboxylic acid head groups in the nHSA organogels and dispersions. 2HSA remained a ‘monomer’, while 3HSA had spectral features for both a free monomer and acyclic dimer. All of the 6HSA through 14HSA had both acyclic and cyclic carboxylic dimers in their SAFiNs.<sup>81</sup>

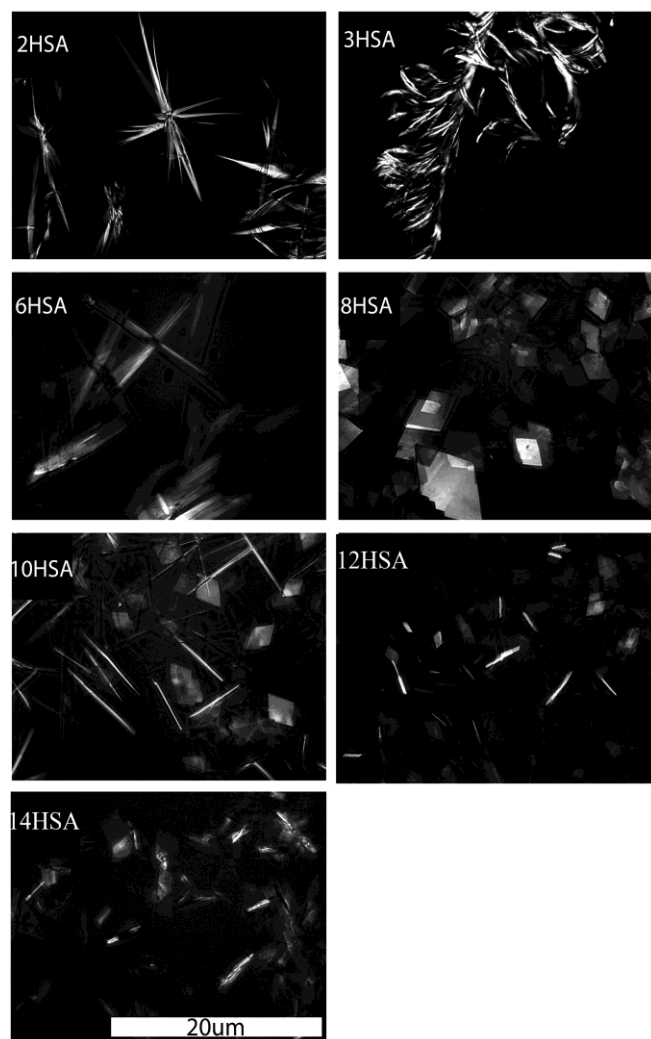


Figure 8: Polarized optical micrographs of positional isomers of 2 wt% gels and dispersions of DL-HSA in mineral oil at 30 °C. The space bar applies to all panels. Reprinted with permission from ref 80. Copyright 2012, the American Chemical Society.

The lack of dimers in the mineral oil dispersion of 2HSA (Figure 9), as well as the lack of wide-angle diffractions, characteristic of highly organized chains within a layer, indicate that when the secondary hydroxyl group is near the carboxylic acid head group, extensive H-bonding of the hydroxyl groups along the secondary axis is absent. The molecular packing of 2HSA promotes (or exists because of) carboxyl-hydroxyl interactions, and is a primary reason why its lamellar spacing is shorter than those of the other **n**HSA isomers (Figure 9) and why the carboxylic acid groups are not in dimeric arrangements. A secondary important consequence of the proximity of the hydroxyl groups to the carboxylic head groups in 2HSA and 3HSA is that the long alkyl chains are less inhibited to undergo motions that lead to conformations different from the *all-trans* ones needed for maximal London dispersive interactions. The data suggest that the hydroxyl group must be located at a relatively long distance from the carboxylic acid group in order to promote crystal growth along the secondary axis; this location also ‘anchors’ the positions of the long chains with respect to each other and, thus, stabilizes London dispersive interactions.

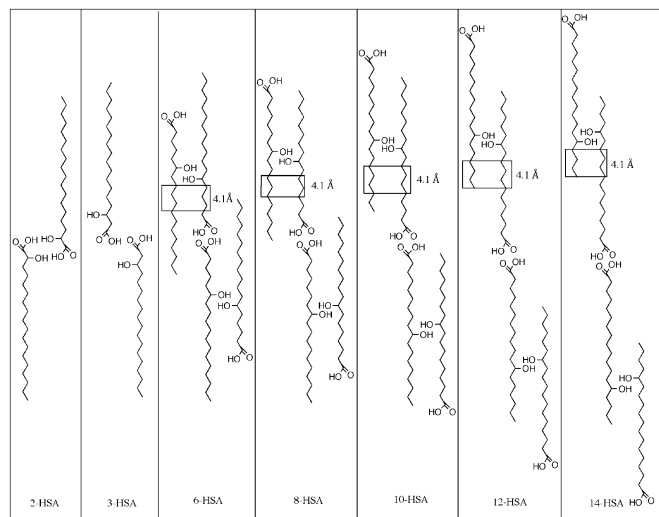


Figure 9: Proposed packing arrangements of **n**HSA isomers in the SAFINs of their gels/dispersions in mineral oil. Distances shown are based on XRD measurements. Reprinted with permission from ref 80. Copyright 2012, the American Chemical Society.

The gelation abilities of a series of positional isomers of ketooctadecanoic acids (**n**KSA; X = HO<sub>2</sub>C, Y = CO, m+o = 16) have been compared in a wide range of liquids. Oxidation of the 12-hydroxy group to a 12-keto group reduces the gelation ability, irrespective of the liquid utilized.<sup>82</sup> The series of **n**KSA-liquid combinations highlights the difficulty in developing tools for predicting gelation *a priori*. Although 2 wt% of D-12HSA and 5 wt% of 12KSA or 14KSA gelled hexane, and 8KSA and 10KSA precipitated when their hexane solutions/sols were cooled. In other lower-polarity liquids, such as CCl<sub>4</sub>, benzene and toluene, all of the isomers of **n**KSA examined formed at least a partial gel. However, 5 wt% **n**KSA sols of higher-polarity liquids, such as CHCl<sub>3</sub>, ethanol, and DMF, did not produce gels.

### D-12HSA derivatives with modified head groups

The importance of introducing a hydroxyl group, a second H-bonding site at C<sub>(12)</sub> of stearic acid, yielding 12HSA as an enantiopure or racemic molecule, and of moving the position of hydroxyl group along the stearic acid chain, have been discussed already. The importance of altering the structure of the carboxylic head group of D-12HSA is discussed here; in all examples mentioned in this section, the chirality at C<sub>(12)</sub> is (*R*).

The general order of gelator efficiency among the D-12HSA derivatives with various head groups is amides ≥ carboxylic acid > secondary amides >> amines. For example, as little as 0.1 wt% of D-12-hydroxystearamide was able to gelate silicone oil or toluene, and the amide gels were generally stable in closed vessels at room temperature for months. The amides gelled a wide range of liquids that includes alkanes, aromatic liquids, DMSO, and acetonitrile, but were insoluble in water. Some of the amide gels are thixotropic (i.e., they recover a part of their viscoelasticity after being destroyed by shear).<sup>83</sup> The recovery was very rapid; in the best case found, a 2 wt% D-12-hydroxystearamide in silicone oil gel was found to recover ca. 90% of its original viscoelasticity within 10 s after the cessation of destructive shear. Also, Ohseido et al. have found that the thixotropic properties of gels with primary alkylamides and alkylhydrazides can be enhanced by using mixtures of the homologues.<sup>84, 85</sup> The authors attribute the enhancement to a

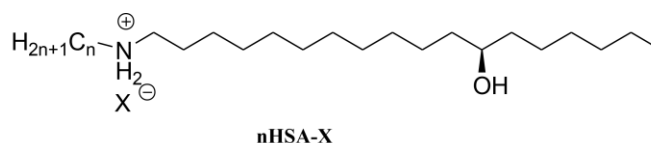
'surfactant-like' effect. We conjecture that the shorter homologues within a mixture may concentrate at junction zones (i.e., the points of attachment between the constituent objects in the SAFiN), creating points of lower order that are more easily re-established after the cessation of destructive shear.

*N*-3-hydroxypropyl dodecanamide (HODA) is another molecule in which a second H-bonding site has been introduced. Although the chain lengths between it and the *N*-alkyl amides of HSA differ, the comparison among them is instructive. In HODA, the hydroxyl group is near the amide head group. Freshly-prepared, fast-cooled, toluene gels with  $7.5 \times 10^{-2}$  mol/L HODA—the gels became suspensions of flat needles after ca. 2 weeks as a result of Ostwald ripening—recovered almost all of their viscoelasticity within 5 min after cessation of destructive shear.<sup>86</sup> Because this remarkable thixotropic behavior can be repeated several times on the same sample, the basic units of the SAFiN must not be destroyed by the mechanical action. A series of spectral and structural studies demonstrated the fibrillar integrity and that the fibrillar aggregates lost their junction zones, becoming aligned along the direction of shear. The interactions among the fibrillar objects were re-established rapidly when the shear was ceased, allowing the aligned fibers to become randomly oriented and, thus, re-entangled. The commonality between the comportment of the HODA and D-12HSA amide gels suggests that the presence of both hydroxyl and amide groups is key to the high thixotropy and fast recovery here; gels of other D-12HSA derivatives and simple amides do not exhibit the same rheological properties. In analogy with the proposed explanation of the enhanced thixotropy of gels with mixtures of alkylamides or alkylhydrazides as molecular gelators, interactions between hydroxyl and amide groups of the *N*-alkyl D-12-hydroxystearamides or HODA may also create junction zones with higher disorder than found within the individual fibers that have a greater capacity for reattachment after the cessation of destructive strain.

Although *N*-alkyl-18-amino-octadecan-7-ols ( $X = \text{RHN}$ ,  $Y = \text{CHOH}$ ,  $m = 11$ , and  $o = 6$ ), from reduction of the *N*-alkyl-12-hydroxystearamides, were not very efficient gelators—high concentrations were usually needed and few liquids were gelated—the  $\text{CCl}_4$  gels of some underwent an unusual, reversible gel-to-gel transition that preceded gel melting. Infrared, X-ray, DSC, and SANS data led to the hypothesis that a first order morphological transition within the fibers of the SAFiNs reduces the amount of intermolecular H-bonding (upon heating) and leads to the rapid expulsion of molecules of  $\text{CCl}_4$  within fiber bundles. Return of the system to the lower temperature phase on cooling was slow due to diffusion related processes.

As opposed to the amines from which they are derived, many of the *N*-alkyl-(*R*)-12-hydroxyoctadecylammonium chlorides (**m**-HSA-*X*, where  $X = \text{Cl}$  and  $n = 0-6, 18$ ) are excellent gelators as a result of enhanced electrostatic interactions that accompany aggregation, and several are able to gelate water as well as organic liquids at  $< 1$  wt% concentrations.<sup>87</sup> The efficiency of the gelators increased with the length of the *n*-alkyl group. Of the large range of liquids examined, 2 wt% 0-HSA-Cl was able to gel none and 2 wt% 1-HSA-Cl gelated only toluene and  $\text{CCl}_4$ . 2-HSA-Cl was able to gelate water and acetonitrile as well and 18-HSA-Cl gelated successfully alcohols, alkanes, aromatic liquids, and  $\text{CCl}_4$ , but not water or acetonitrile (from which its sols precipitated). This progression of liquids gelated correlates qualitatively with the degree of lipophilicity imparted to the gelators by the *n*-alkyl groups. As mentioned above, the **nHSA-Cl** form gels in aromatic liquids, H-bond donor and acceptor liquids, and in a wide range of other liquids.<sup>87</sup> Dielectric

constants provide no clear relationship with gelation ability: although toluene (2.4) and  $\text{CCl}_4$  (2.2) are gelated by **3HSA-Cl**, *n*-dodecane (2.0), cyclohexane (2.0) and *n*-hexane (1.9) are not.<sup>88</sup> The SAFiNs of the 3-HSA-Cl in toluene and in water have been imaged directly by cryo-SEM and indirectly by SANS measurements. The data indicate bundling of twisted fibers in the hydrogel and of cylindrical fibers in the toluene gel. In the hydrogels of the **nHSA-Cl**, the fiber widths increased with increasing *n*-alkyl chain length. This increase may be responsible for the empirical observation that, at a constant **nHSA-Cl** wt%, the gelation temperatures of the hydrogels increase as the alkyl chain length increases. However, there is no obvious correlation between alkyl chain length and the gelation temperatures of the toluene gels although both sets of gels appear to be packed in lamellae. Because the lamellar packing arrangements (by 'powder' XRD data) within the SAFiNs of the gels differ in subtle ways that cannot be analyzed with the data in hand, how the specific electrostatic interactions of the ammonium and chloride groups differ within the series of homologous salts cannot be discerned either.



In addition, the propylammonium cation with different anions (3-HSA-*X*, where  $X = \text{Cl}, \text{Br}, \text{NO}_3$ , and  $\text{BF}_4$ ) were explored.<sup>87</sup> The latter are somewhat better gelators than the corresponding amines in terms of their minimum gelator concentrations, but their range of liquids gelated is limited. 3-HSA-I did not gelate any of the liquids examined, and differences in the molecular packing arrangements of the 3-HSA-*X* within the SAFiNs, caused by the sizes and effective charges of the anions, result in very different gelation abilities that do not follow the Hofmeister series. For example, at the same concentrations, the melting temperatures of the hydrogels of 3-HSA-Br are higher than those of 3-HSA-Cl, 3-HSA- $\text{BF}_4$  formed only hydrogels, and 3-HSA- $\text{NO}_3$  gelated only water and  $\text{CCl}_4$ . Comparisons between gelation temperatures by 'the falling drop' and conductivity methods were used to calculate critical gelation temperatures of the 3-HSA-*X* salts (where  $X = \text{Cl}, \text{Br}, \text{NO}_3$  and  $\text{BF}_4$ ). From those data, it was concluded that the aggregation, nucleation, and gelation steps must occur within very narrow concentration ranges of the 3-HSA-*X*. The gels are strong rheologically at low gelator concentrations, but none was found to undergo the type of gel-to-gel transition found in the analogous amines. Several gelate both water and organic liquids at  $< 1$  wt% concentrations. From X-ray analyses, the morph of the SAFiNs for the hydrogels and the neat solids are the same; different morphs were found for the SAFiNs of the organogels examined.

## Liquid effects on molecular gels of D-12HSA and related molecules

Although the role of **nHSA** structure on gelation ability has been emphasized, the structures and properties of the liquid components are equally important. The nanostructure, microstructure and supramolecular structures of 12HSA gels are influenced by properties of the liquid component, which have been found to correlate with the hydrogen-bonding Hansen solubility parameter ( $\delta_h$ ).<sup>89</sup>

Hansen solubility parameters have been shown to be able to predict the capacity of D-12HSA to form gels in different organic liquids.<sup>89–91</sup> Liquids with  $\delta_h$  less than  $4.7 \text{ MPa}^{1/2}$  produced clear organogels, opaque organogels formed between  $4.7 < \delta_h < 5.1 \text{ MPa}^{1/2}$ , and solutions resulted when  $\delta_h > 5.1 \text{ MPa}^{1/2}$  (Figure 10). Numerous physical properties of the D-12HSA gels also vary based on the nanoscale arrangements of the polymorphs. For example, using free-induction-delay, pulsed NMR, highly ordered D-12HSA molecules have shorter  $T_2$  relaxations (below  $70 \mu\text{s}$ ) than poorly ordered ones, and a linear correlation has been found between the  $T_2$  relaxation times and the CGCs of the gels.<sup>90</sup> These results are consistent with increases in the onset of melting as ‘crystal quality’ increases; shorter  $T_2$  relaxations correlated to higher onsets of melting and longer unbranched fibers. Even extremely small changes in liquid structure (e.g., odd versus even numbers of methylene groups in *n*-alkanes) resulted in differences in the gelation temperature (at constant gelator concentration): chains with an even number of carbon atoms had slightly higher gelation temperatures than those with an odd-number.<sup>10</sup>

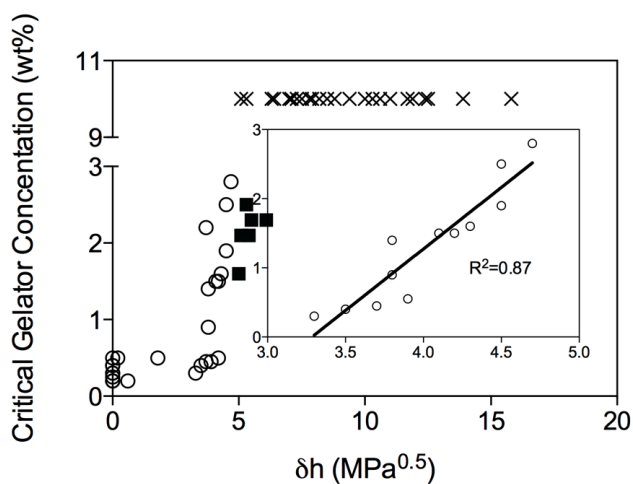


Figure 10: Critical gelator concentrations (determined using the inverted tube technique) as a function of the hydrogen-bonding Hansen solubility parameter ( $\delta_h$ ). Liquids that were not gelled are represented graphically with a CGC of 10 wt%. Clear gel (○); opaque gel (■). Reproduced from ref 91 with permission from The Royal Society of Chemistry.

## Tubules, cones and foams of DL-12HSA and related molecules

Not all of the aggregates of hydroxyalkanoic acids consist of one or two dimensional objects. Douliez and coworkers found that very dilute mixtures of 1,6-hexanediamine and 16-hydroxylhexadecanoic acid can organize into a mixture of tubules (1-D objects), disks (2-D objects), and cones (3-D objects) in water.<sup>92</sup> At room temperature, a 1 wt% sample is a gel in which the gelator molecules are hexagonally arranged in layers. At 0.1 wt%, the mixtures yielded tubules, disks, and cones with different angles and an average diameter of  $5 \mu\text{m}$  (Figure 11). Dilution of a 1 wt% sample without heating and cooling did not yield cones; the cones must be formed by complex nucleation and growth processes. In other work, Douliez and coworkers have demonstrated that, when cooled from their micellar phases, 50–200 mg/mL aqueous mixtures of DL-12HSA and  $\omega$ -amino-1-alkanols are able to form gels in which the SAFiNs consist almost exclusively of tubules.<sup>92, 93</sup> The ratio of the

two gelator components can be varied from 2:3 to 5:2 acid:amine, and the tubules remain stable in the presence of 10–30% (with respect to the gelator components and depending on the additive) of a variety of other acidic or basic additives, as well as the addition of short- and long-chained alcohols. With ethanolamine as the basic component, the tubules were  $> 10 \mu\text{m}$  long and had inner and outer diameters of 400 and 600 nm, respectively. The tubules consisted of bilayers of DL-12HSA (and associated amine) molecules that are separated from each other by water. The diameters of the tubules could be modulated by varying the temperature at which the micellar solutions were cooled.

The same group was able to transform the aqueous dispersions of tubules of DL-12HSA and either ethanolamine or 1-amino-6-hexanol assemblies into foams by passing gas through them.<sup>94</sup> The foams remained stable for months at room temperature, but reverted to micellar species when heated to characteristic temperatures. When the micellar solutions were cooled, the tubules reformed. The reversion of the heated foams was sufficiently slow that it could be stopped after their partial destruction by cooling to room temperature. The mechanical action needed to induce the foams also caused some of the tubules to unfold and the average lengths of the tubules was nearly halved. The component of the acid and base not in the tubules plays an integral role in stabilization of the foams.

The relationship between aggregating properties of the covalently modified DL-12HSA derivatives (including the nHSA-X ammonium salts) described in the sections above and the ammonium carboxylate salts employed by Douliez and coworkers has not been examined explicitly. However, similar surfactants are known to organize (and evolve!<sup>95</sup>) into a variety of objects like those described here.<sup>96–98</sup> It is possible that some of the DL-12HSA gelators do as well.

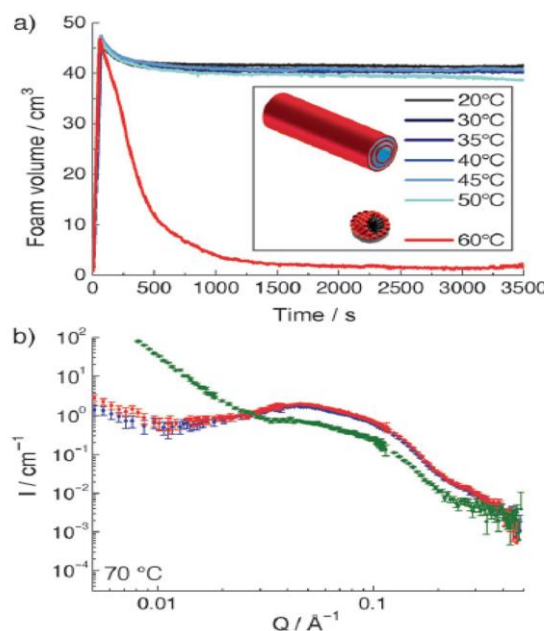


Figure 11: a) Evolution of the foam volume as a function of time at different temperatures for the DL-12HSA/hexanolamine system ( $T_m=60^\circ\text{C}$ ). b) SANS data at  $70^\circ\text{C}$  (in the DL-12HSA/ethanolamine system,  $T_m=70^\circ\text{C}$ ) showing that micelles are formed at that temperature in the foam (green), the stock solution (blue), and the drained solution (red). Reproduced from ref 94 with permission from Wiley-VCH.

## Concluding remarks and ‘perspectives’ for the future

This Perspective has discussed the relationship between the structures of a class of gelators in which the basic unit is the same, a long alkyl chain, and the physical and structural properties of their gels. Starting with the simplest organogelators possible, we have increased incrementally the complexity of the molecular structures in order to identify the features that lead to the most efficient gelators. The conclusions derived from this ‘prototype class’ of gelators are extrapable *qualitatively* to much more complex systems, although direct analogies are not be possible! Quantification of the factors determining how molecules pack in their SAFiNs, their solubilities in different liquids, and the dynamics associated with their aggregation, nucleation, and growth into the basic units that constitute a SAFiN remain outside current capabilities.<sup>1</sup>

Many challenges remain before our understanding of molecular gels will allow *a priori* design of molecules that are able to gelate a specific liquid and yield gels with desired properties. However, clues to such designs are found in how the gelation abilities of the molecular gelators described here vary as their structures are changed.

Before the puzzle of what constitutes an efficient molecular gelator is ‘solved’, one might conjecture about uses for new gelators and their gels. In this regard, we emphasize the word ‘conjecture’ while limiting the possibilities to gels involving molecular gelators based upon derivatives of *n*-alkanes. Of course, the structures of molecular gelators are not limited to derivatives of *n*-alkanes, and we leave, to the reader, to consider other frameworks that might be applicable for making gels with specific uses! With that in mind, one might consider substituting the 12-hydroxyl group in 12HSA (and other related molecular gelators) with thiol groups, so that they might be oxidized to disulfides and reduced again to thiols reversibly as a means to modulate the strengths of fibrillar networks. Also, the hydroxyl groups could be converted easily to vinylic groups capable of being polymerized, so that the fibrillar networks are permanently strengthened. Likewise, the carboxylic acid groups could be esterified with polymerizable groups or the nHSA-X structures could be modified to include polymerizable groups for the same purpose. Finally, it should be possible to develop materials that heretofore have relied upon polymeric gelators. In each of these cases, one can envision usages for the materials in the food, electronics, art conservation, chemical spill abatement, polymer, and pharmaceutical fields. A recent example is the use of polymeric microgels as synthetic platelets for promoting blood clotting.<sup>99</sup>

In each of these fields, molecular gels may be able to play a role that cannot be duplicated by their polymeric counterparts. We invite readers to consider what those molecular gels might be and to add to the list of potential uses. This part of the *Perspective* is for imagining what might be rather than what is!

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Professor Emeritus of Chemistry at the State University of Campinas in Brazil, who died 20 November 2013.

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