Molecular self-assembly and patterning induced by sound waves. The case of gelation

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Recent findings evidence that cavitational and mechanical effects of ultrasound waves trigger molecular assembly and pattern formation, exemplified by organogels and ordered structures. Although sonication-assisted aggregation has become a well-established protocol, the science behind it is often overlooked. In this *tutorial review* various aspects of ultrasound-driven reactions are introduced, highlighting organic and metal coordination compounds, as well as recent applications focused on polymer structures. Given the importance of supramolecular assemblies, especially hydrogels, as biomaterials and vehicles for drug transport and delivery, sound waves thus provide a facile entry to new forms of soft matter and functionalized materials.

1. Introduction and scope

If there is one word that resonates above all in modern chemistry and applied disciplines, it should surely be self-assembly. This is largely the way of nature, in which the organization of components through different kinds of interactions leads to shapes, forms, or periodical patterns.[1] Probably, it is true in nature that there is nothing not self-assembled.[2] Still far from mimicking natural self-organization, human intervention can design stimuli-responsive materials and molecular networks under the action of an external physical field, thus pointing to a biomimetic bottom-up approach. It is within this context that we should adequately place the role and effects of ultrasonic waves to cause aggregation, disruption–recombination, controlled size, exfoliation, or emulsion to name a few. Through this tutorial review we introduce the concepts of gel formation under the influence of microbubbles and describe a series of recent findings and applications that illustrate well the above-mentioned aspects.

It is fair to say, however, that aggregation processes and morphological changes in the presence of an acoustic field are not new. Such transformations have been exploited in materials science, though most applications concentrate on reactive metal powders and metal-containing nanoparticles and catalysts.[3–5] Likewise, ultrasound-induced crystallization—referred to as sonocrystallization—often leads to new crystalline forms (polymorphs) and causes significant changes in both shape and size.[6]

The present tutorial review complements and extends the role of sound waves and mechanical stress to soft matter

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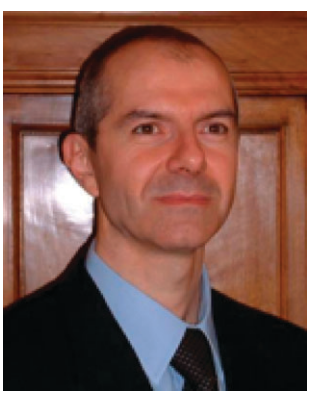

Giancarlo Cravotto

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consisting of organic compounds and macromolecules, which are able to immobilize solvent molecules generating supramolecular structures and networks.

The phenomenon of gelation activated by ultrasound could at first sight be counterintuitive as sonication is also responsible for the breaking of oligomeric and supramolecular entities in the liquid phase. Nevertheless, as we shall see, ultrasonic energy can indeed be a powerful stimulus to cause gelation provided that suitable molecules (gelators) are present. If the acoustic energy is sufficient to induce cavitation of the liquid, there are no doubts that this intriguing non-linear phenomenon constitutes the core of our rationale (*vide infra*). From a chemical viewpoint, activation could take place through different mechanisms. Unfortunately, the literature is not always clear and the field is certainly in its infancy. Thus, gel formation can be induced from apparently homogeneous solutions, and the gels can also be formed from a suspension or precipitate. These aspects are still underestimated and synthetic practitioners also overlook the fact that cavitation is largely dependent on and more influenced by the physical properties of a liquid and dissolved gases than by the physico-chemical properties of a given molecule. Leaving aside the preparation of organic gels and hydrogels assisted by ultrasound waves (sections 5 and 6), application of sonication to the sol–gel process has been known by materials scientists for more than two decades. The resulting sonogels, however, are often hybrid organic–inorganic structures (*e.g.* silica composites) or gels modified by further pyrolysis *en route* to porous architectures. This represents a rather specialized domain; though, to the benefit of interested readers, it will be briefly introduced and discussed (section 4).

It is convenient to bear in mind that gelation is a macroscopic manifestation of a complex process occurring at the nanoscale. In other words, one can visualize nature's patterns under the influence of sound waves. This is closely related to the familiar concepts of forms, shapes, and patterns, which are ubiquitous in organisms and artificial systems.[1,7] Probably, few readers would be aware of the fact that acoustic (pressure) waves are responsible for beautiful forms created in a liquid. Such spatial patterns, described for the first time in the early 19th century, can now be modeled mathematically like chemical oscillations and reaction-diffusion systems. This has little to do with gelation. However, under our perspective, history cannot be ignored and should be enormously instructive. Section 2.1 summarizes how acoustic patterning was actually recognized and visualized in the past and provides a deeper insight into the modern concept of ultrasonically-assisted molecular organization.

Finally, this tutorial review explicitly excludes another emerging and far-reaching application: proteinaceous particles assembled under ultrasound; readers interested in sono-chemically prepared protein microspheres are referred to a recent account instead.[8]

2. Cavitation and mechanochemistry

Sound is made up of (longitudinal) pressure waves, *i.e.* mechanical unlike electromagnetic waves, and requires an elastic medium to propagate. Chemical activation, however, takes place at ultrasonic frequencies (from 20 kHz and usually up to 1 MHz), the range that has found most applications, particularly in synthesis.[9,10] Above an intensity threshold, ultrasound is known to generate cavitation, that is formation, growth, oscillation, and collapse of bubbles in the pressure field. Indeed, it is cavitation that is the key phenomenon responsible for sonochemical effects, releasing enough kinetic energy to drive reactions to completion, as ultrasound frequencies do not even modify ro-vibrational molecular levels. The inside of the microbubble is actually a high-energy microreactor forming excited species as a result of high pressures and temperatures generated during collapse. The mechanical effects of cavitation are more evident at both the interface and the bulk media producing shock waves that induce shear forces. Moreover, one should bear in mind that like any sound wave, ultrasound is transmitted *via* waves which compress and stretch the molecular structure of the medium.[11] Microstreaming generated around the bubbles becomes more complex when solid particles are formed or suspended in the cavitating fluid. This microstreaming is not related to spatial attenuation but rather arises from frictional forces between a boundary layer and a medium carrying vibrations.[12]

2.1. Acoustic patterning in fluids

Although from a historical perspective the birth of sono-chemistry can be traced to Loomis and associates, who in the late 1920s reported the first physical, chemical, and even biological effects on small animals,[13] the mechanical action of sound waves in fluid patterning was observed earlier, even if largely ignored. British genius Michael Faraday (Fig. 1) is to be credited in this field as well. In a paper read at the Royal Society on 12 May 1831 entitled *On a peculiar class of acoustical figures*, and containing an appendix *On the forms and states assumed by fluids in contact with vibrating elastic surfaces*,[14] Faraday reinvestigated previous work and observed rings and periodical patterns in different fluids. He wrote: "when the upper surface of a plate vibrating so as to produce sound is covered with a layer of water, the water usually presents a beautifully crispated appearance in the

Fig. 1 Michael Faraday did observe, as early as 1831, a type of patterning in fluids induced by pressure waves, but disconnected from cavitation.

neighbourhood of the centres of vibration''. In other words, Faraday saw *crispations* that are standing-wave deformations of the fluid surface not only in water but also in different substances such as milk, egg white, alcohol, ink, and terpentine. He also observed patterns in sand and mercury, usually by the naked eye using reflections from the fluid surface, although in the case of milk by shining a light through the fluid from below.

A mathematical treatment of the so-called Faraday waves is complex and obviously beyond the scope of this review; though such surface waves are along with convection and reaction-diffusion (*e.g.* Belousov–Zhabotinsky or Turing models) the commonly studied pattern-forming systems.[15] Typical experiments usually involve sinusoidal vibration, where the effective acceleration (g_e) experienced by the layer adopts the form:

$$g_e(t) = -g + a\cos\omega t \quad (1)$$

where g is the acceleration due to gravity. At low amplitude (a) the surface will remain flat, but standing waves will form beyond a threshold value at which the forced acceleration overcomes viscosity. Non-sinusoidal patterns, such as twelve-fold rotational symmetries,[16] have also been observed and, in this case, evolution of the temporal pattern can be described by eqn (2):

$$g_e(t) = -g + a[\cos\theta\cos 4\omega t + \sin\theta\cos(5\omega t + \varphi)] \quad (2)$$

for constant a, θ, ω and φ. The instability threshold constitutes a complex formalism, otherwise required to account for fluid responses to surface tension, boundary conditions, and time-dependent effective gravity.[15]

3. Sound waves in gels

Faraday waves represent an important milestone in rationalizing shapes and aggregation, although other instability mechanisms have also been suggested such as in geometrical patterns observed in vibrated layers of granular material.[17] These processes are obviously not related to cavitation, a phenomenon only unveiled at the end of the 19th century.[10]

Remarkably, the interaction of ultrasound with soft matter has been known for many years through different therapeutic applications operating within a wide range of frequencies, intensities, and focal pressure amplitudes. Thus, even if gel formation under ultrasound (next sections) was viewed as an unexpected watershed that brought high-frequency sound to a supramolecular viewpoint, chemists have so far overlooked key lessons from medicinal treatments and cellular pathways. Water and gels are considered to be excellent coupling media and preferable to oils and creams. The coupling media is required in order to reach the target tissue as ultrasound will be reflected at the metallic device/air interface. Gels are sufficiently fluid to fill all available spaces, while being viscous enough to stay in place, have a suitable impedance to the media they connect to, and allow ultrasound transmission with minimal attenuation and absorption. In addition, tissues with a higher protein content (*e.g.* cartilage and bone) will absorb ultrasound to a significant extent, though wave reflections are likely to occur thereby decreasing the effectiveness of the applied energy. Softer materials, especially collagen-based materials, are the best absorbers of the ultrasonic energy.[18] Clearly, along with the inherent ability of small molecules to gel a given solvent, one should bear in mind how the resulting medium will absorb, change, or disturb the ultrasound energy.

It is also known that cavitational ultrasound represents a salient contribution to transdermal drug delivery and has been approved for enhanced delivery of bioactive substances through the skin.[19,20] A coupling medium, usually a hydrogel, between the ultrasonic transducer and skin facilitates cavitation. In this case, the expected mechanism is that microbubbles will oscillate and collapse at the skin surface, thus generating localized shock waves and liquid microjets directed at the stratum corneum (the skin's outermost layer preceding the epidermis). This action breaks the stratum corneum lipid structure and increases skin permeability. Beyond the gel phase, cavitational ultrasound is not believed to play a substantial role in transport, a fact that also avoids damage to deeper tissues.

4. Sol–gel processing under ultrasound: sonogels

Gelation, or sol–gel transition, involves transformation of a cross-linking polymeric material from a liquid to a solid phase. This creates a three-dimensional network sustained by physical junctions and weak bonds that can usually be broken by increasing the temperature or adding solvent. The so-called ''inverted test tube'' method has become the common and visual technique to assess this molecular switching of viscosity. Such rheological changes can be induced by electric, magnetic, and photochemical stimuli, with ultrasound incorporated recently into the list of physical fields.[21]

A particular class of gels, which attracted the attention of materials scientists more than two decades ago, are carbonaceous materials synthesized under high-intensity ultrasound.[22–24] The preparation of such sonogels usually involves formation of metal oxides by hydrolysis and subsequent polycondensation reactions assisted by ultrasonic irradiation leading to colloids that then self-assemble. Thus, silica–silica composites have been obtained in a two-step protocol that involves preparation of pure silica sonogels by submitting to the action of ultrasound (20 kHz) on tetraethoxysilane, $Si(OEt)_4$ (TEOS), and an acidic aqueous solution with an initial $[H_2O]/[TEOS]$ molar ratio = 4. A dispersion of fine SiO_2 particles in water was added to the preceding homogenized solution and ultrasound irradiation was then applied. Gelation took place within 3 min at room temperature.[25]

In general sonogels exhibit, upon solvent removal, a finer porosity and more enhanced reticulation than gels obtained by a traditional sol–gel methodology. Carbon sonogels have been synthesized by sonicating (20 kHz with a Ti alloy transducer at different intensities) aqueous mixtures containing resorcinol, formaldehyde, and sodium carbonate, a basic catalyst required for sol–gel polycondensation.[26] The resorcinol–formaldehyde sonogel could be obtained in a shorter reaction time than the conventional gel prepared without ultrasonic irradiation. The gelation time was also dependent on both the catalyst concentration (C/W, the ratio of catalyst to water) and the

ultrasonic intensity. For the same C/W ratio, the higher intensity, the shorter gelation time results. Ultrasonic irradiation was stopped near the gelation point and the resulting materials were allowed to age (in an oven at 348 K), then were freeze-dried and pyrolyzed at 1023 K to yield carbon sonogels, which were examined by SEM imaging (Fig. 2). The sonicated materials showed enhanced mesoporosity, although pore size distributions were also influenced by the catalyst concentration (or pH). At C/W = 80 mol m^{-3} (starting pH = 7.4), the carbon sonogels had good mesoporosity, while such materials showed no mesopores without sonication. Improvements in both mesopore volume and size distribution were also observed at C/W = 20 mol m^{-3} (lower pH), while ultrasound did not influence the porous properties at C/W = 40 mol m^{-3}.

The acceleration in gel formation was primarily attributed to generation of free radicals under irradiation, thereby favoring the first addition step in network formation. Although a satisfactory rationale for mesoporosity could not be established, the authors suggested that pitting of the sonogel surface caused by cavitation would also result in pore size modification. Such sonogels and carbon sonogels should doubtless find further use as catalytic supports and modified materials (electrodes, electro-optic devices, *etc*.).[22,23]

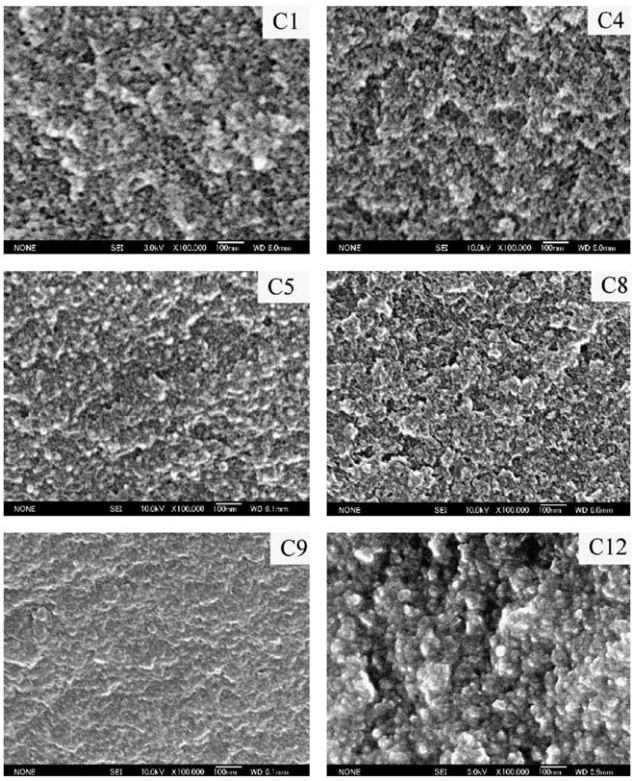


Fig. 2 SEM images of resorcinol–formaldehyde sonogels obtained at different C/W ratios (mol m^{-3}) and different ultrasonic intensities (W cm^{-2}): C1 and C4 (C/W = 20, I = 0 and 106, respectively); C5 and C8 (C/W = 40, I = 0 and 106, respectively); C9 and C12 (C/W = 80, I = 0 and 106, respectively). Reprinted with permission from ref. 26: N. Tonanon, A. Siyasukh, W. Tanthapanichakoon, H. Nishihara, S. R. Mukai and H. Tamon, *Carbon*, 2005, **43**, 525. Copyright 2005 Elsevier Ltd.

5. Formation and fate of organogels

Gelation of solvents with low molecular mass organic compounds under ultrasound was not considered a reliable strategy until 2005 when Naota and Koori reported rapid gelation upon sonication of a solution containing a dinuclear palladium complex, which is stabilized by intramolecular π-stacking interactions.[27] This also represents the first example of ultrasound-induced gelation in a coordination compound (*metallogels*).[28] Thus, clear solutions of complex *anti*-**1** (Fig. 3) were converted into a gel within a few seconds after ultrasonic irradiation (at 40 kHz, 0.45 W cm^{-2}) at room temperature. The *anti*-isomer was able to immobilize a wide range of organic solvents, irrespective of solution concentration and irradiation time. Gels thus obtained were thermoreversible and stable solutions were obtained upon heating at above T_{gel}. Salicylidene derivatives with longer hydrocarbon spacers (n = 6–8) failed to gelate the same solvent system, although precipitation could eventually be observed.

Notably, the protocol exhibits an exquisite stereoselectivity as the *syn* isomer of **1** did not give gels under the same conditions. This fact suggests that molecular assembly takes place with a single conformational arrangement. Moreover, since these metal complexes show planar chirality, the authors further investigated the role of chirality by assessing gelation with enantioenriched solutions of *anti*-**1**. Surprisingly, enantiopure (−)-*anti*-**1** remained in solution after prolonged sonication. In contrast, when a benzene solution of *anti*-**1** with 42% ee was irradiated, gelation did occur, but the resulting gel had no optical activity (*i.e*. 0% ee) (Fig. 4). That gelation proceeds with racemization provides a clue to the chemical nature of the aggregates. Thus, heterochiral association of *R* and *S* monomers should be formed and altering the cofacial bent structure of *anti*-**1** (Fig. 4b). In the absence of sonication this conformation avoids aggregation, but after irradiation self-assembly proceeds *via* an interpenetrative and consecutive stacking of planar monomers. The more stacked conformation in the heterochiral aggregates was inferred from changes in

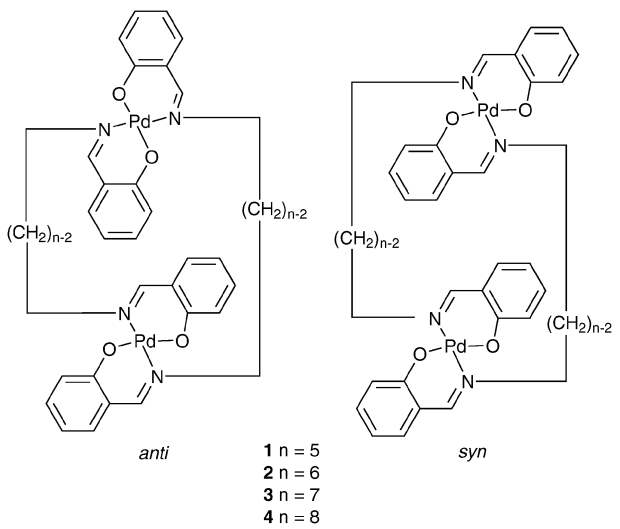


Fig. 3 Pd-Salicylidene complexes evaluated in sonication-induced gelation.

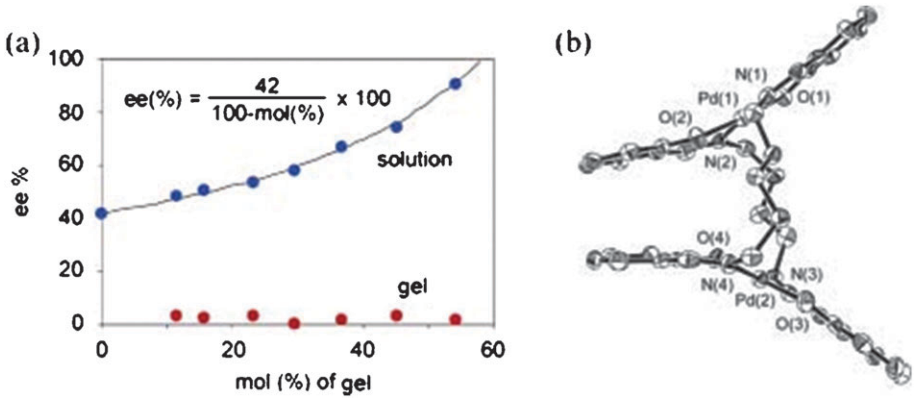


Fig. 4 (a) Enantiomer excesses of *anti*-**1** in the gel state and the remaining liquid. (b) Side view of the (*R*)-enantiomer showing intramolecular π-stacking of the bent conformation. Reprinted with permission from ref. 27: T. Naota and H. Koori, *J. Am. Chem. Soc.*, 2005, **127**, 9324. Copyright 2005 American Chemical Society.

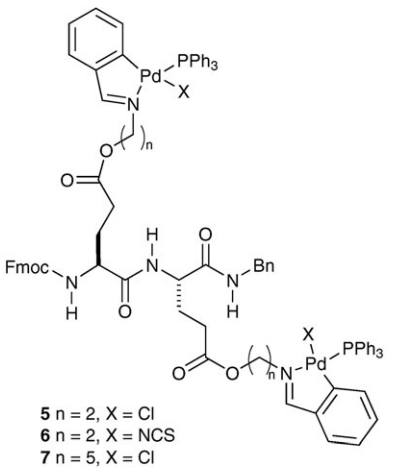
UV spectra and was consistent with the crystal structure found subsequently for *anti*-**2**. It is worth pointing out that chirality effects in self-assembled fibers have been evaluated, comparing homochiral and racemic gels;[29] however, a complete rationale on this fascinating subject is still an open question.

A further feature, evidencing the uniqueness of cavitational activation in the above-mentioned case, is that physical and mechanical stimuli other than sonication were unable to cause gelation including vigorous shaking, rapid heating–cooling, or microwave irradiation.

Naota and associates have also reported a rapid sound-induced gelation (60 s, 40 kHz, 0.45 W cm^{-2}) of palladium-bound peptides. A stable gel, revealing a hydrogen-bonded supramolecular architecture, was obtained from a yellowish solution upon sonication.[30] In the present case, however, the metalated peptides were able to gelate a few organic solvents and the presence of both a chloro ligand and a short spacer (compound **5**, Fig. 5) were crucial for gelation. Neither an isothiocyanate ligand (**6**) nor longer peptides (**7**) afforded stable gels. SEM and AFM images of the xerogels show self-assembly into lamellar aggregates of β-sheets (Fig. 5).

It is plausible to assume that gelation is triggered by re-organization of hydrogen bonding induced by sonication. Intramolecular hydrogen bonding between the chlorine atom and vicinal amide hydrogen atoms (supported by NMR data) prevents intermolecular self-assembly. Ultrasonic irradiation disrupts this situation and induces formation of discrete H-bonded aggregates that spontaneously undergo β-sheet polymerization.

While the field of low-molecular mass organic gelators (LMOGs) is well established,[31,32] instant gelation of organics induced by sound is less familiar. A family of benzylammonium cinnamate salts are capable of gelating various organic solvents, including petrol, which provides a further environmental perspective.[33] Instant gelation of solvents can easily be attained with the aid of a few drops of methanol followed by sonication (42 kHz) for 3–4 s; the minimum gelator concentration lies in the range 4–8.5 wt%. This study has also shown a rationale based on single-crystal structures, revealing that a supramolecular synthon favoring a one-dimensional (1D) hydrogen-bonded network is more important for gelation than



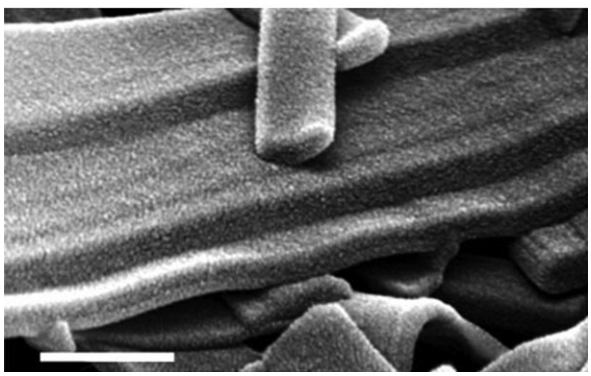


Fig. 5 Metalated peptides and SEM image of gel **5** showing a lamellar structure of β-sheet monolayers (scale bar: 200 nm). Reproduced with permission from ref. 30: K. Isozaki, H. Takaya and T. Naota, *Angew. Chem., Int. Ed.*, 2007, **46**, 2855. Copyright 2007 Wiley-VCH Verlag GmbH & Co. KGaA.

two-dimensional (2D) and three-dimensional (3D) hydrogen-bonded assemblies. This premise suggests that, while ultrasound benefits gel formation by partially destroying hydrogen bonding and/or altering other structural driving forces, multi-hydrogen bonding systems usually only produce precipitates.

A dendron (**8**) based on L-glutamic acid derivatives forming stable gels in both apolar (hexane, toluene) and polar (water)

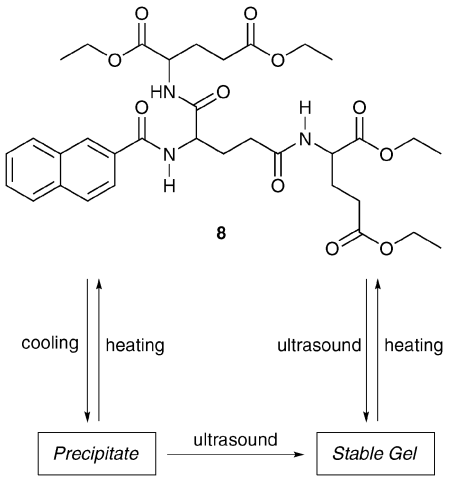


Fig. 6 Sol–gel transitions induced by sonication from hot solutions of a glutamate-based synthon (chirality is not specified).

solvents under ultrasound illustrates the above consideration.[34] The process between the hot solution of the organogelator and either precipitate or gel phase is reversible on heating and cooling. It should be noted that the gel phase could also be obtained from the precipitate by sonication (Fig. 6). Circular dichroism of this chiral glutamic synthon in the gel shows measurable Cotton signals, indicating the existence of supramolecular chirality.

Ureas are suitable derivatives for gelation studies as they may generate multiple intermolecular hydrogen bonds favoring intertwining nanofibers and other morphologies. A C_3-symmetric tris-urea (**9**) produces a translucent gel in acetone after sonication. The gel is stable for several months at room temperature, whereas cooling of the acetone solution resulted in precipitation. Re-gelation may be induced by sonication and compound **9** was also able to immobilize other polar solvents, but not hydrocarbons or dichloromethane.[35] This tris-ureido gelator responds to chemical stimuli and reversible sol–gel transitions may be observed upon addition of anions (Fig. 7). Addition of $BF_3{\cdot}OEt_2$ under ultrasound caused gelation of solutions containing F^-; though they remained unchanged in the presence of Cl^-, Br^-, or I^-. Other Lewis acids ($ZnBr_2$) plus sonication caused re-gelation of acetone solutions containing all the halides as well as the acetate anion. In stark contrast to tris-urea **9**, neither the corresponding tris-amide nor the tris-*N*-methyl urea derivative acted as organogelators.

A family of ureido amphiphiles and bola-amphiphiles derived from chiral aminopolyols (namely D-glucamine and *N*-methyl-D-glucamine) were found to be excellent hydrogelators (Fig. 8).[36] Such non-ionic surfactants can be generated from readily available unprotected aminosugars and hydrophobic isocyanates in one-step protocols and aqueous media, thus enhancing the green character of the synthetic strategy. Although reversible thermal gelation was a general trend, sonication (35 kHz) caused gelation at room temperature and water immobilization may also be obtained at lower concentrations of gelator (1.0 wt% *vs.* 2.0–3.0 wt%). Variable morphologies at the microscale were observed (SEM) for the corresponding xerogels. It is noteworthy that some derivatives also formed lyotropic liquid crystals with lamellar or hexagonal patterns.

Under ultrasonic irradiation, the nucleoside 2′-deoxyadenosine having an octyl hydrocarbon side chain with a urea linker (**14**) also gelates water.[37] Sonication (47 kHz for 30–60 s) creates a network consisting of fibers with a 30–50 nm diameter. Based on FTIR and mass spectra, the assembly of **14** should arise from intermolecular interactions involving water molecules with the ureido group as well as transient hydroxylated species at the adenine moiety, thus producing a hydrophobic–hydrophilic balance that favors gel formation. Clearly, formation of supramolecular aggregates is partially related to radical species from water sonolysis, which are known to cause damage in DNA bases and sugars (Scheme 1). Although the authors of this investigation proposed an initial pathway for water sonolysis producing H^+, hydroxyl radicals ($HO^{\bullet}$) and solvated electrons (from older literature that relates sonolysis to radiolysis-like experiments), the actual species produced by ultrasound are both $H^{\bullet}$ and $HO^{\bullet}$ radicals.[10,11] Such intermediates may then trigger formation of hydroxylated adenine having increased interactions with water molecules during gel formation. Cessation of ultrasonication leads to the parent deoxyadenosine derivative, a less hydrophilic nucleoside that precipitates as an amorphous solid.

Other hydroxylated heterocycles are likewise capable of forming stable hydrogels under ultrasonic treatment, such as in the case of structures formed by the reaction of 1,3,5-benzenetricarboxylic acid and 4-hydroxypyridine.[38]

Peptide solutions which should absorb ultrasonic energy efficiently lead to stable gels in a variety of solvents. A dipeptide prepared in a one-step synthesis from *N*-Fmoc-protected leucine and *C*-benzoyl-protected leucine, only produced precipitates when hot homogeneous alkane solutions (25–100 mM) are cooled. Dispersion of this dipeptide in alkanes (26 mM) followed by sonication at 20 °C for 1–4 min resulted instead in a complete liquid gelation.[39] This transformation appears to be capricious in various structural and physical aspects. Thus, dipeptides lacking the benzoyl group or replacing the Fmoc group by benzoyl did not gelate any solvent under ultrasound. Moreover, only ultrasound as the external stimulus was able to induce gelation, and higher temperatures ($T > 45$ °C, ultrasonic bath) prevented gel formation.

Ultrasound also induces morphological changes depending on exposure times. While short sonication (10 s) favors formation of sheet-like particles, longer exposures (20–60 s) lead to a well-defined network of fibers with an average diameter of 60 nm. Prolonged sonication gives rise to a final architecture composed of ribbon substructures (Fig. 9, top). CP-MAS solid-state ^{13}C NMR spectra point to an initial gel consisting of antiparallel β-sheets *via* hydrogen-bonded amide and carbamate units (Fig. 9, bottom).

This research group has also reported a useful variation of the above strategy: preparation of quantum dots doped gels, which can be harnessed in photoluminescent studies.[40] Quantum dots were based on either CdSe or CdSe/ZnS cores. Alkane solutions of these species were added to a dipeptide and the resulting mixture was sonicated for a few minutes (ultrasonic bath: 40 kHz, 0.28 W cm^{-2}).

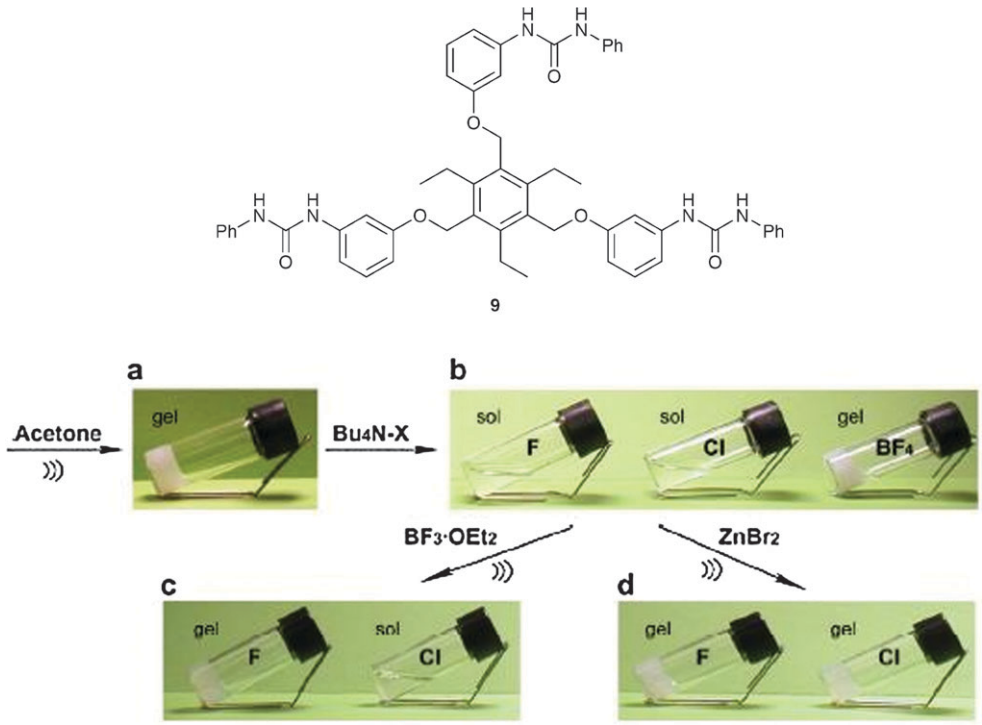


Fig. 7 Sequence of photographs showing the response of a gel of compound **9** in acetone (2.0 wt%) to different chemical agents under sonication. Reproduced with permission from ref. 35: T. Nakagawa and H. Itagaki, *Tetrahedron Lett.*, 2007, **48**, 8990. Copyright 2007 Elsevier Ltd.

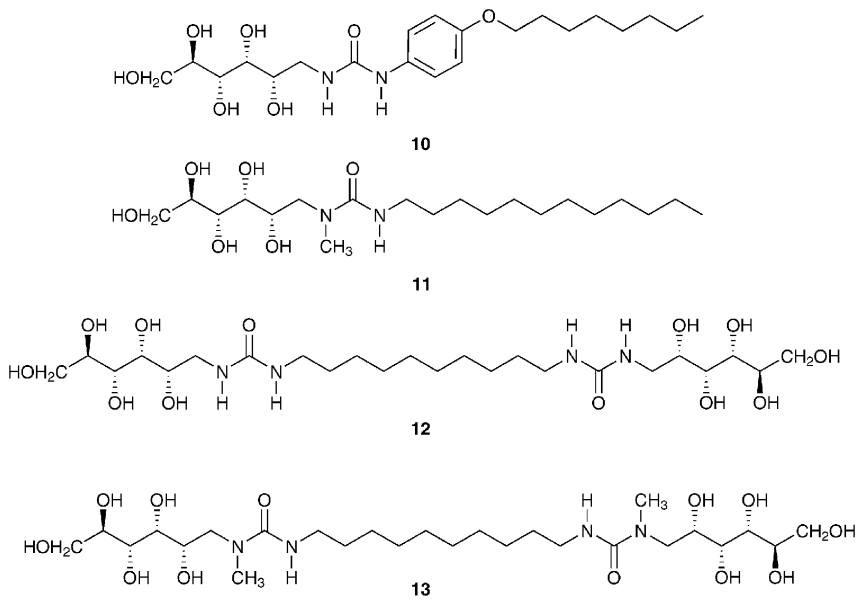
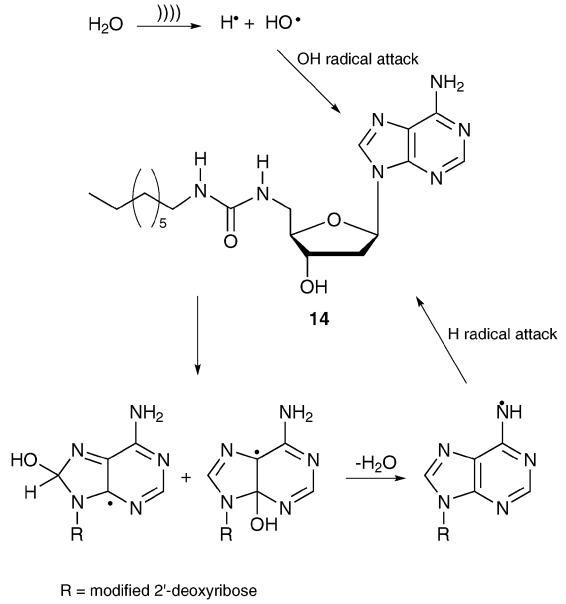


Fig. 8 Representative amphiphiles and bola-amphiphiles derived from aminosugars and producing stable hydrogels upon sonication.

Feng and co-workers have recently investigated the ability of cyclo(L-Tyr-L-Lys) and its ε-amino derivatives to act as both organo- and hydrogelators.[41] The starting cyclodipeptide **15** was easily generated by a one-pot thermal procedure involving deprotection and cyclization of Fmoc-Lys(Fmoc)-Tyr-OMe in a mixture of piperidine and DMF. Subsequent *N*-acylation of the ε-amino group in the Lys residue, either with acid anhydrides or alkyl carboxylic acids, gave rise to derivatives with longer alkyl chains (Scheme 2).

Compound **15** only dissolves in highly polar solvents and gelation was observed in some of them at low concentrations (usually in the range 0.5–2.0 wt%) at room temperature. In fact, the preparation of **15** in DMF led invariably to instant gelation at a very low concentration (0.3 wt%). Although **15** precipitates in water, ultrasound irradiation promotes formation of a weak gel instead of precipitation during the cooling process as observed without sonication. Such hydrogel and precipitate returned to the soluble phase on heating, and



Scheme 1 Ultrasound-promoted hydrogelation with a modified 2′-deoxyadenosine influenced by water sonolysis.

this cycle could be repeated many times. It should be noted that hydrogelation took place even at 56 °C under sonication at a concentration of 1.5 wt%. It seems that ultrasound induces and accelerates an efficient primary nucleation that favors fibrillar aggregation.

The *N*-acylated derivatives **16a–16g** lack their gelation capability in DMF and DMSO, even at relatively high concentrations. In contrast, such substances can immobilize primary alcohols (at 1.0 to 2.0 wt%), although formation of hydrogels was observed as well with the shortest alkyl chains (**16a–16c**), upon cooling their aqueous solutions at 1.0 wt%. Longer alkyl chains (**16d–16g**) resulted in insoluble derivatives in water; though the effect of sonication was not attempted in these cases. Based on NMR and X-ray powder spectra, self-assembly appears to be consistent with a bilayer structure stabilized by hydrogen bonding between amide groups of the diketopiperazine rings, while hydrocarbon tails are packed in the inner part.

5.1. Temporary destruction of gels

An interesting *tour de force* in understanding the mechanical effects of ultrasound has been supplied by Sijbesma and his group through reversible coordination polymers based on palladium. Although not directly related to molecular gel formation, but rather to the well-known covalent-bond breaking induced by ultrasound, these authors did observe a reversible rheological switching during ultrasonic scission of a linear polymer containing diphenylphosphine, Pd(II) chloride, and a polyether spacer (Fig. 10).[42,43] Sonication decreased both molecular weight and specific viscosity (from 5.4 to 1.5) and on standing for 24 h the original weight was fully recovered, thereby suggesting selective breaking between palladium and phosphine groups followed by further recombination. The mechanochemical scission (US probe at 20 kHz under Ar) has also been extended to silver- and ruthenium-carbene coordination polymers, which could serve

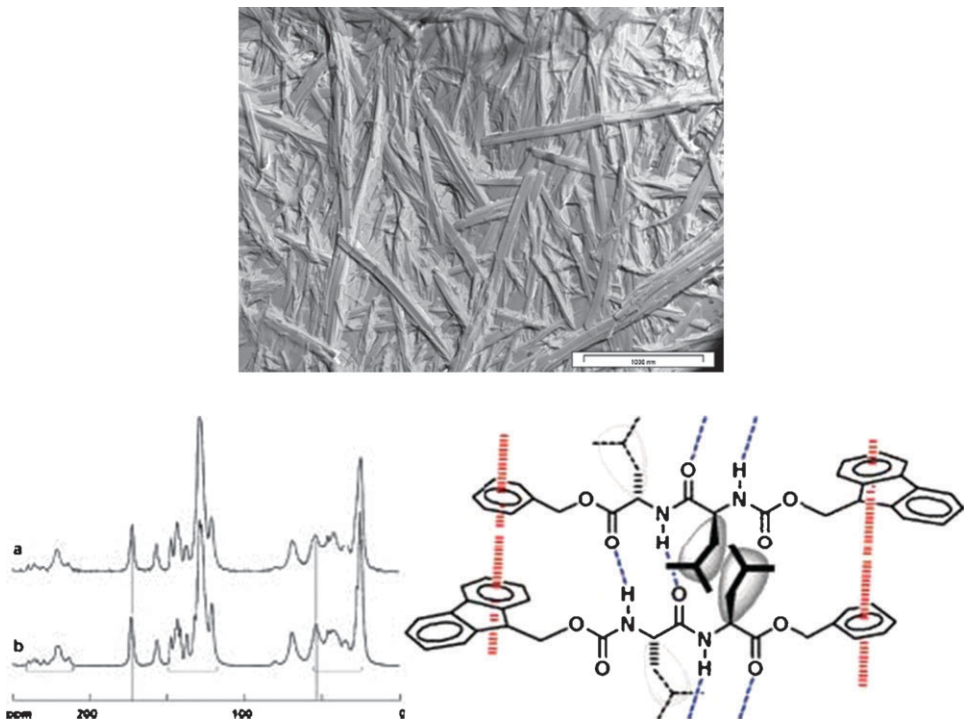
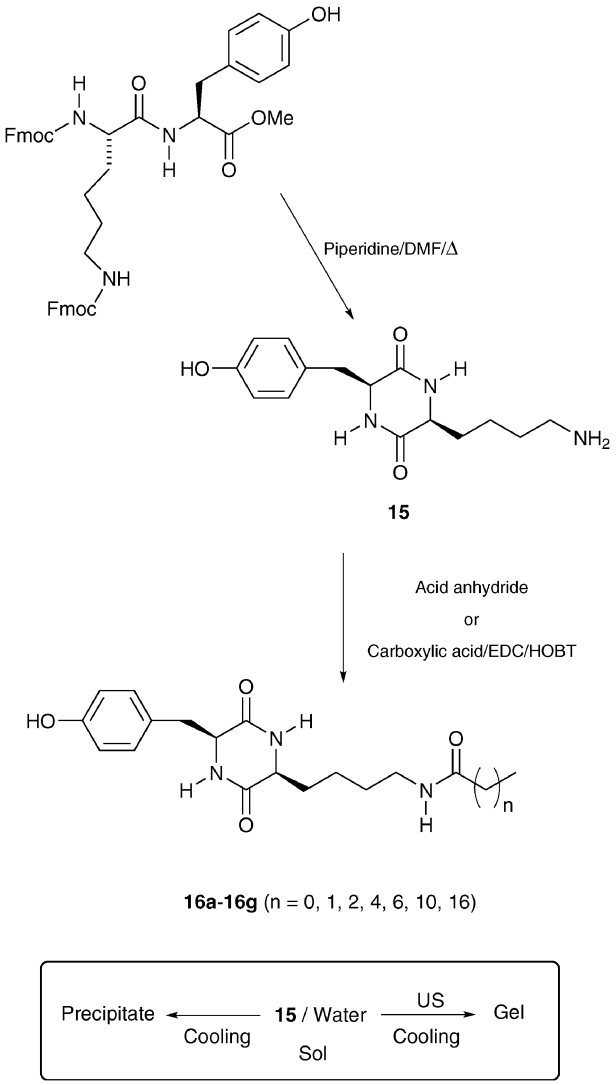


Fig. 9 Top: ribbon structures of a dipeptide organogel (nonane) after a sonication time of 20 s; the image was obtained by freeze fracture electron microscopy. Bottom: proposed antiparallel β-sheet structure based on CP-MAS ^{13}C NMR experiments. Reproduced with permission from ref. 39: D. Bardelang, F. Camerel, J. C. Margeson, D. M. Leek, M. Schmutz, M. B. Zaman, K. Yu, D. V. Soldatov, R. Ziessel, C. I. Ratcliffe and J. A. Ripmeester, *J. Am. Chem. Soc.*, 2008, **130**, 3313. Copyright 2008 American Chemical Society.



Scheme 2 Chiral diketopiperazines derived from amino acids, which are efficient organo- and hydrogelators.

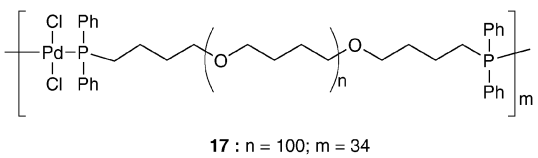


Fig. 10 Polymer that undergoes reversible scission at Pd–P bonds under ultrasonication.

as potential catalysts. Without sonication, the alternative thermal conversion is sluggish.[44,45]

Ultrasound causes stronger rheological effects on gels than on polymer solutions as mechanical effects can act more efficiently. As a proof of concept, reversible switching of the sol–gel transition has been observed for Rh(I) and Ir(I) coordination complexes.[46] Combination of $[RhCl(COD)]_2$ or $[IrCl(COD)]_2$ with a diphenylphosphine polyether polymer in $CHCl_3$ solution gave rise to stable gels (Fig. 11). Contrary to previous findings, sonication of the Rh(I) gel caused liquefaction within 3 min, while re-gelation occurred 1 min after sonication was stopped. Liquefaction occurred similarly for the Ir(I) gel, but re-gelation took longer at room temperature (1.5 h) and more than 10 days at −20 °C. Such facts cannot be accurately interpreted invoking only thermal effects. Based on ^{31}P NMR to estimate ligand exchange rates as well as oscillatory shear experiments, it was concluded that sonication does actually induce ligand exchange but does not modify coordination stoichiometry. Mechanical forces disrupt partially the supramolecular network decreasing the portion of metal centers involved in cross-linking. When sonication is stopped, the metastable system is shifted to the gel state at a rate determined by the exchange kinetics of the organometallic compound.

It should be noted that reversible bond breaking in such assemblies involves the transient formation of coordinatively unsaturated metal complexes. According to the empirical rules of sonochemistry, formation of such species should be the sonication-sensitive step (playing a similar role to radicals or electron-deficient intermediates in organic sonochemistry),[47] which also accounts for the particular effects of ultrasound in the sol–gel transition.

5.2. Ultrasound-induced morphological changes

Previous examples have also illustrated cases of molecular re-shaping by ultrasound, which has its origin in cavitational effects (erosion, dispersion, hole formation, aggregation, *etc.*) leading to variable structures depending on irradiation times. These effects can produce morphologies markedly different to those encountered under silent conditions, thereby representing a valuable route to new materials. Thus, the cooling of a cyclohexane solution containing *N*-Fmoc-octylglycine produces a precipitate consisting of unbranched nanowires. Use of ultrasound as stimulus switches to intermolecular hydrogen bonds that facilitate formation of interconnected nanofibers and hence gelation.[48]

Zhu and associates have equally shown that amphiphilic Janus particles (*i.e.* exhibiting opposite hydrophobic and hydrophilic faces), generated by non-covalent cross-linking of polymeric blocks, tend to self-assemble in aqueous solution leading to nanotubular structures. Upon sonication, TEM provided evidence of the formation of nanosheets having two types of morphologies, either trapezoidal (with short irradiation periods: 20 s) or semicircular (after prolonged exposure).[49] Since this switching occurs quickly, a mechanism based on nanotube dissociation into small particles that further undergo re-assembly seems to be unlikely. Moreover, the regularity of sheets in shape and size is more consistent with plastic deformations induced by sound waves that result in the unwinding and flattening of the tubular aggregates.

Ultrasound-induced morphological switching has also been observed in a coordination polymer that can be constructed by the reaction of $Zn(OSO_2CF_3)_2$ and 4,4′-bis(1-imidazolyl)-biphenyl (Fig. 12).[50] Micro- or nanoparticles obtained show a sheet-like structure, which can be converted into a three-dimensional fibrillar network capable of immobilizing organic solvents upon sonication (40 kHz, 0.45 W cm^{-2}). On the basis of CP-MAS solid-state ^{13}C NMR spectra and crystal data, the authors suggest a rationale for fiber formation owing to

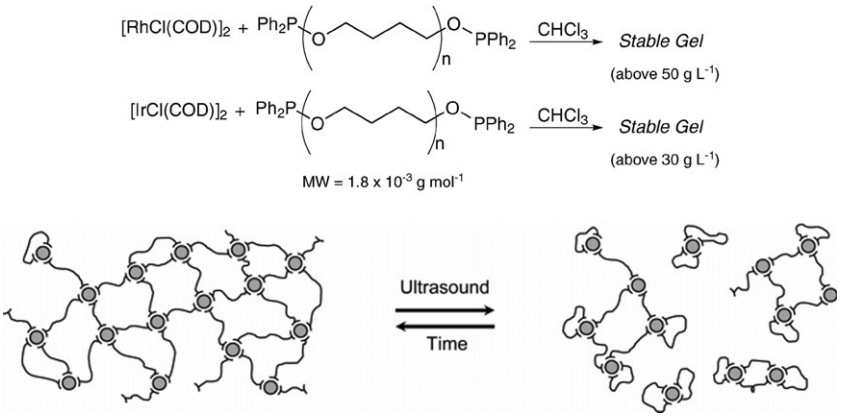


Fig. 11 Formation of stable Rh(I) and Ir(I) gels. Bottom: schematic representation of the ultrasonic scission causing liquefaction. Reproduced with permission from ref. 46: J. M. J. Paulusse, D. J. M. van Beek and R. P. Sijbesma, *J. Am. Chem. Soc.*, 2007, **129**, 2392. Copyright 2007 American Chemical Society.

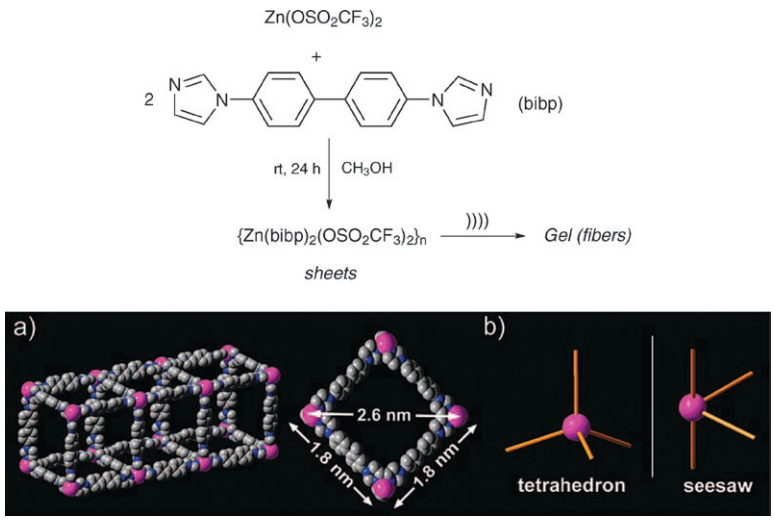


Fig. 12 Synthesis of a Zn coordination polymer and gelation under ultrasound. Bottom: (a) proposed mode of nanofiber organization; (b) Zn ions would adopt a tetrahedral coordination before sonication and a seesaw arrangement after ultrasonic irradiation. Reproduced with permission from ref. 50: S. Zhang, S. Yan, J. Lan, Y. Tang, Y. Xue and J. You, *J. Am. Chem. Soc.*, 2009, **131**, 1689. Copyright 2009 American Chemical Society.

differences in the structural environment of the Zn ions. Thus, Zn would adopt a seesaw arrangement rather than the tetrahedral coordination (Fig. 12, bottom). Although the former should also exhibit some tension, this could be facilitated by ultrasound due to thermal and pressure local changes.

Zhu and co-workers have described a discrete organogelator containing an electroactive tetrathiafulvalene (TTF) core and one urea unit (**18**), whose gelation properties can further be tuned by charge-transfer (CT) complexation and oxidation.[51] The successful idea behind this is that formation of CT complexes causes the TTF unit to acquire a positive charge, and it can also be transformed, either chemical or electrochemically, into the radical cation ($TTF^{+\bullet}$) and even the dication (TTF^{2+}). Overall, these electronic transitions modify the interaction with adjacent TTF units and intermolecular hydrogen bonding through urea groups, thus favoring gelation. When compound **18** was cooled directly from a hot solution in 2-propanol, no gel formation took place leading to precipitation only. However, ultrasonic irradiation for a few minutes before cooling gave rise to gelation.

The gelator reacts with 7,7,8,8-tetracyanoquinodimethane (TCNQ) in cyclohexane and the resulting CT complex generates a dark-green gel. However, in other solvents like 1,2-dichloroethane, complexation of **18** with TCNQ leads to destruction of the gel phase. Likewise chemical oxidation (with $Fe(ClO_4)_3$ or $NOPF_6$) or electrochemical oxidation in 1,2-dichloroethane also caused gel destruction to produce a dark-green suspension. Notably, the structure of the gel changed after formation of the CT complex with TCNQ in cyclohexane. The initial thin fiber structure was converted into a tubular arrangement with diameters of *ca.* 20–60 nm (Fig. 13).

In a recent study, a H-bonding gelator, *N*-lauryl-L-glutamic acid di-*n*-butylamide, which forms separate spherulites in solution, can be transformed into a 3D interconnected fibrillar network by sonication.[52] This substance dissolves in *n*-octanol or propylene glycol, although above the critical gelator

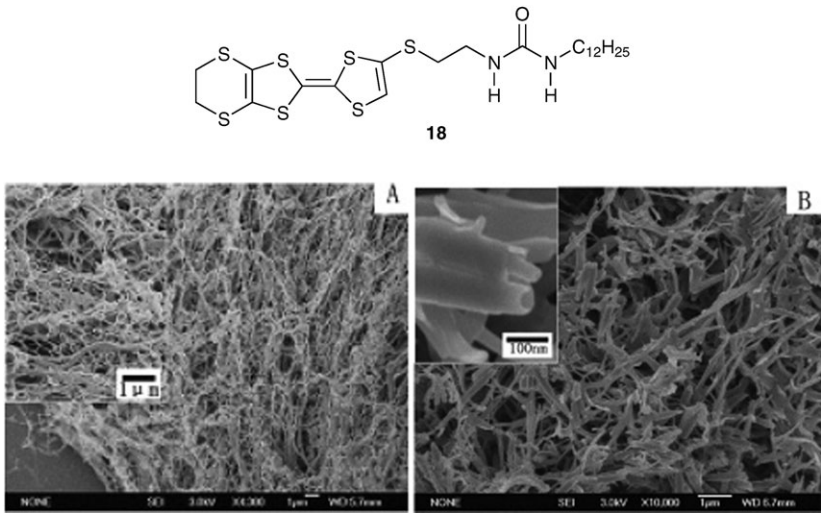


Fig. 13 SEM images of **18** (gel phase) in cyclohexane (A) and after charge-transfer complexation with TCNQ (B). Reproduced with permission from ref. 51: C. Wang, D. Q. Zhang and D. B. Zhu, *J. Am. Chem. Soc.*, 2005, **127**, 16372. Copyright 2005 American Chemical Society.

concentration (~6 wt% and ~2 wt%, respectively) such mixtures are turbid and the gel phases consist of spherulitic domains. The cooling of a hot solution of this organogelator in *n*-octanol (3 wt%) resulted in a non-gelled liquid. However, sonication for about 1 min gave rise to a fibrillar gel as inferred from SEM studies. When the authors applied a heating-and-cooling cycle to the sonicated sample, the liquid phase was obtained again, thus pointing to ultrasonic irradiation as responsible for this morphological switching.

The ability of cholesterol-based fluorescent molecules to form gels under thermal and sonochemical stimuli has been examined recently.[53] Although together with hydrogen bonding, π–π-stacking and hydrophobic interactions should be involved in the aggregation of such molecules, the presence of amide and carbamate linkages (Fig. 14) participating in H-bond formation were indeed key factors for gelation; a similar derivative with an ester linkage did not form gels irrespective of the concentration and solvent. Compound **19** gelated alcohols after ultrasonic treatment only, while **20** produced gels in a variety of solvents upon sonication

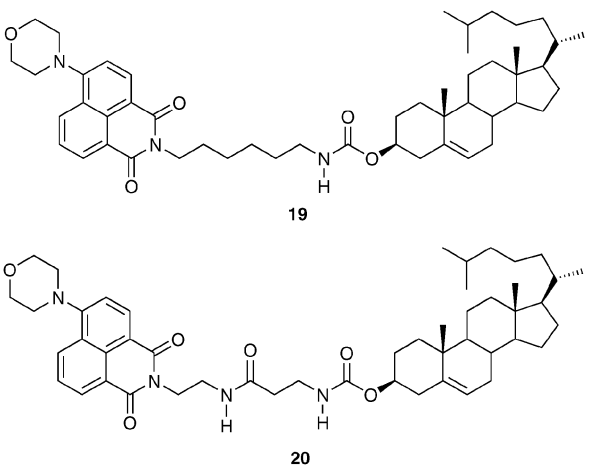


Fig. 14 Cholesterol-based molecules serving as organogelators under thermal and/or ultrasonic conditions.

(40 kHz, 0.16 W cm^{-2}), denoted as S-gel, as well as by cooling hot solutions in *n*-butanol and *p*-xylene (denoted as T-gel). A reversed gel (R-gel) also forms by heating the S-gel to a solution and further cooling to room temperature.

The morphologies of the corresponding xerogels from **19** and **20** were markedly different and depended on the solvents and external activation. Sonication of **19** gave rise to a columnar arrangement, while the T-gel of **20** from *n*-butanol displayed a burl-like three-dimensional structure and 1D fibers in the S-gel. The latter could further be converted into the T-gel morphology following a sol–gel transformation. Although the T- and S-gels showed similar powder X-ray diffraction (XRD) spectra, the authors conjectured the existence of different molecular packings depending on the external stimuli, which were also consistent with geometries calculated at a semiempirical (AM1) level.

Isolated structures of **20** adopt a bent conformation sustained by intramolecular hydrogen bonding between the naphthalimide carbonyl groups and the NH amide groups. The thermal process is then accompanied by a gradual formation of intermolecular H-bonds that unwinds the molecule. Since cavitation is a quasi-adiabatic process (local heat and pressure within the bubbles is followed by extreme cooling rates after collapse), sonication results in a very rapid self-assembly through interpenetrating hydrogen bonding without altering the bent conformation (Fig. 15).

The structures of both the T- and S-gels having different hydrophobic and hydrophilic surfaces provide further insight into their wettability. Thus, when a T-xerogel of compound **20** is coated onto a glass slide, the resulting film is especially hydrophobic and offers a contact angle to water of 159.4°, while the sonicated (S) xerogel gives a contact angle of 104.4°. The surface of a reversed (R) gel (after heating and cooling) gives back a contact angle of 151.3° (Fig. 16). Thus, it is clear that the wettability of xerogels, as a result of morphological variations, can be modified by ultrasound and recovered by a gel–sol process that can be repeated for several cycles.

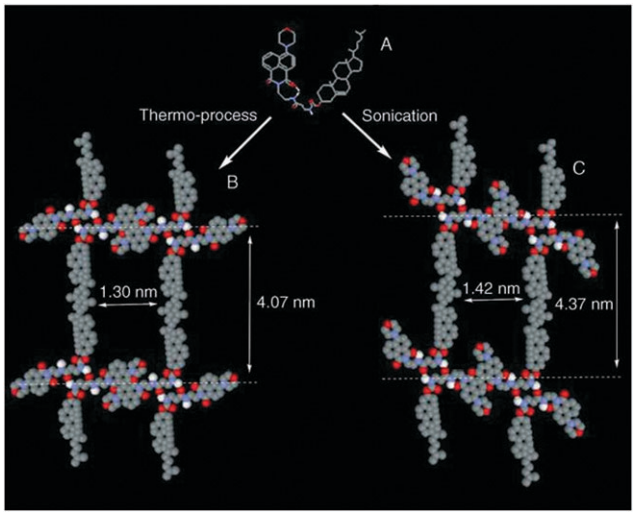


Fig. 15 Model structures proposed for compound **20**: isolated cholesterol-based molecule (A); aggregated structure in the T-gel after heating (B), and assembled structure of the S-gel generated by sonication (C). White spheres represent hydrogen atoms directly involved in hydrogen bonding. Reproduced with permission from ref. 53: J. Wu, T. Yi, T. Shu, M. Yu, Z. Zhou, M. Xu, Y. Zhou, H. Zhang, J. Han, F. Li and C. Huang, *Angew. Chem., Int. Ed.*, 2008, **47**, 1063. Copyright 2008 Wiley-VCH Verlag GmbH & Co. KGaA.

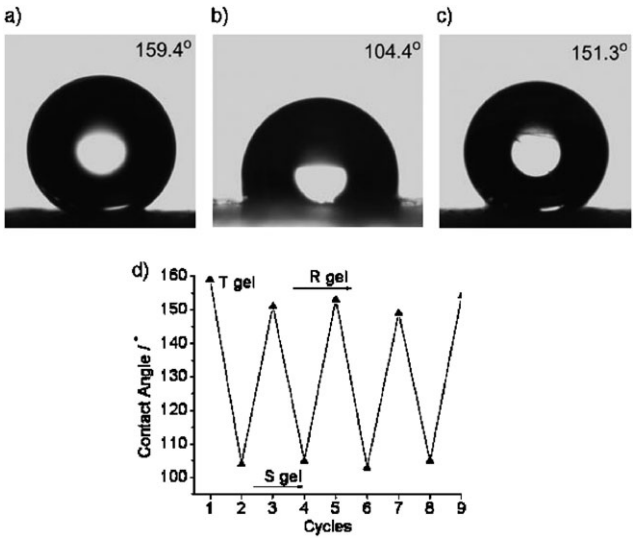


Fig. 16 Microphotographs of a water droplet deposited on films of compound **20** forming a T-xerogel (a), S-xerogel (b), and R-xerogel (c) from *p*-xylene. Fig. (d) shows the reversibility between T- and S-gels for many sol–gel cycles. Reproduced with permission from ref. 53: J. Wu, T. Yi, T. Shu, M. Yu, Z. Zhou, M. Xu, Y. Zhou, H. Zhang, J. Han, F. Li and C. Huang, *Angew. Chem., Int. Ed.*, 2008, **47**, 1063. Copyright 2008 Wiley-VCH Verlag GmbH & Co. KGaA.

The above study provides evidence that predictive behavior can be inferred from structural and crystallographic considerations, which can be modified by an external stimulus. A notable *tour de force* in this context has also been supplied by Steed and associates, revealing the similarities between gelation and crystallization.[54] Thus, despite the presence of donor and acceptor atoms susceptible of hydrogen bonding, both melamine (**21**) and uric acid (**22**) (Fig. 17) are only very

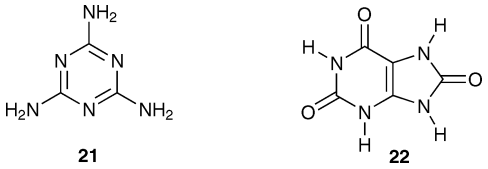


Fig. 17 Structures of melamine (**21**) and uric acid (**22**). While a 1 : 1 mixture in water does not result in dissolution, ultrasound induces the formation of a stable hydrogel whose putative structure was deduced from co-crystallization studies.

sparingly soluble in cold water, and mixing these substances does not produce any observable reaction or dissolution. However, sonication of a 1 : 1 mixture in water at room temperature gives rise to gelation within a few minutes and at a significant low concentration of only 0.8 wt%. Warming or shaking this mixture results in a viscous liquid that gelifies on standing. The process can be accelerated by sonication (for about 10 s) and gelation may always be re-induced (after precipitation of the components) with ultrasound.

6. Biological and medicinal interfaces

The preceding analysis shows how ultrasound induces and modifies the successive self-assembly steps that lead ultimately to supramolecular aggregates, often decorated with fiber-like morphologies. Remarkably, there is a certain formal analogy between ultrasound-responsive materials, which modify their H-bonding and π-stacking interactions, with the biological mechanism by which prion proteins self-assemble into insoluble fibrils.[21] The latter lies at the origin of neurodegenerative diseases and pathological anomalies. As a conceptual proof, sonication of proteins does effectively cause formation of aggregates that resemble amyloid structures.[55] Likewise, a typical 16-residue RADA peptide forming a stable β-sheet structure undergoes self-assembly into nanofibers and gives eventually a hydrogel. Sonication produces smaller fragments that rapidly re-assemble into nanofibers, whose rheological analysis evidences an increase in rigidity.[56]

Although these studies have been conducted at power ultrasound frequencies, therapeutic ultrasound (*e.g.* 1 MHz) with sufficient intensity to cause water sonolysis, also induces structural changes on α-helix or β-sheet motifs.[57] The mechanisms of sonication-induced protein aggregation may be related to both chemical (production of reactive species) and mechanical (shear forces, shock waves, microstreaming, among others) effects, which in turn induce chain reactions, cross-linking, cleavage and re-assembly, such as in gelation processes.

A recent study describes silk fibroin hydrogels generated by sonication of aqueous solutions.[58] Gelation was dependent on the irradiation time and power output. Keeping constant the amplitude (20%), fibroin gelation times decreased with increased sonication time. The sol–gel transition was associated to an increase in β-sheet formation as revealed by changes in circular dichroism (CD) measurements (Fig. 18). The increase in ellipticity at 217 nm (β-sheet structure peak) takes place slowly, which suggests that, while sonication promotes a rapid change from random coil to β-sheet, silk fibroin gelation is then slowed down and an extended β-sheet network resulting

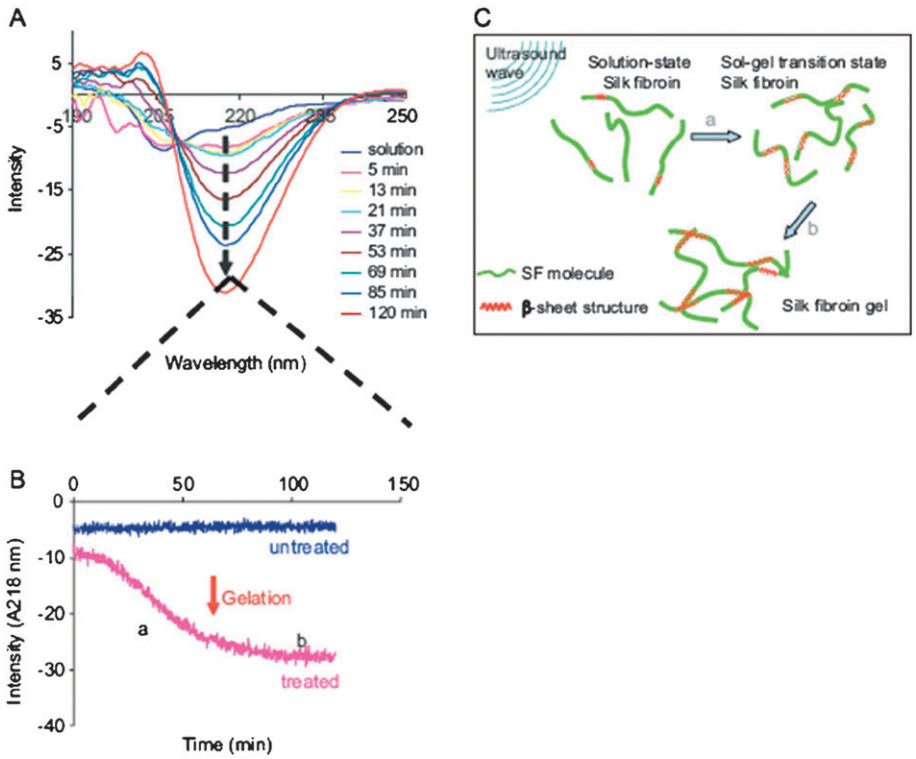


Fig. 18 Formation of silk β-sheet structures under sonication as revealed by CD monitoring (A and B). Scheme C illustrates a two-step process leading to an organized gel network. Reproduced with permission from ref. 58: X. Wang, J. A. Kluge, G. G. Leisk and D. L. Kaplan, *Biomaterials*, 2008, **29**, 1054. Copyright 2008 Elsevier Ltd.

from hydrophobic interactions and inter-chain cross-links occurs within a relatively long timeframe.

The above investigations point out the important implications of ultrasonic irradiation not only in issues such as fabrication of new biomaterials or tissue repair, but also in research on protein aggregation and medical disorders.

7. Conclusions and outlook

Even though a rationale based on the cavitational collapse is far from being fully understood, it is evident that ultrasound represents an effective and distinctive stimulus to promote aggregation and self-assembly. In the past, this ability has largely been exploited with metallic materials, especially *en route* to micro- and nanoparticles. Recent years have witnessed a further extrapolation to discrete organic molecules and polymers leading to a wide range of potential materials and biomaterials. One of such processes, the sol–gel transition, benefits substantially from sonication. Ultrasound not only facilitates and speeds up gelation, even with reluctant substrates, favoring intermolecular hydrogen bonding that leads to aggregates; but also controls molecular orientation and microscale surface features, which may ultimately result in novel structures and morphologies.

Obviously, further interdisciplinary work, especially combining efforts from chemistry, physics, and biosciences will be required to understand the precise influence of ultrasound on weak interactions and self-organization. Within this context, scientists must pay attention to specific aspects of sonochemistry, with a clear-cut estimation of power, frequency, and even instrumental design. Systematic molecular variations should in addition allow us to unveil useful relationships between structure and mechanical effects.

As recognized by Bardelang in a short essay on this subject,[59] the previously thought negative use of ultrasound as destructing assemblies will be progressively replaced by a positive view where gelation and other processes can be preferably favored. Sonication should thus become a future and rewarding research area in soft matter studies.

Acknowledgements

This work is dedicated to the memory of Oleg Abramov (1936–2008). He was an excellent sonochemist who introduced the knowledge and expertise of Russian ultrasonics to the West, a convincing speaker, willing collaborator, and above all a close friend. Financial support from Project NanoIGT (Bando converging technologies, Regione Piemonte, Italy), the Ministry of Science and Education (Spain), and the European Union COST Action D32 (Working Group D32/006/04: *Microwave and high-intensity ultrasound in the synthesis of fine chemicals*) is gratefully acknowledged.

References

1 P. Ball, *The Self-Made Tapestry: Pattern Formation in Nature*, Oxford University Press, Oxford, 1999.
2 G. M. Whitesides and B. Grzybowski, *Science*, 2002, **295**, 2418.
3 K. S. Suslick and G. J. Price, *Annu. Rev. Mater. Sci.*, 1999, **29**, 295.

4 A. Gedanken, X. Tang, Y. Wang, N. Perkas, Yu. Koltypin, M. V. Landau, L. Vradman and M. Herskowitz, *Chem.–Eur. J.*, 2001, **7**, 4546.
5 W. H. Suh, A. R. Jang, Y.-H. Suh and K. S. Suslick, *Adv. Mater.*, 2006, **18**, 1832.
6 G. Ruecroft, D. Hipkiss, T. Ly, N. Maxted and P. Cains, *Org. Process Res. Dev.*, 2005, **9**, 923.
7 For an illuminating discussion on the concepts of pattern and form: P. Ball, *Shapes*, Oxford University Press, Oxford, 2009, pp. 18–25.
8 For a review on sonochemically prepared protein microspheres: A. Gedanken, *Chem.–Eur. J.*, 2008, **14**, 3840.
9 A. Bruckmann, A. Krebs and C. Bolm, *Green Chem.*, 2008, **10**, 1131.
10 G. Cravotto and P. Cintas, *Chem. Soc. Rev.*, 2006, **35**, 180.
11 T. J. Mason, *Practical Sonochemistry. User's Guide to Applications in Chemical and Chemical Engineering*, Ellis Horwood, Chichester, 1999, ch. 1.
12 T. Lepoint and F. Lepoint-Mullie, in *Synthetic Organic Sonochemistry*, ed. J.-L. Luche, Plenum Press, New York, 1998, pp. 7–10.
13 W. T. Richards and A. L. Loomis, *J. Am. Chem. Soc.*, 1927, **49**, 3086.
14 M. Faraday, *Philos. Trans. R. Soc. London*, 1831, **121**, 299.
15 R. Hoyle, *Pattern Formation. An Introduction to Methods*, Cambridge University Press, Cambridge, 2006, pp. 20–22.
16 W. S. Edwards and S. Fauve, *Phys. Rev. E*, 1993, **47**, R788.
17 F. Melo, P. B. Umbanhowar and H. L. Swinney, *Phys. Rev. Lett.*, 1995, **75**, 3838.
18 T. Watson, *Ultrasonics*, 2008, **48**, 321.
19 M. R. Prausnitz and R. Langer, *Nat. Biotechnol.*, 2008, **26**, 1261.
20 S. Mitragotri, *Nat. Rev. Drug Discovery*, 2005, **4**, 255.
21 For a short account: J. M. J. Paulusse and R. P. Sijbesma, *Angew. Chem., Int. Ed.*, 2006, **45**, 2334.
22 E. Blanco, L. Esquivias, R. Litrán, M. Piñero, M. Ramírez-del-Solar and N. de la Rosa-Fox, *Appl. Organomet. Chem.*, 1999, **13**, 399.
23 D. Levy and L. Esquivias, *Adv. Mater.*, 1995, **7**, 120.
24 S. E. Skrabalak, *Phys. Chem. Chem. Phys.*, 2009, **11**, 4930.
25 J. Zarzycki and M. Atik, *J. Mater. Sci. Lett.*, 1994, **13**, 291.
26 N. Tonanon, A. Siyasukh, W. Tanthapanichakoon, H. Nishihara, S. R. Mukai and H. Tamon, *Carbon*, 2005, **43**, 525.
27 T. Naota and H. Koori, *J. Am. Chem. Soc.*, 2005, **127**, 9324.
28 F. Fages, *Angew. Chem., Int. Ed.*, 2006, **45**, 1680.
29 A. Brizard, R. Oda and I. Huc, in *Low Molecular Mass Gelators*, ed. F. Fages, Springer, Berlin, 2005, Topics in Current Chemistry, vol. 256, pp. 167–218.
30 K. Isozaki, H. Takaya and T. Naota, *Angew. Chem., Int. Ed.*, 2007, **46**, 2855.
31 L. A. Estroff and A. D. Hamilton, *Chem. Rev.*, 2004, **104**, 1201.
32 N. M. Sangeetha and U. Maitra, *Chem. Soc. Rev.*, 2005, **34**, 821.
33 D. R. Trivedi and P. Dastidar, *Chem. Mater.*, 2006, **18**, 1470.
34 Y. Li, T. Wang and M. Liu, *Tetrahedron*, 2007, **63**, 7468.
35 M. Yamanaka, T. Nakamura, T. Nakagawa and H. Itagaki, *Tetrahedron Lett.*, 2007, **48**, 8990.
36 M. Ávalos, R. Babiano, P. Cintas, A. Gómez, J. L. Jiménez, M. Lozano, A. L. Ortiz, J. C. Palacios and A. Pinazo, *Chem.–Eur. J.*, 2008, **14**, 5656.
37 S. M. Park and B. H. Kim, *Soft Matter*, 2008, **4**, 1995.
38 Y. Cao, L. M. Tang, Y. J. Wang, B. Y. Zhang and L. K. Jia, *Chem. Lett.*, 2008, **37**, 554.
39 D. Bardelang, F. Camerel, J. C. Margeson, D. M. Leek, M. Schmutz, M. B. Zaman, K. Yu, D. V. Soldatov, R. Ziessel, C. I. Ratcliffe and J. A. Ripmeester, *J. Am. Chem. Soc.*, 2008, **130**, 3313.
40 D. Bardelang, M. B. Zaman, I. L. Moudrakovski, S. Pawsey, J. C. Margeson, D. Wang, X. Wu, J. A. Ripmeester, C. I. Ratcliffe and K. Yu, *Adv. Mater.*, 2008, **20**, 4517.
41 Z. Xie, A. Zhang, L. Ye and Z.-G. Feng, *Soft Matter*, 2009, **5**, 1474.
42 J. M. J. Paulusse and R. P. Sijbesma, *Angew. Chem., Int. Ed.*, 2004, **43**, 4460.
43 J. M. J. Paulusse, J. P. J. Huijbers and R. P. Sijbesma, *Chem.–Eur. J.*, 2006, **12**, 4928.
44 S. Karthikeyan, S. L. Potisek, A. Piermattei and R. P. Sijbesma, *J. Am. Chem. Soc.*, 2008, **130**, 14968.
45 A. Piermattei, S. Karthikeyan and R. P. Sijbesma, *Nat. Chem.*, 2009, **1**, 133.
46 J. M. J. Paulusse, D. J. M. van Beek and R. P. Sijbesma, *J. Am. Chem. Soc.*, 2007, **129**, 2392.
47 P. Cintas and J.-L. Luche, *Synthetic Organic Sonochemistry*, ed. J.-L. Luche, Plenum Press, New York, 1998, ch. 5, pp. 167–234.
48 Y. Wang, C. Zang, H. Fu, X. Li, X. Sheng, Y. Zhao, D. Xiao, Y. Ma, J. S. Ma and J. Yao, *Langmuir*, 2008, **24**, 7635.
49 L. Cheng, G. Zhang, L. Zhu, D. Chen and M. Jiang, *Angew. Chem., Int. Ed.*, 2008, **47**, 10171.
50 S. Zhang, S. Yan, J. Lan, Y. Tang, Y. Xue and J. You, *J. Am. Chem. Soc.*, 2009, **131**, 1689.
51 C. Wang, D. Q. Zhang and D. B. Zhu, *J. Am. Chem. Soc.*, 2005, **127**, 16372.
52 R.-Y. Wang, X.-Y. Liu and J.-L. Li, *Cryst. Growth Des.*, 2009, **9**, 3286.
53 J. Wu, T. Yi, T. Shu, M. Yu, Z. Zhou, M. Xu, Y. Zhou, H. Zhang, J. Han, F. Li and C. Huang, *Angew. Chem., Int. Ed.*, 2008, **47**, 1063.
54 K. M. Anderson, G. M. Day, M. J. Paterson, P. Byrne, N. Clarke and J. W. Steed, *Angew. Chem., Int. Ed.*, 2008, **47**, 1058.
55 P. B. Stathopulos, G. A. Scholz, Y.-M. Hwang, J. A. O. Rumfeldt, J. R. Lepock and E. M. Meiering, *Protein Sci.*, 2004, **13**, 3017.
56 H. Yokoi, T. Kinoshita and S. Zhang, *Proc. Natl. Acad. Sci. U. S. A.*, 2005, **102**, 8414.
57 C. Marchioni, E. Riccardi, S. Spinelli, F. Dell'Unto, P. Grimaldi, A. Bedini, C. Giliberti, L. Giuliani, R. Palomba and A. C. Castellano, *Ultrasonics*, 2009, **49**, 569.
58 X. Wang, J. A. Kluge, G. G. Leisk and D. L. Kaplan, *Biomaterials*, 2008, **29**, 1054.
59 D. Bardelang, *Soft Matter*, 2009, **5**, 1969.