Chemical Science

Cite this: *Chem. Sci.*, 2012, **3**, 295

www.rsc.org/chemicalscience

PERSPECTIVE

Harnessing mechanochemical effects with ultrasound-induced reactions

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Received 29th September 2011, Accepted 9th October 2011
DOI: 10.1039/c1sc00740h

Chemical reactions may experience numerous and varied effects under the influence of ultrasound. This soft radiation, often viewed as a lab trick, induces and improves both physical and chemical transformations by means of efficient agitation, dissolution, mass and heat transfers, and reagents sonolysis, which all arise from the cavitational collapse. An empirical rationale that distinguishes between true chemical effects and mechanical ones, especially in heterogeneous reactions, was introduced more than two decades ago and has been a useful guidance on reporting sonochemical mechanisms. Recent studies have witnessed a truly remarkable data set that boosts sonochemistry over the wall of applied science. This perspective highlights the importance of the so-called *false sonochemistry*-closely related to mechanochemistry-in modern synthesis, thus illustrating the advantages of using pressure waves in chemistry. Emphasis is put on green transformations, mild polymerization reactions and the selective cleavage of functionalized polymers, which may have an effective impact in process chemistry and represent a realistic option in industry.

Introduction: a distinctive chemistry

The use of ultrasound in applied sciences constitutes a common and convenient tool capable of inducing a plethora of chemical and physical effects that can be harnessed from numerous viewpoints, ranging from synthesis and catalysis, materials science, biomedicine and pharmaceuticals, to environmental remediation as an advanced oxidation technology.[1–4] Such effects usually arise from acoustic cavitation generating enough kinetic energy that drives reactions to completion and releasing short-lived, high-energy chemical species to solution after implosive collapse of bubbles. As well-established facts, this process produces enormous heating (4500–5000 K as typical figure) and very high pressures (~1000 atm) for extremely short times (in the range of microseconds), thus rendering cavitation a quasi-adiabatic phenomenon. Cavitational events are still far from a satisfactory understanding, although there have been significant advances in providing more accurate temperature predictions, spatial inhomogeneities, and even the chemistry inside the bubble *via* studies of sonoluminescence and bubble dynamics.[5–8] From the practitioner's point of view, it is generally unnecessary to go into such fundamentals at the bottom, which may certainly be an undecipherable jargon. However, as cavitation gets intimately understood, both empirical observations and effects can be rationalized and controlled. A pedagogical approach to cavitation is probably a must as the phenomenon is largely dependent on and influenced by technical parameters such as frequency, power input, or saturation gas type. The microbubble also provides a particular environment for volatile species and determine the outcome of a given transformation. Physical properties of the bulk medium (vapor pressure, viscosity or surface tension), often neglected in synthesis, become crucial factors.[9]

The mechanisms of sonochemical reactions, focused on the collapse of cavitational bubbles, have always been of interest to those approaching the technique. Historically, the first effects of ultrasound were noticed by Richards and Loomis in their 1927 seminal paper,[10] although the role of ultrasonic vibration in the chemical pathway was rather elusive. These authors, who employed transducers up to 500 kHz, unusual at that time, attributed the observed acceleration of certain chemical reactions to frequency effects. However, a paper unveiling true sonochemical effects on oxidation reactions was published two years later.[11] It is pertinent to quote the authors' observation: "*If an aqueous solution containing dissolved oxygen is radiated, hydrogen peroxide or something analogous to it is formed*". They also noted: "*It seems necessary to assume that every phase of bubble formation is realized in this process, and it must be concluded, therefore, that the mere formation of bubbles in the absence of ultrasonic vibrations is unable to effect the oxidation*".

For decades, sonochemical studies were investigated in aqueous solutions evidencing the similarities between sonolysis and radiolysis. Cavitation does produce H and OH radicals that recombine to yield hydrogen and hydrogen peroxide. Sonolysis of organic solvents and organic molecules may indeed afford a variety of radical species, which dictate the reaction fate. Chemists who began working on ultrasound-assisted reactions

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soon realized that the effects of cavitation could be of both chemical and mechanical origin as the collapse of bubbles is also accompanied by shock waves and shear forces, which are particularly evident in heterogeneous reactions. Discussions about the balance of such effects have been a recurring theme. In the early 1990s and, on scrutinizing numerous organic reactions, Luche introduced a useful, yet empirical, rationale that can be formulated as follows: reactions which can be modified in rate or product distribution by ultrasound irradiation correspond to those proceeding, at least in part, through a radical mechanism.[12] This premise leads to a classification of sonochemical reactions (mostly organic and organometallic),[13] which provides some insight into chemical and/or mechanical effects: a) type I or homogeneous reactions taking place through radical or radical-ion intermediates; the excited species may also include coordinatively unsaturated metal compounds. b) Type II or heterogeneous reactions involving ionic reactions. Here numerous, essentially mechanical, effects can be visible such as surface cleaning, particle size reduction, and enhanced mass transfer. Since such effects could be attained, even improved, with efficient methods of stirring, milling, friction, or grinding (*i.e. mechanochemistry*),[14] type II reactions have often been referred to as *false sonochemistry*. c) Finally, in type III or heterogeneous systems capable of following either ionic or radical mechanism, the latter will usually be favored under sonication. This classification largely circumscribed to synthetic processes may be extended to cover the whole range of ultrasound-assisted transformation for which, as noted by Suslick, a distinction between homogeneous and heterogeneous sonochemistries suffices.[15] We have on the other hand, alluded to the term *cavitational chemistry*, which loosely covers the different and varied effects resulting from microbubble implosion in liquids.[16] The present article summarizes briefly the connection between cavitation and mechanochemistry and focuses essentially on recent developments put at the forefront of applied chemistry, thus evidencing that sound waves deliver efficiently mechanical energy into a given chemical system.

Cavitation as mechano-chemical energy

While able to trigger a chemical reaction after initiating a sonolytic step, the collapse of cavitation bubbles is invariably accompanied by shock waves and shear forces, which are important in heterogeneous processes and contribute to efficient mixing and particle reduction. The tribochemical interpretation, according to which chemical transformations arise from mechanical stress is complex (*vide infra*), although connections with sonochemistry emphasizing both similarities and differences have been previously highlighted.[17] Shock on solids as well as liquids produce numerous events, the final stage being the production of heat. Before reaching this point, other physicochemical transformations may occur, especially if mechanical energy is supplied faster than heat is evolved. These include vibrational and electronic excitation, bond deformation and cleavage, or atom migration. Covalent bonds at specific points, in polymers for instance, can be brought to a pre-dissociation state and then undergo cleavage. On surfaces, the so-called hot-spots (energy-rich domains created by bubble collapse) may initiate chemical reactions *via* ionization or electron-transfer mechanisms. It is uncertain the parameter of importance in the sonochemical activation of solids. Intuitively, the transfer of a solid reagent to a solution involves surface destruction or disorganization, which can be associated with the lattice energy; the lower the energy, the faster the sonochemical reaction.[18] Unfortunately, the lattice energy of numerous compounds remains unknown and, even if this rule has some predictability, the effect will also depend on the acoustic intensity and the cavitational energy of the solvent. The activation of metals, however, occurs by a series of well-studied physical and chemical phenomena. In general, the reactive sites are composed by metal atoms with a minimum number of neighbors on an edge or defects, which are less tightly bound.[19] Surprisingly, the surface area increase has little effect on reactivity, while the energy stored in the disorganized lattice, which can relax either thermally or chemically, is largely responsible of the enhanced reactivity.[17] The loss of activity often results from annealing, sintering or particle agglomeration which are observed after prolonged sonication. Overall, and despite the fact that cavitation at or near solid surfaces is rather poorly understood from a mechanistic point of view, its effects are clearly visible by enabling surface modification of metal oxides and hard ceramic materials, synthesis of metal nanoparticles and their incorporation into mesoporous oxides, as well as changes in crystallinity and metal ion distribution on the surface layer.[20] Most of them, if not all, can be ascribed to the increase of dislocations and vacancies, which absorb preferentially the acoustic energy and guide further plastic deformations.[21] Thus, ultrasonic waves have shown to be a technique of choice in efficiently achieving intercalation and exfoliation of carbonaceous and layered materials,[3,22,23] which occur at defects and are also influenced by both intensity and temperature.

Since ultrasound lacks quantum nature, a long held misconception is that as long as the power is above the cavitation threshold the sonochemical effects will be independent of the frequency. While it is well established that radical production increases at higher frequencies,[24] the relationship between applied frequency, hence radical production, and the extent of mechanical effects in heterogeneous processes is still elusive. By monitoring the abrasive action of sound waves on a glass-filled polystyrene blend by SEM and XPX analyses and measuring weight loss at different frequencies (20, 40, 582, 863 and 1142 kHz), Mason and associates found an inverse dependence of mechanical and chemical effects. Both at 20 kHz (probe) and 40 kHz (bath), the observed high weight loss correlated with significant changes to the surface morphology due to purely mechanical effects such as micro-jetting. These changes were less pronounced at higher frequencies, which can in contrast be ascribed to some surface oxidation by radical species.[25] Previous studies on dextran degradation showed that mechanical effects were important at 35 kHz, whereas degradation at higher frequencies (>500 kHz) occurred chiefly by radical reactions.[26] Thus, the corollary, at least for aqueous processes, is that whenever the frequency increases the mechanical effects decrease, but conversely chemical effects due to radical reactions increase.

The action of ultrasonic waves on nanoparticles and nanostructured materials illustrates well the juxtaposition, often in a synergic way, of mechanical and chemical effects associated

with cavitation. This field constitutes an attractive and green approach to produce catalytic species and environmentally benign formation of oxidizing species and hydrogen by water splitting. A recent and clever design harnesses a piezo-electrochemical mechanism that converts mechanical energy into chemical energy. Hydrothermally synthesized ZnO microfibers and $BaTiO_3$ microdendrites are vibrated with ultrasonic waves, thereby developing a strain-induced electric charge on their surface. This phenomenon may then trigger a redox reaction that produces the formation of H_2 and O_2 from water (Fig. 1).[27]

This process appears to be essentially different from other mechanocatalytic effects in which the parent material undergoes a redox reaction to split water. In contrast, the piezoelectric catalyst (ZnO or $BaTiO_3$) is involved in water splitting by donating strain-induced electrons and holes without any further redox change or decomposition. When ultrasonic waves are applied to such materials, H_2 and O_2 production grows rapidly while gas generation is stopped when ultrasound is turned off. The present miniature device holds promise for a low-cost production of H_2 and O_2 so long as optimum lengths and resonance frequency of the piezoelectric material are found. Fibers with greater lengths may experience a greater bending leading to an increase in strain-induced voltage.[28] Moreover, vibrational energy could in principle be supplied by ecological sources like noise, wind power, or running water. Clearly, supramolecular structures may respond to vibrations of lower frequency, such as in the parallel alignment of nanofibers to the direction of propagation of audible sound.[29]

Sonocatalytic hydrogen production by means of nanoparticles (NPs) equally competes with other well-established technologies such as photocatalysis and catalytic dehydrogenations.[30] However, the actual role played by noble-metal NPs in sonolysis is an open question. In a thorough study that explores the use of alcohols as sacrificial reagents in aqueous solutions and trackes the source of hydrogen *via* H/D isotope exchange, Zhao *et al.* have proven the high efficiency of Au NPs deposited on TiO_2 in

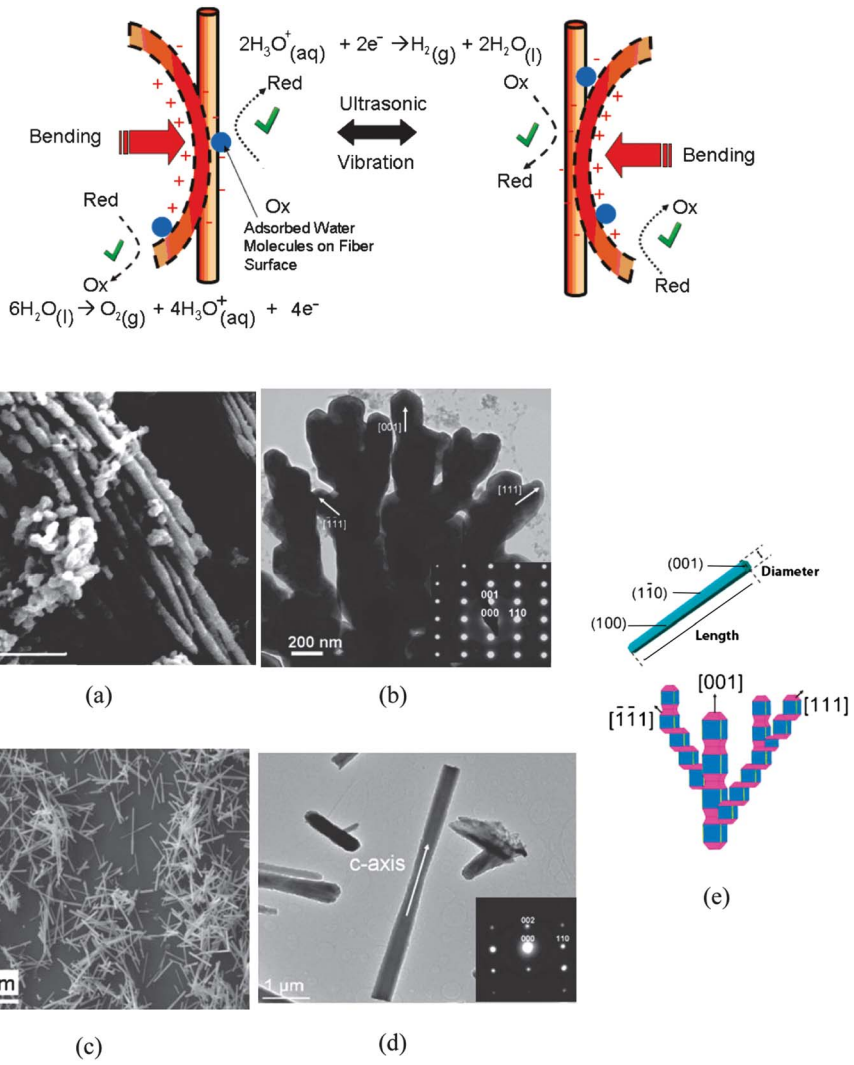


Fig. 1 Top: Microsized ZnO or $BaTiO_3$ are deformed under ultrasonic vibration leading to H_2 and O_2 gases from water *via* redox reactions. Bottom: (a) SEM and (b) TEM images of $BaTiO_3$ dendrites grown on a glass substrate; (c) SEM and (d) TEM images of ZnO fibers grown on a Si(100) wafer. (e) Schematic shapes of a single ZnO fiber (upper) and $BaTiO_3$ dendrite (lower). Reproduced with permission from ref. 27. Copyright 2010 American Chemical Society.

increasing the yields of H and OH radicals as well as hydrogen production in the sonolysis of water-methanol mixtures.

Thus, the addition of methanol in the presence of Au/TiO_2 increased the rate of H_2 production by 12-fold. The acceleration is also significant relative to TiO_2 alone or in the absence of a catalyst. Methanol is volatile enough to readily enter cavitation bubbles and there thermal reforming enhances H_2 evolution by trapping H radicals and scavenging OH radicals (eqn (1) and 2).

Products resulting from methanol pyrolysis and radical recombination (H_2, CO, HCHO and CH_4) are detected. Scavenging of OH radicals occurs not only inside the microbubbles but also at the interfacial region (*ca.* 200–300 nm thick) where the local temperature is still high (*ca.* 1900–2000 K).

$$HO^{\cdot} + CH_3OH \rightarrow H_2O + {}^{\cdot}CH_2OH \quad (1)$$

$$H^{\cdot} + CH_3OH \rightarrow H_2 + {}^{\cdot}CH_2OH \quad (2)$$

The nanostructured catalyst most likely creates solid-gas interfaces that contribute to more efficient water sonolysis[31] (in fact nearly half of the H atoms come from water molecules) and thermal reforming of methanol.[30]

Au NPs intercalated into mesoporous TiO_2 under sonication (20 kHz) at high intensity (51.3 W cm^{-2}) exhibits an enhanced photocatalytic activity. Titania can be doped either with negatively charged Au NPs (provided by EDTA: ethylenediaminotetraacetic acid), up to 15%, or positively Au NPs (in the presence of DMAP: dimethylamino pyridine, 8.1%). The former matrix shows is a superior catalyst due to a larger surface area and greater amount of nanoparticles.[32] Clues to understand the enhanced catalytic activity of Au NPs by sonication also emerge from another independent study.[33] Au NPs on porous carbon (Au/C) prepared under ultrasonic irradiation is actually a better electrocatalyst than conventional Au/C for hydrogen oxidation. TEM data and theoretical calculations agree with a supercooled molten state of Au NPs created during cavitation. The whole structure of such NPs at *ca.* 1100 K has approximately 10% of gold atoms on the surface with small coordination numbers. The existence of coordinatively unsaturated atoms represent sites for further reactions and play the same role as organic radicals, thereby consistent with a true sonochemistry (type I reactions). Cheaper metal NPs produced by sonochemical methods have also met the requirements for a green production of hydrogen as well. Thus, ultrasonically-generated Al NPs containing an oleic acid core do efficiently lead to H_2 (>95% yield) from tap water at ambient temperature.[34] This approach is more benign than the use of bulk micrometre-sized aluminum metal in water and overcomes the passivation caused by aluminum oxide coatings.

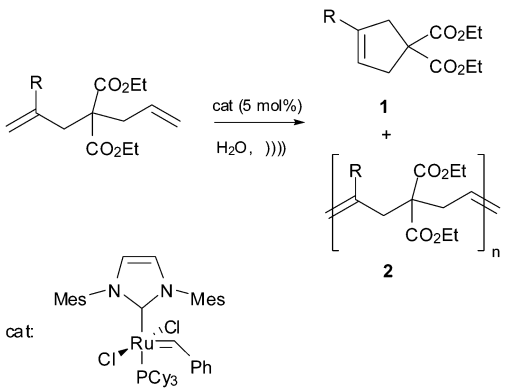
Micromixing and emulsification effects

The mechanical effect supplied by ultrasound manifests itself in liquid–liquid or solid-liquid systems occurring by polar mechanisms and non-volatile substrates, for which a sonolytic step could hardly be formulated. Here, the reaction is primarily influenced by the very asymmetric bubble collapse close to a solid boundary causing high-speed jets of liquid and induced-shock wave emission with enormous local amplitude.[35] As mentioned above, this agrees with Luche's type II reactions denoted collectively as *false sonochemistry*. The main advantage of this technology in chemistry and processing is the possibility of improving the reactivity of stoichiometric and catalytic reactions, often preventing formation of side products. Reactions *on water* or *in water* using water-insoluble reagents benefit from acoustic emulsification as reported in the synthetically useful ring-closing metathesis and cross metathesis (Scheme 1).[36] Products are generally obtained in high yield and selectivity without formation of oligomers (Table 1).

In another green reaction on water, the anticoagulant warfarin could be generated in enantiomerically pure form using (*S*,*S*)-diphenylethylenediamine as catalyst and a carboxylic acid as additive, after prolonged irradiation in an ultrasonic bath at room temperature (Scheme 2).[37] Efficient contact between water and reactants is crucial for success and sonication greatly facilitates the rapid dispersion of solids on water. In fact, under acoustic agitation the process can be scaled up to 2 g with only 2 mol% catalyst. The solid product is readily separated by filtration and does not require any further chromatographic purification; a small amount of hexane for crystallization suffices.

Such purely mechanical effects are most likely behind the positive effects of sonication on numerous heterogeneous reactions where enhanced mass transfer is required.[38] Organocatalytic reactions conducted in organic solvents, for instance, benefit from shorter reaction times and usually lead to high yields and stereoselectivities (Scheme 3).[39]

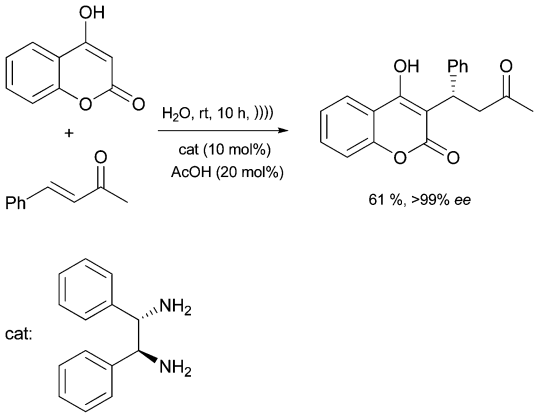
In the context of heterogeneous reactions, applications of ultrasound to a general synthesis of room-temperature ionic liquids (ILs) is particularly noticeable. Sonication does indeed decrease dramatically the overall protocol (comprising both nitrogen quaternization and anion metathesis reactions) and facilitates work-up. ILs represent suitable media for ultrasonically-assisted reactions as they will hardly be involved in the cavitational event due to their negligible vapor pressure. Since anion metathesis occurs in a heterogeneous system and proceeds *via* polar intermediates, it is an appropriate scenario to further check mechanical effects.[40] Best yields are obtained at low frequency and on increasing the acoustic power, the latter linked to the diameter of the probe employed (the lower the diameter, the better the conversions). Such observations are consistent with purely mechanical effects taking place close to the probe tip with enhanced mass transfer and mixing.



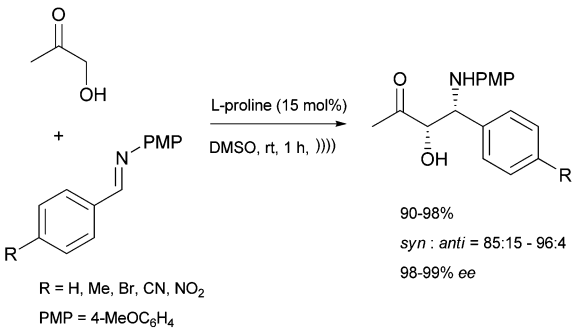
Scheme 1 Metathesis reactions under acoustic emulsification.

Table 1 Sonochemically-induced metathesis reactions with water-insoluble substrates

Conditions	1 (% Yield)	2 (% Yield)
US, H_2O, air, 40 °C, 5 h	R = H (99)	R = H (0)
neat, air, 25 °C, 5 h	R = H (81)	R = H (18)
US, H_2O, air, 40 °C, 5 h	R = Me (99)	R = Me (0)
neat, air, 25 °C, 5 h	R = Me (93)	R = Me (6)

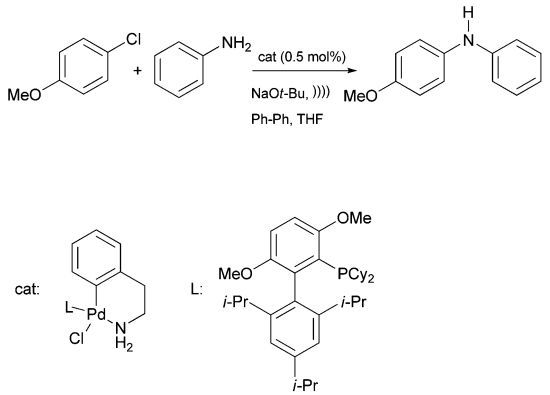


Scheme 2 Ultrasonically-induced asymmetric synthesis of warfarin.



Scheme 3 Asymmetric Mannich reactions of aldimines and hydroxyacetone under sonication.

Efficient micromixing is indeed the key parameter, often the bottleneck, in the intensification of chemical processes through flow reactors that use columns filled with supported catalysts. These can now be coupled to microwave (MW) and/or ultrasound (US) irradiations.[41] Thus, oxidation of alcohols and aldehydes to carboxylic acids as well as oxidation of nitroalkanes to carbonyls (Nef reaction) and carboxylic acids can be conducted in a continuous flow reactor using $KMnO_4$ as oxidant and pulsed ultrasonication. Irradiation avoids blocking of the reactor and provides products in essentially the same yield and purity as for small-scale reactions.[42] Similar benefits have been found in a continuous-flow palladium-catalyzed amination.[43,44] This synthetically useful transformation leading to diarylamines undergoes rate enhancement and affords products in higher yield under acoustic irradiation (Scheme 4). The main plus associated with sonication is to overcome the limitations of bridging and constriction, thereby handling solids efficiently even at high



Scheme 4 Pd-catalyzed amination reactions to give diarylamines.

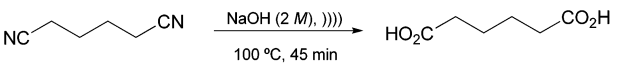
concentrations. The experimental set-up consists of glass syringes to deliver reagents to a microreactor made of polytetrafluoroethylene and placed in an ultrasonic reactor. Upon exiting the reactor, the mixture was collected in a vial under a constant pressure of argon.

Even though efficient mixing may represent the driving force in heterogeneous reactions, the possibility of a truly chemical component involving radical species should not be overlooked. Less volatile solvents can actually be incorporated into sonocatalytic cycles when sonolysis of the solvent acts as a relay. Activated hydroxides, for instance, are efficient catalysts in sonochemical reactions. Adsorbed species may react with the reducing centers on the surface giving rise to a radical anion, which further undergoes hydrogen abstraction by hydroxyl radicals generated during water sonolysis.[45] In a recent example, sonohydrolysis of nitriles to carboxylic acids occur rapidly in high yield under basic conditions, while the process fails in acidic media, which contrasts with conventional thermal conditions. This transformation works well with substrates poorly soluble in aqueous media such as benzonitrile to afford benzoic acid and can be applied to a quantitative synthesis of adipic acid (US probe at 30 kHz, 1.9 Wcm^{-2}), a product of industrial importance (Scheme 5).[46]

A radical mechanism is likely involved assisted by the intermediacy of the oxide anion radical, which can be formed in strong basic medium under ultrasound (eqn (3) and 4). The couple $HO^{\cdot}/O^{-\cdot}$ has a pK_a of 11.9 and may thus have a pivotal role in the hydrolysis mechanism.[47] Under acidic conditions (*e.g.* pH 2.0), HO radicals are rapidly trapped by the acid anion and no reaction is observed at all.

$$H_2O \rightarrow H^{\cdot} + HO^{\cdot} \quad (3)$$

$$HO^{\cdot} + HO^{-} \rightarrow H_2O + O^{-\cdot} \quad (4)$$



Scheme 5 Production of adipic acid induced by water sonolysis in basic medium.

Ultrasound effects on polymer formation

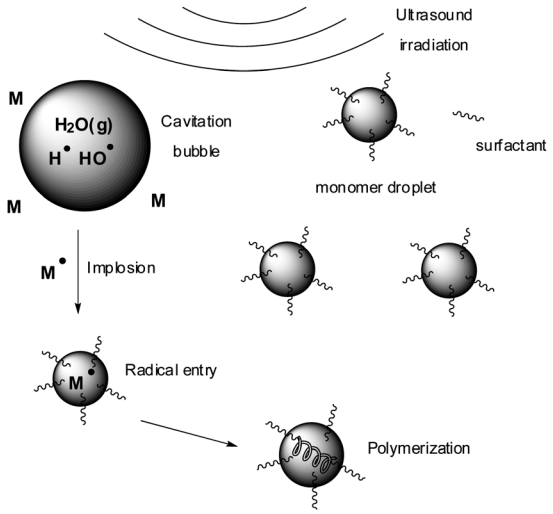
The effects of ultrasound waves on polymers can be summarized in three categories consisting of polymer formation, cleavage or depolymerization, and formation of polymer composites.[48] The latter constitutes an independent research domain and will not be treated here.

Sonochemical polymerization is an attractive surrogate of conventional polymer synthesis and some reactions can be conducted at lower temperatures and with enhanced rates. The starting monomers are activated alkenes that undergo fragmentation and chain growth by mechanoradical reactions induced by cavitation; typical examples being vinyl monomers such as styrene or methyl methacrylate.[49,50] In most cases the primary radicals that initiate the polymerization stem from solvent vapor cleavage in the cavitation bubbles, although monomer pyrolysis can also occur there. Degradation of the polymer chains occurs simultaneously (*vide infra*) and high molecular weight polymers are only formed at early stages of the reaction. Prolonged sonication decreases the rate of conversion and increases the viscosity of the medium, and cavitation can be essentially inexistent (molecules are less mobile and bubbles are difficult to form).

While early studies on sonochemical polymerization were largely performed in homogeneous systems, much attention is now paid to polymerization under heterogeneous conditions with the ensuing polymer products being insoluble in the medium. In this context, ultrasound-assisted gelation has received enormous interest in recent years.[51] Sonication drives sol–gel transition by favoring intermolecular hydrogen bonding between aggregates, which also immobilizes solvent molecules and controls microscale surface morphology.

The polymerization of water-soluble acrylic monomers occurs rapidly with 20 kHz-ultrasound irradiation to form hydrogels. The polymerization does not require the use of chemical initiators, although water-soluble additives (sorbitol, glucose or glycerol, especially the latter) are essential for success.[52] This can be attributed to various effects, notably an increase in the population of secondary alkyl radicals which are more stable than hydroxyl radicals. Furthermore, glycerol leads to more viscous solutions, thereby reducing the polymer solubility and hence avoiding depolymerization side reactions.

A green approach is equally provided by sonochemical emulsion polymerization in aqueous media. Again, the mechanical effects generated by cavitation contribute to an efficient mixing and dispersion of the emulsion components. As a result, no chemical initiators or stabilizers are usually required. In addition, the high shear forces around the microbubbles produce small oil droplets with a narrow size distribution and prevent further droplet aggregation (Ostwald ripening). Emulsion polymerization under ultrasound dates back to the early 1950s, although it has been recognized as a useful synthetic tool from the late 1990s on with application to a wide range of polymers and copolymers.[48,53,54] A plausible rationale for this type of polymerization is shown in Scheme 6. Thus, primary radicals arising from water sonolysis (H˙ and HO˙) may react with free monomer molecules, leading to monomeric radicals in the emulsion system and initiating the polymerization. The unsaturated monomers are often volatile and may evaporate into the microbubble and be decomposed into hydrocarbon radicals (M˙)



Scheme 6 Diagram illustrating the proposed emulsion polymerization under ultrasonic irradiation.

as well. The primary radicals produced are trapped by the solutes adsorbed at the bubble interface and releasing monomeric radicals in the bulk solution. Such radicals enter the monomer droplets and propagate radical polymerization. There has been a certain controversy regarding the role of surfactants as some authors suggest that these large molecules can also be a source of free radicals for the initiation step. Certainly, the conversion of monomer to polymer increases with increasing surfactant concentration and, in the absence of surfactant no polymer product is detected. However, surfactants may be isolated by dialysis and investigations under different conditions of temperature, surfactant concentration, and power intensity suggest that a high surfactant concentration also gives rise to a large number of micelles, which serve as polymerization sites and lead to enhanced reaction rates.[48]

Ultrasound-induced selective polymer cleavage

Polymers exhibit a wide range of responses, ranging from atomic to supramolecular levels, under the action of strain and other mechanical forces.[55,56] As highlighted in the preceding section, polymers undergo ultrasound-induced chain scission by virtue of the shear forces associated with the cavitational collapse. Although such large molecules will usually be excluded from the microbubbles, a polymer near or at the interface of a collapsing bubble may experience harsh enough conditions (transiently up to 2000 K) to fragment thermally without entering the inner cavity.[57] The structural damage can thus be used to degrade both natural and synthetic polymers, whose rate and extent depend on temperature, acoustic intensity, solvent and dissolved gases, as well as the initial polymer composition and molecular weight.

Studies on ultrasonic cleavage reveal that, unlike other chemical or thermal degradations, ultrasound-induced chain scission is not a random process and occurs preferentially near the middle of the chain, which appears to be consistent with a stretching-and-breakage mechanism. Ultrasonic depolymerization is more efficient and occurs at faster rates for higher molecular bond polymers; below a threshold molecular weight

ultrasound has little or no effect. Since fragmentation is caused primarily by the strong forces and velocity gradients arising from fluid flow after bubble collapse, some factors such as dilution are essential as polymer chains will move freely around the bubbles and degradation is expected to be more effective. Likewise, high power intensities will increase the rate and extent of depolymerization due to the creation of a large number of bubbles generating shear forces.[58–60]

The fact that bond breaking reactions occur selectively at weakened linkages leads to the important concept of *mechanophore*, which provides the basis of synthetic innovation using the synergy between ultrasound and polymer scission. In a nutshell, mechanophores are polymer-bound small molecules or substructures located at the chain end or in the center of the chain, which undergo further reactions when mechanical force is transferred to them from the chain segments. These behave therefore as molecular tweezers and detection of mechanochemical effects also requires a critical size of the polymer chain. Some examples have appeared in the recent literature, though the potentialities in synthesis, catalysis and materials design are on the corner.

The concept is nicely illustrated by a violation of the Woodward–Hoffmann rules when a benzocyclobutene mechanophore incorporated into a polymer undergoes thermal ring opening by ultrasound-induced strain. Conventional theory states that such an opening follows a conrotatory motion and a *trans* isomer should produce the *E*,*E*-diene, while the *cis* isomer should afford the *E*,*Z*-configured product. However, when mechanical force is applied both isomers produce the *E*,*E*-diene. Clearly, the *cis* isomer is forced to circumvent the rules in a disrotatory pathway (Scheme 7).[61]

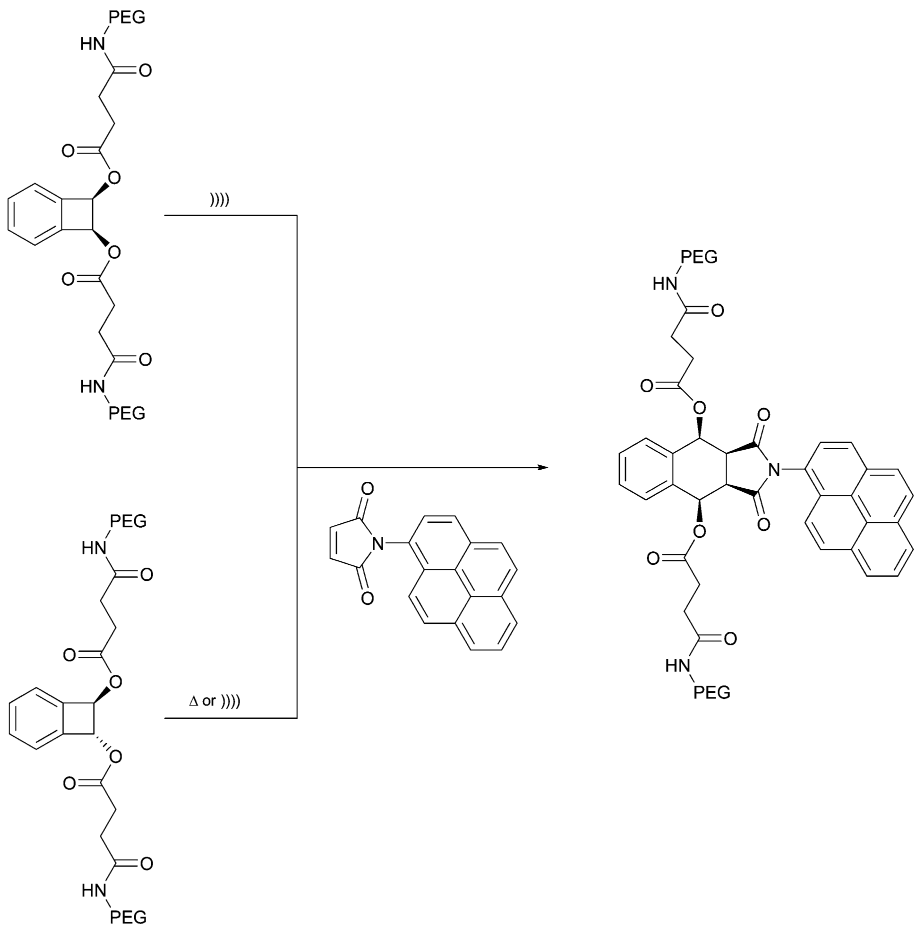
Given the characteristics of cavitational implosion, this phenomenon would hardly be responsible for a stereospecific pathway,[62] although shear forces near a bubble might have directional effects different from those of the bulk solution. The observation demands a rationale and Martínez *et al.* have investigated the mechanical response *via* molecular simulations at *ab initio* level.[63] Calculations evidence that potential energy barriers are lowered for both *trans*- and *cis*-pulling, although the barrier for one sense of rotation is lowered further than that for the opposite sense. An external force applied to *cis*-pulling in cyclobutene lowers the barrier along the disrotatory motion. Similar features are observed for the benzocyclobutene system and the *cis*-pulling conrotatory and disrotatory paths show equivalent barriers. As yet, this study does not explain why the Woodward–Hoffmann rules fail in terms of orbital control. Martínez and co-workers point to single-molecule AFM pulling experiments to work out the problem,[64] though they also suggest that the stereochemistry induced by sonication might be *a posteriori* event, *i.e.* taking place after the ring-opening reaction.[63] As mentioned above, the added value of the sonochemical strategy is that the barrier for the forbidden process drops below that of the allowed process.

Ribas-Arino and associates have instead used catastrophe theory to model not only the local distortions of the mechanophore along the potential energy surface,[65] but also and importantly the effect of polymer chains.[66,67] At forces larger than 0.75 nN the *cis*-conrotatory path disappears and the applied force shifts the system to a *cis*-disrotatory state. These results defy the idea that orbital symmetry is not conserved under mechanical activation; rather the model fails for small forces, particularly in the conrotatory ring opening (the experiment was conducted at low temperatures and the rates of the thermal process should therefore be negligible), and it also leads to inaccurate predictions for large forces.[65b]

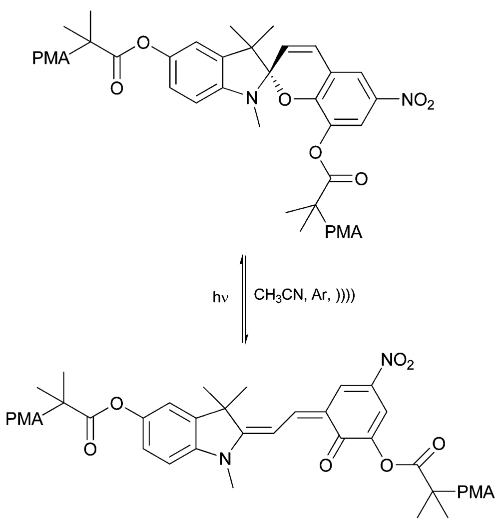
The preceding discussion shows that an interpretational framework accounting for the effects of mechanical loading on chemical kinetics—the emerging field of *chemomechanics*—remains open.[68,69] Despite this hurdle, chemists have long studied the coupling of molecular strain and reactivity and, in addition to the above benzocyclobutene case, some groups have successfully exploited polymer-based sonication.[55] Further examples are summarized below. Thus, ultrasound promotes ring opening of a functionalized spiropyran mechanophore incorporated into the center of a poly(methyl acrylate) polymer (PMA) to give the open merocyanine form.[70,71] As monitored by UV-Vis absorption spectra pulsed sonication converts the original colorless polymer into a pink solution. Notably, visible light irradiation restores the colorless solution (Scheme 8). Again, the location of the mechanophore within the chain was an essential requirement, since no reaction could be observed in a control experiment with a terminally-linked spiropyran.

The spyropyran mechanophore may also undergo stress-induced electrocyclic ring-opening in the solid state as demonstrated by Sottos *et al.*[72] To this end, the heterocyclic moiety was incorporated in both linear elastomeric PMA and cross-linked poly(methyl methacrylate) (PMMA) polymers. Both stretching of the PMA samples and compressing the PMMA-glassy beads result in color changes associated with transformation into the merocyanine form. Again, the transformation reverses upon exposure to light irradiation. Mechanical stress does not induce ring-opening in chain-end functionalized polymers, a fact that reveals the nature of the mechanically-induced reaction. Thus, color appears in regions of high stress such as those located in the center of the spherical beads subjected to compression.

Craig *et al.* have also evaluated the effect of sonication on *gem*-dichlorocyclopropane (*g*DCC) mechanophores incorporated into polybutadiene copolymers. The process lacks selectivity and the reaction probabilities are nearly identical for both *cis*- and *trans*-*gem*-dichlorocyclopropanes, even though the *cis* isomers react ~20 times faster than the *trans* ones under stress-free conditions.[73,74] An extension of this study to *gem*-difluorocyclopropanes (*g*DFCs) embedded in a polymer backbone and subjected to ultrasonication as well, has revealed further surprises.[75] The mechanochemical activation opens the *g*DFCs and generates a 1,3-diradical that can be trapped by a coumarin-based nitroxide radical. The diradical is formally a transition state of the stress-free electrocyclic isomerization. Upon sonication, both *cis*- and *trans*-*g*DFC isomers open to the diradical. When the force is removed, the diradical returns to a point of the potential energy surface where there is no barrier to disrotatory ring closure to the *cis* product. In other words, the 1,3-diradical closes exclusively to the *cis* isomer regardless of the parent geometry. This result mirrors that of the *cis*-pulling for benzocyclobutene; in the present case the *trans*-*g*DFC is pulled down the thermally forbidden conrotatory pathway (Scheme 9). The mechanical nature of polymers is again a characteristic phenomenon supported by a few observations and control



Scheme 7 Electrocyclic ring opening of benzocyclobutene mechanophores under sonication. The product was detected by trapping with *N*-(1-pyrene) maleimide. PEG denotes a poly(ethylene glycol) polymer.

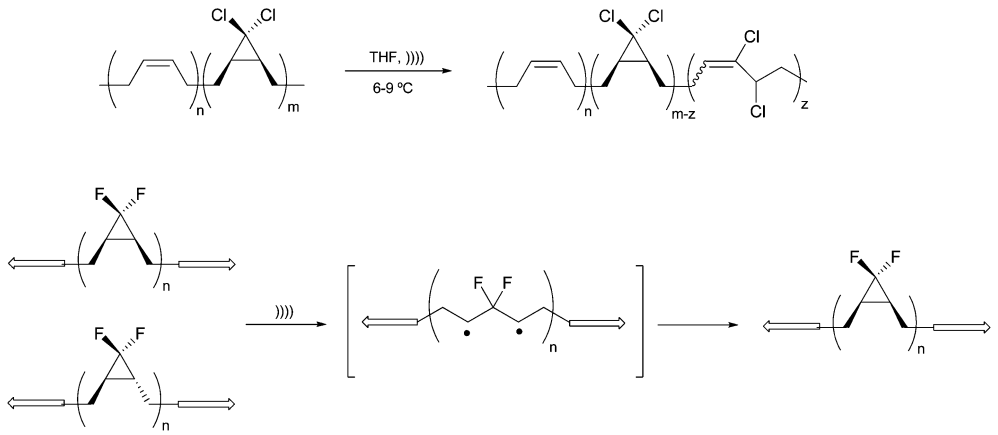


Scheme 8 Isomerization of spiropyran mechanophores. PMA denotes a poly(methyl acrylate) chain.

experiments. Thus, the conversion occurs from more- to less-stable isomer, which rules out purely thermal activation. The kinetics of *g*DFC reactivity exhibits a polymer molecular weight dependence that is similar to those of *gem*-diclorocyclopropanes. A mass of 8.2 kD is below the critical molecular weight to experience significant shear forces for mechanical activation to occur.

It should be also mentioned that the force-induced reactivity and stereochemical outcome of *g*DCCs have been scrutinized recently by *ab initio* simulations.[76] Selectivity of the ring-opening to yield either the *E*- or *Z*-diastereomer of the resulting dichloroalkene depends on the range of forces applied (from 0.7 to 2.2 nN), although in the limit of large forces the predictions point to a rather modest selectivity (60 : 40) between the *Z*,*S*- and *E*,*S*-alkenes.

The issue of mechanostereochemistry has been envisaged again in a thoughtful study by Moore, Bielawski and associates showing that atropisomers can undergo reconfiguration under the action of tensile forces.[77] As depicted in Scheme 10, an (*S*)-configured 1,1′-binaphthyl incorporated into a polymer with an approximate molecular weight of 100 kDa and subjected to pulsed sonication (20 kHz, 10 W cm^{-2}) undergoes progressive racemization (>95% after 24 h). Similar interconversion can be attained with a polymer embedding the opposite (*R*)-1,1′-binaphthyl. These results are certainly interesting and opens the possibility of manipulating thermally stable stereoisomers by the sole action of mechanical forces. It should be noted that only



Scheme 9 Evolution of *gem*-dihalocyclopropane mechanophores under ultrasonication.

a few sonochemical reactions have been shown to exhibit a certain stereoselection, especially on activated surfaces, while cavitational effects occur randomly in the bulk solution.[78]

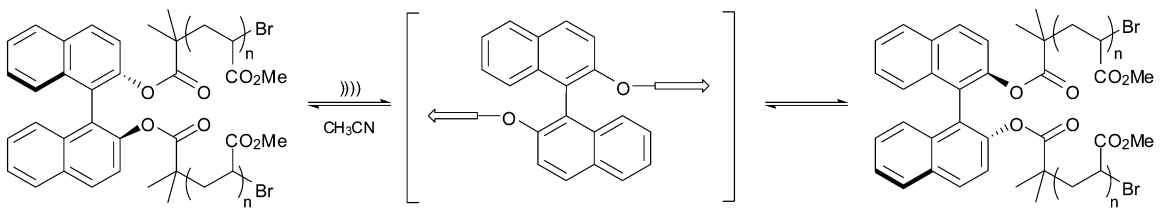
PMAs attached to a cycloadduct derived from maleimide and furan provide the mechanical force in the presence of ultrasound waves to induce retro [4 + 2] cycloadditions (Scheme 11). As in previous studies, the size of the PMA polymer is critical and products from the retro Diels–Alder reaction are observed for chains exceeding 30 kDa.[79] Moreover, polymers with low molecular weight (M_N < 20 kDa), high molecular weight (M_N > 60 kDa) but bearing terminal cycloadducts, as well as non-covalently linked polymers and cycloadducts do not yield any products from the retro cycloaddition.

It is true that retro-Diels–Alder reactions have been previously facilitated by means of single-pulse shock techniques at temperatures exceeding 1000 K (*via* stepwise pathways).[80] However, the ultrasound-induced transformation described above could only be observed when cycloadducts were centrally located in polymer chains of high molecular weight. Clearly, ultrasound enables transformations with prohibitive thermal activation barriers and this particular mechanochemistry can access reactivities not observed from other forms of activation.

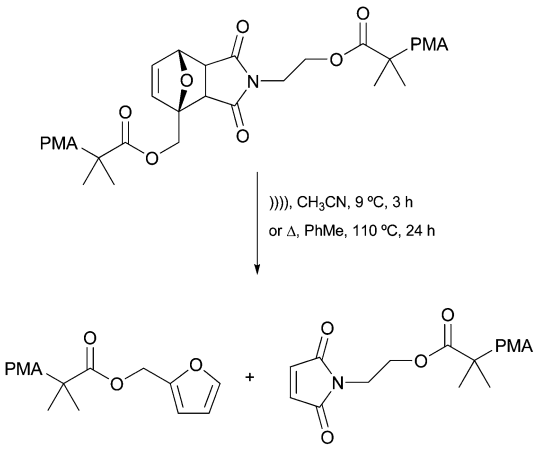
A nice illustration of the latter consideration is the ability of ultrasound to unclick the 1,2,3-triazole moiety, a formally retro [3 + 2] cycloaddition, as reported recently by Bielawski and co-workers.[81] This heterocycle is highly inert and previous attempts at reversing the click reaction under thermal or photochemical conditions led to numerous side products. However, the mechanical effects of ultrasound induce cycloreversion when the triazole fragment is centered within a PMA chain (Scheme 12). As expected, the unclick reaction hinges on a critical polymer length and subjecting an acetonitrile solution of the starting material (M_N = 96 kDa) to ultrasound for 2 h gives rise to a significant decrease in molecular weight (from 96 to 48 kDa). Interesting enough, the polymer chains ended with reactive alkyne and azide functional groups could be reclicked under ultrasonication. Thus, addition of CuI and irradiation with stirring at 80 °C for 19 h resulted in a polymeric material having a molecular weight similar to that of the presonicated material. In short, ultrasound convincingly converts a usually irreversible reaction into a useful reversible process with further expectations. An immediate conclusion is that triazoles are not completely orthogonal to chemical transformations and may also serve as protecting groups; sonication being an effective protocol to selectively unmask azide and alkynyl intermediates.

Sijbesma and coworkers have investigated the sonication of coordination polymers based on transition metals, which give rise to catalytic systems that can promote further chemical reactions.[82] As a proof of concept, ultrasonically-generated shear forces cleave Ag- or Ru-*N*-heterocyclic carbenes which subsequently catalyze transesterification or ring-opening metathesis polymerization (Scheme 13).[83]

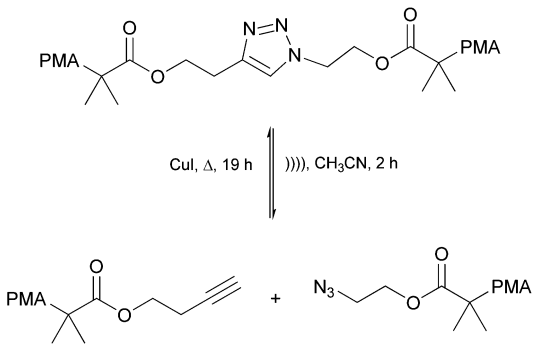
A mechanistic study has been recently conducted on a silver-carbene coordination polymer to ascertain whether ultrasound-induced scission involves thermal, radical, or mechanical pathways. The Ag(I)-*N*-heterocyclic carbene shown in Scheme 14 was dissolved in toluene solutions saturated with Ar, N_2, CH_4 and isobutane, and each exposed to 20 kHz-ultrasound.[84] Scission percentages varied from 6% under isobutane to 11–14% for the other gases, whereas thermal conversions at approximately the same temperature in the absence of ultrasound were less than 1%. Experiments using a radical scavenger showed large



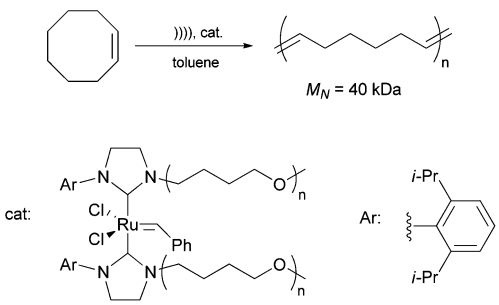
Scheme 10 Reconfiguration of chiral atropisomers by shear forces induced by sonication.



Scheme 11 Mechanically-induced retro [4 + 2] cycloaddition.

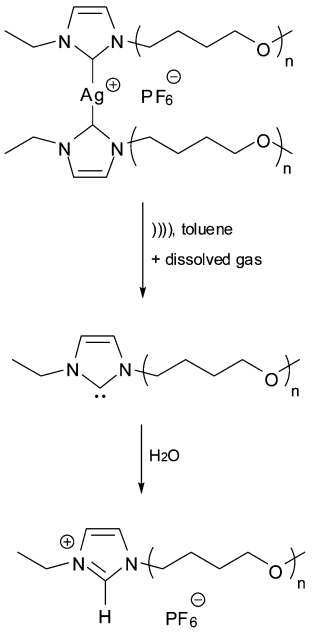


Scheme 12 Triazole cycloreversion (unclick reaction) triggered by ultrasound.



Scheme 13 Polymerization reaction catalyzed by *N*-heterocyclic carbenes generated *in situ* by ultrasound-induced metal–ligand cleavage of polymeric reagents.

differences (by a factor of 10) under these gases and suggest that radical production has a negligible effect on polymer scission. Accordingly, mechanical scission caused by strain after bubble collapse is most likely responsible for polymer cleavage. Numerical simulations also provide a satisfactory rationale as they indicate that critical strain rates for scission can be achieved under sonication at temperatures of 298 K and acoustic pressures of $\sim 10^5$ Pa attained at 20 kHz. The gas solubility greatly affects bubble dynamics, strain rates and hot spot-temperatures. A higher number of isobutane molecules inside the bubbles leads to less intense collapse and a lower strain rate, which correlates well



Scheme 14 Mechanochemical scission of a Ag(I)-NHC polymer catalyst under ultrasound and further trapping of the free carbene with a proton source.

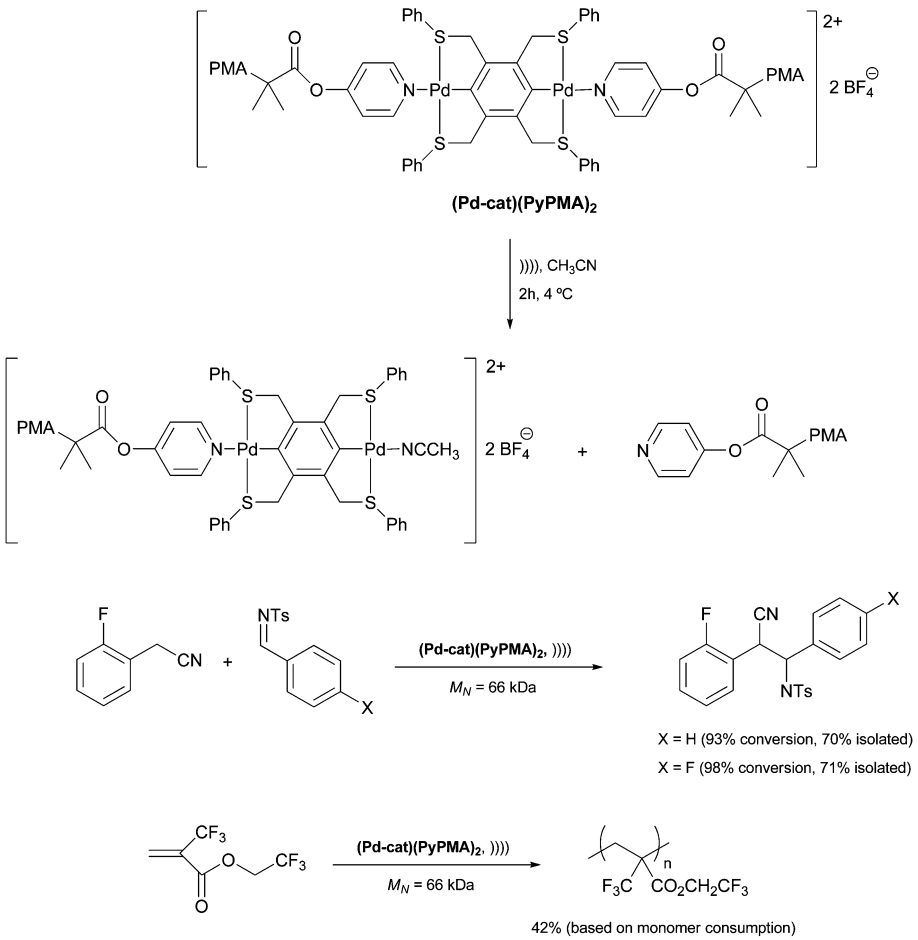
with the lower scission percentage measured in isobutane-saturated solutions.

In a recent work that highlights again the usefulness of these novel catalytic strategies, Bielawski *et al.* have coupled pyridine-capped PMAs to cyclometalated dipalladium complexes, thereby affording coordination polymers that undergo subsequent Pd–pyridine bond scission under ultrasound. A polymer with a molecular weight of approximately 40 kDa is required for chain scission to occur; beyond this threshold M_N an increased rate of chain scission is also observed. The unmasked Pd-based system can efficiently catalyze carbon–carbon bond formation between benzyl cyanides and *N*-tosyl imines. In addition, the pyridine moiety (PyPMA) released during sonication can also catalyze the anionic polymerization of acrylates (Scheme 15).[85] These transformations are unsuccessful under conventional thermal activation.

In related work, the same team has reported pyridine–boronium complexes by coupling two pyridine-capped-PMA chains of different molecular weight to a bis(aryl)boron chloride. As above, ultrasound induces selective scission of the B-pyridine bond when polymers reach average molecular weights (M_N) between 40 and 66 kDa. This mechanical scission liberates the pyridine base capable of effecting colorimetric titrations or catalyzing the polymerization of acrylates.[86]

Perspective and concluding remarks

It has become obvious that ultrasound waves can be remarkably useful in chemical sciences. An ultrasonic field may in principle induce formation of radical species and mechanical force, which arise from the physical phenomenon of cavitation. Ultrasound overcomes numerous technical troubles and facilitates completion of processes conducted under heterogeneous conditions, in



Scheme 15 Preparation of Pd–pyridine–PMA coordination polymers, which can be harnessed to promote, after sonication-induced cleavage, carbon–carbon bond-forming reactions and base-catalyzed polymerizations.

which mass and energy transfers represent rate-limiting steps. It seems that purely mechanical effects can be controlled and fine-tuned at atomic and molecular levels. Of particular importance in both synthesis and catalysis is scission of polymers to activate centrally-appended mechanophores. This raises equally important still-unanswered questions about the nature and action of tensile forces and strain in solution and solid–liquid interfaces. But, sonication clearly offers an opportunity to merge chemistry and physics in the toolbox and an intellectual challenge in terms of a mechanistic rationale. Things would also be easier if scientists entering the field or harnessing occasionally ultrasonic irradiation, were able to realize the importance of a series of key parameters (frequency, acoustic power, temperature), which also influence bulk solvent properties. Moreover, reactor design can be an essential ingredient for efficiency and scaling up considerations.[87] All in all, there is little or no doubt that ultrasound-based methodologies will add further stimuli to basic science and technology.

Acknowledgements

Financial support from different institutions and research agencies is gratefully acknowledged: The MIUR, Italy (PRIN 2008: "A Green Approach to Process Intensification in Organic Synthesis"), the Spanish Ministry of Science and Innovation (Grants MAT2009-14695-C04-C01 and CTQ2010-18938), and the Junta de Extremadura-FEDER (Ayuda a Grupos Catalogados GR10049)

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