

# **SYNTHETIC ORGANIC SONOCHEMISTRY**

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# **EXTRAITS**

waves,<sup>120</sup> we will only consider the case of standing waves in a qualitative description, largely inspired from Leighton.<sup>1</sup>

### 3.4.1. Primary Bjerknes force

The qualitative description of the interaction of a sound field and a bubble requires knowing whether bubbles respond "in phase" or "out-of-phase" with respect to the acoustic pressure, and the nature of the force (in particular, its time-averaged value) acting on the bubble in a resonant field. To solve the first question, the case of a pendulum of length  $l$  can again be taken as a model. Resonant oscillation under a linear regime of the pendulum is forced by an impulsion produced by a second oscillator compensating for any energy loss. If the frequency of the driving oscillator increases, the length  $l$  must be reduced to keep with an in-phase oscillation of the pendulum (stiffness-controlled system). Conversely, if the length  $l$  is increased, the response will be an out-of-phase oscillation (inertia-controlled system). Bubbles in an acoustic field react analogously. Those with an equilibrium radius lower than the resonance radius ( $R < R_{res}$ , Eq. 17, p. 21) oscillate in phase with the acoustic pressure (conversely, for bubbles with  $R > R_{res}$ ). These principles are transposed graphically in Fig. 24 (for the sake of simplicity, the volume changes are assumed to be proportional to the acoustic pressure changes).<sup>1</sup>

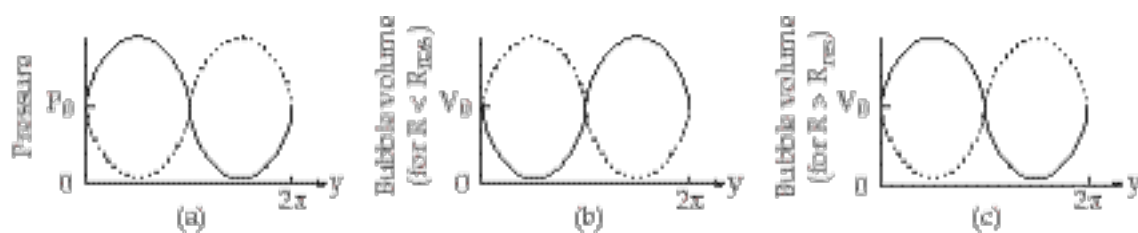


Figure 24 - Evolution of (a) the acoustic pressure in a stationary field, (b) the volume of a bubble with  $R < R_{res}$ , (c) the volume of a bubble with  $R > R_{res}$

The second question is related to the force acting on bubbles. When an acoustic wave propagates in a medium, a pressure gradient is associated with it. The situation with which we are dealing is different because we are concerned with standing waves, but the basis is the same. Let us consider a cube of volume  $V$  immersed in a pressure field. Because of the pressure gradient, the pressure exerted on a side of the cube is not the same as that on the opposite side. The result is the presence of a pressure gradient across the cube ( $\nabla P$  in  $\text{N} \cdot \text{m}^{-2}/\text{m}$ ), acting on the volume of this cube ( $V$  in  $\text{m}^{-3}$ ). The latter is subjected to a force  $F = -V \cdot \nabla P$  (the negative sign comes from the fact that the higher the decrease is in the acoustic pressure in the space, the higher the force will be). In Fig. 25, we present the pressure gradient, the evolution of the forces  $V \cdot \nabla P$ , and the mean value of these forces for bubbles with  $R < R_{res}$  and with  $R > R_{res}$ .

<sup>120</sup> Yosioka, K.; Kawasima, Y. *Acustica* 1955, 5, 167-173.

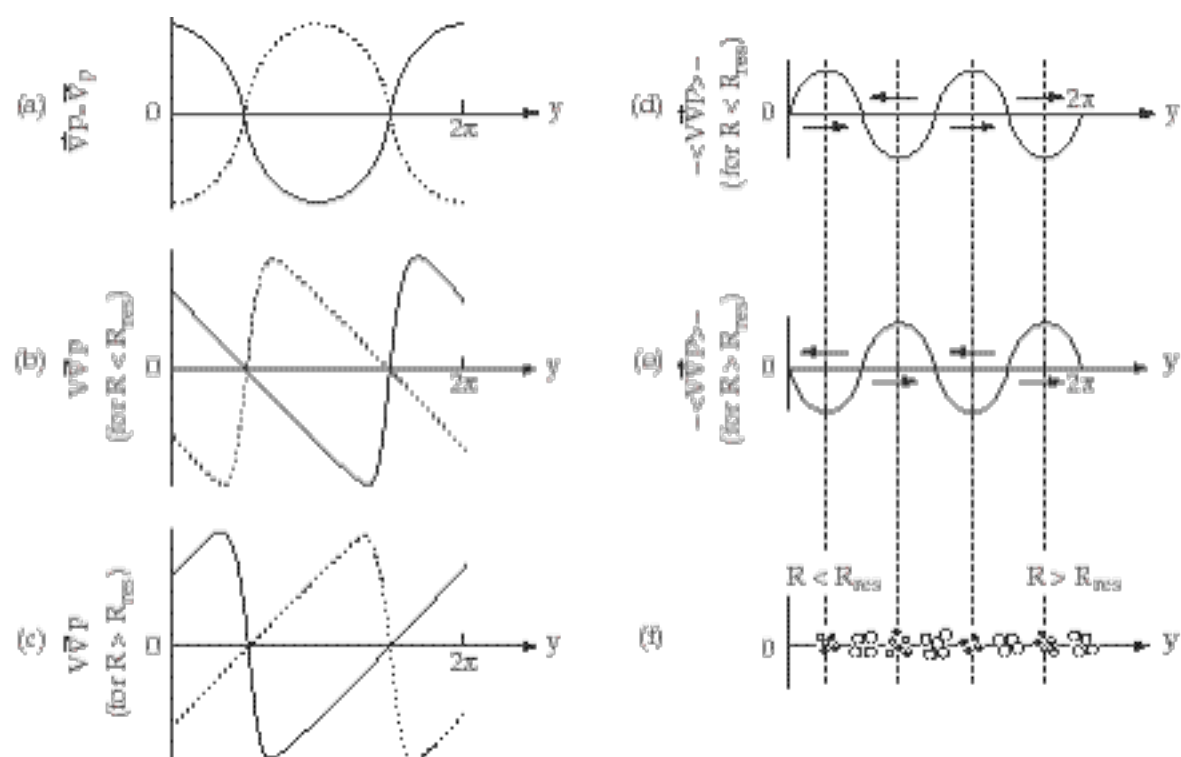


Figure 25 - Graphic representation of the evolution of (a) the pressure gradient, (b) the force  $V \times \nabla P$  for  $R < R_{res}$ , (c) the force  $V \times \nabla P$  for  $R > R_{res}$ , (d) the average force for  $R < R_{res}$ , (e) the average force for  $R > R_{res}$ , (f) distribution of the bubbles in a standing wave field (adapted from Ref. 1)

It may be noted that bubbles with  $R < R_{res}$  are attracted towards the pressure antinodes while bubbles with  $R > R_{res}$  are attracted towards the nodes. Since bubbles at the antinodes experience greater acoustic pressures, their dynamics is more energetic and the chemical and sonoluminescent effects are preferentially detected at pressure antinodes.<sup>121</sup>

### 3.4.2. Secondary Bjerknes force

The problem with which we are dealing in sonochemistry is the relation between a bubble in a bubble cloud interacting with the radiation force. Here, the problem of the interaction between two bubbles in an incident sound field is described qualitatively.<sup>122</sup>

The case of two spherical bubbles, smaller than resonance size, for example (i.e., pulsating in phase), is considered. Of course, the situation can be transposed to bubbles larger than resonance size both vibrating out-of-phase with respect to the acoustic pressure, i.e., in phase with one another. In Fig. 26, the left-hand L and right-

<sup>121</sup> Leighton, T.G.; Walton, A.J.; Pickworth, M.J.W. *Eur. J. Phys.* **1990**, *11*, 47-50.

<sup>122</sup> For quantitative treatments, see Coakley, W.T.; Nyborg, W.L. in *Ultrasound in Medicine and Biology* (Fry, F. Ed.), Elsevier, Amsterdam, **1978**, Part 1, pp. 77-159; see also Refs. 100, 121, 123.

### 2.3.2. Substitutions leading to carbon-heteroelement bonds

A Finkelstein substitution with practical utility was reported some years ago (Fig. 34).<sup>130</sup> An  $\omega$ -bromo fatty acid undergoes halogen exchange with radioactive  $\text{Na}^{123}\text{I}$  to provide the labelled iodo acid, used as a tracer for the medical exploration of cardiac metabolism. The sonochemical reaction conducted in butanone provides quantitative yields of the expensive and thermally labile product, and the presence of water in the solvent, up to 7%, is tolerated. In comparison, the usual method requires heating at *ca.* 180°C and anhydrous conditions, and the purity of the product is much less satisfactory. It can be noticed that the unusually high temperature of the sonochemical reaction, close to the solvent boiling point, makes an interpretation hazardous. A second case of a Finkelstein substitution, a mesylate-iodine exchange, was published recently without experimental detail.<sup>131</sup>

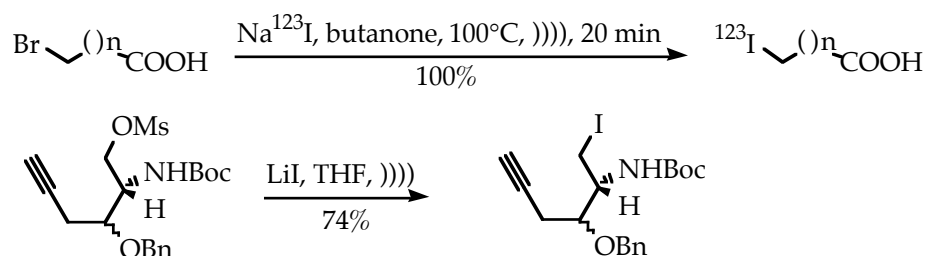
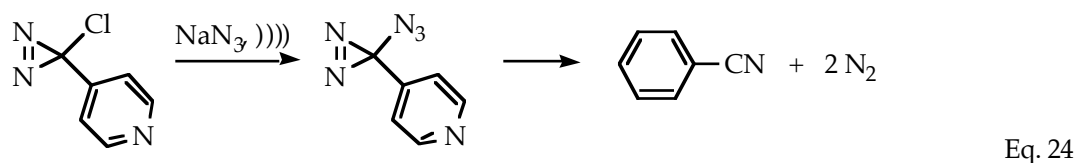
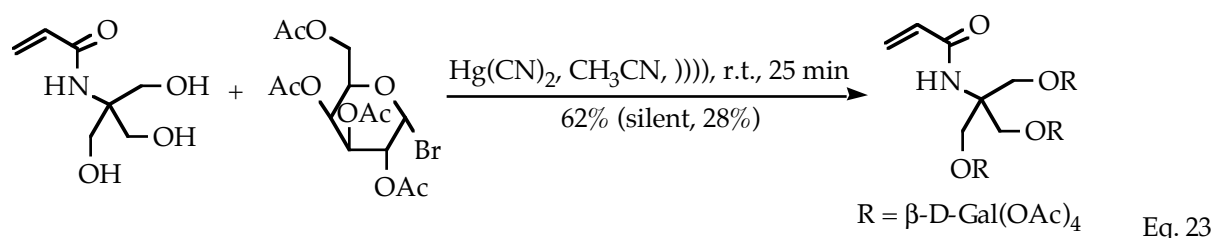


Figure 34 - Finkelstein exchange reactions

A sugar with a bromine atom at the anomeric position undergoes a clean substitution by an alcoholic group in the presence of mercuric cyanide. In comparison with the traditional method, the reaction is much faster and stereoselective (Eq. 23).<sup>132</sup> Only the easily purified  $\beta$ -anomers are obtained, while the silent method gives mixtures.



<sup>130</sup> Mertens, J.; Vanryckeghem, W.; Bossuyt, A.; Van der Winkel, P.; Vanden Driessche, R. *J. Label. Comp. Radiopharm.* **1984**, *21*, 843-856.

<sup>131</sup> Marco-Contelles, J.; Bernabé, M. *Tetrahedron Lett.* **1994**, *35*, 6361-6364.

<sup>132</sup> Polidori, A.; Pucci, B.; Maurizis, J.C.; Pavia, A.A. *New J. Chem.* **1994**, *18*, 839-848.

process leading to a reactive surface, several phenomena are involved which cannot be considered separately. Since no general vision seems to have been proposed until now, we will try to delineate a few important points.

#### 1.1.1.1. Surface cleaning

Metals used for organic synthesis are coated by oxides, hydroxides, carbonates, and sometimes nitrides (e.g., for lithium). The contact between the underlying metal and any "outside" reagent is thus inhibited. Re-establishing the contact between the metal itself and the corrosive solution is the purpose of the physical activation. At this stage, an important role should be played by the mechanical properties of the metal and of the coating and their mutual interaction. It is difficult to decide which parameter predominates in this process, but in a speculative approach, hardness can be taken into account.<sup>13</sup> Two mechanisms, shown in Fig. 1, can then be envisaged, according to the properties of the metal.

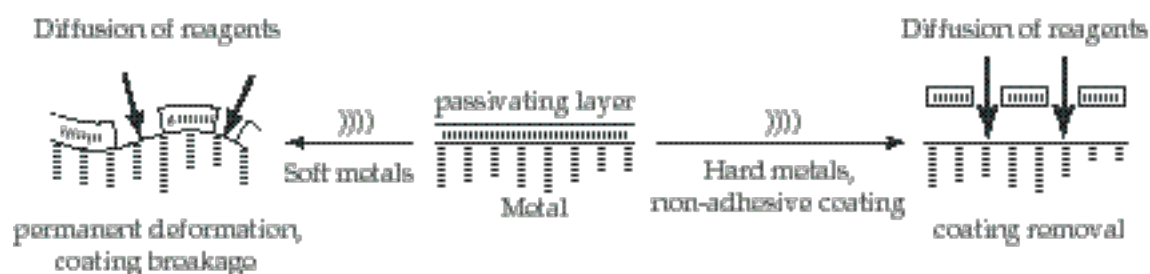


Figure 1 - Metal de-passivation

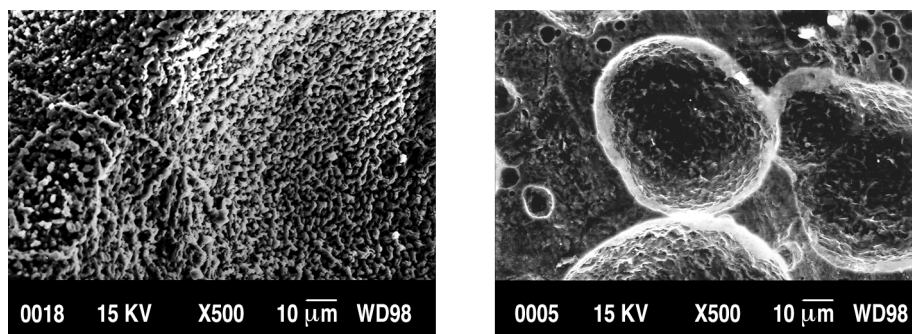


Figure 2 - SEM of sonicated lithium (left) and magnesium (right)

In general, the coatings are composed of non-ductile materials, harder than the metal itself. When submitted to the cavitation microhammering, soft materials, e.g., alkali metals, undergo permanent plastic deformation. Electron microscopy of a lithium

<sup>13</sup> A complication in this approach comes from the important differences, known by metallurgists, in the mechanical properties of a metal according to its "history". The hardness of a metal can be changed on a very broad range by thermal or mechanical treatments. Consequences in terms of reactivity can be considerable, and the activation process, by the involvement of the superficial layers, may be more or less easy for a given metal, always the same as a chemical compound, but with significantly differing properties as a material.

This reaction, described by the authors as a Diels-Alder cycloaddition *via* the *o*-xylylene (p. 99), was employed in carbohydrate chemistry to produce anthracyclinone analogues.<sup>278</sup> No reaction occurs without sonication. The mechanism was not established with certainty, and it can be postulated that a mono-organozinc reagent adds to the activated olefin and the enolate anion undergoes an alkylation from the second benzylic bromide.

The methylenation of carbonyl groups using diiodomethane was attempted but met only with a limited success.<sup>279</sup> Aldehydes provide olefins in good yields, and ketones remain unchanged. The sonication conditions should be systematically investigated to base a synthetic method on these preliminary results.

### 3.6.3. Extensions of the Barbier reaction. The use of aqueous media

Aqueous organic chemistry has recently emerged from being a rare curiosity to becoming a promising research area with the advantage of reducing environmental problems.<sup>280</sup> With metals, these processes were once considered impossible since most organometallics do not survive under such conditions. It is now recognized that not only are organometallic reactions possible in water-containing media, but they offer new approaches in some domains, for instance sugar chemistry. Sonication greatly improves their rates and yields, as the result of the acceleration of electron transfer processes. It can be accepted that the reactions proceed through radical species on the metal surface rather than in solution, even if many questions concerning the mechanism subsist. Reviews on this topic were published recently.<sup>281</sup>

#### 3.6.3.1. Allylation of carbonyl groups

Homoallylic alcohols can be obtained by sonicating a mixture of allylic halides, zinc, and aldehydes or ketones in aqueous THF (Fig. 51).<sup>282</sup> The yields are not always satisfactory, and replacement of the THF-water solvent by THF-aqueous NH<sub>4</sub>Cl greatly improves the method. With these conditions, sonication is unnecessary, and stirring at room temperature is sufficient to provide activation. Allylic bromides react faster than the chlorides and the process is chemoselective, thus enabling allylation of aldehydes in the presence of ketones.<sup>283</sup> In all cases, the allylic group becomes attached to the substrate at the more substituted carbon atom. The stereoselectivity of this reaction was recently studied.<sup>284</sup> Allylation can also be performed with tin,

<sup>278</sup> Chew, S.; Ferrier, R.J. *J. Chem. Soc. Chem. Commun.* **1984**, 911-912.

<sup>279</sup> Yamashita, J. Inoue, Y.; Kondo, T.; Hashimoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2335-2336.

<sup>280</sup> Lubineau, A. *Chem. Ind. (London)* **1996**, 123-126.

<sup>281</sup> (a) Li, C.J. *Chem. Rev.* **1993**, *93*, 2023-2035; (b) Chan, T.H.; Li, C.J.; Lee, M.C.; Wei, Z.Y. *Can. J. Chem.* **1994**, *72*, 1181-1193.

<sup>282</sup> (a) Pétrier, C.; Luche, J.L. *J. Org. Chem.* **1985**, *50*, 910-912; (b) Einhorn, C.; Luche, J.L. *J. Organomet. Chem.* **1987**, *322*, 177-183.

<sup>283</sup> Pétrier, C.; Einhorn, J.; Luche, J.L. *Tetrahedron Lett.* **1985**, *26*, 1449-1452.

<sup>284</sup> Marton, M.; Stivanello, D.; Tagliavini, G. *J. Org. Chem.* **1996**, *61*, 2731-2737.

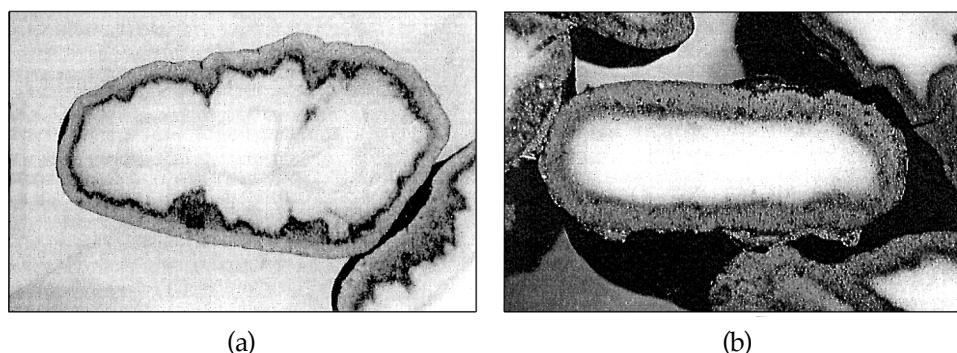
eliminate the more common counter-ions (nitrate, acetate), but the results are completely useless for chloride ions, especially when the support is alumina. The elimination results are barely efficient even when using both dry (flowing H<sub>2</sub>) and humid reduction methods (hydrazine, sodium formate, or borohydride, etc.). The treatment by hydrogen is the most common way in industrial and laboratory practice, but in the presence of chlorine the required temperatures are, in many cases, so high that sinterization of the active metal occurs (Table 3).<sup>43b,47,48</sup>

**Table 3** - Reduction of some supported metals (M<sup>n+</sup>→M<sup>0</sup>) from chloride precursors by hydrogenation

Sample	Rh/SiO <sub>2</sub> <sup>a</sup>	Pd/SiO <sub>2</sub> <sup>a</sup>	Ru/SiO <sub>2</sub> <sup>a</sup>	Ru/Al <sub>2</sub> O <sub>3</sub> <sup>b</sup>	Pt/Al <sub>2</sub> O <sub>3</sub> <sup>c</sup>
T (K)	600	450	>873	1200	>773

<sup>a</sup>See Ref. 34; <sup>b</sup>Ref. 35; <sup>c</sup>Ref. 36.

The third main feature given by using ultrasound during the preparation of supported catalysts is the larger penetration of the active metal inside the pores of the support. To qualitatively study the real penetration of the metal, the catalysts have been prepared using a large-size granular support (both alumina<sup>38</sup> and carbon<sup>49</sup>); after the impregnation of the active metal (Pd or Ru) the support grains were cut and observed by optical microscopy. In the case of the carbon samples, due to the black color of both the support and the supported metal, a particular method was used to create a contrast between the two materials.<sup>50</sup> The supported palladium grains were used for the catalytic decomposition of aqueous cupric formate. Copper separates on the sites of the active component, while carbon remains intact. Sites covered with copper can be readily located optically by their red color on the black support.<sup>49</sup> Figure 3 shows the optical microscope micrograph of two grains of Ru/Al<sub>2</sub>O<sub>3</sub> (Ru 1% wt/wt from RuCl<sub>3</sub>) both reduced simply with hydrazine [Fig. 3(a)] and with hydrazine and ultrasound [Fig. 3(b)].<sup>38</sup>



*Figure 3 - Optical micrographs from a section of a grain of catalyst (Ru 1% from RuCl<sub>3</sub> on alumina): (a) sample reduced with hydrazine; (b) sample reduced with hydrazine and the help of ultrasound*

<sup>47</sup> Narita, T.; Miura, H.; Sugiyama, K.; Matsuda, T. *J. Catal.* **1987**, *103*, 492-495.

<sup>48</sup> Sivasanker, S.; Ramaswamy, A.V.; Ratnasamy, P. *Stud. Surf. Sci. Catal.* **1979**, *3*, 185-196.

<sup>49</sup> Bianchi, C.L.; Gotti, E.; Toscano, L.; Ragaini, V. *Ultrasonics Sonochemistry*, in press.

<sup>50</sup> Cervený, L.; Marhoul, A.; Cervinka, K.; Ruzicka, V. *J. Catal.*, **1980**, *63*, 491-495.



The sample in Fig. 3(a) is a common eggshell catalyst: all the active metal is concentrated on the upper shell of the support grain. As a large grain was used for such a test, it is possible to observe a white heart due to "uncontaminated" alumina. On the contrary, the sonicated sample in Fig. 3(b) is characterized by a black halo due to the ruthenium atoms that migrated inside the support. This kind of catalyst is commonly called egg-white catalyst and is industrially prepared in the presence of citric or tartaric acid. Sonochemically the same result is obtained without using any chemical which could poison the active sites.

From a catalytic viewpoint, the supported catalysts produced sonochemically have been tested in different heterogeneous reactions. Ru/Al<sub>2</sub>O<sub>3</sub> samples have been studied in the Fischer-Tropsch synthesis.<sup>38</sup>

Figure 4 shows the CO conversion curves (calculated from a mass balance on the amount of carbon in CO and of all the hydrocarbons, revealed by the detector of the gas-chromatograph) *vs* time for two Ru/Al<sub>2</sub>O<sub>3</sub> samples (1% Ru w/w). The runs were performed at 275°C, 5 bar in a tubular continuously fed reactor, with a molar ratio H<sub>2</sub>/CO = 2. Pd/C catalysts were tested in the hydrogenation of acetophenone in ethanol at 25°C and atmospheric pressure with flowing H<sub>2</sub> as reactant in a slurry laboratory-scale plant. The activity values were measured by the consumed hydrogen in mL · min<sup>-1</sup>.

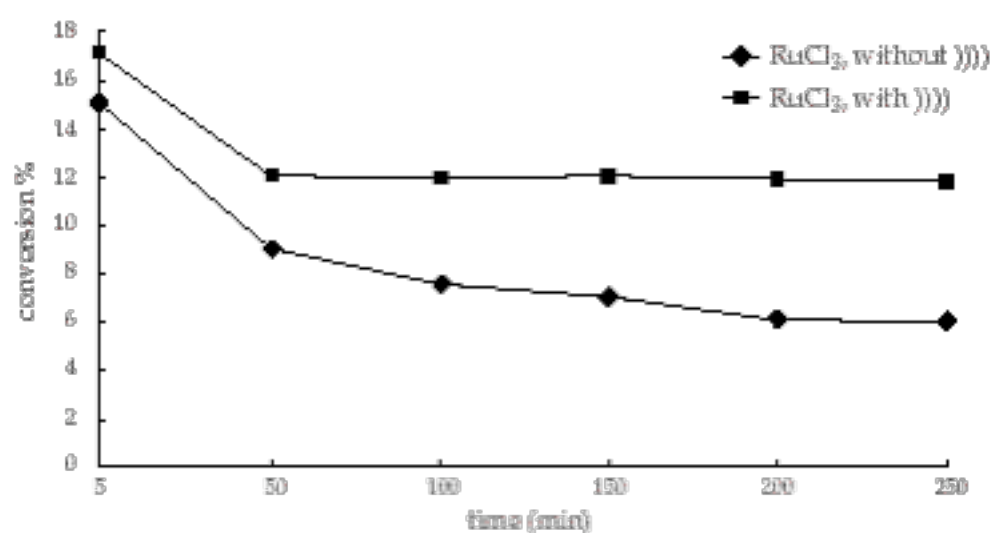


Figure 4 - Fischer-Tropsch synthesis runs performed using Ru/Al<sub>2</sub>O<sub>3</sub> samples

The conversion data (reported in Fig. 5 as the time required to obtain a 90% conversion of acetophenone) for Pd/C catalysts prepared with and without ultrasound have been compared to the data, obtained in the same plant and with the same operating conditions, from two commercial samples, a sample (1) characterized by an eggshell metal distribution and a second one (2) characterized by a penetrated metal distribution. All the samples, both commercial and prepared in the laboratory, have the same metal loading (5% Pd wt/wt) and are supported on the same kind of active carbon. The sonicated sample shows a higher activity than all the catalysts tested, both in Fischer-Tropsch synthesis and in the hydrogenation of acetophenone.

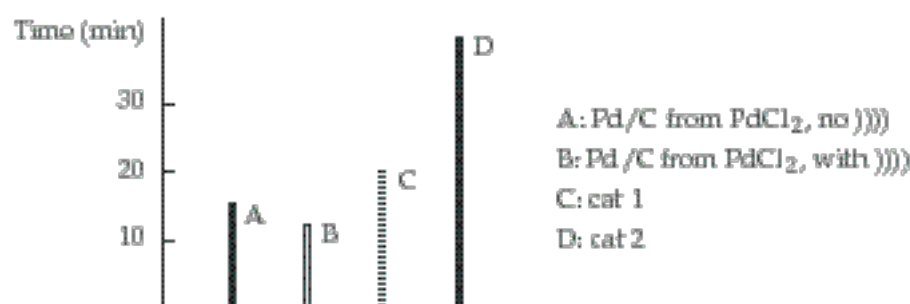


Figure 5 - Activity of Pd/C catalysts as time to reach a 90% conversion of reduced acetophenone

## 2. EFFECT OF SONICATION ON HETEROGENEOUS CATALYTIC REACTIONS

### 2.1. STEPS OF A HETEROGENEOUS CATALYTIC REACTION

Before discussing the influence of ultrasound on a catalytic heterogeneous reaction (liquid/solid, liquid/gas/solid, liquid/liquid/solid), it is useful to illustrate the steps through which such reactions can proceed. Let us refer to a very simple reaction transforming starting material SM to product P as illustrated in Fig. 6. For the sake of simplicity, we suppose that SM and P are both liquids or gases and that these substances are diluted in inert liquids or gases, respectively.



Figure 6 - Reaction steps of a heterogeneous catalytic reaction from SM to P around and inside a catalytic particle with pores of mean diameter  $d_p$ .  
See text for the meaning of numbers 1-7.

The seven steps illustrated in the figure are:

- 1 external diffusion of SM through the solid-fluid interphase to the external part of the solid catalyst particle;
- 2 internal diffusion of SM into the pores of the catalyst;
- 3 adsorption of SM on the catalytic site;
- 4 catalytic reaction from SM producing P species adsorbed on the catalyst;
- 5 desorption of P;
- 6 internal back-diffusion of P through the pores of the catalytic particle;
- 7 external back-diffusion of P in the limit layer and collection of this product in the liquid or gas phase of the reactor.

### 1.2.4. Other types of equipment

Baths, probes, and cup-horns are common laboratory equipment. For large-scale uses, other types of emitters are preferred. Whistles (Fig. 9) can be used for processing liquid mixtures or suspensions. The principle consists of injecting the mixture under a few bar overpressure through a variable slit onto a vibrating blade located in a resonant cavity. The advantage is the simplicity and the compatibility with a flow process; the inconvenience is the erosion undergone by the blade.

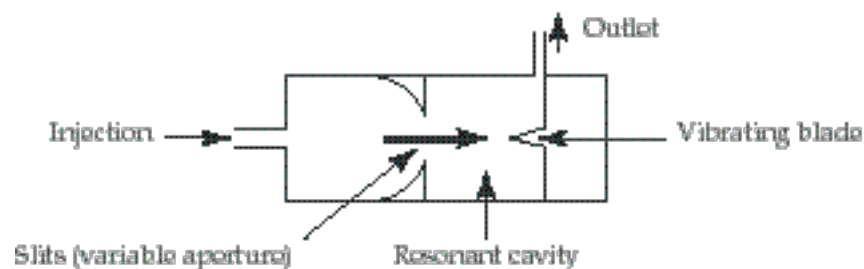


Figure 9 - Principle of the whistle reactor

Equipment involving parallel vibrating plates is probably the best option for on-line use, the product being treated homogeneously during its transfer through the reactor whose walls are vibrating (Fig. 10).<sup>25</sup>

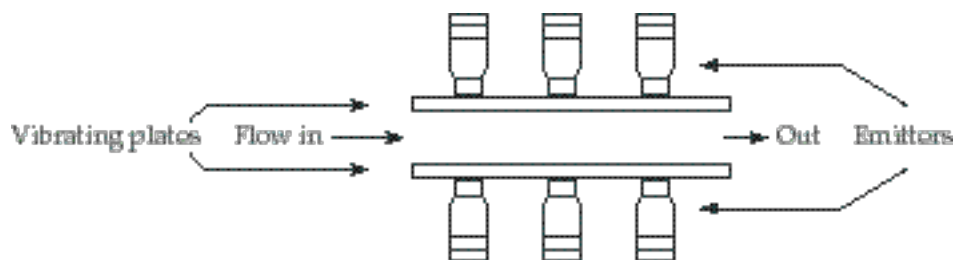
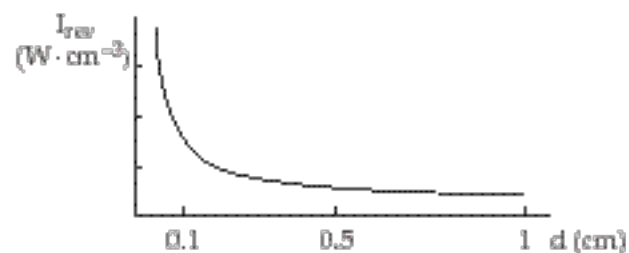


Figure 10 - Parallel-plate device

When the plates are close together, the attenuation of the sound is minimal (Fig. 11) and the "rules" followed in regular sonicated systems (baths, cup horns) involving large volumes and standing wave patterns are not valid in this case.

Figure 11 - Reverberated ultrasonic intensity per unit volume as a function of wall separation ( $d$ )



The advantage of opposite vibrating plates compared to one vibrating surface is that the vibrational energy, before being absorbed by the liquid, is reverberated by the opposite plate. In this way the mechanical effect is maximum. Different but overlapping patents claim the same general cell shape involving parallel vibrating walls with a variable spacing between the plates.

<sup>25</sup> Ref. 1a, p. 108.

## 19. NITROXIDES

### *Oxidation of a secondary amine* (p. 157)

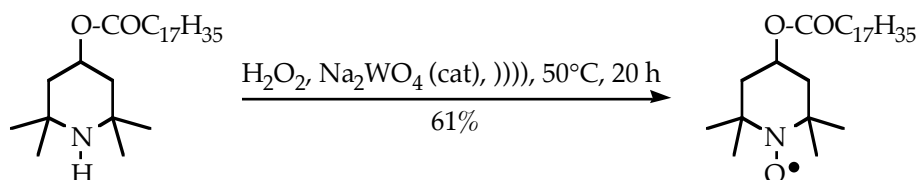
#### *Preparation of 2,2,6,6-tetramethyl-4-stearoyloxypiperidin-1-oxyl*

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Comenius University, Department of Organic Chemistry, Faculty of Sciences, 842-15 Bratislava, Slovakia.

N-Oxyl radicals are commonly prepared by oxidation of secondary amines with 30% hydrogen peroxide without a solvent in the presence of  $\text{Na}_2\text{WO}_4$  as the catalyst.<sup>123</sup> Peroxyacids,<sup>124</sup> dibenzoyl peroxide,<sup>125</sup> and di-*t*-butyl peroxide<sup>126</sup> are also often used as oxidants. These methods suffer from various drawbacks. The oxidation of lipophilic secondary or sterically highly hindered amines with hydrogen peroxide proceeds rather slowly, and oxidation with organic peroxides, e.g., di-*t*-butyl peroxide, can be dangerous, especially when multigram experiments are performed. The procedure described in this paper can be applied to the preparation of N-oxyl radicals on a broad range of 4-hydroxy-2,2,6,6-tetramethyl piperidine derivatives<sup>127</sup> as well as to even more sterically hindered 15-substituted 7,15-diazaspiro[5.1.5.3]hexadecane derivatives.<sup>128</sup>

Sonifications were effected in a Tesson 1 ultrasonic cleaning bath (Tesla Vrable, 37 kHz, 150 W). Its efficiency was characterized by the Weissler test:  $4.7 \cdot 10^{-6} \text{ mol} \cdot \text{L}^{-1}$  of  $\text{I}_3^-$  are formed after 10 min sonication of a 1-M KI solution in water. The experiments were run at 50°C. This temperature is crucial for achieving reasonable yields, since the starting material is only partially soluble in ethanol at lower temperatures. At 30°C, the yield is 31%. Other solvents were used (acetic acid, acetonitrile, DMF), but the yields were lower.



A 100-mL Erlenmeyer flask is charged with 40 mL of ethanol, 4-stearoyl-2,2,6,6-tetramethylpiperidine (prepared from the sodium salt of 4-hydroxy-2,2,6,6-tetramethylpiperidine, 1 g, 2.4 mmol), sodium tungstate dihydrate (0.05 g, 0.15 mmol), Chelaton 3 (disodium salt of ethylenediaminetetraacetic acid, 0.05 g, 0.14 mmol), and hydrogen peroxide (30%, 3 mL). The flask is immersed in the cleaning bath and sonicated  $2 \times 10$  h at 50°C (the mixture is left standing overnight between the two sonication periods).

<sup>123</sup> (a) Forrester, A.R.; Hay, J.M.; Thomson, R.M. *Organic Chemistry of Stable Free Radicals* Academic Press, London, **1967**; (b) Rozantsev, E.G. *Free Nitroxyl Radicals* Plenum Press, New York, **1970**; (c) *Spin Labeling* (Berlinger, L.J. Ed.), Academic Press, London, **1975**; (d) Sosnovsky, G.; Konieczny, M. *Z. Naturforsch.* **1976**, *31B*, 1376-1378; (e) Kagan, E.S.; Mikhailov, V.I.; Rozantsev, E.G.; Scholle, V.D. *Synthesis* **1984**, 895-916.

<sup>124</sup> (a) Toda, T.; Mori, E.; Murayama, K. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 1904-1908; (b) Cella, J.A.; Kelley, J.A.; Kenahan, E.F. *J. Org. Chem.* **1975**, *40*, 1860-1862; (c) Caproin, N.T.; Negoita, N.; Balaban, A.T. *Tetrahedron Lett.* **1977**, 1825-1826.

<sup>125</sup> Freeman, A.M.; Hoffman, A.K. *Fr. 136030; Chem. Abstr.* **1964**, *61*, 13289d.

<sup>126</sup> Kalashnikova, L.A.; Neyman, M.B.; Rozantsev, E.G.; Skripko, L.A. *Zh. Org. Khim.* **1966**, *2*, 1529-1532; *Chem. Abstr.* **1967**, *66*, 75550a.

<sup>127</sup> Kaliska, V.; Toma, S.; Lesko, J. *Chem. Papers* **1988**, *42*, 243-248.

<sup>128</sup> Kaliska, V.; Toma, S.; Lesko, J. *Coll. Czech. Chem. Commun.* **1987**, *52*, 2266-2273.