

Selective Catalytic Oxidations in Supercritical Carbon Dioxide

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Abstract: Supercritical carbon dioxide is ideally suited as reaction medium for catalytic oxidations of organic substrates, and it may be exploited as one of the most promising strategies to realize some fundamental chemical transformations under environmentally benign conditions. The use of supercritical carbon dioxide as solvent for unselective hydrocarbons auto-oxidations is extensively described in the literature. Conversely, only a limited number of reports deal with selective oxidations carried out by molecular oxygen or by other primary oxidants such as hydrogen peroxide, alkyl hydroperoxides, monopersulfate, etc. In this paper recent developments in selective catalytic oxidations are reviewed and particular attention is devoted to those processes in which a metal derivative, capable of selectively oxidizing various substrates, is formed by action of a terminal oxidant such as oxygen or an organic or inorganic peroxide.

1. INTRODUCTION

In spite of the fact that supercritical fluids (scFs) have been known for more than 180 years [1,2], the interest for their applications has almost burst on both academic and industrial areas only twenty years ago and still growing. This renewed interest was initially motivated by concerns about energy costs: the idea was that separations using scFs might be suitable alternatives to distillation and liquid extraction. Indeed, this revealed to be the case only in a limited number of processes and, in particular, when it is possible to avoid pressure reduction in order to recover a solute. For example, the well-known coffee decaffeinating process exploiting scCO_2 [3] is an economically sustainable process only because caffeine is recovered from CO_2 not by depressurisation but rather by extraction into water. More recently, the considerations underlying the research in scFs field are addressed, on one hand, to the replacement of toxic and environmentally hazardous halogenated and/or aromatic solvents and, on the other hand, to the improvement of yields and selectivities by tuning the relevant solvent characteristics of scFs as reaction media.

In the first part of this introduction we will briefly summarize the definition and principal properties of scFs and the practical aspects of reactions performed in these particular media. In the second part, we will mainly focus on the characteristics of supercritical carbon dioxide (scCO_2) regarding its utilization as reaction medium for organic reactions and in particular for oxidative processes.

What is a supercritical fluid? Various definitions of this uncommon state of matter are given by IUPAC [4] and by several dictionaries [5,6]. The definition we use in this review refers to a scF as the physical state of a compound above its critical temperature (t_c) and critical pressure (p_c) but below the pressure required to condense into the solid state. (see the phase diagram of Fig.(1)).

The boundaries of the various regions are defined by the values of pressure and temperature where two phases can co-

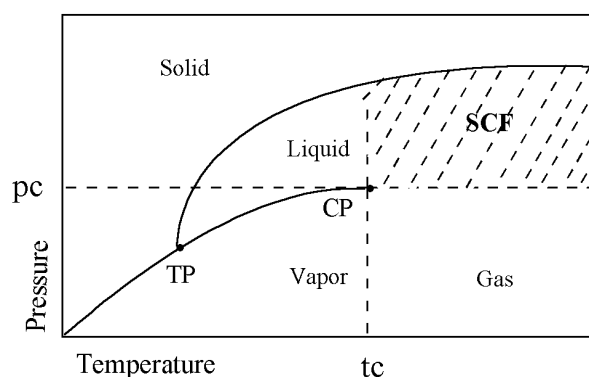


Fig. (1). Phase diagram for a generic substance.

exist. In the case of the liquid/gas and solid/gas boundaries, the pressure vs temperature curve simply represents the dependence of the vapor pressure on the temperature. There is only one couple of pressure and temperature values where the three phases can exist in equilibrium conditions: it is defined the triple point (TP) and is an intrinsic property of the system, totally out of external control. The boundary between liquid and gas regions does not extend beyond the critical temperature (t_c) because above this temperature a liquid phase does not exist regardless of the pressure applied. It is noteworthy that the melting curve extends beyond the critical point so that, in principle, it is possible to achieve condensation of a supercritical phase into a solid one by imposing a sufficiently high pressure. In practice, this is not technically feasible for the major part of substances because of the extremely high pressures required. For example, the pressure required to solidify H_2O at its critical temperature is 14000 MPa [7]. However, in the case of low polarity small molecules this value is greatly reduced and in the case of carbon dioxide is "only" 570 MPa [8]. The supercritical region of many gases and low polarity liquids is easily accessible, *i.e.* $t_c < 100^\circ\text{C}$ and $p_c < 10$ MPa. Supercritical fluids are interesting media for chemical reactions because of their unique properties. The main property that makes them technically attractive is the fact that their densities change

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Table 1. magnitudes of some properties relative to liquid, supercritical and gas phases.

	Liquid	Sc	Gas
Density (gr, cm ⁻³)	1	0.1-0.5	10 ⁻³
Diffusivity (cm ² , s ⁻¹)	10 ⁻⁵	10 ⁻³	10 ⁻¹
Viscosity (Pa, s)	10 ⁻³	10 ⁻⁴ -10 ⁻⁵	10 ⁻⁵

with small variations in the applied pressure and temperature, particularly in the range $1 < t/t_c < 1.1$ and $1 < p/p_c < 2$. Thus, any density dependent property can be manipulated over a wide range. Many of the physical properties of scFs are intermediate between those of a liquid and a gas. Table 1 shows indicative values for some of these properties which are relevant for chemical reactions.

ScFs densities are close to those of liquids and much larger than those of gases so that their solvent power is rather pronounced. Furthermore, the solubility of many compounds can change dramatically under supercritical conditions. For example, naphthalene solubility in super critical carbon dioxide increases by a factor of ten by increasing the pressure from 12.0 to 25.0 MPa [9]. In supercritical water, organic compounds are much more soluble than in the liquid phase, while salts are less soluble [10] as a consequence of the decrease in the dielectric constant. Another example of enhanced solubility in scFs regards permanent gases. In fact, hydrogen, nitrogen, oxygen, etc. are only sparingly soluble in liquid organic solvents but they may be present in much higher concentrations in scFs. Whereas the density of a scF is comparable to that of a liquid, diffusivity and viscosity are more gas-like. Consequently, a diffusion controlled reaction in the liquid phase can be greatly enhanced when carried out under supercritical conditions, by taking advantage of higher diffusivity coefficients. However, not all the properties of scFs show values intermediate to those of gases and liquids. For instance, compressibility and heat capacity, in the proximity of the critical point, are higher than in liquids and gases.

Many low molecular weight inorganic and organic compounds are frequently used as scFs. When a given synthetic process is planned to be carried out in scFs, several parameters should be taken into account and, among these, the price of the starting material is obviously important. The data reported in Table 2 may give a rough idea about the price range of various substances that can be utilized at supercritical conditions.

Equipments may seriously weight upon costs. Specialized high pressure equipments are required for the

processes employing scFs and they may be quite expensive. These operational costs highly depend on the nature of the scF utilized and on its critical parameters. For instance, the operational costs of a plant utilizing highly corrosive scH₂O, which is characterized by a t_c of 374 °C and a p_c of 22.0 MPa, will be much higher than for those using scCO₂ which reaches the supercritical state at 31 °C and 7.4 MPa.

All scFs are compressed gas and therefore contain a great amount of energy, which in the case of equipment failure, can be suddenly released thus potentially causing damages to work environment and persons. Furthermore, intrinsic physical and chemical properties of scFs can present risks and hazards to the experimentalists. For instance, many acids, even weak such as H₂O under supercritical conditions, can corrode standard stainless steel equipment potentially causing catastrophic failures. Many other substances, such as acetylene [11], ethene [12], perfluoroethylene [13], hexane [14] etc., may cause explosive deflagrations at sufficiently high temperatures. Mixing oxygen or even much less efficient oxidizing substances as nitrous oxide [15] with significant amounts of organic compounds in supercritical conditions may lead to explosions.

Following these preliminary remarks, why should scFs be used as solvents to carry out chemical reactions? As a matter of fact, there are many advantages which are essentially based on the combination of the characteristics of the substances employed and those of the supercritical state. These advantages may be roughly divided into four general classes: environmental, health and safety, process, and chemical benefits. Environmental benefits are provided by those scFs that do not contribute to increase the VOC's level in the atmosphere, do not damage the ozone layer and do not exhibit relevant toxicity. Among the various substances that may be employed as scFs, carbon dioxide and water meet all these requirements. We are considering health and safety benefits related to the use of scFs when they are non cancerogenic, non toxic and non flammable. Again, carbon dioxide and water, the most popular substances used under supercritical conditions, present these qualifications. The benefits connected to the manipulations involved in a given process include: absence of solvent residues, facile products recovering by means of adjustable density and solvent power, low viscosity, high diffusion rates and low total operational costs. Once more, carbon dioxide, along with low molecular weight hydrocarbons, assures all these advantages. Finally, the chemical benefits can arise from the complete miscibility of reagents in the case of chemical reactions involving gases, thus implying the elimination of phase barriers. Furthermore, yields and selectivities of a

Table 2. Approximate costs for selected substances that can be utilized at supercritical conditions.

scF	Name	Cost (\$ per Kg)	scF	Name	Cost (\$ per Kg)
Xe	Xenon	4000	N ₂ O	Nitrous Oxide	50
Kr	Krypton	3000	CH ₃ OH	Methanol	18
C ₆ H ₁₄	<i>n</i> -Hexane	300	Ar	Argon	6
C ₂ H ₈ N ₂	Ethylendiamine	200	NH ₃	Ammonia	3
CF ₃ H	Fluoroform	125	CO ₂	Carbon Dioxide	3
C ₂ H ₆	Ethane	100	H ₂ O	Water	<0.0001

chemical reaction can be enhanced by easily tuning some of the main parameters of the scFs, such as the dielectric constant, the local density around solute molecules and the high diffusion rates.

On these premises, supercritical CO₂ could be indicated as a perfect medium for carrying out chemical reactions. Yet, it is to be mentioned that one major drawback of scCO₂ is due to its solvent power that is rather modest so that only a limited number of compounds show appreciable solubilities. At least three different strategies have been developed in order to improve solubilities of organics in compressed CO₂. The first one involves addition of an appropriate co-solvent; thus, relatively small aliquots of methanol or acetone (typically 3-5 % by weight) do not significantly change the mixture's critical properties but may greatly enhance the solvent's loading capacity [16]. In a somehow specular way, addition of CO₂ to an organic solvent with good solubility in CO₂ allows to expand the liquid while decreasing the solubilities of dissolved organics (as compared to the pure liquid) and increasing miscibility of gases. These mixed media allow to replace most of the liquid solvents (typically more than 75% by volume) with CO₂ while combining the advantages of traditional solvents with those of CO₂ [17]. The third technique employed for improving solubility of organics in compressed CO₂ consists in modifying the substrates of interest by attaching CO₂-philic subunits. Thus, it has been shown that perfluoro alkyl [18], perfluoroether [19], silyl [20] groups, and less expensive poly(ether-carbonates) [21] provide excellent CO₂-philicity and therefore improve significantly the solubilities in CO₂. These CO₂-philic moieties can be exploited in the synthesis of amphiphilic molecules specifically designed for acting as surfactants in supercritical CO₂ [22-24]. These compounds can form water/CO₂ micro- and macro-emulsions, which offer several opportunities to perform in supercritical CO₂ aqueous chemistry such as reactions involving enzymes and proteins.

Besides the general potential advantages mentioned above, supercritical CO₂, at least in principle, is ideally suited as a reaction medium for oxidation reactions and applications in both homogeneous and heterogeneous catalytic processes. In fact, CO₂ being fully oxidized, is stable under any oxidative conditions and does not lead to any solvent by-products. Moreover, employing oxygen as terminal oxidant, one may take advantage of its complete miscibility in the supercritical phase and from the liquid-gas barrier elimination. Finally, flammability and explosive conditions are much more reduced in supercritical CO₂ than in organic gas phase, thus minimizing safety concerns when mixing pure organic material with oxygen [25]. As a matter of fact, the majority of the reports concerning oxidations under supercritical conditions deal with unselective oxidations by molecular oxygen promoted by both homogeneous [26] and heterogeneous [27] catalysts. Here, with the term "unselective" we refer to those oxidative processes in which molecular oxygen reacts with a radical generated by the action of a catalyst thus leading to the typical products of a chain process usually known as auto-oxidation. Oxidative processes in supercritical CO₂, in which the ultimate oxidizing agent is an organic or inorganic

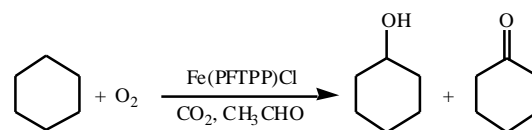
derivative capable of carrying out selective oxidations, are much less explored.

Reviews on supercritical fluids are available and some of the more significant ones mentioned here. Savage reviewed work from 1985 to 1994 [28]; this review provides an excellent introduction to the field and includes a section regarding oxidations in scFs. More recently, Walther published a review, also comprising a short section on catalytic oxidations in scCO₂, mainly addressed to the chemistry of compressed carbon dioxide coordinated to metal centers, and its activation and conversion into organic compounds [29]. Subramaniam and Busch published a review on catalytic oxidation in media containing carbon dioxide, covering the pertinent literature until 2000 [17]; this review is narrowly focused on oxidation performed in CO₂ expanded phases and may be considered complementary to the present review. Additional recent reviews include brief overviews on reactions in supercritical carbon dioxide that highlight the work of Leitner's [30] and Beckman's [31] groups.

In this review, we tried to cover the papers from 1990 to early 2004, dealing with oxidative processes carried on in supercritical carbon dioxide involving selective heterolytic oxidation chemistry or even unselective homolytic chemistry generating selective oxidants *in situ*. For clarity's sake, we divided the papers reviewed into three sections depending on the terminal oxidant employed.

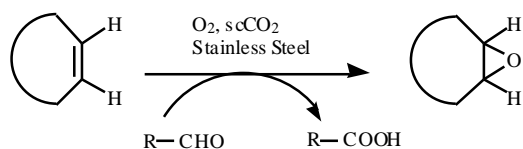
2. MOLECULAR OXYGEN AS TERMINAL OXIDANT

In 1997, Koda reported the oxidation of cyclohexane by dioxygen (1.0 MPa) in the presence of Iron(III) 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin (Fe(PFTPP)Cl) and acetaldehyde in compressed CO₂ at total pressures ranging from 1 to 18 MPa and temperatures from 27 to 70 °C [32]. Under these experimental conditions, cyclohexane is oxidized to cyclohexanol and cyclohexanone with yields up to 5% and TON of 100 (Scheme 1). Since the ratio cyclohexanone/cyclohexanol increases with the reaction time, it has been suggested that at least part of the ketone is produced via cyclohexanol oxidation.



Scheme 1.

Although no further experimental evidence was given, the process probably involves several steps. The first one implies the formation of peroxyacetic acid through the aldehyde auto-oxidation, probably catalyzed by the iron center. In a subsequent step, the peroxyacetic acid leads to an oxometalloporphyrin derivatives which can either acts as a P-450 enzyme mimic, thus yielding cyclohexanol, or as a peroxidase mimic, thus yielding cyclohexanone. The authors reported that the system changes from homogeneous to heterogeneous by lowering the temperature below 70 °C. Interestingly, the maximum hydrocarbon conversion was obtained, depending on the reaction temperature, in the

**Scheme 2.**

proximity of the critical pressure of CO_2 . This is an example of a procedure in which a non selective process, namely the aldehyde auto-oxidation, is exploited in order to produce *in situ* a terminal oxidant, which in turn, gives rise to a selective catalytic oxidation, namely hydrocarbon hydroxylation promoted by metalloporphyrin.

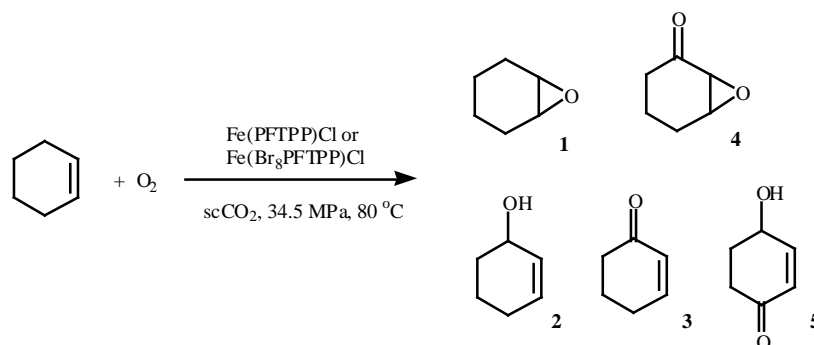
Later on, Leitner showed that selective alkenes epoxidation may be achieved in scCO_2 by oxidation with dioxygen in the presence of an aldehyde as sacrificial co-oxidant and in the absence of added catalysts (Scheme 2) [33].

The results reported showed that the oxidation proceeds smoothly in the case of cyclic olefins: cyclooctene and

oxidation in this medium and the highly effective conversions. Indeed, the results reported show that the oxidation proceeds even in toluene in the presence of added steel shavings, although with a lower efficiency than in scCO_2 . In conclusion, the epoxidation in scCO_2 is promoted by the stainless steel of the reactor wall, which apparently favors the formation of acylperoxy radicals and, in a further step, of peroxyacids that are responsible for the olefin epoxidation.

Tumas published a related paper in 1999 [34]. In this case, cyclohexene was oxidized by oxygen (0.7 MPa) in the presence of halogenated iron porphyrins such as Iron(III) 5,10,15,20-tetrakis(pentafluorophenyl)porphyrin ($\text{Fe}(\text{PFTPP})\text{Cl}$) and Iron(III) -octabromo-5,10,15,20-tetrakis(pentafluorophenyl)porphyrin ($\text{Fe}(\text{Br}_8\text{PFTPP})\text{Cl}$) in scCO_2 at 80 °C and 34.5 MPa, in the absence of any co-reductant. The oxidation yields a mixture of products: cyclohexene oxide **1**, 2-cyclohexen-1-ol **2**, 2-cyclohexen-1-one **3**, 7-oxa-bicyclo[4.1.0]heptan-2-one **4** and 4-hydroxy-2-cyclohexen-1-one **5**, (Scheme 3).

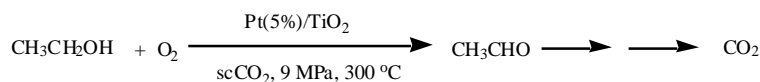
The aerobic oxidation of alkanes and alkenes catalyzed by iron porphyrins in liquid organic solvents has been

**Scheme 3.**

cyclohexene are converted nearly quantitatively into the corresponding epoxides with selectivities approaching 100%. In the case of linear olefins, the epoxidation is nearly quantitative in the case of internal double bond and, in the case of *trans*-3-hexene, *trans*-3-epoxyhexane is the only stereoisomer observed. Lower conversions and selectivities are found in the case of terminal olefins and α,β -unsaturated ketones. However, depending on the substrate, even vinylic oxidation is observed. For example, in the case of propene, under standard experimental conditions, $T=55 \text{ }^\circ\text{C}$, $P=19.0 \text{ MPa}$, the conversion reaches 73% and the major product is acetone with a 67% selectivity. The molecular structure of the aldehyde utilized as co-oxidant has little influence on the epoxidation. Two equivalents of aldehyde over the olefin are sufficient to achieve quantitative conversion, but using only one equivalent of aldehyde, only traces of epoxide are formed. The comparison of the system performances in scCO_2 with those in conventional organic solvents, showed that the oxidation proceeds efficiently in methylene chloride but does not in toluene. Since chlorinated solvents are known to initiate radical auto-oxidation processes, the discrepancy between the results obtained in toluene and scCO_2 can be accounted for. Moreover, Leitner observed that the stainless steel of the reactor plays a crucial role in promoting the

studied in detail and it has been shown to proceed through the decomposition of alkyl hydroperoxides formed *via* hydrocarbons auto-oxidation [35]. This process leads to the formation of alkoxy and alkyl peroxy radicals, which propagate and terminate in free radical reactions, and in the case of cyclohexene, forming allylic oxidation products such as **2** and **3**. This mechanism however does not explain the formation of epoxides **1** and **4**, which may be formed through alternative pathways. Among these, it is reasonable to assume that either the alkyl hydroperoxide reacts with the iron porphyrin to form an iron-oxo-derivatives which, in a subsequent step, epoxidizes the olefin or that the olefin is directly epoxidized by the alkyl hydroperoxide in a reaction catalyzed by the iron porphyrin acting as Lewis acid. The authors chosen cyclohexene as a model substrate because both allylic oxidation and epoxidations are possible and the ratio between radical-derived products and epoxides formed can be taken as a rough measure of the degree of the process selectivity. The results reported clearly demonstrate that supercritical CO_2 may replace traditional liquid organic solvents in the aerobic oxidation of cyclohexene catalyzed by iron porphyrins, with acceptable turnover numbers. For instance, under the same experimental conditions using $\text{Fe}(\text{PFTPP})\text{Cl}$ as catalyst, the turnover numbers for the

process in benzene, methylene chloride and scCO_2 are 1520, 2170 and 580 h^{-1} , respectively. Changes in the process selectivity on moving from liquid solvents to scCO_2 were also observed. Thus, epoxides yields increase, using both the catalysts tested, in reactions performed at $80 \text{ }^\circ\text{C}$ with 3.4 MPa of air; in these conditions cyclohexene oxide **1** constitutes up to 34% of the total products. Furthermore, the process selectivity in scCO_2 can be easily tuned by relatively small changes in temperature. However, according to the authors, it is not clear if these changes in activity and selectivity are due to the reaction medium or simply arise from pressure and temperature effects. In particular, the selectivity enhancement observed in scCO_2 requires that both the reactions involved, namely peroxide decomposition and porphyrin catalyzed epoxidation, are accommodated into a single mechanistic picture. The higher activity registered in



Scheme 4.

liquid solvents (as suggested by TONs) may indicate that, in scCO_2 as reaction medium, the radical chain propagation is disfavored whereas the chain termination is favored. Moreover, the higher amount of epoxides observed in scCO_2 should be related to a major extent of a selective epoxidation carried on by an alkyl hydroperoxide and promoted by the iron porphyrin. The mechanism of these catalyzed epoxidation probably involves the metal porphyrin acting as a Lewis acid, thus enhancing by coordination the electrophilic nature of the oxidant alkylhydroperoxide. In fact, following the authors, a catalytic pathway *via* formation of a high-valent ferryl intermediate should be very unlikely in an apolar and aprotic reaction medium such as scCO_2 .

An analogous study by Shale-Demessiè and co-workers describes the oxidation of cyclohexene by molecular oxygen (0.27-20 MPa) in scCO_2 (20 MPa) at temperatures ranging from 60 to $150 \text{ }^\circ\text{C}$, in the presence of three different heterogeneous catalysts, *i.e.* $\text{cis-}[\text{Fe}(\text{dmp})_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2$ (dmp =2,9-dimethyl-1,10-phenanthroline), 0.5% Pt/Alumina, 0.5% Pd/Alumina [36]. The authors suggest a reaction pathway in which the metal centre can be oxidized by molecular oxygen, or even by hydrogen peroxide, to form an oxo derivatives, which in a second step, oxidizes cyclohexene affording the same products observed by Tumas. Assuming that this is the case, the terminal oxidant molecular oxygen can directly regenerate the actual oxidizing species, namely the metal oxo derivatives, without the need of a peroxide intermediate, through the olefin auto-oxidation. However, independently from the catalyst utilized, cyclohexene oxide is always present in trace amounts and this would suggest that the formation of metal-oxo intermediates capable to transfer oxygen to the olefin is rather unlikely, at least in the case of the iron complex. On the contrary, oxidation over Pd and Pt catalysts yields a mixture of oxygenated products, as those shown in Scheme 3, in addition to products such as benzene and phenol arising from dehydrogenation, according to the features of the platinum group oxides.

Akgerman was probably the first to report a study on selective partial alcohol oxidation with a solid catalyst in scCO_2 . In particular, he studied the catalytic oxidation of ethanol and acetaldehyde over a 4.5% Pt/TiO₂ catalyst at temperatures ranging from 150 to $300 \text{ }^\circ\text{C}$ and at total pressure of 9 MPa, with a 5:1 molar ratio of oxygen to ethanol in the feed [37]. The authors observed that acetaldehyde and trace amount of CO were the only partial oxidation products during the oxidation of alcohol. Acetaldehyde yields are as high as 30% under the experimental conditions employed. Moreover, the aldehyde yield, at constant temperature, increases with increasing time up to a maximum value and then decreases, thus suggesting that it is a primary product which is further oxidized to CO₂ (Scheme 4).

On the basis of the data collected, a parallel and consecutive reaction mechanism was postulated for ethanol oxidation, whereas dissociative adsorption of acetaldehyde on the catalyst surface was indicated for the aldehyde oxidation. A model developed on a detailed reaction mechanism, which assumes a Langmuir-Hinshelwood type mechanism for direct oxidation of ethanol to CO₂ and dehydrogenation of an alkoxy intermediate as the rate controlling step for oxidation of ethanol to acetaldehyde, allows a precise fit of the experimental data.

Willey devoted his attention to an important commercial process, *i.e.* the methanol oxidation to formaldehyde with oxygen over an iron oxide-molybdenum catalyst, in scCO_2 [38,39]. He extended the study to various silica aerogels catalysts containing iron oxide ranging from 1 to 20% (wt) and even to pure iron oxide aerogel. The partial methanol oxidation affords dimethylether, methylformate and formaldehyde, at temperatures between 200 and $300 \text{ }^\circ\text{C}$, in the presence of 1.64 molar equivalent of oxygen and a total pressure of 9 MPa of CO₂. The process selectivity is strongly influenced by the catalyst nature: methanol oxidation using a classic 20% wt Fe₂O₃-MoO₃ aerogel catalyst in scCO_2 mainly affords formaldehyde together with minor amount of dimethylether. Conversely, employing 1% (wt) Fe₂O₃ aerogels, the methanol conversion levels off to 80% at temperatures exceeding $275 \text{ }^\circ\text{C}$ and the major product detected is methylformate with a yield close to 60%. Increasing the percent of Fe₂O₃ relative to the silica support results in an increased production of dimethylether. This trend is confirmed by the observation that in the presence of pure Fe₂O₃ aerogels, the principal product detected is dimethylether at temperatures near about $250 \text{ }^\circ\text{C}$, as shown in Fig. (2).

The dependence of dimethylether formation on the percent of iron oxide suggests that Fe³⁺ acts as a Lewis acid site and promotes methanol dehydration. On the other hand, since methylformate is observed in the presence of pure silica, the author concluded that its formation is

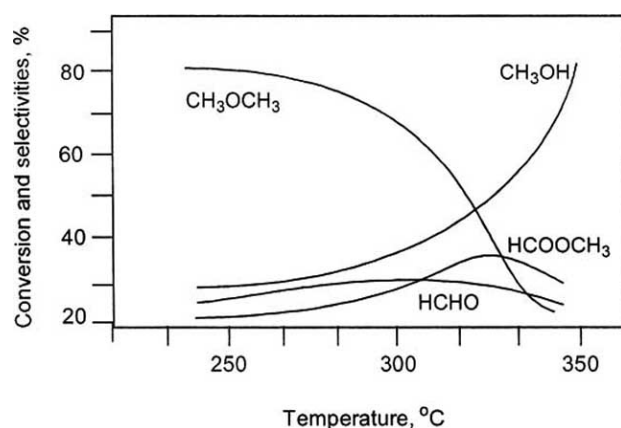
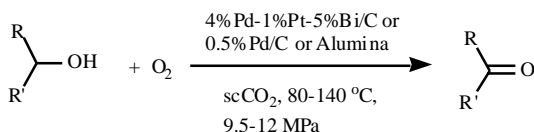


Fig. (2). Oxidation of methanol by oxygen over pure Fe_2O_3 aerogel as a function of temperature.

associated to the activity of silanol sites present on the catalyst support.

In order to overcome some restrictions regarding oxidation of water-insoluble alcohols by oxygen in the presence of noble metal catalysts in organic solvents, namely slow reaction rates and explosion risks, Baiker examined the process in scCO_2 in the presence of a 4%Pd-1%Pt-5%Bi/C [40] and a 0.5%Pd/Alumina or amorphous carbon catalysts [41] (Scheme 5).



R, R' = Phenyl, Alkyl, H

Scheme 5.

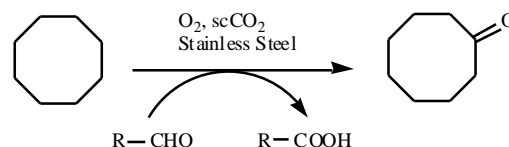
A secondary alkyl alcohol, such as 2-octanol, was converted to octan-2-one with selectivities higher than 99.5% even at relatively elevated substrate conversions (70%). Interestingly, the yield of octan-2-one dependence on oxygen concentration shows a bell shaped curve. The authors attribute the drop after the maximum yield, reached at a molar ratio substrate/ O_2 close to unity, to the so-called over-oxidation of the catalyst, a phenomenon commonly observed with platinum metal catalysts [42]. An additional effect of the increasing oxygen concentration, as pointed out by the authors, is a reduced solubility of reactant and product. A secondary benzyl alcohol as 1-phenylethanol reacts faster than 2-octanol, leading to almost quantitative conversion to the corresponding ketone and with comparable high selectivities. On the contrary, the oxidation of primary alkyl alcohols is fast but non selective. For example, octan-1-ol affords a mixture of octanal, octanoic acid, octyloctanoate and traces of octen-2-ol and dioctylether. Relatively good selectivities could be obtained at lower temperatures (60-80 °C) and with higher contact times. The aldehyde yields however never exceed 20%. Remarkably higher selectivities have been obtained in the oxidation of primary benzyl or allyl alcohols. In particular, the highest aldehyde yield (78%) with the highest selectivity (98%) was obtained in the

oxidation of cinnamyl alcohol, an α,β -unsaturated alkyaromatic alcohol.

In a following related paper, Grunwaldt and Baiker reported structural informations on an alumina supported palladium catalyst obtained by X-ray adsorption spectroscopy while monitoring simultaneously the performances of the catalyst during aerobic oxidation of benzyl alcohol in scCO_2 at 15 MPa and 80°C [43]. The reduction of the catalyst by benzyl alcohol could be monitored by the analysis of the near-edge region of the Pd K-edge. It was found that, under the operating conditions, palladium is mainly in the metallic state. Partial re-oxidation was observed when oxygen was fed in scCO_2 in the absence of alcohol. As observed in octan-2-ol oxidation [40], the rate of alcohol conversion goes through a maximum when the oxygen concentration is increased. It was observed that under the maximum rate conditions part of the palladium is in the oxidized state (up to 10%). Moreover, upon further increase of the oxygen concentration, the activity decreases because of the formation of palladium oxide on the catalyst surface. The reaction rate in scCO_2 is markedly higher than that observed for the corresponding liquid-phase oxidation.

Almost contemporaneous of Baiker's paper, an article by Tsang reported a study on alcohols oxidation by oxygen catalyzed by Pd in scCO_2 drawing similar conclusions [44]. In Tsang's case the model substrate was 9-anthracene methanol for scCO_2 solubility reasons. The results, which distinguish the two previously cited works, are the following: Tsang observed that the oxidation of the model alcohol over a 5%Pt/C catalyst increases rapidly with increasing CO_2 pressure, probably reflecting a solubility effect on the substrate. However, at pressures higher than 10 MPa, the alcohol conversion levels off or even slightly decreases and this was explained as the outcome of a kind of pressure dependent poisoning effect. In particular, high CO_2 pressures hamper the diffusion of water that is formed as a by-product, thus creating a water layer on the catalyst surface, which in turn, reduces the catalyst activity. According to this hypothesis, significantly higher conversions at the same pressure are expected when the catalyst is modified by 1% Teflon as the strongly hydrophobic catalyst may spill off the water, thus preventing the catalyst poisoning. As a matter of fact, over this Teflon modified catalyst the model substrate and some other substituted benzyl alcohols give conversions ranging from 63 and 96%, at temperatures increasing from 60 to 100 °C and pressures from 10 and 15 MPa, with 92-99% selectivities. Worth of note is the fact that high selectivity for the corresponding aldehyde (>92%) can still be achieved when decan-1-ol is the substrate, provided that the Tefloned catalyst is utilized.

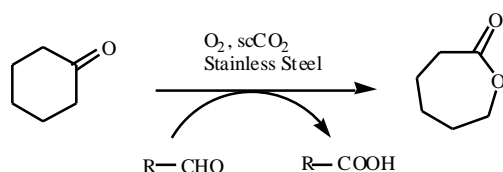
Leitner, after reporting the steel promoted epoxidation of olefins under Mukaiyama-type reaction conditions in scCO_2 [33], described the application of a similar methodology for the oxidation of alkanes (Scheme 6) [45].



Scheme 6.

Cyclooctane was chosen as model substrate because all reaction positions are identical and the main oxidation product, namely cyclooctanone, was proven to be inert towards Baeyer-Villiger oxidation under the experimental conditions adopted. Cyclooctane conversions reach up to 37%, depending on temperature, supercritical phase density and reaction time. The yield of cyclooctanone, at 70 °C and 0.18 gr/mL density of CO₂, may reach 22% with a selectivity of 60%. Other typical by-products detected were cyclooctanol, cyclooctan-1,4-dione, 9-oxabicyclo[3.3.1]nonan-1-ol, cyclooctyl hydroperoxide and adipic acid. The best cyclooctanone yield observed is significantly higher than that reported for cyclohexane oxidation in a related system in scCO₂: only 3% cyclohexanone was obtained in the presence of an iron porphyrin catalyst at 70°C (see reference 32). The occurrence of a free radical pathway is supported by two observations. First, the formation of cyclooctane-1,4-dione as side product is probably ascribed to the intramolecular attack of a cyclooctyl peroxy radical intermediate on the favored 4-position. Secondly, the oxidation of adamantane under similar conditions affords a 1-adamantol/2-adamantone ratio of 4.5:1, thus suggesting the involvement of a radical rather than a metaloxo pathway [46]. Even in the present system, the radical chain is believed to be initiated by the steel promoted formation of the peroxy acyl radical. Subsequently, H-abstraction from cyclooctane followed by addition of molecular oxygen leads to the formation of the cyclooctyl peroxy radical, which can either react with another cyclooctyl peroxy radical or with a peroxy acyl radical. In the first case, the products are cyclooctanol and cyclooctanone whereas in the second are cyclooctanone and peracetic acid. The authors favor the latter pathway on the basis of the high ketone to alcohol ratio observed.

Although under the experimental conditions above mentioned cyclooctanone and even cycloheptanone did not undergo to Baeyer-Villiger oxidation, Leitner showed in a following paper that shorter ring cycloketones and some acyclic ketones undergo ring expansion giving the corresponding lactones or esters (Scheme 7) [47].

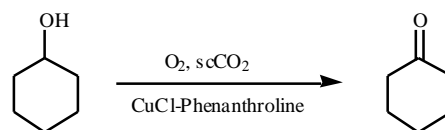


Scheme 7.

Among the various factors potentially affecting the oxidative process, the kind and the amount of aldehyde utilized as co-reductant has the major impact on the reaction course. Various commercially available aldehydes were tested and benzaldehyde gave the best result leading to 75% cyclohexanone conversion under standard conditions. Moreover, high substrate conversions required an aldehyde/substrate ratio of 3:1. Conversely, the partial oxygen pressure does not affect the oxidation significantly in the range 0.5-3 MPa. Substituted small ring cycloketones, such as various 3-substituted cyclobutanone, cyclopentanone and cyclohexanone react smoothly providing the

corresponding lactones with substrate conversions ranging from 70 to 100%. Also some bicyclic ketones were transformed readily to lactones, following the expected regioselectivity, while acyclic substrates such as 3-phenylbutan-2-one and *p*-methoxybenzophenone underwent oxidation too, the higher conversion (79%) being obtained with the latter substrate. Noteworthy is the outcome of the system efficiency *vis a vis* that of traditional liquid organic solvents: in the presence of steel shavings, in each case needed to start the radical process leading to the peroxyacid, the cyclohexanone conversions were: 44% in toluene, 25% in ethyl acetate and 27% in dichloromethane. Again, these results demonstrate that CO₂ is a suitable and green replacement for organic solvents and provides significant advantages in terms of efficiency in the oxidation process.

Han reported a study on the aerobic oxidation of cyclohexanol to cyclohexanone in compressed CO₂ in the presence of CuCl phenanthroline as catalyst [48]. In particular, he studied the effect of phase behavior and of small amount of co-solvents (toluene and fluorobenzene) on the conversion and selectivity of the process (Scheme 8).



Scheme 8.

In order to study the effect of phase behavior of the reaction system on the aerobic oxidation of cyclohexanol, the reaction was carried out in a two-phase region and a single-phase region by controlling the temperature and the density. The authors chosen different densities, named A, B, C, as reported in Table 3. Condition A was in the single phase region, B was close to the phase boundary and C was in the two phase region.

Table 3. Effect of the apparent density on the cyclohexanol conversion and cyclohexanone selectivity at 60 °C and after 6 hours.

Point	Density (g/mL)	Conversion, %	Selectivity %
A	0.77	7.51	98.9
B	0.71	8.20	97.7
C	0.63	10.8	94.0

From the data shown in Table 3, the alcohol conversion in the two-phase region (C) is the highest whereas the selectivity is relatively low. This outcome could be related to a longer contact times between cyclohexanone and catalyst because of the smaller diffusion coefficients in the liquid phase. According to this hypothesis, the selectivity in the single phase system (A) is significantly higher. The main by-product is hexandioic acid. The oxidation reaction was also conducted in various organic solvents and in the absence of solvent. Table 4 shows some pertinent results.

Data of Table 4 show that cyclohexanol oxidation rates in organic solvents are larger than that in scCO₂. The authors

Table 4. Effect of the solvent on the cyclohexanol conversion and cyclohexanone selectivity at 60 °C and after 6 hours.

Reaction medium	Conversion, %	Selectivity %
None	19.8	70.6
Toluene	33.4	77.9
Fluorobenzene	26.5	75.2
scCO ₂ ^a	7.51	98.9
scCO ₂ + Toluene ^{a,b}	18.6	97.3
scCO ₂ + Fluorobenzene ^{a,b}	21.7	99.0

a: apparent density = 0.77 g/mL

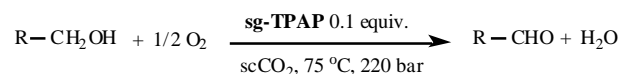
b: amount of cosolvent: 0.5% mol

ascribe this outcome to the fact that the interactions between the reactants and the organic solvents are stronger than those between reactants and CO₂, due to the lower dielectric constant of CO₂. However, the selectivities in the desired product in scCO₂ are much higher than those observed in organic solvents or even in the absence of solvent. The last two entries in Table 4 show that the cyclohexanol conversions are effectively improved by adding a small amount of co-solvents without impairing product selectivity. It is interesting to note that the reaction rate in toluene is higher than that in fluorobenzene, while fluorobenzene is a more effective co-solvent in increasing the reaction rate in scCO₂. In conclusion, the results demonstrate that the selectivity in scCO₂ is in each case higher and therefore it is advantageous to carry on the reaction in such non conventional reaction medium.

In order to further investigate the range of applicability of Pt catalysts for alcohols oxidation in scCO₂, Gläser considered low reaction temperatures, closer to the critical point of CO₂ (T_c=31,1 °C, P_c=7.4 MPa), to fully utilize the strong pressure dependence of the fluid properties in the near critical region [49]. The oxidative dehydrogenation of propan-2-ol and propan-1-ol over 5%Pt/ carbon and 5%Pt/silica catalysts in the presence of dioxygen was chosen as model reaction. In all reactions of propan-2-ol with oxygen over the 5%Pt/C catalyst at 40 °C and 16.5 MPa, complete conversion of the substrate to acetone is achieved. On increasing the oxygen mole fraction, longer time was needed for complete conversion and for the reaction to start. The reason for this delay is presumably the already mentioned catalyst "over-oxidation". Assays of catalyst recycling showed that the relative amount of propan-2-ol converted decreases after each new addition of reactants. Moreover, the conversions proceed at a lower rate, thus indicating that the noble metal catalyst undergoes deactivation even under supercritical conditions. The oxidation of propan-1-ol proceeds with a significantly lower rate than that of propan-2-ol and catalyst deactivation is apparently at the origin of the low conversion values. However, it is of interest the fact that a conversion of propan-1-ol larger than 22% must be reached before that the formation of propanoic acid is observed, thus lowering the aldehyde selectivity. Hence, selective oxidation of primary alcohols in scCO₂ appears also feasible in a continuous reaction mode, providing that conversion or residence time is kept at a sufficiently low level. Platinum catalysts supported on silica with different porosity, *i.e.* a macro porous silica

gel, a mesoporous MCM-41-type material and the micro porous silicalite-1, were also tested in the propan-2-ol oxidation with oxygen in scCO₂. With all the three catalysts, the reactions occurred at a lower rate than with the carbon-supported analog and substrate conversions were incomplete. However, it is remarkable that Pt/MCM-41 and Pt/silicalite-1 did not show any activity in the aqueous phase, thus confirming the potentialities of scCO₂ as reaction medium for catalyzed oxidations.

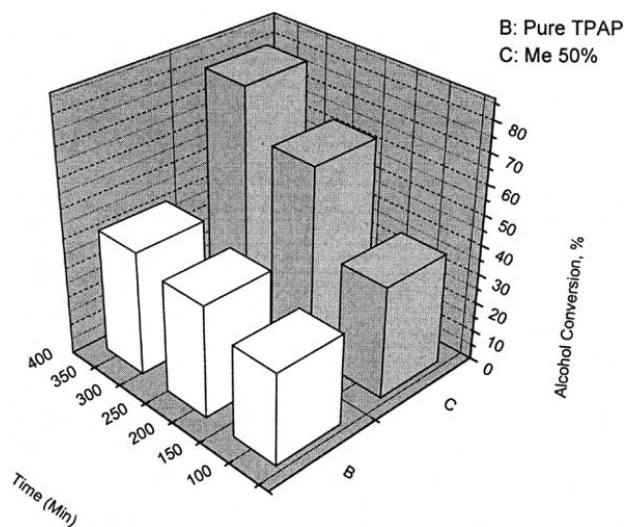
Pagliari recently showed that silica gels organically modified and doped with the ruthenium derivative tetra-*n*-propylammonium perruthenate (TPAP) are leach-proof, selective catalysts for the aerobic oxidation of alcohols to carbonyl compounds with dioxygen at low pressure in compressed carbon dioxide (Scheme 9) [50].



R=Alkyl, Aryl, Alkenyl

Scheme 9.

The authors prepared several sol-gel entrapped TPAP catalysts by varying the methyltrimethoxysilane (MTMS) and tetramethylorthosilicate (TMOS) ratio, in order to study the effect of surface polarity and textural properties on the reactivity in the non polar CO₂ reaction medium. The comparison between the reactivity of unsupported TPAP and that of TPAP encapsulated in the representative 50% methylated sol-gel ormosils in the aerobic oxidation of benzyl alcohol, under the experimental conditions of Scheme 9, shows that sol-gel encapsulation enhances its activity (see Fig. (3)).

**Fig. (3).** Conversions in the aerial oxidation of benzyl alcohol in scCO₂ over unsupported TPAP (white) and entrapped in a gel 50% methylated (grey).

Interestingly, in the case of TPAP catalyzed oxidations terminal alcohols are usually more reactive than the

Table 5. Aerobic oxidation of alcohols mediated by the ormosil 75% methylated doped with TPAP.

Alcohol	Product	Conversion (%) at 4h	TOF (h ⁻¹)
Benzyl alcohol	Benzaldehyde	60	1.5
Octan-1-ol	Octylaldehyde	30	0.8
9-decen-1-ol	9-decenal	8	0.2
4-hexen-1-ol	4-hexenal	4	0.1

Table 6. Activity^[a] and textural properties of sol-gel ormosils doped with TPAP.

Entry	Catalyst	k _{cat} ·x10 ^{3y} (m of ¹ m in ⁻¹)	SSA (m ² g ⁻¹)	PSV (cm ³ g ⁻¹)	Loading (mmol g ⁻¹)
1	C3F-10	4.90	691	0.53	0.046
2	C3F-25	2.14	657	0.42	0.032
3	C3F-50	2.90	458	0.31	0.027
4	C8F-10	1.82	308	0.70	0.028
5	C8F-25	2.07	182	0.59	0.022
6	C8F-50*	1.42	12	0.05	0.012

^[a] Reaction conditions: 0.048 mmol benzyl alcohol, 10 mol% entrapped TPAP, V=10 mL, P=22 MPa, T=75 °C, O₂ (1 atm.); *Xerogel obtained using TBAF as condensation catalyst.

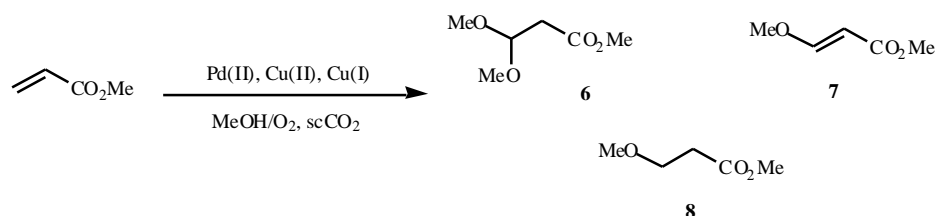
secondary ones, at variance with what is observed in aerobic alcohols oxidation promoted by Pt and Pd. The study of the catalytic activities as function of the methylation degree and synthesis protocol, showed that the best performing catalysts require both, a high degree of surface hydrophobicity and high amounts of water and co-solvent in the sol-gel polycondensation process employed for the catalyst preparation. Results reported in Table 5 show the generality of the method also in the conversion of less easily oxidizable aliphatic and alkenyl alcohols.

Notably, the gel proved to be leach-proof and selective, with no aldehyde over-oxidation or olefinic double bond oxidation. Lower activities are observed but the reaction proceeds for each substrate at the same extent as observed in toluene. The activities of these catalysts, under the batch experimental conditions applied, is still lower than in the liquid phase. However, the interpretation of the structure-activity relationship observed provides useful guidelines for the development of efficient heterogeneous catalysts for oxidative dehydrogenations, towards the requirements for the industrial application as far as catalyst versatility and process sustainability are concerned.

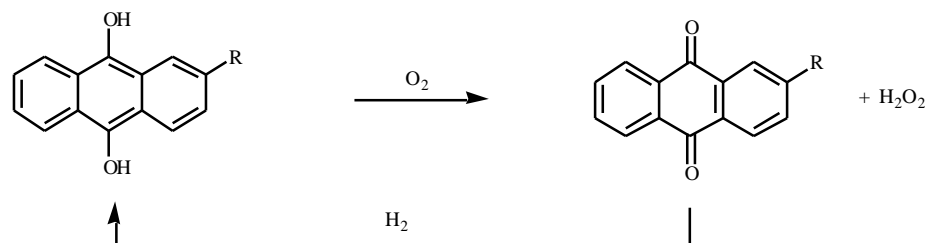
In a following paper Pagliaro extended the investigations concerning the catalytic activity to hybrid organic-inorganic fluorinated silica glasses doped with TPAP [51]. Moderate silica fluorination (10%) by short-chain fluoroalkyl-containing monomers in the sol-gel polycondensation with TMOS affords highly active catalysts which, in scCO₂ at 75 °C and 22.0 MPa, selectively dehydrogenate alcohols with oxygen as primary oxidant. Both the activity and the stability of the fluorinated materials vary with the degree of fluorination and the nature of the fluoroalkyl residue attached to the silica polymeric network. Results reported in Table 6 show that, somehow unexpectedly, fluorination *per se* does not enhance the reactivity of the silica gels and that the materials bearing the shorter fluoropropyl chain (C3F)

are generally more reactive than those modified with the fluorooctyl chain of batch (C8F).

Thus, apparently, increasing fluorination diminishes both surface area and porosity and while the most active catalyst (C3F-10, entry 1) has the biggest pore volume and surface area it also has surprisingly, the lowest degree of fluorination (10%); further fluorination up to 25% (C3F-25, entry 2) more than halves the catalytic activity which only slightly increases with further fluorination (C3F-50, entry 3). On the other hand, all the modified silica gels bearing the perfluorooctyl chain (C8-F) are unstable and during reaction leach a yellow fluorinated compound which results from the hydrolyzed fluorinated carbon chain. The highest activity is observed by using the 25% methylated silica gel (C8F-25) and lowest using the most hydrophobic gel (C8F-50). These results offer the first insight in the behavior of sol-gel fluorinated oxides in aerobic catalysis and provide new valuable information. The enhanced reactivity of the short-chained 10% fluoroalkylated doped gel C3F-10 may be ascribed to the negligible viscosity of the supercritical CO₂ and to the enhanced diffusivity of the dissolved substrate and product molecules through the vast accessible porosity (0.53 cm³ g⁻¹) of the gel that facilitates the transfer of molecules to and from the internal catalyst surface. Partial burying of the hydrophobic TPAP ion pair in the bulk of the resulting silica xerogel makes it inaccessible for catalysis. This may be prevented by the high amount of methanol used in the materials sol-gel synthesis, which disrupts the micellar aggregates typical of the early stages of the sol-gel process. Within such aggregates, the slowly generated R-Si(OH)₃ monomers tend to arrange themselves with the polar -Si(OH)₃ groups at the forefront of the growing sol-gel material and with the hydrophobic non-polymerizable R residue protruding from the interfacial, strongly hydrogen bonding, solvent (water/methanol). This hypothesis would explain the higher reactivities of catalysts of batch C3F with



Scheme 10.



Scheme 11.

lower fluorination. Back to the point, the best performing catalysts require a modest degree of fluorination of the silanes which ensures both a high surface hydrophobicity and an open micro porous network in which the catalytic oxidant is accessible to the reactants.

Oxidation reactions in scCO₂ other than alcohols dehydrogenation are quite rare. One example is the oxidation of terminal olefins bearing electron-withdrawing group upon treatment with alcohols and catalyzed by Pd(II) affording acetals (Scheme 10), reported by Jiang [52].

The author reported that Pd(II)-catalyzed oxidation of methylacrylate can be successfully performed in scCO₂ to give the dimethylacetal **6** as the major product when an excess of methanol is used. It is suggested that the alcohol excess is necessary in order to promote partial solution of the inorganic catalyst in scCO₂. PdCl₂ and PdCl₂(MeCN)₂ were also tested as catalyst and CuCl and CuCl₂ as co-catalysts. The best results *i.e.* 99.7% substrate conversion and 93.5% selectivity for **6** were obtained with PdCl₂ and CuCl. Whereas the oxidation of methylacrylate to acetal was reported to occur at 50 °C in DME [53], the reaction goes to completion at much lower temperatures in scCO₂. Very good conversions (usually >90%) and selectivities for **6** (always better than 80%) were obtained at 40 °C and even at 27 °C, at which temperature CO₂ is liquid, the conversions remain good although the amount of by-products **7** and **8** increases slightly. The pressures of carbon dioxide and oxygen have a great effect on selectivity. The best results were obtained at CO₂ pressures ranging between 12 and 13 MPa. As the pressure of CO₂ is reduced, both conversion and selectivity decrease. Moreover, lower oxygen pressure (0.1 MPa) led to satisfactory conversion with a selectivity for **6** never exceeding 93.4%. The best selectivity (>96%) was obtained as the oxygen pressure was increased to 1.0 MPa. In short, the oxidation of methyl acrylate leads acetal with large conversion and selectivity at relatively low temperatures, when carbon dioxide is used as the reaction medium and in the absence of the promoter HMPA.

In a series of important papers, Beckman addressed the problem of hydrogen oxidation to hydrogen peroxide in

compressed CO₂. Hydrogen peroxide is still currently produced via the sequential hydrogenation and oxidation of 2-alkylanthraquinone (Scheme 11).

The 2-alkyl anthraquinone is dissolved in a mixture of an aromatic and a long-chain alcohol (the so called “working solution”) and then is reduced over a palladium catalyst; the resulting anthrahydroquinone is oxidized by air in a different reactor, leading to hydrogen peroxide and regenerating the anthraquinone. The H₂O₂ is then distilled to remove impurities and increase its concentration. Transport limitations in the reactors and organic contamination of the product during recovery by liquid-liquid extraction are among the main problems relate to this process. Beckman reasoned that the use of CO₂ as the solvent eliminates the need of remediation of the aqueous H₂O₂ solution produced as the CO₂ contamination is benign (lowers the pH in a suitable range for H₂O₂ stability) and is readily reversible. Moreover, hydrogen and oxygen are completely miscible with scCO₂, thus eliminating the gas-liquid interface which is one of the main obstacles to high reaction rates. On the other hand, the solubility of 2-alkylanthraquinones in CO₂ is about 500 times lower than the concentration employed in the actual process. Hence, the author functionalized a number of amino- and hydroxy-anthraquinones with “CO₂-philic” oligomers of hexafluoropropylene oxide in order to enhance solubility in CO₂ [54]. Oxidation of perfluoroether-functionalized anthrahydroquinones (FAQH₂s) was conducted in a high-pressure batch reactor at 23.8 MPa and 25 °C (thus in liquid CO₂). The reaction rate was found first order with respect to both oxygen and FAQH₂. Furthermore, the reactivity of FAQH₂ in the oxidation is not affected by the size of the perfluoro tail or by the nature of the linker between the aromatic ring and the tail. The conclusion of this work is that multiple CO₂-philic tails attached through an ether linker and a methylene spacer to the 2, 3 and 6 positions on the anthraquinone rings would provide an efficient performance of the FAQH₂s in the generation of hydrogen peroxide in CO₂.

The problem of the direct synthesis of hydrogen peroxide starting from oxygen and hydrogen, using noble metals as

Table 7. Formation of H₂O₂ from O₂/H₂ mixtures over various catalysts.

Catalyst	Solvent	T, °C	P, MPa	O ₂ /H ₂	Rate H ₂ O ₂ Formation mmol g(cat) ⁻¹ h ⁻¹
Au/Al ₂ O ₃	CH ₃ OH	2	3.7	1.2	1530
Au:Pd(1:1)/Al ₂ O ₃	CH ₃ OH	2	3.7	1.2	4460
Pd/Al ₂ O ₃	CH ₃ OH	2	3.7	1.2	370
Au/ZnO	ScCO ₂	35	9.2	1.90	9
Au:Pd(1:3)/ZnO	ScCO ₂	35	9.2	1.1	7
Au:Pd(1:1)/ZnO	ScCO ₂	35	9.2	0.8	12
Au:Pd(3:1)/ZnO	ScCO ₂	35	9.2	0.9	8
Pd/ZnO	ScCO ₂	35	9.2	1.3	0

Table 8. Conversions and selectivities for aerobic oxidation of 1-hexene catalysed by Pd(Cl)₂ in various solvents, at 60 °C.

Reaction medium	P, MPa	Conversion, %	2-hexanone selectivity, %
scCO ₂	12.5	98.9	70.5
scCO ₂ + I.L.	12.5	98.2	91.9
I.L.	-	97.0	64.2
Without solvent	-	99.9	63.2

catalysts, is currently addressed by many researchers. However, only in a few cases the feasibility of this process in scCO₂ has been reported. Hutchings has described a supported Au catalyst as very selective for the direct formation of hydrogen peroxide from H₂/O₂ mixtures in both liquid organic solvents and scCO₂ [55]. The initial approach of the authors in designing a process for the direct synthesis of hydrogen peroxide was that to use scCO₂ as a reaction medium. This because earlier studies with Pd catalysts have indicated that H₂ diffusion is a significant problem and this can be expected to be largely bypassed by using a single supercritical phase in which hydrogen and oxygen are completely miscible. In effect, Au and Au:Pd catalysts promote the hydrogen peroxide production, albeit at a low rate. Table 7 summarizes pertinent data.

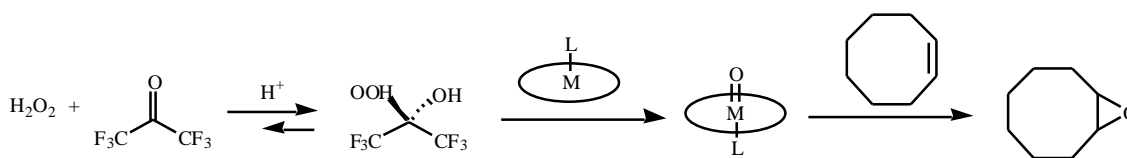
Unfortunately, at the relatively high temperature required to reach the supercritical state (*ca* 35 °C), the hydrogen peroxide formed is unstable and decompose to water and oxygen or even undergoes hydrogenation to water. This outcome was confirmed in separate experiments, in which a H₂O₂ solution was stirred with and without a Pd catalyst under the same conditions in scCO₂: even in the absence of the catalyst, 10% of H₂O₂ was decomposed in 1 hour and more than 30% in the presence of the catalyst. Hence, although scCO₂ can overcome the diffusion limitation, the intrinsic instability of hydrogen peroxide at relatively high temperatures is hardly compatible with the use of this medium.

Beckman also reported a study of the direct formation of hydrogen peroxide from oxygen and hydrogen in compressed CO₂ and indicated that part of the product decomposed probably through interactions with the steel reactor and tubing [56]. In order to determine more accurately the amount of hydrogen peroxide produced, the authors took advantage of the rapid reaction of H₂O₂ with cyclohexene over a titania silicalite catalyst to produce

cyclohexene oxide. They compared the performance of two Pd(II) catalysts (both fluorinated triphenylphosphine and the non fluorinated analog) to two Pd(0) catalyst (Palladium on carbon and a dibenzylideneacetone Pd complex with 8% added chloroform in order to solubilize the catalyst in CO₂). The results obtained indicate that the Pd(0) catalysts are more effective in the generation of H₂O₂ than the Pd(II) catalysts. Interestingly, simple Pd/C produced significant amounts of hydrogen peroxide, likely owing to the solubilization of H₂ and O₂ in water under the high pressures employed (13.1 MPa). Nevertheless, the results suggest that a Pd(0) derivative, which can be dissolved in CO₂, will prove the most active catalyst for H₂O₂ production starting from oxygen and hydrogen in CO₂.

An interesting example of Wacker process, namely the oxidation of alkenes to methyl ketones using oxygen and a Pd or Cu catalyst in scCO₂, was first reported by Jiang [57] and then by Han in scCO₂, ionic liquids and a mixed reaction medium scCO₂/I.L. [58]. In particular, Han studied the oxidation of 1-hexene by molecular oxygen catalyzed by Pd(Cl)₂ in 1-*n*-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF₆]), scCO₂, scCO₂/[bmim][PF₆], and in the absence of solvent. The experiments showed that the main products of the reaction were 2-hexanone and 3-hexanone, being 2-hexanone the desired product. Whereas the olefin conversions approach 100% in all the reaction media, the selectivities span a rather wide range, as shown in Table 8, depending on the solvent.

The relevant outcome is that the selectivity in the mixed scCO₂/[bmim][PF₆] reaction medium is much higher than that observed in the pure solvents or even in the absence of solvent. A rationale for this result can be proposed by taking into account the following facts. The undesired product, 3-hexanone, is generated from 2-hexene which is in turn formed through isomerization of the reactant. The catalyst Pd(Cl)₂ is not soluble in scCO₂ and is mainly present in the



Scheme 12.

I.L.-rich phase. 1-Hexene is soluble in both the $scCO_2$ phase and the I.L. phase. Thus, the CO_2 -rich phase play the role of a reservoir and continuously supplies the reactant to the I.L.-rich phase, where the oxidative process takes place, and keeps low the reactant concentration. As a consequence of this low stationary concentration of the reactant in the phase where the catalyst is present, the isomerization process and, thus, the formation of the undesired product are minimized.

The idea that enzymes display their functions only within an aqueous environment was wiped out when it was shown that enzymes could perform well in organic liquids. However, even in this case there are some practical limitations to their use in organic solvents as they can be hazardous, expensive or simply they are not easily removed. In order to provide a satisfactory answer to such problems, Bright first reported a study on an enzyme catalyzed oxidation occurring within the water core of reverse micelle that have been formed in $scCO_2$ [59]. By using a perfluoropolyether ammonium carboxylate surfactant (PFPE), he was able to form reverse micelle with water cores in $scCO_2$ and showed that the oxidation of cholesterol by cholesterol oxidase (ChOx) obeys classic Michaelis-Menten kinetics. The experiments also show that the best ChOx activity occurs when the molar ratio of H_2O_2 /PFPE (R) exceeds the value of 12 and that the k_{cat} relative to the substrate conversion is similar to that reported using reverse micelle in liquid alkanes. Conversely, the equilibrium constant for the substrate-enzyme dissociation changes with R and, in the best case, is two-fold higher than the value reported for reverse micelle in liquid alkanes. Furthermore, it has been proven that the equilibrium constant is scarcely influenced by the pressure, at least in the range 10.0-26.0 MPa.

3. HYDROGEN PEROXIDE AS TERMINAL OXIDANT

In 1998, Walther reported a study of the solubility in $scCO_2$ of various organometallics of transition metals and of their activity in some catalytic reactions [60]. Among the oxidation reactions, the olefins epoxidation catalyzed by $Ti[OCH(CH_3)_2]_4$, $Mo(CO)_6$ and CH_3ReO_3 , with tert.butylhydroperoxide and hydrogen peroxide is of particular interest. These typical epoxidation catalysts promote the epoxidation of cyclooctene to cyclooctene epoxide in the presence of tert.-BuOOH with yields ranging from 5 to 27% and selectivity higher than 95%. $Ti[OCH(CH_3)_2]_4$ catalyses also the cyclohexene epoxidation although with lower yields (2-8%) and selectivities for the epoxide (28-44%), cyclohexan-1,2-diol and 2-tert.-butoxycyclohexan-1-ol being also formed. The most interesting result is the possibility of exploiting hydrogen peroxide as terminal oxidant in $scCO_2$: Walther showed that $Mo(CO)_6$, in the presence of H_2O_2 can effectively promote

cyclooctene epoxidation with a fair yield (13%) and excellent selectivity (98%). However, the high excess of H_2O_2 over the substrate needed (320) indicates that a large decomposition of the terminal oxidant occurs under the experimental conditions adopted.

Campestrini showed that an efficient heterogeneous oxidation of cyclooctene with hydrogen peroxide catalyzed by a manganese porphyrin supported on silica in the presence of hexafluoroacetone as co-catalyst may be achieved in $scCO_2$ at 40 °C and 20 MPa (Scheme 12) [61].

Under proper conditions, a complete olefin conversion may be obtained with the formation of cyclooctene oxide, as the sole product, using a moderate (3 times) excess of H_2O_2 over the substrate. In this case, the role of perfluoroacetone in the catalytic process is manifold. First of all, it allows to better exploit the oxidative properties of H_2O_2 via the formation of its perfluoroacetone perhydrate, which is soluble in the supercritical phase. Secondly, H_2O_2 fixation by hexafluoroacetone provides a useful tool to preserve hydrogen peroxide from decomposition induced by steel wall and catalase activity of the manganese porphyrin. Furthermore, the formation of perfluoroacetone perhydrate, which is a much better electrophilic oxidant than free H_2O_2 , leads to a fast and clean formation of an oxo-manganese porphyrin, which is the ultimate oxidizing agent capable to epoxidize the olefin. Finally, it has been demonstrated that the Teflon coating of the reactor wall effectively prevents H_2O_2 decompositions: in fact, the epoxide yields are significantly higher with respect to those measured in the uncoated reactor.

In a following paper, Campestrini extended the study of such catalytic epoxidation system exploiting H_2O_2 and perfluoroacetone in $scCO_2$ to heterogeneous catalysts in which the active species, namely a manganese porphyrin, is embedded in polydimethylsiloxane (PDMS) and in organically modified silicates (ORMOSILs) [62]. The aim of catalyst embedding in a solid matrix was that of preventing the catalyst degradation; in fact, at the end of each experiment above described, the manganese porphyrin appeared completely bleached. The best results were obtained by embedding 5,10,15,20-tetrakis-(2',6'-dichlorophenyl)porphyrinate, $(MnTDCPP)Cl$, in a polydimethylsiloxanic membrane. The pertinent results are shown in Table 9.

It is worth of note that $Mn(TDCPP)Cl$ shows a catalytic activity lower than that measured in the best xerogel, also evaluated as matrix, but well above that of the control experiment (run 1). The rate constants relative to $Mn(TDCPP)Cl$ embedded in PDMS apparently do not depend so much on the Mn-complex loading as observed in the case of xerogel matrixes. Furthermore, at variance with the behaviour observed in xerogels, the rate constants

Table 9. Values of k_{cat} relative to cyclooctene oxidation (3.84×10^{-4} mol.) with H_2O_2 (2.00×10^{-3} mol.) catalysed by a $\text{Mn}(\text{TDCPP})\text{Cl}$ (0.9×10^{-6} mol.) embedded in PDMS, in the presence of $(\text{CF}_3)_2\text{CO} \cdot 3\text{H}_2\text{O}$ (3.58×10^{-4} mol.) and 4-*tert*-butylpyridine (1.69×10^{-4} mol.), in 8.5 mL of scCO_2 at 40 °C and 20 MPa.

Run	Mn(TDCPP)Cl Loading mg/mg $\times 10^6$	$k_{\text{cat}} \times 10^3$ min^{-1}
1	-	2.1
2	1.2	31.0
3 ^a	"	21.0
4 ^b	"	10.0
5 ^c	"	10.0
6	2.2	19.0
7	10.2	15.0

a: first catalyst recycle
b: second catalyst recycle
c: third catalyst recycle

decrease with increasing the Mn-porphyrin loading. This outcome suggests that the metal additive does not interfere with the membrane curing and, as a consequence, the catalyst activity is mainly determined by active sites separation at a molecular level, thus increasing with decreasing the metal-complex loading. Finally, the stability of the Mn-complex is significantly enhanced by PDMS embedding. The same catalyst was recycled three times with an efficiency decay slower than that observed in xerogel matrices. In conclusion, it was shown that solid solutions of metal-complexes in ORMOSIL xerogels and PDMS membranes are quite useful heterogeneous catalysts for processes carried on in scCO_2 . In particular, embedding of Mn-porphyrins in PDMS may enhance the life-time of the catalyst in the course of olefin epoxidation by H_2O_2 still preserving a remarkable reactivity.

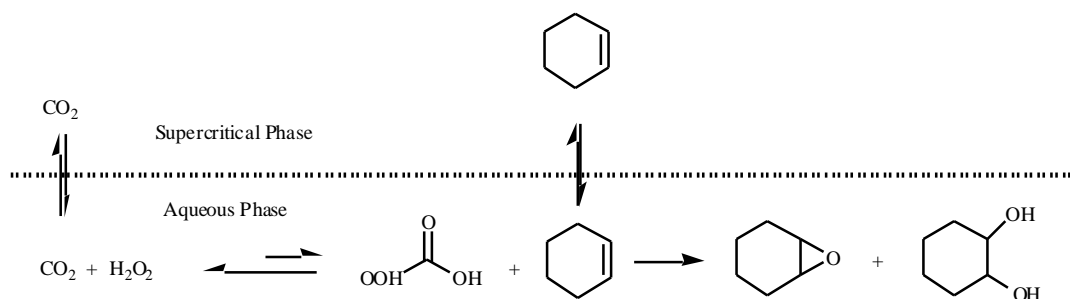
Eckert reported an interesting alternative epoxidation process in which scCO_2 was employed as solvent and reactant, in combination with aqueous H_2O_2 , probably forming *in situ* peroxycarbonic acid [64]. Experiments were conducted at 40 °C and 12 MPa in which the model substrate cyclohexene was epoxidized to 1,2-cyclohexene oxide and 1,2-cyclohexanediol in the aqueous-supercritical fluid biphasic system (Scheme 13).

Although in the absence of any additive the oxidation yields are extremely low (0.02% epoxide and 0.09% diol) they are significantly higher than those obtained with the oxidizing system in which CO_2 was replaced by nitrogen

(0% epoxide and < 0.06% diol). This outcome indicates that CO_2 is involved in the oxidizing process probably through the formation of peroxycarbonic acid. Results from experiments carried on in the presence of NaHCO_3 provided evidence of the existence of peroxycarbonic acid. In fact, the epoxide yield increases from 0.02% to 1.6% in scCO_2 as compared to the increase from 0% to 0.14% in N_2 and this strongly supports the idea that peroxycarbonic acid is formed mainly from CO_2 rather than from a reaction between HCO_3^- and H_2O_2 . The cyclohexene epoxide yield can be enhanced up to 10% by adding a co-solvent, such as DMF, which may improve the solubility of cyclohexene in the aqueous phase where the oxidation process occurs. In order to support the hypothesis that epoxidation occurs in the aqueous phase, it has been studied the epoxidation of a water soluble olefin such as 3-cyclohexen-1-carboxylate sodium salt: in this case, the substrate conversion was 100% being the yield of epoxide 89% and that of a diol 11%. In conclusion, Eckert disclosed an epoxidation technique using CO_2 and H_2O_2 , which may be conveniently applied to oxidation of water soluble olefins; on the contrary, the practical use in the case of non-water soluble olefins is limited by the slow mass transfer of the substrate to the aqueous phase and by H_2O_2 decomposition.

The use of titanium silicalite (TS-1) to generate propylene oxide from propylene and hydrogen peroxide in liquid phase has been investigated extensively over the past decade. It has been concluded that methanol is needed as co-solvent to perform the reaction efficiently. Probably, the addition of methanol improves the solubility of the gases, included propylene, in the aqueous phase thus limiting the mass transfer problem. However, methanol is also the prime source of by-products and it therefore impairs the selectivity for propylene oxide. In order to avoid these complications, Beckman has investigated the use of scCO_2 , as reaction medium for the generation of propylene oxide from propylene and hydrogen peroxide generated *in situ* over a Pd/TS-1 catalyst [64]. The effect of the reaction medium (CO_2 versus water/methanol) was investigated in three sets of experiments in which: a) CO_2 is the solvent, b) water/methanol is the solvent under N_2 pressure, and c) water/methanol is the solvent under CO_2 pressure. The pertinent results are reported in the following Table.

As shown by runs 1-3 the use of CO_2 as reaction medium leads to reasonable olefin conversions and high selectivity for propylene oxide, the desired product. On the contrary, when methanol is present, the selectivity always drops, thus confirming that methanol is the main contributor to by-products formation. However, even when methanol is



Scheme 13.

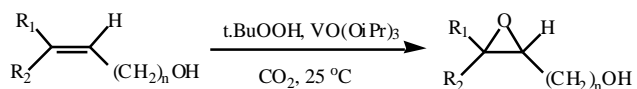
Table 10. Propylene conversions and propylene oxide selectivities for propylene epoxidation in the presence of H₂, O₂ and a Pd/TS-1 catalyst, at 45 °C and a total pressure of 13.1 MPa.

Reaction medium	Catalyst, g	Propylene conversion, %	Propylene oxide selectivity, %
CO ₂	0.1502	9.5	77.1
CO ₂	0.1952	6.5	91.2
CO ₂	0.2998	7.5	94.3
MeOH + H ₂ O + CO ₂	0.1565	3.5	17.4
MeOH + H ₂ O + CO ₂	0.2063	4.7	41.1
MeOH + H ₂ O + N ₂	0.1993	16.0	3.5

present, the replacement of N₂ with CO₂ affords some improvement in selectivities (runs 4-6). Hence, CO₂ revealed to be an excellent reaction medium for the process investigated, where H₂ and O₂ can form *in situ* hydrogen peroxide, the epoxidizing agent. Unlike the mixtures water/methanol, CO₂ can solubilize large quantities of these gases together with propylene, the substrate of choice, providing a non-flammable environment devoid of interfaces which could limit the mass transport. Moreover, CO₂ being chemically inert towards propylene oxide significantly enhances the selectivity.

4. ALKYL HYDROPEROXIDES AND MONOPERSULPHATE AS TERMINAL OXIDANTS

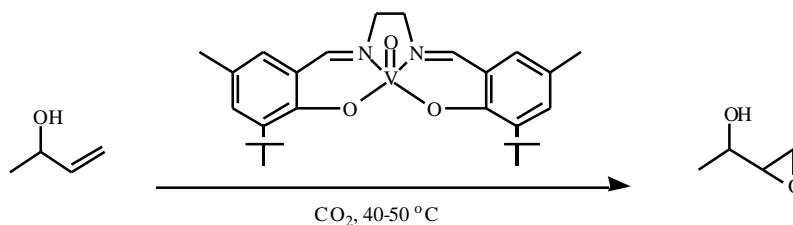
The most useful primary oxidants in selective catalytic oxidations in scCO₂, besides gaseous oxygen, are low molecular weight hydroperoxides thanks to their fair solubility. Probably, the first report of a selective epoxidation using a variety of transition metal catalysts (V, Ti, Mo) and tert.-butylhydroperoxide was published by Tumas in 1998 [65]. This author showed that a wide range of allylic and homoallylic alcohols are oxidized with high conversions and selectivity to the corresponding epoxides, by using VO(OiPr)₃ and tert.-BuOOH in compressed CO₂ at 25 °C (Scheme 14).

**Scheme 14.**

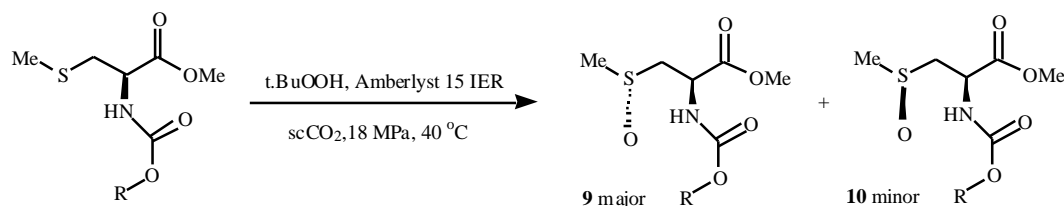
Interestingly, working with a liquid oxidant such as tert.-BuOOH, the authors did not observe any advantage when operating above the critical point of CO₂. Moreover, these reactions are often carried out in conventional solvents at room temperature or below. Under these experimental conditions, after 24 hours reaction time, the substrates conversions are almost quantitative with selectivity ranging from 85 to 99% in favor of the corresponding epoxides. The reactivity of olefins with this oxidizing system parallels that reported in conventional solvents. In fact, activated olefins react faster than simple olefins and allylic alcohols react faster than homoallylic alcohols whereas, under identical experimental conditions, 1-octene and cyclohexene are unreactive. The epoxidation rates were found about three times larger in CO₂ than in hexane suggesting that aromatic solvents may be better models than alkanes for solubility in

the high density carbon dioxide. The oxidizing system tert.-BuOOH/Mo(CO)₆, which was found effective for the oxidation of unactivated alkenes such as cyclohexene, although at elevated temperature (95 °C), was also investigated. In this case the main product is 1,2-cyclohexandiol (73%) along with allylic oxidation products as 2-cyclohexen-1-ol (10%) and 2-cyclohexen-1-one (10%). Quite surprisingly, these results were obtained with aqueous tert.-BuOOH whereas using anhydrous tert.-BuOOH a conversion of cyclohexene of only 15% was observed. Finally, the authors showed that also Ti(OiPr)₄ in the presence of chiral tartrate ligands leads to enantioselective allylic alcohols epoxidation. In CO₂, di-isopropyl tartrate is conveniently used in the place of the diethyl tartrate owing to the limited solubility of the latter ligand. The enantiomeric excess of the product strongly depends on the reaction temperature: it is only 16% at 25 °C but, remarkably, increases to 87% at 0 °C, thus approaching the 94% *ee* reported by Sharpless.

A few months later, a paper was published by Kolis which reported on the alkenes epoxidation in scCO₂ by tert.-BuOOH, catalyzed by Molybdenum hexacarbonyl [66]. In this case, the oxidative process was carried out at temperatures ranging from 86 to 103 °C under a pressure of 51.7 MPa. Under these experimental conditions and using Mo(CO)₆ as catalyst precursor and tert.-BuOOH as final oxidant, the oxidations proceed with nearly quantitative yield. The use of 70% (wt) aqueous solutions of tert.-BuOOH yields the corresponding *trans*-diols, while anhydrous decane solutions of tert.-BuOOH give the epoxides. The highest yields and fastest rates for diol and epoxide formation were observed with *cis*-alkenes, while *trans*-alkenes were considerably less reactive. Furthermore, phenyl substituted olefins exhibit a tendency to break down to their corresponding aldehydes. At variance with Tumas's finding, Kolis observed that the presence of water, besides causing the hydrolysis of epoxides to diols, plays an additional adverse effect by slowing down the reaction rate. Following the rationale provided by Kolis, water can compete with tert.-BuOOH for the coordination sites on the metal, thus reducing the amount of effective epoxidant agent. It should be noted that, while this is probably true in the case of the sole supercritical phase realized by Kolis, in the liquid CO₂ system utilized by Tumas most of the water present probably constitutes a separate phase, thus minimizing the competition with tert.-BuOOH. As far as the catalyst is concerned, Kolis found that Mo(CO)₆ revealed to be the most suitable precursor of the actual catalyst, mainly for its



Scheme 15.



Scheme 16.

solubility; in fact, molybdenum hexacarbonyl, unlike other derivatives such as $\text{MoO}_2(\text{acac})_2$, is fairly soluble in scCO_2 . The authors noted that below 75–80 °C there is no reactivity using $\text{Mo}(\text{CO})_6$ and therefore postulated that the process is temperature dependent due to the dissociation of CO from $\text{Mo}(\text{CO})_6$. This suggestion was confirmed by the good activity observed for a molybdenum precursor bearing a more labile ligand such as $\text{Mo}(\text{C}_8\text{H}_{14})(\text{CO})_5$ at lower temperature.

In a following paper, Kolis extended the study to the epoxidation of allylic alcohols with tert-butylhydroperoxide in the presence of a vanadyl salen oxo-transfer catalyst in supercritical CO_2 (Scheme 15) [67].

The main feature of this catalytic system is that the process takes place in a homogeneous phase, as confirmed by the visual observation that both organic substrates and catalyst are soluble in the supercritical phase under the experimental conditions adopted (the authors report only the initial pressure which is 21.8 MPa; upon heating to the reaction temperatures the pressure should roughly double). The VOsalen/t.BuOOH system in scCO_2 showed an epoxidation reactivity similar to many oxygen transfer catalysts in CH_2Cl_2 . The reactions proceed with yields ranging from fair (33–40%) to high (86–99%) for a wide variety of allylic alcohols, but simple olefins are only sluggishly epoxidized with yields lower than 30%. The reaction rates are apparently slightly lower in scCO_2 than in organic solvents. The reactions are described as very clean and give only minor side products: further oxidation of the allylic alcohol to the α,β -unsaturated ketone is observed in nearly every reaction, but the yield of enone never exceeds 10%. In conclusion, this epoxidation system may replace the traditional environmentally hazardous solvents with comparable yields and selectivity.

The benefits of the supercritical medium in terms of rates and conversions are normally far from impressive, but in some cases the effects on the selectivity of the reaction are quite relevant. For example, Rayner reported the results of a study on the sulfoxidation process of cysteine derivatives using tert-BuOOH in the presence of an Amberlite ion

exchange resin in scCO_2 ; under these conditions, he observed a dramatic, pressure dependent increase in the diastereoselectivity (>95%) when this outcome is compared to that of the same reaction in conventional solvents where no diastereoselectivity is observed (Scheme 16) [68].

Studies on the sulfoxidation of cysteine derivatives in conventional solvents have shown that, although in general they may be expected to give diastereoselective oxidation, in practice this is very difficult to achieve without significant substituent modification, such as those requiring preparation of the MEM esters of sulphur derivatives substituted with bulky groups. For example, CBz methyl cysteine methyl ester was oxidized in high yield by the tert-BuOOH/Amberlite system but no appreciable diastereoselectivity was observed in toluene or dichloromethane. On the contrary, the same reaction carried out in scCO_2 at 40 °C and 20.0 MPa gave the sulfoxides **9** and **10** with high yield and selectivity and, by varying the pressure at a constant temperature of 40 °C, the process was optimized so that the observed diastereoselectivity could reach a value greater than 95%. In particular, the diastereoselectivity reaches a maximum at 18.0 MPa and then falls off as pressure is further increased. The major stereoisomer obtained in the oxidation of CBz methyl cysteine methyl ester has been confirmed by X-ray crystallography to be the anti isomer **9** (R=Bn). The reasons for this dramatic effect are not yet clear; however, there is no doubt that it is potentially very important in the field of stereoselective synthesis.

Another example of tunable selectivity observed in scCO_2 was reported by Campestrini following the study of the oxidation of sulphides by Oxone[®] ($2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$) in the presence of catalytic amount of various manganese porphyrins [69]. Experiments have been carried out in an anhydrous two phase-system (solid Oxone[®], solid catalyst/ scCO_2). Under the experimental conditions employed (40 °C, 20.0 MPa), only the 5,10,15,20-tetrakis(heptafluoropropyl)porphyrinate-manganese(III) chloride turned out to be slight soluble in scCO_2 . In the absence of manganese porphyrin and/or of an aromatic nitrogen base, a slow stoichiometric sulphide

Table 11. Oxidation of *p*-tolyl-methylsulphide (0.74 mmol) by Oxone[®] (0.32 mmol active oxygen), in the presence of 2.4x10⁻⁶ mol of Mn(TFPP)Cl, 0.17 mmol of 4-*tert.*-butylpyridine, in various solvents at 40 °C.

Run	Solvent	<i>p</i> -TolSOMe yield ^a , %	<i>p</i> -TolSO ₂ Me yield ^a , %
1	scCO ₂ ^b	26.3	23.0
2	scCO ₂	16.0	18.3
3	methanol	53.2	16.6
4	hexane	14.3	29.4

a: as determined after 24 h relative to the starting monopersulphate.

b: in the presence of 1% acetone wt/wt.

oxidation leading mainly to sulphoxide is observed in spite of the extremely low solubility of Oxone[®] in scCO₂. Conversely, in the presence of 4-*tert.*-butylpyridine and catalytic amount of manganese porphyrins (0.6% with respect to sulphide), enhanced reaction rates are observed. Furthermore, the selectivity of sulphide oxidation reverses the outcome observed in liquid polar solvents: sulphone is formed in larger (or comparable) amount than that of sulphoxide even when an excess of sulphide relative to oxidant is employed (see Table 11).

Interestingly, the chemo selectivity observed in liquid *n*-hexane, a solvent exhibiting an Et Dimroth and Reichard polarity parameter (Et=31) similar to that of scCO₂ (Et=28-30, depending on pressure), favors the formation of sulphone even more than scCO₂. These observations can be interpreted by assuming that the sulphoxide formed in the first step of the oxidative process remains coordinated to the positively charged catalyst by virtue of its marked dipole moment. Thus, sulphoxide clustering around the catalyst induces a preferential over-oxidation to sulphone which occurs faster than the oxidation of sulphide in liquid *n*-hexane, in spite of the electrophilic character of the oxo-manganese derivative. On the other hand, in methanol, a solvent of remarkable polarity (E_t=55.5), the sulphoxide-catalyst clustering is much less relevant due to strong solute-solvent interactions. Therefore, in methanol, the sulphoxide concentration in the proximity of the catalyst is likely to be similar to that in the bulk phase and the chemo selectivity is determined only by the relative rate constants for sulphide and sulphoxide oxidation, which favor sulphoxide production. A possible rationale for the difference in chemo selectivity observed in the two media of similar polarity, namely scCO₂ and liquid hexane takes into account the different clustering effects experienced in the two phases. In fact, clustering of the sulphoxide intermediate on the catalyst surface could be depressed in supercritical conditions due to the severe constraints imposed on the sulphoxide by the surrounding CO₂ molecules. In other words, solute-solute clustering is apparently favored in scCO₂ whereas solute-catalyst clustering plays a prevailing role in a liquid apolar solvent.

CONCLUDING REMARKS

From the literature results reported in this review, it is predictable that the use of supercritical CO₂ for oxidation processes will be increasingly pursued in order to improve mass transfer, selectivity, and conversion. Catalytic

processes carried out in supercritical CO₂ will also become increasingly important due to advantages offered by phase transfer catalysis and by the realization and use of new transition-metal complexes soluble in scCO₂. Furthermore, progress in a new area such as the development of scCO₂ surfactants will make possible to perform aqueous chemistry in scCO₂ microemulsions thus opening new possibilities for bioreactions.

However, one should take into account that, in spite of its many interesting properties, scCO₂ is not always a panacea. In fact, the cost associated with the compression and containment of the fluid may limit the economic feasibility of scCO₂ applications. Therefore, the most promising applications are those in which the peculiar characteristics of scCO₂ are exploited to make products with specifications that cannot be obtained in traditional solvents or when the possibility to integrate reaction and separation steps of a catalytic process is verified.

ABBREVIATIONS

Bn	=	benzyl
[bmim][PF ₆]	=	1- <i>n</i> -butyl-3-methylimidazolium hexafluorophosphate
CBz	=	carbobenzoxy
ChOx	=	cholesterol oxidase
DME	=	dimethylether
DMF	=	dimethylformamide
Dmp	=	2,9-dimethyl-1,10-phenanthroline
FAQH ₂	=	functionalised anthrahydroquinone
Fe(PFTPP)Cl	=	Iron(III) 5,10,15,20-tetrakis(pentafluorophenyl)porphyrinate chloride
Fe(Br ₈ PFTPP)Cl	=	Iron(III) -octabromo-5,10,15,20-tetrakis(pentafluorophenyl)porphyrinate chloride
HMPA	=	hexamethylphosphoramide
I.L.	=	ionic liquid
MEM	=	methoxyethoxyethyl
Mn(TDCPP)Cl	=	Manganese(III) 5,10,15,20-tetrakis-(2',6'-dichlorophenyl)porphyrinate chloride
MPa	=	mega Pascal
MTMS	=	methyltrimethoxysilane
ORMOSIL	=	organically modified silicates
PDMS	=	polydimethylsiloxane
PFPE	=	perfluoropolyether
ScFs	=	supercritical fluids
TMOS	=	tetramethylorthosilicate
TOF	=	turnover frequency
TON	=	turnover number
TPAP	=	tetra- <i>n</i> -propylammonium perruthenate
TS-1	=	titanium silicalite
Wt	=	weight

REFERENCES

- [1] Cagniard de LaTour, C. *Ann. Chim. Phys.*, **1822**, 21, 127-132.
- [2] Cagniard de LaTour, C. *Ann. Chim. Phys.*, **1822**, 21, 178-182.
- [3] Kosel, Z. *Ang. Chem. Int. Ed. Engl.*, **1978**, 17, 702.
- [4] McNaught, A.D. (Ed.) *Compendium of Chemical Terminology. IUPAC Recommendations*, Blackwell Science Ltd., Oxford, U.K., **1997**.
- [5] Parker, S.P. (Ed.) *McGraw-Hill Dictionary of Scientific and Technical Terms*, McGraw-Hill, Inc., New York, N.Y., **1994**.
- [6] Simpson, J.A., Weiner, E.S.C. *The Oxford English Dictionary*, Vol. XVII, Clarendon Press, Oxford, U.K., **1989**.
- [7] Mishima, O., Endo, S. *J. Chem. Phys.*, **1978**, 68, 4417-4418.
- [8] Bridgeman, P.W. *Phys. Rev.*, **1914**, 3, 126-141, 153-203.
- [9] McHugh, M., Paulaitis, M.E. *J. Chem. Eng. Data*, **1980**, 25, 326.
- [10] Tester, J.W., Holgate, H.R., Armellini, F.J., Webley, P.A., Killilea, W.R., Hong, G.T., Barner, H.E. in *Emerging Technologies in Hazardous Waste Management III*, ACS Symp. Ser. 518, **1993**, 35.
- [11] Urben, P.G. (Ed.) *Bretherick's Handbook of Reactive Chemical Hazards*, Butterworth-Heinemann, **1995**.
- [12] Albert, J., Luft, G. *Chem. Eng. Processing*, **1998**, 37, 55-59.
- [13] Lewis, R.J., *Sax's Dangerous Properties of Industrial Materials*, Van Nostrand, New York, **1992**.
- [14] Ipatiev, V., Dovgalevich, N. *J. Russ. Phys. Chem. Soc.*, **1911**, 43, 1431-1436.
- [15] Hansen, N.B., Hybertson, B.M., Barkley, R.M., Sievers, R.E. *Chem. Mater.*, **1992**, 4, 749-752.
- [16] Smith, W.J., Reid, R.C. *Fluid Phase Equil.*, **1986**, 32, 77.
- [17] Musie, G., Wei, M., Subramaniam, B., Busch, D.H. *Coord. Chem. Rev.*, **2001**, 219-221, 789-820.
- [18] Kainz, S., Koch, D., Baumann, W., Leitner, W., *Angew. Chem. Int. Ed. Engl.*, **1997**, 36, No.15, 1628-1639.
- [19] Campestrini, S., Lora, G., Tonellato, U. *Tetrahedron Lett.*, **2001**, 42, 7045-7048.
- [20] Montilla, F., Rosa, V., Prevett, C., Avilès, T., Nunes da Ponte, M., Masi, D., Mealli, C. *Dalton Trans.*, **2003**, 2170-2176.
- [21] Sarbu, T., Styranc, T., Beckman, E.J. *Nature*, **2000**, 405, 165-168.
- [22] Clarke, M.J., Harrison, K.L., Johnston, K.P., Howdle, S.M. *J. Am. Chem. Soc.*, **1997**, 119, No. 27, 6399-6406.
- [23] Jacobson, G.B., Lee, C.T. Jr., daRocha, S.R.P., Johnston, K.P. *J. Org. Chem.*, **1999**, 64, 1207-1210.
- [24] Jacobson, G.B., Lee, C.T. Jr., Johnston, K.P. *J. Org. Chem.*, **1999**, 64, 1201-1206.
- [25] Xu, X.D., Mouljin, J.A. *Energy Fuels*, **1996**, 10, 305.
- [26] Jessop, P.G., Ikariya, T., Noyori, R., *Chem. Rev.*, **1999**, 99, 475.
- [27] Baiker, A., *Chem. Rev.*, **1999**, 99, 453.
- [28] Savage, P.E., Gopalan, S., Mizan, T.I., Martino, C.J., Brock, E.E., *AIChE Journal*, **1995**, Vol. 41, No.7, 1723-1778.
- [29] Walther, D., Ruben, M., Rau, S. *Coord. Chem. Rev.*, **1999**, 182, 67-100.
- [30] Leitner, W., *Acc. Chem. Res.*, **2002**, 35 (9), 746-756.
- [31] Beckman, E.J., *Environ. Sci. Technol.*, **2003**, 37, 5289-5296.
- [32] Wu, X.-W., Oshima, Y., Koda, S. *Chemistry Letters*, **1997**, 1045-1046.
- [33] Loeker, F., Leitner, W. *Chem. Eur. J.*, **2000**, 6, No. 11, 2011-2015.
- [34] Birnbaum, E.R., Le Lacheur, R.M., Horton, A.C., Tumas, W. *J. Mol. Catal. A*, **1999**, 139, 11-24.
- [35] Ellis, P.E. Jr., Lyons, J.E. *Coord. Chem. Rev.*, **1990**, 105, 181.
- [36] Sahle-Demessie, E., Gonzalez, M.A., Enriquez, J., Zhao, Q. *Ind. Eng. Chem. Res.*, **2000**, 39, 4858-4864.
- [37] Zhou, L., Akgerman, A. *Ind. Eng. Chem. Res.*, **1995**, 34, 1588-1595.
- [38] Wang, C.T., Willey, R.J. *J. of Non-Cryst. Sol.*, **1998**, 225, 173-177.
- [39] Wang, C.T., Willey, R.J., *Catal. Today*, **1999**, 52, 83-89.
- [40] Jenzer, G., Sueur, D., Mallat, T., Baiker A. *Chem. Commun.*, **2000**, 2247-2248.
- [41] Jenzer, G., Mallat, T., Baiker A. *Catal. Lett.*, **2001**, Vol. 73, No. 1, 5-8.
- [42] Besson, M., Gallezot, P. *Catal. Today*, **2000**, 57, 127.
- [43] Grunwaldt, J.D., Caravati, M., Ramin, M., Baiker, A. *Catal. Lett.*, **2003**, Vol. 90, Nos. 3-4, 221-229.
- [44] Steele, A.M., Zhu, J., Tsang, S.C. *Catal. Lett.*, **2001**, Vol.73, No. 1, 9-13.
- [45] Theyssen, N., Leitner, W. *Chem. Commun.*, **2002**, 5, 410-411.
- [46] Khenkin, A.M., Rosenberger, A., Neumann, R. *J. Cat.*, **1999**, 182, 82.
- [47] Bolm, C., Palazzi, C., Franciò, G., Leitner, W. *Chem. Commun.*, **2002**, 15, 1588-1589.
- [48] Chang, Y., Jiang, T., Han, B., Gao, L., Zhang, R., Liu, Z., Wu, W. *Ind. Eng. Chem. Res.*, **2003**, 42, 6384-6388.
- [49] Gläser, R., Josl, R., Williardt, J. *Topics in Catal.*, **2003**, Vol. 22, Nos. 1-2, 31-39.
- [50] Ciriminna, R., Campestrini, S., Pagliaro, M. *Adv. Synth. Catal.*, **2003**, 345, 1261-1267.
- [51] Ciriminna, R., Campestrini, S., Pagliaro, M. *Adv. Synth. Catal.*, **2004**, 346, 231-236.
- [52] Jia, L., Jiang, H., Li, J. *Chem. Commun.*, **1999**, 985-986.
- [53] Hosokawa, T., Aoki, S., Murahashi, S.-I. *Synthesis*, **1992**, 558.
- [54] Hâncu, D., Beckman, E.J. *Ind. Eng. Chem. Res.*, **2000**, 39, 2843-2848.
- [55] Landon, P., Collier, P.J., Papworth, A.J., Kiely, C.J., Hutchings, G.J. *Chem. Commun.*, **2002**, 2058-2059.
- [56] Hâncu, D., Beckman, E.J. *Green Chemistry*, **2001**, 3, 80-86.
- [57] Jiang, H., Jia, L., Li, J. *Green Chemistry*, **2000**, 2, 161.
- [58] Hou, Z., Han, B., Gao, L., Jiang T., Liu, Z., Chang, Y., Zhang, X., He, J. *New J. Chem.*, **2002**, 26, 1246-1248.
- [59] Kane, M.A., Baker, G.A., Pandey, S., Bright, F.V. *Langmuir*, **2000**, 16, 4901-4905.
- [60] Kreher, U., Schebesta, S., Walther, D. *Z. Anorg. Allg. Chem.*, **1998**, 624, 602-612.
- [61] Campestrini, S., Tonellato, U. *Adv. Synth. Catal.*, **2001**, 343, No. 8, 819-825.
- [62] Campestrini, S., Donoli, A., Tonellato, U. *Lett. Org. Chem.*, **2004**, 1, 125-128.
- [63] Nolen, S.A., Lu, J., Brown, J.S., Pollet, P., Eason, B.C., Griffith, K.N., Gläser, R., Bush, D., Lamb, D.R., Liotta, C.L., Eckert, C.A., Thiele, G.F., Bartles, K.A. *Ind. Eng. Chem. Res.*, **2002**, 41, 316-323.
- [64] Danciu, T., Beckman, E.J., Hâncu, D., Cochran, R.N., Grey, R., Hajnik, D.M., Jewson, J. *Angew. Chem. Int. Ed.*, **2003**, 42, No. 10, 1140-1142.
- [65] Pesiri, D.R., Morita, D.K., Glaze, W., Tumas, W. *Chem. Commun.*, **1998**, 1015-1016.
- [66] Haas, G.R., Kolis, J.W. *Organometallics*, **1998**, 17, 4454-4460.
- [67] Haas, G.R., Kolis, J.W. *Tetrahedron Lett.*, **1998**, 5923-5926.
- [68] Oakes, R.S., Clifford, A.A., Bartle, K.D., Thornton pett, M., Rayner, C.M. *Chem. Commun.*, **1999**, 247-248.
- [69] Campestrini, S., Tonellato, U. *J. Mol. Catal. A: Chemical*, **2000**, 164, 263-272.