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Catalytic oxidations in carbon dioxide-based reaction media, including novel CO_2-expanded phases

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Abstract

Environmentally benign oxidations with dense CO_2 (either near-critical, $ncCO_2$, or supercritical carbon dioxide, $scCO_2$) as solvent media have been receiving increased attention during the last decade. This paper reviews catalytic oxidations in dense CO_2 with emphasis on reported homogeneous systems in $scCO_2$, most of which involve transition metal catalysts and dioxygen or organic peroxides as oxidant. Based on recent work in our laboratory, we offer some perspective and provide examples to demonstrate that $scCO_2$ can be adapted to a broader range of homogeneous oxidations including those that utilize CH_3ReO_3 as catalyst and *t*-BuOOH as terminal oxidant, and the oxidation of substituted phenols by dioxygen using Co(salen) complex as catalyst. The advantages of using $scCO_2$ include the total replacement of organic solvents with environmentally benign CO_2, the complete miscibility of the oxidants such as O_2 in $scCO_2$ eliminating interphase transport limitations, and the resistance of CO_2 to oxidation. However, the $scCO_2$-based oxidation has limitations including low reaction rates, inadequate solubilities of a number of transition metal catalysts in CO_2 necessitating high process pressures on the order of hundreds of bars, and the lack of pressure-tunability of the dielectric constant of the reaction medium. We present a new process developed in our laboratory in which the conventional solvent medium is only partially replaced by dense CO_2. We term this a CO_2-*expanded solvent medium*, which offers several advantages as follows: solvent replacement with dense CO_2 by up to 80 mol%, representing a substantial reduction in solvent usage; maintenance of the solubilities of the catalyst and substrate in the reaction mixture while enhancing the miscibility of dioxygen therein; lower process pressures on the order of tens of bars; and pressure-tunable dielectric constants making it possible to realize an optimum reaction medium between $scCO_2$ and neat solvent limits. We distinguish CO_2-*expanded phases* from the traditional concept of a ‘co-solvent’ for a CO_2 based system in the following way. To produce a CO_2 expanded organic solvent medium, we start with the organic solvent and increase its volume by the addition of CO_2, whereas relatively small amounts of ‘co-solvents’ have traditionally been added to dense CO_2 phases to improve solubilities of certain compounds.

We present examples that show enhanced oxidation rates compared to either neat organic solvent or $scCO_2$ for organic substrates (alkenes and phenols) in CO_2-expanded media using dioxygen and metal complexes of both Schiff base and porphyrin ligands. Further, the selectivity toward desired products (alkenes to epoxides; phenols to quinones) is also improved over either neat solvents or $scCO_2$. The CO_2-expanded solvents thus offer excellent potential for exploitation in catalytic oxidations.

Keywords: Oxidation; Dioxygen; Terminal oxidant; Catalysis; Solvent expansion; Supercritical; Carbon dioxide

Nomenclature

acac	acetylacetonato
Br_8PFTPP	octabromotetrakis(pentafluorophenyl)porphinato
CysSMe-OMe	sulfoxo-methionine methyl ester
DMF	*N*,*N*′-dimethylformamide
35DTBP	3,5-di-*tert*-butylphenol
DTBP	2,6-di-*tert*-butylphenol
DTBQ	2,6-di-*tert*-butyl-4,4′-benzoquinone
Me_2B14N4	4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane
Me_3TACN	1,4,7-trimethyl-1,4,7-triazacyclononane
MTO	methyltrioxorhenium
OPr^i	isopropoxide
PFTPP	tetrakis(pentafluorophenyl)porphinato
TACN	1,4,7-triazacyclononane
t-BuOH	*tert*-butyl alcohol
t-BuOOH	*tert*-butyl hydroperoxide
TMP	tetramesitylporphinato
TPP	tetraphenylporphinato
TTDBQ	3,5,3′,5′-tetra-*tert*-butyl-4,4′-diphenoquinone
salen	*N*,*N*′-bis(salicylidene-1,2-diamnoethanato)
salen*	*N*,*N*′-bis(3,5-di-*tert*-butyl salicylidene-1,2-cyclohexane diaminato)
sc	supercritical

1. Introduction

Supercritical and near-critical dense carbon dioxide phases have been heralded as environmentally benign solvents of great promise in many chemical applications, including the long used preparation of materials for decaffeinated drinks, the chemical process industry, and, more recently, to replace the conventional organic solvents used in the cleaning of garments. The low toxicity and limited reactivity of CO_2 make it suitable for use around foods and other consumer goods, and its low cost supports its use in very broad ranges of applications. Reviews of reactions in sc media are provided elsewhere [1].

This review is focused on homogeneous catalytic oxidations in dense CO_2 media. Historically, emphasis has rested on scCO_2, and the many advantages of that medium over traditional solvents are first discussed. Attention is then directed to the still greater advantages of CO_2 expanded organic solvents; these are new media that were first introduced for oxidation reactions in our laboratories. These extremely variable solvent systems retain solubility characteristics of the two combined solvents and still enjoy the environmental advantages of more familiar dense CO_2 media. A CO_2-expanded organic solvent medium is produced by increasing the volume of an organic solvent through the addition of relatively large amounts of CO_2, whereas the 'cosolvent' concept has traditionally been referred to the addition of relatively small amounts of organic solvent to dense CO_2 phases to improve the solubilities of certain compounds. A thumbnail sketch of known homogeneous transition metal catalyst systems is then offered from the viewpoint of investigators concerned with their study in dense CO_2 media. Preferred terminal oxidants are recognized and some well known four-component catalyst systems are mentioned to illustrate those considerations that must be brought along when the newer media are to be used. At this point, the reported catalytic studies of reactions are summarized, with heterogeneous examples described first, followed by the more recently opened subject of homogeneous transition metal catalyst systems in dense CO_2 media. Most of those earlier studies employ $scCO_2$. The authors then turn to their perspective on the subject and present their contribution to the field, including a number of systems explored for the first time and discovery of the potential of chemical reactions in CO_2-expanded organic solvents. Suggestions for future research complete the review.

2. Advantages of $scCO_2$

2.1. General

Carbon dioxide is considered environmentally acceptable, non-toxic, relatively cheap (3–5 cents lb^{-1}), non-flammable, inert toward oxidation and readily available. Supercritical reaction media, in general, have the potential to increase reaction rates, to enhance the selectivities of chemical reactions and to facilitate relatively easy separation of reactants, products, and catalysts after reaction. At ambient temperatures, the solubility of the much-favored terminal oxidant, atmospheric oxygen, in water and conventional organic solvents is limited. However, oxygen and carbon dioxide mixtures are miscible in all proportions under sc conditions. The increased concentration of reactants within an sc phase has the potential to accelerate reaction rates. In addition, the elimination of interphase (gas–liquid) mass transfer resistances may also increase reaction rates. The one-to-two orders-of-magnitude higher intrinsic diffusivities of solutes in sc media compared to organic solvents could also accelerate reactions in the case of processes wherein the overall rate of reaction is limited by diffusion of reactants to form encounter pairs, which subsequently react to form products. The solubilities of solutes in sc fluids depend strongly on pressure and temperature in the vicinity of the critical point. Therefore, the reactants, the products and the catalyst can be separated by relatively simple pressure and/or temperature programming. Furthermore, if the phase behavior of the reaction mixture is such that the products fall out of the reaction mixture at the reaction P and T, in situ product separation is achieved. However, in the case of CO_2, the dielectric constant remains virtually unaffected over a wide range of pressure. Thus, pressure-tuning effects in the sc region on conversion and selectivity may be investigated with minimal change in solvent dielectric constant. Reviews of reactions in sc media are provided elsewhere [1].

2.2. Enhancement of catalyst solubilities in $scCO_2$

A variety of amorphous fluoropolymers exhibit excellent solubilities in $scCO_2$. Yazdi and Beckman show that poly(hexafluoropropylene oxide) with a molecular weight of about 13 500 is completely miscible with CO_2 at 150 bar and room temperature [2]. Kainz and coworkers have shown that perfluoroalkyl substituents increase the solubility in $scCO_2$ of arylphosphanes and their rhodium complexes [3]. Also, Lin and coworkers have reported the extraction of lanthanides and actinides from solid samples with fluorinated β-diketones dissolved in $scCO_2$ [4]. Similarly, fluoropolymers such as poly(chlorotrifluoroethylene) and other fluorinated polyacrylates have solubilities on the order of 10 wt% or more. Copolymers of fluorinated acrylates with methacrylate, *n*-butyl acrylate, styrene and ethylene are also reported to be highly soluble in $scCO_2$ and could actually be synthesized by solution polymerization in $scCO_2$ [5]. These copolymers are additional candidates for enhancing the solubilities of oxidation catalysts in $scCO_2$. More recently, poly(ether-carbonate) copolymers were designed as low-cost, fluorine-free alternatives that readily dissolve in CO_2 at lower pressures [6]. The work of Suleiman et al. shows the possibility of solubilizing quaternary ammonium salts and 18-crown-6 in $scCO_2$ [7]. Exploiting this, the nucleophilic displacement on benzyl chloride by bromide ion in the presence of tetraheptyl ammonium bromide was demonstrated as an example of a phase transfer catalytic process between a solid salt phase and an sc phase. Inorganic salts can therefore be ‘dissolved’ in $scCO_2$ in this manner, including KMnO4, which yields ‘purple CO_2’ which is similar to purple benzene, achieved with crown ethers as the complexing agents. It has also been shown that emulsions and reverse micelles of *water solutions* can be stabilized in $scCO_2$ by fluorinated surfactants [8].

2.3. Advantages of dense CO_2-expanded solvent media

Recent results in these laboratories revealed that dense CO_2-expanded solvent media open a new way towards environmentally benign oxidation catalyst systems for such important chemical reactions as olefin epoxidation and functional group oxidation. Adding CO_2 to solvents having significant solubilities in CO_2 ‘expands’ the solvent while decreasing the solubilities of the dissolved solutes in the mixture [9]. One might also expect the miscibility of gases (such as O_2 and H_2) to be higher in CO_2-expanded solvents relative to the neat organic solvent. Dense CO_2 (mostly at subcritical pressures) is used to replace most of the traditional organic solvent (typically $>75\%$ by volume), such that catalyst solubility is maintained, oxidant solubility in the CO_2-expanded organic phase is enhanced (especially for dioxygen), and the advantages of the traditional solvent are also preserved (polarity, dielectric constant, etc.). In these mixed media, the environmentally benign nature of CO_2

and the advantages of traditional solvents are combined in an optimal manner. Advantages include flexibility of solvent choice, enhanced reaction rates and product selectivity, and much lower operating pressures (tens of bars) compared to processes utilizing $scCO_2$ (hundreds of bars).

3. Suitability of synthetic homogeneous transition metal catalysts for dense CO_2 media

3.1. Essential elements of these catalytic systems

The literature on homogeneous transition metal catalysis constitutes a vast reservoir in which to seek systems appropriate to the elucidation of catalytic oxidation reactions in dense CO_2 media and provides the basis for designing new catalysts. Transition metal catalytic oxidation systems consist of at least four critical components: the catalyst, the substrate, the terminal oxidant, and the medium. Classified on the basis of critical intermediates in the oxidation processes, researchers recognize at least three kinds of such catalytic oxidation systems: those involving high valent oxo complexes of transition metal ions, e.g. $Fe^{n+}=O$ and $Mn^{n+}=O$; those involving peroxy complexes, e.g. derivatives of Ti^{4+} and Mo^{6+}; and those involving organic and/or inorganic radical intermediates, the classic example being Fenton's reagent.

Three terminal oxidants stand out because of their environmentally benign characteristics, and their ready availability and low cost; O_2 from the air, hydrogen peroxide, and a small number of hypochlorite salts (Na^+, Ca^{2+}, and Li^+). Many more relatively expensive or exotic oxidants have also been studied extensively, among which are iodosobenzene and its siblings, peroxy acids like *m*-chloroperoxybenzoic acid and monoperoxysulfuric acid, alkyl peroxides, especially *t*-BuOOH, and amine oxides.

Substrates are global and may be sorted according to reactivity, ranging over saturated hydrocarbons having primary, secondary and/or tertiary hydrogens, aromatic hydrocarbons, alkenes of various reactivities, alkynes, and various functional groups including derivatives of oxygen, sulfur, nitrogen, phosphorus, and other elements.

The transition metals vary with the catalyst type and some compounds of most of these elements show some activity, including manganese, iron, chromium, copper, cobalt, nickel, vanadium, titanium, ruthenium, osmium, rhodium, iridium, palladium, platinum, molybdenum, tungsten, and rhenium. Not uncommonly, a given catalyst system has evolved a favored solvent system and/or a favored terminal oxidant. For obvious reasons, certain systems are restricted to aqueous media, examples including detergent bleach enhancers and lignin oxidants. Others favor such solvents as methanol, *tert*-butanol, methylene chloride and toluene.

The catalyst systems summarized in Table 1 offer one or more advantages for oxidations in dense CO_2 media: related to important commercial systems, miscibility of both oxidant and/or catalyst in the reaction mixture, readily available at

Table 1
Terminal oxidant/homogeneous catalyst complements

Type	Terminal oxidant	Catalyst	Applications
I	H_2O_2 or derivatives	(a) Manganese complexes of 1,4,7-trimethyl-1,4,7-triazacyclononane derivatives; or (b) Manganese bridged cyclam complexes; or (c) CH_3ReO_3, possibly with *tert*-butanol cosolvent and/or phase transfer catalyst. (d) Ti(IV), V(V), and Mo(VI) compounds	Epoxidation of olefins, functional group oxidation and bleach enhancers for the emerging dense CO_2 dry-cleaning industry.
II	O_2	(a) cobalt and other transition metal *salen* derivatives with cosolvent; (b) other cobalt(II) O_2 carriers; (c) (α,β,γ,δ-*tetra*-mesitylporphyrinato) ruthenium with benzene cosolvent; or (d) perhalogenated porphyrin complexes of iron, manganese, chromium, or cobalt with suitable cosolvent.	Vary with catalyst from selective functional group oxidation to olefin epoxidation and even small hydrocarbon oxidation.
III	Aqueous NaOCl	Mn, Fe, or Cr complexes of Schiff bases called salen derivatives; co-solvent; possibly phase transfer catalyst	Olefin epoxidation and functional group oxidation.

reasonable cost, unusual reactivity. As described later, significant advantages of using dense CO_2 media and/or $scCO_2$ with a few of these systems have already been demonstrated. Ligand structures are given in Fig. 1.

Except for Ic, the catalysts are modifiable to some extent, and Ia, Ib, Id, II, and III are easily varied, so that their solubilities can be altered by structural changes and they can be attached to various organic or inorganic supports by covalent linkages.

3.2. Type I systems — those using hydrogen peroxide as a terminal oxidant

The development of detergents [10] that are active in dense CO_2 and the possibility of a new technology for the dry cleaning [11] of clothing in dense CO_2 presages a need for homogeneous catalytic systems that are functional *bleaches* in that medium; i.e. oxidation catalysts that promote the oxidation of stains and soils by peroxides in dense CO_2. This further motivates investigation of catalytic and peroxidatic action of homogeneous catalysts in dense CO_2. Looking more broadly, H_2O_2 is an attractive terminal oxidant because it is readily available, inexpensive, and gives only water as a byproduct when oxidizing a substrate.

A consumer cleaning product [12] containing a dimanganese complex of *N*,*N*′,*N*″-trimethyl-1,4,7-triazacyclononane (Me_3TACN) as a bleach enhancer in the usual aqueous media was marketed in the industry and the possibility exists that such derivatives might be effective in $scCO_2$ (see Fig. 1). Recently, a group of Unilever chemists reported that the related monomeric manganese(IV) complex of Me_3TACN, $[Mn^{IV}(Me_3TACN)(OMe)_3]PF_6$, is a long-lived catalyst for the oxidation of olefins by H_2O_2 in water [13]. Whereas the 4-vinylbenzoic acid yielded only the corresponding epoxide, the styrylacetic acid was converted to a mixture of products, including the epoxide, and its derivatives, a glycol and a lactone. De Vos and Bein found that the competition between O_2 evolution, solvent oxidation, and olefin epoxidation was strongly sensitive to conditions [14]. For styrene in aqueous media, a peroxide/substrate ratio of 100/1 was required to convert most of the substrate to product, because of O_2 evolution, versus complete conversion with 98% selectivity, based on peroxide/substrate ratios of < 2, in acetone at room temperature and 0°C. The reactions of $Mn(Me_3TACN)$ differ from manganese porphyrins [15] in enhanced alkene isomerization and more limited alkane oxidation. Use of $Mn(Me_3TACN)$ in $scCO_2$ will require temperatures in the 35–100°C range.

Enantioselective olefin epoxidation has been reported in the presence of a manganese complex of a chiral 1,4,7-triazacyclononane derivative [16]. A complex of this class has been supported on a mesoporous MCM-41 siliceous material and the catalytic properties of the complex are retained [17]. $Mn(Me_3TACN)$ and Mn(TACN) have also been studied in microporous zeolite environments [18]. A particular advantage of this class of complex is the ease with which the ligand may be modified without substantially altering the chemistry at the active site, as illustrated by the previous studies. This provides the opportunity to modify the structure to enhance solubility in the desired medium and to mount the catalyst on either conventional supports or into macroporous templated polymers.

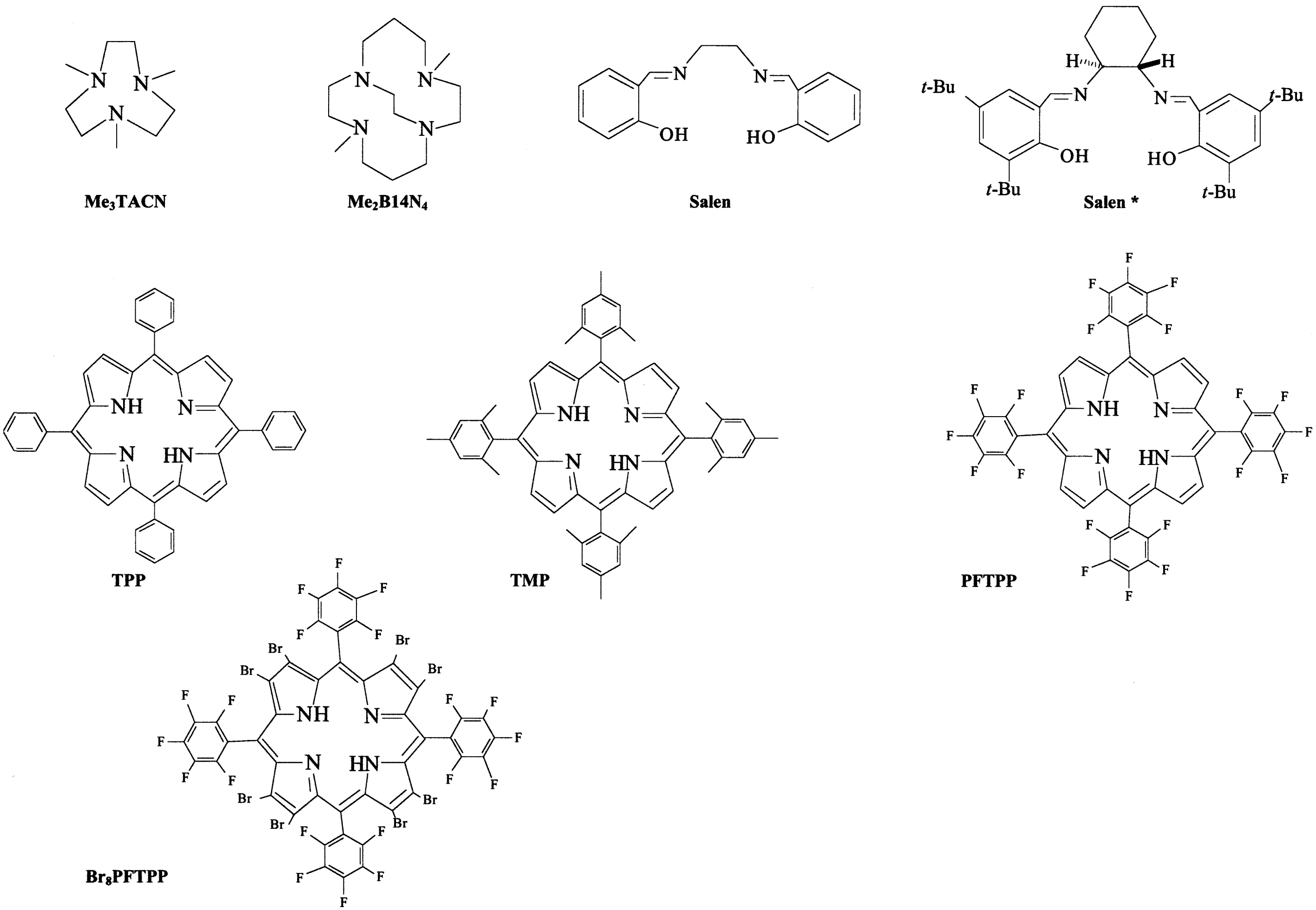

Fig. 1. Structural formulas for the ligands discussed in this review. The abbreviations appearing beneath formulas are used in the chemical formula of complexes to identify the family of the complex.

Methyltrioxorhenium, CH_3ReO_3, is a remarkable catalyst for the oxidation of olefins. It is a volatile, but stable, off-white crystalline solid that is soluble in most solvents ranging from hexane to water [19]. Although many alkyl and aryl trioxorhenium compounds exist, CH_3ReO_3 is uniquely stable and useful in catalysis. In the catalytic epoxidation of olefins by CH_3ReO_3, hydrogen peroxide is used as terminal oxidant and *tert*-butanol is the usual solvent of choice [20]. Catalytically active intermediates are formed by the binding of peroxide to rhenium, one or two peroxide ions replacing oxide ligands [19], $CH_3ReO_2(O_2)$ and $CH_3ReO(O_2)_2$. Thus this catalyst represents those having peroxides as reactive intermediates, in contrast to the porphyrins and salens, for example, in which the high valent metal oxide is the critical structural feature of the active intermediate. The CH_3ReO_3 catalyst shares this property with the molybdenum catalysts of the Halcon process. The reactivity of the CH_3ReO_3/H_2O_2 system is broad-ranging and powerful including as substrates alkenes, alkynes, aromatic compounds, sulfur compounds, amines and other organo-nitrogen compounds, arsines, phosphines, stilbenes, halide ions and oxygen insertion into C–H bonds [21]. Because of its great reactivity, CH_3ReO_3 is an ideal candidate for characterization of this class of oxidation catalysts, using H_2O_2 in $scCO_2$. As discussed in Section 6.2, CH_3ReO_3 is sufficiently soluble in $scCO_2$ in the presence of co-solvents to afford many catalytic oxidations. Furthermore, as H_2O_2 is not soluble in $scCO_2$, two attractive alternatives merit investigation: (1) other similar terminal oxidants (perfluorinated carboxylic acids, for example) that are more soluble in $scCO_2$, and (2) a phase transfer catalyst may facilitate oxidation in the two-phase system. We have developed an entirely new family of catalysts showing great promise in such consumer products as laundry detergents [22]. These compounds are based on the manganese complexes of the 2-carbon cross-bridged tetraazamacrocycles first reported by Weisman (see Fig. 1) [23]. The short *trans-spanning* bridge locks the macrocycle into an ultra rigid folded structure that produces metal complexes of exceptional kinetic stability [24]. The new catalysts effectively promote oxidation of many substrates using hydrogen peroxide as the terminal oxidant, including olefins, certain functional groups and common stains and dyes used to model practical systems. Because of their structures, these cross-bridged macrobicycles are readily modified, for example by adding long chain alkyl groups to alter the solubilities of their complexes in various solvents, or by adding dangling functional groups to incorporate the catalysts in polymer structures. Since the complexes are cations, their counter anions also offer facile control over solubility properties.

3.3. Type II systems — those using dioxygen as terminal oxidant

For reasons basic to environmentally safe catalysis and economy of operations, the dioxygen in the air is particularly attractive as the terminal oxidant for industrial processes. Further, as indicated earlier, the relatively great miscibility of O_2 with $scCO_2$ offers the possibility that, under relatively mild conditions, dioxygen might react more rapidly and vigorously in $scCO_2$ than in water or other common solvents. A few select systems are particularly appropriate for investigation of homogeneous catalytic oxidation reactions using O_2 in $scCO_2$.

Quinn and Groves found that Ru(TMP) (see Fig. 1), catalyzes the epoxidation of olefins by dioxygen, implicating the corresponding dioxoruthenium(VI) complex in the process [25]. They point out the failure of the related (*tetra*-*o*-tolylporphrinato)ruthenium(II) complex to act similarly and that this identifies the critical role played by the *ortho*-buttressing of the mesityl group. Otherwise, the oxidized ruthenium forms oxo-bridged dimers which are catalytically inactive. Hirobe and associates have shown that Ru(TMP) is also effective in the epoxidation of olefins, and in the oxidation of certain alkanes and alcohols, using heteroaromatic *N*-oxides as terminal oxidants [26]. The O_2/Ru(TMP) system has been studied extensively for epoxidation of steroids [27]. The limited data available suggests that the epoxidation is somewhat selective at near-ambient conditions, and the usual solvent medium is benzene, suggesting that the catalyst might have some solubility in $scCO_2$. The catalytic process in the usual solvents is slow and substrates compete with O_2 suggesting that $scCO_2$ could offer some advantages for the system substrate/O_2/Ru(TMP)/$scCO_2$. For a general review, see Mlodnicka and James [28].

The Schiff base condensation of ethylenediamine with salicylaldehyde produces a dinegative linear tetradentate ligand, abbreviated as salen, that has two imine and two phenolate coordinating groups, and much variation in structure can bring by substitution at various positions on the reactants (see Fig. 1). Most of the divalent transition metal ions form complexes with salen and its derivatives and one or two additional ligands may bind, raising the coordination number to 5 or 6. The resulting metal complexes have long been known because their cobalt(II) complexes were the first synthetic compounds found to bind the dioxygen molecule reversibly. In the present decade, the ligands became famous again, this time for the catalysis of oxidation reactions by their manganese and chromium adducts, most specifically, epoxidation of olefins. Both functions are of interest to this discussion. The dioxygen binding abilities, especially of the cobalt(II) complexes are especially interesting because of the substantial literature [29] on substrate oxidations using these as homogeneous catalysts and using O_2 as the terminal oxidant, and because many examples are known and because they are easily prepared at low cost [30].

The O_2 carriers containing cobalt(II) have long been viewed as potential oxidation catalysts. It is, however, unfortunate that these systems have a long history of only being effective in facilitating the oxidation of relatively reactive substrates, such as aldehydes and phenols. Classic work focusing on the oxidation of phenols has implicated phenoxy radicals in the early stages of these reactions, accounting for the reactivity of those substrates [31]. As discussed in Section 6.3, cobalt(II) dioxygen carriers are shown to be more effective for the oxidation of phenols in the CO_2 media. It is tempting to suggest that the higher activity of dioxygen in $scCO_2$ solutions might expand the range of substrates subject to catalysis by these abundant and well known compounds. The same O_2 solubility advantage may accrue to polyhalogenated porphyrin systems first exploited by Lyons and Ellis [32]. These catalysts have attracted attention for oxidation of resistant substrates such as saturated hydrocarbon and lignin under moderate conditions and for their abilities to survive the catalytic process [33].

3.4. Type III systems — those using hypochlorite as a terminal oxidant

Common bleach, aqueous sodium hypochlorite, is the terminal oxidant of choice for epoxidations using manganese complexes of various salen derivatives. Oxidations by the manganese, chromium and nickel complexes of many salens was first reported by Kochi [34], quickly followed by Burrows [35], and much of the early work with these ligands made use of iodosylarenes as oxidants [36]. Yoon and Burrows introduced hypochlorite as a much more desirable oxidant because of its greater effectiveness, extremely low cost, non-explosive nature, and essentially harmless byproduct, NaCl. Epoxidations were performed under phase transfer conditions using aqueous hypochlorite and a CH_2Cl_2 solution of alkene substrate and benzyltributylammonium bromide as the phase-transfer catalyst. Substituted manganese(II) salens are most attractive epoxidation catalysts because of the extensive studies demonstrating the achievement of high levels of enantioselectivity [37]. Phase transfer catalysis between buffered aqueous NaOCl solutions and immiscible organic solvents have been used over a range of scales. The solvent CH_2Cl_2 is convenient in the lab, but 1,2-dichloroethane, toluene, ethyl acetate, and *t*-butyl methyl ether are also used, with little change in catalytic efficacy. The salen derivative catalyst, [*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminato(2-)]manganese(III) chloride has been prepared on the multihundred kilogram level [38].

The several systems described above have been discussed to provide a background for the studies that have been conducted in dense CO_2 media. There are, of course, many more important systems. Porphyrins, especially those of iron, manganese, and chromium, have been most extensively explored [39],[1] providing much of the understanding of the field. Illustrative of other systems are a bleomycin model that is a powerful non-heme oxidation catalyst [40], a possibly more selective lipoxygenase model containing iron and a pentadentate ligand [41], dinuclear complexes that model methane monooxygenase [42], other early transition metal catalysts for peroxide oxidations [43,44] in the mode of the Halcon process [44], and the GIF catalyst systems [45]. Regrettably, because of the vastness of the field, we cannot hope to mention many fascinating systems and results.

4. Heterogeneous catalytic oxidations in $scCO_2$

Despite the attractive nature of $scCO_2$ as a reaction medium, only a small number of catalytic oxidation studies have been reported. The first publications on catalytic oxidation reactions in dense CO_2 involved heterogeneous catalysis. In the year 1987, such an early study by Dooley and Knopf reported aerobic heterogeneous catalytic oxidation of toluene, mostly to benzaldehyde, using a range of oxide and mixed-metal oxide catalysts [46]. The metal oxides were supported on alumina

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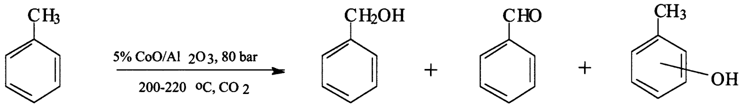
[1] To conserve space, we cite two books that contain excellent summaries of the field by many of its leaders and a few additional selected reviews.

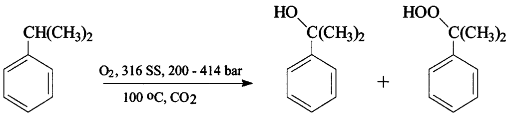
and had the following compositions: 5% CoO, 5% CoO/10% MoO_3, 10.5% MoO_3, 19% W/6% Ni, and Si/Al_2O_3. The latter provided an acid catalyst to compare with the redox catalyst. The 5% CoO/Al_2O_3 was calcined at 200°C to preclude conversion to Co_3O_4, which was found to be less active as a catalyst. Toluene was successfully oxidized to benzaldehyde, benzyl alcohol and cresol isomers, and a small amount of condensation products and carbon dioxide (Scheme 1). Addition of small amounts of benzoic acid to the reaction mixture accelerated the reaction and was reported to have been co-oxidized to CO_2 and water. Benzoic acid is typically one of the most stable products of catalyzed toluene oxidations in conventional solvents. However, the authors indicated that under their experimental conditions (0.7 mol% toluene, 2.0 mol% O_2, 5 wt% N_2, reaction temperature between 400–500 K and total pressure of 80 bar) benzoic acid is unstable.

Also early on, McHugh et al. reported the aerobic oxidation of isopropyl benzene, cumene, in the presence of cumene hydroperoxide to cumyl alcohol and cumene hydroperoxide in $scCO_2$ at 110°C (Scheme 2), and pressures ranging from 200 to 414 bars in stainless steel and gold plated reactors [47]. They proposed a radical chain reaction mechanism and suggested initiating, propagation and termination steps. The oxidation is initiated by homolytic cleavage of cumene hydroperoxide and propagated by converting O_2 to hydroperoxide. The authors also found that polarity and viscosity of the reaction media have a minimal effect both in the oxidation as well as in the critical point of the mixture. However, in the critical region, the presence of metal reactor increased the rate of the termination step and lowered the selectivity to cumene hydroperoxide, when compared to the reaction in the absence of metal.

Akgerman and coworkers reported a high temperature (300°C) and high pressure (89.6 bar) catalytic oxidation of ethanol and acetaldehyde over a 4.45% Pt/TiO_2 catalyst in $scCO_2$ [48]. The oxidation, at 5:1 oxygen/ethanol molar ratio, produced acetaldehyde, carbon dioxide and trace amounts (less than 2%) of carbon monoxide. But at an oxygen/ethanol molar ratio of 4.7:1, acetaldehyde is completely oxidized to carbon dioxide and only trace amounts of carbon monoxide. The authors suggested a combination of parallel and consecutive reaction mechanisms for ethanol oxidation and a dissociative adsorption of acetaldehyde on the catalyst surface with surface reaction rate control for the acetaldehyde oxidation.



Scheme 1. CoO/Al_2O_3 catalyzed aerobic oxidation of toluene.



Scheme 2. Stainless still catalyzed oxidation of cumene.

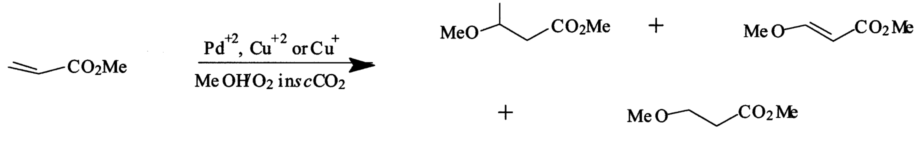
Gaffney and Sofranko [49] examined the feasibility of heterogeneous propylene epoxidation to propylene glycol in a stream of propylene, water, and air in CO_2 at sc conditions (140°C and 140 bar). Of the several solid-supported catalysts evaluated, optimal results were reported with an α-Al_2O_3 supported $CuI/Cu_2O/MnO_2$ catalyst. However, the authors concluded that the production rate was about an order of magnitude too low for commercialization purposes.

Fan et al. [50] reported on the oxidation of isobutane to *tert*-2-butyl alcohol (TBA), using air as an oxidant, using supercritical isobutane ($P_c = 36.5$ bar; $T_c = 135$°C) as the reaction medium. Among various catalysts investigated, SiO_2–TiO_2 and Pd/C were found to be most efficient, albeit with yields $<5\%$ at 54 bar and 255°C.

In 1998, Wang and Willey investigated the aerobic oxidation of methanol on iron oxide or molybdenum aerogels [51]. The partial oxidation of methanol, at temperatures of 200–300°C and a total pressure of 90 bar, yielded dimethyl ether, methyl formate and formaldehyde at conversions greater than 80%. The product distribution was found to be affected by the nature of the catalyst and temperature. Pure iron oxide favored dimethyl ether formation, while low levels of iron oxide on silica favored methyl formate, and iron oxide on molybdenum favored formaldehyde production. At temperatures greater than 300°C, the production of CO_2 was the sole product due to complete combustion of methanol and its intermediate oxidation products. Janzer and coworkers have also reported the aerobic partial oxidation of water-insoluble alcohols in $scCO_2$ over a Pd–Pt–Bi/C catalyst with high reaction rates and up to 98% yields [52].

In a recent study, aerobic oxidation of acrylate esters to acetals by $PdCl_2$, $PdCl_2(CH_3CN)_2$, $CuCl_2$ and CuCl in the presence of methanol in $scCO_2$ was reported by Jia and coworkers [53]. They report that 1 ml of MeOH was added as a co-solvent to partially dissolve the catalysts, but that the MeOH also functions as a reactant. The authors found that the CO_2 pressure, O_2 concentration and temperature affect conversion and selectivity of the reaction. At optimum reaction conditions (120–130 bar total pressure, 40°C, 10 bar oxygen pressure) more than 96% selectivity for the 3,3-dimethoxylpropanoate was obtained (Scheme 3).

Oakes and coworkers reported the diastereoselective oxidation of cysteine derivatives in $scCO_2$ using *t*-BuOOH and Amberlyst 15 ion exchange resin catalyst [54]. The method, even with excess oxidant, produced high yield and good selectivity for the sulfoxide formation (Scheme 4). At constant temperature (40°C), the product selectivity was sensitively tuned with pressure. The major isomer selectivity for the oxidation of CysSMe–OMe was nearly 100% at 180 bar but falls off as the pressure



Scheme 3. Aerobic oxidation of acrylate esters by PdCl, $PdCl_2$, CuCl and $CuCl_2$.

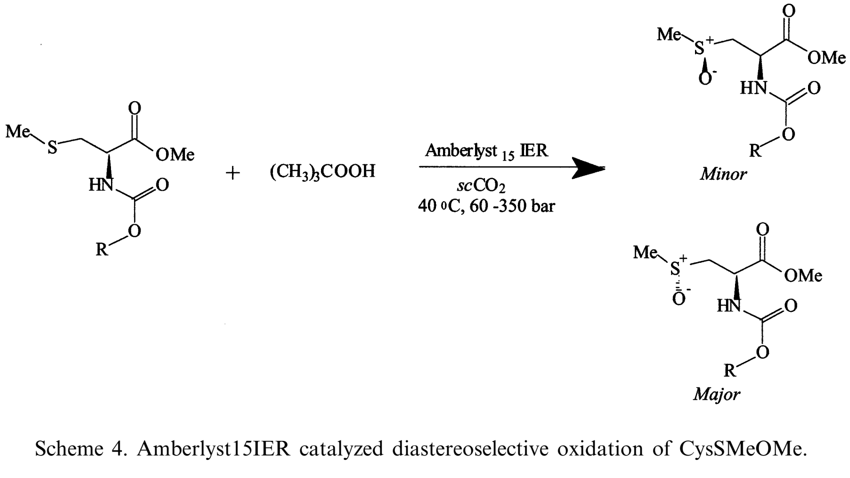
is increased further. The fact that no diastereoselectivity is observed in conventional solvents reveals a clear advantage of $scCO_2$ media in inducing setereoselectivity.

Recently, Loeker and Leitner have reported that steel promotes the aerobic oxidation of olefins in the presence of aldehydes. The authors discovered that the epoxidation is particularly effective for long-chain terminal olefins or for those substrates having internal double bonds [55].

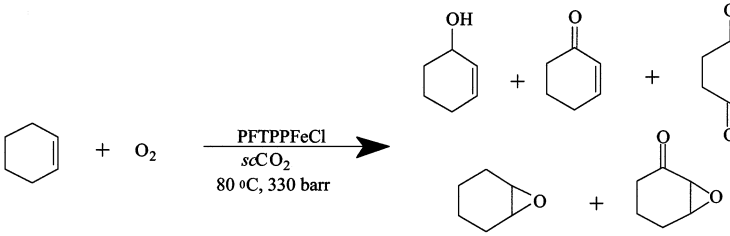
5. Homogeneous catalytic oxidations in $scCO_2$

Relatively recently, homogenous catalytic oxidations in $scCO_2$ and closely related media have been explored by a number of research groups, including ours. The advantages, as stated above, include complete miscibility of the oxygen in $scCO_2$, the replacement of organic solvents by environmentally benign $scCO_2$, and the resistance of CO_2 toward oxidation. The majority of the reported oxidation studies in $scCO_2$ can be grouped into alkene, alkane and alcohol oxidations.

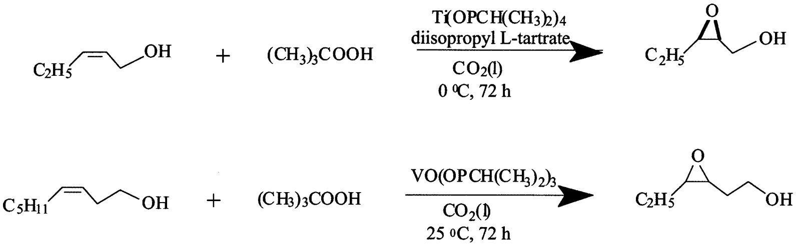
Tumas and coworkers pioneered the homogenous catalytic oxidation of alkenes in $scCO_2$. Cyclohexene was oxidized by oxygen using halogenated porphyrins as catalysts. PFTPPFeCl and Br_8PFTPPFeCl were employed as catalysts under rather harsh conditions, 80°C and total pressure of 345 bar [56]. The oxidation yielded five products, cyclohexene oxide, 2-cyclohexene-1-ol, 2-cyclohexene-1-one, oxabicyclo[4.1.0]heptan-2-one and 4-hydroxy-2-cyclohexene-1-one (Scheme 5). The total replacement of organic solvents was successfully achieved, but the turnover numbers were noticeably lower than those commonly found in such organic solvents as benzene, methylene chloride or acetonitrile. For example, under the same reaction conditions using PFTPPFeCl as the catalyst, the turnover numbers for reactions in benzene, methylene chloride and $scCO_2$ are 1520, 2170 and 580 h^{-1}, respectively. It is also found that the product distribution is influenced by changes of pressure and temperature. Specifically, the selectivity in favor of epoxidation for the



Scheme 4. Amberlyst15IER catalyzed diastereoselective oxidation of CysSMeOMe.



Scheme 5. PFTPPFe^{III}Cl catalyzed aerobic oxidation of cyclohexene.



Scheme 6. Vanadium (V) and titanium (VI)-catalyzed oxidation of allylic and homoallylic alcohols by TBHP.

Br_8PFTPPFeCl catalyzed reaction more than doubled, increasing from 14 to 34%, when the temperature was increased from 40 to 80°C. This sensitivity of the reaction to the temperature and pressure changes suggests relatively easy tunability of reaction conditions.

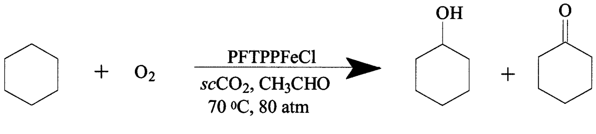
Morgenstern et al. [57] demonstrated the ruthenium-mediated two-phase oxidation of cyclohexene to adipic acid in which high-valent (and more volatile) ruthenium *oxo*-complexes are transferred from an aqueous phase containing the NaOCl catalyst to the $scCO_2$ phase (containing the solubilized organic substrate) in which the reaction occurs.

In another study, Tumas' group has reported selective oxidation of activated alkenes, allylic and homoallyilic alcohols, in dense phase CO_2 using *t*-BuOOH as the terminal oxidant and high valent metal complexes as catalysts [58]. Although superior yields and selectivity were obtained in the case of $VO(OPr^i)_3$, complexes such as $VO(acac)_2$, $Mo(CO)_6$ and $Ti(OPr^i)_4$ showed catalytic activities as well. The authors also found that in the presence of chiral tartrate ligands, such as diethyl tartrate and diisopropyl tartrate, $Ti(OPr^i)_4$ achieved enantioslective epoxidation (Scheme 6). At 25°C, only 16% of enantiomeric excess (ee) was obtained at 93% conversion for the expoxidation of (*Z*)-pent-2-en-l-ol in the presence of diisopropyl L-tartrate. But at a lower temperature (0°C), the enantioselectivity increased to 87% along with a total conversion of 99%.

At about the same time Tumas' group developed the $VO(L)_2$/*t*-BuOOH systems, Hass and Kolis designed and synthesized a vanadium(IV) catalyst using a Schiff base ligand [59]. Epoxidation of a group of allylic alcohols was successful using the new catalyst at 1:1 substrate to *t*-BuOOH mole ratio, 45–50°C and 213 bar of pressure. The authors claimed that the yields and diastereoselectivities obtained in the $scCO_2$ medium are comparable to those obtained in traditional organic solvents.

Possibly because of its ready solubility in $scCO_2$, $Mo(CO)_6$ has been used as an oxidation catalyst by a number of research laboratories. Tumas and coworkers showed selective catalytic epoxidation of allylic and homoallylic alcohols with *t*-BuOOH and $Mo(CO)_6$. To their surprise, they found that the $Mo(CO)_6$ catalyzed oxidation of cyclohexene using 90% *t*-BuOOH/H_2O as terminal oxidant gave significantly higher conversions than corresponding reactions using dry *t*-BuOOH/decane. Independently, Haas and Kolis examined the oxidation of a variety of other unactivated alkenes using the same catalyst [60]. Based on the nature of the applied alkene, epoxidation as well as other C–C bond cleavage products were obtained. Under wet reaction conditions, hydration of the epoxide to produce 1,2-diol was noted. These workers also pointed out that C–C bond cleavage is observed only in instances where the alkene to be oxidized contains phenyl substituents, such as stilbenes and styrenes. For example, at 95°C, 1:3 mole ratio of substrate to peroxide and a total pressure of 213 bar, the oxidation neatly produced 50% conversion to benzaldehyde in a period of 3 h. The authors also found that the rates of diol and epoxide formation are considerably faster for *cis*-alkene than for *trans*-alkene oxidations. Using $Mo(CO)_6$ or $Ti[OCH(CH_3)_2]_4$ as the catalyst and *t*-BuOOH as the oxidant, Kreher and coworkers successfully epoxidized cyclooctene at lower temperatures, 45°C [61].

Wu and coworkers studied the aerobic oxidation of cyclohexane catalyzed by PFTPPFeCl in the presence of acetaldehyde [62]. Cyclohexane was efficiently oxidized to cyclohexanol and cyclohexanone (Scheme 7). Although no rationale was given, the authors found that, depending on the reaction temperature, the maximum conversion was obtained in the vicinity of the critical pressure of CO_2. In a typical reaction condition at 70°C, 1.0 mmol of cyclohexane, 0.25 mmol of acetaldehyde, 0.5 μmol of catalyst and 1.0 mmol of O_2 and total pressure of 90 bar, a total yield of 5% of cyclohexanol and cyclohexanone was obtained in 1 h reaction time. Although the possibility of heterogeneous catalysis is not explicitly mentioned, the authors point that under their experimental conditions, especially at temperatures less than 70°C and low pressures, reaction mixtures were found to be not completely homogeneous.



Scheme 7. PFTPPFeCl catalyzed aerobic oxidation of cyclohexane.

6. A broad approach to oxidation studies in CO_2 media

6.1. Perspective

Building on the elegant foundations provided by those who preceded us in this fascinating realm, we sought to define a broad approach to the investigations of these systems. In the simplest perspective, such a reaction system consists of a substrate, a terminal oxidant, a catalyst, and a medium in which the reactions occur. Further, the vast literature on homogeneous catalytic oxidations, as described above, reveals select combinations that are most effective when one begins to define a specific system. For example, Jacobson's catalyst, Mn(salen*)Cl, a substituted manganese salen, is famous for enantioselective epoxidations, but the favorite terminal oxidant for that catalyst is aqueous sodium hypochlorite. On the other hand, the catalyst itself is most soluble in organic solvents of low polarity — the same as many of its preferred olefin substrates. Clearly this is a system that performs well via phase transfer catalysis.

In contrast, CH_3ReO_3, which is also a highly effective epoxidation catalyst (but not enantioselective), is soluble in most media and its preferred terminal oxidants are peroxides, especially hydrogen peroxide. Many solvents are at least partially miscible with $scCO_2$ and may serve as co-solvents with it. This is not so for water — but common solvents like methanol, DMF, methylene chloride, and acetonitrile do act as co-solvents with $scCO_2$. It follows that, in defining a specific homogeneous catalytic system, it is not enough to define the four key components. They immediately demand more detailed attention in order to handle the special requirements associated with their mutual compatibilities. These are discussed for the few examples that follow.

6.2. Oxidation of alkenes with CH_3ReO_3 and *t*-BuOOH

As our first venture into homogeneous oxidation catalysis in $scCO_2$, we chose CH_3ReO_3 and olefin epoxidation reactions. For this case the substrates and terminal oxidant are readily soluble in $scCO_2$, but the preferred terminal oxidant, hydrogen peroxide, is only conveniently available in aqueous media. Three obvious possible choices were: (1) transfer catalysis between water and $scCO_2$; (2) working with nearly dry hydrogen peroxide; and (3) using a different terminal oxidant. We chose *t*-BuOOH as an appropriate alternative terminal oxidant because it could be used in fully homogeneous systems during those early explorations.

Our initial studies were performed in a 60 ml Jurgeson cell similar to those used in sc precipitation studies [63]. Reactions were run by first introducing known amounts of the substrate, catalyst and oxidant (*t*-BuOOH) into the cell (see footnote of Table 2 for exact composition). Next, CO_2 was pumped into it by bubbling through the reaction mixture until the total cell pressure reached approximately 83 bar at 50°C. We studied the catalytic oxidation of various alkenes (see Table 2) by *t*-BuOOH and CH_3ReO_3 in $scCO_2$. In all cases, the reaction mixture was completely homogeneous. In the absence of the peroxide, however, to our

Table 2
Products and yields of alkenes oxidized with CH_3ReO_3 in $scCO_2$

Alkene	Product(s) (yield %) [a]
Cyclohexene	Cyclohexene oxide (38) Cyclohexanediol (26)
Styrene	Styrene oxide (18) Benzaldehyde (53)
cis-Stilbene	*cis*-Stilbene oxide (35) Benzaldehyde (27)
trans-Stilbene	*trans*-Stilbene oxide (30) Benzaldehyde (30)

[a] Reactions were run with 0.08 mmol of catalyst, 10 mmol of alkene and 20 mmol (2.4 ml) of the 70% w/w *t*-BuOOH (residue is *t*-BuOH) at 83 bar and 50°C, for a reaction time of 48 h.

surprise, the CH_3ReO_3 catalyst showed only slight solubility in $scCO_2$ alone. Fortunately, *t*-BuOOH/*t*-BuOH is an effective cosolvent in addition to being the oxidant in this system. As shown in Table 2, a variety of alkenes, including cyclohexene, styrene, *cis*- and *trans*-stilbenes, were successfully oxidized. Whereas the oxidation of cyclohexene yielded products only by O-atom transfer mechanism, the rest of the substrates also yielded benzaldehyde via C–C bond cleavage. The 1,2-cyclihexanediol is produced by hydration of cyclohexene oxide, presumably from traces of moisture in the reactants and from water formed in the reaction. Hence, in a dry environment, yield of the oxide would be higher. Our results indicate that $scCO_2$ is a viable solvent for this catalyst system.

6.3. Oxidation of substituted phenols with Co(salen) and dioxygen*

Oxygen is completely miscible with CO_2, in sharp contrast the limited solubility of oxygen in most solvents (on the order of a few millimoles per liter). Hence, clear advantages are expected for oxygen in $scCO_2$ and other CO_2 derived media. The cobalt(II) dioxygen carriers have long been studied as catalysts for the oxidation of phenols in organic media, but they are modest oxidation catalysts at best. It follows that there are two good reasons for testing their proficiencies as catalysts in $scCO_2$: (1) they are catalysts that use O_2 as terminal oxidant and (2) they just might be more accomplished catalysts at high concentrations of oxygen. The catalysts chosen were the parent of the family of cobalt/salen complexes, Co(salen) itself, and a second member of the family selected because its ligand imparts high solubility to metal complexes in non-polar solvents; this is the ligand of Jacobson's catalyst.

For these studies, low-volume reactors were custom-fabricated to facilitate oxidations in $scCO_2$, with metered amounts of oxygen [64]. A schematic drawing of the reactor is shown in Fig. 2. The apparatus is capable of operating at pressures up to 400 bar and temperatures from ambient to 300°C. We used two reactors with different capacities (10 and 17 ml effective reactor volume). The reactors are 316 stainless steel hollow cylinders (Thar Designs) with sapphire windows at each end, sealed by o-rings and screw caps. Each reactor has five ports located on the outer body for connections to a gas inlet system, a sampling system, and a pressure transducer (Validyne DP15), and to accommodate a thermocouple and a liquid injection/safety rupture disc (HIP, 336 bar). All experiments were run in batch mode.

Our investigations show that the cobalt(II) dioxygen carrier using Co(salen*) shows both oxidase and oxygenase activities during oxygenation of the substituted phenols in $scCO_2$ [64]. The catalytic oxidation of DTBP and 35-DTBP in $scCO_2$ were studied in the presence of a large excess of O_2, 207 bar total pressure and a reaction temperature of 70°C. The oxidation of 35-DTBP yielded only traces of products under the same experimental conditions that converted DTBP totally to a mixture of DTBQ and the related product of radical coupling, TTDBQ. Conversion and selectivity were studied as functions of temperature, pressure, and concentrations of catalyst, substrate, and terminal oxidant. Selectivity in favor of the oxygen-transfer product DTBQ over the self-coupling of the phenoxy radical (see Scheme 8) was observed upon variation of oxygen concentration and total pressure. In contrast, selectivity remained unaffected over a wide range of temperatures and catalyst concentrations. The oxygen dependence of both the conversion and selectivity showed saturation effects identifying the dioxygen complex as the effective oxidant in both the initial radical formation step and in the oxygenation of that radical. No direct reaction is observed between the electrophilic phenoxy radical and O_2. The observed behavior provides strong support for the previously proposed mechanism for these reactions (see Scheme 9) [64]. As discussed below, the reaction proceeds impressively faster in CO_2-expanded solvent media.

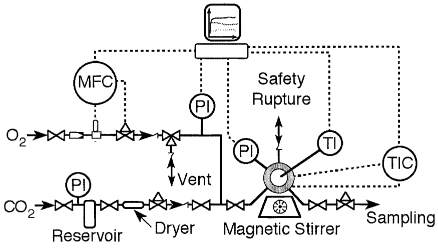
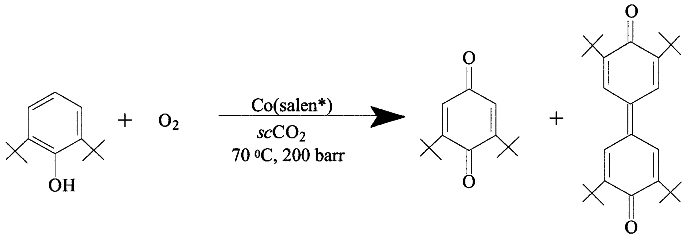
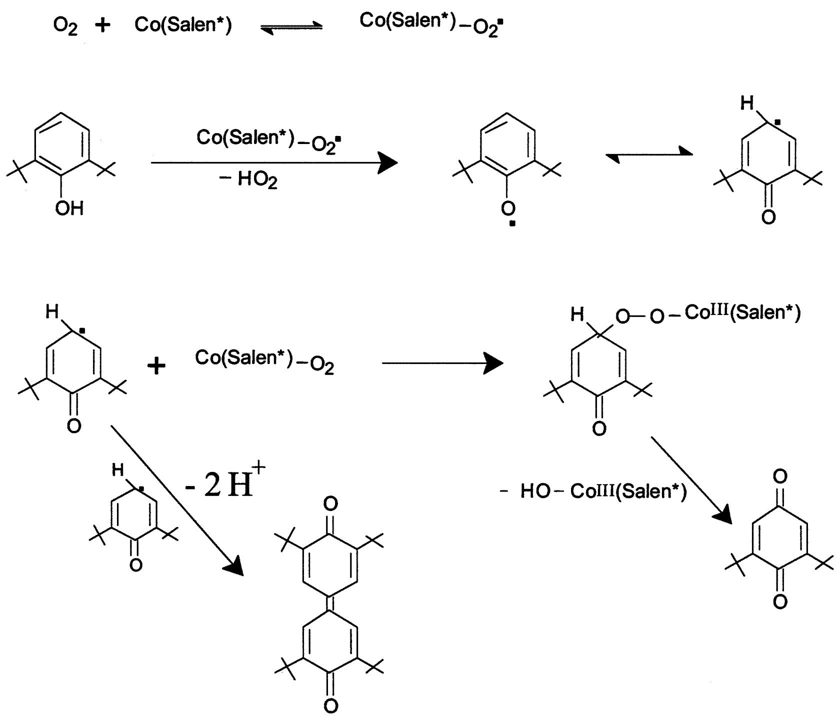


Fig. 2. Schematic of the experimental setup for performing catalytic oxidations in $scCO_2$.



Scheme 8. Co(salen*) catalyzed aerobic oxidation of DTBP.



Scheme 9. Proposed reaction mechnaism for the oxidation of DTBP by Co(salen*).

Table 3
Oxidation of alkenes by Mn(salen*) and *t*-BuOOH/*t*-BuOH

Alkene	Product [a]
Cyclohexene	Cyclohexene oxide (15) 1,2-Cyclohexenediol (12)
Styrene	Styrene oxide (17) Benzaldehyde (23)
cis-Stilbene	*cis*-Stilbene oxide (12) Benzaldehyde (19)
trans-Stilbene	*trans*-Stilbene oxide (16) Benzaldehyde (20)

[a] All reactions were run with 50 μM of catalyst and 83 bar (total pressure) at 50°C and 70% w/w in *t*-BuOOH/*t*-BuOH.

6.4. Oxidation of alkenes with Mn^{III}(salen*) and t-BuOOH

In preliminary studies closely paralleling those for CH_3ReO_3 above, we have shown that Jacobson's catalyst, Mn(salen*), is sufficiently soluble in $scCO_2$ to catalyze the epoxidation of a range of olefins, Table 3, using *t*-BuOOH as terminal oxidant. Epoxidation is accompanied by C=C cleavage in the case of olefins having aromatic rings. Kochi and coworkers have found similar results using other substituted Mn[(5,5′-NO_2)$_2$salen] catalysts and iodosobenzene as terminal oxidant in CH_3CN (Table 4) [65].

7. Oxidations in CO_2-expanded solvent media

7.1. The new concept

The history of the field as summarized briefly above shows that known oxidation catalyst systems are readily adapted to scCO_2. However, the scCO_2-based oxidation has drawbacks including low reaction rates and high process pressure (on the order of hundreds of bars) and only a limited number of transition metal catalysts that exhibit adequate solubility in CO_2 without substantial structural modification. Fluorocarbon additives are known to enhance the solubility of transition metal complexes in scCO_2 at moderate pressures [66]; however, the fluorocarbon compounds are expensive and not considered environmentally benign. The development of catalytic oxidation processes that are selective, environmentally benign, stable and economical continues to be a challenge. The use of CO_2-expanded solvents shows significant promise in accommodating all these attributes.

In the process demonstrated by our research group, the conventional solvent medium is substantially, but not totally replaced by dense CO_2. The retained organic solvent affects the dielectric constant of the reaction medium. According to plan, the CO_2 expansion multiplies the solution volume without causing the substrate, the catalyst, or the terminal oxidant to fall from the reaction mixture. Thus, a completely homogeneous CO_2-expanded reaction mixture consisting of the substrate, catalyst, terminal oxidant, initial solvent and CO_2 is created. The total pressure is on the order of 50–90 bars (much lower than typical pressures for scCO_2) and the CO_2 mole fraction in the solvent is typically between 65 and 80%, a substantial reduction in organic solvent usage. The often preferred terminal

Table 4
Oxidation of alkenes by Mn[(5,5′-NO_2)$_2$salen] and PhIO

Alkene	Product [a]
Cyclohexene	Cyclohexene oxide (56)
Styrene	Styrene oxide (37) Benzaldehyde (10)
cis-Stilbene	*cis*-Stilbene oxide (35) Benzaldehyde (7)
trans-Stilbene	*trans*-Stilbene oxide (40) Benzaldehyde (6)

[a] Reactions were run in 5 ml CH_3CN containing 0.01 mmol of catalyst, 0.15 mmol of iodosylbenzene and 0.30 mmol of olefin.

oxidant dioxygen is about two orders of magnitude more soluble in this medium than in the neat organic solvent [67]. The examples that follow show enhanced oxidation rates for organic substrates (alkenes and phenols) in CO_2-expanded media using dioxygen and metal complexes of both Schiff base and porphyrin ligands. Further, the selectivity toward desired products (alkenes to epoxides; phenols to quinones) is also improved over either neat organic solvents or $scCO_2$.

7.2. Homogeneous expansion of organic solvents containing dissolved catalyst

Fig. 3 describes the experimental setup for measuring the volumetric expansion of organic solvents using CO_2. A measured volume of organic solution containing a known amount of catalyst (mg/ml) is loaded into the thermostated 100 ml view-cell interfaced with a magnetic stirrer assembly; pressure and temperature are monitored. The CO_2 is introduced at a controlled rate into the cell until a certain pressure is reached, the system is equilibrated, and the height of the liquid is noted. The CO_2 addition and equilibration steps are repeated at various multiples of volumetric expansion (twofold, threefold, etc.) until the dissolved catalyst precipitates. The total volume and the pressure at which precipitation occurs are registered as the maximum expansion level for a organic solvent/catalyst system (mg/ml).

Fig. 4 shows plots of volumetric expansions for the solvent methylene chloride at 25°C. The largest homogenous expansion point for each solution is the maximum expansion limit before the catalyst precipitates. For example, the solution with concentration of 2.5 mg/10 ml expands homogeneously up to five times compared to threefold for the 10 mg/10 ml solution. Fig. 5 shows isothermal volumetric expansion profiles at 25 and 50°C for similar initial solution volumes of CH_2Cl_2 (10 ml) but four different concentrations of dissolved Co(salen*). The maximum relative expansion of the solution containing 2.5 mg of Co(salen*) in 10 ml of CH_2Cl_2 is 5. As shown in Fig. 5, the corresponding expansion is 8 for the same concentration of complex at 50°C.

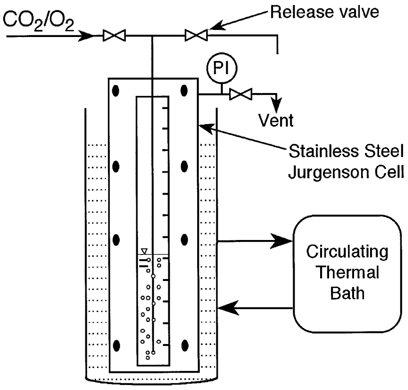


Fig. 3. Schematic of the experimental setup for the expansion of organic solvents by CO_2.

7.3. Catalytic oxidation of substituted phenols by Co(salen) in CO_2-expanded media*

The homogeneous catalytic oxidation of DTBP by Co(salen*) (see Scheme 8) was systematically studied in $scCO_2$ (see above), and in CO_2-expanded and neat organic solvents (for comparison). For oxidation reactions using oxygen, substrate, organic solvent and catalyst were initially charged into the cell and the system was thermostated. Carbon dioxide and oxygen were charged into the cell to achieve the desired concentrations and volume expansion, and the batch reaction was conducted for a predetermined time period. The experimental conditions and conversions are given in Table 5, for results in pure solvents and for the CO_2-expanded solvents. In each case, the molar concentrations of the catalyst and the substrate were held constant. The low solubility of oxygen in neat CH_2Cl_2 limited the molar ratio of oxygen/substrate to a maximum of 2 while the ratio is 10 for the other two media. Due to the low boiling point, 40°C, the reaction in neat CH_2Cl_2 is

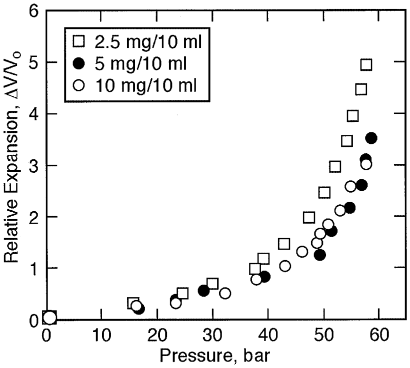


Fig. 4. Expansion curves for varied solution concentrations of Co(salen*) in CH_2Cl_2 by CO_2 at 25°C.

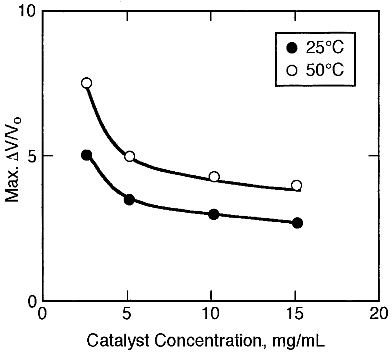


Fig. 5. Maximum limit for homogeneous expansion by CO_2 just before precipitation of Co(salen*) from CH_2Cl_2 at 25 and 50°C.

Table 5
Comparison of DTBP conversion and DTPQ selectivity during DTBP oxidation with Co(salen*) complex in CH_2Cl_2, CO_2-expanded CH_2Cl_2 (roughly twofold volumetrically) and $scCO_2$

P_{total} (bar)	Temperature (°C)	Time (h)	CH_2Cl_2 (ml)	Molar O_2/Sub	Conversion (%)	DTPQ (select%)
2.8	25 [a]	2	10	2	17	88
207	70	21	0	10	80	70
62	70	2	5	10	99	98

Reaction conditions: substrate (68 mg); catalyst (2.5 mg); methyl imidazole (2 μl) and total reaction volume of 10 ml. The reaction time was 2 h except for $scCO_2$ where it is 21.

[a] Boiling point of CH_2Cl_2 is 40°C.

performed at roughly ambient temperature, 25°C. At the given concentrations of reaction components, the conversion at 25°C establishes the base line for the maximum possible DTBP conversion and DTBQ selectivity in neat CH_2Cl_2.

Table 5 shows that the total DTBP conversion and DTPQ selectivity of products in the CO_2-expanded solvent medium (from 5 ml initially to 10 ml by CO_2) are far better than the corresponding values in either $scCO_2$ or neat CH_2Cl_2. Whereas the DTBP conversion in the CO_2-expanded–CH_2Cl_2 is nearly complete, it is only around 20 and 80% in the neat CH_2Cl_2 and $scCO_2$, respectively, despite the fact that the reaction time for $scCO_2$ is more than ten times longer than that for the other two media. More detailed studies have revealed that the turnover frequency (TOF, moles of substrate converted per mole of catalyst per hour) for the oxidation in CO_2-expanded phase is at least forty times higher than that in $scCO_2$ medium.

In addition to the favorable numbers, it should be recalled that the CO_2-expanded solvent operates at only a fraction of the pressure of the $scCO_2$ reaction. Further, compared to reactions in neat organic solvents, higher operating temperatures are safe which may be exploited to attain higher conversions and superior selectivity in shorter times.

7.4. Oxidation of cyclohexene by iron porphyrin complexes in CO_2-expanded media

As summarized above, Tumas and coworkers investigated the catalytic oxidation of organic substrates using iron porphyrins [55]. We have expanded on their data by studying O_2-oxidation of cyclohexene in CO_2-expanded solvent media using the iron porphyrin catalyst, TPPFeCl. The main oxidation products are dictated by the two competing mechanisms involving allylic hydrogen abstraction and oxidation by O-atom transfer. While allylic hydrogen abstraction produces 2-cyclohexene-1-ol, 2-cyclohexene-1-one and 4-hydroxy-2-cyclohexene-1-one as, the cyclohexene oxide and its subsequent hydration product 1,2-cyclihexanediol are produced via the O-atom transfer. 1-Chloro-2-cyclohexanol is also formed, presumably by reaction of cyclohexene oxide with Cl^-.

The cyclohexene conversion and product distribution were sensitively influenced by the CO_2-fraction in the reaction medium. As shown in Fig. 6, when CH_3CN is expanded twofold by CO_2, the conversion increases from 24% in neat CH_3CN to a maximum of 31%. But, further CO_2-expansion decreased the conversion. Epoxidation selectivity showed a similar trend. We attribute these observations to the lower O_2 solubility in neat solvent and the progressively diminishing solvent polarity upon the addition of CO_2. This suggests that a continuum of reaction media with different properties may be realized by varying the CO_2/solvent ratio; and there exists a CO_2/solvent ratio that provided the optimum combination of miscibility (of substrate, catalyst and O_2) and solvent properties (polarity, dielectric constant, etc.) to maximize conversion.

The latter observation was verified further by contrasting with oxidation performed in scCO_2. Although the insolubility of TPPFeCl in scCO_2 prevented direct comparison between the two systems, oxidation by scCO_2 soluble perfluorinated analogue of the catalyst, PFTPPFeCl, can be considered. Besides slight electronic differences on the iron centers of the two catalysts, both are not very different from each other.

Comparison with the work by Tumas and coworkers, who reported the catalytic homogenous oxidation of cyclohexene by the PFTPPFeCl complex, provides further insight. Table 6 compares our results with some of Tumas' group data. Each experiment summarized therein was performed under identical molar ratios of catalyst:O_2:substrate = 1:1500:2000 and batch reaction time of 18 h. The first entry, oxidation in neat CH_3CN at 11 bar total pressure, yielded 15% conversion and 7% selectivity for epoxidation. The second entry, two-fold expanded solvent, at 45 bar yielded 23% conversion and 10% selectivity. The third entry shows no conversion and this is attributed to the insolubility of the fluorine-free tetraphenyl porphyrin complex, TPPFeCl, in scCO_2. The fourth entry, from Tumas's work, shows 12% conversion and 15% selectivity. However, the reaction was carried at a temperature of 80°C and relatively high total pressure, 345 bar. Nevertheless, the conversion is less compared to that achieved in the expanded solvent system with the TPPFeCl catalyst.

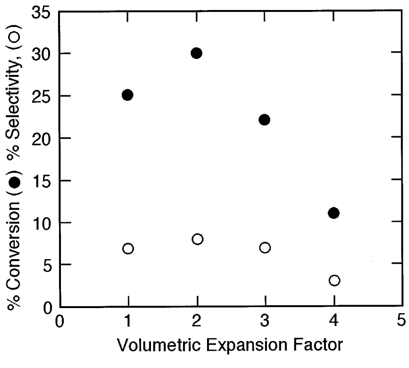


Fig. 6. Variation of cyclohexene conversion with CH_3CN expansion by CO_2. Temperature, 50°C; mole ratio of catalyst/O_2/substrate is 1:1500:2000; and reaction time of 24 h.

Table 6
Comparison of aerobic oxidations of cyclohexene by TPPFeCl and PFTPPFeCl in different solvent systems

Catalyst	Solvent	P_{total} (bar)	% Conversion	% Selectivity
TPPFeCl	CH_3CN	11	15	7
TPPFeCl	1:1 vol (CH_3CN/CO_2)	45	23	10
PFTPPFeCl	1:1 vol (CH_3CN/CO_2)	90	40.9	28.3
PFTPPFeCl	CO_2 [a]	345	12	15

Reaction conditions: Molar ration of catalyst:O_2:substrate of 1:1500:2000 in a total reaction volume of 10 ml. The reaction time was 18 h and except for PFTPPFeCl (80°C), the other reactions were run at 50°C.

[a] From the work of Tumas [56].

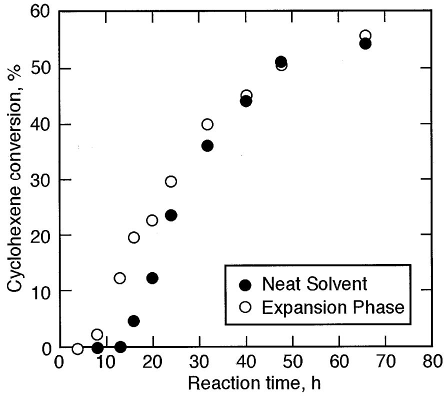


Fig. 7. Cyclohexene conversion profiles in two-fold expanded and neat CH_3CN solvent. Temperature, 50°C; mole ratio of catalyst/O_2/substrate, 1:1500:2000; reaction time 24 h. For expanded media: CH_3CN, 5 ml; total pressure, 60 bar. For neat solvent: CH_3CN, 10 ml; total pressure, 11 bar.

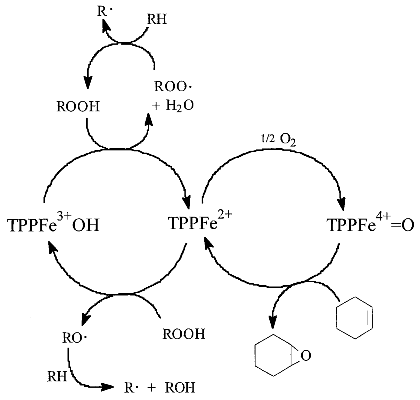
In Fig. 7 are plots of conversions for TPPFeCl, in neat CH_3CN and in two-fold expanded CH_3CN versus reaction time (reaction volume of 10 ml — catalyst:O_2:substrate molar ratio of 1:1500:2000; 2.5 mg of catalyst; 0.50 ml of cyclohexene and 50°C). A significant effect of the expanded solvent is the large reduction of the induction time for the reaction. At longer times, the systems behave in a similar manner.

7.5. Active mechanisms in the oxidation of cyclohexene by iron porphyrins

The catalytic cycle has four major segments, each independently established in the literature as follows: the production of alkyl peroxide, the reduction of $TPPFe^{III}$, the oxidation of $TPPFe^{II}$ and the ferryl intermediate, $TPPFe^{IV}{=}O$. The aerobic oxidation of cyclohexene catalyzed by TPPFeCl has been shown to follow an alkyl peroxide decomposition mechanism (Scheme 10). Similar to many other

$$R\cdot + O_2 \longrightarrow ROO\cdot$$

$$ROO\cdot + RH \longrightarrow ROOH + R\cdot$$



Scheme 10. Proposed reaction mechanism for the oxidation of cyclohexene by PFTPPFeCl.

alkenes, cyclohexene reacts with oxygen to produce a peroxide species which initiates the reaction by reducing and subsequently oxidizing the catalyst while producing alkyl peroxy ($ROO^\bullet$) and alkoxy ($RO^\bullet$) radicals. These radicals are responsible for the allylic H-abstraction of cyclohexene to produce 2-cyclohexene-1-ol, 2-cyclohexene-1-one and 4-hydroxy-2-cyclohexene-1-one. The epoxidation reaction involves a two-electron O-atom transfer by the ferryl intermediate, $TPPFe^{IV}=O$. The catalyst is reduced by two electrons to $TPPFe^{II}$ and either reacts with O_2 to yield the ferryl species or further reacts with ROOH to be oxidized to $TPPFe^{III}$ species and eventually reduced by the peroxide species to $TPPFe^{II}$.

8. Future directions

It follows from the many investigations reviewed herein that while the use of $scCO_2$ in homogeneous catalytic oxidation has certain advantages over conventional solvents (such as total solvent replacement with an environmentally benign solvent, complete O_2 miscibility in the reaction mixture, resistance to oxidation), a major drawback is the high pressures (on the order of hundreds of bars) required to ensure adequate solubility of many transition metal catalysts in CO_2. Fluorocarbon additives are known to enhance the solubility of transition metal complexes in $scCO_2$ at moderate pressures; however, the fluorocarbon compounds are expensive. Recently, poly(ether-carbonate)s copolymers that readily dissolve in CO_2 at lower pressures have been developed [6]. Such research efforts aimed at developing low-cost, fluorine-free alternatives are expected to continue.

Another limitation of $scCO_2$ is the lack of tunability of the dielectric constant and other properties of the reaction medium. By adding a suitable solvent that is miscible with dense CO_2 (CO_2-expanded solvent), such properties as the dielectric constant may be readily varied with mixture composition while maintaining solubility of the substrate, oxidant and catalyst in the expanded phase. There are a number of traditional solvents, such as CH_2Cl_2, CH_3CN, DMF, acetone, methanol, ethanol, *tert*-butanol and isopropanol that can be expanded with dense CO_2. The CO_2-expanded solvent mixtures represent a continuum of reaction media with different physicochemical properties that may be exploited for optimizing conversion and selectivity in well-known catalytic oxidation systems as discussed herein. Further, the low process pressures and the ability to separate and recycle the solvent make homogenous catalytic oxidation in CO_2-expanded solvents environmentally benign and more economical compared to $scCO_2$-based oxidation.

Other kinds of environmentally benign solvents that are receiving increased attention are room temperature ionic liquids such as chloroaluminate(III) ionic liquids, specifically 1-butylpyridinium chloride–aluminum(III) chloride and 1-ethyl-3-methylimidazolium chloride–aluminum(III) chloride. Ionic liquids are extremely good solvents for a wide range of inorganic, organic and polymeric materials. Recently, it was shown that by sufficiently expanding ionic liquids with $scCO_2$, hydrocarbon components can be selectively extracted from the reaction mixture [68]. This suggests that controlled expansion of room temperature ionic liquids with CO_2 should be possible such that the hydrocarbon substrate and catalyst miscibilities in the reaction mixture are maintained while enhancing the solubilities of such oxidants as dioxygen therein. Post reaction, the hydrocarbon components and the catalyst may be fractionated from the reaction mixture by stepwise addition of dense CO_2. Catalytic oxidations in CO_2-expanded ionic liquids thus offer the exciting possibility of developing novel integrated environmentally benign reaction and separation schemes.

It should be clear that the advantages of CO_2-expanded phases can also be realized with heterogeneous catalytic systems in which the solid catalyst particles are exposed to the CO_2-expanded reaction mixture. Another area that shows much promise for exploitation in environmentally benign oxidations is the use of biphasic CO_2/water emulsions [8a]. Water soluble catalysts are sequestered in highly dispersed water phase while the substrate and oxidant (such as dioxygen) are dissolved in the continuous $scCO_2$ phase.

In summary, the outlook for exploitation of dense CO_2 in developing new catalytic oxidation schemes is promising. The emphasis and challenge will be in developing and demonstrating processes that simultaneously display the following attributes — selective, environmentally benign, stable and economical.

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References

[1] (a) G. Kaupp, Angew. Chem. Int. Ed. Engl. 33 (1994) 1452;
(b) M. Poliakoff, M.W. George, S.M. Howdle, in: R. van Eldik, C.D. Hubbard (Eds.), Chemistry Under Extreme or Non-Classical Conditions, Wiley, New York, 1997, pp. 163–188;
(c) E. Dinjus, R. Fornika, M. Scholz, in: R. van Eldik, C.D. Hubbard (Eds.), Chemistry Under Extreme or Non-Classical Conditions, Wiley, New York, 1997, pp. 163–188;
(d) in: P.G. Jessop, W. Leitner (Eds.), Chemical Synthesis Using Supercritical Fluids, Weinheim, Wiley–VCH Verlag GmbH, 1999;
(e) P.G. Jessop, T. Ikariya, R. Noyori, Chem. Rev. 99 (1999) 475;
(f) P.G. Jessop, Y. Hsiao, T. Ikariya, R. Noyori, J. Am. Chem. Soc. 118 (1996) 344;
(g) P.E. Savage, G. Gopalan, T.I. Mizan, C.J. Martino, E.E. Brock, AIChE J. 41 (1995) 1723.

[2] A.V. Yazdi, E.J. Beckman, J. Mater. Res. 10 (1995) 530.

[3] S. Kainz, D. Koch, W. Baumann, W. Leitner, Angew. Chem. 36 (1997) 1628.

[4] Y. Lin, R.D. Brauer, K.E. Laintz, C.M. Wai, Anal. Chem. 65 (1993) 2549.

[5] J.M. DeSimone, US Patent 5,496,901, 1996.

[6] T. Sarbu, T. Styranec, E.J. Beckman, Nature 405 (2000) 165.

[7] D. Suleiman, D.L. Boatright, A.K. Dillow-Wilson, C.L. Liotta, C.A. Eckert, AIChE Annual Meeting, San Francisco, CA, November, 1994.

[8] (a) G.B. Jacobson, C.T. Lee Jr., K.P. Johnston, W. Tumas, J. Am. Chem. Soc. 121 (1999) 11 902;
(b) K.P. Johnston, K.L. Harrison, M.J. Clarke, S.M. Howdle, M.P. Heitz, F.V. Bright, C. Carlier, T.W. Randolph, Science 271 (1996) 624.

[9] (a) P.M. Gallagher, M.P. Coffey, V.J. Krukonis, N. Klasutis, American Chemical Symposium Series, vol. 406, American Chemical Society, Washington, DC, 1989;
(b) J.C. De la Fuente Badilla, C.J. Peters, J. Arons, de Swaan, J. Supercritical Fluids 17 (1) (2000) 13;
(c) C.Y. Tai, C.-S. Cheng, AIChE J. 44 (4) (1998) 989.

[10] J.M. DeSimone, Z. Guan, C.S. Elsbernd, Science 357 (1992) 945.

[11] C. Wu, Science News 152 (1997) 108.

[12] M. Perry, Chem. Br. 31 (1995) 283.

[13] V.C. Quee-Smith, L. DelPizzo, S.H. Jureller, J.L. Kershner, R. Hage, Inorg. Chem. 35 (1996) 6461.

[14] D. De Vos, T. Bein, J. Chem. Soc. Chem Commun. (1996) 917.

[15] P. Battioni, J.P. Renaud, J.F. Bartoli, M. Reina-Artiles, M. Fort, D. Mansuy, J. Am. Chem. Soc. 110 (1988) 8642.

[16] C. Bolm, D. Kadereit, M. Valacchi, Synlett (1997) 687.

[17] Y.V. Subba Rao, D.E. De Vos, T. Bein, P.A. Jacobs, J. Chem. Soc. Chem. Commun. (1997) 355.

[18] D. DeVos, T. Bein, J. Am. Chem. Soc. 119 (1997) 9460.

[19] (a) K.P. Gable, Adv. Organomet. Chem. 41 (1997) 127;
(b) C.C. Romano, F.E. Kuhn, W.A. Herrmann, Chem. Rev. 97 (1997) 3197.

[20] W.A. Herrmann, R.W. Fischer, D.W. Marz, Angew. Chem. Int. Ed. Engl. 30 (1991) 1638.

[21] (a) S. Yamazaki, J.H. Espenson, P. Huston, Inorg. Chem. 32 (1993) 4683;
(b) P. Huston, J.H. Espenson, A. Bakac, Inorg. Chem. 32 (1993) 4517.

[22] D.H. Busch, S.R. Collinson, T.J. Hubin, Catalysts and Methods for Catalytic Oxidation (US patent application); D.H. Busch, S.R. Collinson, T.J. Hubin, R. Labeque, B.K. Williams, J.P. Johnston, D.J. Kitko, J.C. T.R. Burkett-St.Laurent, Bleach Compositions (US patent appliction); D.H. Busch, S.R. Collinson, T.J. Hubin, R. Labeque, B.K. Williams, J.P. Johnston, D.J. Kitko, J.C.T. R. Burkett-St.Laurent, Bleach Compositions Containing Manganese, Iron, or Chromium (US patent application).

[23] (a) R.G. Weisman, E.H. Wong, D.C. Hill, M.E. Rogers, D.P. Reed, J.C. Calabrese, J. Chem. Soc. Chem. Commun. (1996) 947;
(b) G.R. Weisman, M.E. Rogers, E.H. Wong, J.P. Jasinski, E.S. Paight, J. Am. Chem. Soc. 112 (1990) 8604.

[24] T.J. Hubin, J.M. McCormick, S.R. Collinson, N.W. Alcock, D.H. Busch, submitted for publication.

[25] J.T. Groves, R. Quinn, J. Am. Chem. Soc. 107 (1985) 5790.

[26] H. Ohtake, T. Higuchi, M. Hirobe, J. Am. Chem. Soc. 114 (1992) 10 660.

[27] J.C. Marchon, R. Ramasseul, J. Mol. Catal. 51 (1989) 29 (and references therein).

[28] T. Mlodnicka, B.R. James, in: F. Montanari, L. Casella (Eds.), Metalloporphyrins Catalyzed Oxidations, Kluwer Academic, Netherlands, 1994, pp. 121–148.

[29] (a) R.D. Jones, D.A. Summervile, F. Basolo, Chem. Rev. 79 (1979) 139;
(b) G. McLendon, A.E. Martell, Coord. Chem. Rev. 19 (1976) 1;
(c) M. Momenteau, C.A. Reed, Chem. Rev. 94 (1994) 659;
(d) D.H. Busch, P.R. Warburton, in: R.W. Hay, J.R. Dilworth, K.B. Nolan (Eds.), Perspectives in Bioinorganic Chemistry, JAI Press, London, 1973, pp. 1–79;
(e) E.C. Niederhoffer, J.H. Timmons, A.E. Martell, Chem. Rev. 84 (1984) 137;
(f) D.H. Busch, La Transfusione del Sangue 33 (1988) 57;
(g) D.H. Busch, N.W. Alcock, Chem. Rev. 94 (1994) 585.

[30] (a) A. Nishinaga, in: Y. Murakami (Ed.), Supramolecular Assemblies: New Development in Bifunctional Chemistry, Mita Press, Tokyo, 1990;
(b) L.C. Bailey, R.S. Drago, Coord. Chem. Rev. 78 (1987) 321.

[31] (a) Y. Deng, D.H. Busch, Inorg. Chem. 34 (1995) 6380;
(b) M. Yamade, K. Araki, S. Shiraishi, J. Chem. Soc. Perkin Trans. (1990) 2687;
(c) I. Sasaki, D. Pujol, A. Gaudemer, New J. Chem. 13 (1989) 843;
(d) R.P. Perito, B. Corden, J. Am. Chem. Soc. (1988) 110;
(e) D. Wohrle, H. Bohlen, C. Aringer, D. Pohl, Makromol. Chem. 185 (1984) 669;
(f) X. Wang, R.J. Motekaitis, A.E. Martell, Inorg. Chem. 23 (1984) 271;
(g) M. Frostin-Rio, D. Pujol, C. Bied-Charreton, M. Perree-Fauvet, A. Gaudemer, J. Chem. Soc. Perkin Trans. (1984) 1971.

[32] (a) J.E. Lyons, P.E. Ellis Jr., in: R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidation, Marcel Dekker, New York, 1994, pp. 297–324;
(b) A. Bottcher, E.R. Birnbaum, M.W. Day, H.B. Gray, M.W. Grinstaff, J.A. Labinger, J. Mol. Cat. A. Chem. 117 (1997) 229.

[33] (a) D. Mansuy, P. Battioni, in: R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidation, Marcel Dekker, New York, 1994, pp. 99–132;
(b) D. Ostovic, T.C. Bruice, Acc. Chem. Res. 25 (1992) 314;
(c) D. Dolphin, T.G. Traylor, L.Y. Xie, Acc. Chem. Res. 30 (1997) 251;
(d) B. Meunier, in: R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidation, Marcel Dekker, New York, 1994, pp. 133–156.

[34] (a) K. Srinivasan, P. Michaud, J.K. Kochi, J. Am. Chem. Soc. 108 (1986) 2309;
(b) E.G. Samsel, K. Srinivasan, J.K. Kochi, J. Am. Chem. Soc. 107 (1985) 7606;
(c) J.D. Koola, J.K. Kochi, Inorg. Chem. 26 (1987) 908.

[35] J.F. Kinneary, T.R. Wagler, C.J. Burrows, Tetrahedron Lett. 29 (1988) 877.

[36] H. Yoon, C.J. Burrows, J. Am. Chem. Soc. 110 (1988) 4087.

[37] (a) E.N. Jacobsen, in: I. Ojima (Ed.), Catalytic Asymmetric Synthesis, VCH, New York, 1993, pp. 159–202;
(b) N.S. Finney, P.J. Posisil, S. Chang, M. Palucki, R.G. Konsler, K.B. Hansen, E.N. Jacobson, Angew. Chem. Int. Ed. Engl. 36 (1997) 1720 (and references therein).

[38] J.F. Larrow, E.N. Jacobsen, J. Org. Chem. 59 (1994) 1939.

[39] (a) R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidations, Marcel Dekker, New York, 1994;
(b) P.R. Ortiz de Montellano (Ed.), Cytochrome P-450: Structure, Mechanism and Biochemistry, Plenum Press, New York, 1995;
(c) T.G. Traylor, P.S. Traylor, Ann. Rev. Biophys. Bioeng. 11 (1982) 105;
(d) B. Meunier, Chem. Rev. 92 (1992) 1411;
(e) M.J. Gunter, P. Turner, Coord. Chem. Rev. 108 (1991) 115;
(f) P.E. Ellis, J.E. Lyons, Coord. Chem. Rev. 105 (1990) 181;

(g) D. Ostovic, T.C. Bruice, Acc. Chem. Res. 25 (1992) 314;
(h) D. Mansuy, Coord. Chem. Rev. 125 (1993) 129;
(i) D. Dolphin, T.G. Traylor, L.Y. Xie, Acc. Chem. Res. 30 (1997) 251.

[40] G. Roelfes, M. Lubben, S.W. Leppard, E.P. Schudde, R.M. Hermant, R. Hage, E.C. Wilkinson, L. Que Jr., B.L. Feringa, J. Mol. Cat. 117 (1997) 223.

[41] R.T. Jonas, T.D.P. Stack, J. Am. Chem. Soc. 119 (1997) 8566.

[42] (a) S. Mukerjee, A. Stassinopoulos, J.P. Caradonna, J. Am. Chem. Soc. 119 (1997) 8097;
(b) J.P. Caradonna, A. Satssinopoulos, Advan. Inorg. Biochem. 9 (1994) 245;
(c) B.J. Waller, J.D. Lipscomb, Chem. Rev. 96 (1996) 2625;
(d) A.L. Feig, S.J. Lippard, Chem. Rev. 94 (1994) 759.

[43] (a) R.A. Johnson, K.B. Sharpless, in: Iwao Ojima (Ed.), Catalytic Asymmetric Synthesis, VCH, New York, 1992, pp. 103–158;
(b) H. Mimoun, in: S. Patai (Ed.), Chemistry of Functional Groups, Wiley, New York, 1983, pp. 463–482;
(c) in: M. Tsutsui (Ed.), Fundamental Research in Homogeneous Catalysis, vol. 3, Plenum Press, New York, 1979;
(d) K.A. Jorgensen, Chem. Rev. 89 (1989) 431.

[44] R. Landau, G.A. Sullivan, D. Brown, Chem. Technol. (1979) 602.

[45] (a) D.H.R. Barton, D. Doller, Acc. Chem. Res. 25 (1992) 504;
(b) G. Balavoine, D.H.R. Barton, Y.V. Geletii, D.R. Hill, Activation of Dioxygen and Homogeneous Catalytic Oxidtion, Plenum Press, New York, 1993 (p. 225).

[46] K.M. Dooley, F.C. Knoof, Ind. Eng. Chem. Res. 26 (1987) 1910.

[47] G.J. Suppes, R.N. Occhiogrosso, M.A. McHugh, Ind. Eng. Chem. Res. 28 (1989) 1152.

[48] L. Zhou, A. Akgerman, Ind. Eng. Chem. Res. 34 (1995) 1588.

[49] M. Gaffney, J.A. Sofranko, Prepr. Am. Chem. Soc. Div. Pet. Chem. 377 (1992) 1273.

[50] L. Fan, T. Watanabe, K. Fujimoto, Appl. Catal. A. 158 (1997) L41.

[51] (a) C.-T. Wang, R.J. Willey, J. Non-Cryst. Solids 225 (1998) 173;
(b) C.-T. Wang, R.J. Willey, US Patent 5,831,116, 1998.

[52] G. Jenzer, D. Sueur, T. Mallat, A. Baiker, Chem Commun. 22 (2000) 2247.

[53] L. Jia, H. Jiang, J. Li, Chem. Commun. (1999) 985.

[54] R.S. Oakes, A.A. Clifford, K.D. Bartle, M.T. Pett, C.M. Rayner, Chem. Commun. (1999) 247.

[55] F. Loeker, W. Leitner, Chem. Eur. J. 6 (2000) 2011.

[56] D.R. Pesiri, D.K. Morita, W. Glaze, W. Tumas, Chem. Commun. (1998) 1015.

[57] D.A. Morgenstern, R.M. LeLacheur, D.K. Morita, S.L. Borkowsky, S. Feng, G.H. Brown, L. Luan, M.F. Gross, M.J. Burk, W. Tumas, in: P.T. Anastas, T.C. Williamson (Eds.), Green Chemistry: Designing Chemistry for the Environment, ACS Symposiunm Series, vol. 626, ACS, Washington, DC, 1996, p. 132.

[58] E.R. Birnbaum, R.M. Lacheur, A.C. Horton, W. Tumas, J. Mol. Catal. 139 (1998) A-11.

[59] G.R. Hass, J.W. Kolis, Tetrahedron Lett. 39 (1998) 5923.

[60] G.R. Hass, J.W. Kolis, Organometallics (1998) 4454.

[61] U. Kreher, S. Schebesta, D. Walther, Z. Anorg. Allg. Chem. 624 (1998) 602.

[62] X.-W. Wu, Y. Oshima, S. Koda, Chem. Lett. (1997) 1045.

[63] (a) S.-D. Yeo, G.-B. Lim, P.G. Debenedetti, H. Bernstein, Biotechol. Bioeng. 41 (1993) 341;
(b) C.Y. Tai, C.-S. Cheng, AIChE 44 (1998) 989;
(c) C.J. Chang, Y. Liou, J. Chem. Eng. Jpn 26 (1993) 517.

[64] G. Musie, M. Wei, B. Subramaniam, D.H. Busch, submitted for publication.

[65] K. Srinivasan, P. Michand, J.K. Kochi, J. Am. Chem. Soc. 108 (1986) 2309.

[66] (a) J. DeSimone, T.J. Romack, US Patent 5,872,15, 1999;
(b) J.M. DeSimone, E.E. Maury, Y.Z. Menceloglu, J.B. McClain, T.J. Romack, J.R. Combes, Science 265 (1994) 356.

[67] M. Wei, G. Musie, D.H. Busch, B. Subramaniam, submitted for publication.

[68] L.A. Blanchard, D. Hancu, E.J. Brckman, J.F. Brenneeke, Nature 399 (1999) 28.