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Review

Gas-expanded liquids for sustainable catalysis and novel materials: Recent advances

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ABSTRACT

Employing a multiscale systems-based research approach, chemists and chemical engineers at the Center for Environmentally Beneficial Catalysis (CEBC) are collaboratively addressing major grand challenges facing the sustainable manufacture of fuels and chemicals from both traditional and renewable feedstocks. By judiciously combining the principles of green chemistry and green reactor engineering, augmented by valuable insights from industrial partners, CEBC researchers are developing alternative technology concepts that minimize the environmental footprint of chemical manufacturing processes including the reduction of carbon emissions. Such collaborations have resulted in several remarkable discoveries as follows: CO_2-expanded liquids (CXLs) as reaction media for selective and inherently safe O_2 oxidations including that for terephthalic acid production from *p*-xylene with potentially reduced solvent burning (i.e., reduced carbon footprint); propylene oxide production with environmentally benign solvents and oxidant, exploiting the compressibility of propylene at ambient temperatures for process intensification; a novel pressure-intensified ethylene oxide process virtually eliminating CO_2 formation as a byproduct; highly selective hydroformylation of higher olefins employing CXLs and soluble polymer-supported homogeneous Rh-based catalysts that are easily retained in solution while the product is isolated by membrane filtration; and creation of nanoparticles of transition metal complexes with unique functional properties such as reversible oxygen binding and room-temperature nitric oxide disproportionation. Quantitative economic and environmental impact analyses have been employed to benchmark CEBC's novel technology concepts against conventional processes and to guide research and development. Examples of such advances in green processing are discussed in this review.

1. Introduction

There are several megaton industrial catalytic processes that represent marvelous chemical technologies but present challenges

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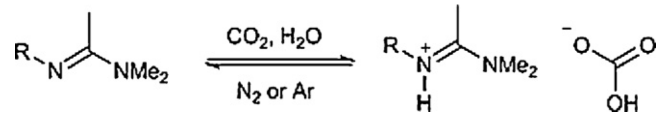
with respect to reducing environmental footprints and enhancing sustainability [1]. Iconic examples of such processes include the homogeneous hydroformylaton of higher olefins, the selective oxidation of light olefins to their corresponding epoxides and the oxidation of *p*-xylene to produce terephthalic acid. The chemical industry has relied on mostly fossil fuel (such as petroleum, natural gas and coal) based feedstock. For a targeted product, there are several possible scenarios for developing sustainable alternatives to conventional technologies. These include (a) developing greener process technologies based on existing feedstock, (b) replacement of conventional petroleum or coal based feedstock with renewable feedstocks such as those derived from biomass (which will also entail the development of new chemistries and process technologies) or (c) replacement of the target product itself, such as polyols and carboxylic acids, with alternate candidates from renewable feedstocks. The focus of this review will be on the first of these scenarios.

The qualitative principles of green chemistry [2] and green engineering [3] provide valuable guidelines for developing greener process alternatives, such as the use of renewable and abundant resources as feedstock, non-hazardous reagents as reaction and separation media, inherently safe process design and process intensification at mild conditions. However, the reliable assessment of overall “greenness” and sustainability requires quantitative comparison with conventional processes using metrics such as atom economy, the *E*-factor (amount of waste produced/unit of desired product) [4], toxic emissions potential [5] and process economics. Such complementary quantitative analyses also provide valuable guidance in identifying potential process improvement opportunities and establishing performance metrics for sustainability.

For a targeted product from a given feedstock, the basic elements of a catalytic process or system include the catalyst, media, multiphase reactor and catalyst/product separator. Effective integration and optimization of these elements into a sustainable technology clearly require a multidisciplinary, multiscale approach involving chemists and chemical engineers [6]. This review highlights examples of such collaborative efforts at the CEBC to develop sustainable alternative process concepts for large-scale catalytic technologies. The examples include the homogeneous hydroformylation of higher olefins, the epoxidations of light olefins such as ethylene and propylene, and the selective oxidation of *p*-xylene to terephthalic acid. The capacity of these processes is growing at 4–6% annually. Hence, the deployment of viable alternative technologies for future expansion of these processes (and also as replacement of existing units when needed) would have a significant impact in reducing environmental footprints. Specifically, the various system elements (i.e., catalysts, solvents, reactors and separators) should be designed such that when integrated, the resulting system displays enhanced rates and selectivity with reduced environmental footprint. In particular, it is shown how the easily tunable physicochemical properties of gas-expanded liquids can be effectively exploited to promote sustainable homogeneous catalysis. An example of quantitative sustainability assessment is also presented to show how it facilitates the design and development of such practically viable catalytic systems.

2. Alternative solvents for sustainable catalysis

Solvent usage has often been linked to waste generation and associated environmental and economic burdens [4]. In addition to creating liquid wastes, solvent emissions have been linked to poor air quality and human illness. During the last two decades, many research groups have investigated benign alternate media for performing chemical reactions [7–11] to reduce the environmental burden in conventional processes. Supercritical CO_2 (*sc*CO_2) [12–19], water [20–22], gas-expanded liquids (GXLs) [23–27], ionic liquids (ILs) [28–30] and switchable solvents [31–35] have received much attention as benign media.



Scheme 1. An amidine-based switchable surfactant (R = C_8H_{17}, $C_{12}H_{25}$, $C_{16}H_{33}$), where the left form is a de-emulsifer and the right form is a surfactant.

The ideal alternative solvent is one that is not only greener in terms of its environmentally benign nature but also satisfies the following criteria: (a) retains the beneficial attributes of the conventional solvent (polarity, catalyst/reactant solubility) being replaced for the given reaction, (b) facilitates facile product/catalyst separation, (c) enhances inherent safety of the process and (d) accommodates mild operating conditions for economic viability. While *sc*CO_2 is “generally regarded as safe”, its non-polar nature renders it unsuitable for most homogeneous catalysis involving polar transition metal complexes. Further, *sc*CO_2 media require operating pressures in excess of 100 bar which adversely impacts process economics. The use of either supercritical or near-critical water ($P_c = 220.6$ bar; $T_c = 373.9\,^{\circ}C$) as a tunable solvent requires rather high operating pressures and temperatures that also limit its use to specific reactions. The use of ionic liquids as tunable media for catalysis either by themselves or in combination with *sc*CO_2 [36] shows promise but demonstrating the economical synthesis of benign ionic liquids remains the key to large-scale applications.

With switchable solvents, the polarity can be completely switched by the addition of a suitable gas to the solvent at ambient pressure. As shown in Scheme 1 (taken from Ref. [35]), incorporation of an amidine functional group into a solvent or a surfactant allows the chemical to have switchable polarity in the presence or absence of CO_2. For example, a long chain amidine can be switched between a surfactant form and a de-emulsifier form by either introduction or removal of CO_2 gas, respectively, at 1 atm. This switchability could be exploited to influence the solubility properties of the solute; a solute in a biphasic water/organic solvent mixture could be made to either partition preferentially into the organic phase without CO_2 presence or partition preferentially into the aqueous phase upon addition of CO_2.

Andreetta et al. [37] demonstrated such a phase-switching solute for catalyst recovery employing Co and Rh complexes with ligands such as $P(CH_2CH_2CH_2NEt_2)_3$ or $P(CH_2CH_2CH_2NMe_2)_3$ that aid transfer of the catalyst from an organic phase to an aqueous phase by CO_2 treatment. The catalyst may be subsequently recovered from the aqueous phase by displacement of the CO_2. The use of switchable solvents for separation applications, including those for recovery of homogeneous catalysts, is an emerging area.

2.1. Gas-expanded liquids

A gas-expanded liquid (GXL) phase is generated by dissolving a compressible gas such as CO_2 or light olefin into the traditional liquid phase at mild pressures (tens of bars). When CO_2 is used as the expansion gas, the resulting liquid phase is termed a CXL. As described elsewhere [24], GXLs combine the advantages of compressed gases such as CO_2 and of traditional solvents in an optimal manner. The dissolved CO_2 (in a CXL) is present in such an amount that it enhances permanent gas (O_2, H_2, CO, etc.) solubilities [38–41] but does not precipitate out the homogeneous catalyst from solution. Further, the dissolved CO_2 also serves to enhance transport properties by increasing the intrinsic diffusivity of solutes in the CXL phase and decreasing the viscosity of the liquid phase.

Because GXLs are generated by partially replacing the conventional solvent (or its benign equivalent) with the expansion gas, they retain the beneficial attributes of the conventional solvent (polarity, catalyst/reactant solubility) but with higher miscibility of permanent gases compared to organic solvents at ambient conditions and enhanced transport rates compared to liquid solvents. The enhanced gas solubilities in GXLs have been exploited to alleviate gas starvation (often encountered in homogeneous catalysis with conventional solvents), resulting in a one to two orders of magnitude greater rates than in neat organic solvent or *sc*CO_2. *Environmental advantages* include substantial replacement of organic solvents with environmentally benign dense-phase CO_2. *Process advantages* include reduced flammability due to CO_2 presence in the vapor phase and milder process pressures (tens of bars) compared to *sc*CO_2 (hundreds of bars). GXLs thus satisfy many of the attributes of an ideal alternative solvent. In the following sections, we review how the several enabling advantages of GXLs may be systematically exploited to develop greener and novel catalytic processes and catalytic materials.

2.1.1. *Generation of GXLs with conventional solvents*

A gas in the vicinity of its critical temperatures [0.9–1.2 T_c (expressed in K)] is highly compressible around the critical pressure and attains liquid-like densities. As an example, consider CO_2 (P_c = 71.8 bar; T_c = 304.1 K) as an expansion gas. At near-ambient temperature (~313.15 K), T/T_c = 1.03 and hence CO_2 is highly compressible attaining liquid-like densities as its critical pressure is approached. When either compressed CO_2 or another compressed gas dissolves in a liquid phase, it volumetrically “expands” that phase forming a GXL. When the system pressure is released, the dissolved gas escapes from the liquid phase “contracting” the liquid phase. Gases whose critical temperatures are far below the reaction temperature do not exhibit compressibility to liquid-like densities and are generally incapable of expanding solvents.

Not all liquids expand equally in the presence of CO_2 pressure, and the differences in behavior are attributed to differences in the ability of the liquids to dissolve CO_2. In this regard, liquids are divided into three general classes [42]. Class I liquids such as water have insufficient ability to dissolve CO_2 (Fig. 1), and therefore do not expand significantly. Glycerol and other polyols also fall into this class. However, by using a solvent such as acetonitrile or methanol that exhibits mutual solubility in CO_2 and water, it is possible to create CO_2-expanded ternary systems containing water [43].

Class II liquids, such as ethyl acetate, acetonitrile and most other traditional organic solvents such as methanol and hexane, dissolve large amounts of CO_2, hence expand appreciably (Fig. 1), and undergo significant changes in physical properties. As shown in Fig. 1, compressed CO_2 at 40 °C is miscible in many conventional solvents such as acetonitrile and ethyl acetate causing them to volumetrically expand several fold, reaching as high as eight for ethyl acetate at around 70 bars. The volumetric expansion of class II solvents is dependent only on the mole fraction of CO_2 in the liquid phase and independent of the choice of solvent [44]. Class III liquids, such as ionic liquids, liquid polymers, and crude oil, dissolve relatively smaller amounts of CO_2 and therefore expand only moderately in volume (Fig. 1).

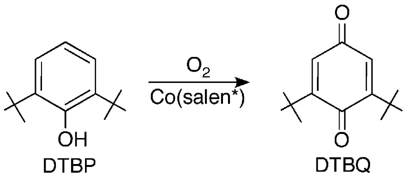
As reviewed elsewhere [24,27], experimental data on the isothermal volumetric expansion of these classes of liquids (class II organic liquids such as alkanes, alcohols, aromatics, ketones, and esters in particular) by CO_2 are abundantly available in the literature. For these solvents, a 2–3 fold volumetric expansion by CO_2 is observed at near-ambient temperatures at relatively mild pressures (50–60 bars). In other words, GXLs may be created at relatively mild pressures with a substantial replacement of the organic solvent with the compressed gas. The expansions have been successfully modeled by the Peng–Robinson Equation of State (PR-EoS) [45] and by molecular simulations [46]. Gases such as ethane, fluoroform and other similar compressible gases are also capable of expanding liquids. As discussed later in this review, gaseous substrates (such as propylene and ethylene) and gaseous oxidants (ozone) have also been exploited as expansion gases to overcome solubility limitations in the liquid phase where reaction occurs. In the following sections, we shall review how GXLs have been systematically exploited at the CEBC to develop sustainable processes that display improved reaction performance with respect to rates, selectivity and separations.

3. Applications of GXLs

3.1. *Oxidation catalysis*

3.1.1. *Oxidation using O_2*

In homogeneous O_2-based oxidations performed in conventional liquid phase with transition metal complexes, O_2 starvation in the liquid phase often limits the reaction rate and also adversely affects product selectivity. Near-ambient temperatures and ambient pressures are typically preferred to maximize the selectivity to the desired product and for safety reasons. We showed that the use of CXLs not only facilitates process intensification at relatively mild conditions but also enhances the inherent safety of the process. Working in collaboration with Professor Busch, we demonstrated these attributes by investigations of the homogeneous O_2 oxidation of 2,6-di-*tert*-butylphenol, DTBP, catalyzed by the cobalt Schiff base [Co(salen*)] (Eq. (1)). The Co(salen*) complexes are well-known O_2 carriers in the liquid phase. Our hypothesis was that the full potential of these O_2 carriers for catalysis may be realized if O_2 availability in the liquid phase (due to solubility and/or mass transfer limitations) is alleviated.



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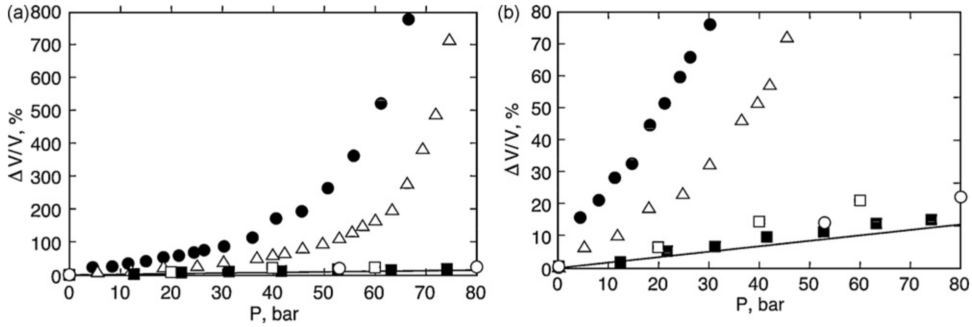


Fig. 1. Expansion of solvents as a function of the pressure of CO_2 at 40 °C, for ethyl acetate (●), MeCN (△), [1-butyl-3methylimidazolium]BF_4 (■), crude oil (line, at 43°C), polypropylene glycol (□), and polyethylene glycol (○) (taken from Ref. [24]).

We investigated the reaction in three different media: neat acetonitrile by bubbling O_2 at ambient pressure, in supercritical CO_2 (*sc*CO_2) at 207 bar with total replacement of acetonitrile; and CO_2-expanded acetonitrile in which the acetonitrile is partially replaced with dense CO_2 in the 60–90 bar range [47,48]. Much higher pressures are required when using *sc*CO_2 in order to solubilize the substrate, catalyst and O_2. As shown in Fig. 2, the maximum TOF in the CO_2-expanded acetonitrile is between one and two orders of magnitude greater than in either *sc*CO_2 or the neat solvent. The observed selectivity toward DTBQ is comparable in *sc*CO_2 and CXLs, but slightly lower in neat acetonitrile.

The enhanced solubility of O_2 in CO_2-expanded acetonitrile relative to neat acetone at 1 bar, the key hypothesis behind this fascinating exploration, was confirmed experimentally by our findings [47] as well as those of Lopez-Castillo et al. [49]. In addition, CXL media provide safety benefits as well. The addition of CO_2, even at low pressures, to potentially flammable hydrocarbon + oxygen vapor mixtures shrinks the flammability envelope [27]. In the case of reactions in CXL media, the vapor phase is dominated by CO_2 (at tens of bars) that is much denser and has a higher heat capacity than ambient-pressure CO_2. In addition, the organic content in the vapor phase above CXLs is lower than in the vapor phase above the neat liquid (acetonitrile) at 1 bar. Both these attributes favor a reduction in the flammability envelope. It is thus remarkable that CXLs can simultaneously provide reaction, environmental and safety benefits in the case of O_2 oxidations.

As summarized in Table 1, we have subsequently demonstrated that the CXL concept can be applied for a variety of industrially significant oxidation chemistries (see Table 1), including *p*-xylene oxidation to terephthalic acid (TPA) and cyclohexane oxidation to adipic acid. Investigations aimed at demonstrating an alternative to the Mid-Century process for TPA manufacture are currently ongoing at the CEBC.

These results show that CO_2-expanded solvents are optimal media that elegantly combine the advantages of dense-phase CO_2 (benign medium, flame retardant, promotes O_2 solubility) and the conventional solvent (chosen to provide polarity to dissolve the catalyst complex and stabilize transition states). The CEBC researchers subsequently applied the concept of gas-expanded liquids to a variety of other homogeneous catalytic systems including H_2O_2 based oxidations, ozonolysis and hydroformylations as discussed in the following sections.

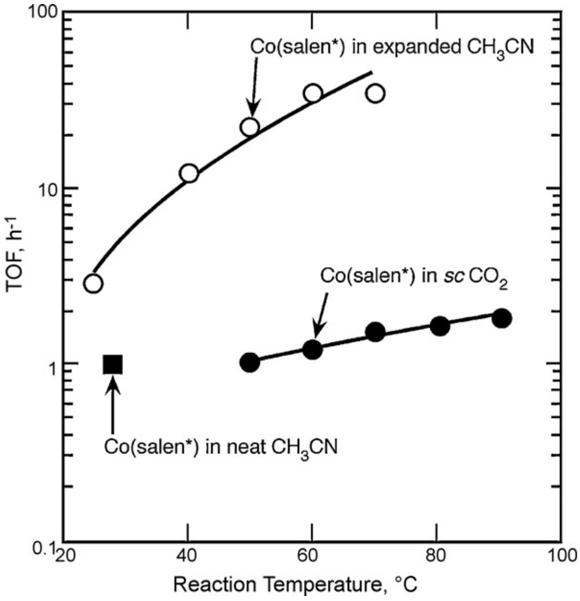
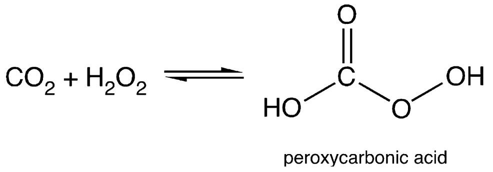


Fig. 2. Turnover frequencies (TOFs) for 2,6-di-*tert*-butyl phenol oxidation with Co(salen*) catalyst at various reaction temperatures. Reaction conditions: total pressure = 1 bar (in neat solvent); 207 bar (in *sc*CO_2) and 50–100 bar (in CO_2-expanded solvent depending on temperature); Catalyst amount = 0.41 μmol; catalyst:substrate:O_2 mole ratio = 1:80:800; volume of methyl imidizole = 2 μL; $V/V_0 = 2$ (in the case of CO_2-expanded solvent media); reaction volume = 10 mL. TOF is defined as moles of substrate converted per mole of dissolved catalyst per hour (taken from Ref. [47]).



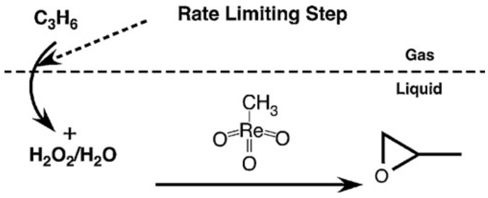
Scheme 2. *In situ* formation of oxidant for the epoxidation of propylene in CXLs.

3.1.2. *Oxidation using H_2O_2*

3.1.2.1. Olefin epoxidations in CO_2-expanded phases. The reaction between H_2O_2 and CO_2 yields a peroxycarbonic acid species (Scheme 2), an oxidant that facilitates olefin epoxidation [51]. Beckman's group [52] reported relatively low conversion (~3%) of propylene to propylene oxide (PO) using percarbonate formed in a biphasic system via reaction of CO_2 and H_2O_2 with NaOH as a base. The low conversions are attributed to mass transfer limitations in the biphasic system.

To alleviate the interphase mass transfer limitations associated with biphasic $CO_2 + H_2O$ systems, we employed acetonitrile as a solvent in which both dense CO_2 and water are appreciably miscible. The resulting ternary system will therefore have miscible regions that can be exploited performing homogeneous catalytic oxidation of organic substrates by water-soluble catalysts and oxidants [43]. Employing CO_2-expanded $CH_3CN/H_2O_2/H_2O$ mixtures as reaction media, we showed that a variety of olefin epoxidations could be performed in a homogeneous phase containing the olefin, CO_2, CH_3CN and H_2O_2 (in aqueous solution). Employing pyridine as the base to stabilize the peroxy acids, one to two orders of magnitude enhancement in rates over the biphasic system was achieved with >85% epoxidation selectivity [43].

3.1.2.2. Propylene epoxidation in CO_2- and olefin-expanded liquid phases. We also demonstrated this concept for the industrially significant *propylene oxidation to propylene oxide* (PO) (Scheme 3). The C_3H_6 solubility in H_2O is $1.36(10^{-4})$ M at 1 bar, 21 °C [53]. By creating a homogeneous mixture of dense CO_2, an organic solvent such as acetonitrile or methanol and water, the solubility of propylene in such a mixture can be substantially increased compared to that in water [54]. When using pyridine as a base, the PO yield at 40 °C is on the order of 10% after 12 h at roughly 48 bar. In the presence of an added catalyst (methyltrioxorhenium or MTO), the PO yield is increased to 80% in 3 h with PyNO as the base. Methyltrioxorhenium (CH_3ReO_3) is an active catalyst for alkene epoxidation at relatively mild temperatures using H_2O_2 as the oxidant [55–59].



Scheme 3. Homogeneous catalytic epoxidation of propylene. The methyltrioxorhenium (MTO) catalyst and oxidant (H_2O_2) are dissolved in the liquid phase and the propylene is supplied from the gas phase.

Table 1
Oxidation of various substrates using $Co(OAc)_2$/NHSI (N-hydroxysuccinimide) catalyst in CO_2-expanded acetic acid (taken from Ref. [50]).

Substrate (S)	Product	Yield (%)	S/NHSI	T (°C)	P_{O_2} (bar)	P_{CO_2} (bar)	Time (h)
p-Xylene	TPA	89	5/1	60	24.14	34.90	1
p-Xylene	TPA	79	5/1	30	23.45	37.03	12
p-Xylene	TPA	68	5/1	21	20.69	20.83	0.5
Cyclohexane	Adipic acid	56	9/1	80	8.28	51.38	6
1,2-Dimethylcyclohexane	2,6-Heptanedione	60	7/1	60	8.28	51.38	6
Cyclooctene	Octanedioic acid	60	18/1	100	8.28	51.38	1
l-Methylpentene	5-Ketohexanoic acid	60	24/1	100	8.28	51.38	1
p-Nitrotoluene	*p*-Nitrotoluic acid	90	4/1	50	8.28	51.38	6

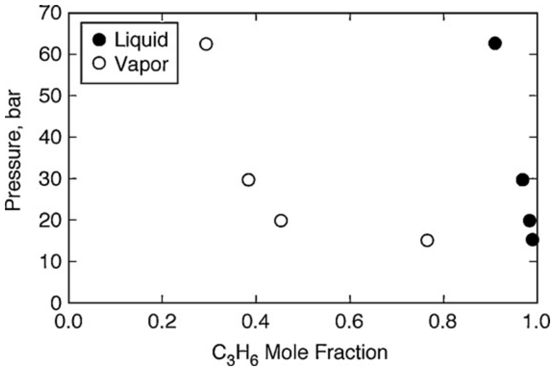


Fig. 3. The N_2/C_3H_6 binary vapor liquid equilibrium data at 22.5 °C [61,62].

We found that if N_2/C_3H_6 (instead of CO_2/C_3H_6) was used as the pressuring medium over the homogeneous H_2O_2/H_2O/MeOH/PyNO mixture containing dissolved MTO catalyst, remarkably high activity (92% PO yield in 1 h) was achieved at roughly 14 bar [60]. When pressurizing with N_2 in a closed system, C_3H_6 ($P_c = 46.1$ bar; $T_c = 92.5$ °C) will condense at this pressure at ambient temperatures (Fig. 3). It should also be clear from Fig. 3 that the equilibrium mole fractions of C_3H_6 in the liquid phase exceed 95% at 15–30 bars.

The use of nitrogen pressure to achieve rate intensification works for two reasons: (i) at ambient temperatures, the propylene is below its critical temperature. At total pressures exceeding roughly 10 bars, propylene condenses and mixes with a soluble liquid phase. Note that in the presence of a solvent such as methanol, pressurization beyond 10 bars increases the C_3H_6 mole fraction in the liquid phase to >30 mol% (Fig. 4)! Either propylene by itself at above 1 bar or a combination of propylene and an inert gas such as N_2 at a similar total pressure may be used to cause this condensation, significantly increasing the concentration of the propylene substrate in the liquid phase. This increased concentration of propylene, along with the availability of excess hydrogen peroxide, results in increased epoxidation rates; (ii) the nitrogen itself is not very soluble in the liquid phase in the range of pressures studied. This lack of N_2 miscibility avoids dilution of the liquid phase observed in dissolving gases, which partially offsets the rate enhancement caused by the increased propylene solubility. It must therefore be noted that CO_2 is not a desirable pressurizing gas since CO_2 will also expand the reaction phase (due to CO_2 dissolution) and lower the reactant concentrations. These results clearly demonstrate that with the proper choice of co-solvent (i.e., methanol for example), pressure (>10 bars at ambient temperature) and pressurizing gas (N_2), the availability of C_3H_6 in the liquid phase containing the catalyst (MTO) and oxidant (H_2O_2) can be dramatically increased by orders of magnitude (compared to C_3H_6 solubility in water) and substrate starvation in the liquid phase is overcome. To the best of our knowledge, this is the first example of utilizing a light olefin as the expansion medium in a GXL and how one might exploit a substrate-expanded liquid phase for process intensification.

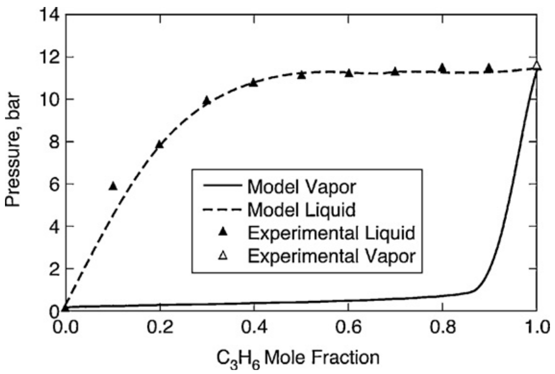


Fig. 4. Vapor–liquid equilibrium for C_3H_6 + MeOH binary system at 21 °C [63,62].

The aforementioned process satisfies the sustainability principles of waste minimization, use of benign reagents and process intensification at mild conditions. Little or no waste is produced compared to the commercial processes. Catalyst durability and recycle studies, aimed at demonstrating a continuous process that is economically competitive compared to existing processes, are currently ongoing at the CEBC.

3.1.2.3. Ethylene epoxidation in olefin-expanded phase. Among industrial chemical processes, ethylene oxide manufacture emits large amounts of CO_2 as byproduct from the combustion of both the ethylene (feed) and ethylene oxide (EO) [64]. Further, the conventional silver-based catalytic process presents safety challenges due to the formation of potentially explosive ethylene oxide/O_2 mixtures in the gas phase. An alternate technology that is selective toward EO alone (eliminating the formation of CO_2 as a byproduct), while also avoiding the formation of explosive vapors, would improve process efficiency and safety, and dramatically reduce the carbon footprint of this large-scale industrial process.

Based on the exceptional activity and selectivity observed with the MTO-catalyzed propylene epoxidation in propylene-expanded liquid phase, the intriguing possibility whether the same process concept would also work for ethylene epoxidation was next investigated. At the near-ambient reaction temperatures, the gaseous ethylene ($P_c = 50.6$ bar; $T_c = 9.5$ °C) is just above the critical temperature. Hence, by compressing the ethylene gas beyond the critical pressure (>50 bars), it is possible to significantly increase its solubility in the liquid reaction phase. As shown in Fig. 5, the solubility of ethylene in methanol at 25 °C (which is in the range of desired reaction temperatures) is on the order of a few tens of mole percent in the 40–60 bar pressure range. Note that N_2 pressure was *not* used in ethylene epoxidation. In contrast to propylene, ethylene is above its critical temperature at the reaction temperature (~25 °C) and therefore does not condense with increasing total pressure. Hence ethylene alone was used as pressurizing gas.

Indeed, by employing MTO, H_2O_2 and a methanol/water mixture as solvent, a homogeneous catalytic system was demonstrated

Table 2
Comparison of conversion and product selectivity obtained in CEBC's process and conventional processes.

Process	Catalyst, oxidant	Pressure, temperature	EO selectivity	CO_2 selectivity	EO productivity (g/g active metal/h)
Conventional[a]	Ag/Al_2O_3, air or O_2	10–20 bar, 200–300 °C	85–90%	10–15%	2–4
CEBC	MTO, H_2O_2	10–50 bar, 20–40 °C	99+%	No CO_2 detected	0.8–4

[a] Taken from Ref. [64].

that eliminates CO_2 formation while producing ethylene oxide at >95% EO selectivity at near-ambient temperatures and rates that are comparable to the conventional EO process [66]. *No* CO_2 was detectable in either the liquid or the vapor phases (Table 2). Furthermore, since H_2O_2 does not decompose at typical reaction temperatures (<40 °C), the vapor phase is void of O_2 and the formation of explosive vapors is impeded.

Thus, the homogeneous liquid phase epoxidation of ethylene to EO with MTO as catalyst and H_2O_2 as oxidant shows much promise as an environmentally benign and inherently safe alternative to the conventional EO process. In addition to the possibility of mitigating the carbon footprint of a large-scale industrial process, the demonstrated technology concept is another example of how the synergy afforded by the facile compressibility of a substrate such as ethylene and the accompanying enhanced solubility in low molecular weight alcohols can be exploited to enhance selectivity and productivity. These encouraging results have paved the way for ongoing research at the CEBC to further enhance the yield of EO while maintaining high EO selectivity and process safety.

3.2. Reactions in ozone-expanded media

Because of its high oxidation potential ($E^0 = 2.075$ V in acid and 1.246 V in base), ozone has been extensively investigated as a powerful oxidant. Even though ozone is considered toxic, it does not persist in the environment and eventually decomposes to molecular oxygen. A particularly attractive reaction of ozone is the cleavage of carbon–carbon double bonds. This oxidation reaction proceeds via meta-stable intermediates that upon further oxidation or reduction yield products that are suitable as building blocks for chemical synthesis. The ozonolysis of unsaturated fatty acids can yield a range of both monoacids and diacids, for which the double bonds of these unsaturated molecules must be cleaved by oxidative methods. For example, the ozonolysis of methyl oleate, $CH_3(CH_2)_7CH{=}CH(CH_2)_7C({=}O)OCH_3$, followed by catalytic reduction in water gives yields of aldehydes approaching 90% [67–69]. Detailed study of the meta-stable initial oxidation products has shown that 90% of the methyl oleate is transformed to 1,2,4-trioxalane, and 10% yield to peroxide oligomers (Scheme 4). The 1,2,4 trioxolane is formed by rearrangement of 1,2,3-trioxolane, the initial product of 1,3 addition of ozone to the double bond.

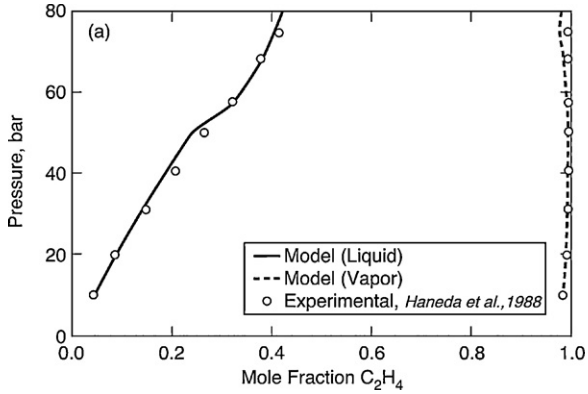
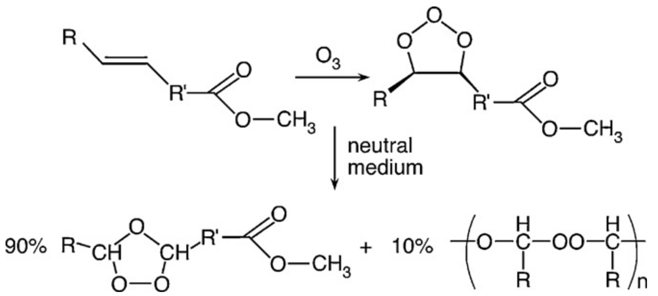


Fig. 5. Phase behavior of ethylene/MeOH system at 25 °C [65,62].

The major drawback of ozonolysis in conventional solvents is that the ozone reacts with most common organic solvents, creating undesirable waste products and consuming the ozone away from the desired reaction. In a collaborative research with Archer Daniels Midland Company, we have recently developed an ozonolysis process concept that utilizes ozone-inert CO_2 as solvent and simple pressure tuning to control ozone solubility in liquid CO_2 [70]. At typical ozonolysis temperatures (0–20 °C), ozone is sufficienty close to its critical temperature (−12.1 °C) such that the ozone density can be increased to liquid-like values by compression beyond its critical pressure (55.6 bar). Conveniently, in the (0–20)°C range and beyond 50 bar, the CO_2 ($P_c = 73.8$ bar; $T_c = 31.1$ °C) will liquefy. The ozone was generated with a pure O_2 source and its concentration in the O_2/O_3 mixture is typically in the range of 3–4 mol%. Thus, if a gas mixture containing O_2, O_3 and CO_2 is compressed beyond 50 bar in the 0–20 °C range, a CO_2-rich liquid phase is created. The miscibility of O_3 in the CO_2-dominated liquid phase was measured using UV–vis spectroscopy. The intensity of the light absorbed by ozone at 580 nm is directly proportional to the O_3 concentration. We observe that the O_3 content in this liquid phase is easily tuned with pressure. For example, the solubility of O_3 in liquid CO_2 at −0.7 °C was determined to be approximately 0.005 absorbance unit at 52.4 bar and 0.05 absorbance unit at 65.5 bar, an order of magnitude increase [70]. This increased dissolution of O_3 in liquid CO_2 created an O_3-expanded liquid phase similar to how the increased dissolution of CO_2 in organic solvents yields CO_2-expanded solvents [46].

Our results to date clearly demonstrate that ozone in liquid CO_2 is highly stable and that ozonolysis in liquid CO_2 provides rapid cleavage of the double bonds of unsaturated substrates at mild temperatures and pressures. The O_3 half-life in liquid CO_2 was found to be approximately 6 h at −1.2 °C [70] and hence the O_3 is stable during the timeframe of both the analysis and reaction. Our initial experimental results (summarized in Table 3) showed that in the case of an insoluble substrate such as methyl oleate, the use of an ultrasound pulse produced an intense emulsion of the oily substrate in liquid CO_2 (containing dissolved O_3), resulting in fast and complete conversion (denoted as X in Table 3) of the methyl oleate to the targeted aldehyde and acid products (Table 3, entry #2). In sharp contrast, mechanical mixing produced only fractional conversion of the substrate even after several hours (Table 3, entry #1). In the case of *trans*-stilbene, which is soluble in liquid CO_2, mechanical agitation was sufficient to appreciably convert the substrate in a few minutes.

The foregoing results clearly show that ozonolysis in liquid CO_2 is a facile, clean and inherently safe oxidation route. Ongoing work



Scheme 4. Initial products of carbon–carbon double bond cleavage by ozonolysis.

Table 3
Ozonolysis in liquid CO_2.

#	Substrate	Mixing	X (%)	Products detected (partial list)
1	Methyl oleate	Mechanical stirring	24	Nonanal; nonanedioic acid, monomethyl ester; nonanoic acid
2	Methyl oleate	Ultrasonic	100	Nonanal; 9-oxo-nonanoic acid, methyl ester; nonanedioic acid, monomethyl ester; nonanoic acid
3	*trans*-Stilbene	Mechanical stirring	95	Benzaldehyde; benzoic acid; benzoic acid, ethyl ester; phenol; 2-hexanone

$P = 44.1$ bar; $T = 0\,^{\circ}C$; substrate loading = 0.1–0.5 g; 1.2 equiv. of O_3 added.

at the CEBC is aimed at exploiting this technology for biomass-derived substrates including the development and demonstration of a continuous CO_2-based ozonolysis reactor.

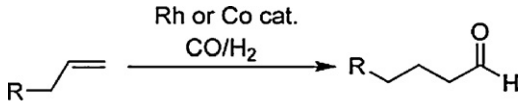
3.3. Hydroformylation of higher (C_{5+}) olefins

Hydroformylation is widely used to convert olefinic petrochemicals into oxygenated hydrocarbon compounds, i.e., linear aldehydes, which are important building blocks for fine chemicals and pharmaceuticals (Scheme 5). The process utilizes syngas as feedstock. Because of its atom efficiency, hydroformylation is considered green.

Industrial processes for the catalytic hydroformylation of higher olefins (>C_5) face several challenges arising from the limited solubilities of the gaseous reactants (H_2 and CO) in the liquid reaction phase and the need for efficient catalyst recovery/recycle [71]. The Rh-based commercial catalysts used in the lower (C_4 or less) olefin processes are not utilized in higher olefin hydroformylation because of their instability at the high temperatures required for product separation/distillation. Hence, the less expensive cobalt-based catalysts are employed. The cobalt catalysts require rather harsh operating conditions (140–200 °C, 50–300 bar) for activation and stabilization. Further, the catalyst recovery steps involve significant quantities of solvents, acids, and bases [72]. The technology challenges are therefore to develop a process that operates at milder temperatures and pressures, and requires a relatively simple and environmentally friendly catalyst recovery method. Recently, Cole-Hamilton and coworkers reported a continuous homogeneous hydroformylation process using dense CO_2 to transport the reactants into and transfer the products out of the reactor leaving behind the insoluble Rh-based catalyst complex in the reactor solution [73].

CEBC researchers have demonstrated a complementary approach that exploits CXLs to develop a Rh-based hydroformylation process that operates at mild pressures (tens of bars) and temperatures less than 100 °C [74–76]. The CXL process is briefly as follows. Compressed CO_2 and syngas are added to the 1-octene + nonanal reaction mixture in which the rhodium complex is dissolved. The compressed CO_2 partially replaces the excess 1-octene substrate used in conventional processes, and serves to expand the 1-octene + nonanal reaction mixture to create a CXL. The syngas solubilities are easily tuned in the CXL at mild pressures. Following reaction, the CO_2 is released and the catalyst complex is separated using either precipitation techniques or solvent filtration membranes (nanofiltration).

We began by investigating ligand-modified rhodium catalysts in CXLs. Toward this end, the most common ligand modifier for rhodium catalysts, PPh_3, was chosen for initial studies. As shown in Fig. 6, fixed-time batch reactor studies conclusively showed that CO_2 enhances the activity (TOF) and n/i selectivity of hydroformylation when compared to equivalent pressures of syngas or an inert gas (N_2).



Scheme 5. Products of Rh-catalyzed hydroformylation of linear olefins.

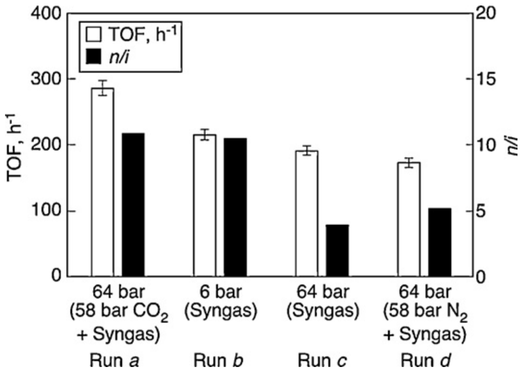


Fig. 6. Effect of pressurizing gas on TOFs and n/i ratio. The solvents used are liquid CO_2 in run *a* and *n*-hexane in runs *b*–*d*. Catalyst: $Rh(acac)(CO)_2$ modified by PPh_3 ligand [L]; L/Rh (molar) = ∼200; $t = 135$ min; $T = 60\,^{\circ}C$; 6 bar syngas (taken from Ref. [75]).

Gas solubility measurements showed the presence of CO_2 at hydroformylation conditions ($T = 40$–$80\,^{\circ}C$ and pressures up to 90 bar) was found to enhance the solubilities of both CO and H_2 in the liquid phase [41]. The enhancement factor, defined as the ratio of the gas (CO or H_2) mole fraction in the neat solvent relative to that in the CXL at identical temperature and gas (CO or H_2) fugacities in the vapor phase, is greater for hydrogen (around 1.8) compared to carbon monoxide (around 1.5). This preferential tuning of the H_2/CO in CXL media (attaining molar H_2/CO >1) is advantageous for enhancing both the TOF and n/i ratio. As shown in Table 4, the use of Rh catalysts with CXL media provides exceptional TOF and chemo-selectivity at very mild pressure (∼40 bar) and temperature (30–60 °C) compared to conventional Co-based processes. As shown elsewhere [75], the presence of CO_2 helps alleviate syngas starvation in the liquid phase that typically leads to the formation of olefinic isomers and adversely affects the aldehyde yield.

A detailed engineering model that takes into account kinetics, phase equilibrium and mass transfer effects was developed to better understand mass transfer and kinetic effects in the CXL-based reactors [77]. The model was deployed to obtain kinetic parameters from real-time conversion and product formation data acquired with a 50-cm^3 stirred autoclave reactor equipped with an *in situ* attenuated total reflectance (ATR) IR probe (ReactIR). The kinetic parameters reveal that the intrinsic rate constants for

Table 4
Enhanced TOFs and selectivity during 1-octene hydroformylation in CXL media.

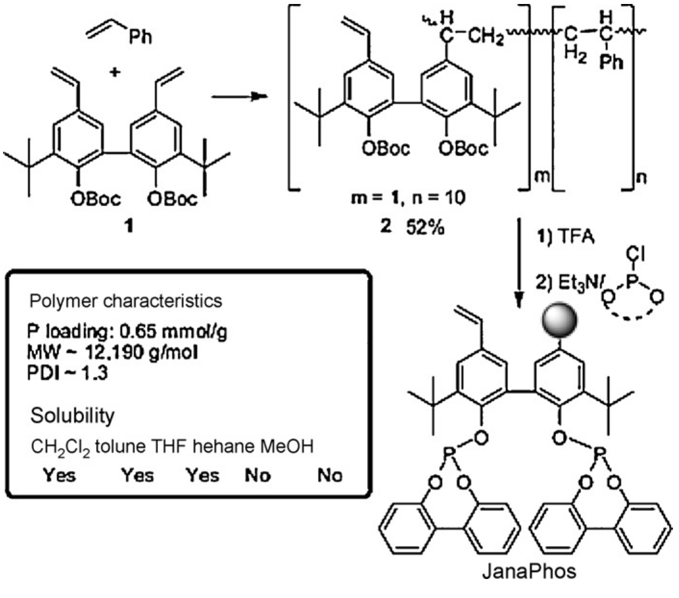
	BASF	Shell	Exxon	CXL
Catalyst	Co	Co/P	Co	Rh/P
P (bar)	300	80	300	38
T (°C)	150	200	165	60
TOF (h^{-1})	35	20	158	316
S_n (%)	50	80	56	89.2

S_n, Selectivity to linear aldehyde.

the key hydrogenation and product formation steps are of similar magnitude with or without CO_2 addition to the reaction mixture [78]. This implies that the enhanced reaction rate in CXL is due to the favorable tunability of the syngas ratio (H_2/CO ratio) in CXLs. Economic analysis of the CXL concept revealed that >99.8% rhodium has to be recovered per pass for the CEBC hydroformylation process to be competitive with a simulated commercial process [79]. Environmental impact analysis revealed that the CEBC process produces less waste and its overall toxicity index is approximately 40 times less than the simulated conventional process.

In efforts to develop catalysts that meet the quantitative criterion for economic viability, the Tunge group synthesized a robust polymer-supported, recyclable rhodium(I) catalyst with chelate capable phosphite functionality (Scheme 6) that subsequently was used to produce a polymer ligand. By controlling of the polymer molecular weight, the solubility was tuned such that the polymer-supported catalyst is soluble in non-polar solvents and insoluble in polar solvents [76]. The polymer support was designed to bind Rh in a bidentate fashion to provide better site-isolation for the rhodium catalysts as well as to inhibit leaching of rhodium from the polymer. The hydroformylation of 1-octene was successfully performed under homogeneous conditions and catalyst recycle was achieved by either precipitation followed by filtration or by membrane nanofiltration methods.

Economically viable levels of Rh recovery were demonstrated in a membrane-based nano/ultra-filtration reactor system [78]. During continuous filtration of a toluene-based solution containing polymer-supported Rh complexes, the Rh and P concentrations in the permeate phase, quantified using ICP analysis, were on the order of a few tens of ppb. During continuous 1-octene hydroformylation studies in the membrane reactor at a syngas pressure of 6 bar and 60 °C, the 1-octene conversion and product (mostly aldehydes) concentrations reached a steady state with the Rh concentrations in the permeate stream being lower than 120 ppb [78]. This is an example of the systems-based, multiscale research approach being employed at the CEBC for developing novel, environmentally beneficial and economically viable process concepts. A patent pertaining to the CXL-based hydroformylation concept [81] has been licensed to a CEBC member company for a defined field of use. The demonstrated technology concept, when fully optimized, should find applications in a variety of other applications in homogeneous catalysis, including hydrogenation and carbonylation of conventional and biomass-based substrates.



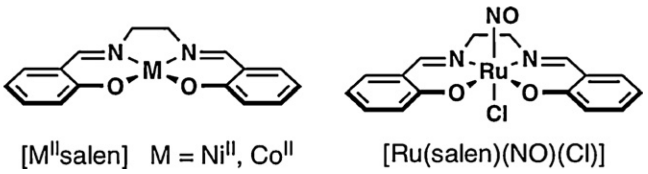
Polymer characteristics

P loading: 0.65 mmol/g
MW ~ 12,190 g/mol
PDI ~ 1.3

Solubility

CH_2Cl_2	tolune	THF	hehane	MeOH
Yes	Yes	Yes	No	No

Scheme 6. Synthesis of polymer-supported ligand [80].



Scheme 7. Molecular structures of compounds used in the PCA studies.

3.4. Synthesis of novel transition metal complexes

We have recently exploited CXLs to recrystallize [M(salen)] molecular complexes as nanoparticles. Just like atom-based nanoclusters, sub-micron particles of molecules could also have unique functional properties but have not been extensively investigated. We deployed the precipitation with compressed antisolvents, or PCA [82], technique on solutions of metal complexes in organic solvents to produce nanoparticulates of metal complexes. In the PCA technology, the non-polar antisolvent such as compressed CO_2 dissolves into the organic solvent containing the dissolved polar compound. The CO_2 dissolution causes the solution to expand and eventually results in substantial supersaturation and nucleation, causing the polar substance to precipitate as fairly uniform particles with length scales between nanometers to microns [83]. The PCA technology has several advantages over conventional methods including higher production output and a one-step route to pure, relatively dry particles that are formed under mild conditions. By spraying the solution as small droplets into dense CO_2, the mass transfer rate between the dense gas and solution droplets is enhanced, producing rapid expansion (and thus supersaturation), resulting in smaller particles [84].

The PCA has been successfully applied to process nanoparticles of pharmaceutical compounds [85–88], including taxol and insulin. CEBC researchers have recently extended the PCA technique to prepare a series of nanoparticles of different metal bis(salicylaldehyde)ethylenediamine (salen) complexes such as those shown in Scheme 7 [89]. Simple [M(salen)] complexes have square planar coordination geometries, resulting in nearly planar molecular units (Scheme 7, left). Additional ligands bind perpendicular to the plane, which give rise to complexes having three-dimensionality (Scheme 7, right).

The geometric differences between the complexes at the molecular level influence the morphology of the PCA-produced nanoparticles. As shown in Fig. 7 (right frame), SEM image of processed [Ru(salen)(NO)(Cl)] complex shows aggregates of primary particles having spherical structures, with average diameter of 50 nm. The spherical morphology is typical of nanoparticles produced by PCA with non-planar molecular structures. In contrast, the SEM image of unprocessed [Ru(salen)(NO)(Cl)] depicted flat irregular particles with sizes ranging from microns to millimeters (Fig. 7, left frame).

In contrast, the SEM images of [Ni(salen)] and [Co(salen)] nanoparticles (Fig. 8) produced by PCA from planar compounds reveal rod-like structures, with average diameter and length of 85 and 700 nm, respectively. These nanoparticles show evidence of unique functions in adsorption [90], controlled release formulation [91] and catalysis [92].

Investigations into the structure–function relationships of the nanoparticles revealed that [Co(salen)] nanoparticles reversibly bind dioxygen at room temperature [90]. Co(salen) complexes are well-known O_2 carriers in solution. In the solid phase, these complexes exhibit some O_2 binding but detailed studies have been complicated because few of the known polymorphs of Co(salen)

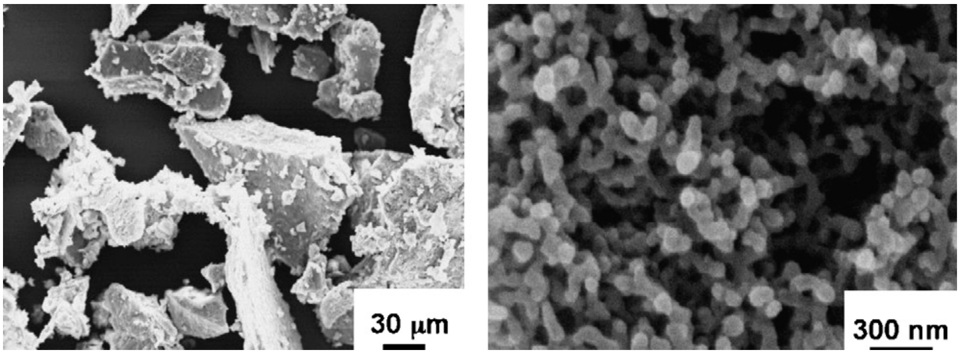


Fig. 7. SEM images of unprocessed [Ru(salen)(NO)Cl)] (left) and the spherical primary particles obtained from the PCA process (right).

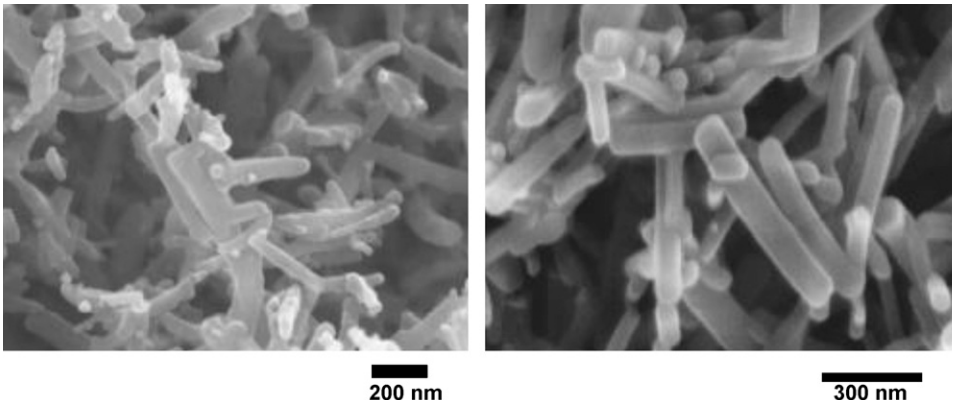


Fig. 8. SEM images of [Co(salen)] (left) and [Ni(salen)] (right) nanoparticles.

actually bind O_2. Temperature programmed desorption (TPD) (Fig. 9), thermogravimetric analysis (TGA) and a Rubotherm magnetic suspension balance measurements reveal a reversible O_2 uptake of approximately 1.51 mmol/(g nanoparticles) at 25 °C, consistent with a binding stoichiometry involving a bridging peroxo unit between two Co centers. In contrast, no measurable O_2 uptake was observed with the commercial Co(salen).

The structure and ligand environment of Co(salen) nanoparticles and unprocessed Co(salen) (i.e., starting precursor) were determined by the combined application of infrared, Raman, X-ray absorption near edge structure (XANES) and extended X-ray absorption fine structure (EXAFS) spectroscopies, and X-ray diffraction (XRD) experiments before and during interaction with O_2 [93]. These studies revealed that the difference in O_2 binding may be rooted in the tetrahedral molecular structure of the [Co(salen)] complexes within the nanoparticles. [Co(salen)] normally adopts a square planar coordination geometry in both solution and the solid-state.

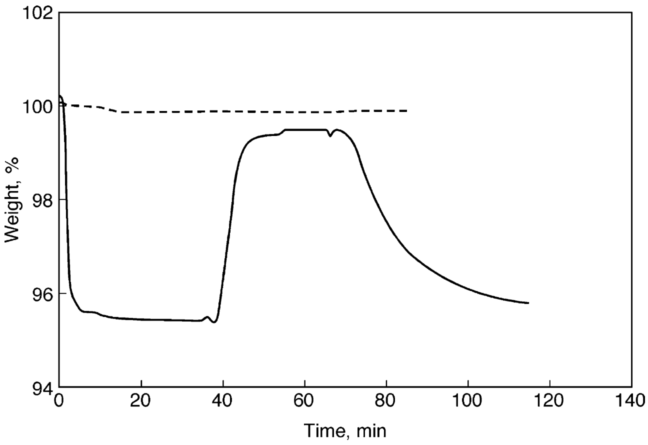


Fig. 9. TGA profiles showing O_2 desorption into flowing N_2 (at 60 °C) followed by subsequent (around 30 min) adsorption from flowing O_2 stream at room temperature (~20 °C): commercial Co(salen) (- -) and Co(salen) nanoparticles (—) (taken from Ref. [90]).

In contrast, the [Co(salen)] nanoparticles do *not* reversibly bind NO but appear to disproportionate NO into other N_xO_y species at room temperature [92]. This is the first example of such reactivity by a solid-state cobalt system at room temperature. These results have stimulated our interest to systematically investigate new functional properties of nanoparticles composed of these and other transition metal complexes.

4. Summary

The foregoing science and technology advances demonstrate the various unique ways in which GXL media may be exploited to develop greener process concepts for O_2 and H_2O_2-based oxidations, hydroformylations and ozonolysis. The demonstrated advantages include *process intensification* at mild conditions by increasing dissolution of the limiting reagent in the GXL reaction phase; the *efficient utilization* of feedstock and reactive gases such as O_3 due to the inertness of CO_2, an often used expansion medium; enhancing *inherent safety* of the process by suppression of flammable vapors; the synthesis of *nanomaterials of transition metal complexes* with unique catalytic function; and *waste minimization* by suppression of side reactions that generate undesired products such as CO_2 and reduced usage of volatile organic solvents. Quantitative analyses are being employed at the CEBC to confirm that these alternate process concepts produce less waste with reduced toxicity compared to conventional processes while being economically viable. Such comparative analyses have been instrumental in licensing the CXL-based hydroformylation technology to a CEBC partner company. The CEBC researchers are currently investigating these CXL-based process concepts for producing industrial chemicals from renewable feedstocks. Such disruptive technology concepts have an especially good chance of being adopted in the biorefineries of the future.

5. Tribute to Professor Daryle Busch

In lieu of a champagne (a CO_2-expanded liquid itself!) toast to Professor Busch's good health on his 80th birthday, we hope that this contribution on the topic of gas-expanded liquids is a fitting tribute to his outstanding contributions to the field of chemistry and to his profession. Most of the science and technology advances discussed in this paper were borne out of research at the Center for Environmentally Beneficial Catalysis (CEBC), an organization initiated with funding from the National Science Foundation Engineering Research Centers (NSF-ERC) program that resulted from our collaboration. It is a distinct privilege and pleasure to have been associated with Professor Busch and to be invited to contribute to this special issue honoring him.

Acknowledgements

The excellent contributions of the many colleagues and collaborators at the CEBC, identified in the cited references, are gratefully acknowledged. Much of the work described in this review was made possible by NSF ERC Grant EEC-0310689, the Kansas Technology Enterprise Corporation and the support of the University of Kansas through the Dan F. Servey Distinguished Professorship.

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