

# Oxidation Reactions in CO<sub>2</sub>: Academic Exercise or Future Green Processes?

E. J. BECKMAN\*

Chemical Engineering Department, University of Pittsburgh,  
1249 Benedum Hall, Pittsburgh, Pennsylvania 15261

Conducting oxidation reactions using CO<sub>2</sub> as the solvent is a promising strategy for creation of greener chemical processes that are also economical, as CO<sub>2</sub> and water are probably the only solvents that can be used in oxidation reactions without the formation of any solvent byproducts. However, it must be noted that the promise of CO<sub>2</sub>-based oxidation still dwarfs the actual realization of CO<sub>2</sub>-based oxidation processes. Nevertheless, there is extensive literature on the use of CO<sub>2</sub> as the solvent for the oxidation of cyclohexane (adipic acid synthesis), cumene oxidation (phenol synthesis), and epoxidation (propylene oxide synthesis). In all of these studies, knowledge of the phase behavior is crucial toward understanding the effects of pressure and temperature on reaction outcomes. To date, much of the research in this field has involved simply using CO<sub>2</sub> as a "drop-in" replacement for a conventional organic solvent; it will be interesting in the future to see if the use of CO<sub>2</sub> can be combined with innovations in catalyst and reactor design to create truly green oxidation processes where the use of CO<sub>2</sub> is not merely tolerated but truly supports process and chemistry innovation.

## Introduction

Oxidation reactions are widely used in the chemical industry to produce high-volume commodity products (1). A number of the commodity processes that have received substantial attention by those endeavoring to create greener chemical syntheses are centered on oxidations, including the industrial syntheses of adipic acid, phenol, terephthalic acid, and caprolactam. While much scientific attention has rightly been directed at the creation of more selective catalysts for these reactions, in this paper we examine the role, if any, that dense carbon dioxide might play in the greening of large-scale oxidations.

Carbon dioxide is widely recognized as a benign yet feeble solvent in the liquid or supercritical state (2). CO<sub>2</sub> exhibits a relatively high TLV, is naturally abundant, and is relatively inexpensive (as compared to other solvents). CO<sub>2</sub> exhibits a particular advantage with respect to oxidation chemistry in that it is nonflammable and cannot be further oxidized; this is certainly not the case for most other organic solvents. From a process perspective, CO<sub>2</sub> is useful in that it is completely miscible with oxygen at temperatures above its critical point (304 K)—this suggests that one *might* be able to eliminate the resistance to transport of oxygen presented by the liquid–vapor interface in a conventional substrate/solvent/oxygen mixture and hence operate the reaction at higher rates in CO<sub>2</sub> than in organic solvents.

In this paper, we will examine situations where CO<sub>2</sub> could provide both process and green advantages if strategically employed and suggest where future research might be directed. Here we focus on larger-scale commodity processes. Although fine chemical synthesis produces more waste on a per mass of product basis (3), the volumes are so high for commodity chemical production that even small improvements would have a substantial impact on waste released to the environment. Furthermore, as noted recently by Blaser and Struder (4), commodity producers are likely to be more receptive to process changes involving alternative solvents than those in the fine chemical industry.

## Impact of Phase Behavior on the Reaction Outcome

It is important to remember that CO<sub>2</sub> is (for the cases under discussion here) only a solvent; hence, it is typically difficult to justify (from either economic or green chemistry grounds) the addition of a solvent to a process that typically operates in bulk (either in the liquid or gas phase). This will usually be the case for gas-phase oxidations, although there are important exceptions to this rule that arise from both phase behavior and safety considerations and which will be noted below. For the case of liquid-phase oxidations, the addition of CO<sub>2</sub> can either be positive or negative, depending upon the characteristics of the system under study.

Several industrially important oxidations are conducted in a two- or three-phase reactor where liquid substrate is contacted with either air or oxygen. The catalyst can be either soluble (homogeneous, two-phase) or insoluble (heterogeneous catalysis, three-phase). The rate of the reaction is often limited not by the inherent kinetics but by the rate at which oxygen finds its way into the liquid phase and to the active sites of the catalyst. This transport rate is often low both due to the low solubility of oxygen in typical organic substrates and due to a low mass transfer coefficient. In these situations, although adding CO<sub>2</sub> dilutes the reaction mixture (ordinarily not a wise move), there are circumstances where this "dilution" can increase the rate of the reaction by eliminating or reducing the transport resistance that slows the migration of oxygen to the catalyst.

The addition of carbon dioxide can reduce or eliminate transport resistance through two mechanisms, one obvious and one more subtle. First, carbon dioxide is completely miscible with oxygen above CO<sub>2</sub>'s critical temperature of 304 K. If one adds the proper amount of CO<sub>2</sub> and adjusts the temperature and pressure accordingly, one can create a single phase (of CO<sub>2</sub>, substrate, and oxygen) where two phases previously existed. In such a case, if the catalyst is soluble, the reaction would move from a transport-limited to a kinetically controlled regime, and hence the rate could increase dramatically. For example, we have previously investigated the oxidation of highly CO<sub>2</sub>-soluble tetrahydroanthraquinones (FTHQ) (5) in CO<sub>2</sub> as one step in a sequence to produce hydrogen peroxide without the use of organic solvent. Use of a single-phase mixture of FTHQ, oxygen, and CO<sub>2</sub> allowed for kinetic control of the reaction; hence, the reactions follow simple second-order kinetics in CO<sub>2</sub>. Moving from transport control to kinetic control in this situation allows for a 5-fold enhancement in the rate of the reaction. Furthermore, elimination of the organic solvent eliminates a principle source of waste (solvent byproducts).

There are disadvantages to conducting the "single-phase" strategy outlined above. First, carbon dioxide is not a particularly strong solvent; hence, high pressures are often required to create a single phase with even nonpolar substrates. To illustrate this, we have performed phase

\* Telephone: (412)624-9630; fax: (412)624-9639; e-mail: beckman@engr.pitt.edu.

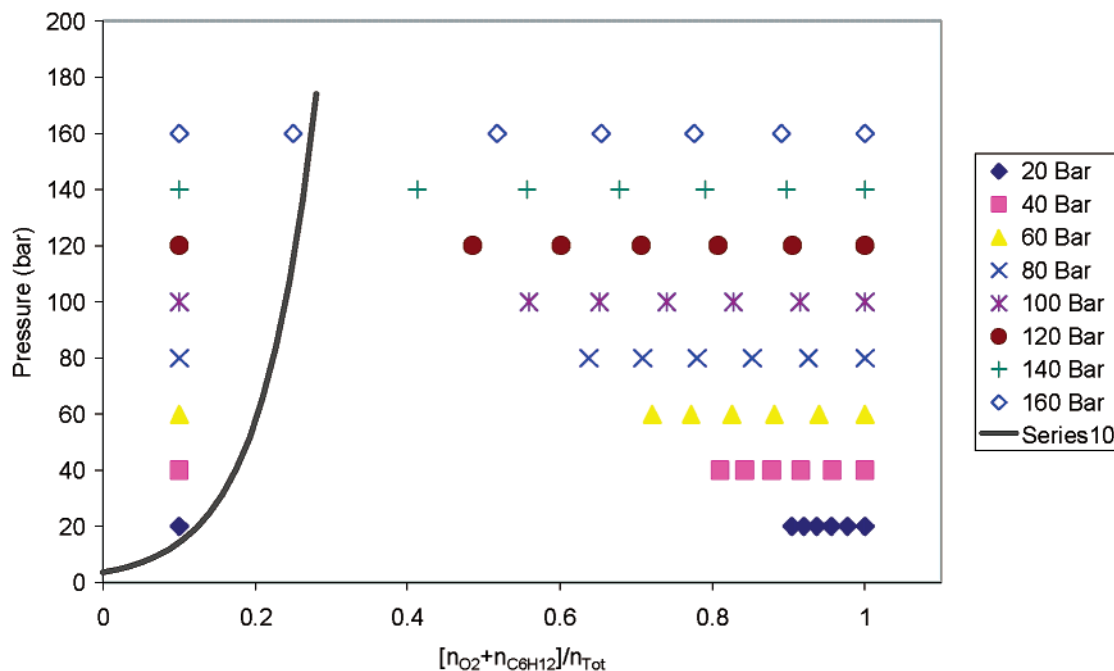


FIGURE 1. Flash calculation results for  $\text{CO}_2/\text{O}_2/\text{cyclohexane}$  mixtures at  $T = 353 \text{ K}$  using the Soave–Redlich–Kwong equation of state. Points to right of solid line represent two-phase mixtures; single-phase mixtures to the left. X-axis shows total mole fraction of oxygen + cyclohexane, where molar ratio of oxygen to cyclohexane = 10.0.

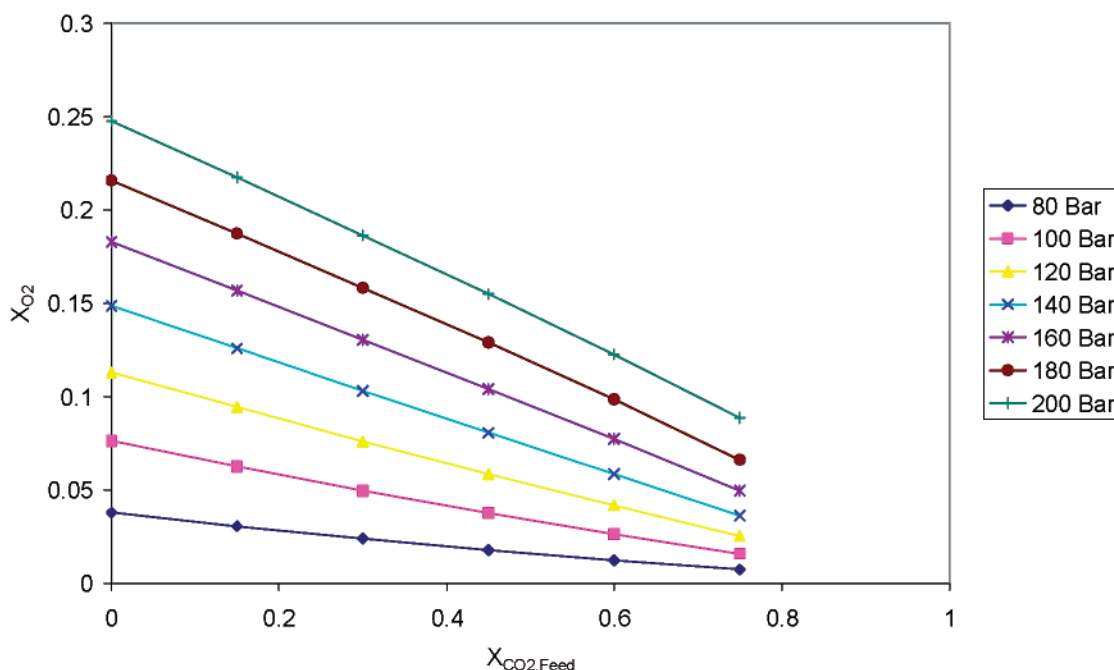


FIGURE 2. Flash calculation results for  $\text{CO}_2/\text{O}_2/\text{cyclohexane}$  mixtures at  $T = 353 \text{ K}$  using the Soave–Redlich–Kwong equation of state. Points show concentrations of oxygen in the liquid phase vs  $\text{CO}_2$  feed (overall) mole fraction at various pressures.

behavior (flash) calculations for the system  $\text{O}_2/\text{cyclohexane}/\text{CO}_2$  using the Soave–Redlich–Kwong equation of state (6). This particular ternary mixture was chosen as it would represent a potential first step in a  $\text{CO}_2$ -based synthesis of adipic acid, a popular target for those interested in the greening of oxidation processes. In Figure 1, we show a preliminary “road map” of flash calculations for a number of concentrations (here the oxygen:cyclohexane ratio remains a constant 2, and we vary the total amount of the reactants on the x-axis) and pressures at 353 K. The solid line on the graph represents the boundary between single- and two-phase mixtures—as can be seen, operation in the single-phase regime requires relatively high pressure and dilute

concentrations of the reactants. Furthermore, there are limits to the concentrations one can attain at economically tractable pressures. Hence, one can create a single phase of  $\text{CO}_2$ , cyclohexane, and oxygen, but one pays a price in terms of elevated operating pressure and dilution of reactants. This dilution effect is also present in the two-phase mixtures (to varying extents), as shown in Figure 2, where liquid-phase compositions are reported. As we add  $\text{CO}_2$  to the system, reactant concentrations decrease in the liquid phase, so no “cosolvent” effect due to  $\text{CO}_2$  is observed. More about the two-phase systems will be reported below.

The second disadvantage to the use of the single-phase strategy is that one might have to chemically alter the

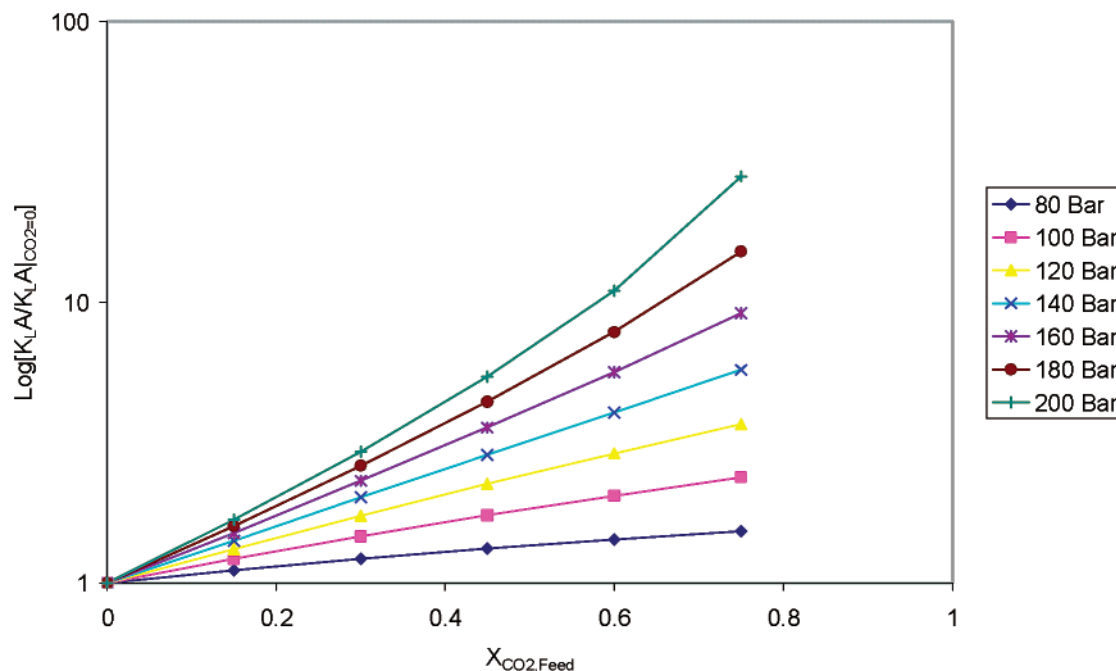


FIGURE 3. Mass transfer coefficients ( $k_L a$ ) calculated using correlation of Albal et al. (17) for two-phase  $\text{CO}_2/\text{O}_2/\text{cyclohexane}$  system using liquid-phase concentrations determined using flash calculations at 353 K. Mass transfer coefficients are normalized against situation where no  $\text{CO}_2$  is added.

homogeneous catalyst to render it soluble in a mixture that is primarily  $\text{CO}_2$ . Carbon dioxide is known to be a relatively feeble solvent and, hence, will not necessarily dissolve the same amount of a traditional homogeneous oxidation catalyst as either the bulk substrate or a conventional organic solvent. The usual method by which to render a catalyst highly  $\text{CO}_2$ -soluble is via functionalization with fluorinated “ponytails”—previous work has demonstrated conclusively that fluorination of catalyst ligands will enhance solubility in  $\text{CO}_2$  (7), allowing one to perform oxidation reactions using analogues to traditional catalysts (8). On the other hand, fluorination increases the cost of the catalyst owing to both the chemistry involved and the significant increase in the molecular weight of the ligands. For the case of oxidation, one may not need to create fluorinated analogues to traditional catalysts, as some of these (in particular metal carbonyls) do exhibit reasonable solubility in carbon dioxide (9).

As noted above,  $\text{CO}_2$  can reduce the effect of transport limitations because it can be used to generate a single phase of oxygen and substrate, although one pays a price in higher operating pressure and reduced reactant concentrations. However, adding  $\text{CO}_2$  to a gas–liquid system, while remaining two-phase, can enhance mass transfer substantially. Returning to our cyclohexane/oxygen/ $\text{CO}_2$  ternary mixture, if the reaction is transport limited (by oxygen migration across the vapor–liquid boundary), then the rate should follow the flux of oxygen into the liquid or:

$$N_A = k_L a^* (C_A^* - C_{A,L}) \quad (1)$$

where  $N_A$  is the flux of oxygen across the interface,  $k_L a$  is the product of the mass transfer coefficient times the interfacial area,  $C_{A,L}$  is the bulk liquid concentration of oxygen, and  $C_A^*$  is the equilibrium concentration at the interface (10). Here we have assumed that the overall transport resistance ( $K_L a$ ) is dominated by the liquid side resistance ( $k_L a$ ) (10). Furthermore, we have assumed a fast reaction in the liquid phase (owing to use of a homogeneous catalyst); hence,  $C_{A,L}$  can be set to zero. We modeled the effect of  $\text{CO}_2$  on the convective mass transfer coefficient using the relationship

derived by Albal and colleagues (11) for mass transfer in a stirred, two-phase agitated batch reactor (eq 2).

$$k_L a^* \left( \frac{L^2}{D} \right) = C^* \left( \frac{\mu}{\rho D} \right)^{1/2} \left( \frac{L^2 \eta \rho}{\mu} \right)^{2/3} \left( \frac{\rho \eta^2 L^3}{\sigma} \right)^{5/4} \quad (2)$$

where  $D$  is the diffusion coefficient of oxygen in the mixture,  $L$  is the diameter of the stirred tank,  $\mu$  is the mixture viscosity,  $\rho$  is the mixture density,  $\eta$  is the stirring speed,  $\sigma$  is the interfacial tension of the gas–liquid mixture, and  $C$  is a constant specific to the reactor in question. The addition of  $\text{CO}_2$  affects  $k_L a$  through its effect on the density, viscosity (and hence diffusion coefficient), and interfacial tension—these parameters were calculated using the equation of state coupled with physical property estimation methods. The results are shown in Figure 3, where it can be seen that addition of  $\text{CO}_2$  to the liquid phase can increase  $k_L a$  by an order of magnitude. To model the effect of  $\text{CO}_2$  on the rate, we must also include the effect of added  $\text{CO}_2$  on the concentration of oxygen in the lower phase, as shown previously in Figure 2. When the results from Figures 2 and 3 are combined (Figure 4), we see that under certain circumstances the rate of oxidation can be increased by an order of magnitude despite operating in the two-phase regime and despite the dilution of the liquid phase by  $\text{CO}_2$ . This enhancement is due primarily to the increases to the convective mass transfer coefficient obtained after the addition of  $\text{CO}_2$  to the liquid phase. Indeed, because creating a single phase requires a significant dilution of the reactants (and hence a rate decrease), use of the two-phase mixture may produce superior results, at least in terms of enhanced rate of reaction.

There are numerous results in the literature that support the conclusions described above. For example, Wu et al. (12) examined the oxidation of cyclohexane in the presence of a soluble (fluorinated) iron porphyrin catalyst. Wu et al. found that the rate of the reaction passed through a maximum in pressure, where the pressure maximum may have corresponded to the point where the system went from two to one phase (initial increases in rate may also have been due

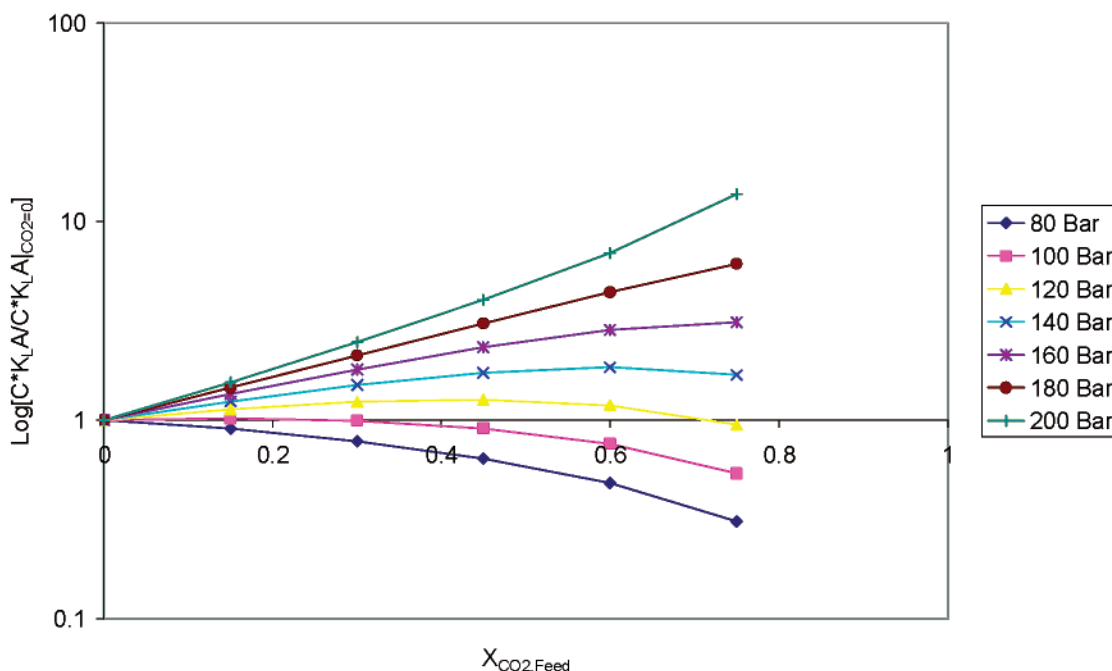


FIGURE 4. Product of oxygen concentration with mass transfer coefficient, where these quantities are calculated as in Figures 2 and 3, vs overall (feed)  $\text{CO}_2$  concentration at 353 K. Y-axis hence represents a measure of the rate of reaction; data are normalized to situation where no  $\text{CO}_2$  is added.

to increases in catalyst solubility with increasing pressure). Srinivas and Mukhopadhyay (13) also examined the oxidation of cyclohexane in  $\text{CO}_2$  at temperatures above 390 K, here without the use of any catalyst. They found that the highest rates could be obtained in the two-phase region where  $\text{CO}_2$  was added as the minor component (diluent). Indeed, Srinivas and Mukhopadhyay (13c) report that “the product formation decreases with a change in phase from two phases (fluid-vapor) to a single vapor phase”. Jenzer and colleagues (14) investigated the oxidation of octanol (using oxygen) in  $\text{CO}_2$  at various temperatures and pressures, where all experiments were conducted in the two-phase regime. They noticed a maximum in octanol yield as pressure increased (at lower temperatures), which they attributed to overoxidation of the catalyst surface at higher pressures (as pressure increased in the two-phase region, the amount of oxygen dissolved in the liquid phase was actually *too large*, causing overoxidation of the catalyst surface). Finally, Hou and colleagues (15) examined the oxidation of cyclohexane over a metal-containing aluminophosphate ( $\text{MnAPO-5}$ ) catalyst in  $\text{CO}_2$  in both the single- and two-phase regimes. As was observed by Srinivas and Mukhopadhyay, the rate of reaction was higher in the two-phase regime, ostensibly because the concentration of cyclohexane was higher in the vicinity of the catalyst when the system split into liquid and vapor phases, while the transport of oxygen between phases remained high.

As described above, operation in the two-phase regime with added  $\text{CO}_2$  can positively affect the outcome of an oxidation reaction owing to enhancements in mass transfer rate and moderate operating pressure. In addition, use of a two-phase mixture more easily allows the use of air as the primary oxidant, a less expensive and more environmentally friendly method than use of pure oxygen. If air were to be used in a single-phase mixture, one would have to operate at a higher pressure to maintain the single phase (given the much higher amounts of low  $T_c$  gases) and would have to conduct extra separation steps to prevent nitrogen buildup (and hence alteration of the phase behavior) in the system.

Subramaniam and colleagues (16) have employed in-depth knowledge of both phase behavior and chemical effects

to optimize conditions for the oxidation of a hindered phenol to the corresponding quinone using a  $\text{Co}(\text{salen})$  catalyst. Here, if one conducts this reaction in organic solvent (acetonitrile), the polar solvent presents the ideal environment for the catalyst (as well as good solvent power), but the solubility of oxygen in the liquid phase is poor. On the other hand, if one conducts the reaction in pure  $\text{CO}_2$ , the solubility of oxygen is excellent, yet the solubility of the catalyst is poor (at moderate pressures) and  $\text{CO}_2$ 's low dielectric constant provides a less than ideal environment for optimal performance of the catalyst. Consequently, Subramaniam and co-workers showed that the ideal solution is to employ a mixture of the organic solvent and  $\text{CO}_2$  (an “expanded liquid”), where one could obtain a polar environment, high oxygen solubility, and high catalyst solubility (without the need to resort to fluorination). Using a mixture of organic solvent and  $\text{CO}_2$  allowed for use of extremely mild operating pressures (less than 100 bar) as well.

One sometimes overlooked *advantage* to  $\text{CO}_2$ 's poor solvent power is reduced metal leaching from catalysts. When operating a heterogeneous catalytic oxidation reaction, a heterogeneous catalyst that releases its active metal into solution will not be stable long-term and may have limited practical utility (17). Sheldon and colleagues have demonstrated that catalysts that are assumed to be heterogeneous can be in fact be homogeneous in that the metal that is leached into solution actually performs the catalysis. In extensive studies, for example, Sheldon's group has found that chromium-substituted molecular sieves, while nominally a heterogeneous catalyst for the oxidation of alcohols, are in fact homogeneous because metal leached from the catalyst forms an active catalytic species. Because  $\text{CO}_2$  is such a poor solvent for ionic and polar species, we would predict a much lower extent of leaching of metal from a catalyst in  $\text{CO}_2$  as compared to bulk substrate or substrate in a traditional solvent. Indeed, Tsang and co-workers (18) observed no leaching of metal during supported Pd or Pt oxidation of alcohols, unlike the situation observed when using water as solvent.



## Case Studies

In this section, we will discuss literature work where oxidation in CO<sub>2</sub> has been used in an attempt to “green” an oxidation reaction of industrial importance.

**Oxidation of Propylene to Propylene Oxide.** Over 4 million t of propylene oxide (PO) are produced each year (19) using either the chlorohydrin or the peroxidation processes. In the chlorohydrin route, propylene is reacted with water and Cl<sub>2</sub> to produce 1-chloro-2-propanol (plus HCl), which is then reacted with base to generate PO plus salt. Over 2 lb of salt waste is produced/lb of PO, which leads to production of wastewater at volumes roughly 40 times that of the PO produced. Peroxidation processes generate PO and a coproduct, either styrene (2.4 mol/mol of PO) or MTBE (3–4 mol/mol of PO). In the styrene process (which predominates), ethyl benzene is first oxidized with O<sub>2</sub> to peroxyethyl benzene, which is then used to oxidize propylene to PO. The residual hydroxyethyl benzene is then dehydrated to styrene. Here 20% waste is produced during the oxidation of ethyl benzene alone, and a sizable number of unit operations must be included to generate and purify the coproduct. In summary, each current PO process produces sizable waste streams and is far more complex and energy-intensive than desired.

Direct oxidation of propylene to PO with O<sub>2</sub> would be highly desirable (20), but the presence of propylene’s highly combustible allylic hydrogens renders this quite difficult (21). Catalysts reported in the literature have yet to be able to support both high conversion of propylene and high selectivity to PO; instead these reactions produce primarily CO<sub>2</sub> via simple combustion. Research has shown that H<sub>2</sub>O<sub>2</sub> will produce PO directly from propylene over the appropriate catalyst, with water as the only byproduct. Many authors (22) have shown that a titanium silicalite (TS-1) catalyst would promote the formation of PO from propylene and hydrogen peroxide at selectivities approaching 100%. Because H<sub>2</sub>O<sub>2</sub> is an environmentally benign oxidant, this route would seem to combine both green and economic advantages. Unfortunately, hydrogen peroxide is currently too expensive to create an economically viable process (23), a condition that seems counterintuitive for such a “simple” chemical.

Although H<sub>2</sub>O<sub>2</sub> is a relatively simple chemical, the anthraquinone (AQ) route, the method by which 95% of the world’s hydrogen peroxide is produced, is not a simple process. In the AQ process, 2-ethylanthraquinone is dissolved in solvent and hydrogenated to the corresponding hydroquinone (HQ) in a three-phase reactor. The HQ is then oxidized back to the AQ, splitting off H<sub>2</sub>O<sub>2</sub> in the process. The H<sub>2</sub>O<sub>2</sub> is then extracted from the organic solvent into water. This scheme allows for continuous H<sub>2</sub>O<sub>2</sub> production without contact between H<sub>2</sub> and O<sub>2</sub>, but it also generates a number of waste streams and consumes relatively large quantities of energy. The high energy input, large number of unit operations, and large waste volumes renders H<sub>2</sub>O<sub>2</sub> production far from green, and the cost of H<sub>2</sub>O<sub>2</sub> is 50% too high to be used in commodity chemical processing.

The use of hydrogen peroxide as a gentle but effective oxidant could be rendered economically viable if it could be generated *in situ* from H<sub>2</sub> and O<sub>2</sub> without the AQ or solvent. Holderich and colleagues (24) have examined the liquid-phase generation of PO from hydrogen, oxygen, and propylene in methanol/water over Pd (alone and with Pt) on TS-1. The choice of MeOH/H<sub>2</sub>O as the solvent mixture arises from the experimental observation that an alcohol (preferably methanol) is needed to perform the reaction efficiently. Clerici and colleagues, for example, propose that the methanol interacts with the catalyst surface at the active site (25), activating it toward epoxidation. However, it is not entirely clear whether the benefits observed while using methanol

derive from a chemical interaction, as proposed by Clerici, or from enhanced H<sub>2</sub> and O<sub>2</sub> solubility in the aqueous phase.

Jenzer et al. have also recently investigated the generation of PO from H<sub>2</sub>, O<sub>2</sub>, and propylene over a Pt/Pd/TS-1 catalyst in a continuous fixed-bed reactor at 43 °C and 50 bar (26). A mixture of methanol and water was employed as the solvent. At the beginning of the reaction, the PO conversion was 3.5% and selectivity was greater than 99%, but both yield and selectivity declined rapidly after 1 h on stream. A variety of byproducts were identified, including acetone, acrolein, acrylic acid, and monomethylated glycols, yet the major byproduct was found to be methyl formate. Many of the byproducts were found to derive from the acid-catalyzed rearrangement and further oxidation of PO (acetone, acrolein) or the reaction between methanol and PO. The formates are created via the oxidation of methanol over Pd, a known reaction that takes place under mild conditions. Although methanol was clearly the primary source of byproducts, the literature (25) maintains that methanol interacts with the active site of the catalyst and is hence vital to successful PO synthesis.

Given this background, we investigated the use of CO<sub>2</sub> as the sole solvent for the generation of PO from hydrogen, oxygen, and propylene over a Pd/TS-1 catalyst (27). CO<sub>2</sub> provides a unique combination of advantages to this process—CO<sub>2</sub> can solubilize large quantities of gases, is immune to oxidative degradation, provides a nonflammable environment in which to mix H<sub>2</sub> and O<sub>2</sub>, and is miscible with both propylene and PO. Note that this case is an exception to the rule that says that adding CO<sub>2</sub> to a gas-phase reaction is not likely to be a good idea; here CO<sub>2</sub> allows for the use of mixtures of O<sub>2</sub> and H<sub>2</sub>, while also solubilizing other necessary components.

The effect of solvent system (CO<sub>2</sub> vs water/MeOH) was compared via three sets of experiments: (a) use of CO<sub>2</sub> as the sole solvent, (b) use of methanol/water and nitrogen to produce the same operating pressure as in set a, and (c) use of methanol/water and CO<sub>2</sub> to produce the same operating pressure as in set a. The results are reported as conversion of propylene and selectivity to PO (total PO divided by total amount of propylene contained in products detected) at the conclusion of the 4.5-h runs. In the case where CO<sub>2</sub> is used as the sole solvent, the byproduct is propane, whereas a number of ring-opening products (products owing to reaction between PO and either water or methanol) and oxidation products are found when MeOH is employed. Decreasing selectivity as one changes the nature of the solvent derives from both chemical and physical effects.

As shown in Table 1, the use of CO<sub>2</sub> as the sole solvent in the reaction allows for high selectivity to PO at reasonable conversions, whereas selectivity drops when methanol/water is added. The latter results are consistent with observations (26) that methanol is a major contributor to byproduct formation (both through reaction with PO and oxidation) and that the use of CO<sub>2</sub> in place of nitrogen leads to improvements. Additional byproducts observed when methanol was present included methyl formate, 1-methoxypropan-2-ol, and 2-methoxypropan-1-ol. Typically, the molar ratio of these three was 12:1.7:1, in agreement with previous observations that methyl formate is the major byproduct when methanol is present.

The presence of the gas–liquid interface (entries 4–6) contributes to decreasing selectivity, as any splashing of the powder catalyst onto the walls of the reactor would lead to the gas-phase hydrogenation of propylene. The last two entries in Table 1 show that use of nitrogen as the pressure transmitting medium leads to enhanced conversion but low selectivity as the significant gas–liquid interface promotes propane formation (it is also possible that methanol can further reduce the palladium to the point where propane

TABLE 1. Comparative Results for Batch Epoxidation in Three Different Systems<sup>a</sup>

solvent system	catalyst mass (g)	propylene conversion (%)	propylene selectivity to PO (%)	propylene selectivity to C <sub>3</sub> H <sub>8</sub> (%)	propylene selectivity to ring opened byproducts
CO <sub>2</sub>	0.15	9.5	77.1	22.9	nd <sup>b</sup>
CO <sub>2</sub>	0.195	6.5	91.2	8.8	nd
CO <sub>2</sub>	0.300	7.5	94.3	5.7	nd
MeOH + H <sub>2</sub> O + CO <sub>2</sub>	0.157	3.5	17.4	75.0	7.6
MeOH + H <sub>2</sub> O + CO <sub>2</sub>	0.206	4.7	41.1	46.5	12.4
MeOH + H <sub>2</sub> O + N <sub>2</sub>	0.199	16	3.5	95.2	1.4

<sup>a</sup> Total pressure = 13.1 MPa, temperature = 318 K, 4.5 h reaction time. In all cases the absolute concentrations were 4 mm for propylene, 1.26 mM for H<sub>2</sub>, and 8.3 mM for O<sub>2</sub>, in 3.84 H 10<sup>-5</sup> m<sup>3</sup> of CO<sub>2</sub>. Conversion continued to change up to 4.5 h, so we believe that the hydrogen had not yet been completely consumed at that point. <sup>b</sup> nd indicates that no PO ring-opening byproducts (propylene glycols, methoxypropanols, or propylene carbonate) were detected by online GC analysis.

hydrogenation is favored over hydrogen peroxide production). The fact that the presence of CO<sub>2</sub> versus N<sub>2</sub> improves conversion and selectivity to PO when used with MeOH/water likely derives from phase behavior effects. CO<sub>2</sub> will swell a mixture of methanol/water (75/25); hence, improvements due to the replacement of nitrogen by CO<sub>2</sub> may derive from increased solubility of the gaseous reactants (O<sub>2</sub>, H<sub>2</sub>, and propylene) in the liquid phase due to the presence of CO<sub>2</sub>. Also, a mixture of N<sub>2</sub>, propylene, O<sub>2</sub>, H<sub>2</sub>, and MeOH/water will likely create a three-phase mixture, while the use of CO<sub>2</sub> (in place of N<sub>2</sub>) will likely create a two-phase mixture, thus reducing the number of interfaces and enhancing transport. When CO<sub>2</sub> is employed as the sole solvent, the gas-liquid interface (a prime source for formation of propane) is eliminated entirely, further enhancing selectivity.

Use of H<sub>2</sub> and O<sub>2</sub> in CO<sub>2</sub> could produce productivity and waste minimization advantages, but would such a process be safe enough to operate? Dupont (28) scaled a H<sub>2</sub> + O<sub>2</sub> → H<sub>2</sub>O<sub>2</sub> process (using biphasic H<sub>2</sub>/O<sub>2</sub>/H<sub>2</sub>O, no CO<sub>2</sub>) to the pilot stage in the early 1990s and only experienced safety problems when an inappropriate material was used in the oxygen handling system. Recent literature (29) shows that CO<sub>2</sub> produces a significantly larger nonexplosive concentration range than N<sub>2</sub> when used with O<sub>2</sub>/H<sub>2</sub> mixtures. Subramaniam's group has recently (30) shown that CO<sub>2</sub> at temperatures near the critical is an ideal medium for absorbing the excess heat that would be created during an uncontrolled 2H<sub>2</sub> + O<sub>2</sub> → 2H<sub>2</sub>O reaction, owing to the maximum exhibit by CO<sub>2</sub>'s heat capacity. Furthermore, contact between O<sub>2</sub> and CO<sub>2</sub> does not create a safety hazard (CO<sub>2</sub> cannot be oxidized), unlike organic solvents. Hence, CO<sub>2</sub> appears to be the ideal solvent for achieving both productivity and safety in the direct route to H<sub>2</sub>O<sub>2</sub>. Note that CO<sub>2</sub> is not used to replace a traditional organic solvent but rather to allow chemistry that would likely be unacceptable on safety grounds in a conventional organic solvent.

**Oxidation of Cyclohexane: Routes to Adipic Acid.** A sustainable process for synthesis of adipic acid (AA) could be described as a "holy grail" of green chemistry given the volume of AA produced (4 billion lb/yr in 1998) and the waste produced by the current process. In the commercial process (31), cyclohexane is first oxidized by a homogeneous cobalt catalyst to a mixture of cyclohexanone and cyclohexanol. The conversion is limited to 4% to inhibit production of byproducts (succinic and other acids); selectivity is still only 85%. Catalyst recovery produces additional waste as a sludge from which some cobalt is recovered. In the second step, the -one/-ol mixture is oxidized to adipic acid by nitric acid, creating a substantial nitrous oxide waste stream (nitrous oxide exhibits potent climate change potential!). Because of both the economic value of AA and the lack of sustainability in the current process, research into cleaner routes to AA has proceeded vigorously over the past 15 yr. Indeed, in late

2000, Solutia announced a new route to AA (32) where benzene is oxidized to phenol using nitrous oxide, the phenol is hydrogenated to cyclohexanone, and finally cyclohexanone is oxidized to AA using nitric acid. The N<sub>2</sub>O produced in the final step is recycled to the beginning, potentially eliminating one of the more potent waste streams from the traditional AA process, although all of the waste associated with nitric acid production still applies. It is not clear at this time whether this process has advanced beyond the pilot stage.

The extensive literature (33) on the oxidation of cyclohexane to first, the -one/-ol mixture, then AA, shows that *tert*-butyl hydroperoxide produces higher conversions than hydrogen peroxide, which produces higher conversion than oxygen. However, the substantially higher price of the peroxy compounds versus oxygen renders their use economically problematic; hence, the cobalt-catalyzed, O<sub>2</sub>-based commercial process endures despite its environmental flaws.

A number of researchers have examined the oxidation of cyclohexane in CO<sub>2</sub>, although the results have not been terribly promising. Armbruster and Martin (34) examined the continuous oxidation of cyclohexane in CO<sub>2</sub> using various metal oxide catalysts; reactions run in CO<sub>2</sub> exhibited substantially lower yields than those conducted in bulk. Hou et al. (15) found that oxidations performed in CO<sub>2</sub> exhibited lower conversions (~3% vs 10%) than oxidations performed without solvent, yet with higher selectivity to products (cyclohexanol/cyclohexanone)—99% in CO<sub>2</sub> versus 88% in bulk and 98% in CCl<sub>4</sub>. Hou et al. suggested that the higher selectivity observed using CO<sub>2</sub> (versus chemistry in bulk) may be due to the ability of the initial products (the -one/-ol mixture) to diffuse out of the catalyst quickly (owing to CO<sub>2</sub>'s low viscosity), preventing byproduct formation.

As noted above, Wu et al. (12) examined the homogeneous oxidation of cyclohexane using a soluble iron catalyst and acetaldehyde; the yields were similar to those found by Hou et al., and selectivities were reported to be high. The use of acetaldehyde and the iron porphyrin renders this approach somewhat impractical for use on a large scale. Finally, Srinivas and Mukhopadhyay (13) examined the oxidation of cyclohexane in detail, in the absence of added catalyst. They report that conversions are low owing to the dilution of the reactants by CO<sub>2</sub> (as compared to liquid-phase oxidation), but the low conversions could perhaps be attributed to lack of catalyst as well. As noted above, the phase behavior exerted considerable influence over the outcome of the reaction; it was found that pressure also influences rate constants and selectivity (to cyclohexanone versus cyclohexanol).

In summary, research into use of CO<sub>2</sub> as the solvent during oxidation of cyclohexane (to cyclohexanol/-one and subsequently to adipic acid) has not yielded promising results to date. However, because in these studies CO<sub>2</sub> was employed in a drop-in capacity (i.e., simply adding CO<sub>2</sub> to a conventional cyclohexane oxidation system), this is not entirely surprising.

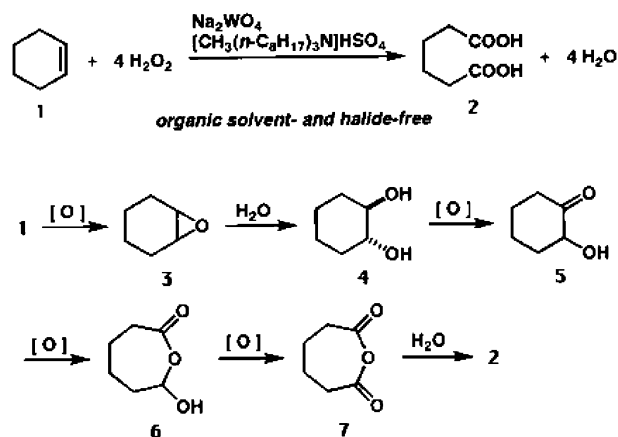


FIGURE 5. New route to adipic acid from cyclohexene and hydrogen peroxide, as explored by Sato et al. (35a).

It may be more advantageous to explore the use of  $\text{CO}_2$  as the solvent in one or more of the newer catalytic schemes to produce adipic acid. These might include Noyori's or Thomas'  $\text{H}_2\text{O}_2$ -based routes (35) or the route developed by Monsanto. For example, in the Noyori route to AA from cyclohexene (using  $\text{H}_2\text{O}_2$  as oxidant, see Figure 5), all of the proposed intermediates are likely to be  $\text{CO}_2$ -soluble, while the product (AA) is not, providing for a potentially straightforward separation/recycle mechanism. Just as Noyori employed a phase transfer ligand to solubilize the tungstate catalyst, one could also solubilize the tungstate in  $\text{CO}_2$  using the appropriate ligand. If one were to use a biphasic  $\text{H}_2\text{O}_2$ – $\text{CO}_2$  system, oxidation would proceed via the percarbonate (formed via reaction between  $\text{H}_2\text{O}_2$ ,  $\text{CO}_2$ , and water), as shown previously by both Eckert's group and our own (36). On the other hand, one could form the  $\text{H}_2\text{O}_2$  in situ, as shown by our group in the synthesis of propylene oxide. In general, it seems hard to imagine that simply addition of  $\text{CO}_2$  to a conventional process could provide benefits (both green and economic) substantial enough for rapid development—new large-scale processes for AA are likely to incorporate innovations in several areas, where alternative solvent use is only one among many.

**Synthesis of Phenol from Benzene.** Approximately 4.5 billion lb/yr of phenol is currently produced from benzene in the three-step cumene process (31). Benzene is first reacted with propylene at  $\sim 200^\circ\text{C}$  to generate cumene, which is then reacted with oxygen at  $80$ – $130^\circ\text{C}$  to form cumene hydroperoxide. The conversion in this step is limited to  $\sim 25\%$  because handling/transport of concentrated cumene hydroperoxide at the temperatures involved is relatively dangerous. In the final step, cumene hydroperoxide (in solvent) is decomposed using sulfuric acid to acetone and phenol. Distillation is used to separate the two coproducts and to remove byproducts (acetophenone and  $\alpha$ -methyl styrene) from the phenol. Aqueous waste derived from the use of the acid and solvent is substantial. As in the coproduct process for generation of PO, the phenol process creates more waste, requires higher energy input, and requires more unit operations than would be needed for generation of the one desired product. The market demands for phenol and acetone are typically not in sync, creating additional problems.

Despite the potential benefits, there has been little research into the use of  $\text{CO}_2$  to help green the phenol process. Suppes et al. (37) explored the oxidation of cumene during the late 1980s. Whereas the physical properties of the medium ( $\text{CO}_2$ ) exerted little influence on the outcome of the reaction, the steel reactor itself lowered the selectivity to cumene hydroperoxide. It was further noted that the oxidation of

cumene to its hydroperoxide (and other species) proceeded faster in neat substrate than in mixtures with supercritical fluids.

Again, it would be more interesting to employ  $\text{CO}_2$  in a greener phenol process that also incorporated innovations in chemistry, catalysis, and/or process design, rather than as a drop-in replacement for a solvent in the conventional cumene process. A number of researchers have shown that one can efficiently oxidize benzene to phenol using hydrogen peroxide. Kumar and Bhaumik, for example (38), found that  $\text{H}_2\text{O}_2$ /TS-1 would produce phenol from benzene (78% conversion, 87% efficiency in  $\text{H}_2\text{O}_2$  usage) at  $333$ – $353^\circ\text{K}$  and selectivity to phenol of 89%. These researchers employed a triphase system (solid catalyst, organic solvent, and aqueous  $\text{H}_2\text{O}_2$ ), which obviously complicates the mass transfer and the recovery of products. Use of in situ generation of  $\text{H}_2\text{O}_2$  (from  $\text{O}_2$  and  $\text{H}_2$ ) in  $\text{CO}_2$  and oxidation of substrate would present simpler transport characteristics and separation issues following reaction. Interestingly, Kitano et al. (39) explored the use of an  $\text{O}_2$ / $\text{H}_2$  mixture (over a Cu–Pd catalyst) to generate phenol from benzene, but this route did not involve  $\text{H}_2\text{O}_2$  as an intermediate. Here, Cu(I) activated oxygen (generating  $\cdot\text{OH}$  and Cu(II)) which then reacted with benzene. Hydrogen subsequently reduced Cu(II) to Cu(I) over Pd. Because the use of  $\text{CO}_2$  as a solvent provides for safe operation using  $\text{O}_2$ / $\text{H}_2$  mixtures and typically also enhances mass transfer (via formation of a concentrated solution of the gases and liquid substrates), the Kitano system could also benefit through use of  $\text{CO}_2$  as solvent.

In summary, clean oxidation of benzene to phenol remains a vibrant area of research in green chemistry. As in the case of adipic acid synthesis, it would be interesting to apply  $\text{CO}_2$  as solvent to one or more of the newer approaches to clean phenol synthesis, such as liquid-phase oxidation using oxygen and a Pd-heteropolyacid catalyst or copper-based catalysts (40). To truly create a greener process, it would appear that innovations in several areas will be needed.

### Coupling use of $\text{CO}_2$ with New Reactor Designs

Finally, another potentially interesting avenue for research on oxidations in  $\text{CO}_2$  might involve coupling of  $\text{CO}_2$  technology with newer reactor designs. In the Dupont process for the oxidation of butane to maleic anhydride (MA) (41), the reaction involves oxidation of the catalyst by air followed by its reduction by butane (with formation of maleic anhydride) and subsequent catalyst recycling. In the Dupont design, the catalyst oxidation and reduction steps are physically separated (a two-bed approach), and the oxidation step is much slower than the reduction. Although the high-temperature conditions for the Dupont MA process make use of  $\text{CO}_2$  impractical ( $\text{CO}_2$  would simply be a gaseous diluent under these conditions), in other such two-bed approaches with slow oxidation steps, the use of liquid  $\text{CO}_2$  could allow for higher  $\text{O}_2$  concentrations and hence more efficient operation.

Microchannel reactors have also been proposed for use in selective oxidations (see ref 41 for a short review) where the high surface-to-volume ratio allows for very efficient removal of heat, and the reactor walls will quench radical reactions. Hence, explosive mixtures have been employed in such reactors without explosions. One might be able to employ  $\text{CO}_2$  as the solvent in such reactions to allow for even higher concentrations of oxygen (or, as noted above, mixtures of  $\text{O}_2$  and  $\text{H}_2$ ).

Conducting oxidation reactions using  $\text{CO}_2$  as the solvent is a promising strategy for creation of greener chemical processes that are also economical, as  $\text{CO}_2$  and water are probably the only solvents that can be used in oxidation reactions without formation of any solvent byproducts, and  $\text{CO}_2$  solubilizes much higher amounts of oxygen than water.



However, it must be noted that the promise of CO<sub>2</sub>-based oxidation still dwarfs the actual realization of CO<sub>2</sub>-based oxidation processes. Furthermore, oxidation in CO<sub>2</sub> has received relatively little attention in the literature as compared to hydrogenation in CO<sub>2</sub>, despite hydrogenation seemingly being a greener process to begin with. Nevertheless, innovations (such as Subramaniam's use of "expanded liquids") appear with increasing regularity; hence, I remain optimistic. As noted above, knowledge of the phase behavior of any CO<sub>2</sub>-based mixture is crucial to understanding the effects of temperature and pressure on the outcome of the reaction. It will be interesting to see if innovations in the use of CO<sub>2</sub> can be combined with innovations in catalyst and reactor design to create greener oxidation processes in the future. Given the volume of products produced each year using oxidation chemistry, this remains a vital target in green chemistry.

## Literature Cited

- (1) Sheldon, R. A.; Kochi, J. K. *Metal Catalyzed Oxidations of Organic Compounds*; Academic Press: New York, 1981.
- (2) Beckman, E. J. *J. Supercrit. Fluids* (in press).
- (3) Sheldon, R. A. *Pure Appl. Chem.* **2000**, *72*, 1233.
- (4) Blaser, H.-U.; Struder, M. *Green Chem.* **2003**, *5*, 112.
- (5) Hancu, D.; Beckman, E. J. *Ind. Eng. Chem. Res.* **2000**, *39*, 2843.
- (6) Hodgdon, T.; Beckman, E. J. *Ind. Eng. Chem. Res.* (submitted for publication).
- (7) Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev.* **1999**, *99*, 475.
- (8) Birnbaum, E. R.; Le Lacheur, R. M.; Horton, A. C.; Tumas, W. *J. Mol. Catal. A: Chem.* **1999**, *139*, 11.
- (9) Haas, G. R.; Kolis, J. W. *Organometallics* **1998**, *17*, 4454.
- (10) Welty, J. R.; Wicks, C. E.; Wilson, R. E. *Fundamentals of Momentum, Heat, and Mass Transfer*, 3rd ed.; John Wiley & Sons: New York, 1984.
- (11) Albal, R. S.; Shah, Y. T.; Schumpe, A.; Carr, N. L. *Chem. Eng. J.* **1983**, *27*, 61.
- (12) Wu, X.-W.; Oshima, Y.; Koda, S. *Chem. Lett.* **1997**, 1045.
- (13) Srinivas, P.; Mukhopadhyay, M. *Ind. Eng. Chem. Res.* **1994**, *33*, 3118. (b) Srinivas, P.; Mukhopadhyay, M. *Ind. Eng. Chem. Res.* **1996**, *35*, 4713. (c) Srinivas, P.; Mukhopadhyay, M. *Ind. Eng. Chem. Res.* **1997**, *36*, 2066.
- (14) Jenzer, G.; Schneider, M. S.; Wandeler, R.; Mallat, T.; Baiker, A. *J. Catal.* **2001**, *199*, 141.
- (15) Hou, Z.; Han, B.; Gao, L.; Liu, Z.; Yang, G. *Green Chem.* **2002**, *4*, 426.
- (16) Wei, M.; Musie, G. T.; Busch, D. H.; Subramaniam, B. *J. Am. Chem. Soc.* **2002**, *124* (11), 2513–2517. (b) Musie, G.; Wei, M.; Subramaniam, B.; Busch, D. H. *Coord. Chem. Rev.* **2001**, *789*, 219–221.
- (17) Arends, I. W. C. E.; Sheldon, R. A. *Appl. Catal. A: Gen.* **2001**, *212*, 175. (b) Sheldon, R. A.; Wallau, M.; Arends, I. W. C. E.; Schuchardt, U. *Acc. Chem. Res.* **1998**, *31*, 485.
- (18) Steele, A. M.; Zhu, J.; Tsang, S. C. *Catal. Lett.* **2001**, *73*, 9.
- (19) Trent, D. L. Propylene Oxide. In *Kirk–Othmer Encyclopedia of Chemical Technology*, Vol. 20; John Wiley and Sons: New York, 1996.
- (20) Monnier, J. R. *Appl. Catal. A: Gen.* **2001**, *221*, 73.
- (21) Lu, G.; Zuo, X. *Catal. Lett.* **1999**, *58*, 67. (b) Murata, K.; Kiyozumi, Y. *Chem. Commun.* **2001**, 1356.
- (22) Laufer, W.; Meiers, R.; Holderich, W. F. *J. Mol. Catal. A: Chem.* **1999**, *141*, 215. (b) Thiele, G. F.; Roland, E. *J. Mol. Catal. A: Chem.* **1997**, *117*, 351. (c) Mantegazza, M. A.; Petrini, G.; Spano, G.; Bagatin, R.; Rivetti, F. *J. Mol. Catal. A: Chem.* **1999**, *146*, 223. (d) Chen, L. Y.; Chuah, G. K.; Jaenicke, S. *J. Mol. Catal. A: Chem.* **1998**, *132*, 281. (e) Li, G.; Wang, X.; Yan, H.; Chen, Y.; Su, Q. *Appl. Catal. A: Gen.* **2001**, *218*, 31.
- (23) McCoy, M. *Chem. Eng. News* **2001**, *79* (43), 19.
- (24) Laufer, W.; Holderich, W. F. *Appl. Catal. A: Gen.* **2001**, *213*, 163. (b) Kollmer, F.; Holderich, W. F. *Pure Appl. Chem.* **2000**, *72*, 1273. (c) Meiers, R.; Holderich, W. F. *Catal. Lett.* **1999**, *59*, 161.
- (25) Clerici, M. G. *Appl. Catal.* **1991**, *68*, 249–261. (b) Bellussi, G.; Carati, A.; Clerici, M. G.; Maddinelli, G.; Millini, R. *J. Catal.* **1992**, *133*, 220. (c) Clerici, M. G.; Ingallina, P. *J. Catal.* **1993**, *140*, 71.
- (26) Jenzer, G.; Mallat, T.; Maciejewski, M.; Eigenmann, F.; Baiker, A. *Appl. Catal. A: Gen.* **2001**, *208*, 125.
- (27) Danciu, T.; Beckman, E. J.; Hancu, D.; Cochran, R.; Grey, R.; Hajnik, D.; Jewson, J. *Angew. Chem., Int. Ed.* **2003**,.
- (28) Gosser, L. W. Catalytic process for making H<sub>2</sub>O<sub>2</sub> from hydrogen and oxygen. U.S. Patent 4,681,751, 1987. (b) Gosser, L. W.; Schwartz, J. T. Hydrogen peroxide production method using platinum/palladium catalysts. U.S. Patent 4,832,938, 1989.
- (29) Pande, J. O.; Tonheim, T. *Proc. Saf. Progr.* **2001**, *20*, 37.
- (30) Jin, H.; Subramaniam, B. *Chem. Eng. Sci.* **2003**, *58*, 1897.
- (31) Weissmehl, K.; Arpe, H.-J. *Industrial Organic Chemistry*, 3rd ed.; VCH: New York, 1997.
- (32) Sobolev, V. I.; Rodkin, M. A.; Uriarte, A. K.; Panov, G. I. Process for making phenol or phenol derivatives. U.S. Patent 6,156,938, 2000.
- (33) Schuchardt, U.; Cardoso, D.; Sercheli, R.; Pereira, R.; da Cruz, R. S.; Guerreiro, M.; Mandelli, D.; Spinace, E. V.; Pires, E. L. *Appl. Catal. A: Gen.* **2001**, *211*, 1. (b) Thomas, J. M.; Raja, R.; Sankar, G.; Bell, R. G.; Lewis, D. W. *Pure Appl. Chem.* **2001**, *73*, 1087. (c) Thomas, J. M.; Raja, R.; Sankar, G.; Johnson, B. F. G.; Lewis, D. W. *Chem. Eur. J.* **2001**, *7*, 2973. (d) Pillai, U. R.; Sahle-Demessie, E. *Chem. Commun.* **2002**, 2142. (e) Mizuno, N.; Nozaki, C.; Kiyoto, I.; Misono, M. *J. Am. Chem. Soc.* **1998**, *120*, 9267.
- (34) Armbruster, U.; Martin, A. *DGMK Tagungsber.* **2002**, *273*, 2002–04.
- (35) Sato, K.; Aoki, M.; Noyori, R. *Science* **1998**, *281*, 1646. (b) Raja, R.; Lee, S.-O.; Sanchez, M.; Sankar, G.; Harris, K. D. M.; Johnson, B. F. G.; Thomas, J. M. *Top. Catal.* **2002**, *20*, 85.
- (36) Hancu, D.; Green, J.; Beckman, E. J. *Acc. Chem. Res.* **2002**, *35*, 757. (b) Nolen, S. A.; Liu, J.; Brown, J. S.; Pollet, P.; Eason, B. C.; Griffith, K. N.; Glaser, R.; Bush, D.; Lamb, D. R.; Liotta, C. L.; Eckert, C. A.; Thiele, G. F.; Bartels, K. A. *Ind. Eng. Chem. Res.* **2002**, *41* (3), 316–323.
- (37) Suppes, G. J.; Occhiogrosso, R. N.; McHugh, M. A. *Ind. Eng. Chem. Res.* **1989**, *28*, 1152.
- (38) Kumar, R.; Bhaumik, A. *Microporous Mesoporous Mater.* **1998**, *21*, 497.
- (39) Kitano, T.; Kuroda, Y.; Mori, M.; Ito, S.; Sasaki, K.; Nitta, M. *J. Chem. Soc. Perkin Trans. 2* **1993**, 981.
- (40) Miyahara, T.; Kabzaki, H.; Hamada, R.; Kuroiwa, S.; Nishiyama, S.; Tsuruya, S. *J. Mol. Catal. A: Chem.* **2001**, *176*, 141. (b) Passoni, L. C.; Cruz, A. T.; Buffon, R.; Schuchardt, U. *J. Mol. Catal. A: Chem.* **1997**, *120*, 117. (c) Masumoto, Y.-K.; Hamada, R.; Yokota, K.; Nishiyama, S.; Tsuruya, S. *J. Mol. Catal. A: Chem.* **2002**, *184*, 215.
- (41) Emig, G.; Liauw, M. A. *Top. Catal.* **2002**, *21*, 11.

Received for review May 30, 2003. Revised manuscript received September 18, 2003. Accepted September 24, 2003.

ES0345401