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Supercritical and near-critical CO$_2$ in green chemical synthesis and processing

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Abstract

Carbon dioxide is often promoted as a sustainable solvent, as CO$_2$ is non-flammable, exhibits a relatively low toxicity and is naturally abundant. However, injudicious use of carbon dioxide in a process or product can reduce rather than enhance overall sustainability. This review specifically examines the use of CO$_2$ to create greener processes and products, with a focus on research and commercialization efforts performed since 1995. The literature reveals that use of CO$_2$ has permeated almost all facets of the chemical industry and that careful application of CO$_2$ technology can result in products (and processes) that are cleaner, less expensive and of higher quality.
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Keywords: Carbon dioxide; Toxicity; Technology

1. Introduction

The use of carbon dioxide as a solvent or raw material has been investigated somewhat continuously in academia and/or industry since 1950; interest in the use of CO$_2$ in these roles has intensified during the past 20 years as large-scale plants using CO$_2$ have been brought on line. While supercritical fluids in general exhibit interesting physical properties [1], specific interest in CO$_2$ is magnified by its perceived 'green' properties—carbon dioxide is non-flammable, relatively non-toxic, and relatively inert. In addition, unlike water, the supercritical regime of CO$_2$ is readily accessible, given its critical temperature of only 304 K.

Whereas the use of carbon dioxide as raw material or solvent could produce product (property) advantages, process (chemistry) advantages, cost advantages, or safety advantages, in this review we will focus explicitly on uses of CO$_2$ that provide practical improvements (as defined in Section 1.7) to the sustainability (or 'green'-ness) of a product or process. Carbon dioxide is often promoted as a green solvent, and its use in this role has permeated throughout the chemical and materials research communities. Here we describe recent advances that are both fundamental and significant.

In summary, rather than present a comprehensive review of CO$_2$-based technology, here we focus on uses of CO$_2$ that are relatively new and appear to provide 'green' advantages. It should be noted that there are examples provided in this paper where a CO$_2$-based process is not particularly 'green', yet is

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generating interest because it produces better quality product than conventional alternatives.

1.1. Physical properties of CO_2

The pVT properties of CO_2 have been known since the 1930s [2]; extensive data sets are available in the literature and on the web in the form of correlations of density, viscosity, dielectric constant, etc., as functions of temperature and pressure [3]. CO_2's critical pressure (and hence its vapor pressure in the 'near-critical' or liquid regime) is significantly higher than analogous values for alkane, fluoroalkane or hydrofluoroalkane fluids. CO_2's anomalously high critical pressure is but one result of the effect that CO_2's strong quadrupole moment exerts on its physical properties. While the high critical pressure is problematic, the most unfortunate outcome of the effect of quadrupole moment on physical properties was the premise, first advanced during the late 1960s, that CO_2 might prove to be a solvent whose strength would rival or surpass that of alkanes and ketones [4]. Because early models employed to calculate CO_2's solvent power relied on a direct relationship between the Hildebrandt solubility parameter (δ) and the square root of the critical pressure $[(P_c)^{1/2}]$, the solubility parameter of CO_2 was over-predicted by 20–100%, leading to early inflated claims as to the potential for using CO_2 to replace conventional organic solvents.

1.2. Environmental and safety advantages to use of CO_2 in chemical processes

Carbon dioxide is non-flammable, a significant safety advantage in using it as a solvent. It is also naturally abundant, with a TLV (threshold limit value for airborne concentration at 298 K to which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effects) of 5000 ppm [5], rendering it less toxic than many other organic solvents (acetone, by comparison, has a TLV of 750 ppm, pentane is 600 ppm, chloroform is 10 ppm [5]). Carbon dioxide is relatively inert towards reactive compounds, another process/environmental advantage (byproducts owing to side reactions with CO_2 are relatively rare), but CO_2's relative inertness should not be confused with complete inertness. For example, an attempt to conduct a hydrogenation

in CO_2 over a platinum catalyst at 303 K will undoubtedly lead to the production of CO, which could poison the catalyst [6]. The same reaction run over a palladium catalyst under the same conditions will by contrast produce lesser amounts of CO as a byproduct [7] and hence knowledge of CO_2's reactivity is vital to its use in green chemistry.

Carbon dioxide is clearly a 'greenhouse gas', but it is also a naturally abundant material. Like water, if CO_2 can be withdrawn from the environment, employed in a process, then returned to the environment 'clean', no environmental detriment accrues. However, while CO_2 could in theory be extracted from the atmosphere (or the stack gas of a combustion based power plant), most of the CO_2 employed in processes today is collected from the effluent of ammonia plants or derived from naturally occurring deposits (e.g. tertiary oil recovery as practiced in the US [8]). Because industrially available CO_2 is derived from man-made sources, if CO_2 can be isolated within a process one could consider this a form of sequestration, although the sequestered volumes would not be high. Ultimately, one should consider the source of CO_2 used in a process in order to adequately judge the sustainability of the process.

CO_2's combination of high TLV and high vapor pressure means that residual CO_2 left behind in substrates is not a concern with respect to human exposure—the same can certainly not be said to be true for many man-made and naturally-occurring organic compounds. Because there is effectively no liability due to 'residual' CO_2 in materials following processing, CO_2 is not considered a solvent requiring process re-evaluation by the US FDA. Only water also enjoys this special situation. Indeed, most of the commercial operations employing CO_2 as a solvent were initiated to take advantage of CO_2's particular advantages in products designed for intimate human contact (such as food), or CO_2's non-VOC designation (such as the foaming of thermoplastics). The recent commercialization of fabric cleaning using CO_2 benefits both from CO_2's advantages in human-contact applications *and* situations where emissions appear unavoidable.

The simultaneous use of both hydrogen and oxygen in a reaction is obviously problematic from a safety standpoint, given that H_2/O_2 mixtures are explosive over a broad concentration range. Addition of CO_2 to mixtures of H_2 and O_2 expands the non-explosive

regime (in the gas phase), more so than if either N_2 or water vapor was added [9]. At this point it is not clear to what extent the non-explosive regime will expand further as one raises the density of the mixture (and hence the heat capacity).

In a final intriguing note regarding safety advantages inherent to use of CO_2 as a solvent, DuPont scientists [10] discovered that addition of CO_2 to tetrafluoroethylene enhances the stability of that notoriously difficult-to-handle monomer, although the exact mechanism for the enhanced stability has not been published. What has been revealed is that addition of CO_2 to TFE vapor inhibits runaway decomposition and explosion of the monomer. In addition, the CO_2/TFE mixture behaves like an azeotrope, in that boiling of a mixture of the two does not significantly change the concentration of either the liquid or the vapor. According to the DuPont patent [10], this 'azeotrope-like' behavior persists over a wide concentration range, behavior that is quite unlike that of typical azeotropic mixtures. The enhanced safety of CO_2/TFE mixtures relative to pure TFE is one of the reasons that DuPont constructed a semi-works polymerization plant employing CO_2 as solvent for the generation of fluoropolymers.

1.3. Environmental and safety disadvantages inherent to use of CO_2 in a process

Because CO_2's vapor pressure at room temperature is >60 bar, use of CO_2 in a process clearly requires high-pressure equipment, creating a potential safety hazard relative to the same process operated at one atmosphere operation. In addition, uncontrolled release of large quantities of carbon dioxide can asphyxiate bystanders owing to air displacement. These issues have not impeded the commercialization of CO_2-based processes nor is it likely they will do so in the future. It should be remembered that the low density polyethylene polymerization process, first commercialized in the 1940s and still in operation today [11], runs continuously at 2000–3000 bar and 520 K with a highly flammable component and hence, safe operation of a 100–200 bar CO_2-based plant is readily achievable using current technology. Operating an exothermic reaction in a high-pressure environment is accompanied by additional safety concerns versus the analogous reaction run at one atmosphere.

Whether to use liquid or supercritical CO_2 is a choice that actually involves safety as well as chemistry considerations. While use of supercritical CO_2 almost always involves use of higher pressure (to achieve the same solubility of a given substrate as in the liquid case), other factors should also be considered. First, supercritical CO_2 will exhibit a higher compressibility than liquid CO_2, and hence the supercritical fluid will be better able to absorb excess heat evolved from an exothermic reaction whose rate suddenly exceeds typical operating conditions. On the other hand, use of saturated liquid CO_2 (in the presence of the vapor phase) would allow boiling to be used as a means to absorb excess heat. Use of supercritical CO_2 (versus liquid) could avoid complications owing to a phase separation occurring upon a departure from established temperature or pressure conditions within a given reactor. For example, if one is employing a mixture of oxygen, substrate, and liquid CO_2 in a particular process, a sudden drop in pressure owing to a perturbation in the process could lead to formation of a flammable gaseous phase—use of a supercritical mixture could avoid this problem as no vapor–liquid separation will be encountered. Indeed, it should also be remembered that the T_c of a mixture of CO_2 and other materials will differ from that of pure CO_2 (see, e.g. Ref. [12] for useful correlations) and hence T-p conditions sufficient for supercritical operation with pure CO_2 may create a liquid in the case of the mixture.

1.4. Chemical advantages to use of CO_2 as a solvent

Carbon dioxide can provide not only environmental advantages, but also chemical advantages when applied strategically, as described below.

1.4.1. CO_2 cannot be oxidized

In essence, carbon dioxide is the result of complete oxidation of organic compounds; it is therefore particularly useful as a solvent in oxidation reactions. Use of almost any organic solvent in a reaction using air or O_2 as the oxidant (the least expensive and most atom-efficient route) will lead to formation of byproducts owing to reaction of O_2 and the solvent. Indeed, the commercial anthraquinone process used to generate H_2O_2 requires the removal and regeneration (or incineration) of substantial volumes of such solvent

byproducts [13]. Oxidation reactions in CO_2 have consequently been investigated extensively over the past decade (see Section 2.8).

Because CO_2 is inert towards oxidation and is also non-flammable, CO_2 is one of the very few organic solvents that could be considered for the direct reaction of hydrogen and oxygen to form hydrogen peroxide [14]. This process has been under investigation for over two decades, yet traditional organic solvents are not sufficiently inert/safe, while water exhibits productivity disadvantages.

1.4.2. CO2 is benign and hence cross-contamination of the other phase during liquid–liquid extraction is not really contamination

There are a number of large-scale chemical processes that employ biphasic (water–organic) mixtures—H_2O_2 production and hydroformylation of low molecular weight alkenes are but two examples [13]. In any contact between aqueous and organic phases, some cross-contamination is inevitable. The aqueous phase will require subsequent remediation to eliminate the organic contamination, while the organic phase may require drying to allow further use in the process.

While CO_2 will 'contaminate' an aqueous phase upon contact in a process, a mixture of CO_2 and water clearly does not require remediation (the CO_2 phase may, of course, require drying for further use). Consequently, CO_2 exhibits a particular advantage in processes where a biphasic reaction or liquid–liquid extraction against water is required. Eckert et al. [15] have, for example, investigated the use of phase transfer catalysts in CO_2/water mixtures. Further, the coffee decaffeination process employs a liquid–liquid extraction between CO_2 and water to recover the extracted caffeine [16].

1.4.3. CO2 is an aprotic solvent

Clearly, CO_2 can be employed without penalty in cases where labile protons could interfere with the reaction.

1.4.4. CO2 is generally immune to free radical chemistry

Because carbon dioxide does not support chain transfer to solvent during free-radically initiated polymerization, it is an ideal solvent for use in such polymerizations, despite the fact that it is typically a poor solvent for high molecular weight polymers. In chain transfer, a growing chain (with a terminal radical) abstracts a hydrogen from a solvent molecule, terminating the first chain. The solvent-based radical may or may not support further initiation, and hence chain transfer to solvent can lead to diminished molecular weight and diminished polymerization rate. Research conducted during the 1990s (primarily by DeSimone et al.) showed that CO_2 does not support chain transfer, as it is inert towards polymer-based free radicals [17]. Other researchers have examined small-molecule free radical chemistry in CO_2 to be viable as well [18]. Indeed, it is likely that most of the polymerizations currently conducted by DuPont in its semi-works facility are precipitation polymerizations, where the improved control over molecular weight and the enhanced safety inherent to use of TFE/CO_2 mixtures (see Section 1.2) more than makes up for any difficulties caused by polymer precipitation during the reactions.

1.4.5. CO2 is miscible with gases in all proportions above 304 °K

The rate of most processes where a gas reacts with a liquid is limited by the rate at which the gas diffuses to the active site (either within a catalyst particle or simply to the liquid reactant). Gases, such as hydrogen and oxygen, are poorly soluble in organic liquids and water and hence in many two- and three-phase reactors, the rate is limited specifically by the rate at which the gas diffuses across the gas–liquid interface.

Although phase separation envelopes exist with gases at lower temperatures, liquid CO_2 can absorb much higher quantities of H_2 or O_2 than typical organic solvents or water [19]. Hence, one can eliminate the dependence of the rate on gas transport into the liquid phase by employing CO_2. Although conventional wisdom might claim that this effect is achieved only through creation of a single phase (of CO_2, gaseous reactant and liquid substrate), recent work in the literature shows that one can achieve high gas solubility and hence high rate while remaining two-phase (see Section 2).

It should be remembered that CO_2 will exhibit total miscibility with gases >304 K only if those gases also exhibit critical temperatures ≦304 K. This includes commonly used reactant gases such as H_2, O_2 and CO,

for example. Further, addition of any third component (here, a gas such as H_2 or CO) to a mixture of CO_2, substrate (and catalyst, perhaps) will alter the phase behavior of the mixture. Because commonly used reactant gases, such as H_2, O_2 and CO, exhibit low critical temperatures [12], at typical reaction temperatures (273–373 K), the density of these gases, even under relatively high pressures used to compress CO_2, will be quite low (more gas-like than liquid-like). As such, we expect these gases to behave as non-solvents towards the substrate and/or catalyst [20]. Thus, addition of large amounts of reactant gas to the mixture may solve one problem (diffusion limitations) and create another (phase separation).

1.4.6. *CO$_2$ exhibits solvent properties that allow miscibility with both fluorous and organic materials*

Carbon dioxide is miscible with a variety of low molecular weight organic liquids, as well as with many common fluorous (perfluorinated) solvents. The literature has shown previously that one can create a homogeneous mixture of certain fluorous and organic liquids at one temperature, where phase separation occurs upon a temperature increase or decrease. Recently, Eckert et al. has shown that one can employ CO_2 as a phase separation 'trigger' in much the same way—the addition of CO_2 (at pressures as low as 20–30 bar) to a mixture of organic and fluorous liquids creates a homogeneous single phase, while removal (through depressurization) returns the system to a two-component, two-phase system [21].

1.4.7. *CO$_2$ exhibits a liquid viscosity only 1/10 that of water*

At liquid-like densities, CO_2's viscosity is only 1/10 that of water and hence Reynolds numbers ($\rho V D/\mu$, where V is fluid velocity, ρ is density and μ is the viscosity) for flowing CO_2 will be approximately ten times those for conventional fluids at comparable fluid velocity. Because convective heat transfer is usually a strong function of Reynolds number, heat transfer in a CO_2 mixture can be expected to be excellent. On the other hand, CO_2's physical properties also lead to significant natural convection causing problems in some coatings processes. The extent to which natural convection is an issue is directly related to the magnitude of the Grashof number [22], which itself scales as ρ^2/μ^2. Because CO_2 exhibits a liquid-like density and a gas-like viscosity, Grashof numbers for CO_2-based processes can be significantly higher than for analogous liquid processes.

The surface tension in carbon dioxide is much lower than that for conventional organic solvents and the diffusivity of solutes is expected to be considerably higher, owing to CO_2's low viscosity. Consequently, CO_2 would be expected to wet and penetrate complex geometries better than simple liquids. Further, solutes would be expected to diffuse faster within catalyst pores where CO_2 is the solvent than in analogous systems using conventional liquids.

1.5. *Chemical disadvantages to use of CO$_2$ as solvent*

Carbon dioxide exhibits some inherent disadvantages where chemistry is concerned; some of these are unique to CO_2 while others are common to any number of solvents.

1.5.1. *CO$_2$ exhibits a relatively high critical pressure and vapor pressure*

As mentioned above, CO_2 exhibits high critical and vapor pressures; these characteristics guarantee higher capital costs for a CO_2-based process relative to one using a conventional solvent, as well as the need for specialized equipment for laboratory work. Exothermic reactions pose special problems for operation in CO_2, given that high pressure is the baseline situation.

1.5.2. *CO$_2$ exhibits a low dielectric constant*

Carbon dioxide exhibits a dielectric constant of ≈ 1.5 in the liquid state; supercritical CO_2 will exhibit values generally between 1.1 and 1.5, depending upon density. This low dielectric can be both a process disadvantage and a chemistry disadvantage. Some reactions, for example, require polar solvents for best results. Further, low dielectric constant also suggests poor solvent power, and hence solubility in CO_2 can require much higher pressures for certain classes of solute than more polar compressible fluids (fluoroform, for example, which exhibits a liquid dielectric of ≈ 10). On the other hand, the thermodynamic interaction between CO_2 and non-polar methylene groups is not particularly favorable and hence, ethane is often a better solvent for hydrocarbons than CO_2.

1.5.3. CO₂ is a Lewis acid

Carbon dioxide will react with strong bases (amines, phosphines, alkyl anions) [23]. When attempting to use amines as reactants, this can be a serious disadvantage, in that carbamate formation can slow the rate of the intended reaction and can also alter the solubility characteristics of the substrate. While alkyl-functional primary and secondary amines react readily with CO_2, tertiary amines are non-reactive. Further, the presence of electron-withdrawing groups in close proximity to the nitrogen atom (as in anilines) prevents formation of carbamates between CO_2 and such compounds. Carbon dioxide will also react (not surprisingly) with metal alkoxides, metal alkyls, and metal hydrides.

CO_2 has been shown to react reversibly with a number of enzymes (lysine residues, specifically), leading to low activity in the presence of CO_2 (although activity returns to normal following removal of the enzyme from the CO_2-rich environment) [24]. Because carbamate formation is reversible, even at high pressure, researchers have employed CO_2 as a protecting group for amines [25] and hence, CO_2's reactivity with amines can be an advantage as well as a disadvantage. Finally, because CO_2 reacts readily with carbanions to form relatively unreactive carboxylates, anionic polymerization cannot be conducted in carbon dioxide.

1.5.4. CO₂ can be hydrogenated in the presence of noble metal catalysts to produce CO

If one is trying to hydrogenate a substrate in CO_2 over a heterogeneous platinum catalyst, production of CO will poison the catalyst and produce toxic byproducts. Unfortunately, this reaction takes place at relatively mild temperatures [6]. There has been a certain degree of controversy recently as to whether the same reaction occurs over palladium catalysts. For example, Hancu and Beckman [14] demonstrated that hydrogenations could be carried out successfully in CO_2 (over palladium), although it should be noted that the hydrogenation in question was very fast and was conducted at 298 K. Subramaniam et al. [26] was able to successfully conduct a hydrogenation reaction over palladium in a continuous reactor; no loss in catalyst activity was observed over a period of 1–2 days. By contrast, Brennecke and Hutchensen [27] found that a palladium catalyst de-activated rapidly during batch

hydrogenations in CO_2. Subramanian [28] recently investigated these apparent contradictions and found that higher temperatures (>343 K) and greater residence times (such as would be found in batch reactions) do lead to the formation of CO which ultimately poisons' the catalyst. This is an area where further research work is certainly merited, given the potential importance of hydrogenation reactions.

In addition to CO, it is likely that some formate could be created through hydrogenation of CO_2 over noble metals; formate has been observed during homogeneous catalysis [29] and could theoretically form under heterogeneous conditions as well.

1.5.5. Dense CO₂ produces low pH (2.85) upon contact with water

Carbon dioxide dissolves in water at molar concentrations [30] at moderate pressures (<100 bar), rapidly forming H_2CO_3. This can render some biocatalytic reactions problematic, in that many enzymes are denatured (unfolded and/or de-activated) by low pH. Johnston et al. has shown that buffering is possible but that impractically high ionic strength (for enzymatic reactions) is needed [31]. On the other hand, one could employ carbonic acid as a reagent, in which case CO_2 could be treated as a very low cost, sustainable acid that does not require addition of base for neutralization. Enick [32], for example, has employed carbonic acid, formed from CO_2/water, to extract contaminants from steel waste into water, where depressurization results in a rapid increase in pH and precipitation of the extracted materials. Carbonic acid formed from CO_2 and water reacts with hydrogen peroxide under basic conditions to produce a percarbonate species, which can then epoxidize alkenes [33].

In summary, the low pH of water in contact with liquid CO_2 can be an advantage or disadvantage, depending upon circumstances. Hancu and Beckman [14], for example, have investigated the generation of H_2O_2 in CO_2, where the product is stripped into water following synthesis in CO_2. The optimum pH for H_2O_2 stability is 2–4, so the low pH of water/CO_2 mixtures is an advantage for this process. The low pH of water in contact with CO_2 also enhances the back-extraction of caffeine in the decaffeination process for coffee. Clearly, however, the low pH of CO_2–water systems is a detriment to the processing of biomolecules.

1.5.6. CO2 is a weak solvent (low polarizability per unit volume, low cohesive energy density)

This is perhaps CO_2's greatest flaw, in that its inability to solvate compounds of interest (hence requiring uneconomically high process pressures) has greatly inhibited its commercial use. This issue will be discussed in more detail in Section 3.3.

1.5.7. CO2 poisons Ziegler-type polymerization catalysts

CO_2 will terminate olefin polymerizations that employ classical Ziegler (titanium halide) catalysts, hence preventing such polymerizations from being carried out in carbon dioxide.

1.6. How we will approach our analysis

Reaction schemes will be critiqued on their ability to provide a more sustainable process compared to existing technology, using the 12 principles of green chemistry as a basis for judgments on sustainability. The basic principles of green chemistry have been outlined by Anastas and Warner [34] and are listed below:

1) Prevention (alter process schemes and chemical pathways to prevent the generation of waste, rather than remediate waste once formed).
2) Atom economy.
3) Less hazardous chemical synthesis.
4) Designing safer chemicals.
5) Safer solvents and auxiliaries (create and employ solvents and process aids that, if emitted to the environment, exhibit a lower impact than currently used materials).
6) Design for energy efficiency.
7) Use of renewable feedstocks.
8) Reduce derivatives.
9) Catalysis (create catalysts that are more selective than current analogs and which therefore produce lower volumes of byproducts during reactions).
10) Design for degradation.
11) Real-time analysis for pollution prevention.
12) Inherently safer chemistry for accident prevention.

If one examines the properties of CO_2 and its many proposed applications, several common trends appear vis-à-vis the twelve principles shown above. CO_2 has been proposed as a benign alternative to common organic solvents, and hence principle (5) comes into play. If one assumes that some proportion of the organic solvent that is employed in any chemical process will be emitted to the environment, then replacement of that solvent with CO_2 is a mode of prevention (principle 1), as CO_2 emissions are less problematic. The toxicity of CO_2 is lower than for many organic solvents (principle 4) and is naturally abundant (principle 7).

It should be noted that while use of CO_2 is within the scope of several of the principles of green chemistry, improper or ill-considered process design could lead to egregious violation of some of the others. Indeed, if use of CO_2 as solvent leads to higher energy consumption or an inherently unsafe process, then some of the 12 principles will be followed while others are violated. Judgment of the net benefit must be done on a case-by-case basis.

Finally, the source of CO_2 used in any process should be considered within the framework of the 12 principles of green chemistry. CO_2 is naturally abundant, yet CO_2 employed in an industrial process is typically not captured from the atmosphere. Carbon dioxide is a byproduct (of sizeable volume) of the commercial ammonia process [13] and much of the commercially available CO_2 is derived from this source (after purification). CO_2 can also be captured from fermentation processes, yet this is not generally practiced commercially (owing to CO_2's low current value). Large deposits of CO_2 exist naturally in the US; these are currently tapped for use in tertiary recovery of petroleum in older fields in West Texas and Oklahoma [8]. Hence, if we examine the source of CO_2, we can come to different conclusions of CO_2's worthiness as a benign solvent. If, for example, CO_2 generated by the ammonia process is employed, then one could consider this as pollution prevention, as this CO_2 would otherwise be emitted to the atmosphere. If we employ CO_2 from natural deposits, this could be construed as 'anti-sequestration', as this CO_2 would ordinarily remain underground. If CO_2 could be captured from the atmosphere (or power plant flue gas) in an energy efficient and economic manner, then used in a process, this would likely be the best source with respect to the 12 principles of green chemistry.

1.7. Process design using supercritical fluids: are CO_2-based plants inherently uneconomical?

The number of processing plants operating worldwide that employ supercritical CO_2 is slightly above 100 and growing steadily [35]. Most of the current plants use CO_2 to process food in some way (extraction or fractionation), yet other types of plants have been or are being brought on stream (e.g. fluoropolymer synthesis by DuPont, hydrogenation by Thomas Swan, coatings by Union Carbide, polyurethane processing by Crain Industries). Despite this steady growth, there is a general sense (or unease) within both the academic and industrial communities that there are elements connected to the design and construction of CO_2-based plants that effectively block greater use of the technology.

Several authors have reviewed aspects of process design and costing of 'supercritical' plants [36]; these reviews typically focus on a specific industry. For example, Perrut reports that for the case of extraction, the relative cost of a supercritical plant scales as $(V*Q)^{1/4}$, where V is the column volume and Q the flow rate. This is consistent with what we report in Section 1.7.1, where minimizing equipment size and flow rate will help to minimize process cost.

Each of the authors who has reviewed process design using supercritical CO_2 emphasizes that one needs access to the relevant fundamental parameters in order to complete and optimize the design. Such parameters include both the relevant thermodynamic model for the mixture(s) in question with the appropriate binary interaction parameters, reaction data (rate constants, heats of reaction, Ahrrenius constants) and transport constants (densities, diffusivities and viscosities). Note that these parameters are exactly the same as would be required to design a one-atmosphere process and hence there is nothing inherently 'foreign' about a CO_2-based process that inhibits design and costing. Indeed, high pressure alone is not sufficient to explain the perceived difficulty of CO_2-based process scale-up, given that hydroformylation operates at 200–300 bar at large scale, while low density polyethylene is produced at over 2000 bar. If one has access to the necessary basic information, one can employ software such as ASPEN to accomplish the process design and ICARUS to handle the costing (the author has carried this out successfully with colleagues).

Hence, we must conclude that, if the inhibition in the scale-up of CO_2-based processes is real rather than perceived, then it must be due to a lack of the fundamental parameters needed for process design, plus other factors that would inhibit the commercialization of any 'new' technology. For example, it is relatively difficult at present to predict the effect of molecular structure on phase behavior in CO_2 of molecules that exhibit any substantial degree of complexity. Carbon dioxide exhibits both non-polar tendencies (low dielectric constant) and 'polar' properties (Lewis acidity, strong quadrupole moment) and hence predictions of phase behavior are not straightforward (as in the case of alkanes or alkenes). Recent work [37] has shown that the statistical associating fluid theory (SAFT) can provide good descriptions of the phase behavior of complex mixtures including CO_2, yet the complexity of this model and/or lack of suitable parameters may currently limit its use industrially. Group contribution models have been applied to CO_2 solutions somewhat narrowly, generally targeting a single class of solutes [38]. What appears to be needed is a means to easily predict the properties of mixtures involving CO_2, such that confident predictions of process requirements and costs can be made using conventional process software such as ASPEN.

1.7.1. Operating a process economically with CO_2: heuristics

While use of CO_2 as a solvent is often considered to be 'green', operation of any process at high pressure typically involves higher costs than the analogous process operated at one atmosphere. If such a process is considered 'green', but cannot be created and operated economically, then the process will be of academic interest only and its potential green benefits unrealized. There are some simple 'rules of thumb' that one can use to render the cost of a CO_2-based process as low as possible.

1.7.1.1. Operate at high concentration. One way in which to minimize the cost of a CO_2-based process is to minimize the size of the equipment. Given that CO_2 is typically proposed as a solvent (rather than a reactant), the most obvious means by which to minimize equipment size is to minimize the amount of solvent (CO_2) flowing through the process. Consequently, one should try to choose or design substrates
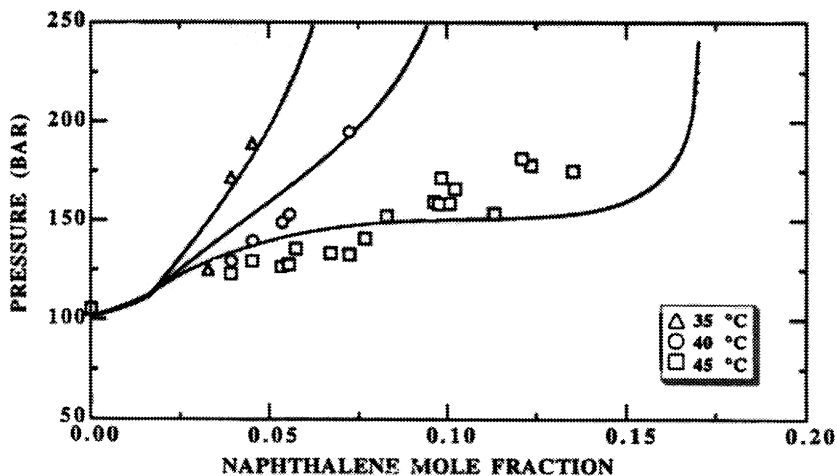
Fig. 1. Solid-fluid phase behavior [1]: CO_2–naphthalene.

such that they exhibit high solubility in CO_2. In addition, those processes where CO_2 is employed as the minor component (use of CO_2 as a plasticizer in polymer processing, for example) are likely to be favored economically.

Another aspect of this issue is reflected in the typical phase behavior of compounds in CO_2 (see Figs. 1 and 2). Note that in the typical phase diagram of a crystalline solid in CO_2, an essentially pure solid phase exists in equilibrium with a solution. Given that the solid phase cannot be processed, one obviously makes use of the solution, where naturally CO_2 is

the major component. For the case of liquid–liquid phase behavior, a CO_2-rich phase exists in equilibrium with a substrate-rich phase. However, because CO_2 has been shown to lower the viscosity of solutions substantially, one can actually pump and process the substrate rich phase. Further, one can operate at lower pressure in addition to at higher concentration. Consequently, it may be beneficial to employ systems where liquid–liquid phase behavior occurs rather than liquid solid. Efficient operation of a process is both economically favorable and more environmentally friendly.
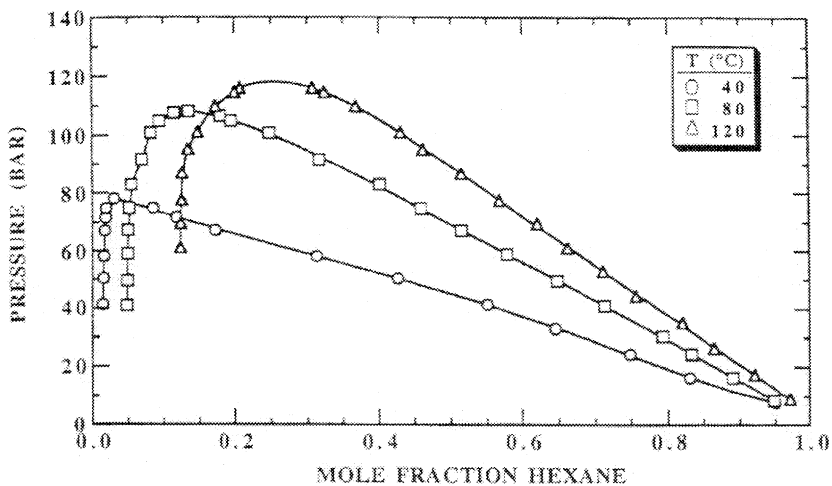

Fig. 2. Liquid–liquid phase behavior [1]: CO_2–hexane.

1.7.1.2. Operate at as low a pressure as possible.
Operation of a process at high pressure is more expensive than at one atmosphere, owing to equipment design and construction, as well as the additional safety features that are necessary. Further, the capital cost of a high-pressure process is not linear with pressure because the pressure ratings of certain vital equipment (flanges, for example) are available in discrete steps (60 and 100 bar, for example). In addition, the number of companies with experience in high-pressure process design drops dramatically as the operating pressure rises above 200 bar.

Clearly, these caveats strongly recommend operating at the lowest pressure possible. One means by which to accomplish this is in the chemical design of reactants and/or substrates. It has been known for a number of years that certain functional groups are more 'CO$_2$-philic' (thermodynamically more CO$_2$-friendly) than others. Use of CO$_2$-philic functional groups in the design of substrates or catalysts can greatly lower the needed operating pressure, although it should be remembered that their use could easily raise raw material costs.

Given that carbon dioxide is a relatively feeble solvent, a classic technique for lowering operating pressure (or raising operating concentration) is to employ co-solvents. Methanol and ethanol are most commonly used [1,39], but a wide range of organic solvents has been employed in this fashion, usually at concentrations <40%. Regarding whether the use of co-solvent/CO$_2$ mixtures is green, one must make a determination on a case-by-case basis. For example, in a conventional chemical process, one must decide whether it is more efficient to use a low pressure process with 100% organic solvent or a high pressure process using only 5–10% organic solvent (for example) with the balance CO$_2$. To date, the typical answer has been to opt for the low pressure, solvent-based process. However, if the solvent (owing to the nature of the process) is to be emitted to the atmosphere, there are examples where the choice has been to opt for the CO$_2$/co-solvent route. In the UniCarb coatings process [40] developed by Union Carbide during the 1980s and 1990s, CO$_2$ was employed to replace one component of a solvent mixture used in spray coating, creating a CO$_2$/co-solvent based process. The foaming of thermoplastics such as polystyrene [41] is often conducted using a mixture of CO$_2$ and an alkane,

a more efficient route than employing either 100% alkane or 100% CO$_2$. One can also employ relatively lower process pressures by operating in the two-phase regime (gas–liquid) rather than employing pressures high enough to maintain a single phase; more about this option will be described in a later section.

Another somewhat obvious route to the lowering the operating pressure is by operating at sub-ambient temperatures. Here, however, one must balance the advantage gained by reducing the operating pressure with other impacts, such as the energy cost for cooling and any reduction in reaction rate owing to reduced temperature. Whereas dropping the temperature is an obvious mechanism to reduce the operating pressure, there are others that have received far less attention. For example, the identification of a minimum boiling azeotrope where CO$_2$ is the majority component could provide a solvent that is both green and exhibits a vapor pressure far lower than that of pure CO$_2$. Azeotropes are desirable in that process steps requiring flashing of the material (or small leaks) will not change the composition of the solvent. Azeotropes can be maximum boiling (where the vapor pressure of the mixture is higher than either of the pure component vapor pressures) or minimum boiling (the opposite, and here desired situation) [42]. Although addition of a second component might lessen the sustainability of the solvent, a solvent that is mostly CO$_2$ is typically better than one than contains no CO$_2$ and the reduction of the pressure through use of a minimum boiling azeotrope might lower the operating pressure sufficiently to allow economical scale-up of the process. Some CO$_2$-based azeotropes have been identified [43] as a result of research by CFC-producing companies in a search for alternative refrigerants. Consequently, most of the known CO$_2$ azeotropes are mixtures with fluorocarbons (it is also known that ethane forms an azeotrope with CO$_2$). Because azeotropes typically form between compounds whose boiling points are separated by 50 K or less, the number of potential azeotrope-forming cosolvents for CO$_2$ is likely limited, but this could provide an interesting route to solvents that are both green and versatile.

1.7.1.3. Recover products without high-pressure drops. It has been mentioned in the literature that use of CO$_2$ as a solvent is advantageous because reduction of the pressure to one atmosphere results

in the complete precipitation of any dissolved material, rendering product recovery easy. This may be true, but use of such a route for product recovery raises costs, as one must then either recompress the CO_2 prior to re-use or compress make-up CO_2. As gas compression is energy-intensive and expensive, a greener route to product recovery is desirable.

One example of product recovery without a high-pressure drop is liquid–liquid extraction against water. A liquid–liquid extraction between an organic and aqueous phase inevitably cross-contaminates the phases, normally requiring remediation of one, and probably both phases. In the case of a water–CO_2 extraction, however, the inevitable cross-contamination is benign (carbonated water!). Indeed, the CO_2-based coffee decaffeination process employs a water–CO_2 extraction to recover the caffeine, allowing the CO_2 to move in loop at relatively constant pressure (see Fig. 3). Further, the cross-contamination here is actually beneficial, as the low pH in the 'CO$_2$-contaminated' water allows for a higher partition coefficient for caffeine, while the 'water-contaminated' CO_2 is a better extractant for caffeine than pure CO_2. Beckman and Hancu also employed a liquid–liquid extraction, here for the recovery of H_2O_2 synthesized in CO_2 [14].

1.7.1.4. Operate the process continuously if possible.
The rationale for operating in a continuous mode is that the equipment can be smaller while maintaining high productivity. While this is usually straightforward for liquid substrates, it can be much more difficult for the processing of solids at high pressure. Indeed, there currently does not exist a viable means for introducing and removing solids continuously from a high pressure (100 bar +) process. Those commercial CO_2-based processes that employ solids use either batch or semi-batch mode. An example of the latter is the coffee decaffeination process, where dual extraction columns are employed, such that one is in extraction mode while the other is being emptied and re-filled [16].

In the late 1980s, Chiang et al. at the University of Pittsburgh developed a process (LICADO) for the cleaning of coal that employed a biphasic mixture of CO_2 and water [44]. Here, the coal was introduced to the process continuously as a slurry in water. If the use of a water slurry of solid substrate is tolerable, this is a useful means by which to introduce solids continuously into a high-pressure process.

A clever example of the use of phase behavior trends to accomplish continuous processing, as well as to recover products without large pressure
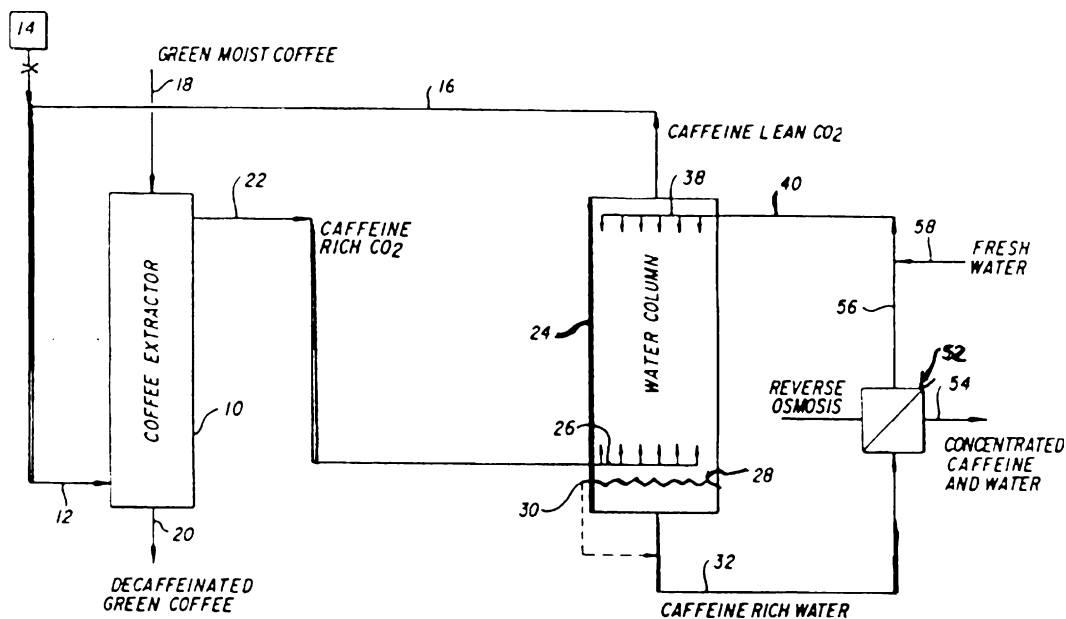

Fig. 3. Process schematic for coffee decaffeination using CO_2 [1].

drops, is shown by Charpentier et al. [45] in the examination of the continuous polymerization of fluorinated monomers in carbon dioxide. Here, the monomers are soluble in CO_2 (as are many vinyl monomers) while the polymers are insoluble (also a relatively general trend). Thus, monomer can be continuously recycled through the continuously stirred tank reactor while the polymer precipitates and is collected.

1.7.1.5. Recover and reuse homogeneous catalysts and CO_2-philes. The discovery of CO_2-philes in the early 1990s allowed for the exploration of a number of processes in CO_2 that had been heretofore untenable owing to CO_2's feeble solvent power. Highly CO_2-soluble surfactants and catalyst ligands became available, leading to a number of important discoveries regarding chemistry in carbon dioxide. However, the new CO_2-philes are significantly more expensive than their CO_2-phobic counterparts and hence it is important to the economics of a CO_2-based process that any CO_2-philes used in the process be recycled as extensively as possible. Note that recycle of CO_2-philes not only makes good economic sense, but is also more sustainable than the case where the CO_2-philes are simply disposed.

Recovery and recycle of homogeneous catalysts is important whenever such catalysts are employed because the metals employed in such catalysts are typically expensive. In the case of a CO_2-based process, the ligands are also likely to be expensive (they must be designed to exhibit high CO_2 solubility) and hence the need for effective catalyst recycle is even more important.

In summary, attention must always be paid to the economic viability of processes employing CO_2 as reactant and/or solvent—while CO_2-based processes are generally thought to be 'green', their benefits will never be realized if the cost of such processes dwarfs conventional analogs.

1.7.2. Where would process improvements enhance opportunities for green chemistry in CO_2?

As in the previous section, examples described here are not directly related to green chemistry, but solution of such problems would greatly enhance the viability of CO_2-based processes and are hence intimately tied

to green chemistry in carbon dioxide. For example, there remains no truly efficient means by which to inject and remove granular solids from a high-pressure system (screw feeders have been tried with limited success). There are clearly a number of areas (food processing) where continuous injection and removal of solids would greatly enhance the economic viability of a CO_2-based process, yet lack of the mechanical means by which to accomplish this relegates the process to batch or semi-batch operation. Note that the chemical basis for continuous polyurethane foam production using liquid CO_2 as the blowing agent (see Section 3.5.2) was established in the early 1960s, whereas commercialization only occurred after development of the proper equipment in the early 1990s.

Over the past decade, there has been significant academic and industrial interest in cleaning processes using CO_2—cleaning of metal parts, electronics components, and fabrics. CO_2 is ideally suited to such applications owing to its low viscosity and environmentally benign nature, yet mechanical issues complicate application of CO_2 to these processes. For each of these applications, individual 'pieces' must be rapidly inserted into a high pressure chamber, the chamber sealed and pressurized, the 'piece' cleaned, the then chamber depressurized and emptied. At one atmosphere, such an operation is trivially simple to conduct and easy to scale (cost per part drops as chamber volume rises). The opposite is currently true for high-pressure operation; scale-up is non-trivial and the cost of the system rises rapidly as the size of the chamber rises. More efficient 'piecework' operations at high pressure will not only render cleaning operations less expensive, but also coating and fabric dying operations. Finally, many proposed CO_2-based processes (including spin coating, lithography and developing, free meniscus coating) that are under examination in academic/industrial laboratories would benefit greatly from breakthroughs in the design of equipment designed to efficiently transfer parts in and out of high-pressure environments.

1.8. Scope of this report

This report will focus on CO_2-based processes where chemical reactions are taking place (i.e. green chemistry) or materials are being processed to create

viable products. Research conducted over the previous 5 years (1997–present) will be emphasized.

Needless to say, this focus will eliminate discussion of processes that contain only separations unit operations (example: extractions and cleaning). This does not mean that such processes are unimportant—on the contrary, several have been commercialized, including extraction of caffeine from coffee beans and tea leaves, certain acids from hops and various components from spice plants [36,46]. In addition, CO_2-based chromatographic instruments have been commercialized at both the analytical and preparative scale [47].

Clearly, a continuing challenge to the reader who is interested or actively involved in research involving CO_2 as a solvent is 'Can the use of CO_2 create new products, eliminate waste, save energy, and/or enhance safety to the point where the costs of the product are reduced ***and*** a more sustainable process created?' The new DuPont fluoropolymer facility may be the first example of this, as the use of CO_2 has eliminated the need for fluorinated solvents, has made working with some of the monomers safer and produces product with better properties than the traditional emulsion process.

In each of the following sections, recent research on various aspects of green chemistry using CO_2 will be summarized. Whereas much of the published work in this area emanates from academic groups, it should be noted that some industrial concerns have also been quite active. Industry quite naturally tends to patent before they publish and consequently a patent search was conducted for the period 1996–2001 where finding the term 'supercritical' in either the patent title or abstract was employed as the criteria defining a 'hit'. This search produced 450 hits for the time period in question. Well over half of these patents described inventions where CO_2 is used as the solvent in natural product extractions or cleaning. Of the remainder, academic inventors filed nearly half. In addition, a search using 'CO_2 or carbon dioxide' in title or abstract (without supercritical) produced 1500 additional 'hits', although the vast majority of these did not involve use of CO_2 as a solvent. For each of the sections on CO_2-based research, a paragraph is appended that describes industrial activity (as described in patents) that is significant but *not* expressly mentioned in the main body of the section. Without question, the most active industrial entities (in producing US

patents) on use of supercritical fluids in green chemistry/processing during 1996–2001 were DuPont, Micell Inc. and Thomas Swan (UK). Not surprisingly, each of these companies also has supported major commercialization efforts in CO_2-based chemistry and processing (DuPont—polymerization of fluoropolymers in CO_2; Micell—dry cleaning in CO_2; Thomas Swan—hydrogenations and alkylations in CO_2). All three have strong research ties to universities.

1.9. A note on cleaning using CO_2

There has been substantial effort made by both the academic and industrial community to employ carbon dioxide in the cleaning of clothing, mechanical parts and the surface of microelectronics components. Whereas this report will not explicitly address the state of the art in cleaning using CO_2, it will evaluate several technological issues that are significant to the advancement of CO_2-based cleaning.

For example, although carbon dioxide is not a particularly strong solvent (see Section 3.3), it will readily solubilize low molecular weight, volatile, non-polar compounds. If the 'contamination' to be removed using CO_2 falls into this category, then no additional fundamental science is required, and the economics of the design and construction of the equipment will determine whether the technology is practiced. Breakthroughs in the design of high pressure cleaning equipment that could rapidly process individual parts would greatly help to promote use of CO_2 as a cleaning solvent.

CO_2 is a weak solvent and hence, cleaning that requires the solubilization of polar, inorganic or high molecular weight material will require the use of CO_2-soluble auxiliaries (surfactants, chelating agents). The discovery that certain fluorinated compounds are 'CO_2-philic' during the early 1990s allow for rapid advancement in the design of such auxiliaries and a discussion of the design of such auxiliaries is included in this report. For the future, the design of CO_2-philic auxiliaries must likely include non-fluorinated building blocks, as fluorinated materials are expensive and some (the fluoroalkyl sulfonate family) are environmentally suspect [48].

For the case of microelectronics processing, cleaning is accompanied by the need to perform chemistry

(photolithography, etching). These topics are included in Section 3.11 and Section 3.12.

Fabric cleaning has recently been commercialized by two groups in the US (Micell, Inc., and Global Technologies/DryWash). Major issues confronting these groups in the future include design of inexpensive surfactants that clean effectively in CO_2, the design of high pressure cleaning equipment that renders the process cost-competitive and competition from other 'benign' cleaning technologies (such as the use of high flash point alkanes, silicones and water). The use of silicones (Green Earth [49]) seems to present significant competition, as these materials are promoted as being more benign than PERC (they are, if TLV is any indication), they are used at one atmosphere (hence, equipment is relatively inexpensive) and their use is backed by some large, relatively wealthy corporations (GE for silicone production, Procter and Gamble for surfactant production [49]). Indeed, even the design of more efficient conventional dry cleaning equipment (i.e. that using perchloroethylene (PERC) as the solvent) represents a commercial challenge [50]; the volume of PERC used by dry cleaners in the US has dropped dramatically over the past decade primarily owing to the use of 'tighter' equipment (lower fugitive losses during cleaning). Indeed, significant consolidation occurred in the CO_2-based dry cleaning industry during early 2002. Chart Industries, Inc., a member of the DryWash consortium, decided to exit the CO_2-based dry cleaning business [51] after several years of disappointing growth ($126,000 net sales in 2001); the connection to the consortium was maintained by some of their employees as a spin-out company (Cool Clean). Cool Clean recently purchased the Hangers franchising operation from Micell. Finally, intellectual property issues could complicate the use of carbon dioxide in fabric cleaning. Unilever, for example, has filed a number of patents (and continuations in part, etc.) on the use of surfactants in CO_2 for the purpose of fabric cleaning [52], as well as on the general process where CO_2 plus a surfactant is employed in fabric cleaning.

In summary, this report will include several issues important to future cleaning applications for CO_2, namely the design of effective, low-cost auxiliaries and the design of lower cost equipment for use in parts cleaning.

1.10. The effect of regulation on use of CO_2 in green chemistry and chemical processing

The extent to which conventional solvents are regulated will have a profound effect on the extent to which CO_2 is used as a solvent in the future. For example, we can examine the recent history of chlorofluorocarbons (vis-à-vis CO_2). Chlorofluorocarbons (CFCs) were preferred as solvents for cleaning because they are non-flammable, relatively non-toxic (TLV of chlorodifluoromethane is 1000 ppm [5]), and inexpensive. As a result of research performed during the 1970s and 1980s, it became apparent that CFCs contributed to the chemical erosion of the stratospheric ozone layer, leading to the Montreal Protocols that outlined a timetable for the withdrawal of CFCs from use as solvents (and refrigerants, etc.). Carbon dioxide is often described as a potential substitute for CFCs in cleaning (and also refrigeration). Because CFCs exhibited a number of highly favorable properties, without the regulation restricting their use, it is not likely that CO_2 would have ever been considered as a viable competitor.

Although CFCs represent a somewhat extreme case, regulation does exert more subtle effects on the use of CO_2. This is most often seen when comparing the pluses and minuses of using conventional solvents to use of carbon dioxide. From an engineering perspective, carbon dioxide is nearly always more difficult to employ as a solvent because one needs high-pressure equipment. Consequently, the extent to which a particular solvent is regulated and hence, the obstacles to the use of such a solvent in a chemical process, can tip the scales either in favor or against use of CO_2. For example, acetone is not currently on the list of compounds that require reporting under section 313 of the Emergency Planning and Community Right-to-Know Act (EPCRA, also known as the Toxics Release Inventory (TRI) [53]). Neither is it listed as a 'Hazardous Air Pollutant' [54] by the Office of Air Quality Planning and Standards at the US EPA. Consequently, if a manufacturer was currently using carbon tetrachloride, for example, in a process where some of the solvent was emitted to the atmosphere, a natural approach to 'greening' the process might be to first determine whether acetone could be substituted for carbon tetrachloride (the latter is included on both the TRI and classified as a hazardous air pollutant). Naturally,

use of acetone in place of carbon tetrachloride would likely not involve any changes to the equipment used in the process, while use of CO_2 would most certainly require equipment re-design. One manifestation of a systematic approach to choosing alternative solvents based on environmental considerations is SAGE, the solvent alternative guide, a web-based interactive tool [55a]. Carbon dioxide is indeed one of the possible choices that might result from an interactive session on SAGE, depending upon inputs, but no economic calculations are performed. An excellent description of the industrial perspective on choosing solvents given both physical property and regulatory constraints may be found in Ref. [55b].

As shown above, current regulations affect application of CO_2 by rendering some conventional solvents better or worse (from the cost of complying with current regulations) than carbon dioxide. In addition, it is possible to envision how future regulations might also affect the use of CO_2 in green processing. Given that CO_2 has been determined to play a role in global climate change, it is conceivable that the emission of CO_2 to the atmosphere will be regulated in the future. Consequently, a number of companies have begun instituting 'trading credits' in CO_2 emissions, primarily on an internal basis. In these systems, CO_2 is assigned a 'negative value' and thus use of CO_2 as a raw material allows one to theoretically reduce the cost of the process or product. If this practice becomes widespread (owing to future regulation on CO_2 emissions) it will likely spur research and development on processes or products that consume CO_2.

Another area where future regulation could greatly impact the use of CO_2 is if restrictions are placed on the use of various fluorinated materials. Certain fluorinated materials have been found to be highly CO_2-soluble (see Section 2.4.1 and Section 3.3) and hence these materials have been applied in the design of highly CO_2-soluble auxiliaries (surfactants and chelating agents). To date, the expense of fluorinated compounds has greatly limited their use in commercial CO_2 technology, yet there are applications areas (such as microelectronics) where the cost of fluorinated compounds will not be an impediment to commercial use of CO_2 processing. However, it has been reported recently that certain fluorinated surfactants persist in the environment, causing concern within the environmental and public health communities. The EPA has proposed a significant new use rule (SNUR) for perfluorooctanesulfonic acid and closely related compounds [48] requiring manufacturers to notify EPA at least 90 days before commencing the manufacture or import of these materials for a significant new use. This may be expanded to include perfluorinated carboxylic acids (and their precursors) as well. If the use of fluorinated compounds is restricted in the future, it could limit the use of CO_2 in certain areas of application. Needless to say, design of non-fluorinated CO_2-philic compounds would therefore become a priority in advancing the state of the science.

2. Reactions using gases

In the following sections, recent significant research and development on the use of CO_2 as solvent (or raw material) to aid in the 'greening' of various classes of reaction or material processing will be discussed. In this section, the use of gaseous reactants (H_2, CO, O_2) in CO_2 will be described.

2.1. Hydrogenation

Hydrogenation is widely used in industry at scales ranging from grams per year to tons per hour [56]. Hydrogenation is conducted at large scale in either the gas or liquid phase; further, while gas phase reactions are performed over a solid catalyst (heterogeneous catalysis), liquid phase reactions are conducted in either two (homogeneous catalyst, liquid and gas each present) or three (heterogeneous catalyst, liquid and gas each present) phase modes. Finally, heterogeneous catalysis is conducted in batch, continuous slurry and fixed bed reactor configurations, although the latter is less common than the former two.

Despite the broad range of potential reactor configurations and reactions, we can, by examining the 12 principles of green chemistry described previously, make some general comments as to how the use of supercritical fluids (CO_2 primarily) can enhance (and possibly detract from) the sustainability and economic viability of a hydrogenation process. We will restrict this discussion to those hydrogenations currently carried out in the liquid phase—addition of a supercritical solvent to a gas-phase reaction will simply dilute the reactant concentrations, reducing the

rate significantly. With some exceptions (described below), it is not likely that use of a supercritical solvent will enhance either the economic viability or the sustainability of a gas-phase hydrogenation.

Two areas where addition of CO_2 might benefit a gas-phase hydrogenation are flammability and catalyst defouling; addition of CO_2 to a mixture of hydrogen and a substrate will enlarge the non-flammable region, while CO_2 could help to prevent catalyst fouling by dissolving compounds that contribute to coke formation [57].

2.2. Liquid-phase hydrogenations: advantages to use of supercritical solvents

A number of hydrogenations (synthesis of unsaturated fatty acids, reduction of fatty esters to alcohols) are conducted commercially in organic solvent and replacement of these solvents with benign carbon dioxide will reduce both liability (reduced flammability, potential toxicity issues) and the potential for VOC emissions owing to fugitive losses. In addition, use of any supercritical fluid in a liquid-phase hydrogenation process can significantly alter the relative importance of fundamental processes governing the rate expression. In a three-phase hydrogenation, the rate can be governed purely by the kinetics of the reaction, but more likely will depend on the rate at which hydrogen diffuses from the gas phase to the active sites on the catalyst. The overall rate of transport is itself governed by three resistances in series: (1) the resistance to transport of H_2 across the gas–liquid interface; (2) the resistance to transport of H_2 through the liquid to the surface of the catalyst; and finally (3) resistance to transport of H_2 within the pores of the catalyst. Given that the overall rate is related to the sum of the resistances in series [58], one term can easily dominate the expression for the overall rate. Use of a supercritical fluid solvent (as opposed to a traditional liquid) eliminates the gas–liquid interface, as low T_c gases such as H_2, O_2 and CO are completely miscible with fluids above their critical point. However, this does not necessarily mean that the reaction will be kinetically controlled, as one must deal with the remaining two resistances to transport (bulk liquid to solid surface, interpore diffusion). Because the diffusion constant is embedded in each of these resistances, the use of a supercritical fluid can also aid in their elimination,

although simply switching from a conventional liquid to a supercritical fluid solvent for hydrogenation by no means guarantees that the reaction rate will depend solely on the underlying kinetics.

It should be noted that significant effort is expended in hydrogenation reactor design to ensure that H_2 is well dispersed in the liquid phase—effective sparging greatly increases the contact surface area between the phases and hence the rate at which H_2 diffuses into the liquid. If use of a supercritical fluid allows for a reactor redesign (for example, plug-flow versus continuous-stirred tank given that gas sparging is unnecessary), then it may be possible to enhance the selectivity of the reaction through reactor design improvement, reducing waste.

Indeed, selectivity is a major concern in any chemical process—hydrogenation is no exception. It is well known that solvents affect the yield and selectivity of various hydrogenation reactions where 'one very useful, although fallible, generality is that in a series of solvents, the extremes in selectivity will be found at the extremes of the dielectric constant...' [56]. The supercritical fluids most often employed as hydrogenation solvents, propane and CO_2, exhibit dielectric constants at the lower end of the scale (1.5–1.7) and we might expect to see an effect on selectivity if a polar solvent is replaced by CO_2. In addition, the physical properties of supercritical fluids are readily varied over a significant range through changes to pressure and temperature and it may be possible to affect selectivity by altering these variables. Finally, the addition of CO_2 or operation above the critical point of the reactant mixture could aid in coke removal from the catalyst, prolonging its life or maintaining favorable selectivity [57]. Clearly, enhancing selectivity of a reaction will ultimately reduce the volume of byproducts generated and potentially the volume of waste emanating from a particular process.

Hydrogenation is generally exothermic and removing heat from the process is thus more of a problem than injecting heat [59]. In this case, the use of a supercritical fluid may or may not be advantageous. Liquids are useful as heat transfer fluids in that one can employ the heat of vaporization to absorb excess heat. Convective heat transfer, which will depend upon both fluid velocity and fluid physical properties, may or may not be more successful in a supercritical fluid, depending upon the exact conditions. For example, the magnitude

of heat transfer is related both to the Prandtl number and Reynolds number [22]; Prandtl numbers for SCFs are typically lower than for liquids, while the Reynolds number for an SCF could be quite a bit higher (given that kinematic viscosity for SCFs is high) at constant velocity. Heat removal is important, in that inability to effectively remove heat could lead to loss of selectivity. Liquid CO_2 could be useful in this regard, as boiling is often employed as a means by which to absorb excess heat, although it must be remembered that CO_2's heat of vaporization is relatively low.

2.3. Heterogeneous hydrogenation in CO_2

As mentioned above, the key 'green' driving force behind the use of a supercritical solvent rather than an organic solvent in a heterogeneous reaction is the elimination of transport resistance (owing to diffusion of the gas across the liquid–vapor boundary) and potentially a more efficient reaction. Ease of separation of products from reactants is also often mentioned, but not typically evaluated. Indeed, products and reactants may be more easily separated in the conventional analog via a simple distillation. Baiker [60] has reviewed progress in heterogeneous reactions in supercritical fluids up to 1999; we will focus on key discoveries prior to 1999 and significant strides made since then.

Harrod et al. [61] have successfully performed the hydrogenation of fats and oils using supercritical propane; propane was employed to allow for solubility of both the substrates (whose solubility in CO_2 is poor) and hydrogen, which is completely miscible with any supercritical fluid. The homogeneous propane/H_2/substrate mixture was fed into a packed bed containing a commercial Pd catalyst—extremely high reaction rates were indeed achieved (gas–liquid transport resistance being eliminated) and the concentration of trans fatty acids (an undesirable byproduct) was reduced. Hence, the green advantages to this reaction would include reduced waste content and smaller, more efficient reactors. However, the use of propane is problematic, and it is not clear whether the process advantages due to faster reaction rate balance the disadvantages deriving from use of a flammable solvent and the problems inherent to high-pressure process design/development. Further, the catalyst deactivated quickly, an important problem for both economic and sustainable reasons [57,59].

Tacke et al. [62] also investigated the hydrogenation of fats and oils (over a supported Pd catalyst), although they employed CO_2 as the supercritical solvent. Again, rates were shown to be significantly higher in the supercritical case (6-fold increase in space-time yields) and selectivity and catalyst lifetime were also improved. Each of these features contributes to enhancing the green potential of the process, while the need for high pressure operation detracts both from the cost and the sustainability (energy, unit operation complexity). Macher and Holmquist [63] also examined the hydrogenation of an oil in supercritical propane; similar results to those found by Harrod were obtained. King et al. [64] examined the hydrogenation of vegetable oil and fatty acid esters over nickel catalysts using both CO_2 and propane as supercritical solvents and under conditions where *either one or two fluid phases* existed in the reactor. This approach is interesting, as it ultimately could prove a useful engineering solution to the problem of solubilizing substrates in CO_2 at moderate operating pressures.

Indeed, Chouchi et al. [65] recently examined the hydrogenation of pinene (over Pd/C) in supercritical CO_2. They found that the rate of the reaction was significantly faster in the two-phase regime (i.e. lower pressures) than when the pressure was raised to the point where only a single fluid phase existed. The reason for this seems clear; the Chouchi study was performed by charging a known amount of each of the ingredients to the reactor, then pressurizing with CO_2. The partitioning of compounds between phases (in the two-phase system) must have been such that the concentration of reactants in the lower phase was higher than under single-phase conditions. In other words, raising the pressure to create a single phase simply diluted the reactants, lowering the rate. Note that the concentration of CO_2 in the lower phase (in the two phase system) was likely to be substantial, as CO_2 should interact favorably with a volatile, low molecular weight compound, such as pinene. Further, the concentration of hydrogen in the lower phase must also have been substantial to support the high rate observed, and hence we see that CO_2 can swell an organic substrate significantly *and* carry substantial amounts of hydrogen into a 'swollen' liquid phase. CO_2 could therefore function as a 'reversible diluent', much in the same way that it is employed as a 'reversible plasticizer' in polymer science [66]. In this case, addition of CO_2

at relatively low pressures would enhance solubility of H_2 in the substrate, raising rates while not impacting process costs precipitously. Even safety could be improved, as previous work has shown that addition of CO_2 to a mixture of hydrogen and air expands the non-explosive regime more so than addition of nitrogen [9]. As such, a sudden leak in the reactor, leading to a mixture of CO_2, air and hydrogen would still be safer than the same case where nitrogen was being used as the pressure-transmitting fluid. Use of CO_2 in such reactions could thus be green, safe and practical.

Bertucco [67] and later Devetta [68], also showed the advantages of using a multi-phase system in their work on the hydrogenation of an unsaturated ketone over a Pd/alumina catalyst. These researchers found that one could eliminate transport resistance while operating in the three-phase (solid catalyst plus liquid plus gas) regime. Here again, the fact that CO_2's presence in the lower liquid phase greatly enhances the solubility of hydrogen in the liquid (substrate plus CO_2) allows one to eliminate transport resistance without the need to apply pressure high enough to create one phase. Consequently, one could conceivably render the reaction more efficient (and hence less wasteful) and economically practical by using moderate pressures.

Arai et al. examined the hydrogenation of unsaturated aldehydes in both CO_2 and ethanol over a Pt/Al_2O_3 catalyst [69]. The selectivity of the reaction towards unsaturated alcohol in CO_2 was significantly better than that in ethanol; while increasing the pressure in the CO_2 case improved selectivity, the opposite occurred when increasing the hydrogen pressure in the ethanol analog. Indeed, here is a case where the use of CO_2 appears to enhance selectivity, and thus reduce waste in a reaction versus the 'liquid' analog. It is not clear from the discussion by Arai whether this improvement in selectivity is enough to offset the difficulties involved in scaling up a high-pressure process and whether the energy input to the CO_2-based analog is more or less than the liquid case. Interestingly, Arai did not observe the rapid catalyst deactivation formerly observed by Minder et al. [70] during hydrogenation in CO_2 over a platinum catalyst. Minder's results were readily explained by formation of CO and other poisoning species owing to the hydrogenation of CO_2 itself; it is unclear why Arai was able to avoid this problem.

Poliakoff et al. [71] have evaluated the efficiency of hydrogenation of a wide variety of substrates in supercritical fluids (propane and CO_2) over a Pd catalyst in a continuous flow reactor. Substrates included aromatic alcohols, aldehydes, ketones, unsaturated cyclic ethers, nitro compounds, oximes and Schiff bases. Reactions were conducted at temperatures ranging from 360 to 670 K at pressures between 80 and 120 bar. All of the substrates examined could be hydrogenated to some extent, with measured space-time yields exceeding 2×10^5 kg h^{-1} m^{-3} for the hydrogenation of cyclohexene. Given the high temperatures employed, the relatively low pressure, the presence of significant amounts of hydrogen and the low volatility of some of the substrates employed, it is highly likely that two or more phases existed in the reactor during the initial phases of the process. CO_2's density will not be 'liquid-like' at these pressures and temperatures, while hydrogen will act as a non-solvent owing to its low critical temperature (and hence low reduced density at the reaction conditions). Poliakoff examined the phase behavior in the cyclohexene-to-cyclohexane system and indeed found that multiple phases exist initially, while a single phase forms near the end of the reaction. Single-phase behavior results because the temperature increases to a point above the critical temperatures of both cyclohexene and cyclohexane. Whereas Poliakoff demonstrated the breadth of continuous hydrogenation in CO_2, lack of comparisons with traditional hydrogenation reactions make it difficult to judge whether the technology will ultimately be deemed 'green'. Catalyst lifetime, for example, is not mentioned—rapid loss in activity could render this technology less than adequate from both green and financial perspectives. If CO_2-based hydrogenation allows for elimination of significant volumes of solvent without greatly increasing energy or catalyst demand, then this technology could ultimately be both economically successful and green.

Subramanian et al. [26] also examined the hydrogenation of cyclohexene to cyclohexane (over Pd/C) in supercritical CO_2, although under conditions where the system remained single phase throughout the reaction and the temperature was held at a constant 343 K. The reaction remained stable over periods exceeding 20 h and catalyst activity was maintained at a high level by pretreating the cyclohexene feed to remove deleterious peroxides. No CO or formate formation

was observed. While this work does not suggest as to how or why such reactions could be considered 'green', it does demonstrate that stable (with respect to temperature and pressure) catalytic hydrogenation in a continuous reactor using CO_2 as solvent is readily achievable. Again, the assumption here is that use of CO_2 will eliminate the gas–liquid interface, rendering the reaction more efficient and potentially less wasteful. Subramaniam has authored a comprehensive review on process design issues inherent to catalytic processes performed in carbon dioxide [59]; interested readers should consult this paper.

Hancu and Beckman [72] examined the hydrogenation of oxygen (production of H_2O_2) in CO_2 under both liquid and supercritical conditions. Hydrogen peroxide is currently produced via hydrogenation (over a Pd supported catalyst), then oxidation of a 2-alkyl anthraquinone (AQ) in an organic solvent (see Fig. 4). Whereas H_2O_2 is widely accepted as a green oxidant, the process by which it is manufactured exhibits a number of less-than-green attributes. First, use of the organic solvent (coupled with the liquid–liquid extraction against water used to recover the product) creates a significant contamination issue, one that is currently remedied using energy-intensive distillation. Further, because each of the reactions are transport controlled (again, by the rate of diffusion of H_2 or O_2 from the gas to liquid phase), CSTRs (continuous stirred tank reactors) are used, allowing for a range of anthraquinone residence times and hence over hydrogenation of the AQ to form waste byproducts.
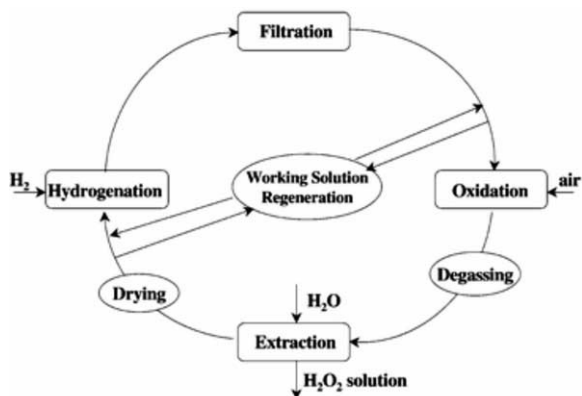

Fig. 4. Schematic of the anthraquinone route to hydrogen peroxide [15].

Gelbein [73] has estimated that one-third of the cost of H_2O_2 can be tied directly to anthraquinone and solvent make-up/regeneration; ≈ 1.5 million pounds of anthraquinone and 15 million pounds of solvent are produced each year simply to support consumption in the AQ process for producing hydrogen peroxide.

Hancu first examined the use of CO_2 as the organic solvent in the anthraquinone process by generating a highly CO_2-soluble analog to conventional alkyl anthraquinones (alkyl AQs exhibit solubilities in CO_2 that are three orders of magnitude below what is employed in the commercial process). These fluoroether-functional AQs exhibited complete miscibility with CO_2; maximum miscibility pressures were sensitive functions of anthraquinone composition and topology. Hancu showed that kinetic control could be obtained in both the hydrogenation and oxidation reactions using CO_2 as the solvent. Here, use of CO_2 eliminates the need for the distillation train, as contamination of the aqueous phase by solvent and other byproducts is not an issue. Further, while the solvent in the conventional process is prone to both hydrogenation and oxidation, this is not the case for the CO_2 analog.

Despite the promising laboratory results, Hancu's process in its original state exhibited a critical economic flaw, yet one that could be corrected given recent results. The fluoroether-functional AQ will be significantly more expensive than an alkyl AQ and pressures required to maintain a homogeneous mixture will be high, despite the use of the CO_2-philic AQ. If, however, we examine the results of Bertucco, Chouchi and Devetta [65,67,68], it is clear that an alternative route exists where one could take advantage of the green aspects of CO_2 use while minimizing the AQ cost issues and reducing the operating pressure. The works cited in the previous sentence show that it is quite possible that one does not need to achieve a single phase of hydrogen, CO_2 and substrate to eliminate gas–liquid diffusional limitations to reaction. In gas–liquid reaction systems, often the primary resistance to transport is the low solubility of the reactant gases in the liquid phase and slow diffusion across the interface. The high degree of swelling of a substrate by CO_2 can allow for significant increases in hydrogen solubility in the liquid phase, while the low viscosity of carbon dioxide enhances diffusion rates. Thus, it is quite likely that one could derivatize an

anthraquinone with an inexpensive oligomer (such as a short chain polypropylene oxide or silicone) that would (a) not raise cost significantly; (b) transform the crystalline, high melting alkyl AQ to a low melting (or amorphous) derivatized AQ that would; (c) swell significantly with CO_2 at moderate pressures (<100 bar); allowing (d) a low viscosity liquid phase with significant hydrogen solubility. This would render the oxidation process more tractable as well, as one could employ air (instead of O_2), where the nitrogen would by and large remain in the upper gas phase. Hence, a CO_2-based version of the AQ process could be rendered greener (through elimination of the solvent waste and energy load reduction) while not detracting from the economics.

As noted in Section 1.5, a key future research issue that will impact heterogeneous hydrogenations in CO_2 is the lifetime of the catalysts, particularly the widely used palladium catalysts. The literature contains examples of successful hydrogenations over Pd in CO_2 and also examples where the rapid formation of CO led quickly to catalyst poisoning and de-activation. Subramaniam et al. has recently presented a rationale [28] for the seemingly contradictory results in the recent literature. They showed (using high pressure FT-IR) that CO forms very quickly (within minutes) on Pd in a mixture of CO_2 and H_2 and then over much longer times alters its mode of binding to reduce catalyst activity. Temperature is a key parameter in this process, where temperatures >343 K seem to greatly accelerate the process. Longer residence times (as would be experienced in batch reactors or CSTRs) also enhance the rate of poisoning.

2.4. Homogeneous hydrogenation in CO_2

2.4.1. CO_2-soluble catalyst design

Clearly, the most pressing issue one must deal with to conduct a homogeneous hydrogenation in a supercritical fluid is that of catalyst and substrate solubility. Carbon dioxide is without question the most popular solvent of those with a readily accessible (<370 K) critical temperature. However, CO_2 is also a feeble solvent [74,75], whose inability to effectively solvate compounds of interest has greatly inhibited commercial development in the past. While many metal-containing catalysts exhibit low solubility in carbon dioxide at moderate pressures, simple metal

carbonyls are known to be miscible with CO_2 under relatively mild conditions [30,76] and as such have been used successfully to catalyze reactions in carbon dioxide. In general, if the catalyst in question is relatively volatile liquid, chances are good that it will exhibit accessible (<500 bar) miscibility pressures in carbon dioxide.

For the case of those metal catalysts whose ligand design renders them poorly soluble in CO_2, work performed since 1990 [77–79] has identified a number of functional groups that are decidedly 'CO$_2$-philic', such that derivatization of catalyst ligands with such groups enhances the solubility of catalysts in CO_2 to the point where homogeneous hydrogenation reactions are feasible. The most widely used of the CO_2-philic groups for catalyst ligand preparation are (CF_2)'s, used in $-(CH_2)_x(CF_2)_y-CF_3$ 'ponytails', where x ranges generally from 0 to 2 and y ranges from 0 to 6. The use of such groups creates a complex optimization problem for those wishing to scale up such processes:

- The solubility of the catalyst is sensitive to the length (and number) of the fluorinated ponytails— longer (or more) tails tends to lower the pressure required to solubilize a given concentration of catalyst [14,80,81]; lower operating pressure means lower capital investment. At the same time, increasing the percentage of fluorine in the catalyst raises the cost owing both to synthetic cost and increased catalyst molecular weight. The presence of the fluorines in the ligands can affect the electronic environment of the metal, either enhancing or detracting from the efficiency of catalysis.
- It has recently been shown that low molecular weight fluorinated sulfonate surfactants (PFOS and analogues, see p. 32) persist in the environment [48,82]. If restrictions associated with PFOS type materials are extended to cover other low molecular weight fluorinated compounds, this would further raise the cost involved with use of fluorinated catalysts.

Whereas conducting homogeneous hydrogenation in an alkane lessens problems owing to the weak solvent power of CO_2, the added liability due to the flammability of the mixture has dampened enthusiasm for such reactions. As mentioned previously, one must be aware that running a hydrogenation reaction in CO_2 can create byproducts owing to reaction of hydrogen

with CO_2 itself—such side reactions can be inhibited through proper catalyst design or choice of operating conditions.

2.4.2. Engineering rationale for homogeneous versus heterogeneous catalysis

In homogeneous hydrogenation, the catalyst has been designed such that it is soluble in the liquid phase; the ligands of the catalyst are usually constructed to produce high selectivity to product. The rationale for conducting homogeneous hydrogenation reactions in CO_2 has three primary thrusts, (1) that operation in CO_2 eliminates the need for organic solvent; (2) operation in CO_2 eliminates the gas–liquid interface and hence allows for kinetic control over the reaction; and (3) use of CO_2 will alter the selectivity of the reaction (hopefully for the better). Much of the recent work on homogeneous hydrogenation has been directed at asymmetric synthesis, with the general hypothesis that use of CO_2 could possibly alter the enantioselectivity of the reactions concerned.

The rate of a homogeneous hydrogenation reaction conducted in an organic solvent or water is likely to be governed by the rate at which hydrogen diffuses across the vapor–liquid interface. As such, elimination of this interface (via operation in CO_2) eliminates this transport resistance. Indeed, because the catalyst in this case is soluble, elimination of the interface entirely eliminates transport resistance. To allow direct replacement of the organic solvent in a homogeneous hydrogenation reaction with CO_2, both the catalyst and the substrate must be soluble in CO_2. Consequently, the majority of the scientific effort in literature works on homogeneous hydrogenation in CO_2 is directed at synthesis of CO_2-soluble analogs of conventional catalysts. Substrates must be chosen that are CO_2-soluble and hence one observes predominantly 'model' compounds employed rather than necessarily compounds of industrial interest.

One could pose the question, 'if a liquid substrate is being employed, why not simply run the reaction using the homogeneous catalyst neat, in the absence of any solvent?' The solubility of hydrogen in organic liquids is typically quite low, and hence running the hydrogenation of a neat substrate will encounter significant transport resistance (of hydrogen across the interface) to reaction. If carbon dioxide readily dissolves or swells the liquid phase (catalyst and substrate), the

rate of reaction can increase owing to enhance hydrogen concentration at the locus of reaction, despite the presence of CO_2, a diluent.

An example of the use of homogeneous catalysis to achieve an engineering goal was shown by Hancu and Beckman [14], who examined the generation of H_2O_2 in CO_2 directly from H_2 and O_2 in a single step using a CO_2-soluble palladium catalyst. This process has been examined in industry for over two decades, as elimination of the anthraquinone from the process eliminates several unit operations and greatly reduces raw material input. If one examines Gelbein's numbers for the economics of H_2O_2 production [73], one would estimate that the using the direct route would reduce the cost of production by over 50%, a significant amount for a commodity process. Hancu proposed that one could generate H_2O_2 in CO_2 (from H_2 and O_2) using a soluble palladium catalyst, where the H_2O_2 is then rapidly stripped into water. The green aspects of this process include elimination of solvent waste and anthraquinone input/byproducts, elimination of the distillation train and the associated energy input, and elimination of several unit operations and the associated energy input. The process could be run continuously and the product recovered from CO_2 without a large pressure drop, rendering the process economics more favorable. Previous work on the direct route to H_2O_2 has focused on the balance between safety and productivity, where most of the patented processes employ water as the reaction medium to maintain safety. However, because the solubility of H_2 and O_2 in water is so low, the productivity of these processes is not sufficient to merit scale-up. In addition, the Pd catalysts employed tend to catalyze degradation of H_2O_2 as well as formation, and hence running the reaction in water does not lead to the desired productivity. Hancu showed that one could employ a CO_2-soluble catalyst, and hence run the reaction in CO_2 without transport limitations and in a non-explosive concentration regime where rates are high. Future work is needed in this area with respect to optimizing catalyst performance and lifetime, yet this is a good example of the use of homogeneous hydrogenation in carbon dioxide to accomplish what are normally perceived to be process goals.

Unlike in the previous example, in cases where a separate aqueous phase is not present, we may be able

to take advantage of the favorable properties of CO_2 (with respect to hydrogenation) while avoiding some of the negative process issues by employing a gas–liquid rather than one-phase system. For example, it is known that H_2 is poorly soluble in most organic liquids and hence it is expected that a hydrogenation in organic solvent would be transport limited. If one knows the fundamental kinetic parameters of the reaction, one should be able to predict at what $[H_2]$ to [substrate] ratio the reaction could be controlled by the underlying kinetics, and hence calculate the target $[H_2]$ for the reaction in the presence of CO_2. If the substrate is a liquid, one should be able to find conditions where a two-phase system (H_2–CO_2-substrate) exists, yet where substantial amounts of hydrogen are dissolved in the lower phase. As described previously, liquid–liquid phase diagrams of CO_2 and larger molecules are typically asymmetric and hence operation at high concentrations of substrate is possible at relatively lower pressures. Further, the catalyst would be required to dissolve in a mixture of (primarily) substrate and CO_2, suggesting that one might not have to fluorinate the catalyst to achieve solubility in the proper phase. Thus, by operating in the two-phase region, one could operate at lower pressure with the original catalyst while also eliminating the need for the organic solvent and the transport resistance to reaction. Ideal substrates would be those that are relatively high in molecular weight, or are polar, yet are also liquids (or low melting solids, where CO_2 can depress the melting point [83]).

Another interesting possibility would, in fact, involve functionalization of the catalyst (fluorination) to allow better solubility in CO_2 while also operating in the two-phase regime. Here, the presence of the CO_2 in the lower phase would serve to not only allow higher hydrogen concentrations but would also solubilize the catalyst. Upon removal of the CO_2, the catalyst would precipitate, allowing recycle. This would present the CO_2-based analogy to recent work by Gladysz et al. [84], where a fluorinated catalyst was developed that was insoluble in the reaction solvent, but dissolved upon heating. Hence, temperature was used as the reversible trigger to allow catalyst use and recovery. Recently, it has indeed been shown that CO_2 itself could also be employed as a reversible solvation trigger [85].

2.4.3. Chemical rationale for homogeneous catalysis

The final reason for conducting a homogeneous hydrogenation in CO_2 is the premise that use of CO_2 would alter the selectivity of the reaction in a positive way. Xiao, for example [86], examined the asymmetric hydrogenation of tiglic acid (2-methyl-2-butenoic acid) in CO_2 using a ruthenium catalyst; ee's (enantiomeric excess's) in CO_2 were essentially no better than those found for the same reaction in methanol. Tumas [87] examined the hydrogenation of dehydroamino acids in CO_2 using a cationic rhodium catalyst—here the fluorinated counteranion (3,5 bis(trifluoromethyl phenyl) borate (BARF) or triflate) enhanced solubility of the catalyst in CO_2. Tumas found somewhat better ee's for some substrates in CO_2 versus hexane or methanol, but overall the performance of CO_2 was comparable to that of the other organic solvents. Leitner [88] has used chiral iridium catalysts to perform the hydrogenation of imines in CO_2. The catalysts were modified (using fluoroalkyl ponytails) to permit solubility in CO_2. Enantiomeric excesses in CO_2 were comparable to those found for the same reaction in dichloromethane, while rates were found to be much higher for some substrates in CO_2 versus CH_2Cl_2.

Recently Tumas [89] and Jessop [90] explored the use of biphasic mixtures of ionic liquids and carbon dioxide to perform hydrogenations. Ionic liquids are salts (typically ammonium or phosphonium) that exhibit melting temperatures near or below room temperature. Ionic liquids behave as polar solvents, yet exhibit vanishingly small vapor pressures. In both the Tumas and Jessop studies, a CO_2-insoluble catalyst was dissolved in the ionic liquid, which is then brought into contact with a mixture of CO_2, substrate and hydrogen. As has been shown by Brennecke [91], ionic liquids absorb large amounts of CO_2 (mole fractions >0.5) at pressures below 100 bar. Further, the ionic liquid does not measurably dissolve in CO_2. Consequently, both Tumas and Jessop were able to conduct reactions in the ionic liquid at very high rates (the high CO_2 swelling allowed for high H_2 solubility), where the product could be stripped from the ionic liquid into CO_2 and the catalyst retained in the ionic liquid for recycle. Note that this is an analogy of the two-phase CO_2/H_2/substrate mixture mentioned above, where the high swelling of the lower phase by

CO_2 eliminates transport limitations while two-phase operation permits use of moderate pressure.

To date, the ionic liquids being explored as solvents are primarily based on imidazolium or pyridinium cations (some work has also been conducted on phosphonium ILs). Whereas these ionic liquids (ILs) are proposed as benign solvents (owing to their near-zero vapor pressures), it must be remembered that the toxicity and fate (in the environment) of such materials is currently not known. Brennecke et al. [92] have recently observed that the toxicity of the butyl imidazolium hexafluorophosphate salts towards *Daphnia magna* is similar to that shown by benzene or dichloromethane, where toxicity of the IL did not depend strongly on the nature of the anion. We expect more such studies in the future in this area. In addition, because large-scale manufacturing processes for these solvents have yet to be established, the impact of such processes on the environment is also not known. In summary, the current crop of ILs may ultimately be judged to be benign solvents or they may not.

2.4.4. Homogeneous hydrogenation and material synthesis

Watkins has explored a novel means by which to apply homogeneous hydrogenation in CO_2 to creation of metal nanoparticles and thin metal films. Watkins has found that certain metal complexes exhibit millimolar solubility in CO_2 at pressures below 100 bar. Exposure of these complexes to hydrogen under mild conditions reduces the metal to the zero valent state, inducing nucleation of pure metal. Watkins first employed this reaction to create small metal particles within polymer monoliths [93]. The complex is added to CO_2, and this solution brought into contact with the polymer, which swells accordingly. Hydrogen is then introduced, which reduces the complex within the polymer, forming the nanoparticles. Recently, Nazem et al. [94] and Howdle et al. [95] have examined the impregnation of polymers with silver particle precursors, performing the reduction in-situ to form the nanoparticle-impregnated material. In Howdle's work, the polymers involved (polylactic acid and analogues) were found to resist attachment by bacteria owing to the antibacterial properties of silver. Use of nanoparticles allowed for useful antibacterial properties despite low loadings of silver.

Watkins has further extended [96] this concept into the realm of green chemistry by adopting the process for use in creating thin metal films. In the microelectronics industry, thin metal films can be generated on an inorganic substrate via vapor deposition, or via dip coating and reduction from an aqueous solution. The former can only be applied to volatile precursors, while the latter route produces very large volumes of metal-contaminated aqueous waste. Watkins has found that homogeneous hydrogenation of metal complexes in CO_2 allows generation of conformal metal films on substrates with sub-micron features and that the only waste produced is a low molecular weight alkane byproduct. Small trenches and pits can be easily coated because CO_2's low interfacial tension permits wetting of even complex features. Watkins has demonstrated this concept with platinum, palladium and nickel—a recent paper [96a] shows that the concept can be extended to copper as well.

This technology is undeniably green, and could be readily applied to a variety of metal film applications, particularly if it can be demonstrated that metal deposition can be targeted (patterned).

2.4.5. How does one economically recover a catalyst and/or a product from CO_2?

Catalyst recycle is a more pressing need for supercritical fluid processes (owing to the custom design of CO_2-philic ligands) than conventional analogs, while also presenting a more difficult problem. Homogeneous catalysts are designed to provide enhanced selectivity and kinetic control of reactions, yet without effective recycle their added cost can prevent economical scale-up. Consequently, any green advantages gained through use of CO_2 as a solvent are more than counteracted by the green and economic disadvantages incurred by use of a homogeneous catalyst. As such, investigations into means by which to recover homogeneous catalysts from CO_2 play a vital role in enhancing the viability of green chemistry in CO_2.

For example, a collaboration between Tumas and the DeSimone group has investigated the design of metal catalysts that are tethered to crosslinked, polyfluoroacrylate polymer beads [97]. As noted earlier, fluoroacrylate polymers are the most CO_2-philic materials yet identified; while the crosslinked versions employed by Tumas cannot dissolve (they are, after all, crosslinked), they will swell in the presence

of CO_2 to 300% of the their initial volume. Because the metal-ligand construct is tethered to the beads, the catalysts can be readily recovered after the reaction and potentially re-used. Crooks [98] has also tried to address the catalyst recycle issue through design of dendrimer-supported metal catalysts; they have created Pd nanoparticles within dendrimers and employed these to support hydrogenation and other reactions. The outer shell of the dendrimers can be decorated with fluoroalkyl groups and hence, these macrocatalysts can be employed in CO_2. Finally, Keurentjes et al. [99] have recently published a method where catalysts are tethered to microporous inorganic supports for use in catalysis in CO_2.

The strategies employed by these three groups are extremely important, in that each has attempted to preserve the benefits of a homogeneous catalyst while co-opting the primary benefit of a heterogeneous catalyst—the ability to easily recover the valuable metal. For each case, then, some key issues remain to be discussed—does each 'supported' catalyst preserve the activity and selectivity of the soluble parent? Are the reactions kinetically controlled or diffusionally limited? How fast does the metal 'leach' from the supported catalysts?

Eckert [15], Tumas [100] and others have examined the use of phase transitions to allow recycle of catalysts and other valuable components in a CO_2 process. Eckert has found that addition of CO_2 to a mixture of organic and fluorocarbon solvents induces mixing, while removal of the CO_2 (by depressurization) rapidly leads to complete phase separation. Consequently, one can employ CO_2 as a reversible and benign 'trigger' to allow a catalytic reaction while ultimately allowing segregation of the catalyst following reaction. Tumas has examined the use of a 'pressure trigger' to attempt to recover the catalyst from a CO_2-continuous emulsion. At elevated pressure, a water-in-CO_2 emulsion forms where the catalyst is localized in the aqueous micellar cores. Reduction of the pressure breaks the emulsion, leading to a distinct aqueous phase housing the catalyst (which could then be re-used).

2.5. Industrial activity: hydrogenation in CO_2

Of the relatively small number of patents (1996–2001) that directly cover hydrogenation in supercritical fluids, two are worthy of special consideration.

First, Harrod et al. [101] describe the hydrogenation of fatty acids in supercritical fluids, technology that has formed the basis for a small start-up company in Europe. Likewise, Poliakoff et al. [102] have described the hydrogenation of a variety of substances in supercritical fluids, technology that has formed the basis/motivation for a pilot scale plant constructed for Thomas Swan Company (Durham, UK) by Chematur (Karlskoga, Sweden). It should be noted that Chematur, a company known for its supercritical water work (assets in both the US and Europe), has acquired the high pressure-related portion of Rauma (Finland), increasing their capabilities in design of processes capable of handling supercritical fluids. The Thomas Swan facility, which was scheduled to start up in September 2001 (and did in early 2002), will be able to generate 1000 tons per year of products, including the results of hydrogenations and Friedel-Crafts acylations and alkylations conducted in supercritical fluids. At this time, it appears that the Swan facility will be used (at least in part) as a pilot-scale or semi-works facility to evaluate the use of supercritical fluids as solvents in various chemical reactions.

2.6. Summary: hydrogenation in CO_2

In summary, hydrogenation in supercritical fluids has been extensively investigated over the past decade and it is clear that hydrogenation reactions can be successfully conducted in CO_2 and other fluids. It is not always clear, however, what if any green advantages are obtained via operation in a supercritical solvent, as many authors do not draw comparisons to conventional processes. Nevertheless, some generalizations can be made:

1) The primary rationale for use of a supercritical solvent in hydrogenation reactions is the elimination of transport limitations to reaction through enhancement of the solubility of hydrogen at the reaction locus. Hydrogen is poorly soluble in conventional hydrocarbon liquids and water and use of CO_2 (and propane, to a lesser extent) as the solvent has been shown to enhance H_2 solubility and hence improve the efficiency of the reaction. Attaining kinetic control over the reaction can lead to reduced byproduct formation and lower energy

input, although in the case of typically exothermic hydrogenations, energy removal is more important than energy addition.

2) A key point that arises if one examines the recent literature is that one does not need to create a single phase (of SCF, substrate and hydrogen) to create a situation where transport limitations can be eliminated [65,67,68]. For example, one can attain kinetic control over the reaction simply by ensuring that a significant amount of CO_2 is present in the liquid phase (maintaining a gas phase of CO_2/H_2). Here the CO_2 functions as a diluent (and viscosity reducer) that enhances the solubility of hydrogen in the lower phase. The enhanced hydrogen solubility more than makes up for the dilution effect from the CO_2. While elimination of the resistance owing to transport of H_2 into the liquid phase does not by definition create kinetic control over the reaction (resistances owing to diffusion to and within the catalyst also exist), the previous work has shown that the solubility of H_2 in the liquid is typically the limiting factor. The use of CO_2 as the 'H_2 solubility enhancing diluent' could have broad ramifications on the practicality for conducting hydrogenations in supercritical fluids, in that it could make the use of benign (and non-flammable) CO_2 more viable. For example, Harrod [61], as well as others, has employed propane as supercritical solvent solely to enable formation of a single phase with substrates whose solubility in CO_2 is poor. It may be possible to both employ CO_2 as the 'diluent' and eliminate transport limitations to reaction, rendering the reaction more efficient while avoiding the flammability problems inherent to propane. The use of CO_2 as 'diluent' could also render the anthraquinone process described by Hancu [72] much more economically efficient as well as greener. This situation obviously best applies to liquids (or low melting solids) that are relatively non-volatile. The use of a two-phase (liquid–vapor) mixture can also help with heat transfer, as the boiling of the liquid can be employed to absorb excess heat.

3) Regarding asymmetric hydrogenations, the key green advantages to this work seem to be the elimination of organic solvent and improved selectivity. However, the results in the literature have not established that significantly greater selectivities are likely to be obtained solely through replacement of a conventional solvent with a supercritical fluid (primarily CO_2). Solvent polarity does impact selectivity, so it is possible that reactions will be identified where use of CO_2 provides selectivity benefits. Most of the work on asymmetric hydrogenation has employed homogeneous catalysts; catalyst lifetime and recovery are unresolved issues in this area.

4) The poisoning of noble metal catalysts via the formation of CO from CO_2 and H_2 could seriously impact the economic viability of hydrogenation processes conducted in carbon dioxide. Subramaniam [28] has begun to elucidate the effect of various process parameters on this process; more research in this area is clearly merited.

2.7. Hydroformylation in CO_2

Hydroformylation, the reaction of hydrogen and CO with an alkene to form aldehydes (Scheme 1), is practiced industrially (the 'oxo' process) on an enormous scale using alkenes of various chain lengths [13].

In one form of the process, cobalt is fed to a reactor containing the oxo gas (H_2 and CO) and the alkene, where a reaction takes place to form the cobalt hydrocarbonyl, the active catalyst species. Alkene is then converted to aldehyde in the liquid phase (the liquid is either a mixture of alkene substrate and alkane solvent or simply the alkene alone). The reaction takes place under rather severe conditions, 200–300 bar and temperatures between 410 and 450 K. The reaction produces the needed aldehyde(s), as well as residual alcohols and alkane. The useful products are recovered and the remainder combusted. The selectivity of the process is $\approx$85% to the aldehyde products. The catalyst is recovered as a cobalt 'sludge' and regenerated/recycled. In a variation on the basic oxo process, a water soluble cobalt catalyst is employed which can be recovered via retention in the aqueous phase at the end of the process. Hence, the reaction is biphasic in nature—poor solubility of higher alkenes limits this process to C_2–C_4 alkenes.
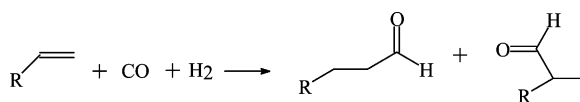
Scheme 1.

The rationale for operating a hydroformylation reaction in a supercritical fluid is similar to that for hydrogenation. Hydroformylation involves the use of two gaseous reactants (CO and H_2) and hence hydroformylation of a non-volatile or low volatility liquid substrate will likely be limited by the solubility and transport of the gaseous reactants from the vapor to the liquid phase. As for the case of hydrogenation in supercritical fluids, research on hydroformylation has been conducted using both homogeneous and heterogeneous catalysts. The 'green' rationale for exploring this class of reactions using SCF solvents is that creation of a more efficient reaction (kinetically controlled, more selective) will result in the production of fewer byproducts and perhaps require lower energy input. Given the conditions under which the process is currently operated, if one could produce the same space-time yield of product using lower pressure and/or temperature, the savings could be significant.

In summary, the green premise behind conducting hydroformylation in CO_2 is not only to replace solvent (only a factor in some oxo processes), but also to create a more efficient reaction, and hence reduce byproduct waste and energy input.

2.7.1. Homogeneous catalysis of hydroformylation in CO_2

Rathke et al. [76] reported the hydroformylation of an olefin in CO_2 in 1991. Here, a cobalt carbonyl catalyst (soluble in CO_2 without modification) was used to promote the generation of butyraldehyde from propylene, CO_2 and hydrogen. Rathke reported that operating the reaction in CO_2 produced a somewhat improved yield of linear to branched aldehyde. The rate of formation of both cobalt intermediates and aldehydes was found to be similar to values found when the reaction was performed in conventional non-polar solvents.

Leitner et al. [103], as well as Erkey et al. [104], reported hydroformylation of an olefin in supercritical CO_2 using a homogeneous rhodium catalyst in 1998, where the now classic strategy of derivatizing the catalyst ligands with fluorinated ponytails was used to enhance catalyst solubility. Leitner found that the reaction (hydroformylation of 1-decene) readily goes to completion in CO_2, with catalyst activities similar to those reported in liquid systems. Erkey's results for 1-octene are similar. As Leitner points out,

the long-chain alkenes employed as substrates for the reactions in CO_2 would likely not be soluble in water and hence the well-known aqueous Rh/triphenyl phosphine trisulfonate catalyst system cannot be used to generate long-chain aldehydes. Here, potentially, is thus a means by which to produce valuable products while replacing an organic solvent with CO_2 (as long-chain aldehydes could only be produced in bulk or in organic solvent). Further, reaction in CO_2 will allow much higher CO and H_2 concentrations and hence potentially much faster rates. Indeed, Erkey et al. suspected that the high CO and H_2 concentrations were potentially the cause for differences in the rate expression between hydroformylation of 1-octene carried out in CO_2 (using a fluorinated phosphine Rh catalyst) versus that in a conventional liquid. Interestingly, Leitner found that internal olefins, which are 'notoriously unreactive' in conventional solvents, are hydroformylated with high rates and excellent yields. Erkey examined the effect of ligand structure (most notably, position and nature of the fluorinated ponytail) on the rate of hydroformylation and found that the activity decreased as the basicity of the ligand decreased. Hence, increasing the fluorine content of the ligand would tend to enhance the solubility of the catalyst in CO_2, but decrease the activity. Indeed, increasing the fluorine content of the ligand will also increase the cost (both through an increase to molecular weight and the inherent cost of fluorinated compounds). Consequently, an optimization problem is created, where increasing fluorine content to the ligand lowers certain capital and operating costs owing to lower required operating pressure, while raising catalyst cost. A possible solution to this problem would be to decouple the effects that create the optimization problem, i.e. find a way to enhance solubility of the catalyst without resorting to fluorination. Xiao et al. at the University of Liverpool has examined this route [105], employing carbonyl groups attached to aryl phosphine ligands to enhance catalyst solubility in CO_2.

Akgerman et al. have investigated homogeneous hydroformylation in supercritical CO_2 for a number of years [106]. In 1997, Guo and Akgerman reported the homogeneous hydroformylation of propylene in CO_2 using a soluble cobalt catalyst. Here, both the rate constant and the selectivity were found to be functions of pressure, each increasing significantly as pressure increased from 90 to 190 bar. The apparent effect of

pressure on the rate constant was attributed to potential limitations in catalyst solubility in the CO_2/propylene mixture—as pressure increased the catalyst solubility should increase, accounting for the observed effect. In a follow-on study published in 1999, Guo and Akgerman employed transition state theory, coupled with partial molar volumes calculated using the Peng-Robinson equation of state, to attempt to explain the selectivity increase with increasing pressure. Calculations reproduced trends in both temperature and pressure-dependence of the rate and the selectivity. It is not clear whether this work has any 'green' ramifications, as the substrate employed (propylene) is a highly compressible fluid itself, and hence might be expected to solubilize significant quantities of hydrogen and CO. In this case, addition of CO_2 would tend to dilute the reactant concentrations, slowing the rate. On the other hand, if it could be shown that addition of CO_2 enhances the concentration of H_2 and CO significantly, then process advantages might be realized.

Xiao et al. [107] have also examined homogeneous hydroformylation in CO_2. They note, for example, that use of fluorinated aryl phosphine ligands (as part of a rhodium catalyst) leads both to higher solubility in CO_2 and higher reaction rates (the latter owing to both electronic affects and solubility limitations of alkylated phosphine catalysts). Comparison of the rates of hydroformylation of acrylates in CO_2 and toluene showed the expected enhancement (in CO_2) owing to the considerable increase in solubility of the reactants (CO and H_2) in CO_2 versus toluene at the same pressure. Selectivities remained the same. Here, as in other research on hydrogenation and hydroformylation in CO_2, the 'green' advantages of the process are suggested to be the increased rates owing to the higher solubility of H_2 and CO in CO_2 versus typical organic solvents, plus the inherently benign nature of CO_2 versus other solvents. However, these attributes may be offset by the high pressure required to operate in CO_2 (energy and capital requirements will likely be higher) and the increased cost and potential environmental problems owing to the use of fluorinated catalyst ligands needed to provide reasonable solubility in CO_2.

It would be quite useful to explore the use of CO_2 as a swelling agent for a liquid hydroformylation system, where the dilution effect is offset by the enhanced solubility of gaseous reactants in the liquid phase owing to the presence of CO_2. Catalysts could still be homogeneous yet not require fluorinated ligands, given that the continuous phase would be primarily alkyl-functional substrate (and product). Consequently, one could eliminate gas–liquid transport resistance while operating at substantially lower pressures than those required for single-phase operation. This indeed might be the process compromise that would provide the 'greenest' operation. Note that this is the opposite to what many authors recommend [108]—whereas a single phase is the best option for some processes, in cases where CO_2/liquid substrate/gas reactive mixtures are being considered, two-phase operation has significant advantages. Indeed, if one could operate a hydroformylation at high space-time yield at lower pressures and temperatures than the current process owing to the presence of CO_2, the process would be both green and economically viable. As in the case of hydrogenation, the use of a two-phase (liquid–vapor) system would allow easy heat removal through boiling (and later condensation) of the liquid.

2.7.2. Heterogeneous hydroformylation in CO_2

Several research groups have evaluated heterogeneous catalysis of hydroformylation in CO_2; generally, yields were good and selectivities to linear aldehyde excellent. For example, Poliakoff [109] used a rhodium complex (aryl phosphine ligands) immobilized on silica—selectivity to linear aldehyde was >90% at 10% alkene (1-octene) conversion. Clearly, use of an immobilized catalyst eases catalyst recovery and re-use issues. Poliakoff found no drop in catalyst activity after 30 h continuous use. Abraham [110] has also examined heterogeneous hydroformylation of propylene, focusing on the design of the catalyst to optimize performance. At first, Abraham's group focused on support design to try to minimize product sorption, while more recent work has targeted the design of 'tethered' rhodium catalysts to try to achieve the advantages of both homogeneous and heterogeneous catalysts. It is again interesting that researchers have neglected to examine the question 'under what conditions will the use of CO_2 provide better results than when using neat substrate?' Given that gases, such as CO and hydrogen, are poorly soluble in organic liquids, if CO_2 will swell the substrate substantially, then conditions may exist where the concentration of hydrogen in the liquid phase (of a

two-phase mixture) may be such that the rate in such a situation is higher than in the neat substrate case, despite the presence of a diluent (CO_2). Such comparisons would be useful for the purposes of determining the viability of such CO_2-based processes.

2.7.3. Industrial activity: hydroformylation in CO_2

Only one industrial patent of note [111], assigned to Mitsubishi Chemical Co. was identified during our patent search. No scale-up work seems to have followed.

2.7.4. Summary: hydroformylation in CO_2

In summary, one could report many of the same conclusions regarding hydroformylation in CO_2 as for hydrogenation in CO_2. In hydroformylation, however, process conditions for the industrial route are rather severe and hence, if one could obtain the high yields and selectivities of the industrial process but at moderate conditions (p, T) via use of CO_2 as a solvent, the process would be both greener and less expensive. A rich area for further work is in hydroformylation in two-phase systems where CO_2 acts as the 'reversible diluent'.
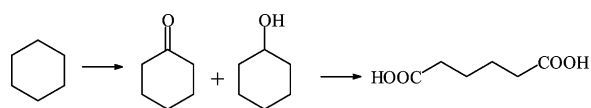
2.8. Oxidation in CO_2

At first glance, CO_2 appears to be an ideal solvent for use in oxidations. Unlike most any organic solvent, CO_2 will not oxidize further in the presence of oxygen and catalysts, and hence use of CO_2 as the solvent eliminates the solvent byproduct waste stream that is usually expected in oxidations.

Many of the conclusions found from recent research on hydrogenation and hydroformylation in CO_2 can also be applied to oxidations conducted in CO_2. However, while hydrogenation and hydroformylation focused exclusively on H_2 (and H_2/CO) as reagents, oxidations conducted in CO_2 have been pursued using a variety of oxidants. The use of O_2 as a benign oxidant has naturally received the most attention, as it is ultimately the least expensive and most atom-efficient route. Research on oxidation of substrates using O_2 in CO_2 has targeted the elimination of transport resistance (as for hydrogenation and hydroformylation) through the elimination of the gas-liquid interface. This is then proposed to enhance the efficiency of the reaction, leading to fewer byproducts. As in the

preceding cases, it would be extremely interesting to examine oxidation in a single-phase system where CO_2 is the minor component (a diluent for the substrate or swelling agent) or in a two-phase system where the substrate resides primarily in the lower phase. Here the role of the CO_2 is simply to enhance the solubility of oxygen in the substrate-rich phase, where we assume that the dilution effect owing to CO_2's presence is more than offset by the enhanced oxygen concentration. This would allow lower pressure operation and might eliminate the need for fluorinated catalyst ligands (for homogeneous processes) in that the catalyst need be soluble in a concentrated substrate–CO_2 mixture, rather than a mixture that is primarily CO_2. Indeed, Wu et al. [112] examined precisely this type of system, although it is not clear from the paper whether they recognized all of the ramifications of the work. Wu studied the oxidation of cyclohexane with oxygen in the presence of an iron porphyrin catalyst and acetaldehyde where CO_2 was the solvent. The yield (of cyclohexanol/cyclohexanone) increased with pressure up to ≈ 100 bar, then decreased sharply at higher pressures. Phase behavior measurements were not made, but qualitative observations (via sapphire windows in the reactor) suggested that the drop in yield coincided with a transformation from two- to one-phase. In this system, the presence of significant quantities of CO_2 in the lower phase of a two-phase mixture allows for solubilization of substantial quantities of oxygen, providing for a high rate of reaction. Transformation to a one-phase mixture merely produced a dilution effect, lowering the rate.

An additional consideration that recommends the use of CO_2 as 'diluent' rather than major component ('solvent') is that oxidations using O_2 are typically carried out using air (O_2/N_2). Air is superior from an economic standpoint, as use of O_2 mandates somewhat energy-intensive O_2–N_2 separation (and hence inadvisable from a green perspective). However, if one were to use O_2/N_2 in a single-phase system where CO_2 is the primary solvent, nitrogen would build up in the system unless a concerted effort (pressure reduction) were made to continuously remove it. In a two-phase mixture where CO_2 is the minor component, the nitrogen concentration in the lower phase would quickly saturate (equilibrium would be established with the upper phase) and hence, this additional
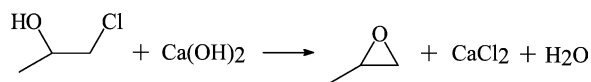
Scheme 2.

Scheme 4.

pressure drop and separation step is not needed (a green advantage).

2.8.1. Oxidations in CO_2: experimental results

Clearly, the oxidation of cyclohexane (first to cyclo-hexanone/cyclohexanol, subsequently to adipic acid) is one of the more commercially important oxidations performed industrially (Scheme 2) [13].

Cyclohexane is oxidized in the liquid phase using air (at temperatures of 395–435 K and pressures in the 10–20 bar range) to a mixture of cyclohexanone and cyclohexanol. Magnesium or cobalt salts are employed to catalyze the reaction. Srinivas and Mukhopadhyay [113] examined the oxidation of cyclohexane in CO_2 with oxygen at temperatures between 430 and 470 K and pressures up to ≈200 bar. Interestingly, a catalyst is not mentioned by the authors, despite the fact that one is employed industrially. The authors found that the condition of the feed (one-phase, two-phase, prox-imity to a phase boundary) exhibited a strong effect on the product profile and the rate of product forma-tion. Not surprisingly, given the discussion above, the highest rates (for both cyclohexane and cyclohexanol formation) were observed in the single phase system where CO_2 was the minor component; i.e. CO_2 was employed to homogenize the mixture of cyclohexane and oxygen, leading to high concentrations of each reactant and hence high rates.

Another oxidation process of great import industri-ally is the formation of epoxides from alkenes. Most important is probably the generation of propylene ox-ide from propylene. Currently, propylene oxide is pro-duced via one of three processes (primarily). First, chlorohydrin (from chlorine and propylene) can be re-acted with base to generate propylene oxide and salt (Scheme 3); a very large volume of wash water is re-quired to work up the product.
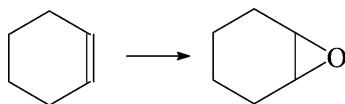

Scheme 3.
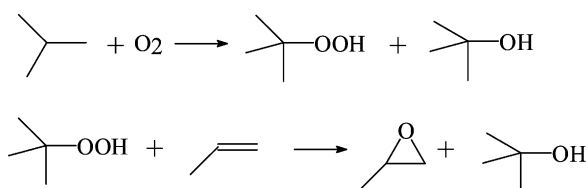
One can also produce propylene oxide via a co-product process where an intermediate is peroxidized with oxygen, and the oxygen transferred to propy-lene, creating propylene oxide and a byproduct alco-hol (which is then transformed to a co-product) [13]. The most widely used co-product processes for PO production also create styrene or methyl tertiary butyl ether (Scheme 4).

There is significant interest in designing a process which only produces PO from propylene and oxygen, as MTBE is now environmentally suspect and the de-mand for styrene tends to fluctuate while that for PO remains consistently strong. As such, propylene oxide production is more energy intensive and wasteful than desired because a co-product must currently be pro-duced along with PO. Consequently, Baiker et al. [114] investigated the oxidation of propylene with an oxy-gen/hydrogen mixture using a Pt/Pd on TS-1 (titanium silicate) catalyst in a two-phase system (methanol was employed as the primary solvent). The reaction pro-ceeds via formation of hydrogen peroxide from H_2 and O_2 over the Pd, followed by oxidation of propy-lene to PO. Both nitrogen and CO_2 were employed as solvents for the H_2/O_2 mixture. Baiker found that the yield of PO increased markedly upon switching from nitrogen to CO_2 in the upper phase of the mixture and that increasing pressure enhanced the yield still fur-ther. As in previous cases, these results may derive from the simple fact that use of CO_2 as the solvent for the reactant gases allows for greatly enhanced concen-trations of these gases in the lower (or liquid) phase, enhancing rates.

Eckert et al. as well as Beckman et al. have inves-tigated an interesting route to alkylene oxides [115]. As shown originally by Richardson et al. [116], hy-drogen peroxide will react with a bicarbonate salt un-der basic conditions to form the percarbonate ion, which will then react with alkenes to form the epox-ide. This reaction is an analogy to epoxidation using

Scheme 5.

a hydroperoxide (such as *t*-BuOOH). Liquid CO_2 will dissolve in molar quantities in water, forming carbonic acid. Beckman and Eckert each showed that a biphasic $CO_2/H_2O_2/water$ mixture will also form percarbonate (upon the addition of appropriate amounts of base) and hence will epoxidize olefins, here cyclohexene oxide (Scheme 5).

Addition of base is critical for achieving high activity. In general, sodium hydroxide is more effective than bicarbonate (likely as it raises the pH more effectively). Given Beckman's results, it would appear that percarbonate is formed both via reaction of H_2O_2 and bicarbonate and via direct reaction between CO_2 and H_2O_2. Further, because the reaction is biphasic, addition of a CO_2-philic surfactant enhanced the rate dramatically, as would be expected. Likewise, addition of a phase transfer catalyst (a tetraalkyl ammonium halide) also enhanced the rate. These epoxidations are intriguing as they employ only water, CO_2 and H_2O_2 as reactants and a catalytic amount of base. The primary drawback to this route is that hydrogen peroxide, although usually considered a commodity chemical, is currently too expensive to use as an oxidant to produce PO.

A number of other researchers have examined the oxidation of alkenes to epoxides using a variety of chemical strategies in carbon dioxide. Birnbaum [117], for example, employed a fluorinated (and hence CO_2-soluble) porphyrin catalyst to oxidize cyclohexene to cyclohexene oxide. Not surprisingly, Birnbaum found that the selectivity was significantly higher in CO_2 than in organic solvent, as operation in CO_2 does not produce solvent oxidation products. Loeker [118] examined the oxidation of olefins in CO_2 using oxygen and aldehydes as sacrificial co-oxidants. Here the reaction was heterogeneous, although it was the steel walls of the high-pressure reaction vessel that were employed as the catalyst. Finally, Haas and Kolis [119] found that one could readily oxidize olefins in CO_2 using *t*-butyl hydroperoxide and a soluble $Mo(CO)_6$ catalyst as an oxygen transfer

medium. Regarding epoxidations, the direct generation of propylene oxide from propylene would be the most significant 'green' advance to be made in this area, yet use of anything but oxygen (or air) as the oxidant is currently too expensive.

Wacker chemistry (the oxidation of an alkene to a ketone using a $PdCl_2/CuCl_2$ catalyst) has also been examined using CO_2 as the sole solvent. Li et al. [120] examined the oxidation of 1-octene in CO_2 and found that operation in a mixture of CO_2 and methanol led to higher selectivity to the methyl ketone than operation in either CO_2 or methanol alone. Because the phase behavior of the system was not measured, the effects reported by Li cannot be completely explained. For example, while it is known that the $PdCl_2$ and $CuCl_2$ catalysts are soluble in methanol and poorly soluble in CO_2, it is not clear as to their solubility in the mixture of MeOH and CO_2. Li et al. also examined the oxidation of acrylic acid to the analogous 3,3 dialkoxy propionate using a similar catalyst system.

In early 2002, Subramaniam et al. [121] published the results of an interesting study on homogeneous oxidation performed in mixtures of carbon dioxide and conventional organic solvents (primarily acetonitrile). This study showed vividly that one can use judicious mixtures of solvent and CO_2 to truly optimize the performance of a reaction. Here, use of CO_2 alone necessitated high pressures (hundreds of bar to dissolve both substrate and catalyst) and the low polarity of pure CO_2 provided a non-ideal medium for the catalyst. On the other hand, while use of pure acetonitrile allowed operation at one atmosphere and provided the catalyst with a suitably polar environment, the solubility of oxygen in the liquid phase was poor. When the right mixture of acetonitrile/CO_2 was employed, the catalyst activity was high, and all components (oxygen, substrate and catalyst) dissolved at pressures of only tens of bar. Study of more examples of this type of system may yield processes that are both greener than current methods and economically practical, particularly if one can ultimately eliminate the need for the organic solvent and work with neat liquid substrates.

2.8.2. Industrial activity: oxidations in supercritical fluids

In a 1997 patent [122], Pitchai et al. (ARCO Chemical Co., now Lyondell Chemical Co., a leading producer of propylene oxide via the co-product process)

describe a process where propylene is converted to propylene oxide directly using a silver catalyst, where addition of CO_2 enhances the efficiency of conversion.

2.9. Summary: gaseous reactants in CO_2

Clearly, carbon dioxide exhibits some significant advantages as a solvent in systems where one or more of the reactants is a gas under typical operating conditions. In such cases, operation in a liquid solvent almost always sets up a situation where the reaction is controlled by diffusion of the gas through the gas-liquid interface. Consequently, use of CO_2 as the solvent can produce (at suitable pressure and temperature conditions) a single-phase substrate-gaseous reactant–CO_2 mixture and hence, eliminate transport resistance owing to the presence of the gas–liquid interface. This, in turn, can render the reaction more efficient and potentially lead to lower energy usage, smaller processes and less waste. In addition, it is clear that use of CO_2 as the solvent exhibits special advantages in certain reactions where oxygen is employed as reactant—because CO_2 will not oxidize, no solvent-based oxidation waste products will be produced in CO_2-based systems. Further, when hydrogen and oxygen are used together in a process (as in Baiker's [114] and Beckman's [14] work), use of CO_2 as the solvent can greatly enhance the safety of the process. Despite the successes noted in the literature, there are some interesting avenues of research in the general area of 'use of gaseous reactants in CO_2' that have not been pursued, yet should be.

First, a minority of the papers published on use of H_2, O_2 and/or CO in CO_2-based reaction systems employ a two-phase mixture in which to conduct the reaction; researchers opt instead to raise the pressure to a point where a single phase forms. Because CO_2 usually swells organic liquids extensively, conducting the reaction in a two-phase mixture could eliminate the transport resistance owing to gas diffusion into the liquid phase while permitting use of relatively low operating pressures. In many cases, if one simply knew the phase behavior of the gas/CO_2/substrate mixture, one could predict those conditions where high (enough) concentrations of gaseous reactant would exist in the lower, substrate-rich phase. Use of lower pressures renders both equipment design and utilities requirements less stringent and is thus a 'green' advantage. In

addition, operation in a two-phase mixture would allow use of air as an oxidant without a slow build-up of nitrogen in the mixture. Finally, as in the case for hydrogenations, use of a two-phase mixture would allow for heat transfer via liquid boiling and condensation.

Another significant point to be made regarding heterogeneous catalysis in CO_2-based systems is that elimination of the transport resistance owing to gas–liquid diffusion may not render the reaction kinetically controlled, as one must also account for liquid–solid transport and pore diffusion within the catalyst. Typically, the effect of pore diffusion on the control of the reaction is mitigated by employing smaller catalyst particles, but this solution is not always practical at larger scales. In addition, it is often easier to operate using a fixed bed of catalyst rather than a slurry of particles. Because CO_2 is a low viscosity fluid, it may be possible in some situations to move from a slurry of particles to a fixed bed without sacrificing rate.

Finally, a number of researchers have shown that one can design catalysts that are soluble in CO_2 and hence one can operate without any transport constraints despite employing gaseous reactants and catalysts. However, recovery of a homogeneous (and typically valuable) catalyst from CO_2 is not a trivial problem and its solution is required to allow homogenous reactions in CO_2 to be both green and economically viable. Naturally, one solution is to design catalysts that are relatively non-toxic and whose activity is high enough such that recovery is not necessary (as is the case currently with ethylene polymerization catalysts). In the case of all catalysts (homogeneous and heterogeneous), the effect of the presence of CO_2 on catalyst deactivation (perhaps through the formation of CO during hydrogenation) is an area that merits further scrutiny.

3. Polymerization and polymer processing

3.1. Introduction

Polymerization and polymer processing in/with CO_2 exhibits some interesting yet seemingly contradictory trends. Some of the most successful commercial processes that employ CO_2 as solvent involve polymeric substrates, yet the vast majority of polymers

produced worldwide are produced in the complete absence of solvent. Indeed, polyolefins (polyethylene), vinyl polymers (styrenics, acrylontrile, butadiene), polyamides (nylons) and polyesters are generated principally in bulk polymerization processes [123]. Further, for the most part, commercial polymers are poorly soluble (many, in effect, are insoluble) in CO_2. However, owing to the asymmetry of amorphous polymer–CO_2 phase envelopes, even polymers that are poorly soluble in CO_2 will swell extensively under moderate CO_2 pressure, allowing for a number of applications using CO_2 as reversible diluent/plasticizer. CO_2 is used extensively in the foaming of polymers (both styrenics and polyurethanes), CO_2 has been used as the solvent in coating processes (Union Carbide's UniCarb process) and CO_2 is currently being explored at the pilot works level in fluoropolymer synthesis (DuPont) and powder coating processing (Ferro Industries).

3.2. Polymerizations: general background

Polymerizations are typically classified by the mode of polymerization (ring-opening, free-radical, etc.), by the type of monomer used (styrenics, acrylates) or by the type of linkage formed during polymerization (polyamides, polyesters). In addition, polymerizations can be conducted in the bulk state, in solution, or in one of many so-called 'heterogeneous modes'—namely precipitation, suspension, dispersion or emulsion.

Because CO_2 is typically proposed/employed as a benign solvent, the following discussion of polymer formation and processing in CO_2 will focus on those applications where solvents are ordinarily used. However, where examples can be found where use of CO_2 in a formerly solvent-less process can provide sustainable and other benefits, such applications will also be discussed.

3.3. CO₂ as a solvent for polymer systems

Polymers present special problems regarding dissolution in any solvent—the very low entropy of mixing in polymer/solvent binaries (owing to the long chains of the polymer) requires a very favorable enthalpic interaction between polymer segments and solvent to ensure dissolution of substantial polymer concentrations [124]. This problem is magnified in the case of

CO_2, given that CO_2's solvent power is admittedly weak.

While a significant portion of academic polymer–SCF phase behavior work has considered solutions where the polymer is the minor component, it is important to remember that the full phase diagram offers several interesting regimes with regards to possible green applications. In Fig. 5, we see a generic phase diagram of a polymer and a SCF [125], showing the various phase separation envelopes and the behavior both above and below the solvent critical temperature. As can be seen in Fig. 6, the liquid–liquid phase envelope is asymmetric (owing to the large disparity in size between polymer and solvent) with the liquid–liquid critical point shifted towards the 100% solvent axis. This is important—it means that solubilization of low concentrations of polymer in solvent will require the highest pressures. Swelling of the polymer by the solvent (moving to the right along the x-axis in Fig. 5) requires significantly lower pressures. Thus, in certain polymer–SCF mixtures, one can observe very high degrees of swelling (>25% in polyacrylate–CO_2 mixtures, for example) at pressures of 100 bar and below [126]. The relatively low pressures required to elicit high degrees of swelling may be one reason why applications where CO_2 is the minor component have been successfully commercialized, while those employing dilute polymer solutions have not.

High-pressure phase behavior studies of polymers and supercritical fluids have been conducted since the late 1940s; the early work was performed to support the high-pressure polyethylene process. Ehrlich's group performed some of the best early work on the phase behavior of polyolefins in supercritical alkanes and alkenes [127]; these studies have been followed by numerous others on polyethylene:alkane or polyethylene:alkene mixtures [128].

In the late 1960s, Giddings suggested a simple correlation between solubility parameter and critical pressure that indicated that CO_2's solvent power should be similar to that of pyridine [4]. However, the strong quadrupole moment of carbon dioxide affects CO_2's pVT properties (including the critical pressure) without influencing its solvent strength. Consequently, early calculations of the solubility parameter were invariably inflated. This was actually confirmed by the very study that proposed that CO_2's solubility parameter should approach that of pyridine;
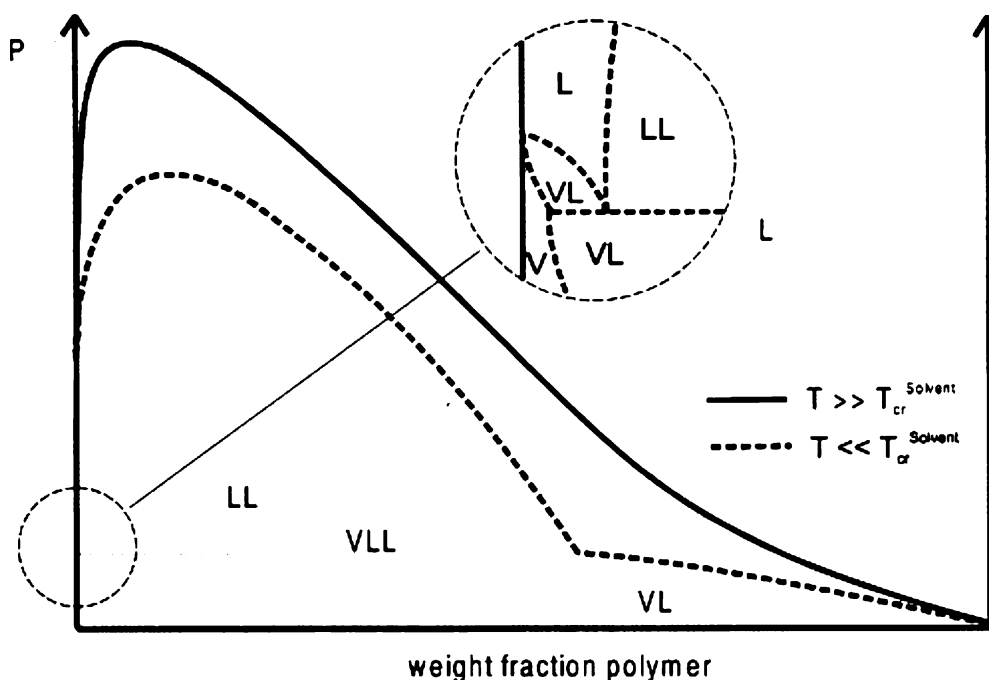
Fig. 5. Qualitative *P-x* diagram of a polymer–CO₂ binary mixture, both above and below the critical temperature of the solvent [125]. This fiigure includes liquid–liquid (LL), vapor–liquid (VL) and three-phase vapor–liquid–liquid (VLL) types of phase envelopes.

polymers that would dissolve in pyridine were not soluble in carbon dioxide. Subsequent calculations performed during the early 1980s (see, for example, Ref. [129]) using CO_2's equation of state strongly suggested that CO_2's solubility parameter should approach that of normal alkanes. However, experimental work by Heller's group on the phase behavior of polymers performed during that time [130] clearly demonstrated that CO_2's solvent power is inferior to that of *n*-alkanes—very few polymers tested by Heller showed any significant solubility in carbon dioxide at moderate (<200 bar) pressures. Experimental work by Johnston et al. [131] suggested that solubility parameter was not the best means by which to characterize the solvent power of compressible fluids, such as carbon dioxide. Johnston suggested instead that polarizability/volume is a better measure of solvent power; by this standard CO_2 is judged to be a feeble solvent, in line with experimental evidence.

During this same time period, a number of researchers found that silicones [132] and fluorinated materials [1,75,133] exhibited miscibility with CO_2 at pressures well below those of alkanes of comparable

chain length. Indeed, a calculation of the solubility parameter of CO_2 using the heat of vaporization and molar volume (of the liquid) would suggest values similar to those of fluoroalkanes or silicones [134]. In 1992, DeSimone et al. published the first reports that describe a truly 'CO_2-philic' polymer, a fluorinated polyacrylate [79]. Further work [135] showed that block copolymers of fluorinated acrylates and 'CO_2-phobic' polymers were both soluble and able to form micelles in carbon dioxide.

It is interesting that the role of fluorine in the design of CO_2-philic materials has not been completely established. For example, while the poly (perfluoroacrylates) are the most CO_2-philic polymers known, it is also true that more poorly soluble fluoropolymers have been identified than highly soluble variants [128,136]. Samulski et al. [137] have found experimentally that fluorine interacts specifically with the electron-poor carbon on CO_2, which would explain why addition of one or two fluorine atoms to aryl phosphine ligands or chelating agents tends to enhance CO_2-solubility significantly. Calculations using various levels of theory tend to predict no specific
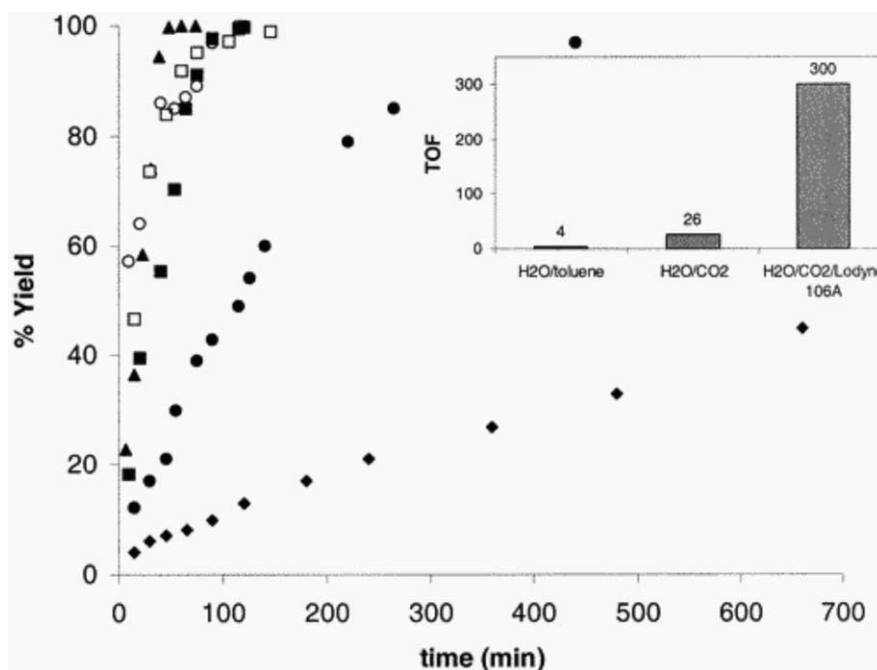
Fig. 6. Time profile of formation of ethyl benzene from hydrogenation of styrene performed in biphasic water/toluene (♦), biphasic water/CO_2 (●) and in emulsions using PFPE MW=2500 (▲), PFPE MW=740 (■), Lodyne 106A (○) or PBO-PEO (□) as surfactants. Reaction conditions: 50/50 wt.% water/CO_2, 1.5% surfactant, 80 mM styrene, 1 mol.% catalyst (to substrate), Rh/L=1/6, 40C, 4000 psi. TOF values at 50% conversion are given as a comparison for biphasic H_2O/toluene, H_2O/CO_2 and H_2O/CO_2 emulsion systems [310].

interactions with fluorine [138], suggesting that fluorine's role in the design of CO_2-philic materials is simply to lower the cohesive energy density. McHugh has recently suggested that fluorination can significantly enhance the 'CO_2-philicity' of polymers if the fluorination creates a dipole in the material, providing a locus for quadrupole–dipole interactions with CO_2 [136a]. This appears to be an area where more fundamental research would help to create a clearer picture of the underlying phenomena.

As interest in applications for CO_2-philic polymers exploded in the 1990s [139], a small group of researchers continued to probe the fundamentals of CO_2 behavior with special regards to polymer solubility. Johnston's and Eckert's groups, using IR spectroscopy and computer calculations, proposed that Lewis acid-base interactions between CO_2 and carbonyl groups could explain the high swelling of polyacrylates by carbon dioxide [140,141]. Calculations using various levels of theory tend to support the experimental evidence, at least where carbonyl

groups are concerned [142]. Further, the specific interactions between Lewis base groups and CO_2 exhibits a much more significant effect on polymer–CO_2 phase behavior than small molecule–CO_2 phase behavior. McHugh's group published several seminal papers [128,143] on the phase behavior of CO_2 and various homo- and copolymers in the mid-1990s. Conventional wisdom of the time would suggest that because CO_2 is a low dielectric, low cohesive energy density solvent, it should only solvate polymers of similar characteristics. However, for the case of ethylene–acrylate copolymers, McHugh found that increasing the acrylate content lowered miscibility pressures, despite the fact that the acrylate is the polar comonomer. McHugh postulated quadrupole–dipole interactions as the cause; clearly Lewis acid-base interactions could have played a role as well. For the case of *n*-alkyl acrylates, McHugh found that increasing the side chain length of the polymer initially would lower miscibility pressures, ostensibly due to the increased polymer free volume (and hence entropy

of mixing). However, because enthalpic interactions between CO_2 and methylene groups are not favorable, increasing the side chain length beyond a certain point led to decreased miscibility. Johnston recently reported that polymers that exhibit low interfacial tensions (and hence low cohesive energy densities) tended to also exhibit low miscibility pressures in carbon dioxide [74].

Clearly, the phase behavior of polymers in CO_2 is tied to CO_2's low cohesive energy density, but its Lewis acid character will also play a significant role if the polymer contains Lewis base groups. For example, Beckman found that polybutadiene, a very low cohesive energy density polymer, is more 'CO_2-philic' than other vinyl polymers of higher cohesive energy density [144]. However, both polypropylene oxide and polyvinyl acetate exhibit lower miscibility pressures than polybutadiene, likely owing to the presence of Lewis base groups in each of the latter polymers despite exhibiting higher cohesive energy densities than polybutadiene.

Topology also plays a role in determining phase behavior. Beckman and Lepilleur [145] found that increases to polymer chain branching generally lowers miscibility pressure in CO_2. This result confirms earlier results on branched polyolefins in alkanes [146]. Finally, McHugh found that topology can play an extraordinary role in determining the phase behavior of polymers in CO_2. The miscibility pressures of polyvinyl acetate, for example, lie at pressures hundreds to thousands of bar lower than those for polymethyl acrylate (an isomer of PVAc) [143]. The underlying mechanism for this behavior is entirely unknown.

In the late 1990s, Beckman's group [147] proposed a hypothesis for design of CO_2-philic polymers that incorporated the earlier conclusions reached by both McHugh and Johnston. Beckman et al. proposed that CO_2-philic polymers should incorporate monomers (or functional groups) that contain several features: high flexibility (and thus low Tg), low cohesive energy density and also Lewis base groups to provide loci for specific interactions between the polymer and CO_2. They demonstrated the effectiveness of the hypothesis by designing highly CO_2-soluble ether-carbonate copolymers. Modified polydimethyl siloxane (PDMS) was also examined [148]—experimental work by Kiran [149] had shown that PDMS exhibits UCST type

phase behavior at room temperature, suggesting that the enthalpic interaction between PDMS and CO_2 is non-optimal. Fink et al. then showed that addition of Lewis base groups (in side chains) to PDMS lowered miscibility pressures in CO_2 by hundreds of bar. Finally, Wallen [150] has proposed that CO_2 can exhibit specific interactions other than simple Lewis acid-base type. Wallen has found, via both simulation work and experiment, that an aldehyde will exhibit interactions between the carbonyl oxygen and the carbon atom in CO_2 as well as a weak hydrogen bonding interaction between the aldehyde H and the oxygen in CO_2.

In summary, we have made great strides in our understanding of CO_2–polymer phase behavior since the days when 'CO_2 is like hexane' was conventional wisdom. However, as shown by recent work from McHugh, Beckman, and Johnston, a fundamental understanding of CO_2–polymer thermodynamic behavior is still lacking. Poly(fluoroacrylates) are the most CO_2-philic polymers known, but their high cost renders their application problematic. If one could, from first principles, design a non-fluorinated, truly CO_2-philic polymer, this would greatly enhance the potential for industrial application of CO_2, both in polymer science and general chemical processing.

3.4. Chain polymerization and CO_2

In chain polymerizations, an initiating species is formed which then contacts a monomer, creating the beginning of an active chain. This chain then grows rapidly to form the polymer molecule. Finally, a chain-terminating event may take place (or monomer may be depleted), ending growth of the chain in question. The various chain polymerization types are then further subdivided based on the type of initiating species and also the relative rates of initiation and growth [151].

3.4.1. Free radical solution polymerization

In free radical chain polymerization, an initiator (through thermal, chemical or photochemical stimulation) forms an active radical that contacts a vinyl monomer, forming the growing chain. Termination takes place either through chain coupling or disproportionation. Molecular weight distributions can be broad (>2.0) and average molecular weight rises rapidly with conversion, leveling off as long chains

are continuously formed. Low-density polyethylene, polyacrylates, polystyrene, polyvinyl chloride and other materials are formed using free radical initiation. Much of the total commercial volume of such polymers is synthesized in the absence of solvent in continuous processes containing only monomer, polymer and initiator at temperatures sufficient to create a pumpable polymer melt.

As described above, the solubility of most polymers in carbon dioxide is relatively poor, and hence it is not surprising that early work on polymerization in CO_2 was relegated to precipitation polymerizations [152]. Although it could be claimed that the plasticizing effect of CO_2 on the precipitated polymer might enhance transport of monomer to the growing chain end, no significant advantages (versus the added complication of working at elevated pressure), green or otherwise, were realized from such processes, possibly because the presence of the monomer itself tended to plasticize the polymer. Consequently, one would only expect to observe a significant effect of added CO_2 during the later stages of polymerization, when the presence of CO_2 might inhibit the well-known Trommsdorf, or autoacceleration effect (the latter occurs when the increased viscosity of a polymer melt inhibits chain termination, leading to rapid increases in rate). Because CO_2 is a diluent, its presence would also lower the rate in general, a disadvantage [153]. Finally, vinyl polymerizations are exothermic and hence, great care would need to be taken to prevent uncontrolled pressure increases. In summary, the disadvantages inherent to operating a vinyl polymerization in CO_2 have greatly outweighed any advantages to date. In general, it is very hard to justify (from a 'green' perspective) adding solvent to a solvent-less process.

One exception to this rule is in the surfactant-free precipitation polymerization of fluoromonomers [154], recently scaled up by DuPont to a semi-works size in North Carolina. Typically, fluoropolymers are generated via suspension polymerization in water; the use of carbon dioxide as the solvent provides for a chain-transfer free solvent and eliminates the need for the surfactant (as noted previously, the EPA has recently filed a SNUR regarding fluorinated surfactants of the fluorosulfonate variety, possibly restricting their use in future [48]). Interestingly, most fluoromonomer polymerizations are precipitation polymerizations (as shown by McHugh [136], many fluoropolymers are

insoluble in CO_2). However, addition of CO_2 stabilizes tetrafluoroethylene, eliminates the need for fluorinated solvents and surfactants, and eliminates chain transfer to solvent. Indeed, a recent conversation with a DuPont customer [155] revealed that the fluorinated copolymers produced in CO_2 exhibit superior performance during extrusion, owing to fewer gels and a tighter composition distribution. Hence, in fluoropolymer polymerization, CO_2 provides green advantages, safety advantages and product advantages.

Another possible application for precipitation polymerization in carbon dioxide involves acrylic acid [156]. Poly(acrylic acid) is currently generated in an emulsion or suspension polymerization in a hydrocarbon continuous phase; removal of the alkane from the product is both energy intensive and waste forming. Use of CO_2 as the continuous phase allows the generation of dry, free-flowing, granular material.

Carbon dioxide has also been proposed as a diluent (reversible plasticizer) for reactions on preformed polymers, reactions that often take place within extruders during polymer processing. In theory, the plasticizing effect of CO_2 will reduce transport limitations of the reactants (in the otherwise highly viscous melt), leading to enhanced rate and thus more complete reaction in the same residence time. However, O'Neill and Beckman [153] found that in the case of the polyvinyl acetate-to-butyrate transition (a highly successful industrial process) the presence of the low molecular weight reactants was sufficient to plasticize the melt. Here CO_2 acted merely as a diluent, lowering the rate by reducing the concentration of the active species.

3.4.2. Heterogeneous free radical polymerizations

Heterogeneous polymerizations are those where the polymer is not soluble in the continuous phase, or solvent [151]. These polymerizations can be further sub-divided based on the thermodynamic affinity of the monomer for the solvent and the nature of the polymer stabilization:

1) Emulsion
2) Dispersion
3) Suspension

While simple precipitation can be considered as a form of heterogeneous polymerization, it has been considered separately in the previous section.

3.4.2.1. Emulsion polymerization in CO_2. In emulsion polymerization, neither the monomer nor the polymer is soluble (to any appreciable extent, there is always some measurable monomer solubility) in the continuous phase and sufficient surfactant is present to form micelles (the locus of the polymerization) and to stabilize the large droplets of monomer that are also present (the latter form monomer reservoirs). The kinetics of the emulsion polymerization are such that (unlike in bulk or solution free radical polymerization) both high rate and high molecular weight are possible. Carbon dioxide, while not a powerful solvent, is miscible with a large variety of volatile, low molecular weight vinyl monomers [157]. As such, identifying a suitable candidate for emulsion polymerization is problematic, as one must find a monomer that exhibits a sizeable phase envelope under the conditions of interest, yet under conditions where the surfactant to be employed is miscible (in CO_2, the converse is much simpler to identify—a mixture where the monomer is miscible and the surfactant is not!). This has proven to be difficult and to date only acrylamide, acrylic acid and *N*-vinyl formamide have been investigated in any detail [158]. The case for acrylamide is further complicated by the fact that it is a solid at temperatures below 353 K and hence has been employed as an aqueous solution—the presence of the water renders subsequent polymer particle size analysis difficult. Emulsion polymerization of water soluble monomers in CO_2 is a viable target in the context of green chemistry, in that the commercial route employs an organic continuous phase and also requires significant energy input to separate product from emulsion following polymerization.

The key issue in emulsion polymerization is the design of the surfactant—it must be soluble in CO_2 at moderate pressures, effective and relatively low cost. Early work employed fluorinated surfactants (nonionic and anionic), as these were known to be CO_2-philic [158]. Results showed that one could indeed generate high polymer at high rates, but the surfactants employed were more valuable (even at 1% loading and below) than the polymers being generated and recycle is difficult to achieve economically. Although silicone-functional surfactants have also been evaluated [159] in emulsion polymerization, their performance is not as good as their fluorinated cousins, and their cost can be quite high (for siloxane-based materials generated from the cyclic tetramer (D_4), cost is approximately five to ten times as high as traditional hydrocarbon surfactants. For mono-functional materials created from the D_3 cyclic trimer, the cost approaches that of fluorinated materials.) The practicality of the process would be greatly enhanced by discovery of an effective yet low cost surfactant. In work to date, AIBN (azo bis(isobutyrnitrile)) was usually employed as the initiator and hence process temperatures were set at 330–340 K to achieve reasonable polymerization rates (AIBN half-life at 343 K is ≈4 h). As such, process pressures were relatively high (>200 bar). Clearly, use of an initiating system that operates at lower temperatures (photochemical or redox [151]) would lower the required process pressure and hence also render emulsion polymerization in CO_2 more practical (see, for example Ref. [160]). It should be noted that such an initiator system would be more expensive than that currently employed, an added cost that must be factored into the total.

3.4.2.2. Dispersion polymerization in CO_2. Dispersion polymerization [161], where the monomer is soluble in the continuous phase (here CO_2) while the polymer is not, has seen extensive research activity over the past decade. Because most, if not all vinyl monomers are miscible with CO_2 at relatively modest pressures (complete miscibility below 100 bar at 313 K in many cases), while high polymers are notoriously insoluble, dispersion polymerization seems well suited to adaptation to carbon dioxide. If one were to conduct a dispersion polymerization in a conventional liquid, a low molecular weight alcohol or alkane would be the preferred continuous phase and thus CO_2 could replace a significant volume of organic solvent. Separation of the product polymer from the continuous phase in a CO_2 system would not require drying/devolatilization, a potentially significant energy savings. Because many vinyl monomers lend themselves to dispersion polymerization in CO_2, the key requirement to successful demonstration was finding a suitable stabilizer. Finally, because a successful dispersion polymerization produces a stable latex that can then form the basis for a coating formulation, it was hoped that the analogous process in CO_2 would produce a coating formulation that could be sprayed without VOC release.

Stabilizers for dispersion polymerization in conventional systems require a soluble component and an anchoring component—DeSimone's group prepared the first successful stabilization system from homo- and co-polymers of fluoroacrylate monomers [162]. Small amounts of these copolymers permitted the rapid polymerization of methyl methacrylate (MMA) in CO_2 in the form of monodisperse particles ≈1 micron in size. Johnston et al. later showed that stabilization of the particles was due in large part to effective solvation of the CO_2-philic, fluorinated blocks of the copolymer [163]. If conditions (temperature and pressure) were such that the fluorinated chains would collapse, flocculation of the particles would take place. Beckman and Lepilleur [164] also examined the dispersion of MMA in CO_2; here comb-type copolymers (acrylate backbone and fluoroether side chains) were employed. Once the backbone was above a certain chain length, monodisperse, micron size particles could be rapidly formed. Finally, Howdle et al. [165] found that one could create a very simple but effective stabilizer for MMA polymerization—a fluoroether carboxylic acid. Hydrogen bonding between the acid and MMA's carbonyl provided anchoring sufficient to stabilize the dispersion and hence form small PMMA particles.

As in the case for emulsion polymerization, practical dispersion polymerization in CO_2 will ultimately require a stabilizer that is both sustainable and inexpensive and hence the fluorinated materials investigated heavily during the 1990s are not likely to be applied industrially. A reactive silicone (polydimethyl siloxane, acrylate terminated) has been applied as a stabilizer in MMA polymerization [166], but its performance was far less satisfying than the various fluorinated stabilizers that have been evaluated. As in the case of emulsion polymerization, use of an initiating system that operates at low temperature (versus the typical thermally triggered azo- and peroxide compounds) would lower process temperature (and hence pressure) substantially. Finally, although micron-size particles of MMA (and other monomers) were readily formed, latex stability was relatively poor, with material settling out in a matter of hours (versus the desired days and weeks). This is not entirely surprising, as the low viscosity of CO_2 (1/10 that of water) produces a relatively high terminal settling velocity. If the cost of the stabilizer could be lowered and the stability of the latex improved, a CO_2-based dispersion could form the basis of a low VOC coating system.

A potentially sustainable CO_2-based (and hence solvent-free) coating formulation might be developed even if the rapid settling of the latex cannot be corrected. If polymer particles, produced either in water or in CO_2 then recovered and dried, could subsequently be re-dispersed in CO_2, then one could ship the dry particles from manufacturer to remote customer and still employ a non-VOC (CO_2-based) spray coating system. Use of such a system would save the large amount of energy needed to transport essentially solvent (CO_2 or water) long distances. Johnston et al. have investigated the mechanics of particle re-dispersal and also the design of surfactants that would allow such polymerization and re-dispersal [167]. Their initial results are promising. Although not entirely similar, the commercial UniCarb process [40] was an early attempt to address the stability versus sustainability balance in spray coatings. The conventional coatings process employed polymer beads dispersed in a mixture of a good solvent and a poor yet volatile solvent. The UniCarb process replaced the poor solvent with CO_2 (also a poor-yet-volatile solvent) while retaining the good solvent to maintain the stability of the dispersion. Replacement of the poor solvent with CO_2 reduced VOC emissions by 60%.

One area where CO_2 would exhibit advantages over both water and organic solvents would be dispersion polymerization of hydrolytically sensitive monomers. In such a case, water would be green but technically infeasible, while apolar organics would be technically feasible yet not sustainable. DeSimone and Shiho have illustrated this using a glycidyl methacrylate monomer [168]. Again, if an effective yet inexpensive surfactant could be identified, use of CO_2 in such an application would be both green and technically efficient.

3.4.2.3. Suspension polymerization in CO_2. In suspension polymerization, neither the monomer nor the polymer are soluble in the continuous phase, but the stabilizer structure and concentration are such that only droplets are formed (no micelles) and hence the kinetics of the polymerization resemble that of bulk polymerization. Suspension polymerization is typically applied to hydrophobic vinyl monomers in water, a process that is itself relatively green

(although water remediation and energy use for drying represent targets for improvement). CO_2 has been used in the suspension polymerization of acrylic acid in CO_2 in the hope of replacing the conventional hydrocarbon continuous phase. Polyacrylic acid is a very low-cost commodity material, and hence such a process must produce dry, free-flowing powder at relatively low pressure and with an inexpensive stabilizer [169].

3.4.2.4. CO_2 as non-solvent in heterogeneous polymerizations. Cooper et al. [170] have explored a novel application of CO_2 in heterogeneous polymerization. Here, CO_2 is used as the porogen in the suspension polymerization of styrene/divinyl benzene, where the resulting porous beads form the basis for ion exchange resins. Typically a hydrocarbon porogen is employed and hence must be separated from the product and disposed after use. A good porogen must be miscible with the monomer (as is the case with CO_2 and styrene) yet immiscible with the polymer (as in CO_2/polystyrene). Generally, one alters the pore size and total surface area of the beads through alterations to porogen composition; Cooper showed that one could achieve the same tunability through pressure alterations to CO_2.

3.4.3. Other chain polymerizations in CO_2

Carbon dioxide has been employed as a solvent for cationic and metal-catalyzed ring-opening polymerization of various monomers in CO_2. Biddulph and Plesch first examined cationic chain polymerization of isobutylene in CO_2 in 1960 [171]; Kennedy later also examined this reaction [172]. This work demonstrated that cationic polymerization is indeed viable but that the premature precipitation of the polymer lessens any advantages one might have derived from use of a green solvent. DeSimone later applied knowledge of CO_2-philic compounds to greater advantage by examining the homogeneous cationic polymerization of fluorinated monomers (both vinyl and functional oxetane) in CO_2 [173]. As the DeSimone group demonstrated earlier, polymerization of fluorinated monomers in CO_2 is a very effective technique for polymer production without the use of hydro fluorocarbon solvents.

Metathesis polymerization is also viable in CO_2, yet the hydrocarbon monomers employed produce polymers that rapidly precipitate upon attaining even modest chain length [174]. The same is true for oxidative polymerizations of either pyrrole or dimethyl phenol. It has been shown that one can prevent the seemingly inevitable precipitation through use of fluorinated stabilizers (and hence formation of a dispersion), but the high cost of the stabilizers has inhibited further consideration of such routes.

Not surprisingly, anionic polymerization in CO_2 produces at best carboxy-terminated oligomers, as the terminal anion reacts quickly with CO_2 to produce the less reactive carboxylate. Carbon dioxide is also an efficient chain terminator in Ziegler-Natta and metallocene type catalyst systems—as such, CO_2 cannot currently be used as a solvent in controlled olefin polymerizations, the largest volume polymerizations currently. Because these polymerizations tend to be low pressure gas-phase reactions of ethylene and propylene, it is not clear what role carbon dioxide could play even if the catalysts could tolerate its presence.

3.4.4. Industrial activity: chain polymerizations in CO_2

DuPont has filed a number of patents [175] describing the use of CO_2 as a solvent for chain polymerization of fluorinated monomers. This technology, plus patents filed by coworkers at the University of North Carolina [154], formed the basis for the construction of a semi-works facility in North Carolina with an annual capacity of over 1000 tons of fluoropolymer (there are plans to expand this capacity significantly by 2006). 3M and Xerox have also obtained recent patents in this area [176], although their supercritical CO_2 research efforts appear to have been discontinued several years ago.

The EU funded (1.5 million Euros, 12/97–12/00) a multi-year study (Superpol project) linking four universities with polymer manufacturers Solvay, Goldschmidt and DSM to explore the use of supercritical fluids in polymer production. While the consortium includes both prestigious universities and well-known companies, the results to date [177] have not significantly added to the information described above. Solvay has recently acquired the fluoropolymers business of Ausimont, and hence may invest in CO_2-based fluoropolymer polymerization technology in the future.

3.5. Condensation polymerizations

3.5.1. Polyester, polyamides, polycarbonates

Condensation polymerization [151] occurs through the step-wise addition of difunctional monomers to each other, usually in a reaction that produces a small molecule byproduct (water or alcohol, for example). Polyesterification (reaction of diol with diester or diacid) and polyamidation (diamine with diacid or diester) are two classic examples of great industrial importance. Because of the nature of these polymerizations, there are key differences with respect to chain polymerizations. Condensation polymerizations are usually endothermic, and hence heat must be applied to achieve high rate of reaction. Unlike chain polymerization, molecular weight builds slowly in condensation reactions. Indeed, the statistics of condensation polymerization show that the extent of reaction of the active end groups must reach at least 95% to create polymer chains of reasonable length. Because each condensation (chain building) reaction is governed by equilibrium, removal of the small molecule byproduct is crucial in achieving high extent of reaction and hence high chain length.

Continuous industrial condensation polymerization processes all exhibit the same general elements [123]. The two monomers are added to the system in the correct proportions and then heated and pumped into a U-shaped tubular reactor with the appropriate catalyst. Steam (or alcohol) is flashed from the reactor at its exit, and the resulting oligomer is pumped to a 'finishing stage'. Here, vacuum or flowing N_2 is applied to remove the small molecule, while slow mixing creates surface area to enhance the reaction rate. Here the oligomers are transformed to polymers. Temperatures in the process must be high enough to melt the polymer and hence temperatures of 520–570 K are not uncommon.

Given the nature of condensation polymerizations, CO_2 has been applied as a diluent/plasticizer to enhance the removal of the small molecule, hence increasing molecular weight [178]. By dissolving in the polymer melt, CO_2 should reduce the viscosity and increase the rate of removal of the condensation byproduct. Clearly, for the process to be most successful, the small molecule should partition preferentially to the CO_2 phase. The green aspect of such a scheme is that use of CO_2 could allow better removal of the condensation byproduct at lower temperature, saving energy. The best example of this use of CO_2 is probably the work of Kiserow and DeSimone on the CO_2-enhanced solid-state polymerization of polycarbonate. In bisphenol A polycarbonate production, diphenyl carbonate is reacted with bisphenol A to produce the polymer plus phenol. Many end users of polycarbonate (as well as nylon 6.6) practice 'solid-state polymerization', where the purchased polymer is charged to a vacuum oven to increase molecular weight through additional reaction and byproduct removal. DeSimone showed that CO_2 could be employed to remove phenol from polycarbonate oligomers at temperatures well below the T_g of the polymer (420 K), raising molecular weight substantially [179]. Later work [180] by Shi et al. showed that limitations to the increase in molecular weight are due primarily to an imbalance in the concentration of the two types of endgroup on the polymer (hydroxyl and terminal carbonate)—this is a common problem in the solid state polymerization of condensation polymers.

A general problem with using CO_2 to enhance condensation byproduct removal is the low solubility of some common byproducts in carbon dioxide. Water, the most common byproduct in polyamide generation, is poorly soluble in CO_2. In the formation of polyethylene terephthalate (the highest volume polyester), the polymer is formed via the self-condensation of the adduct of 2 mol of ethylene glycol and dimethyl terephthalate (see Scheme 6); the byproduct is hence ethylene glycol, also poorly soluble in CO_2. Indeed, the use of CO_2 to plasticize polymer melts and remove condensation byproducts is sound, sustainable processing, but this technique will only be truly effective if the byproduct is designed to partition strongly to CO_2.
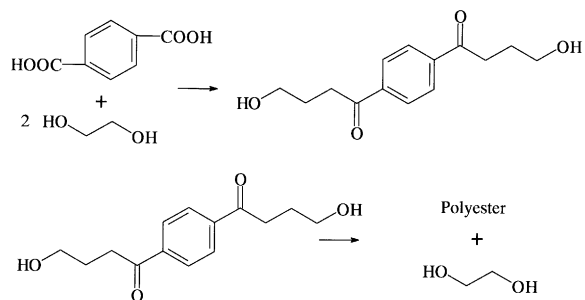
Scheme 6.

While energy reduction is an admirable part of green chemistry, the most significant targets for green chemistry in condensation polymers are probably not the polymerizations themselves, but rather the synthesis of the monomers. For example, diphenyl carbonate (monomer for polycarbonate) is synthesized from phosgene and phenol and a sizeable effort has been made by industry to optimize the catalytic production of DPC from phenol and CO [181]. Bisphenol A (also a precursor to polycarbonate) is under scrutiny for possible deleterious effects on humans. Terephthalic acid (precursor for polyesters) is generated via an oxidation of *p*-xylene that produces some problematic waste streams [13]. DuPont has expended considerable effort in a joint venture with Genencor to create a biochemical route to propane diol, another precursor to aromatic polyesters. Pilot scale biological production of propane diol has been achieved and full-scale production is planned for the future [182]. Non-phosgene routes to di-isocyanates (precursors to polyurethanes) using CO_2 as a raw material have been investigated by both industry and academia [183]. Finally, the oxidation route to adipic acid (precursor to nylon 6.6) and the synthesis of caprolactam (precursor to nylon 6) are frequent targets of scientists involved in green chemistry, given the significant waste streams emitted by current processes [184]. Consequently, it would appear that real breakthroughs in green chemistry applied to condensation polymers will and should come in the area of more sustainable monomer synthesis. In some of these cases CO_2 could play a significant role, but the primary research need appears to be more atom efficient synthetic routes.

3.5.2. Polyurethanes

Polyurethanes are condensation polymers but represent a special case, in that a small molecule is not produced during the primary polymerization reaction (where a hydroxyl group and an isocyanate react to form a urethane linkage). Whereas polyurethanes are applied as fibers, coatings and thermoplastics, their primary relevance to this report owes to their extensive use in foamed articles.

Polyurethane flexible slabstock foam has been produced via the 'one-shot' process since the late 1950s [185]. Here a stream of polyol (a multi-functional hydroxy-terminated oligomer, typically a polyether) is blended with water, catalysts, surfactants and 'blowing agents', then injected into a high-intensity mixing chamber with a multi-functional isocyanate. The resulting liquid blend is pumped evenly onto a moving belt, where polymerization occurs as hydroxyl groups react with isocyanates to form urethane linkages. Further, water reacts with isocyanate to form an amine group plus CO_2, where the amine subsequently reacts with another isocyanate to form a urea linkage. The heat of reaction boils the 'blowing agent'; this plus the CO_2 released during the polymerization creates the foam, which is stabilized until cure by the added surfactant.

For decades, the preferred blowing agent was either a chlorofluorocarbon or methylene chloride; note that these blowing agents were simply emitted to the atmosphere during foam formation. Following adaptation of the Montreal Protocols in 1986, foam producers searched for alternatives. Compounds such as pentane and hydrofluoropropane have been evaluated and applied, yet these do not fully ameliorate the emissions problem (and, of course, hydrocarbons are flammable). In the late 1980s and early 1990s, Crain Industries created a CO_2-based process (CarDio, [186]) where liquid CO_2 (3–5% by weight) is injected into the polyol stream at pressures above the vapor pressure of CO_2. The pressure is then gradually reduced, such that the pressure in the high intensity mixer is only 10–20 bar. The pressure is then reduced further via the use of a 'gate-bar' assembly that expands the mixture to one atmosphere and spreads it evenly onto the moving belt. The liquid mixture remains single phase through the mixing chamber because polyols absorb significant amounts of CO_2, even at low pressures. Plants operate the CarDio process in both Europe and the US. Bayer Corporation has also commercialized a CO_2-based, continuous polyurethane process [187]. In both the CarDio and Bayer processes, CO_2 directly replaces a large volume of organic solvent that would have been emitted to the atmosphere with little additional energy input (cooling the liquid CO_2). Consequently, polyurethane foam production using CO_2 as the blowing agent is an excellent example of green chemistry using carbon dioxide. It is interesting to note that the first patent proposing the use of CO_2 as the blowing agent for polyurethane foam was filed in 1959 [188]—it was only after perfection of the gate bar assembly in 1991 that Crain was able to successfully scale up a CO_2-based polyurethane foam line.

Thus, the success of a green, CO_2-based chemical process can depend as much on mechanical design as on chemical design.

3.6. Carbon dioxide as a monomer

It has been known since 1969 that carbon dioxide can be copolymerized with oxiranes to form poly(ether-carbonates) [189]. Production of a polycarbonate using CO_2 instead of phosgene (the usual route) is indeed a green process, in that not only is a harmful chemical replaced with a benign alternative, but the production of substantial quantities of salt (the usual byproduct in polycarbonate production) is avoided. Poly(ether-carbonates) formed from oxiranes and CO_2 could be applied as degradable surfactants (using ethylene oxide) or low energy alternatives to polyesters polyols in polyurethane manufacture (using propylene oxide). They have also been found to be the most CO_2-philic, non-fluorinated materials yet identified [147] and hence they themselves could enhance the wider use of CO_2 as a benign solvent. There are, however, some key technical hurdles that have substantially prevented the commercialization of a CO_2-based route to a polycarbonate to date:

1) Most of the catalysts developed to date have not demonstrated particularly high activity when used with either ethylene oxide or propylene oxide, the comonomers most likely needed to produce economically viable copolymers [190]. On the other hand, a number of catalyst systems have been shown to be highly effective in the copolymerization of CO_2 with cyclohexene oxide [191], although this copolymer has not attracted any significant industrial interest owing to monomer cost versus polymer properties.
2) Those catalysts that *have* shown high activity in CO_2/propylene oxide copolymerizations have not permitted significant incorporation of CO_2 into the copolymer (typically <10% carbonate) [192].
3) Catalysts developed to date tend to produce substantial amounts of low molecular weight, cyclic carbonate when used with either ethylene oxide or propylene oxide. In many cases, over 80% cyclic material is produced. The low molecular weight

cyclic cannot be polymerized, and hence current catalysts could not be employed economically.

Early work (1970s–1980s) focused on the assessment of zinc catalysts for the copolymerization of oxiranes and CO_2 [190]. These catalysts typically employed a reaction between a dialkyl zinc and a multi-hydroxyl containing compound to create the active catalyst. Polymerization times were relatively long, significant amounts of cyclic carbonate were produced, yet alternating copolymer (100% carbonate) could be generated. Molecular weight distributions in these polymerizations could be very broad, often >5.0. Nevertheless, a zinc system was eventually used to synthesize an ethylene oxide–CO_2 alternating copolymer that was applied commercially (PC Corp., Wilmington, DE) as a ceramic binder (this copolymer degrades cleanly to gaseous byproducts at temperatures >470 K).

Recent work in this area has focused on the development of 'single-site' style catalysts to allow better control over molecular weight [191]. However, while these new catalysts have proven to be very effective in the copolymerization of cyclohexene oxide and CO_2, none have been able to solve the problems observed during copolymerizations of CO_2 and either ethylene oxide or propylene oxide. In general, in copolymerizations of CO_2 and propylene oxide, catalysts derived from aluminum exhibit high activity and produce predominantly copolymer with a narrow molecular weight distribution, yet allow little CO_2 incorporation into the copolymer [192]. Zinc catalysts allow for high levels of CO_2 in the copolymer, yet produce predominantly low molecular weight alkylene carbonate.

Indeed, the generation of copolymers of CO_2 and either propylene or ethylene oxide would represent green chemistry, as these materials would have ready markets and alternative routes to their production (via phosgene) are highly problematic from a sustainable viewpoint. Until the technical hurdles to efficient copolymerization (see above) can be overcome, a CO_2-based route to aliphatic polycarbonates, and indeed, aliphatic polycarbonates in general, will not enjoy widespread use. Whereas a variety of other polymers have also been generated from CO_2 [193], either the properties of these new materials (vis-à-vis their cost) have not been promising or the efficiency of the polymerization low and hence, they are techni-

cal curiosities rather than potential avenues for green chemistry. Indeed, to achieve the highest impact (with respect to green chemistry), research should be directed at creating catalysts that target the efficient copolymerization of propylene oxide (or perhaps ethylene oxide) and CO_2.

Generation of an aliphatic polyester from CO_2 and an olefin would be a superb example of green chemistry with a ready market for the material. Aliphatic polyesters, while 'green' materials in their own right (they degrade cleanly to non-toxic fragments in the environment), require multiple steps to prepare the monomers and then the polymer, and also significant energy input along the way. A chain polymerization route to aliphatic polyesters starting from olefins and CO_2 would be both greener and less expensive than the current method. With the exception of one or two references in the late 1970s [194] and a 1949 patent [195], there has been no published scientific activity on this problem, despite the technical and commercial importance. Calculations performed at the University of Pittsburgh suggest that formation of a lactone (the immediate precursor to a polyester) from CO_2 and several olefins should be thermoneutral, and hence the reaction is at least theoretically tractable.

3.7. Industrial activity: condensation polymers and CO_2 as monomer

As mentioned above, both Crain and Bayer have commercialized the use of CO_2 as the blowing agent in continuous polyurethane foam production—20+ plants currently operate using this technology. Further, PC Corp. (DE, USA) sells aliphatic polycarbonate (used as a ceramic binder) generated via the copolymerization of CO_2 and ethylene oxide.

Xerox has patented [196] a process where bisphenol A polycarbonate is generated from bisphenol A and diphenyl carbonate using CO_2 to extract the residual phenol. Further, Akzo-Nobel patented [197] the formation of a degradable surfactant via the copolymerization of ethylene oxide and CO_2, where the polymerization is terminated by a fatty acid. However, it appears that Xerox has ceased their research efforts on polymerization in CO_2, while Akzo-Nobel appears to have shut down their research efforts on CO_2/alkylene oxide copolymerizations in early 1998.

3.8. Post-polymerization processing of polymers using CO_2

Polymers require far more post-synthesis processing than do small molecules, and hence it is not surprising that CO_2 plays a role in green post-polymerization processing of polymers. First, as mentioned previously, CO_2 will swell many polymers extensively, even those normally considered 'CO_2-phobic'. As shown in the generic phase diagram (Fig. 5), this is because of the asymmetry of the liquid–liquid phase envelope, itself arising from the disparity in size (and hence vapor pressure) of the solvent and solute. Swelling a polymer with CO_2 will drop its viscosity significantly (depending upon temperature, by orders of magnitude). This large drop in viscosity allows for a number of CO_2-enhanced processes. For example, Berens and Huvard [198a] demonstrated that the swelling of a polymer by carbon dioxide enhances the rate of infusion of model compounds. Kazarian and Eckert [198b] later exploited this effect in a novel way; they have shown that one can greatly enhance the kinetics of mixing of a CO_2-incompatible dye with a polymer. In this work, the dye and polymer are thermodynamically compatible, but the rate of infusion of the polymer by the dye is glacially slow. CO_2 plasticizes the polymer (while not actually dissolving very much, if any, of the dye), lowering the viscosity and allowing fast blending. The dying of fabric and fibers using CO_2 has been extensively examined in Europe and the US [199,200]; here again the dye and polymer are thermodynamically compatible while the dye is sparingly soluble in CO_2. Consequently, the dye partitions preferentially into the swollen polymer, where the CO_2 diluent enhances the kinetics of the thermodynamically favorable process. It is interesting to note that Johnston [201] outlined the fundamentals for such a process several years ago using a silicone polymer, CO_2 and toluene as the model 'infusant'. The green aspect to this work is a reduction in energy required for mixing, as well as elimination of the aqueous waste stream commonly associated with dying operations. Further, use of CO_2 in place of water reduces air emissions and the need for drying of the fibers after dying [202]. It is important to note that here CO_2 is being employed as a sustainable alternative to water–water is indeed a green solvent but it can be applied in ways (and in locales) where

its use is not sustainable (the same can be said for CO_2!).

Major challenges remaining in this process are in many ways 'mechanical'—how does one design a treatment chamber that allows fast charging, fast sample changeover, and rapid dying? Is there sufficient thermodynamic and transport information available to model and hence scale-up the process? Note that this situation is analogous to that described for continuous polyurethane production using carbon dioxide—the chemical challenges were overcome long before the mechanical issues were settled. A further challenge would include redesigning conventional dyes to allow for higher CO_2 solubility, which would provide for more even coating.

Applying the concept of carbon dioxide as 're-versible plasticizer', Shine and Gelb [203] showed that one could mix a thermally labile bioactive compound (here a vaccine) into polycaprolactone. Howdle et al. [204] recently expanded this work into the tissue engineering field. Here, CO_2 was used to swell an aliphatic polyester, depressing its T_g to well below room temperature. A temperature and shear-sensitive enzyme was then mixed with the swollen polymer; upon depressurization the enzyme was found to be dispersed throughout the now foamed polymer and to have retained its activity. Such a process allows the blending of temperature sensitive compounds with polymers without the need for additional solvent-based processing.

Powder coating processing provides another potential application for CO_2 as a sustainable and reversible plasticizer. Powder coatings (blends of low molecular weight functional polymer, crosslinking agent, pigments, and stabilizers) are themselves considered green materials, as they can be applied directly to automobile and appliance bodies without any solvent. However, the means for production of powder coatings is itself wasteful and expensive. The raw materials are charged to an extruder for high shear mixing; the resulting pellets are then ground and sieved to create the proper size distribution. Waste from the grinding process cannot be re-extruded, as the polymers are quite naturally thermally sensitive. Ferro Corporation [205] first patented a process where CO_2 is used to swell the polymer, depressing its T_g (normally 310–320 K) to well below 270 K. The additives (pigments, etc.) are then mixed with the swollen

polymer. Finally, the material is rapidly depressurized through a nozzle to form a granular mixture. Note that material processed in this way can actually be recycled if necessary, as temperatures employed are low (313 K). PPG Corporation [206] also supported work in this area using hydrofluorocarbon fluids; this work was targeted at small colored batches. Other patents have also appeared recently [207]. Challenges remaining here include elimination of a significant degassing problem upon film formation and the need to lower the operating pressure as much as possible to remain economical. Regarding the degassing problem, conventional powder coating formulations use benzoin as the degassing agent (to help eliminate air during film formation). However, it is not currently known why benzoin is effective as a degassing aid in conventional formulations, and hence the design of analogs for use in material processed in CO_2 is not currently possible. Indeed, both Ferro Corporation and PPG have ceased (at least for now) their research and development efforts in this area, owing to an inability to rapidly overcome these technical hurdles.

3.9. Extrusion-foaming using CO_2

The extrusion-based foaming of polymers [41] is inherently sustainable in that small amounts of raw material (the polymer) are used to create valuable, lightweight parts. The low weight and/or low thermal conductivity of these parts ultimately saves energy in applications ranging from home and appliance insulation to transportation components. Although the parts themselves can be considered sustainable, the conventional method of fabrication releases a large volume of solvent to the atmosphere. Prior to the late 1980s, chlorofluorocarbons (CFCs) were often employed as blowing agents (pore-forming agents), as these solvents are low boiling, non-toxic, and non-flammable. Subsequent to the acceptance of the Montreal Protocols (1986), most foam producers switched from CFCs to hydrofluorocarbons, hydrocarbons, or mixtures of hydrocarbons and CO_2. There is generally a desire within the foam producing industry to move to 100% CO_2 as the blowing agent in extrusion foaming, although some serious technical hurdles remain. A variety of polymers are extrusion-foamed, including polyolefins, polystyrene and polyesters. It should be noted that while injection of a volatile blowing agent

to the extruder is probably the most common means to induce foaming, 'chemical' blowing agents, i.e. compounds that thermally decompose to form gases, are also employed.

The extrusion based foaming of polymers is conceptually simple, yet requires complex analysis to fully understand the system. In the case of polystyrene, a fluid is injected into the extruder, where the pressure and temperature are sufficient (ostensibly) to create a single-phase mixture of blowing agent and polymer. Mixing is enhanced through strategic screw design. Following mixing, the melt is cooled (in some cases in a second, tandem extruder) to build melt strength, as the addition of the fluid greatly lowers the melt viscosity. The die is cooler still. Upon exiting the die, the rapid pressure drop creates a supersaturated solution, where small pores containing CO_2 nucleate and grow (nucleating agents are often added to stimulate this process). The pores grow until the rapidly rising viscosity of the polymer (owing to cooling and loss of blowing agent) restricts further expansion. In conventional extruded foam, the cells are of order 100–1000 microns in diameter. Microcellular foam [208], formed in much the same way albeit with higher concentration of CO_2 in the polymer melt, exhibits cells 50 microns and below in size.

The generation of foamed thermoplastics using CO_2 as the sole blowing agent is most definitely 'green' processing, as the CO_2 replaces either organic or hydrofluorocarbon agents that would otherwise directly enter the atmosphere. A number of researchers have investigated the fundamentals of foam formation using high pressure CO_2, and several important conclusions have arisen [209]:

- The number of cells nucleated during a pressure quench in a CO_2–swollen polymer depends directly upon the degree of swelling of the polymer. Swelling, in turn, rises as pressure rises and as temperature falls. To create more cells one must adjust conditions to ensure higher degrees of swelling.
- The growth of cells is dependent upon the degree to which CO_2 diffuses into the nuclei and also the degree to which CO_2 expands as pressure drops. At the same time, growth is inhibited by the retractive force of the polymer melt, which increases as the temperature drops and CO_2 diffuses from the melt. Hence, to make smaller cells, one must restrict

growth soon after nucleation, by vitrifying the system before the pressure drops to the point where CO_2 begins to expand significantly. If one desires to make a large number of very small cells, then in theory one should start with a high degree of swelling of the polymer by CO_2 and vitrify the material as soon as possible after nucleation of pores. Unfortunately, very high degrees of swelling lower the melt strength (related to viscosity) significantly and hence pores tend to coalesce during growth [210].

- Our understanding of the fundamental processes that control foam morphology derives in large part to fundamental studies performed in academia and industry during the late 1980s and early 1990s. For example, early studies of the effect of pressure on the swelling of polymers by CO_2 by Berens and Huvard [211], Liao and McHugh [212] and Wissinger and Paulaitis [126] paved the way for future work on polymer foaming. Wang and Kramer [213] first explored the behavior of the glass transition of a polymer versus CO_2 pressure in 1983; this was followed by a seminal study by Condo and Johnston [66]. Fundamental studies of the viscosity of polymer–CO_2 melts, for example, were performed by Manke and also by Khan [214]. These studies provided the data that made later studies of foam formation more tractable. While it is likely that similar work was performed in industry, little of it can be found in the open literature and hence the academic work has been vital in providing a basis for recent foam research.

Foam formed using CO_2 as the sole blowing agent has been commercialized in a number of cases, yet the process is non-optimal, as foam properties using CO_2 still do not approach those when CFCs are employed as blowing agents. While the foam-forming process is understood from an academic sense, a number of scientific/technical challenges remain before optimization can occur. These include:

- **Shear effects on phase behavior**: The phase behavior of CO_2–polymer mixtures is generally measured (in academia) under static conditions; there have been reports that the phase behavior of CO_2–polystyrene, for example, depends significantly on shear [215]. Measurement of high pressure phase behavior under shear presents a significant experimental challenge, yet one which

may have to ultimately be conquered if a full understanding of extrusion foaming is to be found.

- **Pressure limitations in conventional extruders**: While extruders can theoretically be operated at very high pressures (300 bar+), the typical operating pressure for a polystyrene foam extruder is ≈100 bar at temperatures in excess of 470 K. At the same time, the swelling of polymers such as polystyrene is not sufficient under these conditions to produce foam of the same quality as can be produced with liquid blowing agents. While raising the pressure is the usual remedy for insufficient swelling, it is not a viable one in this case, and hence additives must be developed that will allow enhanced swelling of 'CO$_2$-phobic' polymers by CO$_2$ [216]. Further, these additives must be designed in order to be effective at low loadings (or else foam physical properties and cost will be adversely impacted).
- **Rapid diffusion of CO$_2$**: Compared to conventional blowing agents, CO$_2$ diffuses rapidly from foam pores—this rapid diffusion in practice contributes to foam collapse [217]. Consequently, there is a need to develop additives that will partition to the CO$_2$–polymer interface, then set up a barrier against CO$_2$ diffusion.
- **High thermal conductivity of CO$_2$**: Insulation is a prime application for foamed polymeric materials. Further, the effective thermal conductivity of a polymer foam, at low foam density, is a strong function of the thermal conductivity of the gas inside the pores. Because CO$_2$ exhibits a significantly higher thermal conductivity than CFCs [218], one may have to employ larger quantities of foam to accomplish the same insulation job if CO$_2$ is employed as the blowing agent. The blowing agent, although originally entrapped within the foamed polymer, will eventually diffuse out and be replaced by air diffusing in—the high diffusion coefficient of CO$_2$ renders this exchange faster with CO$_2$ than with chlorofluorocarbons. Thus, an additional challenge is to achieve high insulating value while employing CO$_2$.

Finally, a general conclusion that one can draw from the extensive previous work on foaming is that, using the 'swell-quench' method, one can generate a foam with either small pores (<10 microns) or low bulk density (<0.05 g/cc), but not both. Low bulk density requires the generation of very large numbers of small pores, and hence high swelling (and hence high nucleation density) but limited growth. Unfortunately, as mentioned previously, high swelling also leads to low melt strength and hence pore coalescence. The lower limit for cell size in extruded foam with low bulk density (<0.1 g/cc) appears to be approximately 50 microns. Consequently, researchers have explored new strategies for forming low bulk density, fine-celled foams. For example, Enick et al. [219] have generated molecules that will dissolve in CO$_2$, then self assemble to form gels. Removal of the CO$_2$ (via depressurization) leaves behind a porous structure with submicron cell size and bulk density below 0.05 g/cc.

In summary, the foaming of thermoplastics using CO$_2$ as the sole blowing agent is undeniably green polymer processing, in that use of CO$_2$ directly replaces organic solvent that would ultimately enter the atmosphere. The challenges to efficient use of CO$_2$ in foam production are given above—it should be noted that these are entirely technical and hence would provide excellent targets for future research.

3.10. Industrial activity: post-polymerization processing

As mentioned above, a large number of patents have been issued for both the foaming of polymers with CO$_2$ and the use of CO$_2$ to dye textiles. For the case of polymer foaming, the technology has achieved commercial status, both macrocellular foam formation (Dow, for example) and microcellular foam formation (Trexel has licensed technology developed at MIT by Nam Suh et al. [220]). The textile work has been advanced to the pilot stage in Germany and in the US.

3.11. Use of CO$_2$ in polymer science applied to the microelectronics industry

The preparation of an eight-inch silicone wafer requires hundreds of individual process steps, of which approximately half involve washing [221]. It has been estimated that a single fabrication line will use over one million gallons of solvent each year. In photolithography, the technique used to create patterned microelectronic components, a polymer layer is applied to an inorganic substrate by spin coating

from solvent, then selectively imaged and developed (washed off) to create a pattern. To create the pattern, a mask is applied to the polymer layer, after which radiation is employed to either crosslink the accessible areas (leaving the hidden areas uncrosslinked) or degrade the accessible areas (leaving the hidden area intact). The mask is then removed and the soluble material (in either case) is washed away. Photolithography currently employs significant volumes of either solvent or water to accomplish the developing (washing) step and hence generates a substantial liquid effluent stream. The key to successful developing is to be able to efficiently change the solubility characteristics of the exposed portion of the resin. Carbon dioxide is a particularly intriguing solvent for use in microelectronics applications, not only because it is environmentally benign, but also because its vanishing low interfacial tension allows it to successful wet and penetrate very small features on a component.

Initial work to apply carbon dioxide to the coating and photolithography processes dates to the mid-1990s; researchers at IBM and Phasex Corporation examined the design of resins specifically for use in CO_2-based developing [222]—the work by DeSimone's group on the miscibility of perfluoropolyacrylates showed the IBM researchers that such as process was feasible. A number of fluorine and silicon-containing polymers were examined, and a photoacid generator employed to develop the patterns; the most viable system seemed to be one where a random copolymer of a fluorinated acrylate and *t*-butyl methacrylate was used. Ober et al. [223] have also designed a photolithography system that could be developed using carbon dioxide. Here, a block copolymer of a fluoroacrylate (CO_2-soluble) and tetrahydropyrano methacrylate was synthesized. The polymer was spun-cast onto a substrate from a conventional solvent and a photoacid generator added. The system was masked, patterned (using 193 nm radiation) and developed with CO_2, demonstrating that 0.2-micron features could be produced. DeSimone has also postulated the design of fluorinated copolymers for use in photolithography [224]; both negative and positive resist systems are described. Interestingly, fluorinated materials are both highly CO_2-soluble and are known to be relatively transparent to radiation in the 130–190 nm range [225] (the wavelengths to be employed in next generation systems).

DeSimone et al. have described a free-meniscus coating methodology using CO_2 to apply polymers to inorganic substrates, potentially eliminating the significant volume of solvent currently used for that purpose [224,226]. DeSimone has demonstrated the concept using fluorinated polyethers, polymers whose high solubility in CO_2 is well known.

As suggested in a recent articles in Chemical and Engineering News [227] and Technology Review [228], interest in the use of CO_2 in microelectronics processing is growing. To date, most of the industrial ventures involve partnerships between large, well-known chemical suppliers to the electronics industry (Praxair, Air Products) or microelectronics companies (IBM) and small firms with expertise in the design of high-pressure equipment (Supercritical Systems [229] (Fremont, CA; purchased by Tokyo Electron) and SC Fluids (Nashua, NH)). The efforts to date have focused on the use of mixtures of CO_2 and cosolvents, as a means to overcome the feeble solvent power of CO_2 without having to resort to the design of CO_2-philic materials. Clearly, technical challenges for the future include the ability to design CO_2-philic materials for use in microelectronics processing that are also acceptable (from both technical and environmental perspectives) to the industry. Indeed, do we possess a firm understanding as to the underlying molecular foundation for high CO_2 solubility as well as transparency to radiation of a particular wavelength? Today, the answer is 'no'. Will these underlying mechanisms ultimately conflict with one another? Further, given the rapid throughput in the industry, can high-pressure systems be developed that will allow use of CO_2 at the throughputs required? Finally, the work to date on polymers for use in lithography has created materials where the exposed portion of the polymer is rendered insoluble in carbon dioxide (through action of a photochemically-generated acid on a protected carboxylic acid). It is somewhat surprising that we have yet to see a system created where the exposed portion of the material is rendered soluble in CO_2 instead.

It is clear that if CO_2 can make significant inroads into the microelectronics processing industry, then potentially large volumes of organic solvents and just as importantly water, could be replaced with CO_2—once again there are clear technical challenges to be overcome.

Table 1
Production and E-factors for various industry segments [315]

Industry segment	Production (tons/annum)	E-factor (mass waste/mass product)
Oil refining	10^6–10^8	≈ 0.1
Bulk chemicals	10^4–10^6	<1–5
Fine chemicals	10^2–10^4	5–50
Pharmaceuticals	10–10^3	25–>100

3.12. Industrial activity: CO_2 and polymers in microelectronics manufacture

It was recently announced that Air Products and Chemicals had agreed to purchase equipment from SC Fluids for use in photoresist development using carbon dioxide [230]. SC Fluids is also working with ATMI (chemical supplier to the microelectronics industry) and IBM on photoresist development using CO_2. Ashland Specialty Chemicals has formed an alliance with Dainippon Screen and Kobe Steel to develop technology for microelectronics processing using CO_2 [230].

In addition to using CO_2 to strip material from wafer surfaces, industry has applied carbon dioxide processing to create porous materials that will function as a low dielectric substrate or film [231].

4. Other reactions in CO_2

Researchers in both academia and industry (although most of the publications come from academic laboratories) have conducted a large number of reactions in carbon dioxide, demonstrating the feasibility for use of CO_2 in a broad range of applications. Again, the question we must pose is 'is this green chemistry'? And further, what is the impact of this work on the greater chemical industry?

If we examine the 'E-factors', or mass of waste per mass of product for various industries, we find chemicals and pharmaceuticals produce waste at a rate several orders of magnitude higher than that for bulk chemicals or petrochemicals (see Table 1). However, if we examine the impact of each industry (related to the E-factor times the production rate), we see that the commodity segments still exercise the greater impact.

Hence, if one had to choose which industry segments upon which to focus research efforts in use of CO_2 in green chemistry, it would seem that the obvious choice would be bulk chemicals and petrochemicals. On the other hand, because fine chemicals are typically produced in batch mode in small volumes, the cost of high-pressure equipment for these industries may not be as much of an impediment as it would be for their commodity cousins.

Finally, as we note in a later section, the education of scientists and engineers in the use of CO_2 as a solvent has a value of its own, and as such the publication of papers on reactions that fall into this chapter has done much to 'demystify' CO_2. Hence, these papers have significant educational/outreach value.

4.1. Enzymatic chemistry

At first glance, enzyme/CO_2 mixtures appear as ideal reaction systems for the performance of green chemistry. Enzymes are naturally derived catalysts that are highly selective, while CO_2 is a naturally abundant, benign solvent. However, research into enzymatic reactions in CO_2 has dropped precipitously since the mid-1990s and no commercialization of such processes is currently anticipated. The reasons for this are straightforward and scientifically based, deriving from the substantial research performed in this area during the 1990s.

Enzymes are naturally derived catalysts, proteins whose primary, secondary and tertiary structure has evolved to create a catalyst that is highly selective and very active under a set of narrowly defined conditions. Enzymes themselves are green catalysts, and their means of production (fermentation) is also typically a green process. In nature, enzymes perform their catalytic function in water, yet Klibanov (and others) showed that enzymes would function adequately (not as well as in water) in organic media provided that a small amount of water remains bound to the enzyme [232]. Further, while lipases (and other analogous enzymes) naturally perform hydrolysis reactions in an aqueous environment, these same enzymes were shown to perform esterification in an organic environment. Because enzymes do not dissolve in the organic solvents under consideration, enzymatic chemistry in organic solvents is governed by heterogeneous reaction kinetics. This, however, is not a drawback, as catalyst recovery is easier than for a homogeneous system. Given this background, enzymatic reactions

in CO_2 seemed an ideal combination of green solvent with green catalyst.

During the early 1990s, a number of enzymes were evaluated in carbon dioxide, primarily in support of esterification reactions [233]. For the most part, activities were very low, much lower than for the same reaction conducted in a conventional organic solvent. In addition, rates in CO_2 were substantially lower than rates in other compressible fluids (ethane, propane, fluoroform). In some key publications, Russell et al. outlined the reason for CO_2's low activity—apparently carbon dioxide reacts with primary amine residues (primarily from lysine) to form carbamic acid and/or ammonium carbamates [234]. This derivatization was observed experimentally and is apparently responsible for the reduced activity of many enzymes in CO_2 (note that not all enzymes suffer from this reduced activity, consistent with the fact that enzymes exhibit a range of protein sequences, secondary and tertiary structures). Carbamate formation is reversible, as removal of the enzyme from CO_2, followed by examination of the rate in either water or another organic solvent reveals no change in inherent activity. Even bubbling of gaseous carbon dioxide through a suspension of enzyme in organic solvent can produce the reversible drop in activity. Consequently, interest in enzymatic chemistry using enzyme powder in CO_2 diminished greatly.

At this same time, advancements in the design of CO_2-philic surfactants allowed for the possibility of performing enzymatic chemistry in the aqueous core of micelles formed in carbon dioxide, a situation that would eliminate the problems due to carbamate formation (polar solvents destabilize the carbamates). Indeed, work by Randolph and Johnston [235], as well as Beckman et al. [236], showed that one could solubilize an enzyme in the core of a micelle, and then recover the protein via depressurization. However, CO_2 dissolves in water and forms carbonic acid and not surprisingly the pH within the micelles was shown to be <3.0. While Johnston showed that one could buffer such a system to a pH from 5.0 to 6.0 [31], the ionic strength required was far higher than would normally be recommended for use with an active enzyme. Thus, realization of the full 'green' potential of enzyme–CO_2 systems was again blocked by technical realities.

Other issues to note regarding use of enzymes in CO_2 include the need by the enzyme for a certain amount of bound water and the equilibrium nature of many of the reactions. Although CO_2 is usually considered a non-polar solvent, it will solubilize ≈2500 ppm water at moderate pressures (100 bar, room temperature). Because enzymes will not function in organic media if stripped of all of their water, care must be taken to prevent CO_2 from dehydrating the enzyme. In addition, many of the enzymatic reactions that one might wish to perform in CO_2 are governed by equilibrium and hence, one must examine means by which to remove the byproduct or product from the neighborhood of the enzyme.

A final obstacle to use of enzymes in supercritical fluids lies in the poor solubility of many of the polar substrates that one might wish to transform. For example, while many of the literature studies performed during the early 1990s examined esterifications, the starting material (carboxylic acid) was usually not particularly soluble in CO_2 (hardly surprising given what is known about CO_2).

The previous paragraphs make plain the technical hurdles that would need to be overcome to render enzymatic chemistry in CO_2 generally practical and useful. Either enzymes must be identified (or developed through a directed evolution-like process) that do not form carbamates with CO_2 (or where carbamate formation does not impede activity) or a way must be found to buffer a CO_2/water mixture without resorting to an ionic strength that will harm the enzyme. Conversely, identification of enzymes that thrive at low pH or high ionic strength would also be worthwhile in this regard.

If one could overcome the problems described above, then one could evaluate a number of issues regarding the use of enzymes in compressible fluids. For example, work by Russell [237] using fluoroform showed that pressure (through its effect on fluid properties) could be used to tune enzyme activity and also, to a certain extent, selectivity for a given reaction path. However, given the preference for CO_2 versus other compressible fluids, until the problems regarding CO_2 and enzymes are dealt with, enzymatic chemistry in compressible fluids will likely continue at only a very low level of research activity.

4.2. Diels-Alder chemistry

The Diels-Alder reaction is employed on a large scale industrially to help to purify cyclopentadiene,

and to a lesser extent to manufacture anthraquinone [13]; it should be noted that these reactions proceed without solvent. A substantial body of literature exists concerning Diels-Alder chemistry in supercritical fluids, CO_2 in particular. For the most part, research on this particular reaction has been used (via analysis of the rate constants), to confirm the influence of concentration fluctuations (present near the critical point) on the rate of the reaction. In general, the rate reaches a maximum near T_c, dropping at both higher and lower pressures. However, this work is currently of scientific interest only, as control of a reaction in the neighborhood of a critical point is problematic at large scale. Tester et al. [238] report that most Diels-Alder rate constants in CO_2 can be correlated using a simple Arrhenius expression provided that the pre-exponential term varies linearly with fluid density, similar to what Roberts [239] observed using propane as the solvent. Lewis acid catalysts are effective (if soluble), as shown by Matsuo et al. using a scandium triflate in CO_2 [240].

Although the literature on Diels-Alder chemistry in CO_2 at first glance appears uninteresting (from a green chemistry viewpoint), there are some publications that merit closer scrutiny. For example, Ikushima et al. [241], published the results of a study of the cycloaddition of isoprene and methyl acrylate (Scheme 7), reporting that while one atmosphere conditions produced primarily the para isomer of the methyl acetoxy cyclohexene product, operation in CO_2 produced significant amounts (at some pressures the major component) of the meta isomer. If true, such a result suggests that use of CO_2 can alter product selectivities, and hence would significantly impact the
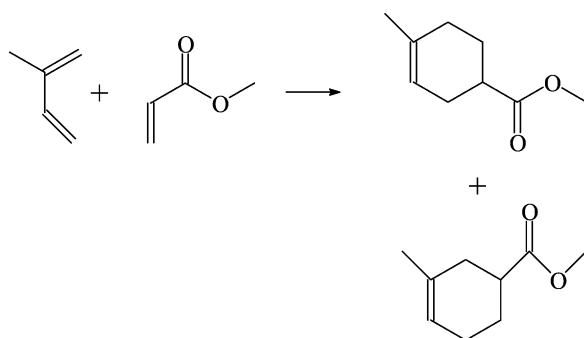
field of green chemistry in critical fluids. However, subsequent work by Danheiser and Tester [242] revealed that Ikushima et al. failed to note that multiple phases were present in the reactor, and that adequate sampling of the phases revealed that all conditions produced a 67–31 split of para and meta isomers. This again shows the importance of understanding the phase behavior of any reaction mixture under evaluation. Indeed, subsequent work by Danheiser and Tester on a wide range of Diels-Alder substrates revealed no effect of CO_2 pressure on regioselectivity.

Some additional observations on Diels-Alder chemistry in CO_2 include reports by Clifford et al. [243] that the endo:exo ratio of products in the reaction between methyl acrylate and cyclopentadiene exhibits a maximum versus pressure in CO_2. Totoe et al. [244] also observed differences in product selectivity between toluene and CO_2 in a 1,3 dipolar cycloaddition.

In summary, although there have been some intriguing reports on variations in selectivity in CO_2 versus conventional solvents, most of the research on Diels-Alder chemistry in CO_2 has been directed at deriving fundamental parameters rather than creating opportunities for green chemistry per se. The work by Danheiser and Tester should stand as a warning to those involved in chemistry in supercritical fluids—one ignores phase behavior effects at one's peril!

4.3. Lewis acid catalysis/Friedel-Crafts chemistry

Friedel-Crafts chemistry is used extensively to perform liquid-phase alkylations and acylations, although it should be noted that the largest scale industrial processes do not employ solvent and some have switched from the typical aluminum halide 'catalyst' to supported acidic catalysts [13]. However, fine chemical syntheses often employ relatively toxic solvents during Friedel-Crafts reactions, and hence this reaction presents a viable target for use of CO_2. Because Friedel-Crafts chemistry is usually performed in polar media, an obvious question is whether CO_2 (with its low dielectric constant) can actually support such reactions. Further, the primary environmental drawback to Friedel-Crafts chemistry is the need for large amounts of aluminum halide and hence, much recent research has focused on finding true catalysts for the various alkylations and acylations. Interestingly,

Scheme 7.

many of the newer Friedel-Crafts 'catalysts' are fluorinated, and hence highly CO_2-soluble.

Chateauneuf and Nie [245] examined the alkylation reaction between methoxy benzene and triphenyl methanol using trifluoroacetic acid as catalyst. Kobayashi et al. [246] found that rhenium triflate promoted the acylation of aromatic compounds (as in Chateauneuf's work, if electron donating substituents were present on the aryl compound) with an anhydride. The reaction proceeded smoothly in either organic solvents or CO_2. Finally, Poliakoff's group first examined the Friedel-Crafts alkylation of various activated aryl compounds using a supported (Deloxan) acid catalyst in CO_2 [247]. Although not large, the literature on Friedel-Crafts chemistry in CO_2 demonstrates that this reaction is indeed feasible, and that many of the Lewis acids proposed as catalysts are readily CO_2-soluble.

Olah et al. [248] examined the acid catalyzed isobutene-isobutylene reaction in carbon dioxide; they found that CO_2 acted as a weak base and use of CO_2 as solvent lowered the acidity of the system and hence the alkylate quality. However, in cases where the acidity was increased to counteract this effect, the use of CO_2 decreased the amount of acid needed to perform the alkylation. Further, use of CO_2 increased the octane number of the product.

In a final intriguing note, Pernecker and Kennedy [249], during an investigation into the Lewis acid catalyzed polymerization of isobutylene in CO_2, found that addition of only the Lewis acid to carbon dioxide formed a product, either a solid precipitate or a second liquid. Removal of the CO_2 regenerated the original Lewis acid. On the other hand, incubation of a Lewis acid with the polymerization initiator, followed by addition to CO_2, resulted in no 'CO_2-product' formation. Pernecker's results suggest that one might activate CO_2 itself for further reaction using a Lewis acid, but if the Lewis acid is presented with a more reactive substrate, it will preferentially bind to this substrate.

In summary, Friedel-Crafts chemistry is (in fine chemical synthesis) performed in solvent, and hence CO_2 represents a potentially useful and green substitute. Catalysts that one would ordinarily use to perform such reactions are soluble in CO_2 without further modification. The effective use of CO_2 then depends upon substrate solubility.

4.4. CO_2 as reactant and solvent

In this section, those reactions where CO_2 is employed as reactant and solvent, yet where small molecules (rather than polymers, see Section 3) are formed as products, will be discussed. A large number of reactions using CO_2 as a raw material have been demonstrated in the laboratory, but very few such reactions are practiced commercially. For example, it has been shown in the literature that one can generate formic acid [250], dimethyl formamide [251], carboxylic acids [252] and methanol [253] using CO_2 as reactant (and in many cases the solvent as well). To date, however, the economics of such processes have not been sufficiently favorable to warrant significant industrial attention. Part of the problem is that use of CO_2 to create commodities, such as those listed above competes directly with use of highly reactive CO to create the same molecules. For example, methanol is produced from CO and hydrogen (synthesis gas, or syngas) in an atom-efficient process [13]. Further, one can readily generate the needed synthesis gas from coal, natural gas or petroleum. To form methanol from CO_2, one would need an additional clean and inexpensive source of hydrogen. Further, the thermodynamics of the two routes are such that one can obtain twice the yield of methanol from the syngas route (e.g. at 470 K) than the CO_2 route [254]. At present, CO_2 is only used to supplement syngas during methanol production if the ratio of hydrogen to CO is significantly higher than 2.0 (which can occur when natural gas is used as the syngas source). Other small molecules such as formic acid, formates, and formamides are then generated from methanol (plus CO, ammonia, alkyl amines)—this chemistry is also atom-efficient and hence alternative routes using CO_2 as a starting material have been unable to compete. In general, it is presumed that CO_2-based routes for basic commodity chemicals would be competitive if a relatively inexpensive, non CO_2-producing source of hydrogen can be developed [254]. Granted, CO is a much more toxic material than CO_2, yet syngas has been used successfully for decades in chemical processes, so this factor carries little weight currently.

The generation of dialkyl carbonates presents a similar example to those described above—a number of researchers have investigated the synthesis of dialkyl carbonates from CO_2 and alcohols using alkoxy tin

catalysts [255]—in this process one must push the equilibrium towards product via the removal of alcohol. Meanwhile, the commercial process operates very effectively from CO and alcohol over relatively inexpensive copper catalysts [256].

Despite the negative results described above, it is important to note that ≈110 megatons of CO_2 are consumed each year to produce low molecular weight products [254]. Most of this is consumed to generate urea; in addition salicylic acid is synthesized (Kolbe-Schmitt reaction) from CO_2 and a phenolic salt while alkylene carbonates are generated from the analogous alkylene oxides and CO_2. The alkylene carbonates are considered relatively benign solvents (they exhibit low toxicity and low vapor pressure), and hence their synthesis from CO_2 is an example of green chemistry. Monsanto, as well as academic researchers, have studied the synthesis of isocyanates from CO_2 [183]. While the traditional route reacts amines with phosgene, creating the isocyanate plus salt, the CO_2-based routes react the amine with CO_2 in the presence of strong dehydrating agent. The yields of such CO_2-based reactions are excellent, yet the cost of the dehydrating agent (or rather, its regeneration) has inhibited commercialization of such chemistry. Behr, among others, has reviewed a range of small molecule reactions that employ CO_2 as a reactant [257].

In summary, CO_2 has the potential to be a useful C_1 synthon but recent work, while scientifically interesting, has not led to processes that can effectively compete with existing routes/plants. Further, when considering CO_2 as a green reactant, one must always be cognizant of any energy differences required to employ CO_2 in a synthetic scheme versus a conventional reactant (such as CO). If use of CO_2 is more energy intensive, then one might create a situation where more CO_2 is created than chemically 'sequestered'.

4.5. Other organic reactions

As was mentioned previously, volatile metal carbonyls (for example) exhibit sufficient solubility (or sufficiently low miscibility pressures) to support catalysis in CO_2 without catalyst modification. As such, there are a number of examples in the literature where CO_2 has been used as a 'drop-in' replacement for catalytic reactions ordinarily carried out in organic solvents. Nevertheless, once Leitner and Tu-

mas demonstrated in 1997 that one could perform homogeneous catalysis in CO_2 if the catalyst ligands were properly designed, a number of researchers have extended this work, examining a wide range of name reactions in CO_2. The importance of the Leitner and Tumas papers was perhaps to demonstrate that effectively any catalyst could be rendered CO_2-soluble, if the fluorination of the ligands could be accomplished synthetically. Consequently carbonylation [258], Heck and Stille couplings [259], vinylic substitution [260], hydrosilation [261], isocyanate trimerization [262], dechlorination [263], Pauson-Khand cyclization [264] and others have been successfully performed in carbon dioxide. The use of fluorinated catalyst ligands is common, providing the solubility needed for the reaction to proceed smoothly.

While these papers demonstrate the scope of 'chemistry in CO_2', it is not clear as to the impact of such work on the overall aims of green chemistry. Granted, such reactions would ordinarily be performed in an organic solvent, and hence use of CO_2 replaces such solvent use. On the other hand, the reactions described above are typically used for small volume, batch reactions and hence, the overall impact of this work on the greening of industrial chemistry will be small. Perhaps the most significant impact of this work on green chemistry is in its ability to show chemists that CO_2 is a viable solvent for a variety of reactions, and hence the greatest value of the work may be to educate the next generation of chemists.

4.6. Industrial activity: Friedel-Crafts chemistry and other name reactions

Both Poliakoff [265] and Subramaniam [266] have patented alkylations in supercritical fluids, albeit using different types of catalysts. Each of these academic groups is/was working with an industrial partner (Thomas Swan and Engelhard, respectively [267]) and hence the work may ultimately be transferred to industry.

Schiraldi et al., as well as Harris et al. [268] have patented the esterification of specific substrates in carbon dioxide. Finally, a group at BASF has patented the generation of α-tocopherol (and derivatives) in carbon dioxide [269]. It is not clear at this time if these inventions are being pursued further by the companies involved.

4.7. Inorganic chemistry

Obviously, most inorganic compounds are not soluble in carbon dioxide and hence, inorganic chemistry performed in or with CO_2 has been accomplished by finding ways around this seemingly intractable thermodynamic hurdle. The first inorganic chemistry performed in a supercritical organic solvent was probably the work by Matson [270] at Battelle PNL in the late 1980s—here an emulsion was formed in a supercritical alkane and inorganic particles generated via a reaction at the micellar interface between an inorganic and an organic precursor (note that when Matson performed his study, it was not possible to form micelles in CO_2!). Recently, several research groups have adopted the same strategy to create metal nanoparticles within micelles formed in carbon dioxide. Naturally, the great strides made during the 1990s in the identification and application of CO_2-philes paved the way for this research. Both Fulton [271] and Roberts [272] have reported the formation of metals particles with diameters <20 nm by (a) creating an emulsion in CO_2 where the aqueous cores of the micelles contain metal ions as well as water; and (b) adding a reducing agent to the CO_2, such that a reaction occurs at the micellar interface between ion and reducing agent to nucleate the particles. Particle growth then occurs through micelle–micelle collisions—Roberts has shown that one can control the particle growth rate via control over the degree to which the micelles can collide and exchange contents. Further, changing the physical properties of the compressible continuous phase can alter the micellar collision rate.

An obvious question is 'is this green chemistry?' Because there is currently no sizeable industrial process for the manufacture of metal nanoparticles, this question is difficult to answer. Production of metal nanoparticles in a CO_2-continuous emulsion will likely be more environmentally friendly than the analogous reaction in an organic solvent. However, if such metal nanoparticles are ultimately applied commercially, there may also be other means by which to synthesize them, means that require no solvent at all. As can be seen by this and other such situations, it can be difficult to judge whether a process is green unless taken in context with competing processes—green seems not to be an absolute but rather a relative concept.

4.7.1. Inorganic chemistry: metal chelates

Although separations will not expressly be covered in this report, the use of chelating agents for metal extraction should be noted. While many conventional chelating agents and their associated metal complexes are poorly soluble in carbon dioxide, concepts on the design of CO_2-philic materials were applied very early to the design of CO_2-soluble chelating agents [273], showing that fluorination improved solubility. On the other hand, tri-alkyl phosphates and tri-alkyl amines, known to bind several types of metals, have been shown to be miscible with CO_2 at moderate pressures despite containing no fluorine. Various research groups [274] have demonstrated that one can extract metals (using the appropriate agent) from both solid and liquid matrices at high yields. It has also been shown that the phase behavior of the metal chelate can be substantially different from that of the agent (not surprising, since at the very least the molecular weight of the chelate is much greater than that of the agent). Finally, one of the first advances in the design of non-fluorous CO_2-philes came about as a result of work by Siever's group on chelating agent structure–solubility relationships [275]. It was shown that, in the case of copper-β-diketone complexes, the solubility of analogs containing branched alkyl groups was superior to fluorinated analogs.

Again, we must pose the question, is the use of chelating agents in carbon dioxide green chemistry/processing? The two most important cases for examination, that where metals are processed/purified for sale, and that where metals must be removed from solid or liquid matrices to remedy an environmental problem, will be examined here.

Regarding the first case, both copper and precious metals (platinum groups metals; PGMs) are purified using solvent extraction. In the case of copper, solvent extraction and electrowinning (SX-EW) have captured ≈15–20% of the total amount of copper produced worldwide [276], replacing the significantly less green (owing to energy use and air emissions) conventional smelting process. In SX-EW, the metal is first extracted from the ore using sulfuric acid (along with substantial amounts of silver, lead, iron, zinc and arsenic, plus a wide variety of minor components) via heap leaching, where the acid is simply allowed to flow by gravity through an ore pile. This acidic solution is then contacted with an organic solvent

containing an extractant (one of a variety of amines, phosphates or oximes) to draw the copper selectively into the organic phase (usually a high flash point alkane mixture). The copper is then back-extracted into water, from where it is electrochemically reduced (electrowinning) to pure (99.99%+) copper. The solvent extraction step is, from a process perspective, somewhat simple, consisting of a series of mixer-settler tanks that are open to the environment.

Previous work has shown that one can extract copper into carbon dioxide; further it is likely that one could synthesize a highly CO_2-soluble analog to one of the currently used commercial extractants for copper. Hence, one could construct a CO_2-based analog to the current solvent extraction process. However, it is not likely that the cost of such a step would justify the move away from the currently used organic solvents. At present, the solvent extraction/back extraction steps contribute $\approx$10–20% of the $0.2/lb processing cost of copper using SX-EW, assuming that >90% of the extractant is recovered after each use [277]. Indeed, perhaps a far better target for green processing applied to copper refining would involve either conversion of the remaining traditional smelters over to SX-EW [278] or finding ways in which to lower the energy demand of the ore excavating/crushing/grinding process or the electrowinning step [279]. A further complication is that most copper refining is performed in either South America or Africa, where the regulatory and/or societal driving force for adopting green chemical processing is substantially less than in either Europe or the US.

Platinum group metals, either those derived from ore or during the recycling of catalytic converters or electronics components, are also refined using solvent extraction [280]. Here, the metal is extracted using strong acid (usually HCl), then purified by extraction into organic solvent using an auxiliary, where selectivity is achieved via both the design of the auxiliary and subsequent aqueous washing steps to remove unwanted trace metals. The extraction is multi-step, in order to sequentially remove the gold, platinum, palladium and other PGMs. The metals are then reduced either chemically or electrochemically and recovered. The opportunities for the use of carbon dioxide to replace organic solvents in such processes mirror those in copper refining; here, however, the value of the metal is five orders of magnitude greater. Further, it has

been shown that one can design CO_2-soluble analogs to those compounds used to extract PGMs into organic solvents [281]. However, just as the value of PGMs makes the use of CO_2 more viable, so too does it promote the development of competing technologies. For example, IBC (Utah) has developed solid metal absorbents comprised of macrocycles tethered to polymeric resins [282]. These resins have been shown to selectively bind PGMs of various types, where the metals are recovered by back extraction following processing. If CO_2 is to be competitive in this arena, the ligands must be selective, should be as inexpensive as possible and/or one must be able to recover them following binding and release of the metal. Both the ligands and their metal complexes must be highly soluble at low pressures (preferably CO_2's vapor pressure) as throughputs in this application will be very high. As in the case of coffee decaffeination, it would be highly preferable to reduce and/or capture the metals without depressurization of the CO_2. Given Watkin's research, it may be possible, for example, to reduce the metals using added hydrogen. Unlike in the case of conventional organic solvents, adding hydrogen to CO_2 produces neither safety nor mass transport problems. There are two features of this process that weigh in favor of CO_2: (a) the metal concentration is relatively low, meaning that employing a high ligand:metal ratio still allows for dilute ligand concentrations; and (b) aqueous flow rates can be higher than the point that causes breakthrough problems for solid sorbents. Hence, there may be opportunities for use of CO_2 in this industry.

Another application of potential interest is in the upgrading of so-called vacuum resid (or vacuum residual) in petroleum refineries [283]. Vacuum resid refers to low vapor pressure (hence relatively high molecular weight) fractions of the initial petroleum stream. In addition to hydrocarbons, this fraction contains a substantial quantity (over 1000 ppm) of a wide spectrum of metals (owing to the concentration effects of numerous upstream unit operations). Included in this mix of metal contaminants are considerable amounts of vanadium and nickel, metals that can de-activate the catalysts employed to crack petroleum into useable (salable) materials. Further, both the nickel and vanadium are complexed by porphyrin type materials present in the vacuum resid. If these metals could be easily and economically extracted, more of the initial

petroleum stream could be employed to create salable products, meaning less is simply burned.

Aqueous waste from electroplating operations generally contains substantial amounts of dissolved metals in a low pH (2.0 and below) medium. Chelating agents dissolved in carbon dioxide can be used to extract many of the relevant metals from such low pH media [284], provided that the agents are designed to operate under such conditions. Generally, the strategy by which chelating agents are rendered CO_2-soluble involves the attachment of 'CO$_2$-philic' functional groups to a moiety known to bind certain metals, and as such there are in theory no restrictions as to the type of chelating agent employed, so long as the functionalization chemistry can be performed. The competing technologies for CO_2 extraction include the use of precipitants, compounds that react with dissolved metals to form insoluble species, as well as chelating agent-functional ion exchange resins (solid sorbents). Precipitants are inexpensive, yet they produce a sludge that must be collected and disposed. Ion exchange resins (following back extraction) produce instead a concentrated (ideally) solution of the metals, which must be subsequently treated to recover the metal.

The most problematic application to analyze is that where CO_2 plus a chelating agent is being used to remove metals from a matrix to accomplish remediation. Indeed, the primary focus of green chemistry is the elimination of waste production, rather than the clean up of existing problems, yet the use of CO_2 to remediate metal contamination may be considered green processing in some circumstances. First, it has been shown by various research groups that one can extract a variety of metals from solid matrices (including soil [285]) using chelating agents dissolved in carbon dioxide. If CO_2 was to be used to replace either an organic solvent or water in the washing of contaminated soil, this could be considered green processing, provided that the energy required for the process was equal to or less than that employed for the conventional route. A large amount of sludge (as much as 15% of soil throughput, created from suspended fine particles) is produced, for example, when soil is washed with water. Because carbon dioxide is a low density, low viscosity, low interfacial tension fluid, it is likely that sludge production would be greatly reduced if CO_2 were used to wash soil. On the

other hand, because soil washing typically involves excavation of the contaminated material, remediation strategies that eliminate the problem without excavation (in-situ remediation) should be preferred. Such strategies range from the use of green plants to absorb and concentrate metals, to the addition of agents to the oil that stabilize the metals, preventing their transport.

4.7.2. Inorganic chemistry: industrial activity

Materials Technology Limited has obtained several patents [286] describing the use of high pressure CO_2 to enhance the rate of curing of concrete, where the CO_2 actually dissolves in the concrete mixture and reacts with the matrix. While one might consider this as sequestration of CO_2 and hence green chemistry, it should be remembered that the preparation of the concrete precursor involves the calcining of the raw material, where CO_2 is driven off while injecting significant energy. Thus, more CO_2 is probably produced during this sequence than is sequestered.

Both Texas Instruments [287] and Micron Technology [288] have patented inventions where inorganic chemistry is performed in CO_2 to support cleaning/processing of silicone wafers. The Micron patent describes the use of mixtures of CO_2 and etching chemicals to pattern inorganic substrates, while the Texas Instrument patent describes a process where inorganic contamination on wafers is first derivatized, then dissolved in CO_2 and removed. Note that in these patents, the use of CO_2 is designed to replace the use of water. In many parts of the world, significant water usage by industry is not sustainable and hence, there is a need to find replacement technologies for large-scale water usage.

4.8. Reactions at interfaces and/or multi-phase mixtures

Reactions at interfaces (or transport across interfaces to facilitate reaction) in CO_2-based systems have been proposed as a useful means by which to support green chemistry in carbon dioxide while easing separation problems post-reaction. Indeed, if one can effectively segregate catalyst, reactants and products in various phases in the reactor, downstream separation is certainly easier. However, one is now also faced with thermodynamic (phase behavior) and transport limitations to reaction. A key proviso in attempting

to use a biphasic system (with CO_2) to perform green chemistry is that the continuous component of each phase (CO_2 and the second component) should either both be environmentally benign (and hence cross-contamination is irrelevant) or should be immiscible over essentially the entire concentration regime. Thus, only the components of interest (reactants, products) are moving across the phase boundary.

Reactions making use of the CO_2/water biphasic mixture have long been proposed as green alternatives to conventional reactions. Each of these solvents is inherently benign, they are immiscible over a broad range of concentrations, and the inevitable cross-contamination that occurs upon phase contact does not require remediation. Eckert et al. [289] first examined the use of a conventional phase transfer catalyst in a CO_2/water mixture and found that despite the lack of 'CO_2-philic' ligands, the tetraalkyl ammonium bromide was effective at catalyzing the reaction across the interface. While Eckert employed a phase transfer catalyst, Johnston et al. (and later Tumas) enlarged the interfacial surface area through creation of an emulsion [290]. The enhanced surface area in the emulsion greatly enhanced the rate of the model reactions performed by these two groups (see Fig. 6). Beckman and Hancu [33](b) also examined the use of added surfactant to enhance reactivity in a CO_2/water biphasic system. Here, CO_2 dissolves in aqueous hydrogen peroxide, forming percarbonate (through two distinct mechanisms). The percarbonate ion (basic conditions are employed) then reacts with an alkene at the interface, forming the epoxide. The addition of surfactant to this system substantially enhanced the reaction rate, as did the addition of a phase transfer catalyst. The usual caveat in CO_2/water biphasic mixtures is that the low pH can cause problems for some reactions [291]. Quadir et al. [292] used the CO_2/water biphasic system in an intriguing way; here CO_2 was employed to alter the particle size distribution emanating from an emulsion polymerization in water.

The recent intense scientific interest in ionic liquids has created another possible biphasic system for use with carbon dioxide. Ionic liquids are salts (to date, ammonium and phosphonium salts) that exhibit melting temperatures close to or below room temperature. These materials exhibit manageable viscosities and essentially negligible vapor pressures and are hence
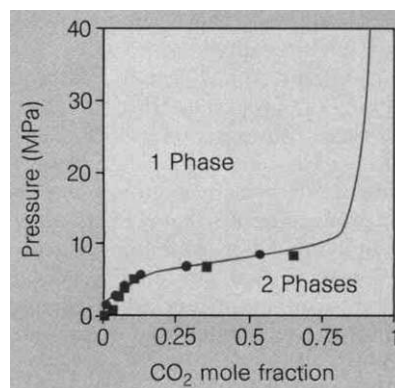

Fig. 7. Phase behavior of carbon dioxide with the ionic liquid 1-butyl-3-methyl imidazolium hexafluorophosphate [293].

considered potentially benign solvent media. In 1999, Brennecke [293] observed that ionic liquids would absorb large quantities of CO_2 at relatively low pressure (mole fractions of ≈ 0.6 at pressure below 100 bar), yet the amount of ionic liquid dissolved in CO_2 was below the detection limit of the instrument employed (and thus below 10^{-5} mole fraction). As such, the phase behavior of an ionic liquid in equilibrium with CO_2 resembles that of a crosslinked polymer in equilibrium with CO_2 (Fig. 7). Further, like polymer–CO_2 mixtures, the apparent volume change upon mixing for an IL–CO_2 mixture is large and negative, such that the volume change upon swelling of the IL is rather small, despite the amount of CO_2 absorbed. Further, because CO_2 dissolves readily in the ionic liquid, transport across the interface is rapid.

A number of researchers have since exploited ionic liquid/CO_2 biphasic mixtures as media for green chemistry. Tumas [89] employed CO_2 as a reactant in the formation of dimethyl formamide from amines, postulating that the ionic liquid would stabilize the polar intermediate in the reaction. Both Cole-Hamilton [294] and Leitner [295] conducted catalytic reactions in an ionic liquid, employing CO_2 to both extract products (leaving the catalysts behind) and enhance the solubility of gaseous reactants in the ionic liquid phase. Jessop and Eckert [90] examined asymmetric hydrogenation in an ionic liquid, again where the product is stripped into CO_2, leaving the catalyst behind. It would not be surprising to see other such efforts in the future. The previously stated (Section 2) caveats regarding ionic liquids naturally still apply.

In theory, one could also conduct reactions across a CO_2–solid interface (other than heterogeneous catalysis) and a CO_2–organic liquid interface, although little work has been reported to date. The one notable example here is the work by Eckert's group [15], where a phase transfer catalyst (PTC) is used to promote the displacement reaction of benzyl chloride with solid potassium bromide (no reaction occurs in the absence of the PTC). Brennecke [296] found that a simple esterification reaction conducted in a biphasic CO_2/organic mixture, proceeded to a greater degree of conversion, possibly because the product partitioned preferentially to the upper, CO_2-rich phase. In order to render any of these interfacial reactions practical, the thermodynamics of the system must be well understood. Clearly, the extent to which reactants, products, byproducts and solvents partition between the phases will determine the rate of reaction and the ability to recover both products and catalysts. In the case of ionic liquids, data and or models on the pVT and mixture behavior is entirely lacking and hence, partitioning behavior must still be determined experimentally.

5. Formation of fine particles using carbon dioxide

The controlled formation of particles (or powders) is important to several disparate industries, including those that manufacture pigments, pharmaceuticals and catalysts. Needless to say, these diverse applications mandate a diverse set of specifications for the production of such particles. Not surprisingly, supercritical fluids (and carbon dioxide in particular) have made inroads into particle production to varying degrees, with penetration more significant in some industries versus others. In particular, the benign properties of carbon dioxide (vis-à-vis intimate contact with humans) have created substantial interest within the pharmaceutical production community for use of CO_2 in the generation of therapeutic particulate products. In some cases, the use of CO_2 is proposed to supplant the use of organic solvents, and hence such a process could rightly be termed green processing. In other cases, the use of CO_2 (plus auxiliaries, as will be described below) might actually be less 'green' than a current process, but the characteristics of the product are superior, providing a performance rather than an environmental advantage. Further, because regulatory approval on new

products or processes (in the pharmaceutical industry) can require years to obtain, the industrial impact of CO_2 processing of pharmaceutical powders make not occur for some time (if at all, naturally). However, recent industrial investment (by entities in the pharmaceutical industry) in supercritical fluid technology suggests that the level of interest remains high.

5.1. Production of particles using carbon dioxide: RESS

The earliest particle formation process using CO_2 as the solvent is probably the oft-cited paper by Hannay and Hogarth in the 19th century, where depressurization of a CO_2-based solution created a precipitate 'like snow' (see Ref. [1] for description). During the 1980s, researchers at Battelle's Pacific Northwest Laboratories created the rapid expansion of supercritical solution (RESS) process, where a solution (here, of solid in supercritical alkane) was sprayed through a nozzle (where the outlet was at atmospheric pressure), creating fine particles [297]. Other researchers have explored the use of RESS to form particles since then, both from an experimental and theoretical standpoint [298]. As mentioned previously, CO_2 is not a particularly powerful solvent and hence, many of the solutes one might like to process using RESS require very high pressures (500 bar and above) to dissolve even small quantities of material—high CO_2 throughput will be needed to produce relatively small amounts of particles. The high CO_2 throughput (with its associated costs, capital and operating) has effectively inhibited the use of RESS on a commercial basis. This has rendered RESS generally less interesting than some competing CO_2-based particle formation technologies; these will be described below.

The most successful (from a developmental, if not yet truly commercial point of view) particle forming processes are those that have taken what is known about CO_2's thermophysical properties and applied these characteristics strategically. For example, as has been mentioned previously, it is well known that CO_2 is a rather feeble solvent—while problematic when attempting to use CO_2 in a RESS process, this characteristic is quite useful when CO_2 is employed as a non-solvent to induce precipitation of a solute from organic solvent. Further, whereas high pressure is required to create dilute solutions of large

molecules in CO_2, low pressures are sufficient to create solutions of CO_2 in large molecules (or solutions of compounds in organic solvent), as suggested in Fig. 5. Hence, saturated solutions of CO_2 (in either polymers or solute/solvent mixtures), sprayed through nozzles, have been used to generate fine particles.

5.2. Creating fine particles using CO_2: non-solvent modes of operation and PGSS

Jung and Perrut have written an excellent review of the use of supercritical fluids to generate fine particles [298]; other reviews have appeared recently as well [299]. These reviews describe the wide variety of materials that have been micronized via CO_2-based processing, and the various modes in which such particle processes operate.

During the 1980s, Krukonis et al. [300] found that one could employ CO_2 as a non-solvent to induce controlled precipitation of various solutes from organic solvent solution. The success of this approach derives from CO_2's generally feeble solvent power yet its miscibility with a variety of volatile organic solvents. The use of CO_2 as a non-solvent to produce particles has expanded significantly since then, where the typical 'process' employs one of several nozzle designs in order to create an aerosol simultaneous with the induced phase separation. As shown in the review by Jung and Perrut [298], an extraordinary variety of materials (many bioactive compounds) have been processed via one of the many non-solvent routes, typically generating micron-size particles and smaller.

As noted in the section on polymer processing, the pressure required to create a concentrated mixture of polymer and CO_2 is significantly lower than that required to create a dilute solution of polymer in CO_2 (see Fig. 5). As such, a number of researchers have explored the use of gas-saturated solutions (of either CO_2 in a polymer, or CO_2 in an organic solvent/solute mixture) to produce fine particles. Here the CO_2-saturated mixture is sprayed through a nozzle and the rapid vaporization of CO_2 creates an aerosol and removes any organic solvent. The work by Ferro Corporation on the generation of powder coating formulations using CO_2 is an example of this type of processing, sometimes referred to as PGSS (particles from gas-saturated solutions).

Although a variety of materials have been micronized using carbon dioxide, it is clear that most of the industrial interest in such processes arises from pharmaceutical manufacturers. As such, we will focus on bioactive particle manufacture in discussing the green potential of these processes.

5.3. Production of fine pharmaceutical powders: is this green processing?

To determine whether CO_2-based particle formation processes are 'green', one must first examine the ways in which particles are generated currently. First, it seems clear that the pharmaceutical industry is truly interested in the production of fine powders (particles) of controlled size and known purity. The design and testing of inhalable drugs is an ongoing area of significant research and business activity.

The CO_2-based particles processes described in the literature are green (and economical!) to varying degrees. For example, while RESS employs CO_2 as the only solvent, the need for high CO_2 throughputs (owing to low solubility of target compounds) means that the energy budget for such a process will be high (energy needed for compression and purification of large volumes of CO_2). On the other hand, processes such as PGSS or the various non-solvent modes of operation employ carbon dioxide at relatively low pressure and flow rates. Many of the anti-solvent processes employ organic solvents (DMSO most frequently), and hence care must be taken to 'close the loop' on these solvents to avoid lowering the sustainability of the process. Because CO_2-based particle production processes are, at most, at the pilot scale, it is not clear to what extent the organic solvent can actually be recycled. Further, if the particle process requires regulatory approval (for use in manufacture of pharmaceuticals), it is not clear to what extent solvent recycle will be permitted.

Many pharmaceutical compounds are readily soluble in water, while being poorly soluble in even polar solvents such as DMSO. Researchers at Bradford Particle Design (BPD) dealt with this situation in a CO_2-based non-solvent process by incorporating a co-solvent (an alcohol) that is miscible with both water and CO_2 [301]. Use of a coaxial nozzle and this co-solvent allowed BPD to produce fine particles from a variety of water-soluble compounds. Sievers et al. [302] have dealt with this problem via use of colliding

streams of aqueous solution and CO_2 (prior to exiting the high pressure environment at a nozzle), where the CO_2 helps form (and dry!) an aerosol of the aqueous solution. These two processes are noted because they each accomplish the formation of small particles of valuable compound using entirely sustainable solvent systems—CO_2/water/ethanol by BPD and CO_2/water by Sievers et al. This mode of operation would seem to exhibit the highest green potential of the various CO_2-based powder processes.

5.4. Comparisons with current processes

The literature suggests that milling, crystallization and spray drying are currently the most common means by which to generate powders (particles) from pharmaceuticals [299,303]. Milling [304] is a relatively energy-intensive process, but requires no solvent and is readily scalable. Milling (including jet pulverizing) has been demonstrated to be able to create particles in the 1–5 micron range. The design and performance characteristics of various types of mills are known and the process is readily scalable and can be rendered continuous [305]. However, temperature increases during milling can damage labile compounds and strict control over particle size and particle morphology may either be lacking or inconsistent. Milling can create substantial waste if the distribution of particle sizes exhibits a substantial tail at the lower end of the scale. Replacement of milling with a CO_2-based process would seem to owe more to product concerns than to 'green' concerns, if one of the various CO_2 processes can generate product consistently with the correct characteristics (size, distribution, shape, morphology).

Spray drying [305,306] involves the atomization of a solution (product in solvent), the mixing of the droplets with a hot gas (usually air) followed by the drying of the droplets to form the particles. Particles can be produced whose sizes range from 2 up to 500 microns; theory on design and operation of spray dryers has been well-studied. If one is employing water as the solvent, then the only significant 'green' complaint that one might have with spray drying is that water's high heat of vaporization requires a significant energy input to the process. On the other hand, as in the case of milling, if the CO_2-based process generates particles of higher quality (closer adherence to size

and morphology constraints), at a competitive price, then the CO_2 process could dominate despite potentially being less green. Obviously, if one is spray drying from organic solution, then recycle of the solvent is an additional consideration.

As for the cases of both milling and spray drying, crystallization is an often-used industrial process where numerous variations are possible [305,307]. Design principles for crystallizers have been investigated in depth in the past and hence, procedures for the design of crystallizers are readily available. If water is being used as the solvent, crystallization is already a relatively green process where perhaps high-energy input owing to the use of water as solvent (recall the need to dry the product) or the need to treat the wastewater from the process could be seen as negatives. Again, however, crystallization may not be able to produce the particle characteristics desired by the end-users.

In summary, the use of carbon dioxide as a nonsolvent for the production of particles (primarily pharmaceutical particles) is not substantially more 'green' than competing technologies (in some cases it could be less green). However, the use of CO_2 could provide better product, and hence its relatively green status provides no complications from a sustainability perspective. What seems to differentiate CO_2-based processes from their conventional competitors (crystallization, spray drying, milling) is a general lack of basic design equations that would allow ready creation of a design schematic given product specific inputs (the usual situation in computer-aided design of a unit operation or process). Research by DeBenedetti et al. during the 1990s [308] suggested that the process by which particles are created during spraying of a solution into CO_2 could be modeled by considering the formation of fluid droplets and the transport of both CO_2 and solvent between the continuous phase and the droplet phase. However, recent work by Randolph et al. [309] suggests that true droplets never form in the spray process and that particle formation can be described by gas phase nucleation and growth within the expanding plume. Whereas this may seem (to an outsider) as merely an academic debate, accurate models of the particle formation process inevitably result in the identification of the correct dimensionless groups associated with the phenomena and the underlying mathematical relationships that will ultimately permit process design from first principles. While there is

general agreement that phase behavior (thermodynamics) and transport play roles in the effects of process conditions on particle characteristics, it is not clear that a universal set of design guidelines currently exists.

Hence, in summary, what appears to be needed in this CO_2-based sub-field is research on building a true engineering model for such processes, where the input of fundamental thermophysical parameters allows for the design and operation of equipment that can deliver product with the desired characteristics. Indeed, the proliferation of acronyms associated with CO_2-based particle production (see Ref. [298]) lends the impression that the various processes are in some way fundamentally different from one another and thus, that one must experimentally evaluate each option (for a particular solute) to determine the proper operating mode to produce a given particle size and distribution. The lack of a defined 'unit operation' with acknowledged theoretical underpinning makes it difficult to perform an engineering design and scale-up of such processes, hindering their wider use. Equipment for CO_2-based particle production is rather treated as 'custom'.

Another avenue of research (in this area) that has received relatively scant attention in recent years is the use of CO_2 to process/produce well-defined particles from pigments. It is known that pigment particle size (and extent of particle agglomeration) exhibits a strong effect on the ultimate color of the article receiving the pigment. Pigments are usually milled mechanically; the use of a CO_2-based anti-solvent process could allow for the production of pigments with good control over the size and size distribution. Texter [310] has reviewed a number of solution based methods (homogeneous and multi-phase systems) for generating fine particles from pigments—most seem to rely upon controlled precipitation of pigment from a precursor solution (or emulsion) to form the particles. Here, naturally, CO_2 presents some advantages as it can be readily separated from the organic solvent and it is itself benign. Whether such advantages allow CO_2-based processes to supplant traditional milling (which obviously uses no solvent) remains an open question, although preliminary results are promising [311].

5.5. Industrial activity

There has been an interesting spate of industrial activity on particle formation using carbon dioxide

over the past 3 years, much of it not expressly technology based. Bradford Particle Design (UK) helped pioneer the development of the 'SEDS' process (solution-enhanced dispersion by supercritical fluids), where ethanol is added to an aqueous solution while it is sprayed into CO_2 to form particles. In early 2001, Inhale Therapeutics acquired Bradford Particle Design, demonstrating the interest by the pharmaceutical community in this technology. Interestingly, Bradford has previously announced that Bristol-Myers-Squibb had licensed their technology for use in pharmaceutical manufacture; it is not clear as to the state of that alliance at this time. At nearly the same time (late 2000) as the Bradford acquisition, Lavipharm (Greece) announced the acquisition of Separex (France) and the purchase of a 30% stake in Phasex (US). Both Separex and Phasex are well known to the supercritical fluid community, having each worked on the fundamentals and design of numerous supercritical fluid processes.

The review by Jung and Perrut lists many of the patents awarded on CO_2-based processing for the generation of fine particles. In addition to Bradford Particle Design [301], a number of academics have patented aspects of the non-solvent route to particle production, including Randolph [312] and Sievers [302], at the University of Colorado and Subramaniam at the University of Kansas [313].

Regarding the PGSS type processes, many of the patents that have appeared are related to applications in the coatings industry, including the Unicarb Process (mentioned previously), and powder coatings applications from Ferro (mentioned previously) and Morton [314].

6. Milestones in green chemistry using CO_2

Designating particular achievements as milestones is, of course, subjective. There are several types of milestones that one can consider with regards to green chemistry in carbon dioxide—purely scientific milestones, milestones in the dissemination of information on use of CO_2 and milestones in commercialization. Perhaps the first true commercially successful 'green' applications of CO_2 were the coffee decaffeination and CO_2-based thermoplastic foaming processes scaled-up during the 1980s; these are milestones as they showed that one could successfully scale a CO_2-based process

and operate such a process economically, given a good design.

Regarding scientific milestones, in the 1980s conventional wisdom claimed that CO_2's solvent power resembled that of n-alkanes, despite a large body of experimental evidence to the contrary. During the period 1988–1992, a number of research groups (Smith, Johnston, Enick and Brady, Beckman) reported that fluorinated materials, as well as silicones, exhibited significantly better thermodynamic compatibility with CO_2 than alkanes. The paper in *Science* by the DeSimone group on the CO_2-philicity of poly(perfluoroacrylates) in 1992 was a milestone both from the scientific standpoint *and* from a dissemination perspective, as this publication served to quash the 'CO₂ is like hexane' heuristic and introduce a wide audience to the notion that true CO_2-philes did indeed exist. Interestingly, it was not for another 3 years before the information of the CO_2-philicity of fluorinated materials found its way into the synthetic organic chemistry community. With publications by Leitner's and Tumas' groups, showing the use of fluorinated ligands in homogeneous catalysis in CO_2, green chemistry in CO_2 began to rapidly permeate the chemistry community. Once it was demonstrated that effectively any catalyst could ultimately be rendered CO_2-soluble, CO_2 was applied broadly as a solvent in organic transformations by both the academic and industrial communities. In 1999, Brennecke published a study demonstrating the potential for use of ionic liquid/CO_2 biphasic mixtures as media for green chemistry—the first papers exploiting this biphasic system appeared in 2001.

A number of researchers examined the strong potential for CO_2 to plasticize polymers, with several important papers appearing between 1985 and 1994 (the work by Wang and Kramer introduced the concept). Exploitation of this science appeared in 1996 through 2001, as both industry (Ferro, PPG) and academia (Howdle, Eckert) employed the plasticizing effect to enhance mixing in polymer systems.

Regarding commercial successes, the introduction of the CarDio process for continuous production of polyurethane foam using CO_2 as the blowing agent has been extremely important, in that it is both green chemistry and commercially successful. However, because the development of CarDio was conducted entirely by industry, with no R&D support from academia, it is little known within academic circles. Much more widely known is the construction (by Dupont) of a semi works facility to polymerize fluorinated monomers in carbon dioxide, as this technology was transferred (in part) from academia (work by DeSimone's group at North Carolina). The same is probably true for the cleaning of fabrics (dry cleaning) using CO_2.

The introduction of CO_2 to microelectronics processing began with preliminary work by the Phasex Corporation and IBM in 1995–1996, given the DeSimone *Science* paper showing that perfluoroacrylate polymers are readily miscible with CO_2. Again, because the preliminary work was conducted primarily by industry and was disseminated to a relatively narrow audience (the microelectronics industry), extensive interest in this topic did not begin until several years later, when both Ober's group (Cornell University) and the DeSimone group (UNC) began to play active roles. Now, the use of CO_2 in microelectronics processing is considered sufficiently noteworthy to merit an article in Chemical and Engineering News. The work by Watkins on creation of thin metal films via chemistry in CO_2 [96] will likely enhance interest still further.

Another series of commercial milestones occurred in late 2000 to early 2001, when the pharmaceutical industry purchased (either in their entirety or substantial portions) Bradford Particle Design, Separex and Phasex—three of the more significant commercial enterprises relying primarily on supercritical fluids technology. It will be interesting to see whether this leads to more rapid commercialization of CO_2-based processes or the reverse.

In summary, milestones in green chemistry using CO_2 have occurred upon scientific achievement, as was the case with the discovery of CO_2-philic polymers by DeSimone in 1992, and also the dissemination of fundamental science to industries or communities for whom CO_2 had previously been considered an exotic technology. In this report a number of technical hurdles to increased use of CO_2 in green chemistry have been outlined—it is hoped that future milestones will occur by overcoming these hurdles. Finally, it should be noted that some scientific milestones that have occurred in this field might be considered the result of a particular researcher recognizing the broader

implications of a narrowly focused study published previously.

7. Areas for future research on CO_2 technology

In each of the previous sections, mention has been made of potentially useful avenues for future research; these will be summarized below (in no particular order).

- The use of biphasic systems (including carbon dioxide as one component) for conducting reactions using gaseous components.
- A greater focus on oxidations and hydroformylations, versus hydrogenation in CO_2; the former reactions generate more waste and require more stringent conditions than hydrogenation, yet have received relatively less attention in the literature (with respect to the sub-field of reactions in CO_2).
- Group contribution or better yet, first principles models for the prediction of phase behavior in multi-phase, multi-component systems where carbon dioxide is one of the components. Prediction of basic transport properties is needed as well. In order to do this, one needs a fundamental understanding of the effects of chemical structure and topology on the phase behavior of molecules in carbon dioxide; this should also result in the design of 'CO_2-philes' that do not include fluorine.
- An understanding of the fundamentals behind solvation of hydrophilic compounds (including water) in CO_2-based emulsions; also thermodynamics and transport properties of the CO_2–water interface. This would address the frustrating observation that not all CO_2-soluble amphiphiles can solubilize water.
- The design of equipment that would allow rapid injection and removal of solids from high pressure, CO_2-rich environments. Also, the design of systems for the rapid high-pressure treatment of solid articles (as in the development of silicon wafers) or the continuous coating of material using a CO_2-based solution. Such work would benefit diverse CO_2 applications, including microelectronics processing, the dyeing of textiles, cleaning and extraction.
- The use of CO_2 in microelectronics processing. This is an application where concurrent design at the molecular and process level is needed.

- An in-depth understanding of the mechanism for generation of CO and subsequent poisoning of noble metal catalysts in the presence of hydrogen and CO_2 and hence, the design of catalysts that can effectively perform hydrogenations for extended time periods in carbon dioxide.
- The design of catalysts for the generation of polyesters and commodity chemicals (aromatic acids) from CO_2; activation of CO_2 at low pressures.
- Also, IT would be useful to explore the use of co-solvents for CO_2 in a more systematic manner, to find mixtures that are technically, environmentally and economically successful. The use of 'expanded' solvents in reactions is included here.
- The design of additives that would allow greater use of CO_2 in the extrusion foaming of polymers. Also, the generation of low density, fine-celled foams using CO_2 as the blowing agent.
- The development of a set of fundamental design principles for the formation of particles via phase separation from mixtures that include CO_2 (under flow in a known geometry).
- Programs that focus on overcoming the various technical hurdles to the use of CO_2 in coating processes. For example, while problems in using CO_2 to process powder coating formulations differ greatly from problems encountered in preparing emulsion coating formulations using CO_2, the problems are inherently technical in nature.
- Identification of applications where CO_2 might replace water, whose use in arid climates is not always sustainable. These include fabric dyeing, cleaning and microelectronics processing—are there others?

Whether one agrees with these areas of emphasis or not, the list shown above reveals that while the use of carbon dioxide as a solvent as part of a green processing scheme might be considered (in 2002) a relatively mature technology, it remains a rich area for future research. Further, while use of carbon dioxide is often prompted by environmental concerns, recent commercialization efforts show that use of CO_2 in a process can provide product quality and safety advantages as well as enhanced sustainability. Successful commercial implementations of CO_2-based technology show clearly that a close collaboration between scientists and engineers is needed to bring promising ideas to fruition. Carbon dioxide is without question a benign

solvent, yet equivalent attention must be paid to the monetary 'green' as to the sustainable 'green' to create commercially successful processes that use CO_2.

Acknowledgements

References

[1] (a) M.A. McHugh, V.J. Krukonis, Supercritical Fluid Extraction, second ed, Butterworth-Heinemann, Boston, MA, 1994;
(b) G. Brunner, Gas Extraction, Steinkopff Verlag, Darmstadt, Germany, 1994.

[2] (a) A. Michels, C. Michels, Proc. Roy. Soc. (Lond.) A 153 (1936) 201;
(b) A. Michels, C. Michels, H. Wouters, Proc. Roy. Soc. (Lond.) A 153 (1936) 214.

[3] S. Angus, B. Armstrong, K.M. de Reuck, Carbon Dioxide (On the basis of surveys and equations produced by V.V. Altunin) Oxford University Press, New York, 1976.

[4] (a) J.C. Giddings, M.N. Myers, L. McLaren, R.A. Keller, Science 162 (1969) 67;
(b) J.C. Giddings, M.N. Myers, J.W. King, J. Chromatogr. Sci. 7 (1969) 276.

[5] (a) Praxair Material Data Safety Sheet, P-4574-H, May, 1999;
(b) D.R. Lide, (Ed.), CRC Handbook of Chemistry and Physics, seventy-sixth ed., CRC, Boca Raton, FL, 1996, Chapter 16.

[6] B. Minder, T. Mallat, A. Baiker, Third International Symposium on High-Pressure Chemical Engineering, Zurich, 1996, p. 139.

[7] (a) F. Solymosi, E. Erdohelyi, M. Lancz, J. Catal. 95 (1985) 567;
(b) A. Erdohelyi, M. Pasztor, F. Solymosi, J. Catal. 98 (1986) 106.

[8] (a) L.W. Lake, Enhanced Oil Recovery, Prentice Hall, Englewood Cliffs, NJ, 1989;
(b) A. Chakma, M.R. Islam, F. Berruti (Eds.), Enhanced Oil Recovery, Am. Inst. Chem. Eng. Symp. Ser. 280, New York, 1991.

[9] J.O. Pande, J. Tonheim, Proc. Safety Progr. 20 (2001) 37.

[10] D.J. Van Bramer, M.B. Shiflett, A. Yokozeki, US Patent 5,345,013, 1994.

[11] F. Rodriguez, Principles of Polymer Systems, fourth ed, McGraw-Hill, New York, 1996.

[12] R.C. Reid, J.M. Prausnitz, B.E. Poling, The Properties of Liquids and Gases, fourth ed, McGraw-Hill, New York, 1987.

[13] K. Weissermel, H.-J. Arpe, Industrial Organic Chemistry, third ed, Wiley, VCH-Weinheim, Germany, 1997.

[14] D. Hancu, E.J. Beckman, Green Chem. 3 (2001) 80.

[15] C.A. Eckert, C.L. Liotta, C.W. Culp, D.R. Lamb, in: P.G. Jessop, W. Leitner (Eds.), Chemical Synthesis Using Supercritical Fluids, Wiley VCH, Weinheim, Germany, 1999, p. 446.

[16] (a) K. Zosel, US Patent No. 3,806,619, 1974, April 23;
(b) R. Prasad, M. Gottesman, R.A. Scarella, US Patent No. 4,246,291, 1981, Jan. 20.

[17] J.L. Kendall, D.A. Canelas, J.L. Young, J.M. DeSimone, Chem. Rev. 99 (1999) 543.

[18] (a) J.M. Tanko, J.F. Blackert, Science 263 (1994) 203;
(b) S. Hadida, M.S. Super, E.J. Beckman, D.P. Curran, J. Am. Chem. Soc. 119 (1997) 7406.

[19] C.Y. Tsang, W.B. Street, Chem. Eng. Sci. 36 (1981) 993.

[20] Y.-L. Hsiao, J.M. DeSimone, J. Polym. Sci. Part A: Polym. Chem. 35 (1997) 2009.

[21] C.A. Eckert, Presentation at the International Symposium on Supercritical Fluid Technology, Myrtle Beach, SC, August 18–23, 2001.

[22] The convective heat transfer flux is proportional to the heat transfer coefficient (h), where h is correlated to physical properties through a correlation of the form $h = k(\text{Re})^x(\text{Pr})^y$ where Pr (the Prandtl number) $= \mu Cp/k$ and Re (the Reynolds number) $= \rho Dv/$. Here μ is the viscosity, ρ is the density, v the fluid velocity, k the thermal conductivity and Cp the heat capacity. For the case of natural convection (convection induced by temperature gradients in the fluid), the heat transfer coefficient correlates with the thermal conductivity, the Prandtl number and the Grashof number (Gr), where $\text{Gr} = \beta g \rho^2 D^3 \Delta T/\mu^2$; where ΔT is the temperature difference between the surface and the fluid, while β is the coefficient of thermal expansion. See, for example, J.R. Welty, C.E. Wicks, R.E. Wilson, Fundamentals of Momentum, Heat, and Mass Transfer, third ed., Wiley and Sons, New York, 1984.

[23] (a) S. Inoue, N. Yamazaki, Organic and Bioorganic Chemistry of Carbon Dioxide, Wiley and Sons, New York, 1982;
(b) K.N. West, C. Wheeler, J.P. McCarney, K.N. Griffith, D. Bush, C.L. Liotta, C.A. Eckert, J. Phys. Chem. A 105 (2001) 3947.

[24] A.J. Mesiano, E.J. Beckman, A.J. Russell, Chem. Rev. 99 (1999) 623.

[25] Y. Wu, US Patent No. 4,483,888, 1984, Nov. 20.

[26] V. Arunajatesan, B. Subramanian, K.W. Hutchenson, F.E. Herkes, Chem. Eng. Sci. 56 (2001) 1363.

[27] K.W. Hutchensen, F.E. Herkes, D.J. Walls, T.K. Das, J.F. Brennecke, Presentation at the ACS Annual Meeting, 2001.

[28] V. Arunajatesan, B. Subramanian, K.W. Hutchensen, F.E. Herkes, Presentation 176d at AIChE Annual Meeting, Reno, NV, 2001.

[29] P.G. Jessop, Y. Hsiao, T. Ikariya, R. Noyori, J. Am. Chem. Soc. 118 (1996) 344.

[30] R. Wiebe, V.L. Gaddy, J. Am. Chem. Soc. 62 (1940) 815.

[31] J.D. Holmes, K.J. Ziegler, M. Audriani, C.T. Lee, P.A. Bhargava, D.C. Steytler, K.P. Johnston, J. Phys. Chem. B 103 (1999) 5703.

[32] R.M. Enick, E.J. Beckman, C.M. Shi, J.H. Xu, L. Chordia, Energy Fuels 15 (2001) 256.

[33] (a) S.A. Nolen, J. Liu, J.S. Brown, P. Pollet, B.C. Eason, K.N. Griffith, R. Glaser, D. Bush, D.R. Lamb, C.L. Liotta, C.A. Eckert, G.F. Thiele, K.A. Bartels, Ind. Eng. Chem. Res. 41 (2002) 316;
(b) D. Hancu, E.J. Beckman, Acc. Chem. Res. 35 (2002) 757.

[34] P.T. Anastas, J.C. Warner, Green Chemistry, Theory and Practice, Oxford University Press, New York, 1998, p. 30.

[35] L. Chordia, Presentation at Fifth International Symposium on Supercritical Fluid, Atlanta, GA, April 8–12, 2000.

[36] (a) M. Perrut, Ind. Eng. Chem. Res. 39 (2000) 4531;
(b) W.H. Hauthal, Chemosphere 43 (2001) 123;
(c) C.W. Smith, G. Huse, in: J. McHardy, S.P. Sawan (Eds.), Supercrital Fluid Cleaning, Noyes, Westwood, NJ, 1998, p. 245;
(d) M. Cygnarowicz-Provost, in: J.W. King, G.R. List (Eds.), Supercritical Fluid Technology for Oil and Lipid Chemistry, AOCS Press, Champaign, IL, 1996, p. 155;
(e) R. Gani, G. Hytoft, C. Jaksland, Appl. Therm. Eng. 17 (1997) 889.

[37] (a) C.M. Colina, C.K. Hall, K.E. Gubbins, Fluid Phase Equil. 194–197 (2002) 553;
(b) F.J. Blas, A. Galindo, Fluid Phase Equil. 194–197 (2002) 501;
(c) H.-S. Byun, K. Kim, M.A. McHugh, Ind. Eng. Chem. Res. 39 (2000) 4580;
(d) Z.-Y. Zhang, J.-C. Yang, Y.-G. Li, Fluid Phase Equil. 169 (2000) 1.

[38] (a) S. Diaz, S. Espinosa, E.A. Brignole, Comp.-Aid. Chem. Eng. 8 (2000) 319;
(b) M. Artal, J. Munoz Embid, I. Velasco, C. Berro, E. Rauzy, Fluid Phase Equil. 178 (2001) 119;
(c) S. Espinosa, S. Diaz, E.A. Brignole, Comp. Chem. Eng. 24 (2000) 1301;
(d) J.-N. Jaubert, L. Coniglio, Ind. Eng. Chem. Res. 38 (1999) 5011;
(e) A. Keshtkar, F. Jatali, M. Moshfeghian, Fluid Phase Equil. 140 (1997) 107.

[39] (a) C.A. Eckert, D. Bush, J.S. Brown, C.L. Liotta, Ind. Eng. Chem. Res. 39 (2000) 4615;

(b) F.P. Lucien, N.R. Foster, J. Supercrit. Fluids 17 (2000) 111.

[40] (a) L. Chinsoo, K.L. Hoy, M.D. Donohue, US Patent No. 4,923,720, 1990, May 8;
(b) L. Chinsoo, K.L. Hoy, M.D. Donohue, US Patent No. 5,027,742, 1991, July 2;
(c) K.L. Hoy, K.A. Nielsen, L. Chinsoo, US Patent No. 5,108,799, 1992, April 28.

[41] K.W. Suh, Polystyrene and structural foam, in: D. Klempner, K.C. Frisch (Eds.), Polymeric Foams, Oxford University Press, New York, 1991, p. 151.

[42] F.M. Khoury, Predicting the Performance of Multi-Stage Separation Processes, second ed, CRC Press, Boca Raton, FL, 1995.

[43] Azeotropes.

[44] S.-H. Chiang, G.E. Klinzing, US Patent No. 4,613,429, 1986, Sept. 23.

[45] (a) P.A. Charpentier, J.M. DeSimone, G.W. Roberts, Chem. Eng. Sci. 55 (2000) 5341;
(b) P.A. Charpentier, K.A. Kennedy, J.M. DeSimone, G.W. Roberts, Macromolecules 32 (1999) 5973.

[46] (a) M.V. Palmer, S.S.T. Ting, Food Chem. 52 (1995) 345;
(b) K.K. Tiwari, Chem. Ind. Dig. 9 (1996) 71;
(c) P. Jusforgues, M. Shaimi, D. Barth, Chromat. Sci. Ser. 75 (1998) 403. Supercritical Fluid Chromatography with Packed Columns;
(d) G.A. Montero, T.D. Giorgio, K.B. Schnelle, Envir. Progr. 15 (1996) 112.

[47] R.M. Smith, J. Chromat. A. 856 (1999) 83.

[48] Perfluorooctyl Sulfonates; Proposed Significant New Use Rule, Fed. Regis. (2000), 65 (2002) 62319.

[49] (a) http://www.greenearthcleaning.com.;
(b) D.R. Berndt, J.M. Griffiss, US Patent No. 5,942,007, 1999, August 24.

[50] B.J. Feder, New York Times (2000), February 15, Section C, p. 1.

[51] http://www.chart-ind.com/news.html

[52] (a) S.H. Jureller, J.L. Kerschner, D.S. Murphy, US Patent No. 6,148,644, 2000.;
(b) S.H. Jureller, J.L. Kerschner, R. Harris, US Patent No. 5,683,473, 1997.;
(c) S.H. Jureller, J.L. Kerschner, M. Bae-Lee, L. Del Pizzo, R. Harris, C. Resch, C. Waja, PCT Int. Appl. WO 9627704 (1996).

[53] US EPA, Office of Environmental Information, EPA 260-B-01-001, March, 2001.

[54] Air toxics website—CAA: Original list of hazardous air pollutants: http://www.epa.gov/ttnatw01/orig189.html

[55] (a) http://www.clean.rti.org;
(b) W.M. Nelson, in Green Chemical Syntheses and Processes. P.T. Anastas, L.G. Heine, T.C. Williamson, eds., ACS Symp Ser 767 (2000) Chapter 24.

[56] P.N. Rylander, Hydrogenation Methods, Academic Press, Orlando, FL, 1985.

[57] (a) B. Subramaniam, Appl. Catal. A: Gen. 212 (2001) 199;
(b) B. Subramaniam, V. Arunajatesan, C.J. Lyon, Stud. Surf. Sci. Catal. 126 (1999) 63;

(c) B. Subramaniam, J. Ashraf, in: Innovations in Supercritical Fluids, ACS Symposium Ser. 608, 1995, p. 24;
(d) D.M. Ginosar, B. Subramaniam, Stud. Surf. Sci. Catal. 88 (1994) 327;
(e) D.M. Ginosar, B. Subramaniam, J. Catal. 152 (1995) 31;
(f) S. Baptiste-Nguyen, B. Subramaniam, AIChE J. 38 (1992) 1027.

[58] C.N. Satterfield, Heterogeneous Catalysis in Practice (As an example), McGraw-Hill, New York, 1980.

[59] B. Subramaniam, C.J. Lyon, V. Arunajatesan, Appl. Catal. B: Environ. 37 (2002) 279.

[60] A. Baiker, Chem. Rev. 99 (1999) 453.

[61] (a) S. van den Hark, M. Harrod, P. Moller, J. Am. Oil Chem. Soc. 76 (1999) 1363;
(b) S. van den Hark, M. Harrod, Appl. Cat. A: Gen. 210 (2001) 207.

[62] T. Tacke, S. Wieland, P. Panster, Third International Conference on High Pressure Chemical Engineering, Zurich, 1996, pp. 17–21.

[63] M.B. Macher, A. Holmqvist, Eur. J. Lip. Sci. Tech. 103 (2001) 81.

[64] (a) J.W. King, R.L. Holliday, G.R. List, J.M. Snyder, J. Am. Oil Chem. Soc. 78 (2001) 107;
(b) M.B.O. Andersson, J.W. King, L.G. Blomberg, Green Chem. 2 (2000) 230.

[65] D. Chouchi, D. Gourgouillon, M. Courel, J. Vital, M.N. da Ponte, Ind. Eng. Chem. Res. 40 (2001) 2551.

[66] (a) P.D. Condo, D.R. Paul, K.P. Johnston, Macromolecules 27 (1994) 365;
(b) P.D. Condo, K.P. Johnston, J. Polym. Sci. Part B: Polym. Phys. 32 (1994) 523.

[67] A. Bertucco, P. Canu, L. Devetta, A.G. Zwahlen, Ind. Eng. Chem. Res. 36 (1997) 2626.

[68] L. Devetta, A. Giovanzana, P. Canu, A. Bertucco, B.J. Minder, Catal. Today 48 (1999) 337.

[69] B.M. Bhanage, Y. Ikushima, M. Shirai, M. Arai, Catal. Lett. 62 (1999) 175.

[70] B. Minder, T. Mallat, K.H. Pickel, K. Steiner, A. Baiker, Catal. Lett. 34 (1995) 1.

[71] M.G. Hitzler, F.R. Smail, S.K. Ross, M. Poliakoff, Org. Proc. Res. Dev. 2 (1998) 137.

[72] (a) D. Hancu, E.J. Beckman, Indust. Eng. Chem. Res. 38 (1999) 2824;
(b) D. Hancu, E.J. Beckman, Indust. Eng. Chem. Res. 38 (1999) 2833;
(c) D. Hancu, E.J. Beckman, Ind. Eng. Chem. Res. 39 (2000) 2843.

[73] A.P. Gelbein, Chemtech 28 (1998) 1.

[74] M.L. O'Neill, Q. Cao, M. Fang, K.P. Johnston, S.P. Wilkinson, C.D. Smith, J.L. Kerschner, S.H. Jureller, Ind. Eng. Chem. Res. 37 (1998) 3067.

[75] K.A. Consani, R.D. Smith, J. Supercrit. Fluids 3 (1990) 51.

[76] (a) R.J. Klingler, J.W. Rathke, J. Am. Chem. Soc. 116 (1994) 4772;
(b) J.W. Rathke, R.J. Klingler, US Patent 5,198,589, 1993;
(c) J.W. Rathke, R.J. Klingler, T.R. Krause, Organometallics 10 (1991) 1350;

(d) R.P. Warzinski, C.-H. Lee, G.D. Holder, J. Supercrit. Fluids 5 (1992) 60.

[77] R. Fink, D. Hancu, R. Valentine, E.J. Beckman, J. Phys. Chem. B 103 (1999) 6441.

[78] K. Harrison, J. Goveas, K.P. Johnston, E.A. O'Rear, Langmuir 10 (1994) 3536.

[79] J.M. DeSimone, Z. Guan, C.S. Elsbernd, Science 257 (1992) 945.

[80] D.R. Palo, C. Erkey, Organometalltics 19 (2000) 81.

[81] D.C. Smith, E.D. Stevens, S.P. Nolan, Inorg. Chem. 38 (1999) 5277.

[82] (a) Chem. Eng. News 78 (21) (2000) 9;
(b) Chem. Eng. News 79 (5) (2001) 7.

[83] P.G. Jessop, S. DeHaai, D.C. Wynne, Chem. Commun. (2000) 693.

[84] M. Wende, R. Meier, J.A. Gladysz, J. Am. Chem. Soc. 123 (2001) 11490.

[85] (a) P.G. Jessop, M.M. Olmstead, C. Ablan, M. Grabenauer, D. Sheppard, C.A. Eckert, C.L. Liotta, Inorg. Chem. 41 (2002) 3463;
(b) P.G. Jessop, R.A. Brown, P. Pollet, E. McKoon, T. Ngo, C.A. Eckert, C.L. Liotta, in: P.G. Jessop, R.A. Brown, P. Pollet, E. McKoon, T. Ngo, C.A. Eckert, C.L. Liotta (Eds.), The Use of Neoteric Solvents for Hydrogenation and Other Asymmetric Reactions, 2001.

[86] J. Xiao, S.C.A. Nefkins, P.G. Jessop, T. Ikariya, R. Noyori, Tetrahed. Lett. 37 (1996) 2813.

[87] M.J. Burk, S. Feng, M.F. Gross, W. Tumas, J. Am. Chem. Soc. 117 (1995) 8277.

[88] S. Kainz, A. Brinkman, W. Leitner, A. Pfaltz, J. Am. Chem. Soc. 121 (1999) 6421.

[89] F. Liu, M.B. Abrams, R.T. Baker, W. Tumas, Chem. Commun. (2001) 433.

[90] R.A. Brown, P. Pollet, E. McKoon, C.A. Eckert, C.L. Liotta, P.G. Jessop, J. Am. Chem. Soc. 123 (2001) 1254.

[91] L.A. Blanchard, D. Hancu, E.J. Beckman, J.F. Brennecke, Nature 399 (1999) 28.

[92] Anonymous, Chem. Eng. News 80 (2002) 44.

[93] J.J. Watkins, T.J. McCarthy, Chem. Mat. 7 (1995) 1991.

[94] N. Nazem, L.T. Taylor, A.F. Rubira, J. Supercrit. Fluids 23 (2002) 43.

[95] K.S. Morley, P.C. Marr, P.B. Webb, A.R. Berry, F.J. Allison, G. Moldovan, P.D. Brown, S.M. Howdle, J. Mat. Chem. 12 (2002) 1898.

[96] (a) J.M. Blackburn, D.P. Long, A. Cabanas, J.J. Watkins, Science 294 (2001) 141;
(b) N.E. Fernandes, S.M. Fisher, J.C. Poshusta, D.G. Vlachos, M. Tsapatsis, J.J. Watkins, Chem. Mat. 13 (2001) 2023;
(c) J.M. Blackburn, D.P. Long, J.J. Watkins, Chem. Mat. 12 (2000) 2625;
(d) D.P. Long, J.M. Blcakburn, J.J. Watkins, Adv. Mat. 12 (2000) 913;
(e) J.J. Watkins, J.M. Blackburn, T.J. McCarthy, Chem. Mat. 11 (1999) 213.

[97] S.A. Crette, J.M. DeSimone, R.G. Carbonell, W. Tumas, J.T. Brady, Abstracts of papers for ACS Meeting, August 20, 2000 220: 413, Part 2.

[98] R.M. Crooks, B.I. Lemon, L. Sun, L.K. Yeung, M.Q. Zhao, Top. Curr. Chem. 212 (2001) 81.

[99] L.J.P. van der Broek, E.L.V. Goetheer, A.W. Verkerk, E. de Wolf, B.J. Deelman, G. van Koten, J.T.F. Keurentjes, Ang. Chem. Int. Ed. 40 (2001) 4473.

[100] G.B. Jacobsen, C.T. Lee, K.P. Johnston, W. Tumas, J. Am. Chem. Soc. 121 (1999) 11902.

[101] M. Harrod, P. Moller, US Patent No. 6,265,596, 2001, July 24.

[102] M. Poliakoff, T.M. Swan, T. Tacke, M.G. Hitzler, S.K. Ross, S. Wieland, US Patent No. 6,156,933, 2000, Dec. 5.

[103] (a) D. Koch, W. Leitner, J. Am. Chem. Soc. 120 (1998) 13398;
(b) S. Kainz, W. Leitner, Catal. Lett. 55 (1998) 223;
(c) G. Francio, W. Leitner, Chem. Commun. (1999) 1663.

[104] (a) D.R. Palo, C. Erkey, Ind. Eng. Chem. Res. 37 (1998) 4203;
(b) D.R. Palo, C. Erkey, Ind. Eng. Chem. Res. 38 (1999) 3786;
(c) T. Davis, C. Erkey, Ind. Eng. Chem. Res. 39 (2000) 3671.

[105] Y. Hu, W. Chen, L.J. Xu, J.L. Xiao, Organometallics 20 (2001) 3206.

[106] (a) Y. Guo, A. Akgerman, Ind. Eng. Chem. Res. 36 (1997) 4581;
(b) Y. Guo, A. Akgerman, J. Supercrit. Fluids 15 (1999) 63;
(c) B. Lin, A. Akgerman, Ind. Eng. Chem. Res. 40 (2001) 1113.

[107] A.M. Banet Osuna, W. Chen, E.G. Hope, R.D.W. Kemmitt, D.R. Paige, A.M. Stuart, J. Xiao, L. Xu, J. Chem. Soc. Dalt. Trans. 22 (2000) 4052.

[108] J. Kie, B. Han, M.W. George, H. Yan, M. Poliakoff, J. Am. Chem. Soc. 123 (2001) 3661.

[109] N.J. Meehan, A.J. Sandee, J.N.H. Reek, P.C.J. Kamer, P.W.N.M. van Leeuwen, M. Poliakoff, Chem. Commun. (2000) 1497.

[110] (a) A.R. Tadd, A. Marteel, M.R. Mason, J.A. Davies, M.A. Abraham, Ind. Eng. Chem. Res. (2002), ASAP;
(b) G. Snyder, A. Tadd, M.A. Abraham, Ind. Eng. Chem. Res. 40 (2001) 5317;
(c) S. Dharmidhikari, M.A. Abraham, J. Supercrit. Fluids 18 (2000) 1.

[111] I. Ojima, H. Urata, US Patent No. 5,962,744, 1999, Oct. 5.

[112] X.-W. Wu, Y. Oshima, S. Koda, Chem. Lett. (Jpn.) 10 (1997) 1045.

[113] P. Srinivas, M. Mukhopadhyay, Ind. Eng. Chem. Res. 36 (1997) 2066.

[114] G. Jenzer, T. Mallat, M. Maciejewski, F. Eigenmann, A. Baiker, Appl. Catal. A: Gen. (2001) 125.

[115] (a) S.A. Nolen, J. Lu, J.S. Brown, P. Pollet, B.C. Eason, K.N. Griffith, R. Glaeser, D. Bush, D.R. Lamb, C.L. Liotta, C.A. Eckert, G.F. Thiele, K.A. Bartels, Ind. Eng. Chem. Res. 41 (2002) 316;
(b) D. Hancu, J. Green, E.J. Beckman, Industr. Eng. Chem. 41 (2002) 4466.

[116] (a) H. Yao, D.E. Richardson, J. Am. Chem. Soc. 122 (2000) 3220;
(b) D.E. Richardson, H. Yao, K.M. Frank, D.A. Bennett, J. Am. Chem. Soc. 122 (2000) 1729.

[117] E.R. Birnbaum, R.M. Le Lacheur, A. Horton, W. Tumas, J. Mol. Cat. A: Chem. 139 (1999) 11.

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

[119] G.R. Hans, J.W. Kolis, Organometallics 17 (1998) 4454.

[120] H. Jiang, L. Jia, J. Li, Green Chem. 2 (2000) 161.

[121] D.H. Busch, M. Wei, G.T. Musie, B. Subramaniam, J. Am. Chem. Soc. 124 (2002) 2513.

[122] R. Pitchai, A.P. Kahn, A.M. Gaffney, US Patent No. 5,625,084, 1997, Apr. 27.

[123] A. Kumar, R.K. Gupta, Fundamentals of Polymers, McGraw-Hill, New York, 1998.

[124] P.J. Flory, Principles of Polymer Chemistry, Cornell University Press, Ithaca, NY, 1953.

[125] V. Wiesmet, E. Weidner, S. Behme, G. Sadowski, W. Arlt, J. Supercrit. Fluids 17 (2000) 1.

[126] (a) R.G. Wissinger, M.E. Paulaitis, J. Polym. Sci. Part B: Polym. Phys. 25 (1987) 2497;
(b) R.G. Wissinger, M.E. Paulaitis, J. Polym. Sci. Part B: Polym. Phys. 29 (1991) 631.

[127] (a) P. Ehrlich, J. Polym. Sci. A3 (1965) 131;
(b) P. Ehrlich, G.A. Mortimer, Adv. Polym. Sci. 7 (1970) 386.

[128] C. Kirby, M.A. McHugh, Chem. Rev. 99 (1999) 565, for a review.

[129] S.R. Allada, Ind. Eng. Chem. Proc. Des. Dev. 23 (1984) 344.

[130] F.M. Orr, J.P. Heller, J.T. Taber, R.J. Card, Chemtech (1983) 482.

[131] G.J. McFann, S.M. Howdle, K.P. Johnston, AIChE J. 40 (1994) 543.

[132] (a) M.E. Sikorski, J.L. Lundberg, Abstract HS 22, American Physical Society Meeting, Detroit, MI, 1983;
(b) T.V. Harris, C.A. Irani, W.R. Pretzer, US Patent No. 5,045,220, 1991, Sept. 3.

[133] (a) A. Iezzi, P. Bendale, R.M. Enick, M. Turberg, J. Brady, Fluid Phase. Equil. 52 (1989) 307;
(b) T.A. Hoefling, R.M. Enick, E.J. Beckman, J. Phys. Chem. 95 (1991) 7127;
(c) T.A. Hoefling, D.A. Newman, R.M. Enick, E.J. Beckman, J. Supercrit. Fluids 6 (1993) 165;
(d) T.A. Hoefling, D.A. Newman, R.M. Enick, E.J. Beckman, J. Supercrit. Fluids 6 (1993) 205.

[134] G.G. Ghenciu, Extraction of Proteins in Liquid Carbon Dioxide, PhD Thesis, Univ. of Pittsburgh, 1997.

[135] J.B. McClain, D.E. Betts, D.A. Canelas, E.T. Samulski, J.M. DeSimone, J.D. Londono, H.D. Cochran, G.D. Wignall, D. ChilluraMartino, R. Triolo, Science 274 (1996) 2049.

[136] (a) M.A. McHugh, I.-H. Park, J.J. Reisinger, Y. Ren, T.P. Lodge, M.A. Hillmyer, Macromolecules 35 (2002) 4653;
(b) T.P. DiNoia, S.E. Conway, J.S. Lim, M.A. McHugh, J. Polym. Sci. Part B: Polym. Phys. 38 (2000) 2832;
(c) M. Lora, J.S. Lim, M.A. McHugh, J. Phys. Chem. B. 103 (1999) 2818;

(d) C.A. Mertogan, M.A. McHugh, W.H. Tuminello, J. Appl. Polym. Sci. 74 (1999) 2039.

[137] (a) A. Dardin, J.M. DeSimone, E.T. Samulski, J. Phys. Chem. 102 (1998) 1775;
(b) A. Dardin, J.B. Cain, J.M. DeSimone, J.C.S. Johnson Jr, E.T. Samulski, Macromolecules 30 (1997) 3593.

[138] P. Diep, K.D. Jordan, J.K. Johnson, E.J. Beckman, J. Phys. Chem. A 102 (1998) 2231 (An example).

[139] Chemical Reviews devoted an entire issue to supercritical fluids, 1999, p. 99; many of the articles in this issue describe the use of CO_2-philic materials.

[140] J.C. Meredith, K.P. Johnston, J.M. Seminario, S.G. Kazarian, C.A. Eckert, J. Phys. Chem. 100 (1996) 10837.

[141] S.G. Kazarian, M.F. Vincent, F.V. Bright, C. Liotta, C.A. Eckert, J. Am. Chem. Soc. 118 (1996) 1729.

[142] M.R. Nelson, R.F. Borkman, J. Phys. Chem. A 102 (1998) 7860.

[143] F. Rindfleisch, T.P. DiNoia, M.A. McHugh, J. Phys. Chem. 100 (1996) 15581.

[144] E.J. Beckman, Unpublished results.

[145] C. Lepilleur, E.J. Beckman, Fluid Phase. Equil. 134 (1997) 285.

[146] (a) L.A. Kleintjens, R. Koningsveld, M. Gordon, Macromolecules 13 (1980) 303;
(b) S.-J. Chen, M. Banaszak, M. Radosz, Macromolecules 28 (1995) 1812.

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

[148] R. Fink, D. Hancu, R. Valentine, E.J. Beckman, J. Phys. Chem. B 103 (1999) 6441.

[149] Y. Xiang, E. Kiran, Polymer 36 (1995) 4817.

[150] S. Wallen, International Symposium on Supercritical Fluid Technology, Myrtle Beach, SC, 2001.

[151] G. Odian, Principles of Polymerization, third ed, Wiley and Sons, New York, 1991.

[152] K. Fukui, T. Kagiya, H. Yokota, Y. Toriuchi, F. Kuniyoshi, US Patent No. 3,522,228, 1970.

[153] M.L. O'Neill, D. Newman, E.J. Beckman, Polym. Eng. Sci. 39 (1999) 862.

[154] (a) T.J. Romack, J.M. DeSimone, Macromolecules 28 (1995) 8429;
(b) T.J. Romack, J.M. DeSimone, US Patent No. 5,674,957, 1997;
(c) T.J. Romack, J.M. DeSimone, US Patent No. 5,939,501, 1999;
(d) T.J. Romack, J.M. DeSimone, US Patent No. 5,939,502, 1999;
(e) T.J. Romack, J.M. DeSimone, US Patent No. 5,981,673, 1999.

[155] E.R. George (Zeus, Inc.), personal communication, 2002.

[156] T.J. Romack, E.E. Maury, J.M. DeSimone, Macromolecules 28 (1995) 912.

[157] J.A. Hyatt, J. Org. Chem. 49 (1984) 5097.

[158] (a) F. Adamsky, E.J. Beckman, in: J.C. Salamone (Ed.), The Polymeric Materials Encyclopedia, vol. 1A–B, CRC Press, Boca Raton, FL, 1996, p. 54;
(b) E.J. Singley, Development of Fluoroether Amphiphiles and their Applications in Heterogeneous Polymerizations in Supercritical Carbon Dioxide, PhD Thesis, University of Pittsburgh, 1997.

[159] (a) R. Fink, E.J. Beckman. V. Hildebrandt, PCT Int. Appl. (2000) WO 0053639;
(b) R. Fink, E.J. Beckman, Ind. Eng. Chem. Res. (2002) (submitted).

[160] W.C. Bunyard, J.F. Kadla, J.M. DeSimone, J. Am. Chem. Soc. 123 (2001) 7199.

[161] K.E.J. Barrett, Dispersion Polymerization in Organic Media, Wiley and Sons, New York, 1975.

[162] (a) J.M. DeSimone, E.E. Maury, Y.Z. Mencelogu, J.B. McClain, T.R. Romack, J.R. Combes, Science 265 (1994) 356;
(b) D.A. Canelas, D.E. Betts, J.M. DeSimone, Macromolecules 29 (1996) 2818;
(c) D.A. Canelas, J.M. DeSimone, Macromolecules 30 (1997) 5673.

[163] (a) M.L. O'Neill, M.Z. Yates, K.L. Harrison, K.P. Johnston, D.A. Canelas, D.E. Betts, J.M. DeSimone, S.P. Wilkinson, Macromolecules 30 (1997) 5050;
(b) M.Z. Yates, M.L. O'Neill, K.P. Johnston, S. Webber, D.A. Canelas, D.E. Betts, J.M. DeSimone, Macromolecules 30 (1997) 5060.

[164] C. Lepilleur, E.J. Beckman, Macromolecules 30 (1997) 745.

[165] P. Christian, M.R. Giles, R.M.T. Griffiths, D.J. Irvine, R.C. Major, S.M. Howdle, Macromolecules 33 (2000) 9222.

[166] K.A. Shaffer, T.A. Jones, D.A. Canelas, J.M. DeSimone, S.P. Wilkinsonj, Macromolecules 29 (1996) 2704.

[167] (a) M.Z. Yates, G. Li, J.J. Shim, S. Maniar, K.P. Johnston, K.T. Lim, S. Webber, Macromolecules 32 (1999) 1018;
(b) G. Li, M.Z. Yates, K.P. Johnston, K.T. Lim, S. Webber, Macromolecules 33 (2000) 1606.

[168] H. Shiho, J.M. DeSimone, Macromolecules 34 (2001) 1198.

[169] T.J. Romack, E.E. Maury, J.M. DeSimone, Macromolecules 28 (1995) 912.

[170] C.D. Wood, A.I. Cooper, Macromolecules 34 (2001) 5.

[171] R.H. Biddulph, P.H. Plesch, J. Chem. Soc. (1960) 3913.

[172] T. Pernecker, J.P. Kennedy, Polym. Bull. (Berl.) 33 (1994) 13.

[173] (a) M.R. Clark, J.M. DeSimone, Polym. Prepr. (Am. Chem. Soc. Div. Polym. Chem.) 35 (1994) 482;
(b) M.R. Clark, J.M. DeSimone, Macromolecules 28 (1995) 3002.

[174] (a) C.D. Mistele, H.H. Thorp, J.M. DeSimone, J. Macromol. Sci. A 33 (1996) 953;
(b) US Patent No. 5,840,820, 1998.

[175] (a) E.F. Debrabander, P.D. Brothers, US Patent No. 6,051,682, 2000, Apr. 18;
(b) R.C. Wheland, P.D. Brothers, US Patent No. 6,107,423, 2000, Aug. 22;
(c) R.C. Wheland, P.D. Brothers, C. Anolick, C.W. Stewart, US Patent No. 6,228,963, 2001, May 8;
(d) P.D. Brothers, US Patent No. 6,103,844, 2000, Aug 15.

[176] (a) M.F. Cunningham, H.K. Mahabadi, US Patent No. 6,057,409, 2000, May 2;
(b) G.L. Eian, C.L.S. Elsbernd, US Patent No. 5,559,198, 1996, Sept. 24.

[177] http://europa.eu.int/comm./research/growth/gcc/pressroom.
html

[178] (a) A.L.C. Burke, R.D. Givens, M. Jikei, J.M. DeSimone,
Polym. Prepr. 38 (1997) 387;
(b) R.D. Givens, M. Jikei, J.M. DeSimone, Polym. Prepr.
38 (1997) 468.

[179] S.M. Gross, G.W. Roberts, D.J. Kiserow, J.M. DeSimone,
Macromolecules 33 (2000) 40.

[180] C. Shi, J.M. DeSimone, G. Roberts, D.J. Kiserow, Macro-
molecules 34 (2001) 7744.

[181] R.V. Chaudhari, S.P. Gupte, A.A. Kelkar, S. Kanagasaba-
pathy, S. Radhakrishnan, US Patent No. 5,917,077, 1999,
June 29.

[182] Chem. Eng. News 79 (21) (2001) 27.

[183] W.D. McGhee, M.K. Stern, T.E. Waldman, US Patent No.
5,233,010, 1993, Aug 3.

[184] W.F. Hoelderich, G. Dahlhoff, Chem. Innov. 31 (2001) 29.

[185] D. Klempner, K.C. Frisch, Handbook of Polymeric Foams,
Oxford University Press, New York, 1991.

[186] (a) C. Fiorentini, A.C.M. Griffiths, US Patent No. 5,629,027,
1997, May 13;
(b) C. Fiorentini, A.C.M. Griffiths, US Patent No. 5,665,287,
1997, Sept. 9;
(c) C. Fiorentini, A.C.M. Griffiths, US Patent No. 5,639,483,
1997, June 17.

[187] H.-M. Sulzbach, H. Steilen, R. Raffel, R. Eiben, W. Ebeling,
US Patent No. 6,127,442, 2000, Oct. 3.

[188] P. Merriman, US Patent No. 3,184,419, 1965, May 18.

[189] (a) S. Inoue, H. Koinuma, T. Tsuruta, Makromol. Chem.
130 (1969) 210;
(b) S. Inoue, H. Koinuma, T. Tsuruta, J. Polym. Sci. B 7
(1969) 287.

[190] (a) S. Inoue, Chemtech 588 (1976);
(b) A. Rokicki, W. Kuran, Macromol. Sci. Rev. Macromol.
Chem. C21 (1981) 135;
(c) W. Kuran, Prog. Polym. Sci. 23 (1998) 919.

[191] (a) T. Aida, S. Inoue, Macromolecules 15 (1982) 682;
(b) T. Aida, M. Ishikawa, S. Inoue, Macromolecules 19
(1986) 8;
(c) D. Darensbourg, M. Holtcamp, Macromolecules 28
(1995) 7577;
(d) M. Super, E. Berluche, C. Costello, E.J. Beckman,
Macromolecules 30 (1997) 368;
(e) M. Cheng, D.R. Moore, J.J. Reczek, B.M. Chamberlain,
E.B. Lobkovsky, G.W. Coates, J. Am. Chem. Soc. 123 (2001)
8738.

[192] E. Buzdugan, E.J. Beckman, Presentation at the Sixth
International Conference on CO$_2$ Utilization, Breckenridge,
CO, September 10–14, 2001.

[193] M. Super, E.J. Beckman, Trends Polym. Sci. 5 (1997) 236.

[194] (a) K. Soga, S. Hosoda, Y. Tazuke, S. Ikeda, J. Polym. Sci.
Polym. Lett. 13 (1975) 265;
(b) K. Soga, M. Sato, S. Hosoda, S. Ikeda, J. Polym. Sci.
Polym. Lett. 13 (1995) 543.

[195] D.E. Sargent, US Patent No. 2,462,680, 1949.

[196] P.G. Odell, US Patent No. 5,698,665, 1997, Dec. 16.

[197] K.-S. Kim, S. Danishevsky, C.B. Peterson, US Patent No.
6,100,372, 2000, Aug. 8.

[198] (a) A.R. Berens, G.S. Huvard, R.W. Korsmeyer, F.W. Kunig,
J. Appl. Polym. Sci. 46 (1992) 231;
(b) S.G. Kazarian, N.H. Brantley, B.L. West, M.F. Vincent,
C.A. Eckert, Appl. Spectr. 51 (1997) 491.

[199] (a) G.A. Montero, C.B. Smith, W.A. Hendrix, D.L. Butcher,
Ind. Eng. Chem. Res. 39 (2000) 4806 for recent review;
(b) E. Bach, E. Cleve, E. Schollmeyer, Rev. Prog. Colorat.
Rel. Top. 32 (2002) 88 (for recent review).

[200] (a) E. Bach, E. Cleve, E. Schollmeyer, M. Bork, P. Korner,
Melliand. Int. 3 (1998) 192;
(b) E. Bach, E. Cleve, E. Schollmeyer, T. Vardag, P. Korner,
2 (1999) 165;
(c) M.D. Argyle, W.A. Propp, US Patent No. 5,709,910,
1999, Jan. 20;
(d) R. Eggers, J. von Schnitzler, K. Truckenmuller, US Patent
No. 5,938,794, 1999, Aug. 17;
(e) E. Schollmeyer, E. Bach, E. Cleve, M. Bork, M.
Steinhauer, J.-P. Korner, US Patent No. 5,953,780, 1999,
Sept. 21;
(f) R. Eggers, J. von Schnitzler, R. Huber, G. Worner, US
Patent No. 5,958,085, 1999, Sept. 28;
(g) R. Eggers, J. von Schnitzler, G. Worner, US Patent No.
5,972,045, 1999, Oct. 26;
(h) C.B. Smith, G.A. Montero, W.A. Hendrix, US Patent
No. 6,048,369, 2000, Apr. 11;
(i) N. Poddevin, J. Fages, R. Guidoin, US Patent No.
6,120,558, 2000, Sept. 19;
(j) W.A. Hendrix, G.A. Montero, C.B. Smith, D.L. Butcher,
US Patent No. 6,261,326, 2001, July 17.

[201] (a) J.J. Shim, K.P. Johnston, AIChE J. 37 (1991) 607;
(b) J.J. Shim, K.P. Johnston, AIChE J. 35 (1989) 1097.

[202] W.A. Hendrix, J. Industr. Tex. 31 (2001) 43.

[203] A.D. Shine, J. Gelb, US Patent 5,766,637, 1998.

[204] S.M. Howdle, M.S. Watson, M.J. Whitaker, M.C. Davies,
K.M. Shakesheff, V.K. Popov, F.S. Mandel, D.J. Wang,
Chem. Commun. (2001) 109.

[205] (a) F. Mandel, US Patent No. 6,054,103, 2000, April 25;
(b) F. Mandel, US Patent No. 5,993,747, 1999, Nov. 30;
(c) F. Mandel, C.D. Green, A.S. Scheibelhoffer, US Patent
No. 5,548,004, 1996, Aug 20.

[206] E.J. Beckman, M. O'Neill, US Patent No. 6,184,270, 2001,
Feb. 6.

[207] G. Mura, S. Pozzoli, Eur. Pat. Appl. 94119470.6, 1994, Dec.
9.

[208] D. Pierick, The MuCell Molding Technology: Microcellular
Foam. Paper presented at Molding '99 (1999), New Orleans,
March 1–3.

[209] (a) S. Goel, E.J. Beckman, AIChE J. 41 (1995) 357;
(b) C.M. Stafford, T.P. Russell, T.J. McCarthy, Macro-
molecules 32 (1999) 7610;
(c) K.A. Arora, A.J. Lesser, T.J. McCarthy, Macromolecules
31 (1998) 4614.

[210] D. Sparacio, E.J. Beckman, Generation of microcellular
biodegradable polymers using supercritical carbon dioxide,
in: M. Hunt, T. Long (Eds.), Solvent-Free Polymerizations

and Processes: Minimization of Conventional Organic Solvents, vol. 713 (ACS Symposium Series), 1998, pp. 181–195.

[211] A.R. Berens, G.S. Huvard, Supercritical Fluid Science and Technology (ACS Symposium Series 406), 1989, p. 207.

[212] I.S. Liau, M.A. McHugh, High pressure solid polymer—supercritical fluid phase behavior, in: J.M.L. Penninger, M. Radosz, M.A. McHugh, V.J. Krukonis (Eds.), Supercritical Fluid Technology, Elsevier, Amsterdam, 1985, p. 415.

[213] W. Wang, E.J. Kramer, W.H. Sachse, J. Polym. Sci. Polym. Phys. Ed. 20 (1982) 1371.

[214] (a) C. Kwag, C.W. Manke, E. Gulari, J. Polym. Sci. Polym. Phys. 37 (1999) 2771;
(b) J.R. Royer, Y.J. Gay, J.M. DeSimone, S.A. Khan, J. Polym. Sci. Polym. Phys. 38 (2000) 3168.

[215] K. Suh, Extruded Thermoplastic Foams Produced with Supercritical Fluids. Paper presented at the Conference on Supercritical Fluids in Materials Processing and Synthesis, Davos Switzerland, 1999, 9/26-10/1.

[216] G.R. Wilkes, K.A. Bly, H.A. Dunbar, E.R. Uhl, J.L. Zwynenburg, US Patent No. 5,993,706, 1999, Nov. 30.

[217] J. Cebien, Bayer Corporation, personal communication.

[218] R.H. Perry, C.H. Chilton, Chemical Engineering Handbook, fifth ed, McGraw-Hill, New York, 1973.

[219] C. Shi, Z. Huang, S. Kilic, J. Xu, R.M. Enick, E.J. Beckman, A.J. Carr, R.E. Melendez, A.D. Hamilton, Science 286 (1999) 1540.

[220] C.B. Park, N.P. Suh, D.F. Baldwin, US Patent No. 6,051,174, 2000, Apr. 18.

[221] International Roadmap for Semiconductors, Semiconductor Industry Association, San Jose, CA, 1999.

[222] R.D. Allen, G. Wallraff, US Patent No. 5,665,527, 1997, Sept. 9.

[223] (a) H.G. Pryce Lewis, G.L. Weibel, C.K. Ober, K.K. Gleason, Chem. Vap. Dep. 7 (2001) 195;
(b) N. Sundararajan, S. Yang, K. Ogino, S. Valiyaveettil, J. Wang, X. Zhou, C.K. Ober, S. Obendorf, R.D. Allen, Chem. Mat. 12 (2000) 41;
(c) S. Yang, J. Wang, K. Ogino, S. Valiyaveettil, C.K. Ober, Chem. Mat. 12 (2000) 33.

[224] (a) D.K. Taylor, R. Carbonell, J.M. DeSimone, Ann. Rev. Energy Envir. 25 (2000) 115;
(b) J. Kendall, J.M. DeSimone, R.G. Carbonell, C.L. McAdams, PCT Int. Appl. (2002), WO 0231596.

[225] C. Brodsky, J. Byers, W. Conley, R. Hung, S. Yamada, K. Patterson, M. Somervell, B. Trinique, H.V. Tran, S. Cho, T. Chiba, S.-H. Lin, A. Jamieson, H. Johnson, T. Vander Heyden, C.G. Willson, J. Vac. Sci. Tech. B 18 (2000) 3396.

[226] (a) R.C. Carbonell, J.M. DeSimone, B.J. Novick, US Patent No. 6,083,565;
(b) J.M. DeSimone, R.C. Carbonell, US Patent No. 6,001,418.

[227] M. McCoy, Chem. Eng. News 79 (38) (2001) 10.

[228] D. Voss, Tech. Rev. 105 (2002) 27.

[229] Chem. Eng. News 79 (38) (2001) 10.

[230] Chem. Eng. News 79 (50) (2001) 14.

[231] (a) V.K. Agarwal, US Patent No. 6,306,754, 2001, Oct. 23;
(b) H-J. Lee, D.G.-K. Jeng, US Patent No. 6,319,858, 2001, Nov. 20.

[232] A.M. Klibanov, Trends Biotech. 15 (1997) 97.

[233] A. Mesiano, E.J. Beckman, A.J. Russell, Chem. Rev. 99 (1999) 623.

[234] (a) S. Kamat, J. Barrera, E.J. Beckman, A.J. Russell, Biotech. Bioeng. 40 (1992) 158;
(b) S. Kamat, G. Critchley, E.J. Beckman, A.J. Russell, Biotech. Bioeng. 46 (1995) 610.

[235] K.P. Johnston, K.L. Harrison, M.J. Clarke, S.M. Howdle, M.P. Heitz, F.V. Bright, C. Carlier, T.W. Randolph, Science 271 (1996) 624.

[236] (a) E. Ghenciu, A.J. Russell, E.J. Beckman, Biotech. Bioeng. 58 (1998) 572;
(b) E.G. Ghenciu, E.J. Beckman, Industr. Eng. Chem. 36 (1997) 5366.

[237] A.K. Chaudhary, E.J. Beckman, A.J. Russell, J. Am. Chem. Soc. 117 (1995) 3728.

[238] R.D. Weinstein, A.R. Winslo, R.L. Danheiser, J.G. Harris, J.W. Tester, J. Phys. Chem. 100 (1996) 12337.

[239] J.T. Reaves, C.B. Roberts, Ind. Eng. Chem. Res. 38 (1999) 855.

[240] J. Matsuo, T. Tsuchiya, K. Odashima, S. Kobayashi, Chem. Lett. (2000) 178.

[241] Y. Ikushima, N. Saito, M. Arai, J. Phys. Chem. 96 (1992) 2293.

[242] A.R. Renslo, R.D. Weinstein, J.W. tester, R.L. Danheiser, J. Org. Chem. 62 (1997) 4530.

[243] R.S. Oakes, T.J. Heppenstall, N. Shezad, A.A. Clifford, C.M. Rayner, Chem. Commun. (1999) 1459.

[244] H. Totoe, A.E. McGowin, K. Turnbull, J. Supercrit. Fluids 18 (2000) 131.

[245] J.E. Chateauneuf, K. Nie, Adv. Envir. Res. 4 (2000) 307.

[246] (a) A. Kawada, S. Mitamura, J. Matsuo, T. Tsuchiya, S. Kobayashi, Bull. Chem. Soc. Jap. 73 (2000) 2325;
(b) S. Kobayashi, K. Manabe, Pure. Appl. Chem. 72 (2000) 1373.

[247] M.G. Hitzler, F.R. Smail, S.K. Ross, M. Poliakoff, Chem. Commun. (1998), 359.

[248] G.A. Olah, E. Marinez, B. Torok, G.K. Surya Prakash, Catal. Lett. 61 (1999) 105.

[249] T. Pernecker, J.P. Kennedy, Polym. Bull. (Berl.) 32 (1994) 537.

[250] (a) R. Fornika, H. Gorls, B. Seemann, W. Leitner, Chem. Commun. (1995) 1479;
(b) W. Leitner, Angew. Chem. Int. Ed. Eng. 34 (1995) 2207.

[251] P.E. Jessop, Y. Hsiao, T. Ikariya, R. Noyori, J. Am. Chem. Soc. 118 (1996) 344.

[252] M. Shi, K.M. Nicholas, J. Am. Chem. Soc. 119 (1997) 5057.

[253] K. Ushikoshi, K. Mori, T. Watanabe, M. Takeuchi, M. Saito, in: T. Inui, M. Anpo, K. Izui, S. Yanagida, T. Yamaguchi (Eds.), Advances in Chemical Conversions for Mitigating Carbon Dioxide. Studies in Surface Science and Catalysis, vol. 114, Elsevier Science, New York, 1998, p. 357.

[254] H. Arakawa, et al., Chem. Rev. 101 (2001) 953.

[255] N. Yamazaki, S. Nakahama, F. Higashi, Ind. Eng. Chem. Prod. Res. Dev. 18 (1979) 249.

[256] A.-A.G. Shaikh, S. Sivaram, Chem. Rev. (1996) 951.

[257] (a) A. Behr, Carbon Dioxide Activation by Metal Complexes, VCH, New York, 1988;
(b) M.M. Halmann, Chemical Fixation of Carbon Dioxide: Methods for recycling CO2 into Useful Products, CRC Press, London, 1993;
(c) D.H. Gibson, Chem. Rev. 96 (1996) 2063 Also, see Ref. [124] from our Ref. [245].

[258] (a) L. Jia, H. Jiang, J. Li, Green Chem. 1 (1999) 91;
(b) Y. Kishimoto, T. Ikariya, J. Org. Chem. 65 (2000) 7656.

[259] (a) D.K. Morita, D.R. Pesiri, S.A. David, W.H. Glaze, W. Tumas, Chem. Commun. (1998) 1397;
(b) W. Chen, L. Xu, J. Xiao, Org. Lett. 2 (2000) 2675;
(c) B.M. Bhanage, Y. Ikushima, M. Shirai, M. Arai, Tetrahed. Lett. 40 (1999) 6427;
(d) T. Osswald, S. Schneider, S. Wang, W. Bannwarth, Tetrahed. Lett. 42 (2001) 2965.

[260] S. Cacchi, G. Fabrizi, F. Gasparrini, C. Villani, Synlett 3 (1999) 345.

[261] L.-N. He, J.-C. Choi, T. Sakakura, Tetrahed. Lett. 42 (2001) 2169.

[262] F. Montilla, E. Clara, T. Aviles, T. Casimiro, A. Aguicar Ricardo, M. Nunes de Ponte, J. Organomet. Chem. 626 (2001) 227.

[263] A. Kabir, W.D. Marshall, Green Chem. 3 (2001) 47.

[264] N. Jeong, S.H. Hwang, Angew Chem. Int. Ed. Eng. 39 (2000) 636.

[265] M. Poliakoff, T.M. Swan, T. Tacke, M.G. Hitzler, S.K. Ross, S. Wieland, F.R. Smail, US Patent No. 6,303,840, 2001, Oct. 16.

[266] B. Subramaniam, M.C. Clark, US Patent No. 5,907,075, 1999, May 25.

[267] S.K. Ritter, Chem. Eng. News 79 (40) (2001) 63.

[268] (a) R. Harris, S.H. Jureller, J.L. Kerschner, P.T. Trzasko, R.W.R. Humphreys, US Patent No. 5,977,348, 1999, Nov. 2;
(b) D.A. Schiraldi, J.S. Brown, K. Chandler, C.A. Eckert, J.S. Hurley, D.R. Lamb, P.H. Lesutis, C.L. Liotta, US Patent No. 6,204,386, 2001, March 20.

[269] R. Lowack, J. Meyer, M. Eggersdorfer, P. Grafen, US Patent No. 5,523,420, 1996, Jun. 4.

[270] D.W. Matson, J.L. Fulton, R.D. Smith, K.A. Consani, US Patent No. 5,238,671, 1993, Aug. 24.

[271] M. Ji, X.Y. Chen, C.M. Wai, J.L. Fulton, J. Am. Chem. Soc. 121 (1999) 2631.

[272] J.P. Cason, K. Khamwasadkar, C.B. Roberts, Ind. Eng. Chem. Res. 39 (2000) 4749.

[273] K.E. Laintz, C.M. Wai, C.R. Yonker, R.D. Smith, J. Supercrit. Fluids 4 (1991) 194.

[274] (a) C. Erkery, J. Supercrit. Fluids 17 (2000) 259, for a review;
(b) C.M. Wai, S. Wang, J. Chromatogr. A 785 (1997) 369, for a review;
(c) N.G. Smart, T. Carleson, T. Kast, A.A. Clifford, M.D. Burford, C.M. Wai, Talanta 44 (1997) 137, for a review.

[275] (a) A.F. Lagalante, B.N. Hansen, T.J. Bruno, R.E. Sievers, Inorg. Chem. 34 (1995) 5781;
(b) W.C. Anderson, R.E. Sievers, A.F. Lagalante, T.J. Bruno, J. Chem. Eng. Data 45 (2001) 1045.

[276] (a) W. Dicinoski, Min. Mag. 182 (2000) 258 (also pp. 260 and 262);
(b) R.H. White, Copper Leaching, Solvent Extraction and Electrowinning, Society of Mineral and Metallic Exploration, Littleton, CO, 1999, p. 229;
(c) B. Townsend, K.J. Sievers, Min. Mag. 162 (1990) 26 also pp. 29, 32, 35;
(d) D.S. Flett, Inst. Min. Met. Trans. Sect. C 83 (1974) C30.

[277] (a) M. Olper, M. Maccagni, C.J.N. Buisman, C.E. Schultz, In: S.K. Young (Ed.), Proceedings of the Copper 99-Cobre Ninety-ninth International Conference, vol. 4, (fourth ed.), Mineral, Metallic and Materials Society, 1999, p. 597;
(b) D. Valic, A.S. Tombalakian, A. Alfantazi, R.R. Moskalyk, In: S.K. Young (Ed.), Proceedings of the Copper 99-Cobre Ninety-ninth International Conference, vol. 3, (fourth ed.), Mineral, Metallic and Materials Society, 1999, p. 711.

[278] W.G. Davenport, In: S.K. Young (Ed.), Proceedings of the Copper 99-Cobre Ninety-ninth International Conference, vol. 1, (fourth ed.), Mineral, Metallic and Materials Society, 1999, p. 55.

[279] T.B. Braun, J. Met. 33 (1981) 59.

[280] (a) L.S. Benner, T. Suzuki, K. Meguro, S. Tanaka (Eds.), Precious Metals: Science and Technology, Institute of Precious Metals Institute, Allentown, PA, 1991;
(b) G.B.A. Harris, in: R.K. Mishra (Ed.), Precious Metals, Pergamon Press, Toronto, Canada, 1993, p. 351.

[281] C.J. Powell, E.J. Beckman, Ind. Eng. Chem. Res. 40 (2001) 2897.

[282] (a) R.M. Izatt, J.S. Bradshaw, R.L. Bruening, Pure Appl. Chem. 68 (1996) 1237 (for example);
(b) List of publications on IBC web site: http://www.ibcmrt.com/publications

[283] (a) J.H. Sherman, J.W. Hershberger, R.T. Taylor, G.M. Garrett, PCT Int. Appl. (2000), WO 0056842;
(b) B.J. Bertus, D.W. Walker, US Patent No. 4,727,053, 1988;
(c) J.C.D. Macedo, M.A.I. Duarte, Appl. Cat. A 110 (1994) 87;
(d) Roussel, J.-C., Boulet, R., Pet. Refin. (1995) 1 (Crude Oil, Petroleum Products, Process Flowsheets), 1–15, 453–60;
(e) C.D. Pearson, J.B. Green, Energy Fuels 7 (1993) 338;
(f) P.C.H. Mitchell, Catal. Today 7 (1990) 439;
(g) J.G. Reynolds, US Patent No. 4,789,463, 1988.

[284] (a) J.-T. Li, E.J. Beckman, Ind. Eng. Chem. Res. 37 (1998) 4768;
(b) K.E. Laintz, C.D. Hale, P. Stark, C.L. Rouquette, Anal. Chem. 70 (1998) 400.

[285] (a) J.-J. Yu, K.-H. Chiu, S. Wang, J. Chin. Inst. Chem. Eng. 32 (2001) 263;

(b) Y. Lin, H. Wu, N.G. Smart, C.M. Wai, Sep. Sci. Tech. 36 (2001) 1149;

(c) F. Gervais, C. Perre, S. Sarrade, P. Moszkowicz, L. Barna, Rec. Prog. Gen. Proc. 13 (1999) 197;

(d) M. Shamsipur, A.R. Ghiasvand, Y. Yamini, J. Supercrit. Fluids 20 (2001) 163;

(e) C.M. Wai, B. Waller, Ind. Eng. Chem. Res. 39 (2000) 4837;

(f) C. Kersch, G.F. Woerlee, G.J. Witkamp, in: K.C. Liddell (Ed.), Metal Separation Technologies Beyond : Integrating Novel Chemistry with Processing, Mineral, Metallic and Material Society, Warrendale, PA, 2000, p. 2002.

[286] (a) F.G. Baglin, US Patent No. 5,897,704, 1999, April 27.;
(b) R.H. Jones, US Patent No. 5,965,201, 1999, Oct. 12.

[287] M.A. Douglas, A.C. Templeton, US Patent No. 5,868,856, 1999, Feb. 9.

[288] B.A. Vaartstra, US Patent No. 6,149,828, 2000, Nov. 12.

[289] K. Chandler, C.W. Culp, D.R. Lamb, C.L. Liotta, C.A. Eckert, Ind. Eng. Chem. Res. 37 (1998) 3252.

[290] G.B. Jacobsen, C.T. Lee, K.P. Johnston, J. Org. Chem. 64 (1999) 1201–1207.

[291] R.J. Bonilla, B.R. James, P.G. Jessop, Chem. Commun. (2000) 941.

[292] M.A. Quadir, R. Snook, R.G. Gilbert, J.M. DeSimone, Macromolecules 30 (1997) 6015.

[293] L.A. Blanchard, D. Hancu, E.J. Beckman, J.F. Brennecke, Nature 399 (1999) 28.

[294] M.F. Sellin, P.B. Webb, D.J. Cole-Hamilton, Chem. Commun. (2001) 781.

[295] A. Bosmann, G. Francio, E. Janssen, M. Solinas, W. Leitner, P. Wasserscheid, Angew Chem. Int. Ed. Eng. 40 (2001) 2697.

[296] L.A. Blanchard, J.F. Brennecke, Green Chem. 3 (2001) 17.

[297] D.W. Matson, R.C. Peterson, R.D. Smith, J. Mater. Sci. 22 (1987) 1919.

[298] J. Jung, M. Perrut, J. Supercrit. Fluids 20 (2001) 179.

[299] (a) B. Bungert, G. Sadowski, W. Arlt, Ind. Eng. Chem. Res. 37 (1998) 3208;
(b) U.B. Kompella, K. Koushik, Crit. Rev. Ther. Drug. Carr. Sys. 18 (2001) 173;
(c) E. Reverchon, G. Della Porta, Pure Appl. Chem. 73 (2001) 1293;
(d) R. Marr, T. Gamse, Chem. Eng. Proc. 39 (2000) 19;
(e) S. Palakodaty, P. York, Pharm. Res. 16 (1999) 976;
(f) E. Reverchon, J. Supercrit. Fluids 15 (1999) 21.

[300] P.M. Gallagher, M.P. Coffey, V.J. Krukonis, N. Klasutis, K.P. Johnston J.M.L. Penninger (Eds.), Supercritical Science and Technology (1989) American Chemical SocietyWashington, DC. ACS Symp. Ser. 406.

[301] (a) M. Hanna, P. York, World Patent WO 95/01221, 1994;
(b) M. Hanna, P. York, World Patent WO 96/00610, 1995;
(c) M. Hanna, P. York, US Patent 6,063,138, 2000.

[302] (a) R.E. Sievers, U. Karst, Eur. Pat. 0 677 332, 1995; and US Patent No. 5,639,441, 1997;
(b) R.E. Sievers, U. Karst, P.D. Milewski, S.P. Sellers, B.A. Miles, J.D. Schaefer, C.R. Stoldt, C.Y. Xu, Aer. Sci. Tech. 30 (1999) 3;
(c) R.E. Sievers, U. Karst, US Patent No. 6,095,134, 2000.

[303] Y.-F. Maa, S.J. Prestrelski, Curr. Pharma. Biotech. 1 (2000) 283.

[304] R. Thibert, R. Tawashi, Microspheres, Microcapsules, and Liposomes (Preparation and Applications), 1 (1999) 327.

[305] R.H. Perry, C.H. Chilton, Chemical Engineers Handbook, fifth ed, McGraw-Hill, New York, 1973.

[306] (a) M. Kileen, Powd. Bulk. Eng. 8 (1994) 39;
(b) S. Mortensen, D. Lohmann, Chem.-Tech. 21 (1992) 72;
(c) J. Weers, Innov. Pharm. Tech. 1 (2000) 111–114;
(d) K. Jono, H. Ichikawa, Y. Fukumori, Powd. Tech. 113 (2000) 269.

[307] B.Y. Shekunov, P. York, J. Cryst. Growth 211 (2000) 122.

[308] (a) M. Weber, L.M. Russell, P.G. Debenedetti, J. Supercrit. Fluids 23 (2002) 65;
(b) J.O. Werling, P.G. Debenedetti, J. Supercrit. Fluids 18 (2000) 11;
(c) J.O. Werling, P.G. Debenedetti, J. Supercrit. Fluids 16 (1999) 167;
(d) X. Kwauk, P.G. Debenedetti, J. Aerosol. Sci. 24 (1993) 445;
(e) J.W. Tom, P.G. Debenedetti, J. Aerosol. Sci. 22 (1991) 555;
(f) P.G. Debenedetti, AIChE J. 36 (1990) 1289.

[309] C.S. Lengsfeld, J.P. Delplanque, V.H. Barocas, T.W. Randolph, J. Phys. Chem. B 104 (2000) 2725.

[310] J. Texter, Surfact. Sci. Ser. 100 (2001) 577. Reactions and Synthesis in Surfactant Systems.

[311] L. Hong, J. Guo, Y. Gao, W.-K. Yuan, Ind. Eng. Chem. Res. 39 (2000) 4882.

[312] (a) M.C. Manning, T.W. Randolph, E. Shefter, R.F. Falk, US Patent No. 5,981,474, 1999;
(b) M.C. Manning, T.W. Randolph, E. Shefter, R.F. Falk, US Patent No. 5,770,559, 1998.

[313] (a) B. Subramaniam, S. Saim, R.A. Rajewski, V. Stella, US Patent No. 5,874,029, 1999;
(b) B. Subramaniam, S. Saim, R.A. Rajewski, V. Stella, US Patent No. 5,833,891, 1998.

[314] (a) A.T. Daly, O.H. Decker, R. Wursthorn, US Patent No. 5,766,522, 1998;
(b) A.T. Daly, N.B. Shah, G.D. Cornell, K.R. Wursthorn, US Patent No. 5,708,039.

[315] R.A. Sheldon, in: P. Tundo, L. Clemenza, A. Perosa (Eds.), College Lectures of Summer Schools on Green Chemicals, 2001, p. 41.