SUPERCRITICAL CARBON DIOXIDE AS A UNIQUE REACTION MEDIUM

Reported by Melissa Witmer November 26, 2001

INTRODUCTION

Supercritical fluids are becoming increasingly important in industry partly in response to the adverse environmental impact of solvent use and disposal. Carbon dioxide has received special attention as a result of its easily accessible supercritical point (31 °C, 75.8 bar). Supercritical carbon dioxide (SC-CO_2) is a desirable replacement for organic solvents because it is inexpensive, non-toxic, non-flammable, and exhibits ease of recycling and disposal.[1] These properties make it an especially suitable solvent for large-scale industrial synthesis. In fact, two small-scale plants using SC-CO_2, one owned by Thomas Swan & Co. and the other by DuPont, have been in operation for several years. Thomas Swan & Co. has very recently completed a large plant for the use of supercritical carbon fluids in industrial scale synthesis. In addition, DuPont has allocated $40 million for the construction of a plant for the production of fluoropolymers that is expected to be fully functional by 2006.

At the First International Symposium on Supercritical Fluid in 1998, Dr. Val Krukonis, an expert in the field and founder of Phasex corporation, stated, "There's no point in doing something in supercritical fluid just because it's neat. Using the fluids must have some real advantage."[2] In deference to this sound advice, this review will be focused on reactions in which the outcome either cannot be obtained using traditional organic solvents or is influenced to a great extent by the unique properties of SC-CO_2.

The first part of this review will focus on how the physical properties of SC-CO_2 can affect the reaction rates and product distributions of several organic reactions. The second part will provide some examples in which SC-CO_2 is used both as a solvent and reactant.

PROPERTIES OF SUPERCRITICAL CO_2

The boundaries between the solid, liquid and gas phases are shown in a typical phase diagram (Figure 1). The supercritical fluid state occurs above the critical temperature when increasing the pressure no longer causes a phase change to liquid. Unlike the gas, solid, and liquid phases; the supercritical fluid phase of CO_2 near the critical point is inhomogeneous.[3] Low and high-density regions exist in equilibrium throughout the medium. The loss of entropy when a molecule of CO_2 moves from a low density to high-density region is balanced by the increase in favorable intermolecular interactions. As a consequence, SC-CO_2 is easily compressed near its critical point; and many bulk properties such as solvent density, dielectric constant, and solubility parameter change dramatically with small changes in pressure. Thus, SC-CO_2 is a tunable solvent which can be adjusted to accommodate a wide variety of reactions.

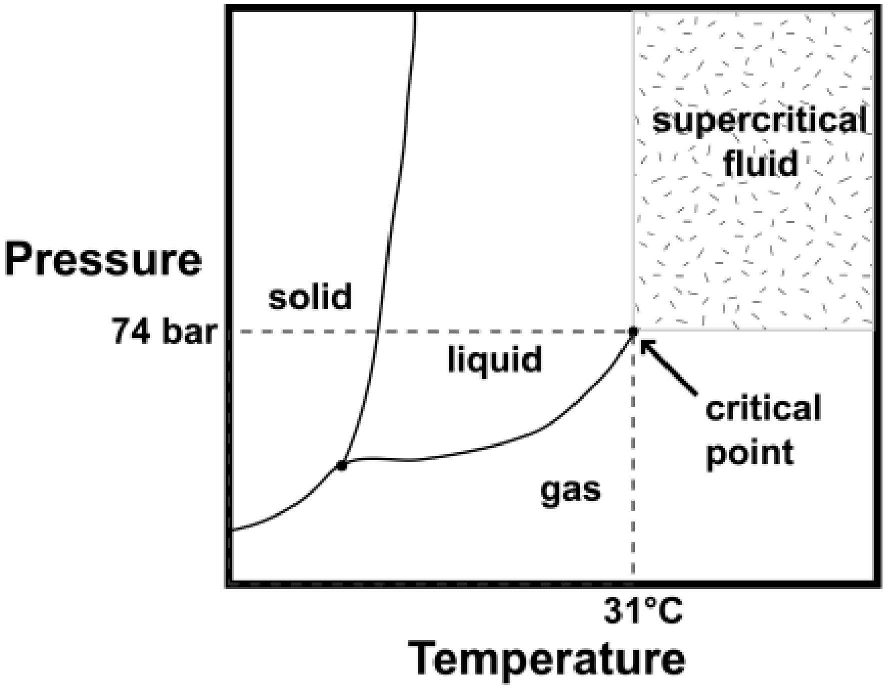
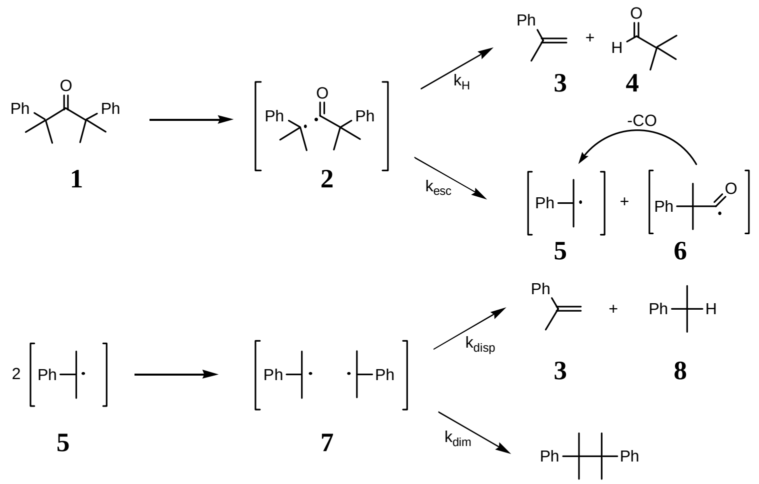


Figure 1. Representative phase diagram for CO_2

Many studies have reported the effects of solvent heterogeneity in SC-CO_2. It is believed that when solutes are placed in SC-CO_2, they are surrounded by the more dense regions of the supercritical fluid. This effect is called “clustering,” and may result in enhanced solvent cage effects. Recent studies by Tanko and coworkers have probed the solvent cage effects of both geminate and diffusive caged radical pairs.[4]

The photolytic cleavage of dicumyl ketone **1** leads to the formation of various products (Scheme 1). Hydrogen abstraction within solvent cage **2** yields **3** and **4**. By contrast, escape from the solvent cage **2** gives radical **5.** This radical can associate to form the diffusion radical cage **7** which leads to the disproportionation products of **8** and **3,** resulting from hydrogen abstraction or to **9** by dimerization. A comparison of the quantities of products obtained provides information on the rates of escape and rates of hydrogen abstraction occuring in geminate solvent cage **2**. The ratio of products (**8** + **9**):**4** reveals the relative rate of escape (k_{esc}) from radical cage **2** versus the rate of hydrogen abstraction within the solvent cage(k_H). In addition, the ratio of k_{dim}/k_{disp} is directly related to the ratio of products **9/8**. The relative rates of dimerization versus disproportionation are a sensitive probe of local solvent density because there are more geometric constraints for the dimerization reaction than for the disproportionation. Since the local density affects the ease of rotation of the solute, k_{dim}/k_{disp} is expected to decrease with increasing local solvent density.

Scheme 1



The photolysis reaction was performed under various pres 9 of SC-CO_2 to probe the effects of increasing viscosity and local solvent density on the various rates. Two interesting results were obtained. Above 1800 psi both k_{esc}/k_H and k_{dim}/k_{disp} diminish with increasing pressure of SC-CO_2. This decrease is anticipated because the increase in viscosity slows the rate of radical escape from the solvent cage and slows the rotation of **5** within solvent cage **7**. However, the ratios are about half of what would be expected based on viscosity studies in conventional solvents. These results indicate that at pressures above 107.5 bar, SC-CO_2 displays enhanced solvent cage effects compared to organic solvents. In contrast, k_{esc}/k_H and k_{dim}/k_{disp} *increases* with increasing pressure below 107.5 bar. In fact, k_{ecs}/k_h is about the same at 77.5 bar and 588.3 bar. These results support the theory of a clustering effect where the local solvent density is greater than that of the bulk fluid. Computer simulations suggest that the cause of these effects is the favorable interaction of SC-CO_2 with aromatic compounds through polarization of one of the C==O bonds. These results show that SC-CO_2 demonstrates special properties near the critical point which are not found in traditional organic solvents. The effects of clustering and increased cage effects can explain unexpected rates and product distributions found in some of the reactions discussed herein.

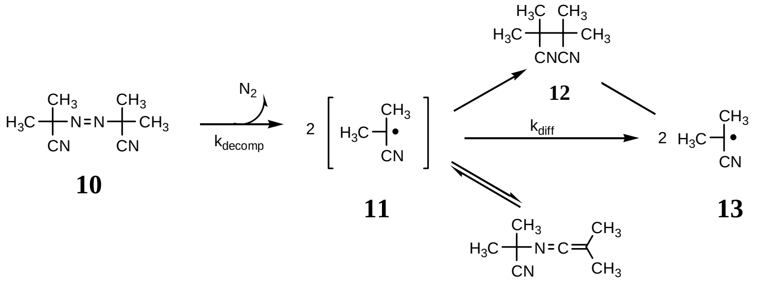
EFFECTS OF SC-CO_2 PROPERTIES ON ORGANIC REACTIONS

Radical decomposition

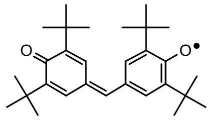
Similar to the free radical studies described above, DeSimone and coworkers have extensively studied the decomposition of free radical initiator 2,2’-azobis(isobutyronitrile) **10** (AIBN) in SC-CO_2.[5,6]

The rate of decomposition of **10** to **11** was found to be slower in SC-CO_2 than in traditional organic solvents. For example, the rate of AIBN decomposition in SC-CO_2 is $3.5 \times 10^{-6}s^{-1}$ and $8.4 \times 10^{-6}s^{-1}$ in benzene at ambient temperature. The lower rate of decomposition in SC-CO_2 is believed to result from the lower dielectric constant of this medium compared to organic solvents. This is further supported by the observation that the addition of small amounts of THF greatly enhances the rate of decomposition (Scheme 2).

Scheme 2



Trapping studies using the radical trap galvinoxyl **14** show that AIBN has a higher efficiency factor in SC-CO_2 (0.83) than in benzene (0.53).[5] The efficiency factor is a measure of the fraction of radicals that propagate through the solution to those that either dimerize to **12** or participate in a disproportionation reaction (Scheme 2). The higher efficiency factor is attributed to the low viscosity of SC-CO_2. Higher initiation efficiency and tunable rates of dissociation of AIBN have important implications in the field of polymer chemistry in which AIBN is a commonly used free radical initiator.



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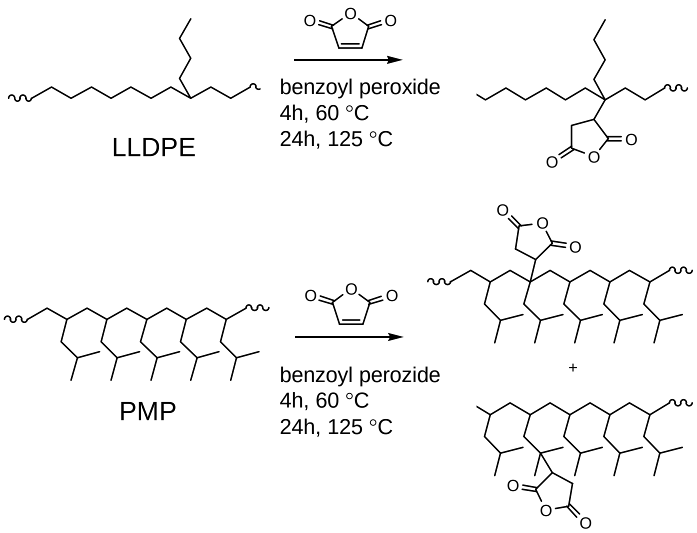
Polymerizations in SC-CO_2

The first homogeneous free radical polymerization in SC-CO_2 was reported in 1992 by DeSimone and coworkers.[5] SC-CO_2 is an ideal solvent for the polymerizations of fluoropolymers and silicon-based polymers which display limited solubility in organic solvents. Moreover, although most commercial polymers are not soluble in SC-CO_2, they can be synthesized in biphasic dispersion and emulsion polymerizations.[7,8] The molecular weights and polymer properties obtained in SC-CO_2 are similar to those obtained by analogous polymerization methods in organic solvents. Therefore, the incentives of using SC-CO_2 as a solvent lie not in the polymerization reaction, but in the decreased cost of polymer processing.[9] Polymers synthesized in SC-CO_2 can be isolated simply by depressurization of the reaction vessel. The CO_2 is easily collected and recycled, eliminating the cost of solvent disposal. In addition, the costly and energy intensive drying procedure, typical in polymer manufacturing using traditional solvents is greatly reduced.[7] Moreover, due to the increased plasticity of polymers in SC-CO_2, residual monomer and catalysts are easily removed from the polymer matrix.[9]

SC-CO_2 can also be used to incorporate monomers for the generation of polymer blends or other small molecules for polymer modification.[10,11,12] McCarthy and coworkers used the SC-CO_2 as a carrier of maleic anhydride to functionalize linear low density polyethylene (LLDPE) and poly(4-methyl-1-pentene) (PMP) (Scheme 3). Maleation to the extent of 2.96-3.52 % by weight in LLDPE and 2.06-2.62 % by weight in PMP was reported. This is a significantly higher level of functionalization than is available in commercial maleated polymers which have nearly undetectable levels of maleation.

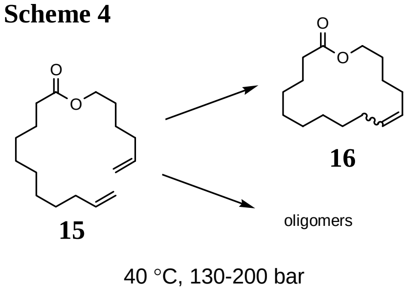
Scheme 3



Olefin metathesis

Tuning the properties of SC-CO_2 through changes in pressure can also affect the outcome of olefin metathesis.[13] At 130 bar, 8% ring closing metathesis product **16** was obtained from **15** and 68% of the product was oligomer (Scheme 4). However, increasing the pressure to 200 bar increased the percent of product **16** to 87% and decreased oligomer formation to about 2%. Isothermal increases in pressure increase the density of SC-CO_2, favoring improved yields of the intramolecular ring closing metathesis product **16** versus intermolecular formation of oligomers. This observation at first seems counterintuitive and is the opposite to the behavior observed in traditional organic solvents. Usually increased pressure favors intermolecular reaction in order to decrease the number of moles in solution. But within a certain range, increasing the pressure of SC-CO_2 at a constant volume forces more molecules of CO_2 between solute molecules thus, mimicking the effects of increased dilution in traditional solvents.

Scheme 4



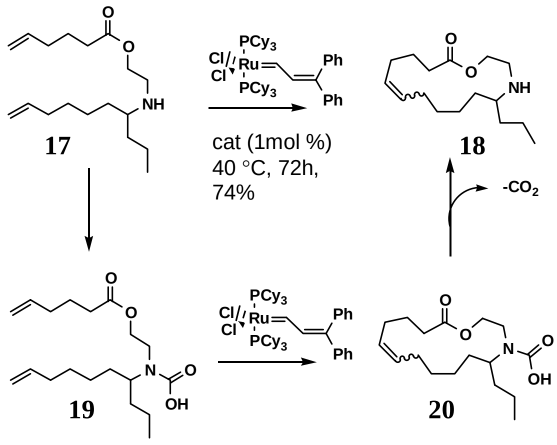
SC-CO_2 AS A REACTANT

In addition to acting as a solvent with unique physical properties, SC-CO_2 proves to have synthetic utility a variety of reactions. Furstner and coworkers report the use of SC-CO_2 as a labile protecting group for secondary amines whereas Noyori *et al.* use SC-CO_2 as a C1 building block.[13,14,15]

CO_2 as a protecting group

The volatility of carbon dioxide allows it to act as a temporary *in situ* protecting group for secondary amines. Recent reports by Furstner *et al.* show the metathesis of **17** to give **18** in 74% yield in SC-CO_2 without protection of the secondary amine (Scheme 5).[13] This is a convenient solution to one of the few limitations of the metathesis reaction; secondary amines poison ruthenium metathesis catalysts in traditional organic solvents.[16] In SC-CO_2 protection is not necessary because the carbon dioxide itself acts as a temporary protecting group for the amine. When the reaction vessel is vented, the carbamic acid **20** reverts spontaneously to the amine **19** without the need for an additional deprotection step.

Scheme 5



SC-CO_2 as a carbon source

Noyori and coworkers use SC-CO_2 as a carbon source in the formation of formic acid, methyl formate, and dimethyl formamide.[14,15] Noyori *et al.* report the homogeneous hydrogenation of SC-CO_2

to give formic acid (Equation 1). Additives such as water, methanol and DMSO all accelerate the rate of reaction as long as only one phase is observed in the reaction vessel. Yields, product distributions, and rates of reaction are all sensitive to temperature, the addition of co-solvents, and H_2 pressure. The yields and rates observed are also very sensitive to the phase behavior of SC-CO_2.

Under optimized conditions, formic acid was produced at turnover frequencies exceeding 4000 h^{-1} (turnover frequency = moles product/moles catalyst per hour) (Equation 2). Methyl formate was produced with turnover number (TON) of 3500. The TON, which is a measure of moles of product/mol catalyst, is one order of magnitude greater than any pervious reported result at any temperature. DMF was produced at a turnover frequency of 8000 h^{-1} and a TON of 420 000. This result is two orders of magnitude greater than any previously published TON.

1) $$CO_2 + H_2 \xrightarrow[\text{SC-}CO_2]{\text{cat., base}} HCO_2H$$

2) $$CO_2 + H_2 + CH_3OH \xrightarrow[\text{SC-}CO_2]{\text{cat.}} HCO_2CH_3 + H_2O$$

3) $$CO_2 + H_2 + NHR_2 \xrightarrow[\text{SC-}CO_2]{\text{cat.}} HCONR_2 + H_2O$$

The high degree of solubility of H_2 gas in SC-CO_2 is one factor contributing to the improved results of these reactions in this medium. Only in super critical fluids can the catalyst and all of the reagents be dissolved in the same phase. A weaker coordination sphere surrounding the catalyst may also contribute to an increase in the reaction rate. Furthermore, it is believed that the lifetime of the catalyst is longer in SC-CO_2 than in organic solvents. The increased rate paired with the increased lifetime of the catalyst lead to significantly higher product yields.

CONCLUSIONS

Many unique properties of SC-CO_2 make it a useful solvent for a wide variety of reactions. Unlike traditional organic solvents, SC-CO_2 is a tunable solvent with the density, dielectric constant, and viscosity dependant on pressure. The utility of SC-CO_2 as a reactant has also been demonstrated in a number of reactions.

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