LA-UR- 99-1246

Title: "Supercritical Fluids: Reactions, Materials and Applications"

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Submitted to: 6th Conference on Supercritical Fluids
Oxford University
Nottingham, England
April 9 - 16, 1999

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Supercritical Fluids: Reactions, Materials and Applications

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INTRODUCTION

A number of important processes utilizing supercritical fluids have been either implemented or are emerging for extractions, separations and a wide range of cleaning applications. Supercritical fluids can be reasonable solvents yet share many of the advantages of gases including miscibility with other gases (i.e. hydrogen and oxygen), low viscosities and high diffusivities. Carbon dioxide has the further advantages of being nontoxic, nonflammable, inexpensive and currently unregulated. The use of compressed gases, either as liquids or supercritical fluids, as reaction media offers the opportunity to replace conventional hazardous solvents and also to optimize and potentially control the effect of solvent on chemical and material processing. The last several years has seen a significant growth in advances in chemical synthesis, catalytic transformations and materials synthesis and processing.

We will report on results from an exploratory program at Los Alamos National Laboratory aimed at investigating the use of dense phase fluids, particularly carbon dioxide, as reaction media for homogeneous, heterogeneous and phase-separable catalytic reactions in an effort to develop new, environmentally-friendly methods for chemical synthesis and processing. This approach offers the possibility of opening up substantially different chemical pathways, increasing selectivity at higher reaction rates, facilitating downstream separations and mitigating the need for hazardous solvents.

Developing and understanding chemical and catalytic transformations in carbon dioxide could lead to greener chemistry at three levels:

1. Solvent replacement
2. Better chemistry (e.g. higher reactivity, selectivity, less energy consumption)
3. New chemistry (e.g. novel separations, use of CO_2 as a C-1 source).

HOMOGENEOUS CATALYSIS

The last decade has seen enormous growth in the scientific literature on chemical reactions and catalytic processes in supercritical carbon dioxide and other fluids. A recent Chemical Review issue has been dedicated to the field and provides an excellent review of catalytic reactions (1). It is becoming clear that there are a number of avenues to capitalize on the properties of carbon dioxide for new or improved chemistry. An excellent opportunity for identifying potential areas could include one or more of the following:

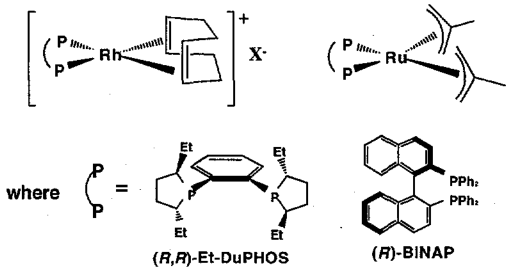
1. reactions with gaseous reagents such as oxygen or hydrogen (i.e. gas miscibility)
2. reactions involving oxidation, i.e. oxidation stability of the solvent
3. reactions that require hazardous solvents, e.g. some high-value pharmaceuticals
4. reactions that exhibit sigificant solvent effects, e.g. "pressure tunability"
5. reactions that are highly exothermic, i.e. heat transfer medium
6. reactions that could benefit from enhanced downstream separations

We and others have found that dense phase fluids, particularly carbon dioxide, are effective solvents for a wide range of homogeneous catalytic transformations. A major focus of our research program at Los Alamos over last few years has been to benchmark reactivities and selectivities of catalytic reactions in liquid and supercritical carbon dioxide by comparing rates and yields of known homogeneous catalytic transformations with those obtained in conventional organic solvents. We will discuss product distributions, selectivity, kinetics, temperature/pressure effects and mechanistic studies of three important classes of catalytic reactions, catalytic oxidations, asymmetric hydrogenations/reductions and carbon-carbon bond forming reactions. Experimental details and reactor concepts have been described elsewhere (2,3). Reactions investigated in our laboratory to date include:

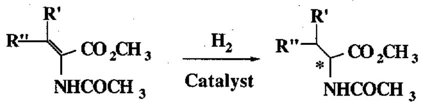
- dihydroxylation or cleavage of olefins by Ru and Os phase transfer catalysts (2)
- vanadium and titanium-catalyzed epoxidation of allylic and homoallylic alcohols (4)
- iron-porphyrin catalyzed oxidation of cyclohexene (5)
- cobalt-catalyzed ring-opening of cyclohexane to adipic acid (3)
- rhodium and ruthenium catalyzed asymmetric hydrogenation/reduction of olefins (6)
- Lewis acid catalyzed acylations and alkylations (3)
- palladium-catalyzed Stille and Heck coupling reactions (7)
- use of CO2 as a solvent and reagent for isocyanate synthesis (3) and epoxide ring-opening polymerization (2).

In an effort to capitalize on the oxidative stability of carbon dioxide and its miscibility with molecular oxygen, we have examined a number of catalytic oxidation reactions. We have found that a wide range of catalytic oxidations of alkenes can be carried out in liquid or supercritical carbon dioxide using a number of transition metal complexes and oxidants such as alkylhydroperoxides or oxygen. The rate law for the well-studied vanadium (V) catalyzed epoxidation of allylic and homoallylic alcohols using t-butyl hydroperoxide was found to be the same in CO_2 and several organic solvents. Rates are several times faster in carbon dioxide than hexane and comparable to those measured in toluene (4). In an attempt to use molecular oxygen as the primary oxidant, we have examined the catalytic activity of highly fluorinated iron porphyrins. Highly fluorinated metalloporphyrins are soluble in supercritical CO_2 and can catalyze the oxidation of alkenes with molecular oxygen (5). Catalytic amounts of 5,10,15,20-tetrakis(pentafluorophenyl)-porphyrinato-iron(III) chloride and 2,3,7,8,12, 13,17,18-octabromo-5,10,15,20-tetrakis(pentafluorophenyl)porphyrinato iron(III) chloride react with cyclohexene at 80°C in CO_2 to form products derived from allylic oxidation and epoxidation. Selectivities in carbon dioxide were found to be higher than those observed in benzene, dichloromethane and acetonitrile. Our results suggest that the selectivity enhancements are likely due to the oxidative stability of carbon dioxide and the lack of unselective chain-carrying radicals typically derived from the organic solvents.

The design of stereoselective reactions that provide only one of two possible product enantiomers remains a primary goal of modern organic and organometallic chemistry. Asymmetric catalysis, which involves the use of chiral transition metal or main group complexes, has emerged as one of the most powerful, cost-effective methods for the generation of a wide variety of enantiomerically enriched compounds. There has been considerable interest in investigating homogeneous and heterogeneous catalytic hydrogenation reactions in supercritical fluids (1). We (6) and others (8) have found that asymmetric catalytic hydrogenations of prochiral olefins proceed cleanly with high enantioselectivities in supercritical carbon dioxide. Our work has focused on rhodium and ruthenium catalysts containing chiral biphosphine ligands, 1,2-bis(trans-2,5-diethylphospholano)benzene (DuPHOS) or 2,2'-bis(diphenyl-phosphino)-1,1'-binaphthyl (BINAP).



The cationic rhodium catalysts can be made soluble in supercritical CO_2 by using the highly lipophilic anion (tetrakis(3,5-bis(trifluoromethyl)-phenyl)borate ($B(Ar_F)_4^-$) as the counterion. The ability to solubilize cationic catalysts has broad implications for catalysis in supercritical fluids. A wide range of prochiral unsaturated substrates, including enamides, α-enamide esters and N-acyl hydrazones have been found to under hydrogenation with high enantioselectivity. Of particular note, we have observed (6) enhanced enantiomeric excesses for the β,β-disubstituted α-enamides (Table 1) in carbon dioxide relative to methanol and hexane.



Substrate	% ee in MeOH	 Hexane	 SC CO_2
R' = H, R'' = H	98.7	96.2	99.5
R' = H, R'' = Et	98.7	96.8	98.8
R' = H, R'' = Ph	97.5	98.3	99.2
R' = H, R'' = $3,5\text{-}CF_3Ph$	93.2	96.6	91.9
R', R'' = cyclohexyl	81.8	76.2	96.8
R' = Me, R'' = Me	62.6	69.5	84.7

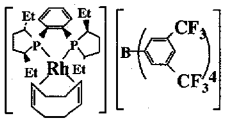


Table 1. Enantiomeric excesses for asymmetric hydrogenations of α-enamide esters.

We have also investigated several palladium-catalyzed coupling reactions in supercritical CO_2. Palladium catalyzed carbon-carbon bond forming reactions have found widespread applications in organic synthesis. We have examined ligand effects on the Stille coupling reaction of trimethylvinyltin and iodobenzene (to produce styrene) catalyzed by palladium (0) precursors and added phosphine ligands. While ligands such as triphenylphosphine were found to give low conversions due to catalyst insolubility, fluorinated phosphines, such as tri-(3,5-bis(trifluoromethyl) riphenyl)phosphine led to homogeneous solutions and high conversions. Rates in CO_2 were found to be within a factor of two of those measured in toluene. Higher conversions for Heck (4) and Suzuki (9) coupling reactions were also observed for fluorinated phosphine ligands.

RECENT ADVANCES IN CO_2-PHILIC LIGANDS AND BIPHASIC CATALYSIS

The nonpolar nature of dense phase CO_2 can limit the scope of homogeneous catalytic reactions that can be effectively run in this medium to only those which involve nonpolar substrates. Recently, there have been extensive efforts to enhance the solubility and reactivity of homogeneous catalysts in supercritical carbon dioxide by incorporating "CO_2-philic" moieties into phosphine ligands. Leitner (10) and others (1) have focused on incoporating "ponytails" containing fluoro, fluoroether or siloxane groups into phosphines for catalytic reactions CO_2. The fluorinated ligands were initially advanced by Horvath (11) for reactions in fluorocarbons. We have been investigating the "pigtail" phosphines, $R_2PCH_2CH_2R_f$, and phosphinites, $R_2POCH_2CH_2R_f$, (where R_f = perfluoroalkyl) in supercritical CO_2. Several examples involving homogeneous catalyzed hydrogenations and hydroborations (12) will be presented to illustrate the versatility of these ligands, which are relatively easy to prepare, (13) for controlled variation of the steric and electronic properties of the phosphine, a key element for controlling reactivity and selectivity.

In addition to developing more "CO_2-philic" catalytic systems, we have explored three other mechanisms for enhancing the range of reactions, catalysts and substrates that can be employed in carbon dioxide:

1. Phase-separable catalysis utilizing tailored catalysts and surfactants in CO_2/water emulsions and microemulsions.

2. Utilization of more polar dense phase fluids for homogeneous catalysis, e.g. dimethyl ether (DME).

3. Synthesis of CO_2-soluble polymers chemically modified with ligand sites for enhanced binding and separation of metal ions.

The recent development of surfactants capable of forming emulsions and microemulsions of H_2O in CO_2 has led to micellar systems (14) which are good solvents for both hydrophilic and hydrophobic species. We have been examining catalytic reactions using water soluble catalysts and lipophilic substrates in two-phase systems where the catalyst and product are obtained in separate phases after completing the reaction and changing the pressure. For example, we have found that the rates and conversions of the hydrogenation and hydroformylation of long chain alkenes using water soluble rhodium-phosphine complexes are significantly higher in CO_2/water emulsions than in two-phase CO_2/water or toluene/water mixtures. We will discuss preliminary results on the effect of surfactant concentration, pressure, temperature, and catalyst on the conversion and selectivities.

Compressed dense phase dimethyl ether (DME) is significantly more polar than CO_2 (15). We have found that DME is well suited to reactions that are typically carried out in more polar organic solvents such as diethyl ether or tetrahydrofuran. Conversions and selectivities, as well as measured rates in some instances, will be used to compare the reactivity of a number of homogeneous palladium-catalyzed cross-coupling reactions, including Heck, Stille and Suzuki reactions. Rates for palladium catalyzed coupling reactions in DME rival those measured for tetrahydrofuran (16). DME may be a viable alternative solvent given that it is not peroxidizable (17) and can easily be separated as a gas through pressure changes.

In collaboration with DeSimone at the University of North Carolina, we have been investigating the chemical modification of polymers known to be soluble in carbon dioxide (18) in order to develop novel ligand systems for metals. We have found (19) that random copolymerization of functionalized monomers with fluorinated acrylate monomers leads to functionalized polymers that are soluble in liquid and supercritical carbon dioxide. We have been able to incorporate a wide range of ligands either in the monomer or through chemical attachment at reactive sites after polymerization. These polymeric systems are capable of extracting metal ions into carbon dioxide, as determined by spectroscopic and extraction experiments.

ACKNOWLEDGMENTS

We gratefully acknowledge our collaborators Dr. Mark McCleskey, Dr. Kim Powell, Dr. Steve Buelow, Prof. Joe DeSimone (University of North Carolina), Prof. Keith Johnston (University of Texas), and Dr. Mark Burk (Chirotech). This work is part of the Los Alamos Catalysis Initiative and was funded predominantly by Department of Energy LDRD funding through Los Alamos National Laboratory. We also thank the US EPA Office of Pollution Prevention and Toxics, the EPA Risk Reduction and Engineering Lab and the Green Chemistry Institute for funding portions of this work.

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