Homogeneous And Phase-Transfer Catalysis In Supercritical Fluids

Phase Transfer Catalysis (PTC) is an important method for industrial reactions. Typical solvents used are often polar, high-boiling, chlorine-containing organics, which are not only environmentally undesirable, but also pose other problems such as limitations on mass transfer and solvent removal and recovery. We eliminate or ameliorate these limitations by using safe, cheap, nontoxic supercritical CO₂ as a replacement.

PTC provides an attractive and effective method for conducting heterogeneous reactions. A catalyst (quaternary ammonium salts or cyclic ethers) is employed to transport ionic reactants into a nonpolar phase. Many advantages accrue to processing such reactions in supercritical fluid (SCF) solvents. We have demonstrated the feasibility and studied the kinetics for a variety of PTC catalysts on reactions of importance in the chemical and pharmaceutical industry, including chiral syntheses.

SCF’s have unique properties that make them especially attractive solvents for PTC. The most common SCF solvent is CO₂, which provides environmentally benign processing and facile separation of reaction products. Typically SCF’s have viscosities two orders of magnitude lower than liquids and higher molecular diffusivities, both of which should ameliorate the mass transfer limitations that often occur in liquids.

PTC represents an important advance in heterogeneous reaction processes. In the early 1990’s sales of products made with phase-transfer catalysis exceeded $10 billion/year -- about $5 billion in polymers, $3 billion in pharmaceuticals, $2 billion in agricultural chemicals, $1 billion in monomers, and unestimated sales of general chemicals, flavors and fragrances, dyes, surfactants, explosives, and others.

During the last two decades a great deal of research has been reported regarding heterogeneous enantioselective syntheses involving chiral phase transfer catalysis. The asymmetric induction accompanying these reactions varied greatly from just a few percent enantiomeric excess to the high nineties. At present there are no reported examples of the use of a supercritical fluid phase in chiral phase transfer catalysis.

We are conducting a program of research that investigates the chemistry and engineering of supercritical fluid phase-transfer catalysis and permit its application to problems of specific interest. We first demonstrated phase-transfer catalysis in SCF’s for reaction between a solid salt phase and a supercritical fluid (SCF) solvent -- the nucleophilic displacement on benzyl chloride by bromide ion and by cyanide ion in the presence of tetraheptylammonium bromide.

\[
\begin{align*}
\text{CH}_2\text{Cl} & \quad \text{PTC, KBr} \quad \text{SCF CO}_2 \\
\text{CH}_2\text{Br} \\
\end{align*}
\]
Further, we are pursuing a number of other attractive PTC reactions in SCFs, including chiral syntheses. One example, is the base-promoted alkylation reaction of phenyl acetonitrile with ethyl bromide to make 2-phenyl-butyronitrile, an important intermediate for a wide variety of pharmaceuticals.

\[
\text{CH}_2\text{CN} + \text{CH}_3\text{CH}_2\text{Br} \xrightarrow{\text{KOH}} \text{CH}_3\text{CH}_2\text{CHCN}
\]

SCF PTC provides enormous opportunities for heterogeneous reaction processes with several distinct advantages:

- Environmentally benign solvents -- SCF technology offers great flexibility in the choice of solvent. We shall use cheap, nontoxic, nonflammable CO2 pure and with small amounts of benign modifiers.
- Elimination of mass transfer limitations -- SCF solvents have viscosities nearly two orders of magnitude less than liquids and molecular diffusivities 10-50 fold higher.
- Milder reaction conditions -- SCF solvents often exhibit extreme rate variations and faster rates may be achieved at milder conditions.
- Higher yield and selectivity -- supercritical fluid solvents can be tailored to achieve a variety of process goals.