

Fig. 7.20 Fluorous catalysis without fluorous solvents.

time of fluorocarbons in the environment which, even though they are chemically inert, essentially nontoxic and are not, in contrast to their cousins the CFCs, ozone-depleting agents, is still a matter for genuine concern.

In this context it is interesting to note the recent reports of *fluorous catalysis without fluorous solvents* [68]. The thermomorphous fluorous phosphines, $\text{P}[(\text{CH}_2)_m(\text{CF}_2)_7\text{CF}_3]_3$ ($m=2$ or 3) exhibit ca. 600-fold increase in *n*-octane solubility between -20 and 80°C . They catalyze the addition of alcohols to methyl propiolate in a monophasic system at 65°C and can be recovered by precipitation on cooling (Fig. 7.20) [68]. Similarly, perfluoroheptadecan-9-one catalyzed the epoxidation of olefins with hydrogen peroxide in e.g. ethyl acetate as solvent [69]. The catalyst could be recovered by cooling the reaction mixture, which resulted in its precipitation.

Presumably this technique can be applied to other examples of (organometallic) catalysis. We also note that catalysis can also be performed in supercritical carbon dioxide (scCO_2) as solvent (see next section).

7.5 Supercritical Carbon Dioxide

7.5.1 Supercritical Fluids

Supercritical fluids (SCFs) constitute a different category of neoteric solvents to the rest discussed in this chapter since they are not in the liquid state. The critical point (Fig. 7.21) represents the highest temperature and pressure at which a substance can exist as a vapor in equilibrium with a liquid. In a closed system, as the boiling point curve is ascended, with increasing pressure and temperature, the liquid becomes less dense, owing to thermal expansion, and the gas becomes denser as the pressure increases. The densities of the two phases converge and become identical at the critical point, where they merge and become a SCF. Hence the properties, e.g. density, viscosity and diffusivity, of a SCF are intermediate between a liquid and a vapor. SCFs also mix well with gases, making them potentially interesting media for catalytic reactions with hydrogen, carbon monoxide and oxygen.

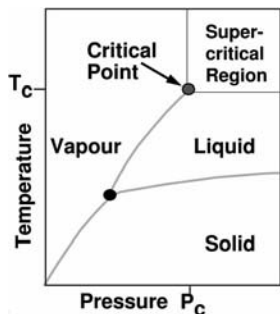


Fig. 7.21 A phase diagram illustrating the supercritical region.

7.5.2

Supercritical Carbon Dioxide

Several features of scCO_2 make it an interesting solvent in the context of green chemistry and catalysis. For carbon dioxide the critical pressure and temperature are moderate: 74 bar and 31 °C, respectively. Hence the amount of energy required to generate supercritical carbon dioxide is relatively small.

In addition, carbon dioxide is nontoxic, chemically inert towards many substances, nonflammable, and simple depressurization results in its removal.

It is miscible with, e.g. hydrogen, making it an interesting solvent for hydrogenation and hydroformylation (see below). Although it is a greenhouse gas its use involves no net addition to the atmosphere; it is borrowed as it were. Its main uses are as a replacement for VOCs in extraction processes. For example it is widely used for the decaffeination of coffee where it replaced the use of a chlorinated hydrocarbon. More recently, it has been commercialized as a replacement for trichloroethane in dry cleaning applications [70]. In the last decade attention has also been focused on the use of scCO_2 as a solvent for green chemistry and catalysis [71–74]. The pre-existence of an established SCF extraction industry meant that the necessary equipment was already available.

7.5.3

Hydrogenation

The most extensively studied reaction is probably hydrogenation. The miscibility of scCO_2 with hydrogen, as noted above, results in high diffusion rates and is a significant advantage. It provides the basis for achieving much higher reaction rates than in conventional solvents. The use of scCO_2 as a solvent for catalytic hydrogenations over supported noble metal catalysts was pioneered by Poliakoff [75–77]. For example, the Pd-catalyzed hydrogenation of a variety of functional groups, such as C=C, C=O, C=N and NO_2 was shown [75, 76] to proceed with high selectivities and reaction rates in scCO_2 . The high reaction rates allowed the use of exceptionally small flow reactors. Chemoselectivities with multifunctional compounds could be adjusted by minor variations in reaction parameters.

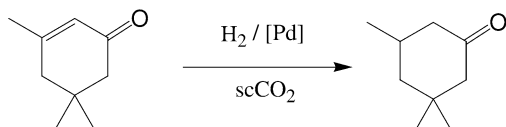
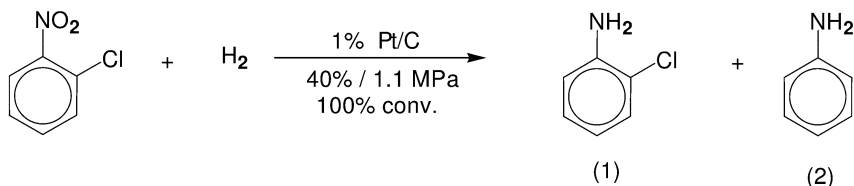


Fig. 7.22 Catalytic hydrogenation of isophorone in $scCO_2$.

The technology has been commercialized, in collaboration with the Thomas Swan company, for the manufacture of trimethyl cyclohexanone by Pd-catalyzed hydrogenation of isophorone (Fig. 7.22) [77].

The multi-purpose plant, which went on stream in 2002, has a production capacity of 1000 tpa (100 kg h^{-1}). The very high purity of the product and high productivities, together with the elimination of organic solvent, are particular benefits of the process. It is a perfect example of the successful transfer of green chemistry from academia to industry. Presumably it will stimulate further industrial application of the technology. Ikariya and coworkers [78], another pioneering group in the area of catalytic hydrogenations in $scCO_2$, recently reported that chemoselective hydrogenation of halogenated nitrobenzene (Fig. 7.23) proceeds very effectively over Pt/C catalysts in $scCO_2$. The rate is significantly enhanced compared to that with the neat substrate and competing dehalogenation is markedly suppressed, affording a higher chemoselectivity. The increased selectivity in $scCO_2$ was tentatively attributed to the generation of small amounts of CO which preferentially cover the more active sites on the platinum surface which are responsible for dehalogenation. Indeed, the addition of small amounts of CO to the neat reaction system caused a marked suppression of competing dehalogenation.

Catalytic asymmetric hydrogenations have also been performed in supercritical carbon dioxide [79–81]. For example, α -enamides were hydrogenated in high enantioselectivities comparable to those observed in conventional solvents, using a cationic rhodium complex of the EtDuPHOS ligand (Fig. 7.24) [79]. More recently, catalytic asymmetric hydrogenations have been performed in $scCO_2$ with



	Time (h)	Selectivity (%)	
		<u>1</u>	<u>2</u>
neat	5	95.6	2.1
$sc \text{ CO}_2$	2.5	99.7	0.3

Fig. 7.23 Chemoselective hydrogenation of *o*-chloronitrobenzene in $scCO_2$.

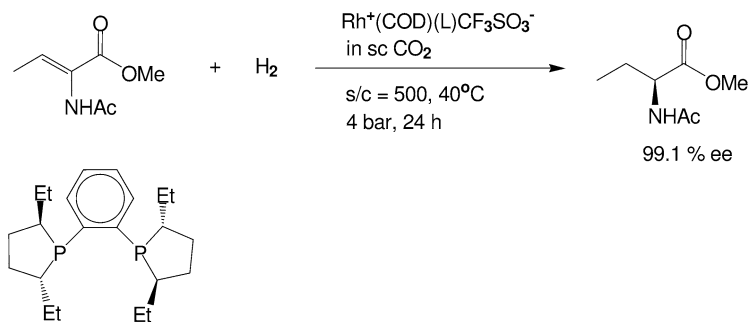


Fig. 7.24 Catalytic asymmetric hydrogenation in scCO_2 .

Rh complexes containing monodentate perfluoroalkylated chiral ligands [80]. By using a chiral Rh complex immobilized onto alumina, via a phosphotungstic acid linker, asymmetric hydrogenations could be performed in continuous operation using scCO_2 as the solvent [81]. Jessop and coworkers [82] compared a variety of neoteric solvents – scCO_2 , ionic liquids (ILs), ILs with cosolvents and CO_2 -expanded ionic liquids (EILs) – in the asymmetric hydrogenation of prochiral unsaturated acids catalyzed by chiral ruthenium complexes. They concluded that the optimum solvent was dependent on the specific substrate used and no one solvent clearly outperforms all others for all substrates. Solvents thought to dissolve significant amounts of hydrogen gave good enantioselectivities for substrates known to be dependent on high H_2 concentrations. Solvents dissolving low amounts of hydrogen, e.g. ionic liquids, were ideal for substrates dependent on minimum H_2 concentrations for high enantioselectivities. Similarly, olefin hydroformylation has been conducted in scCO_2 using an immobilized Rh catalyst [83].

7.5.4

Oxidation

Supercritical carbon dioxide is, in principle, an ideal inert solvent for performing catalytic aerobic oxidations as it is nonflammable and completely miscible with oxygen. It is surprising, therefore, that there are so few studies in this area. A recent report describes the aerobic oxidation of alcohols catalyzed by PEG-stabilized palladium nanoparticles in a scCO_2 /PEG biphasic system [84]. Recently, much interest has also been focused on catalytic oxidations with hydrogen peroxide, generated *in situ* by Pd-catalyzed reaction of hydrogen with oxygen, in scCO_2 /water mixtures [85]. The system was used effectively for the direct epoxidation of propylene to propylene oxide over a Pd/TS-1 catalyst [86]. These reactions probably involve the intermediate formation of peroxycarbonic acid by reaction of H_2O_2 with CO_2 (Fig. 7.25).

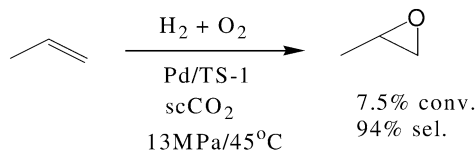


Fig. 7.25 Oxidation of propylene with H_2/O_2 in scCO_2 .

7.5.5

Biocatalysis

scCO_2 is also an interesting solvent for performing bioconversions. The first reports of biocatalysis in scCO_2 date back to 1985 [87–89] and in the intervening two decades the subject has been extensively studied [90]. Enzymes are generally more stable in scCO_2 than in water and the *Candida antarctica* lipase (Novozym 435)-catalyzed resolution of 1-phenylethanol was successfully performed at temperatures exceeding 100°C in this solvent [91]. Matsuda et al. found that the enantioselectivity of alcohol acylations catalyzed by Novozyme 435 in scCO_2 could be controlled by adjusting the pressure and temperature [92]. The same group recently reported a continuous flow system in scCO_2 for the enzymatic resolution of chiral secondary alcohols via Novozyme 435 catalyzed acylation with vinyl acetate (Fig. 7.26) [93]. For example, the kinetic resolution of 1-phenyl ethanol at 9 MPa CO_2 and 40°C afforded the (*R*)-acetate in 99.8% *ee* and the (*S*)-alcohol in 90.6% *ee* at 48% conversion ($E=1800$).

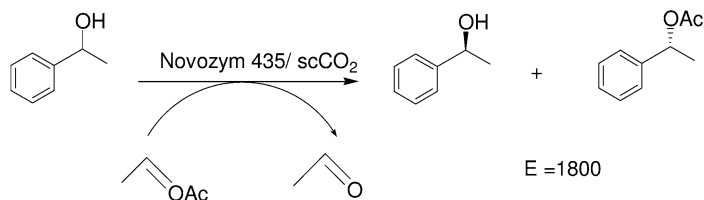


Fig. 7.26 Lipase catalyzed enantioselective transesterification in scCO_2 .

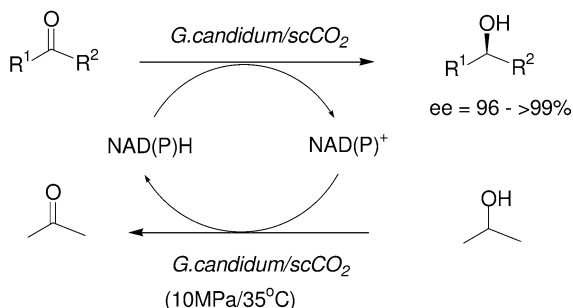


Fig. 7.27 Biocatalytic enantioselective reduction of ketones in scCO_2 .

Similarly, the enantioselective reduction of prochiral ketones catalyzed by whole cells of *Geotrichum candidum* proceeded smoothly in scCO₂ in a semi-continuous flow system (Fig. 7.27) [94].

Enzyme catalyzed oxidations with O₂ have also been successfully performed in scCO₂ e.g. using cholesterol oxidase [95] and polyphenol oxidase [88]. The use of scCO₂ as a solvent for biotransformations clearly has considerable potential and we expect that it will find more applications in the future.

7.6

Ionic Liquids

Ionic liquids are quite simply liquids that are composed entirely of ions [96, 97]. They are generally salts of organic cations, e.g. tetraalkylammonium, alkylpyridinium, 1,3-dialkylimidazolium, tetraalkylphosphonium (Fig. 7.28). Room temperature ionic liquids exhibit certain properties which make them attractive media for performing green catalytic reactions. They have essentially no vapor pressure and are thermally robust with liquid ranges of e.g. 300 °C, compared to 100 °C for water. Polarity and hydrophilicity/hydrophobicity can be tuned by a suitable combination of cation and anion, which has earned them the accolade, ‘designer solvents’.

Ionic liquids have been extensively studied in the last few years as media for organic synthesis and catalysis in particular [98]. For example, the hydroformylation of higher olefins, such as 1-octene, was performed in ionic liquids [99]. Good activities were observed with rhodium in combination with the water-soluble ligand, tppts, described above but the selectivity was low (*n*/*iso* ratio=2.6). In order to achieve both high activities and selectivities special ligands had to be designed (Fig. 7.29). No detectable (less than 0.07%) Rh leaching was observed and the IL phase containing the catalyst could be recycled after separating the product which formed a separate phase. However, the need for rather exotic ligands will presumably translate to higher costs for this process.

As would be expected, high rate accelerations can result when reactions proceeding through ionic intermediates, e.g. carbocations, are performed in ionic liquids. For example, Seddon and coworkers [100] studied the Friedel-Crafts acylation of toluene, chlorobenzene (Fig. 7.30) and anisole with acetyl chloride in [emim][Al₂Cl₇], whereby the ionic liquid is acting both as solvent and catalyst. They ob-

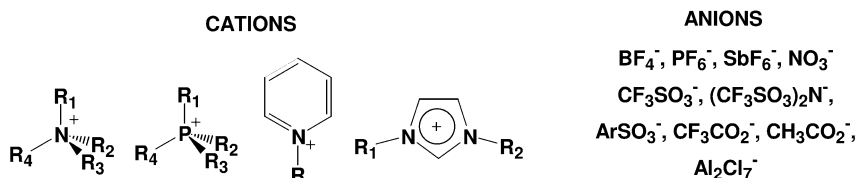


Fig. 7.28 Structures of ionic liquids.