Available online at www.sciencedirect.com

SCIENCE DIRECT

ELSEVIER

Tetrahedron

Tetrahedron 60 (2004) 815–833

Tetrahedron report number 666

Recent advances in the application of supercritical fluids for carbon–carbon bond formation in organic synthesis

Dipak Prajapati* and Mukut Gohain

Medicinal Chemistry Division, Regional Research Laboratory, Jorhat, 785 006 Assam India

Received 18 October 2003

Contents

1. Introduction

Reactions under supercritical conditions have been used for large-scale industrial production for most of the twentieth century, but the application of supercritical fluids (SCFs) in the synthesis of complex organic molecules is only just emerging. Research in this field has been particularly active in the last decade of this century, because the special properties of SCFs make them attractive solvents for modern synthetic chemistry. The idea of using supercritical fluids as reaction solvents has, however, been emerging ever since the discovery of a 'peculiar state of matter' early in the nineteenth century by Baron Charles Cagniard de LaTour, an experimental physicist[1] in France. Supercritical fluids may be alternatives to liquid solvents, but they are neither simple nor simply replacements of solvents. The experimental chemist could not modify a written synthetic method by simply crossing out the word 'benzene' and replacing it with the words 'supercritical carbon dioxide'. Many other modifications to the procedure would be necessary, because of the inferior solvent strength and need for the pressurized equipment for many SCFs.

Supercritical fluids may be defined as the state of a compound, mixture or element above its critical pressure (P_c) and critical temperature (T_c), but below the pressure required to condense it into a solid. They occupy a point where pure and applied science meet head on. This is a feature that has attracted many workers to the field. The importance of SCFs and their applications have been summarised quite effectively by Garrabos et al.,[2] who also

---

Keywords: Supercritical fluids; Carbon–carbon bond formation reactions; Supercritical carbon dioxide.

* Corresponding author. Fax: +91-376-2370011;
e-mail address: dr_dprajapati@yahoo.co.uk

0040–4020/$ - see front matter
doi:10.1016/j.tet.2003.10.075

Nomenclature

acac	acetylacetonate
ADMET	acyclic diene metathesis
AIBN	2,2′-azobis(isobutyryl nitrile)
BINOL	*R*(+)-1,1′-naphthalene-2,2′-diol
BINAP	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
BINAPHOS	2-(diphenylphosphino)-1,1′-binaphthen-2′-yl-1,1′-binaphthen-2,2′-diylphosphite
cod	1,5-cyclooctadiene
CNT	carbon nanotubes
DELOXAN	polysiloxane-based solid acids
DABCO	1,4-diazabicyclo[2.2.2]octane
dppb	1,4-diphenylphosphinobutane
DME	dimethyl ether
de	diastereomeric excess
DBU	diazabicyclo[5.4.0]undecene
H–H	head-to-head dimer
H–T	head-to-tail dimer
hfacac	1,1,1,5,5,5-hexafluoroacetylacetonate
LAB	linear alkylbenzenes
MWCNT	multiwalled carbon nanotube
PTC	Phase-transfer catalysis
ROMP	ring-opening metathesis polymerisation
RCM	ring-closing metathesis
SCF	supercritical fluid
SCW	supercritical water
TPPTSS	triphenylphosphine trisulphonate sodium salt
TON	turnover number
THAB	tetraheptyl ammoniumbromide
THAC	tetraheptyl ammoniumchloride

describe a series of interesting applications, as well as outlining the sometimes-overlooked effects of gravity on fluids near their critical point. The properties of SCFs are different from those of ordinary liquids and gases and are tunable simply by changing the pressure and temperature. In particular, the density and viscosity change drastically at conditions close to the critical point. It is well known that the density-dependent properties of an SCF solvent (e.g. solubility, diffusivity, viscosity and heat capacity) can be manipulated with relatively small changes in temperature and pressure. In catalysis applications, the resulting effects of these tunable solvents feature in a variety of ways, such as enhancing component[3] and catalyst[4] solubilities, influencing Kinetic rates through both temperature and pressure effects, as well as shifting equilibrium constants to favour the desired products,[5] increasing selectivity and yields (e.g. by manipulating the solvent dielectric constant[6] or viscosity,[7]) reducing mass transfer limitations in diffusion-limited reactions,[8] controlling the temperature in highly-exothermic reactions through adjustment of the solvent heat capacity[9a] and minimising heterogeneous catalyst deactivation through the prevention of coking and extraction of fouling products.[9b]

The most popular supercritical fluid, carbon dioxide, has the added benefit of being a natural, unregulated solvent, with low toxicity and high availability.[10] When carbon dioxide is used as the supercritical solvent, additional advantages can be realised. The chemical industry has become increasingly aware of environmental concerns over the use of volatile organic solvents and chlorofluorocarbons in the manufacture and processing of commercial polymer products. The use of water alleviates these problems somewhat, but it still results in large amounts of hazardous aqueous waste that require treatment. Green chemistry is much more than simply replacing hazardous materials (solvents, reagents) with less hazardous substances and can be defined as elegant chemistry on the basis of three factors,[11] environmental friendliness, chemical efficiency (selective), and economic viability. As a result of these environmental concerns, supercritical CO_2 represents a more environmentally friendly alternative to the traditional solvents. Although supercritical CO_2 has been touted as a modern remedy for many commercial problems, the use of CO_2 as a solvent is complicated by the low solubility of many reactants, even under supercritical conditions.[12] Many industrial applications are therefore hindered by this obstacle, as well as by the fact that high-pressure equipment can be quite costly. Despite these difficulties, the attraction of combining natural catalysts with natural solvents has been the driving force behind a growing body of literature concerning the stability, activity and specificity of enzymes in supercritical carbon dioxide.[13–15]

The trend towards using supercritical fluids in chemical practice[16] intensified only at the beginning of 1980s, and their use as reaction media is becoming an alternative for the reactions in which the previously described options are not suitable. The projected advantages of the reactions in supercritical fluids are the increased reaction rates and selectivities resulting from the high solubility of the reactant gases, rapid diffusion of solvents, weakening of the solvation around the reacting species and the local clustering of reactants or solvents.[17] It is also interesting to note, in a practical sense, that these fluids are easily recycled and allow the separation of dissolved compounds by a gradual release of pressure. Sequential and selective precipitations of the catalyst and product would be possible. Several recent reports have shown that scCO_2 can replace the conventional organic solvents in various transformations, such as radical reactions,[18] Diels–Alder reactions,[19] polymerisations,[20] homogeneous hydrocarboxylations[21] and asymmetric hydrogenations.[22] Broadly, the authors have reviewed those papers, published in recent years, which concern some aspects of carbon–carbon bond formation reactions in organic synthesis and which are considered to be of the greatest value to the synthetic organic chemist.

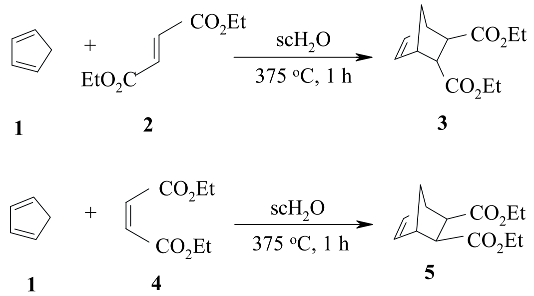
The most intriguing aspect of organic synthesis of paramount concern is that of the carbon–carbon bond-formation reaction.[23] The efficient generation of a carbon–carbon bond forms the backbone and is the essence of synthetic organic chemistry, organometallic reactions, metal-catalysed reactions and cycloaddition reactions leading to the formation of new carbon–carbon bonds figuring prominently in both synthetic and mechanistic organic chemistry.[24] Moreover, the development of new and more selective reagents in carbon–carbon bond-forming reactions has accelerated exponentially and still constitutes one of the most vigorous areas of organic synthesis. Two major types of reagents are the carbon nucleophiles and carbon electrophiles and these are widely used to form carbon–carbon bonds in organic synthesis. The C-nucleophile group includes numerous organometallic reagents, carbanions, enolates and their precursors. The familiar alkylating, acylating and cyclopropanating reagents, together with Michael acceptors and other electron-deficient olefins, comprise a fundamental group of C-electrophiles.

The efficient formation of carbon–carbon bonds with good and, preferably, predictable stereocontrol is still a synthetic challenge in organic chemistry. On this issue during the last decade, a unique reactivity and remarkable selectivity has been exhibited on removing organic solvents in carbon–carbon bond-forming reactions, which is an important drive towards the development of environmentally benign chemical technologies. In addition, organic solvents are high on the lists of toxic or otherwise damaging compounds, because of the large volumes used in industry and the difficulties in containing volatile compounds. Replacement reaction media include ionic liquids[25,26] supercritical fluids,[27] water[28–30] and solvent-free conditions.[26,31,32] Due to the broad applicability and the vast diversity of C–C bond formation reactions in organic synthesis and, for the sake of simplicity, this review has strived to include the relevant information on the current status of the developments in the application of SCFs in C–C bond-forming reactions.

2. Carbon–carbon bond formation reactions in supercritical fluids

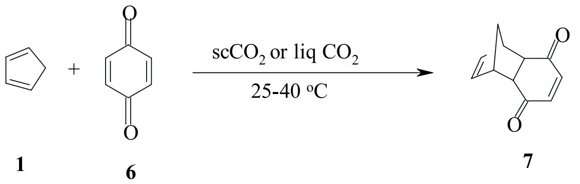
2.1. Diels–Alder reactions

The Diels–Alder reaction is the most widely-used synthetic method for the synthesis of polycyclic ring compounds. Ikushima et al.[33] examined the Diels–Alder reaction in $scCO_2$ and found specific changes in the isomer distribution and in the rate of reaction near the critical point.[34] In the early 1980s, Breslow et al.[35] and Grieco et al.[36] reported that the rates of Diels–Alder reactions were greatly improved by using water instead of conventional organic solvents as the reaction media. Kolis et al.[37] have reported the possibility of performing Diels–Alder reactions in superheated and scH_2O due to the unique properties[38] of scH_2O. The reactions tested were the cycloadditions of cyclopentadiene **1** with diethyl furmarate **2** and diethyl maleate **4** using scH_2O as the solvent. They obtained yields of 10 and 86% for **3** and **5**, respectively, after 1 h. Although the yield of the *endo*/*exo*-2,3-diethyl ester of 5-norbornene **3** was low, equal amounts of both isomers of **5** were formed in good yield from the *cis* diene (Scheme 1).



Scheme 1.

Renslo et al.[39] have examined the reaction selectivity in some Diels–Alder reactions in $scCO_2$ and conventional solvents. They showed that the product distribution in $scCO_2$ at pressures of 49–118 bar and at temperatures of 50 and 150 °C was very similar to that obtained in conventional solvents such as toluene. This is different from the previous observations under similar conditions[33] and Renslo et al. pointed out the importance of phase behaviour when sampling CO_2 reaction mixtures for results. Isaacs and Keating[40] carried out the Diels–Alder reaction between *p*-benzoquinone **6** and cyclopentandiene **1** in CO_2 at 25–40 °C, to form **7**. It was shown that the reaction effectively occurred throughout the liquid and supercritical ranges with no discontinuity and that the rates of the reaction were about 20% greater than those obtained in diethyl ether (Scheme 2).

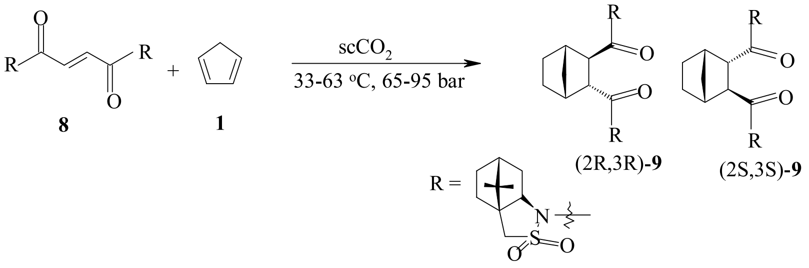


Scheme 2.

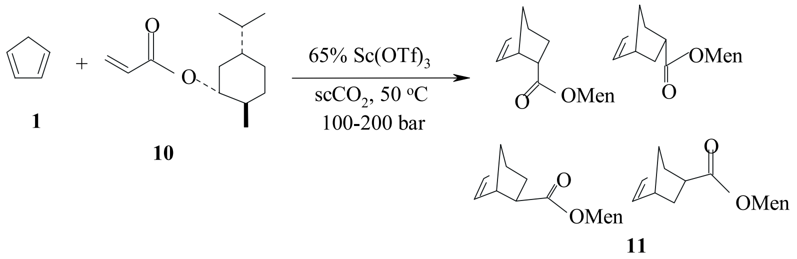
Weinstein et al.[41] studied the Diels–Alder reaction of cyclopentadiene **1** and ethyl acrylate in CO_2 from 38 to 88 °C and from 80 to 210 bar. The rate of the reaction was shown to increase with pressure (or density) for the whole range examined at a constant temperature. Paulaites and Alexander reported the earliest findings on the Diels–Alder reaction in supercritical media.[42] The first Diels–Alder reaction in $scCO_2$ controlled by a chiral auxilary[43] was reported by Chapuis et al. As part of a study into the solvent effects on stereoselectivity, the reaction between cyclopentadiene **1** and the dienophile **8** to produce **9** was performed in $scCO_2$. In conventional solvents, the *de* generally increased with polarity (58% *de* in CCl_4, 92% *de* in water), although several anomalies were observed such as in diethyl ether (87% *de*) and hexane (70% *de*). In $scCO_2$, the best selectivity was observed around the critical point (65% conversion, 93% *de* at 33 °C, 74 bar), although a similar result was obtained at a slightly higher temperature and pressure (100% converison, 92% *de* at 43 °C, 78 bar) (Scheme 3).

The Lewis acid-catalysed distereoselective Diels–Alder reaction between (−)-menthyl acrylate **10** and cyclopentadiene **1** was also investigated using scandium triflate as the catalyst.[44] The poor rate and selectivities in the uncatalysed reaction can be improved by using a Lewis acid i.e. scandium triflate, which was investigated by Oakes et al. in 1999. A moderate diastereocontrol was observed, which was once again optimised by tuning the pressure of the $scCO_2$ solvent. At a pressure of 155 bar and a temperature of 50 °C an *endo* to *exo* ratio of 9.25:1 of **11** was achieved, with a diastereomeric ratio of 3.6:1 (Scheme 4).

In 1998, Clifford et al.[45] investigated reaction controlled and

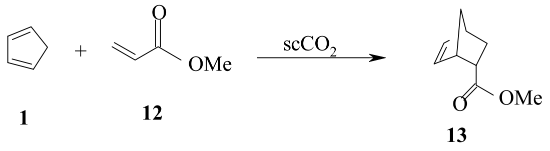


Scheme 3.



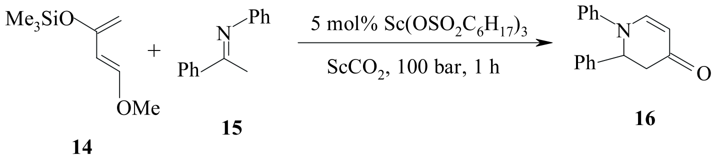
Scheme 4.

potential tuning in the Diels–Alder reaction between cyclopentadiene **1** and methyl acrylate **12** in $scCO_2$ to give **13** (Scheme 5). The theoretical explanation is based on a tuning function. The calculation using the tuning function suggested that the maximum selectivity could occur at a density of 0.540 $g\ ml^{-1}$, significantly above the critical density of 0.465 $g\ ml^{-1}$ (Scheme 5).



Scheme 5.

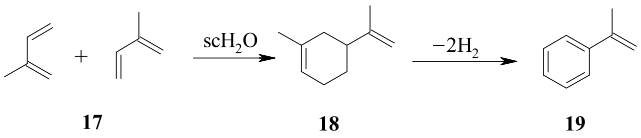
In a recent finding, Kobayashi has reported the use of scandium perfluoro-alkanesulfonates as Lewis acid catalysts for the Diels–Alder reaction in $scCO_2$.[46] It was disclosed that the catalyst activity was improved by increasing the length of the perfluoroalkyl chain and, hence, its solubility. This catalyst was also used in the aza-Diels–Alder reaction of Danishefsky's diene **14** with the imine **15** in $scCO_2$ to obtain the corresponding aza-Diels–Alder adduct **1b** in 99% yield (Scheme 6).



Scheme 6.

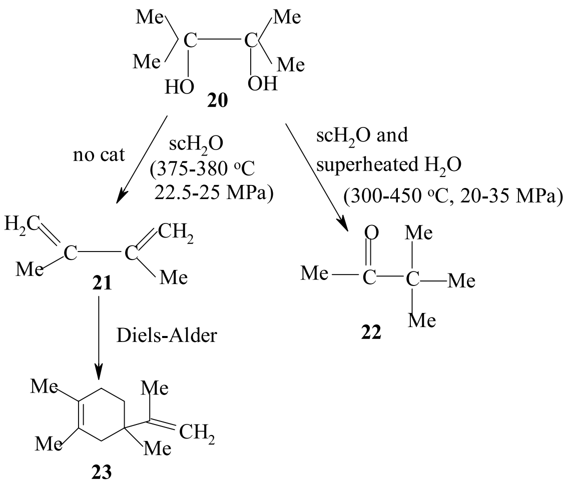
The silica-catalyzed Diels–Alder reaction in $scCO_2$ was carried out by Danheiser et al.[47] Here, the silica was found to significantly enhance the rate and selectivity of the reaction. Roberts investigated[48] the effect of pressure on the bimolecular rate constant of the Diels–Alder reaction between maleic anhydride and isoprene in $scCO_2$ at 35 °C.

There are various other reports[49] on the selectivity of the Diels–Alder reaction in supercritical fluids. The reaction of isoprene **17** in supercritical H_2O was conducted in batch mode, in the temperature range of 300–410 °C at 25 MPa with an initial concentration of 8 wt%. The residence time was 1 h. The main products were Diels–Alder adducts such as dipentene **18** and some terpenes **19**. No hydration products could be detected[50] (Scheme 7).



Scheme 7.

Supercritical water could be used as an acid catalyst for dehydration and other reactions if its own 'acidity' could be changed. Pinacolone **22** was the sole product under scH_2O and superheated water reaction conditions. In the very limited near-critical region of 375–380 °C at 22.5–25 MPa, however, the formation of 1,2,4-trimethyl-4-isopro-penyl-cyclohexene **23**, rather than pinacolone **22**, from pinacol **20** was observed for the first time.[51] The conversion of **20** to **23** was 50–70%. Here, pinacol was completely dehydrated into 2,3-dimethyl-1,3-butadiene **21** and the intermolecular Diels–Alder reaction of **21** then results in the formation of **23**. Diels–Alder reactions have already been confirmed to occur in supercritical water in the absence of acid catalysts[52] (Scheme 8).



Scheme 8.

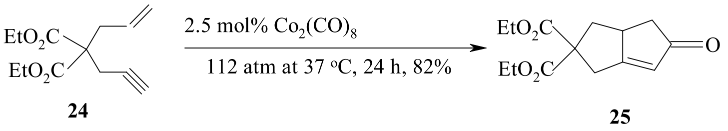
2.2. Catalytic Pauson–Khand reactions

The cocyclisation of alkynes with alkenes and carbon monoxide by cobalt, leading to cyclopentenones (known as the Pauson–Khand reaction), has been accepted as one of the most powerful tools in the synthesis of cyclopentenones. Recent developments in the Pauson–Khand reaction include the discovery of promoters, such as silica gel, tertiary amine *N*-oxides and DMSO for the stoichiometric reaction, enantioselective reactions and catalytic versions of the reaction.[53] Jeong et al.[54] have reported the first catalytic intramolecular Pauson–Khand reaction in supercritical fluids. The catalytic intramolecular Pauson–Khand reactions e.g. **24** to **25** were first performed in $scCO_2$ with dicobalt octacarbonyl as the catalyst and enynes, followed by correct pressurisation with carbon monoxide and carbon dioxide. The reaction mixture requires a higher carbon monoxide pressure (15–30 atm) to make the catalytic metal species as intact as possible (Scheme 9).

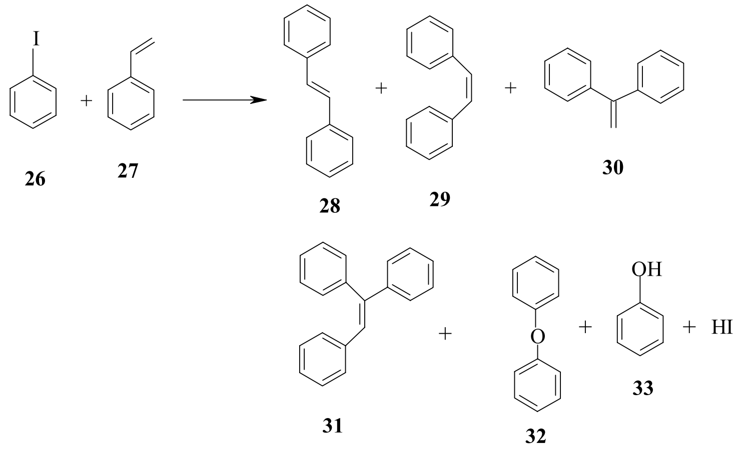
2.3. Inter- and intramolecular Heck reactions

The Heck reaction is an extremely valuable method for carbon–carbon bond formation and is now widely used in the fine chemical and pharmaceutical industries.[55] The Heck arylation of alkenes has been carried out in hot compressed water (533 K) and in scH_2O (673 K) in the presence of Pd catalysts.[56,57] Ikushima et al.[58] have recently reported the Heck coupling reaction of iodobenzene **26** with styrene **27** in supercritical water without using any catalyst, in which several alkylarenes, such as stilbene **28** and **29** and 1,1-diphenylethylene **30**, were formed, as shown in Scheme 10, besides hydrogen iodide and other products **31** to **33**. They demonstrated[59,60] a remarkable stimulation of rearrangement or disproportionation using scH_2O, which might be due to the acid and base difunctionality of scH_2O. The unusual properties of water near its critical point provide a novel method for extending the Heck reaction into water. It was shown that a high reaction rate and selectivity are possible near its critical point. The choice of base had a significant effect on the product selectivity. The best result was obtained using KOAc, which is a relatively mild base. The conversion reached 70% and the yield of stilbene was 55.6% (both *trans* and *cis* stilbene) within 10 min (Scheme 10).

Recently various approaches to the Heck reaction has been developed,[61–65] but its practical application has been restricted, due to the disadvantage of using environmentally damaging solvents and transition-metal catalysts and to problems associated with catalyst-product separation and side reactions such as decomposition. The Heck reaction using fluorinated phosphine–palladium complexes in $scCO_2$ with electron-deficient alkenes occurs in a superior yield to that reported for conventional solvents, i.e. 90% conversion and 90% selectivity for the coupling of PhI **26** with acrylic acid and styrene.[66] Similar results were obtained in the Heck coupling by Holmes[67] using isolated

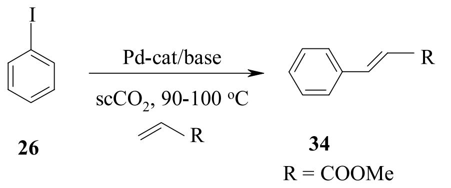


Scheme 9.



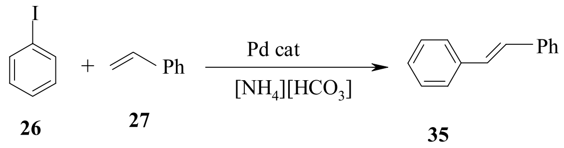
Scheme 10.

complexes of the formula $[PdL_2X_2]$, where L= $PhP[(CH_2)_2(CF_2)_6F]_2$ and X=Cl or OAc. At 100 °C, a 91% isolated yield of methyl cinnamate **34** from PhI **26** and methyl acrylate acid was achieved using 5 mol% of the acetate complex (Scheme 11).



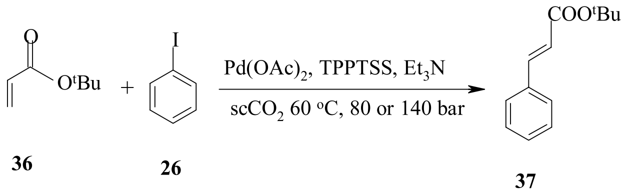
Scheme 11.

The Heck reaction has also been studied in metal-catalysed organic synthesis in SCFs other than CO_2. Supercritical and, especially, superheated water have been found to be suitable solvent media for this reaction for the synthesis of **35** using various palladium complexes without phosphine ligands[68] (Scheme 12).



Scheme 12.

Heck reactions in $scCO_2$ using fluorinated phosphine ligands[69] or trifluoroacetate counterions,[70] or non-fluorinated phosphines[71,72] and solid-supported reactions have been reported. The application of supported reagents[73] in $scCO_2$ has received little attention.[74] Cacchi has successfully used Pd/C as a heterogeneous catalyst to facilitate the Heck reaction in $scCO_2$, although these conditions required extended reaction times to release reasonable yields[75] Arai has reported a Heck reaction using water-soluble catalysts in $scCO_2$–water biphasic systems.[76] The coupling of iodobenzene **26** with butyl acrylate **36** in $scCO_2$ to form **37** was

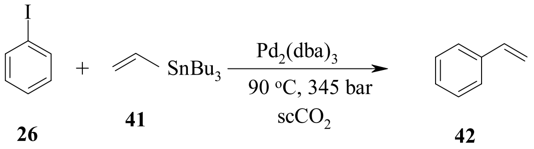


Scheme 13.

investigated[77] using $Pd(OAc)_2$ and triphenylphosphine trisulphonate sodium salt (TPPTSS) as water-soluble ligands (Scheme 13). In the absence of a co-solvent, the catalyst remains insoluble and the yields are low (<5% at 80 bar), but the addition of a polar co-solvent such as water increases the rate. The use of a more CO_2-philic co-solvent such as ethylene glycol offered a further enhancement (Scheme 13).

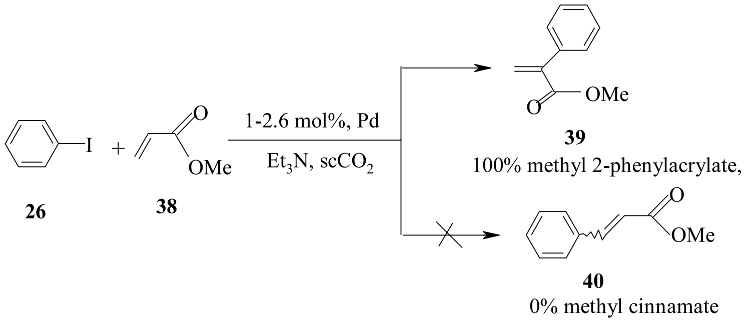
In a recent report,[78] dendrimer-encapsulated nanoparticles were shown to be versatile catalysts for both the Heck heterocoupling of iodobenzene with methyl acrylate and the hydrogenation of styrene in supercritical CO_2. Iodobenzene **26** can be coupled with methyl acrylate **38**, which is a benchmark reaction for the Heck coupling,[79] to yield exclusively methyl 2-phenylacrylate **39** (Scheme 14). The selectivity of **39** is remarkable when compared with standard palladium complexes or colloidal nanoparticles[80,81] used for Heck couplings in organic solvents, which result in only the *cis* and/or *trans* cinnamate **40**. The high selectivity is due in part to the steric environment the dendrimer template imposes on the reaction intermediates.

Tumas et al.[69] have investigated palladium-catalysed carbon–carbon bond coupling reactions, namely the Heck and Stille reactions in $scCO_2$. The reaction between iodobenzene **26** and vinyl(tributyl)tin **41** was carried out with a number of ligands using $Pd(dba)_3$ as the source of palladium. The nature of the ligand was found to significantly affect the yield of **42**. Using Ph_3P, a 49% conversion was achieved, which was only slightly better than that observed with no ligand present (38%). Tris(2-furyl)phosphine, however, showed good activity (86% conversion) (Scheme 15).

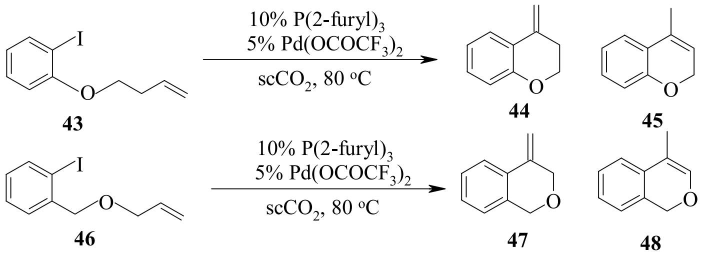


Scheme 15.

The intramolecular Heck cyclisation reaction in supercritical CO_2 has also been studied.[82] The intramolecular cyclisation of **43** and **46** in acetonitrile as the solvent gave complete conversion, but the isomerised exocyclic products **45** and **48** accounted for 76 and 80% of the yields, respectively. It has, however, been shown that, by carrying out the reaction in $scCO_2$, not only is a complete conversion



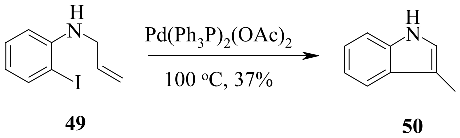
Scheme 14.



Scheme 16.

achieved, but suppression of the double bond isomerisation reaction is also observed. The desired exocyclic products **44** and **47** account for 83 and 93% of the yield, respectively (Scheme 16).

The intramolecular Heck reaction of **49** has been investigated[67] by Holmes et al. using fluorinated phosphine ligand complexes in supercritical carbon dioxide and the corresponding substituted indole **50** was obtained in superior yield to that reported for conventional solvents (Scheme 17).



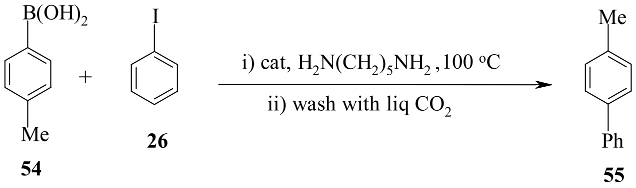
Scheme 17.

2.4. C–C bond-forming Baylis–Hillman reactions

The Baylis–Hillman reaction[83] is considered to be one of the most facile coupling protocols between activated alkenes **12** and aldehydes **51**, allowing the introduction of a hydroxyalkyl moiety at the α-position of Michael acceptors **52**. This reaction can be efficiently carried[84] out in $scCO_2$ with enhanced reaction rates relative to the comparable solution-phase reactions. At low pressure, an unprecedented dimerisation and formation of **53** is observed, which has led to the development of a novel one-pot three-component coupling reaction to form highly-functionalised ethers derived from Baylis–Hillman products (Scheme 18).

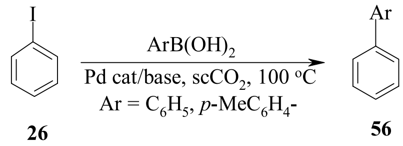
2.5. Suzuki coupling reactions

Suzuki coupling reactions[85] have been investigated in the supercritical phase in recent years.[63] Treatment of *p*-tolylboronic acid **54** with iodobenzene **26** and the base *N*,*N*,*N*,*N*-tetramethylhexanediamine in the presence of the polymer-supported phosphine–palladium catalyst in $scCO_2$ afforded the biaryl product **55**, which was isolated by venting the liquid CO_2 isolation into a beaker containing EtOAc. Washing the remaining resin and the amine salt with liquid CO_2 afforded the product in 64% yield (Scheme 19).



Scheme 19.

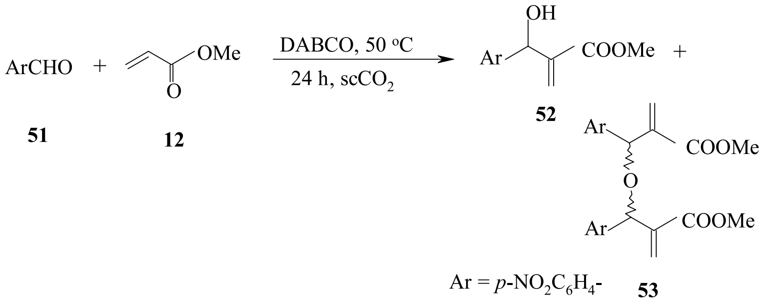
The Suzuki coupling with arylboronic acids[86] using phosphine ligands which play a crucial role in stabilising the active intermediate in $scCO_2$ has been studied. The reaction is believed to proceed via a Pd^0 intermediate, generated in situ from Pd^o or Pd^{II} precursors (Scheme 20). The fluorinated phosphine–palladium complex-mediated coupling of boronic acids with aryl or vinyl halides to yield biaryl **56**, the Suzuki reaction, has certain advantages for the coupling of two sp2 centres. This too can be conducted in $scCO_2$ in yields that are comparable to those achieved in conventional solvents.[67]



Scheme 20.

2.6. Alkylation reactions

Poliakoff and his co-workers introduced the supercritical phase to the Friedel–Crafts alkylation reactions by using $scCO_2$ or by making propene, one of the reactants, the



Scheme 18.

supercritical fluid.[87] The effect of the supercritical fluid operation on catalyst deactivation has been studied by Gao et al.[88,89] using the alkylation of benzene with ethylene on a Y-type zeolite as an example. Li Fan et al.[90] have investigated the effect of the SCF on the alkylation reaction on Y-type zeolites. Two types of alkylation reactions were studied, isopentane (T_c=188 °C, P_c=33 MPa) with isobutene and isobutane (T_c=135 °C, P_c=3.6 MPa) with isobutene. The paraffins acted as both reactant and supercritical fluid. The supercritical-phase reaction exhibited a higher catalytic activity, along with a remarkably longer lifetime, compared to the reaction in the liquid or gas phase. Recently, Clark and Subramaniam reported the 1-butene/isobutane alkylation in $scCO_2$ with USY zeolite as the catalyst. The utilisation of $scCO_2$ was considered mainly to lower the reaction temperature, as the higher reaction temperatures in other supercritical phase systems could have increased the cracking and coking reactions.[91] They showed that, using a molar excess of a low T_c diluent such as $scCO_2$, the alkylation can be performed at supercritical conditions at temperatures lower than the critical temperature of isobutane (<135 °C), resulting in a virtually steady alkylate (trimethylpentanes and dimethylhexanes) production for experimental durations of nearly 2 days.

Hitzler et al.[87] investigated the continuous Friedel–Crafts alkylation of mesitylene [$C_6H_3(Me)_3$], and anisole (C_6H_5OMe) with propene or propan-2-ol in supercritical carbon dioxide using polysiloxane-supported solid (DELOXAN) acid as catalyst in a small fixed-bed reactor (10 ml volume). Mesitylene **57** was alkylated in sc-propene (T_c=91.9 °C, P_c=46.0 bar) and the corresponding mono alkylated species **58** was obtained as the major product (25%) and the di and tri alkylated product **59** and **60** as the minor products. This work clearly demonstrates the feasibility of continuous and sustainable Friedel–Crafts alkylation in SCF solution, although no comparison was made with continuous alkylation in a conventional solvent using the same catalyst (Scheme 21). Suzuki et al.[92] have also performed Friedel–Crafts reactions, alkylations and etherifications at 350 °C, 152 bar and residence times of 120 min in the absence of any acid catalysts in scMeOH.

2.7. Photochemical reactions

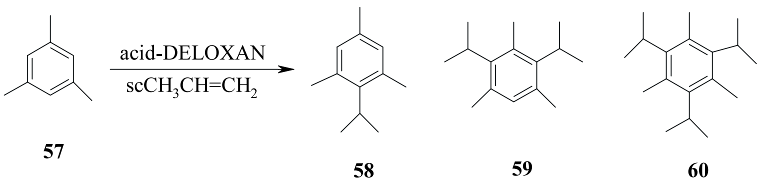
Johnston et al.[93] investigated the [2+2] photodimerisation of isophorone **61** in $scCO_2$ (38 °C) and $scCHF_3$ (34.5 °C). Three dimers were produced: a head-to-head dimer ($H-H_{anti}$), and two diasteromeric head-to-tail dimers ($H-T_{anti}$ and $H-T_{syn}$). In conventional solvents, Chapman found that more polar solvents favour the production of the more polar product.[94] Analogous results were obtained in SCF solvents, the more polar product ($H-H_{anti}$) being a major product in the more polar solvent and only a minor product[93] in CO_2 (in which the $H-H$:$H-T_{total}$ ratio was essentially 0.10, independent of pressure). These observations are explicable on the basis that, over the range of pressures examined, the dielectric constant varies more for CHF_3 (from 2.5 to 8.4) than for CO_2 (from 1.34 to 1.54) (Scheme 22).

Weedon et al. have examined the photo-Fries rearrangement[95] of naphthyl acetate **62** in $scCO_2$ at 35 and 46 °C. Photolysis of **62** leads to a caged pair [**63/64**] and the reaction in the cage yields the photo-Fries products, 2- or 4-acetylnaphthol (**65** or **66**). A cage escape, however, followed by hydrogen abstraction (isopropanol was present as a hydrogen-atom donor) leads to α-naphthol **67** (Scheme 23).

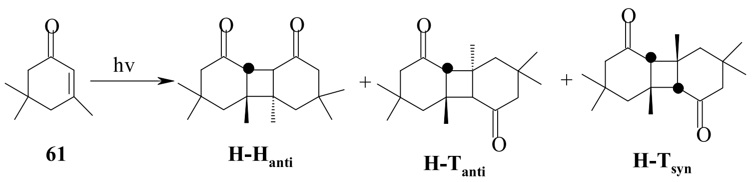
Photochemical carbonylation of the C–H bonds of liquid propane was achieved by Sakakura et al.[96] with the use of $RhCl(CO)(PMe_3)_2$ as catalyst and 3 atm of CO at 15 °C. Excellent selectivity for linear butanal (97% selectivity, 20 TON after 484 h) was obtained with only traces of 2-methylpropanal and acetaldehyde being observed.

2.8. Cyclopropanation reactions

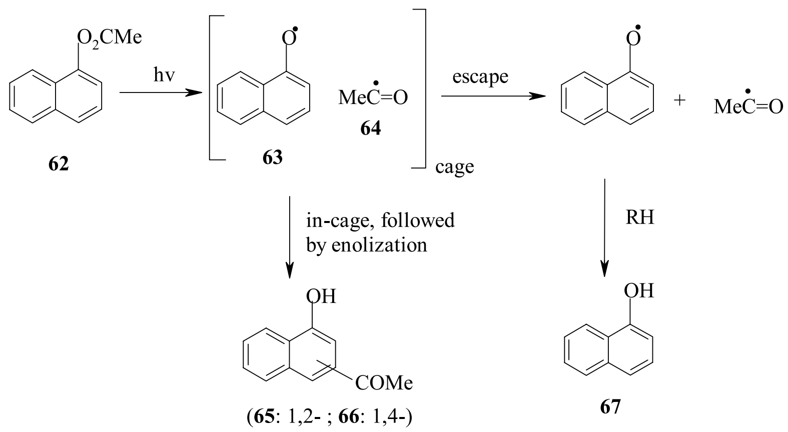
Supercritical fluoroform ($scCHF_3$) is yet another SCF that provides highly interesting opportunities for metal-catalysed C–C bond-formation reactions. Rhodium-catalysed asymmetric cyclopropanation was investigated, as it exhibits a marked selectivity dependence on solvent polarity in the liquid state[97,98] The cyclopropanation of styrene **27** with methyl phenyldiazoacetate **68** catalysed by



Scheme 21.

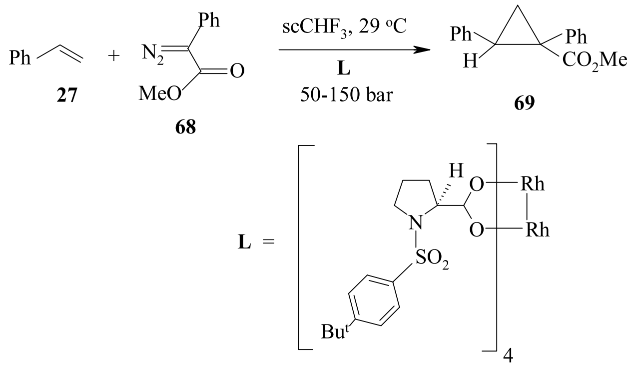


Scheme 22.



Scheme 23.

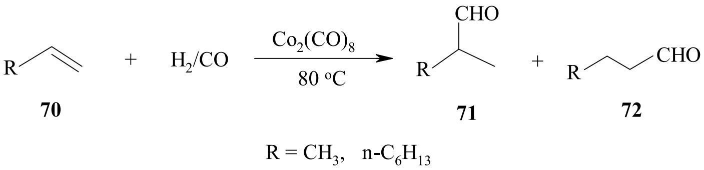
the dimeric rhodium(II) carboxylate complex L proceeds, to form **69** with a higher enantioselectivity in non-polar than in polar liquid solvents. Indeed, a strong dependence of the enantioselectivity on pressure was observed when the same reaction was performed in scCHF$_3$ at various pressures[99] (Scheme 24).



Scheme 24.

2.9. Hydroformylation reactions

The addition of CO and H$_2$ to a C=C double bond to yield aldehydes or, with subsequent reduction, alcohols is referred to as hydroformylation This reaction is one of the most important processes catalysed by homogenous organometallic catalysts on an industrial scale.[100] The hydroformylation catalysts are classified according to the metal used, with cobalt and rhodium-based catalysts being by far the most successful systems. The catalytic cycle proposed by Heck and Breslow[101] consists of a number of elementary steps. Depending on the catalyst and other factors, the rate-limiting step can be the reaction with H$_2$[102] and a rate increase could therefore be observed for some hydroformylation systems in SCFs.

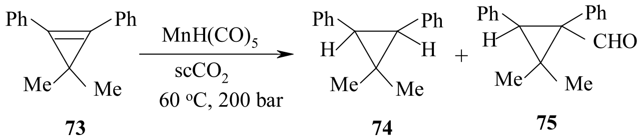


Scheme 25.

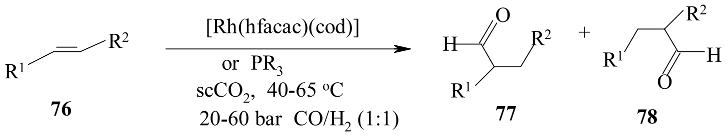
The first hydroformylation reaction of propylene in scCO$_2$ catalysed by dicobalt octacarbonyl was reported by Rathke et al.[103] The propylene **70** hydroformylation proceeded smoothly at 80 °C at $P_{\mathrm{H2}}=P_{\mathrm{co}}=56$ atm with Co$_2$(CO)$_8$ (10 mol%), hydrogen (42 bar) and carbon monoxide (42 bar), giving *n*-butyraldehyde **72** (88%). The selectivity for the desired linear aldehyde, butanal (88%), is higher than the value (83%) measured in benzene at slightly higher pressures ($Pco=80$ atm). The linear-to-branched ratio is slightly influenced by the pressure and temperature.[104] When the temperature is constant at 88 °C, the linear product selectivity increases from 73 to 81% as the pressure doubles (Scheme 25).

Noyori and his co-workers[105] reported the stoichiometric reaction of the olefin **73** with MnH(CO)$_5$ in scCO$_2$,which gave a similar selectivity for the hydroformylation product **75**, over the hydrogenation product **74**, to that found in alkane solvents. This suggested that the aldehyde **75** was primarily formed by non-radical pathways, which were independent of the solvent viscosity (Scheme 26).

As in conventional solvents, rhodium-based systems are generally much more active than cobalt catalysts in scCO$_2$ (Scheme 27). Various alkenes **76** have been hydroformylated in scCO$_2$ to yield **77** and **78** with [Rh(hfacac)(cod)] (cod=1.5-cyclooctadiene) as the catalyst precursor without additional ligands, at substrate/Rh ratios as high as 2600:1.[106] The reaction rate was found to be considerably higher in scCO$_2$ than in liquid organic solvents, this effect

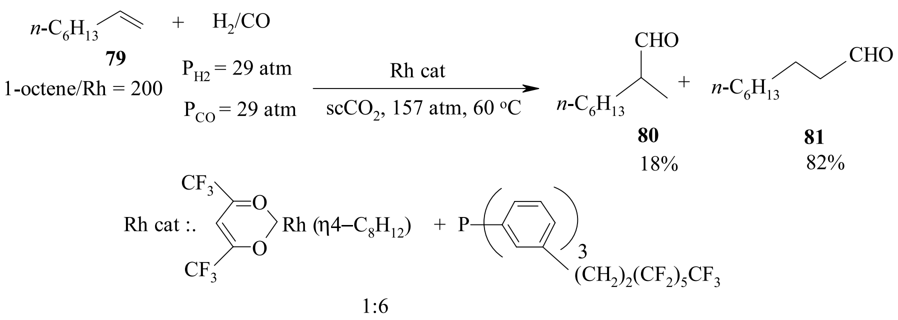


Scheme 26.



$R^1 = n$-C_6H_{13}, $R^2 = H$; $R^1 = R^2 = Et$;
$R^1 = Ph$, $R^2 = H$; $R^1 = CH_2OAc$, $R^2 = H$;

Scheme 27.



Scheme 28.

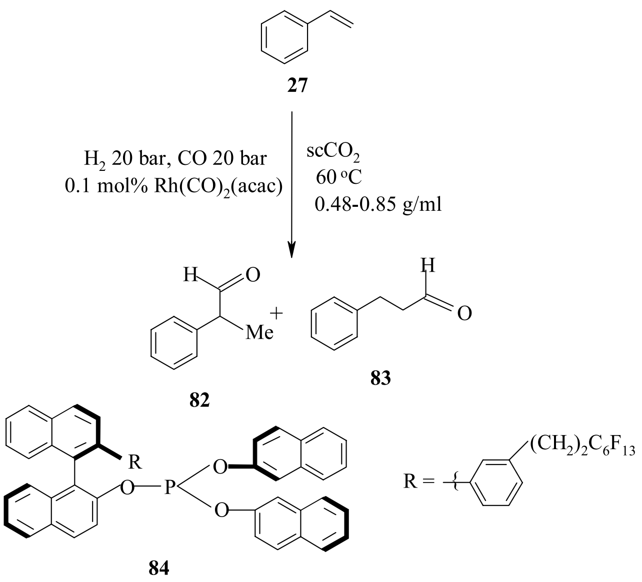
being the most pronounced for internal alkenes such as *trans*-3-hexene.

Leitner et al.[107] investigated a CO_2-soluble Rh complex with a polyfluoroalkyl substituted triarylphosphine ligand (Rh/phosphine 1:6) in $scCO_2$, which effected the hydroformylation of 1-octene **79** to give the linear aldehyde **81** in good yield and with 82% selectivity (Scheme 28). The reaction proceeds smoothly in the homogeneous supercritical phase without any side reactions such as hydrogenation or isomerisation (to **80**) of the olefin.

The introduction of fluorinated side-chains on the aromatic rings of the phosphine ligands results in an increase in the solubilities of the complexes in $scCO_2$, quantified by UV/vis spectroscopy of the Rh-hexafluoroacetylacetonate complexes with these ligands.[107] Under supercritical conditions at 45 °C and 91 atm, these complexes give bright yellow solutions with saturation concentrations of 6.3×10^{-5} and 7.5×10^{-5} mol l^{-1}, respectively.

Recently, a rhodium-catalysed hydroformylation reaction in $scCO_2$ using trialkylphosphines as simple alternatives to fluorinated arylphosphines, in order to achieve solubility, was investigated.[108] The catalyst prepared in situ from $Rh_2(OAc)_4$ (0.74 mol%) and PEt_3 (4 mol%) gave complete conversion of hex-1-ene within 2 h at 100 °C. The equivalent reaction in toluene solution showed an equivalent rate, but a poorer product ratio of 2.1:1.

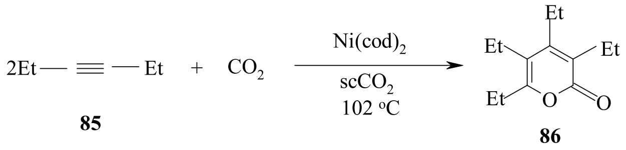
Asymmetric hydroformylation in $scCO_2$ also provides viable routes to important anti-inflammatory drugs starting from simple vinylarenes. Rhodium catalysts bearing the chiral phosphine/phosphite ligand (*R*,*S*)-BINAPHOS allow very high levels of enantiocontrol.[109] Investigations with a catalyst made up from 1,5-cod and (*R*,*S*)-BINAPHOS revealed that the ligand-bound rhodium species have insufficient solubility in the supercritical phase. Even a moderate asymmetric induction could only be obtained at low CO_2 densities, when an additional liquid phase was present at some stage of the reaction.[110] The ligand solubility problem was addressed by the addition of fluorinated chains, leading to the development of the fluorinated BINAPHOS ligand **84**. Thus the asymmetric hydroformylation of styrene **27**, using (*R*,*S*)-BINAPHOS **84** as the catalyst, favoured the asymmetric hydroformylation product **82** over its achiral regioisomer **83** with an appreciable asymmetric induction 68% ee. The use of this ligand with $Rh(CO)_2(acac)$, leads to increased levels of enantioselectivity and greater regioselectivity both in a conventional benzene solvent and in $scCO_2$ with quantitative conversions (17 h, 60 °C, 0.1 mol% cat, 0.2 mol% **84**).[111] (Scheme 29).



Scheme 29.

2.10. Coupling reactions in $scCO_2$

Reetz et al.[112] investigated the formation of tetraethyl 2-pyrone **86** from 3-hexyne **85** and CO_2 using a catalyst generated in situ from $Ni(cod)_2$ and the chelating diphosphine 1,4-diphenylphosphinobutane (dppb)$[Ph_2P(CH_2)_4PPh_2]$ in $scCO_2$. The selectivity and TON of 7, although only moderate, were similar to those reported in conventional solvents. Although the phase behaviour of the low-density reaction mixture and the solubility of the metal complex were not mentioned, these results demonstrated that Ni catalysts allow catalytic C–C coupling reactions with CO_2 under conditions beyond T_c and P_c Changing the catalyst from dppb to trimethylphosphine as the ligand increased the activity, allowed lower temperatures (51 °C) to be used and gave a higher TON of 18. The catalyst did, however, have a shorter lifetime in $scCO_2$ compared with conventional solvents[113] (Scheme 30).

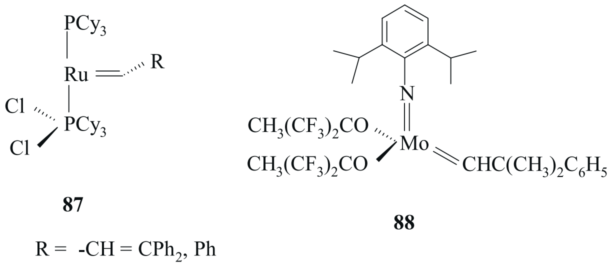


Scheme 30.

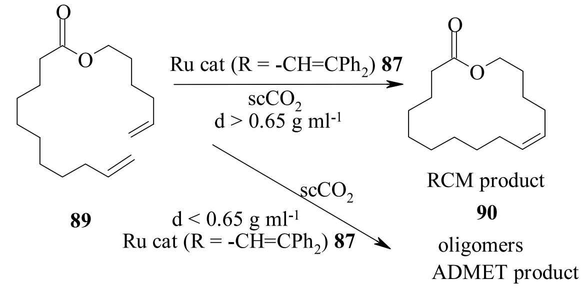
2.11. Olefin metathesis in $scCO_2$

Recent literature reveals that supercritical fluids are useful reaction media for the metathesis of olefins.[114–116] DeSimone found that $[Ru(H_2O)_6](OTs)_2$ (Ts=*p*-toluenesulfonyl) catalysed the ROMP (ring-opening metathesis polymerisation) of norbornene at 65 °C in $scCO_2$ (67–296 atm). The product, an off-white spongy textured polymer, was isolated by venting the CO_2.[117] Leitner et al.[118] have reported transition metal-catalysed olefin metathesis reactions in compressed CO_2 media. Using the conventional metathesis catalysts **87** and **88** (Scheme 31) ROMP of norbornene and cyclooctene gave the corresponding polymer in excellent yields, both in liquid CO_2 and in $scCO_2$.

Ring-closing metathesis (RCM) was also investigated[118,119] using the same carbene complexes and some remarkable observations were made. It was found that the RCM of **89** was extremely sensitive to density, with the 16-membered ring **90** being formed in excellent yield at densities $>0.65\ g\ ml^{-1}$ whereas mainly oligomers (70%, with 10% **89**) were produced at low densities (ADMET product) (Scheme 32). The density effect on the reaction pathway is not fully understood, but may be caused by the compressibility of the supercritical phase. Furstner et al. speculate that increasing the density at constant volume leads to a high dilution reaction condition, favouring the intramolecular reaction pathway.[119] A number of other cyclisations were performed in good yield. An interesting observation was that the catalyst **87** (R=–CH=CPh_2) (Scheme 31), which is normally deactivated in the presence of basic N–H groups, was active under such conditions in CO_2 solution.



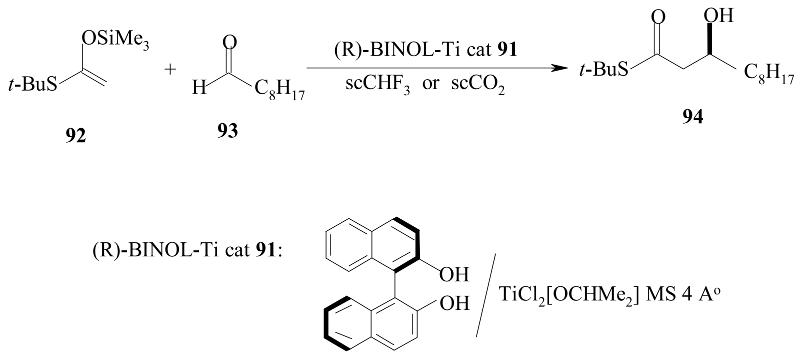
Scheme 31.



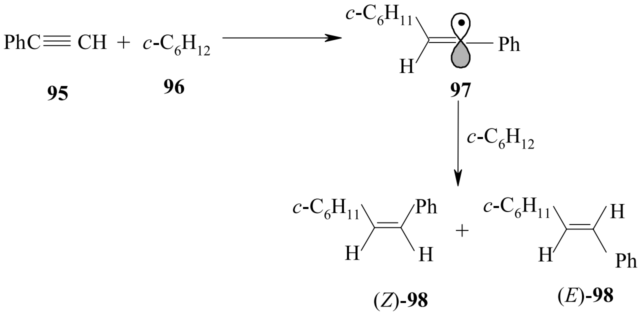
Scheme 32.

2.12. Asymmetric Mukaiyama aldol reactions in $scCHF_3$

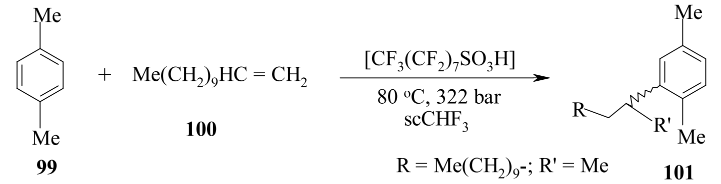
Asymmetric Lewis acid-catalysed carbon–carbon bond formation in Mukaiyama aldol reactions mediated by a β-naphthol-derived chiral titanium(IV) complex **91** proceeds smoothly in a supercritical fluid[120] such as fluoroform ($scCHF_3$). The chemical yield and enantioselectivity of the reaction in SCFs are found to be tuned by changing the supercritical fluids, ($scCHF_3$ versus $scCO_2$) and adjusting the matched polarities by varying the pressure of the CHF_3. The reaction in SCFs containing the chiral



Scheme 33.



Scheme 34.



Scheme 35.

Table 1. Dodecene alkylation of *p*-xylene with $CF_3(CF_2)_7SO_3H$ catalyst

Solvent	Conv. to LAB (%)	Isomerisation products[a] (%)
None[b]	0	<1
CO_2[c]	1	68
CHF_3[c]	90	7–9

[a] Value shown represents conversion of the non-alkylated α-olefin to an internal olefin mixture with 85% being close to thermodynamic equilibrium.

[b] 100 °C, 1 bar.

[c] 80 °C, 322 bar.

catalyst[121] and a ketene silyl acetal of the thioester **92** and an aldehyde **93** (1:2:3=1:20–40:20 molar ratio) proceeds smoothly to give a trimethylsilyl ether of the aldol product **94** in moderate yields (Scheme 33). The outcome of the reaction was found to be influenced by tuning the SCFs ($scCO_2$: T_c=31.0 °C, P_c=72.8 atm).

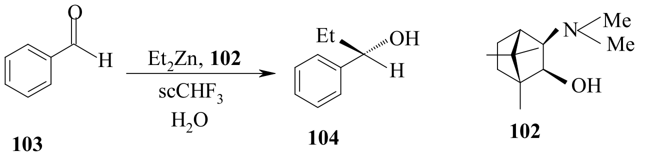
2.13. Addition of supercritical cyclohexane to phenylethyne

Metzger et al.[122] examined the addition of cyclohexane **96** to phenylethyne **95** in the temperature range from 20 to 340 °C in supercritical cyclohexane (ratio 1000:1). The addition proceeds via a 2-cyclohexyl-1-phenylethenyl radical **97** to provide 1-cyclohexyl-2-phenylethene **98**, as shown in Scheme 34. The radical chain is initiated by a bimolecular reaction of cyclohexane with phenylethylene to give a cyclohexyl radical and a 1-phenylethenyl radical. No effect on the reaction rate constant near the critical point was observed.

2.14. Formation of alkylbenzenes

Hutchenson and his co-workers[123] demonstrated the formation of linear alkylbenzenes (LAB) using a perfluorosulfonic acid catalyst in supercritical fluid reaction media. An enhanced alkylation activity was observed in fluoroforms (CHF_3) compared to carbon dioxide. The results indicates that $scCO_2$ solubilises the long-chain perfluorosulphonic acid $CF_3(CF_2)_7SO_3H$ which initiates the catalytic activity of these molecules. The poor conversion to the LAB product suggests, however, that the availability of the acid sites is still limited under these conditions despite the apparent solubility of the catalyst. The authors found that the dodec-1-ene **100** alkylation of *p*-xylene **99** using SCF fluoroform as the solvent proceeds in high yield to form **101**. The isomerisation of the α-olefin is primarily observed using $scCO_2$, with only a small yield of the alkylated product. This demonstrates tuning of the reaction pathway depending upon the solvent characteristics within the SCF media. This example illustrates the use of an SCF solvent to define the reaction chemistry in a catalysis application (Scheme 35 and Table 1).

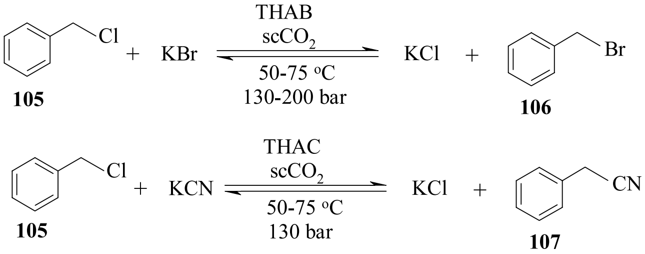
The asymmetric alkylation of benzaldehyde **103** catalysed by **102** in supercritical fluoroform (Scheme 36) to form the alcohol **104** was studied by Jessop et al.[99,124] Preliminary investigations of the reactions of benzaldehyde **103** with diethylzinc in $scCHF_3$ showed that the enantioselectivity was pressure dependent.



Scheme 36.

2.15. Phase-transfer catalysis

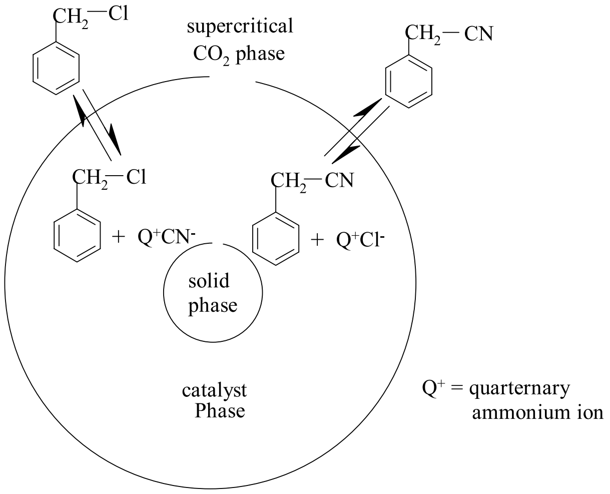
Phase-transfer catalysis (PTC) has also been used for carrying out reactions in supercritical media. The first PTC reaction in SCF was the displacement reaction of benzyl chloride **105** with potassium bromide in supercritical carbon dioxide[125,126] with 5 mol% acetone, in the presence of tetraheptylammonium bromide (THAB), to yield benzyl bromide **106** (Scheme 37). Chandler et al.[127] investigated the reaction between benzyl chloride **105** and potassium



Scheme 37.

cyanide in $scCO_2$ in the presence of tetraheptylammonium chloride (THAC) to yield benzyl cyanide **107**.

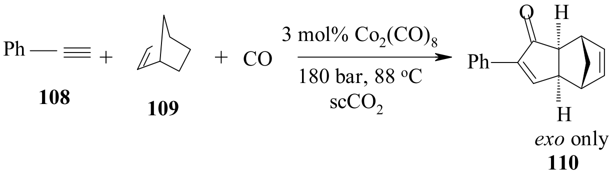
Scheme 38 depicts the three-phase system and the concentrated catalyst phase where the reaction is believed to occur. In the presence of acetone as a cosolvent, the reaction rate decreased, perhaps due to the increased solubility of the catalyst in the SCF and the detection of catalyst in the ω-phase. Although it is customary to add co-solvents to SCFs to increase the solubilities, in this case the increased solubility appears to be detrimental to the reaction rate.



Scheme 38.

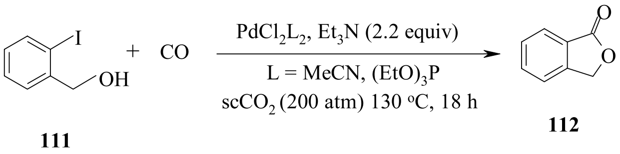
2.16. Miscellaneous reactions

An intermolecular reaction was also carried out in $scCO_2$ where[54] phenylacetylene **108** can couple with excess norbonadiene **109** catalysed by dicobaltoctacarbonyl and a CO pressure of 15 bar, to give the bicyclic compound **110** in 87% (Scheme 39).



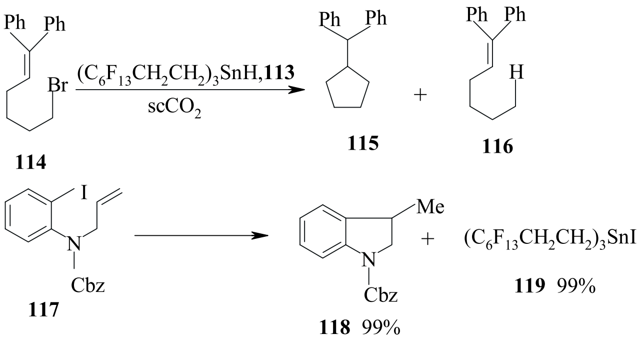
Scheme 39.

Ikaria et al. have reported[128] an efficient carbonylation of aryl halides catalysed by CO_2-soluble palladium complexes with trialkyl or triaryl phosphite ligands in $scCO_2$. The intramolecular carbonylation of 2-iodobenzyl alcohol **111** catalysed by $PdCl_2(MeCN)_2$ in $scCO_2$ proceeded efficiently to give the phthalide **112** with a TON of 1880 after 18 h (Scheme 40). Changing the ligand to the more soluble triethylphosphite gave an increase in rate, showing that the reaction is faster in $scCO_2$ than in conventional organic solvents.



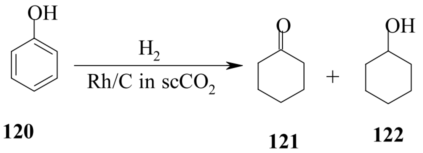
Scheme 40.

An intramolecular cyclisation[129] via the reduction of 1,1-diphenyl-6-bromo-1-hexene **114** under supercritical CO_2 conditions with the fluorous tin hydride **113** provided the 5-*exo* cyclised product **115** in 87% isolated yield, along with 7% of the reduced product **116**. Interestingly, the reduction of **114** with liquid benzotrifluoride (1 atm) provided only the cyclised product **115**, which was isolated in 75% yield. Significantly, the reduction of **114** with tributyltin hydride produced neither **115** nor **116** but recovered the starting materials, along with some tin formate. In addition, reduction of the aryl iodide **117** with the fluorous tin hydride **113** provided **118** in 99% yield, along with 99% of the tin iodide **119** (Scheme 41).

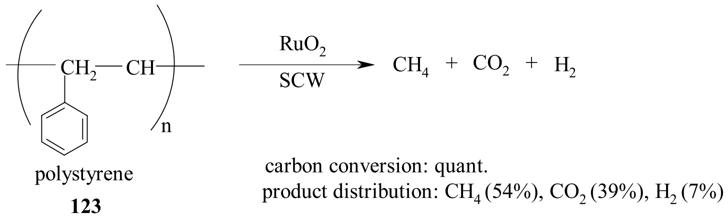


Scheme 41.

A very recent study by Shirai et al.[130] found that a charcoal-supported rhodium catalyst was highly active for the ring hydrogenation of phenol and cresols under supercritical carbon dioxide. Commercially available catalysts were used in this work viz 5 wt% carbon-supported palladium (5% Pd/C), rhodium (5% Rh/C), platinum (5% Pt/C), and ruthenium (5% Ru/C). During hydrogenation of phenol, it was found that both the hydrogenation activity and selectivity to cyclohexanol increased with increasing hydrogen pressure at 10 Mpa carbon dioxide. Phenol hydrogenation is a successive reaction in which phenol **120** is first hydrogenated to cyclohexanone **121** followed by hydrogenation of the latter to cyclohexanol **122** (Scheme 42). Cyclohexanol was, however observed at low phenol conversion under high hydrogen pressure, indicating that it would be formed not only via the cyclohexanone intermediate, but also directly from phenol. The hydrogenation activity also increased with increasing carbon dioxide pressure. Bhange et al. have observed higher conversions with increasing CO_2 pressure in the case of cinnamaldehyde under supercritical carbon dioxide.[131]



Scheme 42.



123

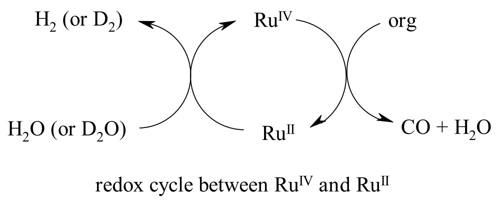
Scheme 43.

Table 2. Summary of the results on the gasification reaction of organic compounds by RuO_2 in SCW

Organic compounds (org)	Molar ratio [org]/[RuO_2]	C-conv. (%)	Product distribution (%)		
			CH_4	CO_2	H_2
Naphthalene	5.12	96.7	48.8	42.7	8.4
Carbazole	3.94	87.9	52.7	40.6	6.7
Diphenyl ether	3.87	99.9	45.8	48.8	5.4
Dibenzofuran	3.92	101.7	51.0	43.6	5.5
Polyethylene	23.5	100.6	66.6	28.0	5.3
Polypropylene	15.7	99.9	66.5	26.9	6.5
Polystyrene	6.32	100.7	53.7	39.4	6.9
Poly(ethylene terephthalate)	3.44	97.2	37.3	51.0	11.5
Cellulose	4.07	97.0	34.2	50.9	14.6

In a recent breakthrough by Tomiyasu et. al,[132] complete gasification of organic compounds by ruthenium(IV) oxide (RuO_2) in SCW has been achieved, where aromatic compounds, as well as other organic compounds including plastics, are converted into CH_4 and CO_2, accompanied by the production of H_2. The stoichiometry of the conversions strongly suggests that the hydrogen source of the fuel products is water and that the catalytic effect of RuO_2 results from a redox couple of Ru^{IV}/Ru^{II} induced by SCW. In fact, direct evidence supporting this has been obtained by a gasification experiment of polystyrene **123** in a RuO_2-supercritical deuterium oxide system. (Scheme 43 and Table 2).

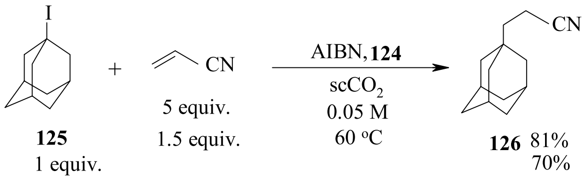
Organic molecules are partially oxidised by RuO_2 to form CO and H_2O, where Ru^{IV} is reduced to the lower oxidation sate of Ru^{II}. In order to oxidise an excess number of organic molecules, Ru^{II} must be re-oxidised to Ru^{IV}, which is carried out with the reduction of SCW to H_2. The Ru^{IV} regenerated is reduced again to Ru^{II} for further partial oxidation of organic molecules. The CO produced is converted into CH_4 and CO_2 through [mCO+$n$$H_2$] reactions with H_2 derived from SCW. A redox cycle between Ru^{IV} and Ru^{II} is induced by SCW, in which the gasification reaction of organic compounds proceeds catalytically (Scheme 44).



redox cycle between Ru^{IV} and Ru^{II}

Scheme 44.

Curran et al. have reported[129] radical reactions in supercritical carbon dioxide. The standard Giese reaction shown in Scheme 45 was conducted by the addition of iodoadamantane **125** to acrylonitrile (5 equiv), which provided the radical adduct **126** in 81% yield after flash chromatography when carried out in the presence of tris(2-perfluorohexyl)ethyl)tin hydride **124** in $scCO_2$. Additionally formed in this experiment was an acetone-soluble material, polyacrylonitrile.[133] When 1.5 equiv. of acrylonitrile was used, the compound **126** was isolated in 70% yield and the formation of this acetone-soluble material was not observed (Scheme 45).

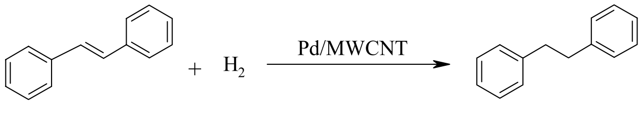


125 **126**

124: $(CF_3(CF_2)_5CH_2CH_2)_3SnH$

Scheme 45.

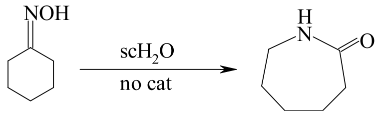
In a very recent paper, Wai et al.[134] reported a rapid, direct and green procedure to decorate multiwalled CNTs (MWCNTs) with catalytic palladium nanoparticles by a simple hydrogen reduction of a Pd(II)-β-diketone precursor using $scCO_2$ as the medium. The resulting Pd nanoparticle-MWCNT composite is an effective catalyst for the selective hydrogenation of olefins in CO_2 and for the electrochemical reduction of O_2. The catalytic capability of the Pd-MWCNT composite was tested for hydrogenation of a CO_2-soluble olefin *trans*-stilbene in liquid CO_2. The conversion of this stilbene **127** to 1,2-diphenylethane **128** was about 80 and 96% after 5 and 10 min. respectively, and indicates that the Pd-MWCNT composite exhibits a high catalytic activity for the hydrogenation of olefins in CO_2. This simple and green nanoparticle deposition technique is not limited to Pd and may be used to prepare a variety of metal nanoparticles on MWCNT surfaces for catalytic applications (Scheme 46).



127 **128**

Scheme 46.

A high-pressure and high-temperature FTIR method was used to study the non-catalytic Beckmann rearrangement using supercritical water.[135] A significant acceleration of the Beckmann rearrangement was achieved by using scH_2O, especially near the critical point, and even in the absence of any acid catalysts. It has been demonstrated that scH_2O acts effectively in place of the conventional acid catalysis for the rearrangement. In the case of the Beckmann rearrangement of cyclohexanone-oxime **129** into ε-caprolactam **130**, in the IR spectrum near the critical point a new CO stretching band assigned to ε-caprolactam appeared, whereas no bands for cyclohexanone-oxime were observed. The rate constant for the formation of ε-caprolactam greatly increased as the temperature approached the critical temperature of water. The accelerated rates of reaction may be attributed to a large increase in the local proton concentration around the organic reactants (Scheme 47).



129 **130**

Scheme 47.

3. Conclusions

The various examples illustrated in this review have demonstrated the considerable potential of supercritical fluids as alternative media for carbon–carbon bond-formation reactions in organic synthesis. Although the favourable features of using supercritical CO_2 as a reaction medium for organic synthesis have been widely cited for over a decade, it is still not very clear what types of reactions to run in supercritical CO_2 and how to run them. In order to exploit the potential of $scCO_2$, the fundamental principles behind its role must be understood and to do this requires true interdisciplinary research involving academic synthetic chemists and industrial process chemists, physical chemists and chemical engineers, all of whom have an important role to play. Further studies are therefore surely needed, and the wholesale apportioning of this reaction class to supercritical CO_2 now seems like a viable possibility. In addition, the use of highly CO_2-soluble fluorous reagents and catalysts should prove to be a valuable strategy to transport other reaction classes to CO_2. Although much work has been carried out in this area, the field of SCF reaction chemistry is far less developed than the extraction of materials. Part of the reason is undoubtedly the understandable caution of reaction chemists to embark on experiments that involve high pressures, high temperatures or even both. Nevertheless, this review has shown that new chemistry is beginning to emerge and that SCFs do provide access to new compounds. Most importantly, it is clear that SCFs offer chemists increased opportunities to control reactions. In supercritical media, chemists can manipulate the phase behaviour of a mixture and they can control the concentrations of dissolved gases, alter the morphology of the products and carry out their reaction in a cleaner, greener way. At the end of many reactions, however, the problem of separating the products from spent and unspent reagents remains. The use of environmentally friendly reaction solvents such as supercritical CO_2 makes little sense if the reactions are followed by standard extractions or chromatographies with traditional organic solvents: extractions and chromatographies invariably require more solvent volumes than the reactions that precede them. It seems probable, however, that the large differences in solubility in supercritical CO_2 between fluorous and organic compounds can be transferred into practical separation procedures. In the long run, the potential of supercritical fluid applications will continue to expand, driven by research uncovering new opportunities and substantiating their known potential for controlling surface reactions and for the synthesis of new catalytic materials.

Acknowledgements

We thank the Department of Science and Technology (DST), New Delhi for financial support and the Director, Regional Research Laboratory, Jorhat for his encouragement to perform this work.

References and notes

1. Cagniard de LaTour, C. *Ann. Chim. Phys.* **1822**, *21*, 127–132, see also 178–182.
2. Garrabos, Y.; Lenaindra, B.; Subra, P.; Canoall, F.; Pommiol, C. *Ann. Chem. Sci. Metor.* **1992**, *17*, 55.
3. (a) Jessop, P. G.; Leitner, W. *Chemical Synthesis using Supercritical Fluids*; Wiley-VCB: Weinheim, 1999. (b) Sun, Y.; Landav, R. N.; Wang, J.; LeBold, C.; Blackmond, D. G. *J. Am. Chem. Soc.* **1996**, *118*, 1348.
4. Bosk, M. J.; Feng, S.; Gross, M. G.; Tomas, W. *J. Am. Chem. Soc.* **1995**, *117*, 277.
5. Johnston, K. P. *Nature* **1994**, *368*, 187.
6. Wynne, D. C.; Jessop, P. G. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1143.
7. Aida, T.; Squires, T. G. In *Supercritical Fluids: Chemical and Engineering Principles and Application. ACS Symposium series No. 329*; Squires, T. G., Paulaitis, M. E., Eds.; American Chemical Society: Washington, DC, 1987; p 58.
8. Jessop, P. G.; Kariya, T. I.; Noyori, R. *Nature* **1994**, *368*, 231.
9. (a) Bochniak, D. J.; Subramaniam, B. *AIChE J.* **1998**, *44*, 1889. (b) Subramanium, B.; Torma, A. In *Innovations in Supercritical Fluids Science and Technology*; *ACS Synposium series No. 608*; Hutchenson, K. W., Foster, N. R., Eds.; American Chemical Society: Washington, DC, 1995; p 246. (c) Eckart, C. A.; Chandler, K. *J. Supercrit. Fluids* **1998**, *13*, 187.
10. Braker, W.; Mossman, A. L. *Matheson Gas Data Book*; Matheson Company: Lundhurst, NJ, 1980.
11. (a) Anastas, P. T.; Williams, T. C. *Green Chemistry: Frontiers in Benign Chemical Synthesis, Processes and*

Protocols; Oxford University Press: Oxford, 1998. (b) Xie, W.; Jin, Y.; Wang, P. G. *Chem. Tech.* **1999**, *2*, 23.

12. Rondolph, T. W. *Trends Biotechnol.* **1990**, *8*, 78.
13. Nakamura, K.; Chi, Y. M.; Yamada, Y.; Yano, T. *Chem. Eng. Commun.* **1985**, *45*, 207.
14. Paulaites, M. E.; Krokonis, V. Y.; Kurnik, R. T.; Raid, R. C. *Rev. Chem. Eng.* **1982**, *1*, 179.
15. Morty, A.; Chulalaksananukul, W.; Condoret, J. S.; Willemot, R. M.; Durand, G. *Biotechnol. Lett.* **1990**, *12*, 11.
16. See for example: In *Supercritical Fluids Methods*; Williams, J. R., Clifford, A. A., Eds.; Humana: New Jersey, 2000.
17. McHungh, M.; Krukonis, U. Supercritical Fluids Extraction; Butterworth: Stockham, MA, 1986.
18. (a) Kaupp, G. *Angew. Chem. Int. Ed. Engl.* **1994**, *34*, 1452. (b) Tanko, J. M.; Blackert, J. F. *Science* **1994**, *263*, 203.
19. (a) Ikushima, Y.; Saito, N.; Sato, O.; Ari, M. *Bull. Chem. Soc. Jpn* **1994**, *67*, 1734. (b) Ikushima, Y. *J. Phys. Chem.* **1992**, *96*, 2293.
20. (a) Combes, J. R.; Guan, J. M.; De Simone, J. M. *Macromolecules* **1994**, *27*, 865. (b) Guan, Z.; Combes, J. R.; Menceloglu, Y. Z.; De Simone, J. M. *Macromolecules* **1993**, *26*, 2663. (c) De Simone, J. M.; Guan, Z.; Flebernd, C. S. *Science* **1992**, *257*, 945.
21. (a) Ikariya, T.; Jessop, P. G.; Noyori, R. Japan Patent. Appl. No. 274221, 1993. (b) Jessop, P. G.; Ikariya, T.; Noyori, R. *Nature* **1994**, *368*, 231. (c) Jessop, P. G.; Ikariya, T.; Noyori, R. *Science* **1995**, *269*, 1065.
22. (a) Jessop, P. G.; Hsiao, Y.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996**, *118*, 344. (b) Burk, M. J.; Feng, S. G.; Gross, M. F.; Tumas, W. J. *J. Am. Chem. Soc.* **1995**, *117*, 8277.
23. (a) Metzger, J. O. *Angew. Chem. Int. Ed.* **1998**, *37*, 2975. (b) Verma, R. S. *Green Chem.* **1999**, *1*, 43. (c) Deshayes, S.; Liagre, M.; Loupy, A.; Luche, J. L.; Patil, A. *Tetrahedron* **1999**, *55*, 10851.
24. (a) Gohain, M.; Gogoi, B. J.; Prajapati, D.; Sandhu, J. S. *New J. Chem.* **2003**, 1038. (b) Saikia, P.; Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **2002**, 7525. (c) Thakur, A. J.; Saikia, P.; Prajapati, D.; Sandhu, J. S. *Synlett* **2001**, 1299. (d) Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **2000**, 8639. (e) Boruah, B.; Baruah, A.; Dutta, M. P.; Prajapati, D.; Sandhu, J. S. *Synlett* **1999**, 409. (f) Illias, Md.; Barman, D. C.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **2002**, *43*, 1877.
25. (a) Holberg, J. D.; Seddon, K. K. *J. Chem. Soc., Dalton Trans.* **1999**, 2139. (b) Welton, J. *J. Chem. Rev.* **1999**, *99*, 2701. (c) Baruah, B.; Dutta, M. P.; Boruah, A.; Prajapati, D.; Sandhu, J. S. *Synlett* **1999**, 409.
26. (a) MacFarlane, D.; Meakin, P.; Sun, J.; Amini, N.; Forsyth, M. *J. Phys. Chem. B.* **1999**, *103*, 4164. (b) Scott, J. L.; MacFarlane, D.; Raston, C. L.; Teoh, M. *Green Chem.* **2000**, *2*, 123.
27. (a) Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev.* **1999**, *99*, 475–493. (b) Oakes, S. R.; Cliffor, A. A.; Rayner, C. M. *J. Chem. Soc. Perkin Trans. 1* **2001**, 917. (c) Shezad, N.; Clifford, A. A.; Rayner, C. M. *Tetrahedron Lett.* **2001**, *42*, 323. (d) Darr, J. A.; Poliakoff, M. *Chem. Rev.* **1999**, *99*, 495.
28. (a) Anastas, P. T.; Williamson, T. C. *Green Chemistry: Frontiers in benign chemical synthesis and processes*; Oxford University: Oxford, 1998. (b) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, 1998. (c) Xie, W.; Jin, Y.; Wang, P. G. *Chem. Tech.* **1999**, *2*, 23.
29. (a) Laskar, D. D.; Gohain, M.; Prajapati, D.; Sandhu, J. S. *New J. Chem.* **2002**, 193. (b) Thakur, A. J.; Prajapati, D.; Gogoi, B. J.; Sandhu, J. S. *Chem. Lett.* **2003**, 258. (c) Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **2001**, 7883. (d) Strauss, C. R. *Aust. J. Chem.* **1999**, *52*, 83, and references cited therein.
30. (a) Li, C.; Chan, T. *Organic reactions in aqueous media*; Wiley: New York, 1997. (b) Li, C. H.; Zhang, W. C. J. *J. Am. Chem. Soc.* **1998**, *120*, 9102. (c) Prajapati, D.; Laskar, D. D.; Gogoi, B. J.; Devi, G. *Tetrahedron Lett.* **2003**, *44*, 6755.
31. For reviews see: Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480.
32. (a) Cave, G. W. V.; Raston, C. L. *J. Chem. Soc. Chem. Commun.* **2000**, 2199. (b) Toda, F.; Tanaka, K. *Chem. Rev.* **2000**, *100*, 1025.
33. Ikushima, Y. *J. Phys. Chem.* **1992**, *96*, 2293.
34. Ikushima, Y.; Saito, N.; Sato, O.; Arai, M. *Bull. Chem. Soc. Jpn* **1991**, *64*, 282.
35. (a) Rideout, D.; Breslow, R. *J. Am. Chem. Soc.* **1980**, *102*, 1897. (b) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159.
36. (a) Grieco, P. A.; Garner, P. *Tetrahedron Lett.* **1983**, *24*, 1897. (b) Grieco, P. A. *Aldrichim. Acta* **1991**, *24*, 358.
37. Korzanski, M. B.; Kolis, J. W. *Tetrahedron Lett.* **1997**, *38*, 5611.
38. Gao, J. *J. Am. Chem. Soc.* **1993**, *115*, 6893.
39. Renslo, A. R.; Weinstein, R. D.; Tester, J. W.; Danheiser, R. L. *J. Org. Chem.* **1997**, *62*, 4530.
40. Isaacs, N. S.; Keating, N. *J. Chem. Soc. Chem. Commun.* **1992**, 876.
41. Weinstein, R. D.; Renslo, A. R.; Danheiser, R. L.; Harris, J. G.; Terter, J. W. *J. Phys. Chem.* **1996**, *100*, 12337.
42. Paulaites, M. E.; Alexander, G. C. *Pure Appl. Chem.* **1987**, *59*, 61.
43. Chapuis, C.; Kucharska, A.; Rzepecki, P.; Jurezak, J. *Helv. Chim. Acta* **1998**, *81*, 2314.
44. (a) Oakes, R. S.; Heppenstall, T. J.; Shezad, N.; Clifford, A. A.; Rayner, C. M. *J. Chem. Soc. Chem. Commun.* **1999**, 1459. (b) Oakes, R. S., Ph.D. thesis, University of Leeds, 2000..
45. Clifford, A. A.; Popli, K.; Gaskill, W. J.; Dartti, K. D.; Ruyner, C. M. *J. Chem. Soc. Faraday Trans* **1998**, *94*, 1451.
46. Matsui, J.; Tsuchiya, T.; Odashina, K.; Kobayashi, S. *Chem. Lett.* **2000**, 179.
47. Washstein, R. J.; Renslo, A. R.; Danheixer, R. L.; Tester, J. W. *J. Phys. Chem. B* **1999**, *103*, 2878.
48. Reaves, T.; Roberts, C. B. *Chem. Eng. Commun.* **1999**, *171*, 117.
49. (a) Kim, S.; Johnston, K. P. *Chem. Eng. Commun.* **1988**, *63*, 49. (b) Ikushima, Y.; Ito, S.; Asano, T.; Yokoyaman, T.; Saito, N.; Hatakeda, K. *J. Chem. Eng. Jpn* **1990**, *23*, 96.
50. (a) Akiya, N.; Savage, P. E. *AlChE J.* **1998**, *44*, 405–415. (b) Broll, D.; Kaul, C.; Kramer, A.; Krammer, P.; Richter, T.; Jung, M.; Vogel, H.; Zehner, P. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 2998.
51. Ikushima, Y.; Kiyotaka, H.; Sato, O.; Yokoyama, T.; Arai, M. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 2910.
52. Katritzky, A. R.; Allin, S. M. *Acc. Chem. Res.* **1996**, *29*, 399.
53. Park, K. H.; Uk Son, S.; Chung, Y. K. *J. Chem. Soc. Chem. Commun.* **2003**, 1898.
54. Jeong, N.; Hwang, S. H.; Lee, Y. W.; Lim, J. S. *J. Am. Chem. Soc.* **1997**, *119*, 10549.
55. Berthiol, F.; Doucet, H.; Santelli, M. *Tetrahedron Lett.* **2003**, *44*, 1221.
56. Gron, L. U.; Tinsley, A. S. *Tetrahedron* **1999**, *40*, 227.

57. Gron, L. U.; Lacroix, J. F.; Higgins, C. J.; Steelman, K. L.; Tinsley, A. S. *Tetrahedron Lett.* **2001**, *42*, 8555.

58. Zhang, R.; Zhas, F.; Sato, M.; Ikushima, Y. *J. Chem. Soc. Chem. Commun.* **2003**, 1548.

59. Ikushima, Y.; Hatakeda, K.; Sato, O.; Yokoyama, T.; Masahito, A. *Angew. Chem. Int. Ed. Engl.* **2001**, *40*, 210.

60. Ikushima, Y.; Hatakeda, K.; Sato, M.; Sato, O.; Arai, M. *J. Chem. Soc. Chem. Commun.* **2002**, 2208.

61. Mukhopadhyay, S.; Rothenberg, G.; Joshi, A.; Baidossi, M.; Casson, Y. *Adv. Synth. Catal.* **2002**, *344*, 348.

62. Jeffery, T. *Tetrahedron Lett.* **1994**, *35*, 3051.

63. Gordon, R. S.; Holmes, A. R. *J. Chem. Soc. Chem. Commun.* **2002**, 640.

64. Fujita, S.; Yuzawa, K.; Bhanage, B. M.; Ikushima, Y.; Arai, M. *J. Mol. Catal. A* **2002**, *280*, 35.

65. Camichael, A. J.; Earle, M. J.; Holbrey, J. D.; McCormac, P. B.; Seddon, K. R. *Org. Lett.* **1999**, *1*, 997.

66. Morita, D. K.; Pesiri, D. R.; David, S. A.; Calaze, W. H.; Tumas, W. *J. Chem. Soc. Chem. Commun.* **1998**, 1397.

67. Carrol, M. A.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1998**, 1395.

68. (a) Reardon, P.; Metts, S.; Crittendon, C.; Daugherity, P.; Parsons, E. *J. Organometal.* **1995**, *14*, 3810. (b) Dimimuie, J.; Mett, S.; Crittendon, C. *J. Organometal.* **1995**, *14*, 4033.

69. Morita, D. K.; Peseri, D. R.; David, S. A.; Glaze, W. H.; Tumas, W. *J. Chem. Soc. Chem.Commun.* **1998**, 1397.

70. Shezad, N.; Oakas, R. S.; Difford, A. A.; Rayner, C. M. *Tetrahedron Lett.* **1999**, *44*, 2221.

71. Osswall, T.; Schnesder, S.; Wang, S.; Bannwarth, W. *Tetrahedron Lett.* **2001**, *42*, 2965.

72. Early, T. R.; Gordon, R. S.; Qrrol, M. A.; Holmes, A. B.; Shuta, R. E.; Macenvay, I. F. *J. Chem. Soc. Chem. Commun.* **2001**, 1966.

73. Ley, S. V.; Baxandale, I. R.; Bream, R. N.; Jackson, P. S.; Leerh, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. T.; Taylor, S. J. *J. Chem. Soc. Perkin Trans. 1* **2000**, 3816.

74. Desimon, J.; Solva, M.; Tando, P. *J. Org. Chem.* **2001**, *66*, 4047.

75. Cacchi, S.; Fabrizi, G.; Gasparrini, F.; Villani, C. *Synlett* **1999**, 345.

76. Bhanage, B. M.; Ikushima, Y.; Shirai, M.; Arai, M. *Tetrahedron Lett.* **1999**, *40*, 6427.

77. Yeung, L. K.; Lee, T., Jr.; Johnston, K. P.; Crooks, R. M. *J. Chem. Soc., Chem. Commun.* **2001**, 2290.

78. DeMeijuere, A.; Meyet, F. E. *Angew. Chem. Int. Eng. Engl.* **1994**, *33*, 2379.

79. Belle, M.; Fischer, H.; Kuchlein, K.; Reisinger, C. P.; Hermann, W. A. *J. Organometal. Chem.* **1996**, *520*, 257.

80. (a) Reetz, M. T.; Lohmer, G. *J. Chem. Soc. Chem. Commun.* **1996**, 1921. (b) Reetz, M. T.; Westermann, E. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 165. (c) Kingelhofer, S.; Heitz, W.; Creiner, A.; Oestreich, S.; Forster, S.; Antonietti, M. *J. Am. Chem. Soc.* **1997**, *119*, 10116.

81. Yeung, L. K.; Crooks, R. M. *Nano. Lett.* **2001**, *1*, 14.

82. Shezad, N.; Clifford, A. A.; Rayner, C. M. *Tetrahedron Lett.* **2001**, *42*, 323.

83. (a) Li, G.-G.; Gao, J.-J.; Wei, H.-X.; Enright, M. *Org. Lett.* **2002**, *2*, 617. (b) Shi, M.; Xu, Y.-M. *J. Org. Chem.* **2003**, *68*, 4784. and references cited therein. (c) Basvaiah, D.; Jaganmohan, R. A. *J. Chem. Soc., Chem. Commun.* **2003**, 604.

84. (a) Paul, R. M.; Anthony, C. A. *J. Chem. Soc., Chem. Commun.* **2002**, 968. (b) Bedford, R. B.; Blaki, M. Ta.; Butts, C. P.; Holder, D. *J. Chem. Soc., Chem. Commun.* **2003**, 466.

85. Zhao, Y.; Zhou, Y.; Ma, D.; Liu, J.; Li, L.; Zhang, T. Y.; Zhang, H. *Org. Biomol. Chem.* **2003**, *1*, 1643.

86. (a) Show, B. L.; Perera, S. D. *J. Chem. Soc. Chem. Commun.* **1998**, 1361. (b) Riermeirs, T. H.; Zapf, A.; Beller, M. *Top. Catal.* **1997**, *4*, 301.

87. Hitzler, M. G.; Snail, F. R.; Koss, S. K.; Poliakoff, M. *Chem. Commun.* **1998**, 359–360.

88. Gao, Y.; Liu, H. Z.; Shi, Y. R.; Yuan, W. K. *The Fourth International Symposium on Supercritical Fluids; Sendai, Japan* **1997**, 531–534.

89. Gao, Y.; Shi, Y. F.; Zhu, Z. N.; Yoan, W. K. *Fourth International Symposium on High presume Chemical Engineering; Zurich, Switzerland* **1996**, 151–156.

90. Fan, L.; Nakamura, I.; Ishita, S.; Fujimoto, K. *Int. Eng. Chem. Res.* **1997**, *36*, 1458–1463.

91. Clark, M. C.; Subramaniam, B. *Int. Eng. Chem. Res.* **1998**, *37*, 1243–1250.

92. Suzuki, T.; Okada, A.; Ohhashi, K.; Sasaki, T.; Saka, T.; Kamizawa, C. *Proc. Annu. Meet. Chem. Eng., Jpn* **1998**, *3*, 208.

93. Hrojez, B. J.; Mehta, A. J.; Fox, M. A.; Johnston, K. R. *J. Am. Chem. Soc.* **1989**, *111*, 2662–2666.

94. Chapman, O. L.; Nelson, P. J.; King, R. W.; Trecker, D. J.; Griswold, A. *Rec. Chem. Prog.* **1967**, *28*, 167.

95. Andrew, D.; Des Islet, B. T.; Margaritis, A.; Weedon, A. C. *J. Am. Chem. Soc.* **1995**, *117*, 6132–6133.

96. Sakakura, T.; Ishiguro, K.; Okano, M.; Sako, T. *Chem. Lett.* **1997**, 1089–1090.

97. Doyle, M. P.; Zhou, Q. L.; Charnsangarej, C.; Longoria, M. A. *Tetrahedron Lett.* **1996**, *37*, 4124.

98. (a) Davies, H. M. L.; Doan, B. D. *Tetrahedron Lett.* **1996**, *37*, 3967. (b) Davies, H. M. L.; Hudcheson, D. K. *Tetrahedron Lett.* **1993**, *34*, 7243.

99. Wynme, D.; Jessop, P. G. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1143.

100. Frohning, C. D.; Kohlpainter, C. W. *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Eds.; VCH: Weinheim, 1996; Vol. 1, p 47.

101. Heck, B. P.; Breslow, D. A. *J. Am. Chem. Soc.* **1961**, *83*, 4023.

102. Parshall, G. W.; Ittel, S. D. Homogeneous Catalysis; 2nd ed. Wiley: New York, 1992.

103. Rathke, J. W.; Klingler, R. J.; Krause, T. R. *Organometallics* **1991**, *10*, 1350.

104. Gee, Y.; Akgerman, A. *Ind. Eng. Chem. Res.* **1997**, *26*, 4581.

105. Jessop, P. G.; Ikariya, T.; Noyori, R. *Organometallics* **1995**, *14*, 1510.

106. Koch, D.; Leitnet, W. *J. Am. Chem. Soc.* **1998**, *120*, 13398.

107. Kainz, S.; Koch, D.; Baumann, W.; Leitner, W. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1628.

108. Bach, I.; Cole-Hamilton, D. J. *J. Chem. Soc., Chem. Commun.* **1998**, 1463.

109. (a) Nozaki, K.; Takaya, H.; Hiayama, T. *Top. Catal.* **1997**, *4*, 175. (b) Nozaki, K.; Sakai, N.; Mano, S.; Higashijima, T.; Horiuchi, T.; Takaya, H. *J. Am. Chem. Soc.* **1997**, *119*, 4413.

110. Kainz, S.; Leitner, W. *Catal. Lett.* **1998**, *55*, 223.

111. Francio, G.; Leitner, W. *J. Chem. Soc. Chem. Commun.* **1999**, 1663.

112. Reetz, M. T.; Konen, W.; Strack, T. *Chimia* **1993**, *47*, 493.

113. Walther, D.; Schonberg, E.; Dinjus, E.; Sieler, J. *J. Organomet. Chem.* **1987**, *334*, 377.

114. Ivin, K. J.; Mol, J. C. Olefin Metathesis and Metathesis Polymerisation; Academic: New York, 1997.
115. Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446.
116. Schrock, R. R.; Mundzek, J. S.; Bazan, G. C.; Robbins, J.; Dimare, M.; O'Regan, M. *J. Am. Chem. Soc.* **1990**, *112*, 3875.
117. Mistele, C. D.; DeSimone, J. M.; Thorp, H. H. *J. Micromol. Sci., Pure Appl. Chem.* **1996**, *A33*, 953.
118. Furstner, A.; Koch, D.; Langemann, K.; Leitner, W.; Six, C. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2466.
119. Kainz, S.; Loch, D.; Leitner, W. In *Selective Reaction of Metal Activated Molecules*; Werner, H., Schreier, W., Eds.; Vieweg: Wiesbaden, 1998.
120. Mikami, K.; Matsukawa, S.; Kayaki, Y.; Ikariya, T. *Tetrahedron Lett.* **2000**, *41*, 1931.
121. (a) Mikani, K.; Matsukawa, S. *J. Am. Chem. Soc.* **1994**, *116*, 4077. (b) Mikani, K.; Matsukawa, S. *J. Am. Chem. Soc.* **1993**, *115*, 7039.
122. Metzger, J. O.; Bangert, F. *Chem. Ber.* **1994**, *127*, 673.
123. Harmer, M. A.; Hutchenson, K. W. *J. Chem. Soc., Chem. Commun.* **2002**, 18.
124. Jessop, P. G.; Wynne, D. C. *Proceedings of the Sixth Meeting on Supercritical Fluids; Nottingham, England* **1999**, 301.
125. Boatright, D. L.; Suleiman, D.; Liotta, C. L.; Eckart, C. A. *Solid Supercritical Fluid Phase Transfer Catalysis; ACS 207th National Meetings; San Diego, CA, March 15* **1994**, 15.
126. Dillow, A. K.; Yun, S. L. J.; Suleiman, D.; Boatright, D. L.; Liotta, C. L.; Eckert, C. A. *Ind. Eng. Chem. Res.* **1996**, *35*, 1801.
127. Chander, K.; Culp, C. W.; Lamb, D. R.; Liotta, C. L.; Eckert, C. A. *Ind. Eng. Chem. Res.* **1998**, *37*, 3252.
128. Kayaki, Y.; Naguchi, Y.; Iwasa, T.; Ikaria, T.; Noyori, R. *J. Chem. Soc Chem Commun.* **1999**, 1235.
129. Hadida, S.; Super, M. S.; Beckman, E. J.; Curran, D. P. *J. Am. Chem. Soc.* **1997**, *119*, 7406.
130. Rode, C. V.; Joshi, U. D.; Sato, O.; Shirai, M. *J. Chem. Soc., Chem. Commun.* **2003**, 1960.
131. Bhange, B. M.; Ikushima, Y.; Shirai, M.; Arai, M. *Catal. Lett.* **1999**, *62*, 175.
132. Park, K. C.; Tomiyasu, H. *J. Chem. Soc. Chem. Commun.* **2003**, 694.
133. Desimone, J. M.; Gvan, Z.; Elsbernd, C. S. *Science* **1992**, *257*, 945.
134. Ye, X. R.; Lin, Y.; Wai, C. M. *J. Chem. Soc., Chem. Commun.* **2003**, 612.
135. Ikushima, Y.; Hatakeda, K.; Yokoyama, K.; Sato, O.; Yokoyama, T.; Arai, M. *J. Am. Chem. Soc.* **2000**, *122*, 1908.

Biographical sketch

Dipak Prajapati was born on 16th November, 1956 at Tinsukia, a small town in Assam (India). He graduated in Chemistry from Dibrugarh University in 1977 and obtained M.Sc. from Dibrugarh University in 1980, then a Ph.D. from the same University in 1985 under the guidance of Dr. J. S. Sandhu, FNA. He become a post doctoral fellow at University of Konstanz, Konstanz (Germany) to work under Professor Dr. R. R. Schmidt on a Alexander von Humboldt Research Fellowship (1988–1990). In 1990 he returned to India and joined Regional Research Laboratory, Jorhat as a Scientist C. Since then he become Scientist E-1 in 1993, Scientist E-II in 1998, a post he presently holds. He was awarded Dr. B. M. Das memorial science award in 2002 for his outstanding scientific contribution in synthetic organic chemistry. His research interests concentrate on the molecular manipulations of the pyrimidine nucleobases and chromone derivatives for the search of newer anticancer, antiviral and antibacterial agents and application of metal and bio-catalysts for the development of new reaction and reagents. He has also worked in the area of inter- as well as intramolecular cycloaddition reactions, particularly 1,2-, 1,3-, and 1,4- and in site selective reactions that dipoles have preferences when more than one dipolarophilic site is available in the substrate.

Mukut Gohain was born in Tinsukia, Assam, India in 1975. He received his B.Sc. (Chemistry) degree in 1977 from Dibrugarh University, Dibrugarh and M.Sc. (Chemistry) in 2000 from Assam University, Silchar. After completion of his M.Sc. he joined the Medicinal Chemistry Division of Regional Research Laboratory (CSIR), Jorhat, to pursue for his Ph.D. degree under the guidance of Dr. J. S. Sandhu, FNA. Presently he is working in the same laboratory under the supervision of Dr. Dipak Prajapati, Scientist E-II. His research interests are synthesis of potent bioactive molecules and development of new synthetic methods. He currently works on the application of organoindium and organosamarium reagents in organic synthesis.