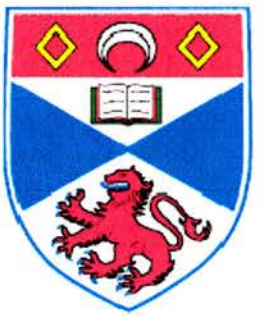
CONTINUOUS FLOW HYDROFORMYLATION OF LONG CHAIN ALKENES USING SUPERCRITICAL FLUID-IONIC LIQUID BIPHASIC SYSTEMS



A thesis presented by

Thulani E Kuncnc

to the

University of St Andrews

in Application for

The Degree of Doctor of Philosophy

January 2005

Declarations

I, .hereby certify that this thesis, which is approximately 50,000 words in length, has been written by me, that it is the record of work carried out by me and that it has not been in any previous application for a higher degree.

Date....12-04-05.....**Signature of Candidate**.....

I was admitted as a research student in February 2001 and as a candidate for the degree of .CHEMISTRY/PhD..in February 2001; the higher study for which this is a record, was carried out in the University of St Andrews between 2001 and 2005.

Date.....12-04-05.....**Signature of Candidate**.....

I hereby certify that the candidate has fulfilled the conditions of the Resolution and Regulations appropriate for the degree of..CHEMISTRY../PhD.....in the University of St Andrews and that the candidate is qualified to submit this thesis in application for that degree.

Date.....12-04-05.....**Signature of Supervisor.**

In submitting this thesis to the University of St Andrews I understand that I am giving permission for it to be made available for in accordance with the regulations of the University Library for the time being in force, subject to any copyright vested in the work not being affected thereby. I also understand that the title and abstract will be published, and that a copy of the work may be made and supplied to any bona fide library or research worker.

Date..12-04-05.....**Signature of Candidate**.....

Acknowledgements

"UJesu Krestu Ulidwala, konke okunye kuzondlula. Ngingeze ngathemba okwami ngiyophaswa yidwala lami." God has been a constant theme throughout this journey. My heart has been kept beating, through thick and thin. He has never failed me. Through this experience I hope to take something home and that is to trust him and not fail Him. Honor, Praise and Thanks be unto Him.

People come to our lives and leave footprints. I would like to take this opportunity to pass my gratitude to the following people:

- ⇔ Prof D.J. Cole-Hamilton for his supervision. He has been patient and supportive all the way, not only as my supervisor but also as my mentor.
- ⇔ Dr Paul Webb for his day to day guidance with the running of the continuous flow rig. He allowed me to wake him up in the middle of the night whenever I had a problem with the rig.
- ⇔ Dr Mike Green, for his support when I left South Africa for Scotland all the way back to South Africa and up until now. I thank Dr Green's contributions and guidance as my Sasol supervisor.
- ⇔ If it was because of you guys (Dr Douglas Foster, Mr Peter Porgozelec, Sylivia Williams, Malanja Smith), my thesis would be incomplete without your analysis of the products.
- ⇔ Bob Cathcart, thank you for putting up with my mechanical problems.
- ⇔ I thank Dr Kenny Tenza and DOH (Prof O'Hagan) group in St Andrews, Dr Stacey Polas (Sasol St Andrews, UK), Dr Arno Neveling and the Organic Synthesis group at Sasol, Dr Neil Grimmer (Hydroformylation Team at

Sastech R&D), Dr Fanie Otto (Hydroformylation Team at Sastech R&D), Prof William Bradley (RAU) for their help, especially with the ligand syntheses.

⇔ How can I forget the DJCH group (Cole-Hamilton group). I had a family far away from home. I thank you guys for the support and help you showed.

⇔ Dundee SDA church Scotland, you do not know what person you shaped in me. You guys, you were a shoulder to cry on. The reception and support we got from as a family was unbelievable.

⇔ I also like to thank Dr Hendrik van Rensburg and his family, Dr Jannie Steynberg and Irene Steynberg for the support showed to us, especially during the times of need and grief.

⇔ I have to mention these people for their help and support: The Lesars, The Waltons, Marcel and Claudette Ghiaolda, Alan and Cladia Mcgurk, Les and Tracy Simpson and Karl Da Silva.

In a special way I would like to thank my beautiful "Natural African beauty Queen" Khabo and my gorgeous "Scottish" daughter Sphesihle for being by my side through thick and thin. These people mean everything to me. These are the people who would share my stresses, joys and worries whether they like or not. I thank God for you "Bantwana Bami". I cannot forget the rest of my Family in Ladysmith and Soweto. May God richly bless you.

My Friends, ngiyabonga! Lastly, I would like to than Sasol for giving me this opportunity and financially supporting me.

Abbreviations

$scCO_2$	Supercritical carbon dioxide
TPP	Triphenylphosphine
dppe	1,2-Bis(diphenylphosphino)ethane
dppp	1,3-Bis(diphenylphosphino)propane
dppb	1,4-bis(diphenylphosphino)butane
P-M-P	Phosphorus-metal-phosphorus bond
β	Beta
IL	Ionic liquid
[BMIM][Br]	1-Butyl-3-methylimidazolium bromide
[BMIM][Cl]	1-Butyll-3-methylimidazolium chloride
$[BMIM][BF_4]$	1-Butyl-3-methylimidazolium tetrafluoroborate
$[BMIM][PF_6]$	1-Butyl-3-methylimidazolium hexafluorophosphate
$[BMIM][NTf_2]$	1-Butyl-3-methylimidazolium Bis(trifluoromethanesulfonyl)amide
$[EMIM][PF_6]$	1-Ethyl-3-methylimidazolium hexafluorophosphate
[EMIM][Cl]	1-Ethyl-3-methylimidazolium chloride
[MMIM][Cl]	1,3-dimethylimidazolium chloride
$[OctMIM][PF_6]$	1-Octyl-3-methylimidazolium hexafluorophosphate
OctMIM][Cl]	1-Octyl-3-methylimidazolium chloride
$[PentMIM][PF_6]$	1-Pentyl-3-methylimidazolium hexafluorophosphate
$[HexMIM][PF_6]$	1-Hexyl-3-methylimidazolium hexafluorophosphate
$[HepMIM][PF_6]$	1-Heptyl-3-methylimidazolium hexafluorophosphate
$[EMIM][AlCl_4]$	1-Ethyl-3-methylimidazolium aluminium chloride
$[EMIM][CF_3SO_3]$	1-Ethyl-3-methylimidazolium trifluoromethanesulfonate
$[BMIM][CF_3SO_3]$	1-Ethyl-3-methylimidazolium trifluoromethanesulfonate
$[BMIM][SnCl_3]$	1-Butyll-3-methylimidazolium tin chloride
[TPPMS]	Monosulfonated Triphenylphosphine
SCF	Supercritical Fluid

HPIR	High pressure Infra Red
HPNMR	High pressure Nuclear Magnetic Resonance
n-BuLi	Normal Butyllithium
TMEDA	Tetramethylethylenediamine
TLC	Thin Layer Chromatograph
HPLC	High Pressure Liquid Chromatograph
DMSO	Dimethylsulfoxide
sec-BuLi	Secondary Butyllithium
ppb	Part per billion
Pr	Propyl
J	Coupling constant
%	Percent
°C	Degree Celsius
Ac	Acetyl
l:b	Linear to branched ratio
b:l	Branched to linear ratio
DCM	Dichloromethane
cod	1,5-cyclooctadiene
^{1}H NMR	Proton Nuclear Magnetic Resonance
^{31}P NMR	Phosphorus Nuclear Magnetic Resonance
DMF	Dimethylformamide
equiv.	Equivalent
Et	Ethyl group
EtOH	Ethanol
g	Grams
GC	Gas Chromatography
h	Hours
H_z	Hertz
ICP	Inductively coupled plasma spectroscopy
K	Degrees Kelvin
L	Ligand

M	Molar concentration, in mole/liter
Me	Methyl group
MeOH	Methanol
mg	Milligram
min	Minute
cm^3	Centimeter cube
mmol	Millimole
mol	Mole
MS	Mass Spectrometry
nm	Nanometer
NMR	Nuclear Magnetic Resonance
OAc	Acetate
Ph	Phenyl group
ppm	Parts per million
psi	Pounds per square inch
r.t.	Room temperature
SASOL	South African Coal, Oil and Gas Company
STP	Standard temperature and pressure
THF	Tetrahydrofuran
TOF	Turnover frequency
TON	Turnover number
δ	Chemical shift relative to tetramethylsilane
ee	equitorial-equatorial
ea	equitorial-axial

Abstract

This work describes a continuous flow process, which uses a $scCO_2$-ionic liquid biphasic hydroformylation of linear higher alkenes (1-octene) using a rhodium catalyst. The catalyst used is ionic. The catalyst is dissolved in an ionic liquid while $scCO_2$ is used as a transport vector for the substrate (1-octene) and the gaseous reagents (CO/H_2) into the reactor. The system is decompressed downstream to yield the product, which is free of the catalyst and solvent. The use of rhodium complexes of 1-propyl-3-methylimidazolium diphenyl(3-sulfonatophenyl)phosphine ([PMIM][TPPMS]) in 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF_6]) leads to slow reaction (TOFs of between 5 and 10 h^{-1}) due to mass transport limitation. The use also of rhodium complexes of 1-propyl-3-methylimidazolium diphenyl(3-sulfonatophenyl)phosphine yields poor product selectivity towards linear aldehydes (l:b ratio of 3.5).

Increasing the alkyl chain length on the cation (i.e. 1-alkyl-3-methylimidazolium cation) and exchanging the hexafluorophosphate (PF_6) anion with a bigger anion, bis(trifluoromethanesulfonyl)amide [$(CF_3SO_3)_2N$] improves the solubility of the substrate in the ionic liquid, thus yielding higher reaction rates. This lead to catalyst TOFs as high as 500 h^{-1} with 1-propyl-3-methylimidazolium diphenyl(3-sulfonatophenyl)phosphine in [OctMIM][NTf_2].

The use of rhodium complexes of [NixantphosPMIM][Cl] in [OctMIM][NTf_2] yielded catalyst turnover frequencies of 255 h^{-1} when compared to 500 h^{-1}, though this catalyst system achieved product linearity as high 97.5% when compared to 78% with

1-propyl-3-methylimidazolium diphenyl(3-sulfonatophenyl)phosphine. The rhodium leaching was found to be about 200 ppb, which can be reduced down by increasing the ionic character of the ligand by attaching more than one ionic liquid moeties on the nixantphos backbone. Oxygen impurities in the substrate, CO_2, and CO/H_2 feeds can lead to oxidation of the phosphine ligand, leading to higher rates; lower selectivities to linear aldehyde; increasing isomerisation and greater rhodium leaching.

Table of Contents

Table of Tables

Table of Figures

Table of Schemes

1 General Introduction

1.1. Hydroformylation reaction

Hydroformylation is a reaction where a carbon monoxide molecule and a hydrogen atom are introduced to the double bond of an alkene to form an aldehyde or alcohol depending on the catalyst used (Figure 1.1). Usually the reaction yields two geometric isomers of the product, the linear and the branched, where the linear version of the product is usually the most desired.

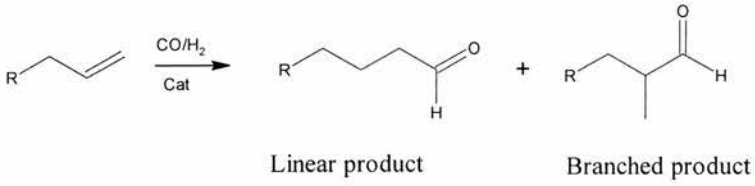


Figure 1.1 Hydroformylation reaction

The first hydroformylation catalysts were discovered by Otto Roelen in 1938[1]. They are based on cobalt carbonyl compounds, such as dicobalt octacarbonyl [$Co_2(CO)_8$]. The reaction proceeds as outlined by the mechanism suggested by Heck and Breslow[2] (Figure 1.2). Reaction conditions are harsh (200-400 bar and 150-200°C) for this unmodified type of catalysis because of low activity and stability of the cobalthydridotetracarbonyl [$HCo(CO)_4$] species, which is the active catalyst precursor. Apart from the fact that the process requires large reactor vessels, this catalyst system gives poor selectivity towards linear product and there are many by-products such as alkanes, ketones, and aldol condensation products. It was realized subsequently that the addition of a trialkylphosphine donor ligand improves the catalyst selectivity towards linear product and further hydrogenates aldehydes to

alcohols which are often the desired final products[3], though it slows down the reaction and still requires relatively harsh conditions.

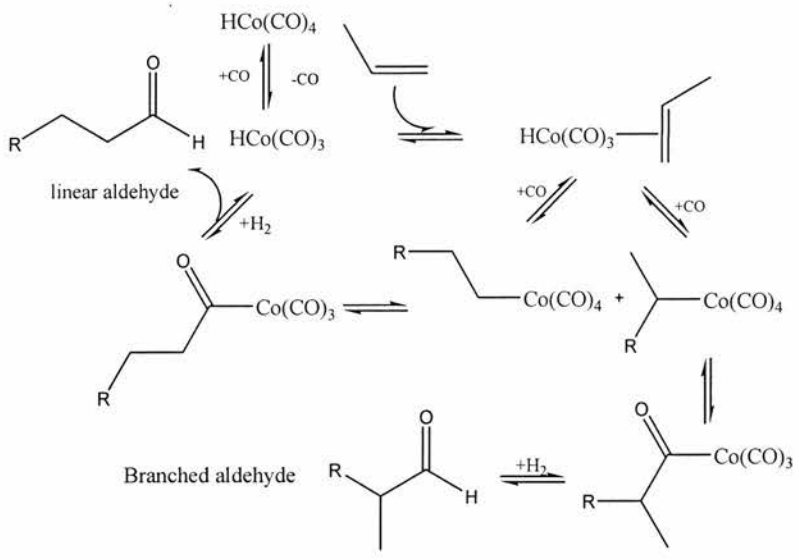


Figure 1.2 Cobalt hydroformylation reaction mechanism

Later, the focus shifted to rhodium as a metal centre. Wilkinson discovered that triarylphosphine (TPP) modified rhodium complexes were extremely active hydroformylation catalysts and selective towards linear aldehydes under mild conditions[4-7]. He suggested the reaction mechanism shown in Figure 1.3. The catalyst precursor is usually $[RhH(PPh_3)_3(CO)]$ which is in equilibrium with two active species, $[RhH(PPh_3)_2(CO)_2]$ and $[RhH(PPh_3)_2(CO)]$, in the presence of carbon monoxide and hydrogen. The monophosphine complex is believed to be less selective. Addition of excess triphenylphosphine shifts the equilibrium towards the bisphosphine complex, thus improving the selectivity and suppressing isomerisation. The process was commercialised in 1974 by Celanese and in 1976 by Union Carbine

Corporation using this finding and it is reported that selectivity greater than 90 % can be achieved[8].

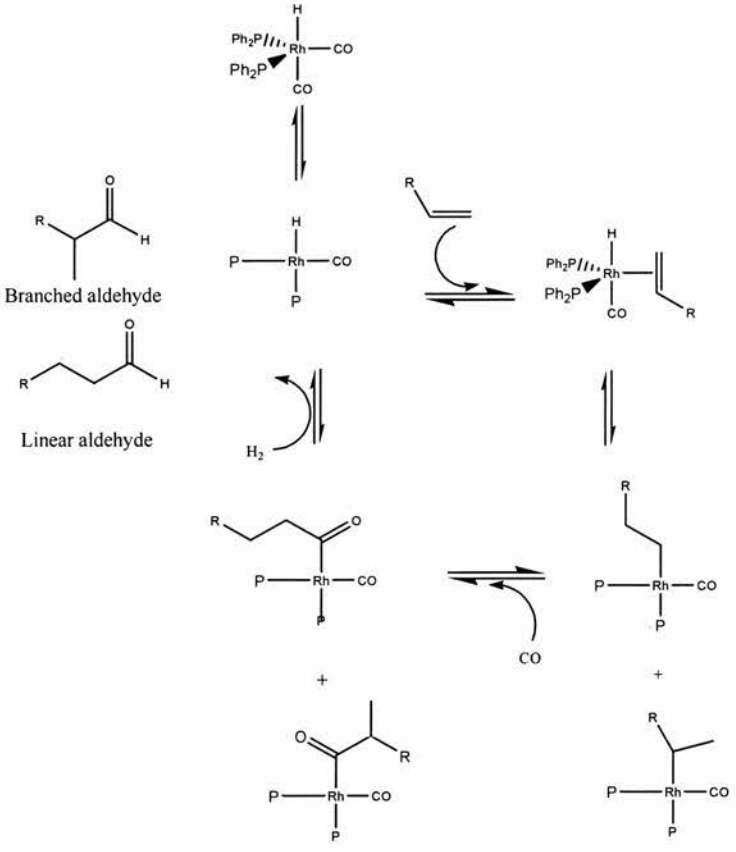


Figure 1.3 Rhodium hydroformylation reaction mechanism by Wilkinson

Diphosphines form relatively stable bisphosphine rhodium complexes (L_2Rh). Favourable effects of diphosphines were reported as early as 1966 by Iwamoto[9]. He found that bis(diphenylphosphino)propane [dppp] was the preferred ligand for the codimerisation of butadiene and ethene using iron catalysts. During the seventies, chiral DIOP was found to be suitable ligand for asymmetric hydrogenation[9] (Figure 1.4). The use of diphosphines in hydroformylation reactions has recently become of

interesting importance. This has been due to reports that they can give improved selectivity to linear aldehydes over monophosphines. This was based on the hypothesis that the intermediate which gives high regioselectivity was the two phosphines on the equatorial plane[4-7], hence diphosphines which were thought to favour that type of a coordination (Figure 1.5) should give higher linear selectivities.

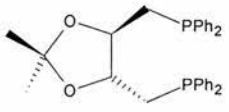


Figure 1.4 DIOP

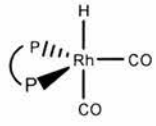
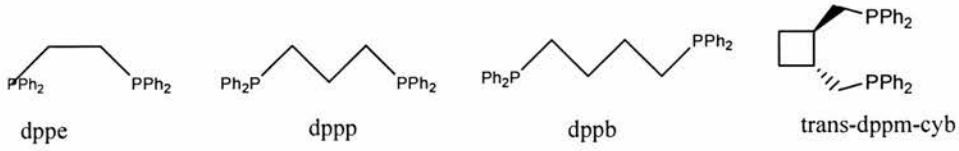


Figure 1.5 Chelating effect (ee plane)

However, the diphosphines dppe, dppp and dppb were found by Pittman[10-12] to yield lower selectivity to linear aldehydes in the hydroformylation of propene because they were found to rather occupy equatorial and axial sites in the trigonal bipyramidal structure (Figure 1.6). For the alkene molecule to coordinate into the rhodium complex, the complex most lose one CO molecule, leading to a four coordinate square planar complex. The complex is more likely to let loose one phosphine and the ligand be bound through one phosphine, which will favour lower l:b ratio. The first ever improved selectivity to linear aldehyde with rhodium/diphosphine catalyst system in hydroformylation was achieved by Consiglio in 1973[13]. The diphosphine used was

DIOP. Later in 1981, high selectivity (l:b) was also reported with trans-dppm-cyb ligand by Hughes and Unruh[14].



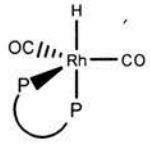
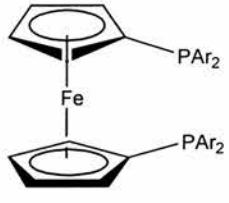


Figure 1.6 ea coordination

It seems as if the steric bulk and the chelate effect of a ligand plays an important role in the selectivity of a catalyst. In 1982 Unruh and Christenson[15] studied the use of ferrocene based diphosphine ligands (Figure 1.7). The diphosphines were based on 1,1'-bis(diphenylphosphino)ferrocene (dppf).



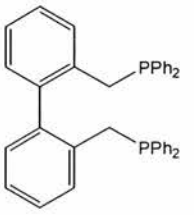
Ar = Ph
= 4-ClC_6H_4
= 3-FC_6H_4
= 4-$CF_3C_6H_4$

Figure 1.7 Ferrocene based diphosphine ligands

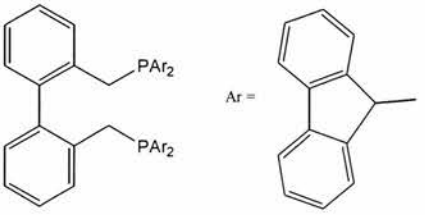
van Leeuwen and co-workers[16] described ferrocenyl diphosphines as flexible diphosphine ligands with bite angles ranging from 92 to 120°, with a strong preference for values around 97±2°. Rotation of the cyclopentadienyl fragments with

respect to one another could help to accommodate a variety of structures. This led to a study of different electronically modified ferrocene diphosphine ligands with electron withdrawing ferrocenyl ligands being studied (Figure 1.7. It was found that the more electron withdrawing the ligand becomes, the faster the reaction, which is attributed to the fact that π-back-donation to CO decreases. This favours easy CO dissociation and easy alkene coordination because of the electrophilic nature of the rhodium centre. It was also found that there is a large increase in l:b ratio as the ligand:Rh ratio increases (with 1.5 ratio the optimum). However, electronwithdrawing ligands favour isomerisation of the alkene. The increased l:b ratio can at least in part be attributed to the branched alkyl intermediate undergoing ß-H abstraction rather than carbonylation. The l:b ratio is determined by two factors. The first is the intrinsic preference for H migration to the coordinated alkene to give the linear alkyl species (this can be determined from the ratio of linear aldehyde and branched aldehydes plus isomerised alkene). The second one is the relative rates of ß-H abstraction and migration of CO to the branched aldehyde (reflected in the isomerised alkene:branched aldehydes ratio). A better comparison of the effectiveness of complexes in the hydroformylation of terminal alkenes is the yield of linear aldehyde.

In 1987, Devon and coworkers[17] studied a new class of diphosphine ligand. The ligands were based on 2,2'-bis(phosphinomethyl)-1,1'-biphenyls. They were found to give high l:b ratio, with BISBI (figure 1.9) the best one with l:b ratio of 25.1:1 compared to 2.4:1 when using TPP in much larger excess. They subsequently improved on this result using 2,2'-bis(dibenzophosphinomethyl)-1,1'-biphenyls[18], obtaining a l:b ratio of 288:1.



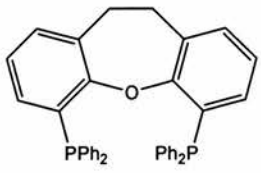
BISBI



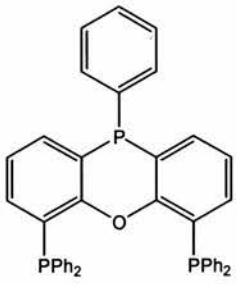
2,2'-bis(dibenzophosphinomethyl)-1,1'-biphenyl

In 1992, Casey and coworkers[19,20] carried out a study of the regiochemistry based on steric or electronic differences between bis-equatorial and equatorial-axial diphosphine complexes. It was thought that the complexes with either ee configuration, or with wider bite angles lead to higher l:b ratios due to steric bulk. The diphosphine ligand dppe with a 90° bite angle is known to prefer ea configuration and it gives low l:b ratios as compared to BISBI with a bite angle of 120°, which gives higher l:b ratios. They then hypothesised that diphosphine ligands with bite angles of 90° or less would prefer an ea configuration and would lead to a different regioselectivity than those with bite angles of 120°, which prefer ee configuration. They therefore, suggested that bite angle has an important role in determining the regioselectivity of the catalyst.

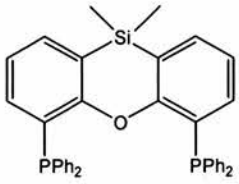
In 1990, van Leeuwen *et al*[21,22] investigated new diphosphine ligands with bite angles outside the common range of 75° to 99° based on xantphos backbone structures (Figure 1.8). From Table 1.1, it is clear that increasing the bite angle increases the rate and selectivity to the straight chain product with the exception of ligands **7** t o **8**. The breaking of this correlation is said to be due to the donating character of the N atom on ligands **7** and **8**. No clear correlation between the ee:ea ratios and bite angles was observed.



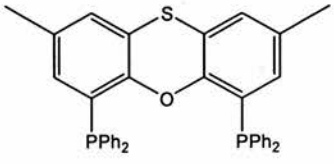
Homoxantphos (**1**) 102.0°



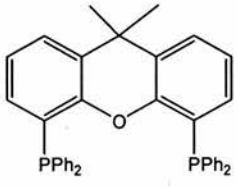
Phosxantphos (**2**) 107.9°



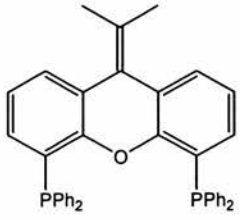
Sixantphos (**3**) 108.5°



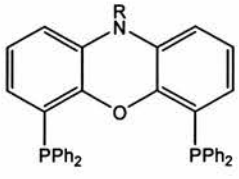
Thixantphos (**4**) 109.6°



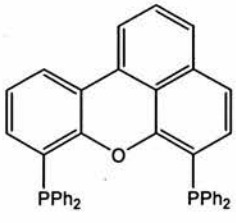
Xantphos (**5**) 111.4°



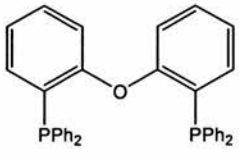
Isopropxantphos (**6**) 113.2°



R = H, Nixantphos (**7**) 114.0°
R = Bn, Benzylnixantphos (**8**) 114.2°



Benzoxantphos (**9**) 120.6°



DPEphos (**10**) 102°

Figure 1.8 Xantphos type ligands

Table 1.1 Hydroformylation of 1-octene using xantphos based type ligands[a]

Ligand	Bite angle/ deg	ee:ea[b]	l:b ratio[c]	%Linear aldehyde[c]	%Isom.[c]	TOF[c,d]
1	102.0	3:7	8.5	88.2	1.4	37
2	107.9	7:3	14.6	89.7	4.2	74
3	108.5	6:4	34.6	94.3	3.0	81
4	109.6	7:3	50.0	93.2	4.9	110
5	111.4	7:3	52.2	94.5	3.6	187
6	113.2	8:2	49.8	94.3	3.8	162
7	114.1	7:3	50.6	94.3	3.9	154
8	114.2	8:2	69.4	94.9	3.7	160
9	120.6	6:4	50.2	96.5	1.6	343

[a]Conditions: CO/H_2 = 1, $P(CO/H_2)$ = 20 bar, Ligand:Rh = 5, substrate:Rh = 637, [Rh] = 1.00 mM, No. of experiments = 3. No hydrogenation observed.

[b]calculated from $J_{P\text{-}H}$ NMR data

[c]Linear to branched ratio, isomerisation to 2-octene, turnover frequency determined at 205 conversion.

[d]Turnover frequency = (mol aldehyde) (mol Rh)$^{-1}$h^{-1}.

1.2 Room temperature ionic liquids (IL)

Ionic liquids are salts that are liquid at low temperature (even at room temperature and below), which represent a class of solvents with non-molecular, ionic character. They can be briefly described as having the following properties[23] :

⇔ They are usually composed of poorly co-ordinating ions, so they can be highly polar yet non-co-ordinating;

⇔ They are immiscible with a number of organic solvents and provide a non-aqueous, polar alternative for two phase systems;

⇔ They are non-volatile solvents, hence they can be used under high vacuum conditions, and can avoid the polluting properties of volatile organic compounds; and

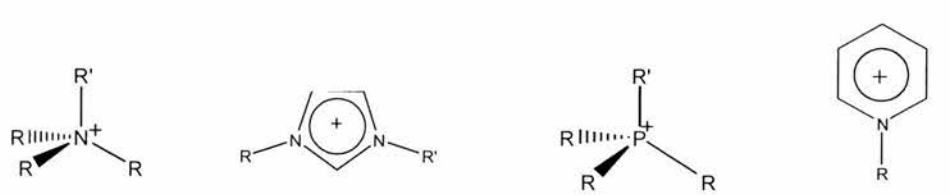
⇔ They are good solvents for a wide range of both organic and inorganic materials, thus bringing unusual combinations of reagents into one phase.

Ionic liquids were developed as far back as 1914. The first ionic liquid to be reported was ethylammonium nitrate[23]. It was found that this salt is liquid at room temperature but usually contains small amounts of water[24]. Hurley and Weir at the Rice Institute in Texas developed the first ionic liquids with chloroaluminate ions in 1948 as bath solutions for electroplating aluminium[25]. These systems did not receive further attention until the groups of Osteryoung and Wilkes rediscovered them in the late 1970s where they succeeded in preparing room temperature liquid chloroaluminate melts for the first time[26,27]. Research and development concentrated mainly on electrochemical applications at that time[24].

In the early 1980s, Hussey, Seddon and co-workers[28] began to use chloroaluminate melts as non-aqueous, polar solvents for the study of transition metal complexes, where they started looking at the electrochemical aspects of the relevant transition metal complexes. Ionic liquids were first published as new reaction media and catalysts for organic synthesis at the end of the 1980s[29] and their use in homogeneous catalysis was first published by Chauvin *et al*[30]. and by Osteryoung *et al*[31] in 1990. It eventually became clear, based on Wilkes *et al*'s[32] work, that ionic liquids are not restricted to chloroaluminate melts but a whole range of cation/anion combinations can form low melting salts. Since then publications have been concentrating on the synthesis of new ionic liquids, investigating their physical and chemical properties and their applications as solvents in synthesis and catalysis[23,33-36]. Under this section we will be discussing in brief their synthesis, characteristic properties and applications.

1.2.1 Synthesis of ionic liquids

Ionic liquids are either organic salts or contain at least one organic component. The most commonly used salts are those with alkylammonium, N,N-dialkylimidazolium alkylphosphonium, and N-alkylpyridinium cations (Figure 1.9)[1,24].



Ammonium ion **Imidazolium ion** **Phosphonium ion** **Pyridinium ion**

Figure 1.9 Important cations in ionic liquids

One of the methods for preparing ionic liquids is metathesis of a halide salt with for instance, a silver, group 1 metal or ammonium salt of the desired anion and acid-base neutralisation reactions.

The next section presents some examples of the synthesis of ionic liquids based on different salts:

In 1992, the first of the new ionic liquids (1-ethyl-3-methylimidazolium tetrafluoroborate) was synthesised *via* metathesis of 1-ethyl-3-methylimidazolium iodide with $Ag[BF_4]$ in methanol[32]. The imidazolium halide can be prepared by a simply reaction of the appropriate halogenoalkane and imidazole. This is carried out by heating the halogenoalkane and imidazole under reflux[37]. The preparation of 1-ethyl-3-methylimidazolium hexafluorophosphate ($[EMIM][PF_6]$) shortly followed. It was prepared by reaction of [EMIM][Cl] with HPF_6[38].

⇔ Tetraalkylammonium tetraalkylborides are usually prepared by metathesis of tetraalkylammonium bromide with the lithium tetraalkylboride[39].

⇔ Monoalkylammonium nitrate salts are made by the neutralisation of the amine with nitric acid[23,40].

⇔ The halogenoaluminates (III) are prepared by direct combination of a halide salt with aluminium halide[23,41] These compounds are usually sensitive to oxygen and water[42].

⇔ Other ionic liquids are prepared by quarternization of the appropriate amine e.g. the synthesis of 1-alkyl-3-methylimidazolium triafluoromethanesulfonate salts[23,43].

1.2.2 Solvent strength and Solubility Characteristics

Solvent properties are usually derived from the solvent polarity. The simplest rule in as far as solvents are concerned is that like dissolves like i.e. polar solvents dissolve and stabilise dipolar or charged solutes[24]. Based on this simple rule, it can be said that ionic liquids are polar solvents. One of the differences, which make ionic liquids unique as compared to conventional solvents, is that their solubility characteristics can be tuned by careful choice of the cation/anion combination[24]. The solubility of a non-polar compound like 1-octene in tri-n-alkylmethylammonium tosylate melts can be increased by increasing the non-polar character of the cation[24,44].

The anion also affects the solubility of compounds in an IL e.g. water is soluble in [BMIM][Br] but insoluble in [BMIM][PF_6][45]. The bigger the anion the more non-polar the ionic liquid becomes. It is reported that the solubility of gases in [BMIM][NTf_2] varies significantly with CO_2 being highly soluble whilst H_2, CH_4, N_2 are less soluble[45]. Anthony *et al*[46] also reported the solubility of gases in [BMIM][PF_6]. Once again CO_2 was found to be highly soluble while H_2, CO, CH_4, O_2, C_2H_6 are much less soluble.

1.2.3 Melting point, Density and Viscosity

The cation/anion combination affects the melting point of an ionic liquid. It has been found that high melting points are characteristic for alkali metal chlorides, whereas chlorides with organic cations melt at temperatures below 150°C[47] (Table 1.2).

Table 1.2 Melting points of selected chloride salts

Salts	**Melting points/°C**
NaCl	803
KCl	772
[MMIM][Cl]	125
[EMIM][Cl]	87
[BMIM][Cl]	65

On the other hand it has been found that increasing the size of the anion with the same charge decreases the melting point[24] (Table 1.3).

Table 1.3 Effect of increasing the size of the anion on the melting point of the salt

Salt	**Melting points/°C**
[EMIM][Cl]	87[47]
[[EMIM][$AlCl_4$]	7[48]
[EMIM][BF_4]	6[35]
[EMIM][CF_3SO_3]	-9[43]

The density of an ionic liquid generally decreases with an increase in bulkiness of the organic cation[24]. The density is also affected by the N-alkyl chain length on the imidazolium cation, with the density decreasing with an increase in alkyl chain length[24]. The anion also affects the density.

The viscosity of an ionic liquid is usually determined by the tendency to form hydrogen bonds and by the strength of the van der Waals interactions[43] (Table 1.4). The lowest viscosities are usually found for ionic liquids containing 1-ethyl-3-methylimidazolium [EMIM] ion, in which a side chain with sufficient mobility is combined with a low molar mass[24].

Table 1.4 Effect of an anion on viscosity of an ionic liquid

Salts	**η{cP]**
[BMIM][CF_3SO_3]	90
[BMIM][n-$C_4F_9SO_3$]	373
[BMIM][CF_3COO]	73
[BMIM][n-C_3F_7COO]	182
[BMIM][$(CF_3SO_2)_2N$]	52

1.2.4 Vapour pressure and Thermal Stability

Ionic liquids have virtually no vapour pressure[24]. This is a great advantage from a process engineering point of view since separation by distillation of a reaction mixture becomes more efficient as a method of product isolation. The well known problem of

azeotrope formation between the solvent and the products does not exist in ionic liquids.

The liquid range for the application of an ionic liquid e.g. as a solvent in a technical process is not only limited by its melting point but also by its thermal stability. The stability of ionic liquids is determined by their heteroatom-carbon and heteroatom-hydrogen bonds. For ionic liquids prepared by alkylation of an amine or a phosphine, the stability is mainly related to its anion. [EMIM][BF_4] is reported to be stable to about 300°C[45] and [EMIM][NTf_2] is stable up to more than 400°C[43].

1.2.5 Environmental Aspects

In contrast to volatile organic solvents and extraction media, ionic liquids have no measurable vapour pressure, therefore there is no loss of solvent through evaporation. With all the problems associated with the volatility of organic solvents, the use of ionic liquids eliminates that. However, Garcia *et al*[49] found that the butylmethylimidazolium type ionic liquids proved to show little or no biodegradability and they were also found to be more toxic than conventional organic solvents. They also found that methyl(propxycarbonyl)-imidazolium ionic liquids showed higher levels of biodegradability, though none of the ionic liquids were readily biodegradability. This though suggests that the biodegrability of ionic liquids can be tuned like its solvent properties.

1.2.6 Hydroformylation in Ionic liquids

In today's environmentally conscious world, among other problems of homogeneous catalysis, is that it uses organic solvents such as chlorinated hydrocarbons, acetonitrile, dimethylformamide etc., which are not environmentally benign[50-53]. As a result it is rapidly becoming clear that the way in which organic solvents are used should be given serious attention. One opportunity is to use environmentally friendly solvents. In this respect, ionic liquids can be considered as they are not corrosive and have essentially zero volatility among other advantages[50]. They can be used in many reactions[23,24]. They are possible solvents for homogeneous catalysis as they are generally able to dissolve organometallic compounds, especially if they are ionic. Some of the factors, which make ionic liquids attractive in homogeneous catalysis, are:

- ⇔ Ionic liquids are environmentally friendly[24,50];
- ⇔ They are easy to synthesize;
- ⇔ Their solvent properties are tunable[24,54];
- ⇔ Most of them are thermally stable[24];
- ⇔ They have virtually zero vapour pressure[24,55];
- ⇔ There is the possibility of easy separation of the catalyst from the substrate/product stream[55];
- ⇔ Most ionic liquids act as inert solvents in most reactions[24]. In this case the ionic liquid just provides a polar, weakly co-ordinating medium for the catalyst.
- ⇔ Ionic liquids sometimes stabilise the catalyst[24,56].

Ionic liquids have been used as solvents for many transition metal catalysed reactions e.g. hydrogenation of alkenes, oxidation, hydroformylation etc.[57-59]. Ionic liquids based on methylimidazolium and non-nucleophilic PF_6^-, SbF_6^-, BF_4^-, and $CuCl_2^-$ ions are easy to prepare and handle, air stable, and have a wide liquidus range. They remain liquid at room temperature, and they have relatively favourable viscosity and density characteristics [32,38,54]. We will briefly discuss the hydroformylation reaction in ionic liquids.

The main point behind using ionic liquids is that a medium is required which will dissolve the catalyst and to a certain extent the substrate and be able to separate the organic product from the ionic liquid leaving the catalyst in the ionic liquid without deactivation. Separation can be either by distillation or by simple decantation depending on the solubility of the products in the ionic liquid. If separation is by distillation, this system still has an advantage over the conventional systems because of the fact that ionic liquids have virtually no vapour pressure and can stabilise the catalyst to a certain extent[60].

Most recently used ionic liquids include alkylmethylimidazolium hexafluorophosphates which are easy to prepare, air and water stable and immiscible with water, saturated hydrocarbon solvents, dialkyl ethers but miscible with alkyl halides, alcohols and amines[61]. Most of the hydroformylation reactions reported here are carried out in this type of ionic liquid [23,24,61,62].

1.2.6.1 Hydroformylation using non-ionic catalysts

Parshall[59] described the first hydroformylation reaction in ionic liquids in 1972. He described the platinum catalysed hydroformylation of ethene in tetraethylammonium trichlorostannate. However, he does not give details of the catalytic activity of the platinum catalyst. Wasserscheid *et al*[63] studied hydroformylation of methyl-3-pentenoate (M3P) (Figure 1.10) and 1-octene later in [BMIM][$SnCl_3$] using [$PtCl_2(PPh_3)_2$] as the catalyst. The overall activity of the platinum catalyst was higher in the ionic liquid (Yield = 6.3 %, TOF = 37 h^{-1}) than in dichloromethane (Yield = 1.5 %, TOF = 9 h^{-1}). This was thought to be due to the enhancement of the catalyst life time in the ionic liquid, as it was found that the catalyst deactivates in dichloromethane even if a five fold excess of the catalyst is added to try and stabilise the catalyst. Hydrogenation was more prominent in the ionic liquid than in dichloromethane, hence better selectivity was obtained in dichloromethane. The higher hydrogenation in the ionic liquid was thought to be because of the low solubility of gases in the ionic liquid, especially CO.

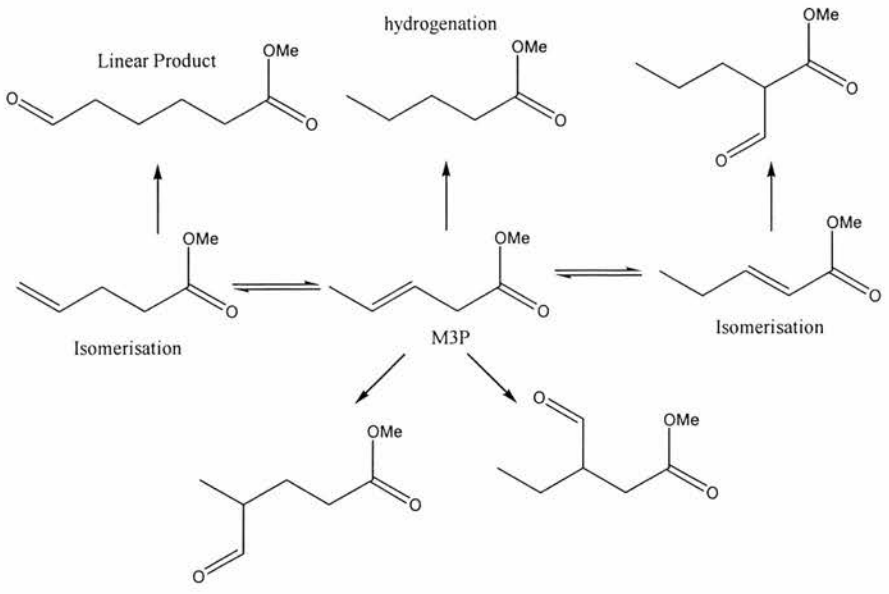


Figure 1.10 Products during the hydroformylation of Methyl-3-pentenoate (M3P)

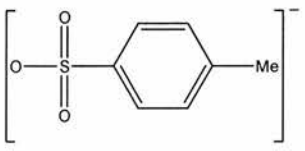
The catalyst in the hydroformylation of 1-octene showed a lower rate in the ionic liquid (Yield = 22.3 %, TOF = 126 h^{-1}) than in dichloromethane (Yield = 25.7 %, TOF = 140 h^{-1}). Hydrogenation in the ionic liquid was found to be even more pronounced during the hydroformylation of 1-octene. 1-Octene is less soluble in the ionic liquid than methyl-3-pentenoate, hence the lower rate with 1-octene.

Chauvin *et al*[24,64] showed that organic/IL two-phase 1-pentene hydroformylation could be achieved, as hexanals are poorly soluble in ionic liquids. It has been reported that the catalyst shows higher activity in 1-butyl-3-methylimidazolium hexafluorophosphate [BMIM][PF_6], with TPP as ligand, (Yield = 99 %, TOF = 333 h^{-1}, l:b = 3) than in toluene (Yield = 95 %, TOF = 297 h^{-1}, l:b = 2). The product was separated from the catalyst and solvent by decantation and the ionic phase was reused. Though the catalyst system was found to give similar activity when recycled, a small part of the active Rh catalyst was extracted into the organic phase. The reason might

be that the catalyst system is neither polar nor ionic, so one would expect the catalyst to prefer to dissolve in the organic phase as opposed to the ionic liquid. As a result, a polar ligand (e.g. mono (TPPMS) or trisulfonated triphenylphosphine (TPPTS) which would be expected to dissolve in the ionic liquid as opposed to the organic phase, was used. The reaction rates (TOF = 59 h^{-1}, Yield = 16 %) were lower in this case when compared with the [$Rh(acac)(CO)_2$]\TPP] system. It has been suggested that this might be due to the low solubility of permanent gases in the ionic liquid and the oxidation of the catalyst in the ionic liquid[62] and also because the catalyst is in the IL phase and the substrate is in the organic phase. It has also been shown that the low rates are almost certainly caused by the low solubility of the sodium salt, NaTPPMS in the ionic liquid[62]. Somewhat improved conversions could be obtained if other solvents (e.g.THF) were added. Even so, conversions were about 33 %. Nevertheless, the l:b ratios were found to be similar to those found with the TPP ligand. This improvement may rightly be because the reaction takes place in the organic phase.

Karodia *et al*[53] investigated the effect of using different phosphonium tosylates in the hydroformylation of 1-hexene with [$Rh_2(OAc)_4$]/TPP as the catalyst. They found that the substituents attached to the central phosphorus atom of the phosphonium salts affect the catalyst performance (Table 1.5). The catalyst with no added excess phosphine ligand (no TPP) yielded conversions ranging from 49 % in **C** to 96 % in **B** and the l:b ratios from 2.5:1 in **D** to 1:4 in **B.** Upon addition of excess TPP, conversions were above 95 %, although the l:b ratios were different. It was thought that in this case the [$RhHCO(TPP)_3$] catalyst species forms from [$Rh_2(OAc)_4$] in the presence of TPP, H_2 and CO and is then the catalytic species in all the salts. In the case where there is no added TPP, the salts themselves might be acting as ligands. All

these salts will solubilise 1-hexene and gases differently, which could explain the results. At the end of the reaction, the product was decanted off and from rhodium analysis, there is little or no leaching. The IL/catalyst solutions were used several times and the catalyst retains its activity.



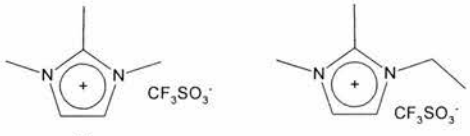
A R = Phenyl and R* = Ethyl
B R = Phenyl and R* = Butyl
C R = Phenyl and R* = Octyl
D R = Buty and R* = Ethyl

Table 1.5 Hydroformylation reaction with in different phosphonium salts

Salt	TPP	%Conv	%Linear Product	%Branched Products	l:b ratio
A	No	80	29.4	56.6	1:1.3
	Yes	95	55.7	39.3	1.5:1
B	No	96	18.4	66.4	1:4
	Yes	99	20.8	67.9	1:3.2
C	No	49	18.9	30.1	1:1.7
	Yes	100	69.1	29.9	2.2:1
D	No	90	62.6	27.4	2.5:1
	Yes	100	69.3	29.7	2.2:1

Stenzel *et al*[65] have recently reported the hydroformylation of 1-hexene and 1-dodecene in three different ionic liquid salts (Figure 1.11) using both chiral and achiral catalyst precursors i.e. [Rh(I)(cod)(2,4,7-trimethylindenyl)] and [RhCl $(TPP)_3$]. The reason for using ionic liquids **E** and **F,** as oppose to commonly used 1,3-

dialkylimidazolium salts, was to inhibit ionic liquid degradation. It is reported that such ionic liquids can be deprotonated (at the 2 position) under basic conditions to form the corresponding carbene compounds[66]. High alkene conversions of 68 % to 100 % were achieved at 80 bar CO/H_2 pressure after 6 hours reaction time, though catalyst precursor $RhCl[(TPP)_3]$ showed higher conversions than [Rh(I) (cod)(2,4,7-trimethylindenyl)]. The activity of the catalysts was lower in all the ionic liquids than toluene. This is probably due to the lower solubility of gases and the substrate in the ionic liquids. Selectivity to linear product (l:b varied from 1:0.4 to 1:2.2) was found to lower in all the ionic liquids than in toluene, which was thought to be a result of higher hydrogenation of the olefin to an alkane. Ionic liquids **E** and **F** and toluene favoured the formation of the linear product when using catalyst [Rh(I) (cod)(2,4,7-trimethylindenyl)]. Isomerisation was more prevalent in ionic liquids than in toluene and this could be explained by the fact gases have lower solubility in the ionic liquid, thus promoting[64]. Isomerised 1-dodecene can give rise to six different aldehydes of which five are chiral and 1-hexene can give rise to three of which two are chiral. Due to the high reaction temperatures, kinetic discrimination of the diastereomorphic catalytic transition states is low, resulting in low selectivity and enantiomeric excess.

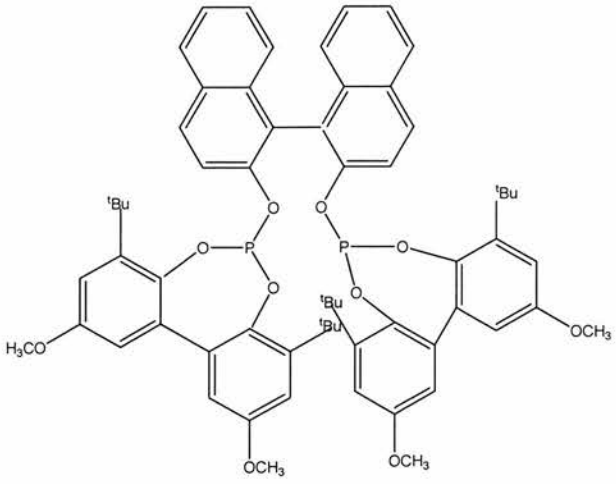


E F

Figure 1.11 Different ionic liquids

1.2.6.2 Rhodium hydroformylation with phosphites in ionic liquids

Ligand **11** was synthesised and hydroformylation of methyl-3-pentenoate in [BMIM][PF_6] as a solvent was carried out with [Rh(acac)$(CO)_2$] as the catalyst precursor[56]. The results were compared with the results obtained when the reaction was performed in toluene. Keim *et al*[56] chose methyl-3-pentenoate as a substrate in order to demonstrate the great potential of ionic liquids as solvents for homogeneous catalysis even in cases where the reaction mixture is monophasic. In this case, the substrate and the product are soluble in the ionic liquid, making the mixture monophasic. The product was therefore recovered by distillation. It was found that the catalytic activity in the [BMIM][PF_6] solvent (TOF = 180 h^{-1}) was better than in toluene (TOF = 89 h^{-1}) whereas the l:b ratios (l:b = 1) were similar. The catalyst was then recycled in both solvents and it was found that the use of an organic solvent leads to a complete deactivation of the catalyst after the first distillative product separation . However, in the case of [BMIM][PF_6], the remaining ionic catalyst phase was found to be active after the first product separation and could be successfully reused for catalysis. Even though the catalyst could be reused, its activity decreased to almost zero after four cycles. It was also found that TPP is less thermally stable when compared to ligand **11.** It was concluded that the presence of an ionic liquid is essential for the successful stabilisation of the Rh-catalyst under the thermal stress of the product distillation.

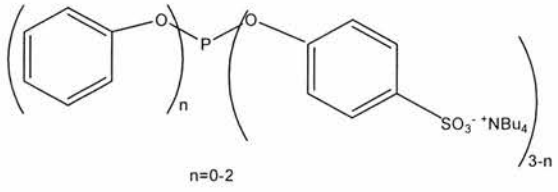


11

Sellin *et al*[62] have also reported the hydroformylation of 1-hexene in [BMIM][PF_6] using [$Rh_2(OAc)_4$] and triphenylphosphite [$P(OPh)_3$]. The catalyst system gave poor selectivity to aldehydes (TOF = 178 h^{-1}, selectivity to aldehydes = 15.7 %) and a poor linear to branch ratio (2.4) although conversions were high. It was found that the dominant products arose from aldol condensation of aldehydes, hence the low aldehyde selectivity. On adding $scCO_2$, the rate of reaction decreased but the selectivity to aldehydes increased to about 82 % and the l:b ratio increased to 6:1. The product was extracted by $scCO_2$ and the ionic liquid phase, which includes the catalyst, was reused. The catalyst was found to retain its activity and selectivity for 2-3 runs before losing both its selectivity and activity. This was due to the catalyst decomposing as a result of water formation during the reaction. The water reacts with PF_6^- to give $O_2PF_2^-$ and HF, which reacts with $P(OPh)_3$ to give $PF_n(OPh)_{3-n}$, where n = 1 or 2.

Favre *et al*[67] also studied the hydroformylation of 1-hexene in [BMIM][PF_6], using [$Rh(acac)(CO)_2$] as a catalyst precursor and ligand **12**. It was found that ligand **12**

gave good catalytic activity (TOF = 240 h^{-1}, Total Yield = 96 %, Yield aldehydes = 88 %, l:b = 13). The product was separated by decantation and the catalyst was reused in two more cycles before loosing all its activity. The l:b ratio remained high for the three cycles and the leaching of rhodium was low (2 % of the initial Rh). Ligand **12** is ionic whereas triphenylphosphite is not and that could explain the difference in performance between the two systems. The two ligands are very similar except that ligand **12** is ionic which makes it more soluble in the ionic liquid, hence it gives higher catalyst activity.



n=0-2

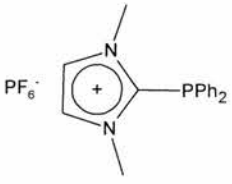
12

1.2.6.3 Rhodium catalysed hydroformylation with ionic phosphine ligands in ionic liquids

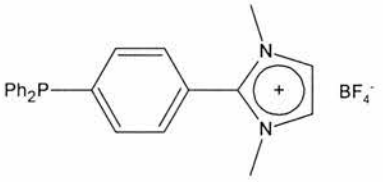
Solubility of the catalyst in the ionic liquid solvent and/or the leaching of the catalyst from the ionic solvent to the organic phase are among problems encountered in carrying out hydroformylation in ionic liquids. So, the ideal catalyst would be one, which will be soluble in the ionic liquid and be retained in the ionic phase after product separation. Several monodentate and bidentate ligands were synthesised and used in hydroformylation reactions in ionic liquids with $[Rh(acac)(CO)_2]$ as a catalyst precursor.

1.2.6.3.1 Monodentate Ionic Ligands

Brauer *et al*[68] have reported phosphine ligands containing imidazolium moieties which have been used in the rhodium catalysed hydroformylation of alkenes. The IL/organic biphasic 1-octene hydroformylation showed higher turnover frequency with ligand **13** (TOF = 552 h^{-1}, l:b ratio = 1.1) when compared with ligand **14** (TOF = 52 h^{-1}, l:b = 2.8). The reason for this difference was attributed to the proximity of the positive charge to the phosphorus atom, which enhances the catalytic activity.

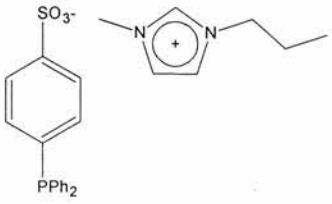


13



14

Sellin *et al*[62] synthesised monosulfonated triphenylphosphine **15** with the imidazolium cation as a counter ion instead of sodium. It was used together with $[Rh_2(OAc)_4]$ as a catalyst precursor for the hydroformylation of 1-nonene in $scCO_2$-[BMIM][PF_6]/biphasic system with flushing of the product with $scCO_2$ out of the reactor. It was shown that the catalyst could be used for at least 12 runs with TOFs ranging from 160-320 h^{-1} with the l:b ratio dropping from 3.7 to 2.5. Rhodium leaching (<0.003 %) was not observed until the 9th run. Rhodium leaching after the 9th run was attributed to the oxidation of the ligand so that the active species becomes $[RhH(CO)_4]$ which is soluble in $scCO_2$ and which gives more isomerisation and lower l:b ratios.

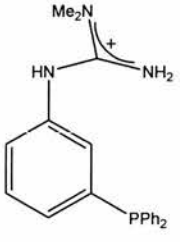


15

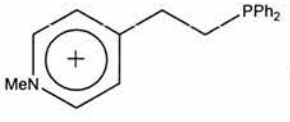
Favre *et al*[67] studied the effect of using different ligand counter anions on Rh retention in the ionic phase and the effect of the proximity of the positive charge to the phosphorus centre. It was found that ligands **16** and **17** gave similar catalytic performances (TOF = 180 h^{-1}, l:b = 4, product yield = 80 %, Yield aldehydes = 75 %) in [BMIM][BF_4], but the loss of Rh to the organic phase was found to be below the detection limits for ligand **16** whereas with ligand **17**, about 0.8 % of the initial Rh content was detected to have leached out of the ionic liquid phase. This could be attributed to the fact that ligand **16** has the same counter anion (BF_4^-) as the ionic liquid as opposed to ligand **17** (PF_6^-), so the ligand **16** will be preferentially retained by the ionic liquid. Ligand **18** showed much higher reaction rates than ligands **16** and **17** (TOF = 240 h^{-1}, Product yield = 87 %, Yield aldehydes = 96 %, l:b = 2.6). This result is not conclusive since a lower ligand to rhodium ratio (L/Rh) was used for ligand **18** (L/Rh = 4 as compared to L/Rh =10 for ligand **16** and L/Rh = 7 for ligand **17**). Decreasing the L/Rh ratio favours high reaction rate but reduces the l:b ratio, which is evident from comparing ligand **18** with ligands **16** and **17**.

Brasse *et al*[69] conducted a comparison of ligand **19** with TPP in [BMIM][PF_6] in the hydroformylation of 1-octene. TPP showed better catalytic activity (Yield = 69.1 %, TOF = 680 h^{-1}, l:b = 2.8) than ligand **19** (Yield = 32.1 %, TOF = 276 h^{-1}, l:b = 2.0), but a significant part of the hydroformylation reaction was found to be taking place in

the organic phase as 53 % of the used Rh was found to have leached out of the ionic liquid phase. The catalytic activity dropped after the first cycle with TPP (Yield = 10.2 %, TOF = 100 h^{-1}, l:b = 2.7), whereas with ligand **19,** the activity was retained (Yield = 35.3 %, TOF = 330 h^{-1}, l:b = 1.7). Rh leaching was found to be less than 0.07 % per run with ligand **19.** It was also found that ligand **19** performs better than the most widely used ligand for immobilisation of Rh catalysts in aqueous biphasic systems, NaTPPTS (Yield = 7.8 %, TOF = 80 h^{-1}, l:b = 2.6). The reason for this difference is mainly due to the solubilities of ligand **19** and NaTTPTS. NaTPPTS has been reported to have low solubility in the ionic liquid[62]. Encouraged by these results, Wassserscheid *et al* sought to address the poor l:b ratios given by using ligand **19**.

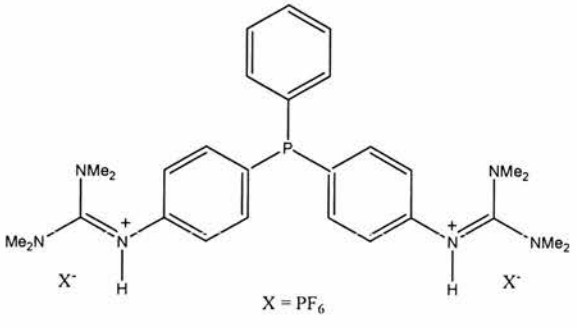


X⁻



16 X = BF_4^-
17 X = PF_6^-

18

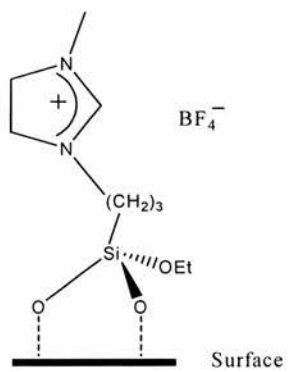


19

Wasserscheid *et al*[70] recently reported the use of ligand **19** in [BMIM][n-$C_8H_{17}OSO_3$] for the hydroformylation of 1-octene. Most of the ionic liquids used, especially in hydroformylation reactions have anions which contain halogens. Wasserscheid *et al*[70] demonstrated that [BMIM][n-$C_8H_{17}OSO_3$] is the first halogen-free ionic liquid which fulfils the technically desired combination of properties i.e. melting point below 40°C, hydrolytically stable, possible disposal by combustion without forming any HF or HCl, possible biodegradation of the used anion in ordinary waste treatment, cheap and available raw material. It was noted that the reaction mixture was monophasic before the reaction and after the reaction, meaning that 1-octene and the aldehyde products were completely soluble in [BMIM][n-$C_8H_{17}OSO_3$]. A clear colourless product was extracted using cyclohexane. The catalyst activity was found to be higher in [BMIM][n-$C_8H_{17}OSO_3$] (TOF = 892 h^{-1}, l:b = 2.9) than in [BMIM][PF_6] (TOF = 276 h^{-1}, l:b = 2.0) and [BMIM][BF_4] (TOF = 317 h^{-1}, l:b = 2.6). This was explained by the higher solubility of 1-octene in [BMIM][n-$C_8H_{17}OSO_3$] than the corresponding hexafluorophosphate and tetrafluoroborate ionic liquids.

Mehnert *et al*[71] investigated the hydroformylation of 1-hexene in [BMIM][BF_4] supported on a modified silica, **20,** using Rh/TPPTS. Comparison was made with the biphasic ionic liquid systems. The supported system exhibited a slightly enhanced activity with comparable l:b ratios. The supported system containing the ionic liquid [BMIM][BF_4] produced n-heptanal with a higher TOF (Yield = 33 %, TOF = 65 min^{-1}, l:b = 2.4) than the biphasic system (Yield = 58 %, TOF = 23 min^{-1}, l:b = 2.2). This improved activity could be attributed to a higher concentration of the active rhodium species at the interface and the generally larger interface area of the solid support in comparison to the biphasic system. Both systems were found to exhibit similar

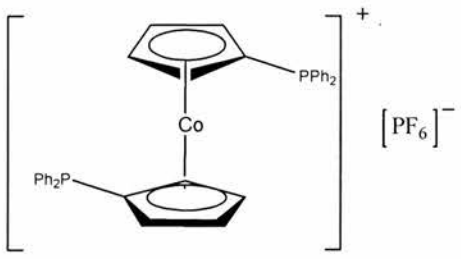
rhodium leaching to the organic phase. Although the rhodium species formed are insoluble in the organic phase, it was found that the ionic liquid partially dissolved in the organic phase at high aldehyde concentration and facilitated the leaching of the rhodium complex. The increase in aldehyde concentrations was also found to deplete the supported ionic layer, which shortened the catalyst lifetime.



20

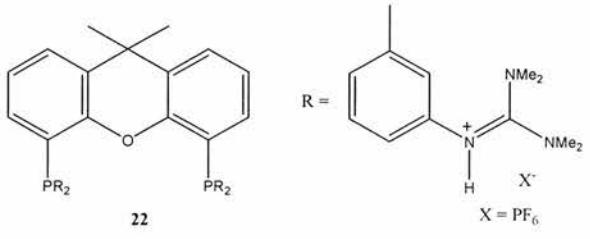
1.2.6.3.2 Bidentate Ionic Ligands

Brasse *et al*[72] have reported that using a cobaltocenium based phoshino ionic ligand **21** with $[Rh(acac)(CO)_2]$ as a catalyst precursor, gives high activity and selectivity (TOF = 810 h^{-1}, selectivity to normal aldehyde = 94 %, l:b = 16.2) in the hydroformylation of 1-octene in $[BMIM][PF_6]$ (IL/organic biphase). It was found that Rh leaching to the organic layer was less than 0.2 % of the overall amount of rhodium used.



21

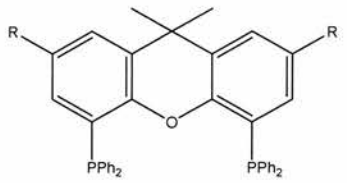
Brasse *et al*[69] also synthesized and tested a phenylguanidium modified xantphos **22**. After each run, the product was decanted off. The conversion was found to steadily increase as the catalyst was reused (from 10.6 % on the 1st run to 44.3 % on the 7th run) and a much better l:b ratio of 20:1 was obtained. The increase in conversion was explained by the formation of the active catalyst species. Rh leaching was found to be less than 0.07 %.



22

Dupont *et al*[73] also investigated the use of xanthene type ligands (sulfonated xanthene **24**) in [BMIM][PF_6] for the hydroformylation of 1-octene. It was found that the catalytic system formed by the immobilisation of Rh(acac)$(CO)_2$/xanthphos **23** in [BMIM][PF_6] is more active (TOF = 245 h^{-1} at 99 % conversion) than with the sulfonated xanthphos **24** (TOF = 47 h^{-1} at 18 % conversion) under similar conditions. It was found that after the first cycle, most of the rhodium complex leached to the organic phase with the xanthphos ligand **23**. This was evident from the drop in

conversion from 99 % to 60 %. This also explains the higher catalyst activity observed with xanthphos on the first cycle, most of the catalysis takes place in the organic phase rather than the ionic liquid phase. The Rh/sulfonated xanthphos could be recycled and almost complete conversion (Yield = 99 %, TOF = 41 h^{-1}, l:b = 1.7) was obtained by increasing the reaction time from 4 to 24 hours. The l:b ratio increased to 42 when the ligand:Rh ratio was increased to 5. Dupont *et al*[73] have recently reported that the same catalytic species exist in ionic liquids as in conventional solvents by investigating the catalyst species present in [BMIM][PF_6] using [Rh(acac)$(CO)_2$] in the presence of sulfoxantphos ligand **23** by HPIR and HPNMR.

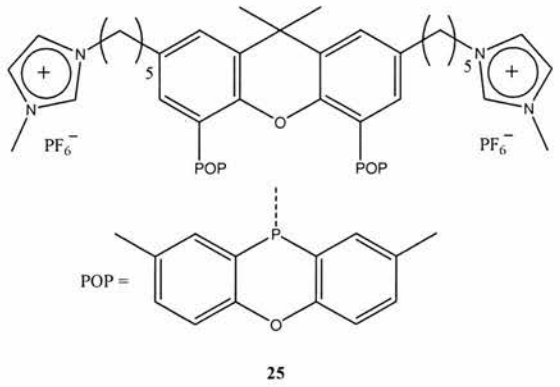


23 R = H, Xantphos
24 R =SO_3Na, Sulfonated Xantphos

Favre *et al*[67] also showed that it is possible to optimise the rhodium hydroformylation activity by adjusting the nature of the anions and cations forming the ionic liquid. Adjusting the solvent nature affects the solubility of the substrate, in this case 1-hexene, which in turn affects the catalyst performance. It was found that the TOF of 1-hexene hydroformylation using [Rh(acac)$(CO)_2$] as a precursor and monosulfonated triphenylphosphine as ligand, increased with increasing 1-hexene solubility in different ionic liquids.

Bronger *et al*[74] recently reported the use of ligand **25** for the hydroformylation of 1-octene at 100°C under 17 bar CO/H_2 (1:1) in [BMIM][PF_6] ionic liquid. At approximately 30 % conversion, the reaction was stopped, vented, cooled and the product decanted. The IL/catalyst solution was used for seven consecutive recycling experiments. Stable catalysis was observed from the 4th cycle, which meant that it needed about 4 cycles for the catalyst to be fully activated. The catalyst activity (TOF of about 100 h^{-1} on average) was found to be low, though the l:b ratio (about 40 on average) was high. The red colour of the ionic solution and the low catalyst activity observed was thought to be due to the formation of a dimeric species. They overcome this by increasing the hydrogen partial pressure, whilst keeping that of CO constant. As a result, the catalytic activity was improved threefold, to TOFs greater than 300 h^{-1}, with l:b ratio of about 50. The isomerisation on the other hand increased from 8 % to 15 %. No phosphorus (< 100 ppb) or rhodium (< 5 ppb) leaching was detected at all. The catalyst was found to be air stable. An experiment was carried out after the catalyst solution had been exposed to air for 14 days and it retained its activity but with slightly higher isomerisation. The observed increased in isomerisation was thought to be due to the formation of acidic impurities caused by some anion hydrolysis with moisture from air.

Recently a full paper by Bronger *et al*[75] has been published. They have reported an improved TOF (TOF = 6200 h^{-1}) by increasing the stirring rate and reducing the ligand concentration. The isomerisation was found to be 13 %.



25

1.2.6.4 Conclusions

From section 1.4.2.2 above, it can be concluded that the hydroformylation reaction catalysts seem to generally give similar activity and selectivity when carried out in either an ionic liquid or a conventional organic solvent media. Ionic liquids seem to stabilize the catalyst, especially during product distillation. The solubility of either the substrate or the catalyst influences the product separation and product yields. In most cases for the catalyst to perform better, one needs to immobilize the catalyst system on the ionic liquid by sometime making the ligand ionic as well. Sometimes functionalising the ligand would affect the electron density around the metal centre, thus altering the catalyst performance.

1.3 Supercritical Fluids (SCFs)

1.3.1 A brief history of SCFs

The idea of using SCFs as reaction media has been emerging ever since the discovery of this "peculiar state of mater" early in the nineteenth century by Baron Charles Cagniard de LaTour, an experimental physicist in France[76,77]. Denys Papin[76,78] prompted this in 1680 when he designed a high pressure vessel, which he used to prove that the boiling of water could be suppressed under an applied pressure. Baron Cagniard de Latour[78,79] speculated that suppression of boiling must have a limit, which he proved in 1822 by observing the changes in sound a marble made upon rolling inside a sealed gun barrel containing alcohol. Upon heating the barrel in a flame and rolling it from side to side the marble appeared to bounce as though the liquid no longer existed. He went on to use sealed glass tubes, so that he could visually observe the liquid to supercritical transition, noting that the liquid disappeared after reaching double its original volume. In this way he proved the existence of the critical point. It was referred to as *'Cagniard de LaTours point'* up until 1869 when Dr Thomas Andrews introduced the term 'critical point' during his extensive studies on the behaviour of carbon dioxide[80]. He found the critical point of carbon dioxide to be +31.1°C and 73.8 bar[81].

1.3.2 Definition and a brief description of SCFs[76-78]

A supercritical fluid is a defined 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 (Figure 1.12).

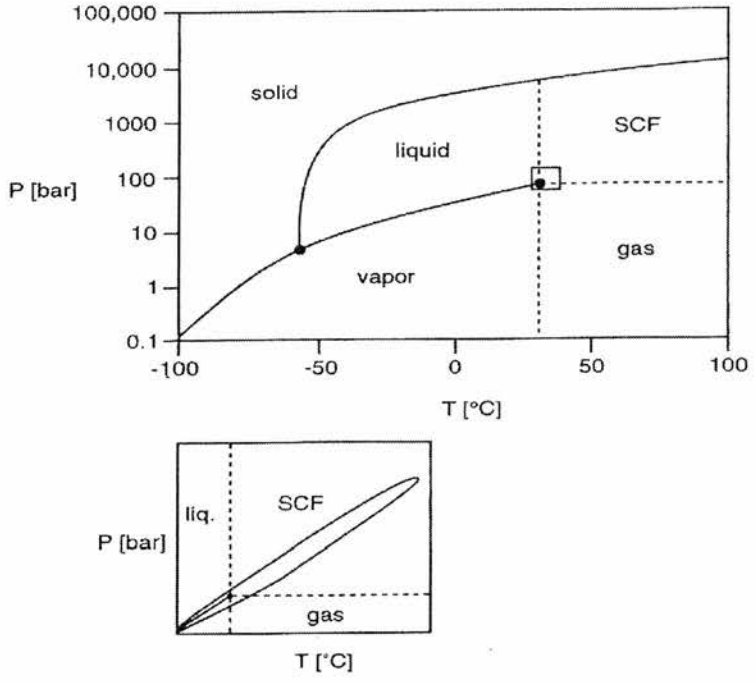


Figure 1.12 The phase diagram of CO_2. The critical and triple points are shown as filled circles. The inset (with a linear pressure scale) shows an expanded view of the area around the critical point; the tear-shaped contour indicates the compressible region[76].

It is technically a *gas* (anything which takes the volume of the container) but not a *vapour* (a gas whose temperature is less than the critical temperature). The conditions under which a compound is investigated are often described in terms of reduced

temperature (T_r), reduced pressure (p_r) and reduced density (d_r) (see eqs 1.1, 1.2 and 1.3)

$T_r = T/T_c$ **Equation 1.1**

[T = the actual temperature & T_c = the critical temperature]

$p_r = p/p_c$ **Equation 1.2**

[p = the actual pressure & p_c = the critical pressure]

$dr = d/d_c$ **Equation 1.3**

[d = the actual density & d_c = the critical density]

The properties of SCFs are frequently described as being intermediate between those of a gas and a liquid. This is derived from the fact that the gaseous and liquid phases merge together and become indistinguishable at the critical point. Nonetheless, not all properties of SCFs are intermediate between those of gases and liquids. Compressibility and heat capacity are among other properties, which are not intermediate between those of gases and liquids but are significantly higher near the critical point than they are in liquids or gases. Although the properties of a compound may change drastically with pressure near the critical point, most of them show no discontinuity. The changes start gradually, rather than with a sudden onset, when the conditions approach the critical point. This region is usually referred to as the "near-critical" region, which is usually used to refer to the non-supercritical section only. Another similar expression, "compressible region" refers to the area around the critical point in which the compressibility is significantly greater than would be predicted from the ideal gas law. Although a significant proportion of the

compressibility region lies inside the SCF section, there is an overlap with the liquid and vapour regions as well. Thus, even liquids do have significant compressibility near the critical point, although they are virtually incompressible at $T_r<<1$. One interesting property of SCFs is that above the critical point, the substance cannot be liquefied by compression alone. As a result of this, it is possible to vary continually the density and other thermodynamic related properties of the SCF from gas-like phase to liquid-like phase without any phase separation. A fluid in its supercritical state can therefore have appreciable density, sufficient enough to exhibit liquid-like solvent properties, whilst maintaining the gas-like characteristics of mass transport. The most important property of SCFs is their tuneable solvent strength, which can be changed by changing the fluid's density. From Figure 1.13, it is interesting to note that the change in density occurs sharply and continuously with pressure in the compressible region. At higher pressures, the density changes gradually.

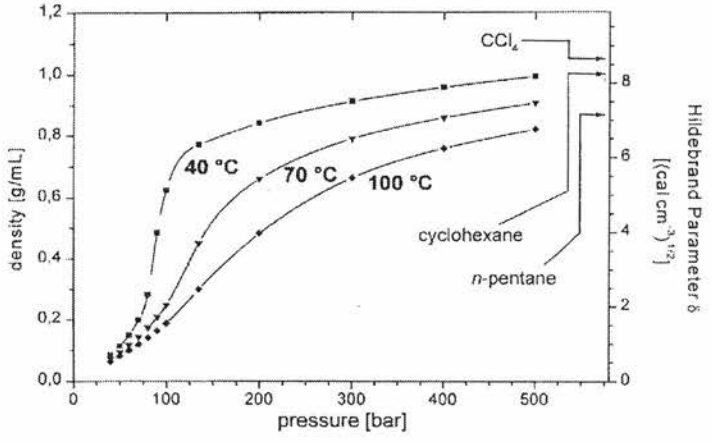


Figure 1.13: The density and the solvent power of $scCO_2$ as a function of temperature and pressure[76]

The critical parameters of several substances are listed below in Table 1.6 in order of increasing critical temperature. In general, the critical temperature of a substance

increases with increasing molecular weight as illustrated by the simple hydrocarbons highlighted in Table 1.6. Highly polar molecules, or those that exhibit extensive hydrogen bonding in the liquid phase, have very high critical temperatures despite their low molecular weight. These high values of T_c reflect the large quantities of thermal energy required to overcome extensive hydrogen bonding in the liquid phase.

Table 1.6 Critical parameters of selected solvents[78]

Solvent	**T_c (°C)**	**p_c (bar)**
Helium	-267.95	2.28
Hydrogen	-240.21	12.84
Nitrogen	-146.89	33.99
Carbon Monoxide	-140.35	34.94
Argon	-122.29	49.06
Oxygen	-118.57	50.43
Methane	**-82.60**	**45.98**
Ethylene	9.19	50.40
Xenon	16.59	58.21
Carbon dioxide	31.06	73.84
Ethane	**32.18**	**48.71**
Propane	**96.70**	**42.48**
Butane	**152.01**	**37.96**

1.3.3 Advantages of using SCFs as media for chemical synthesis and chemical reactions

The first reactions in SCFs were observed in the nineteenth century. There are numerous advantages of using SCFs as opposed to conventional organic solvents for chemical synthesis and reactions. They are mostly based on the unique properties of the supercritical state. The advantages of SCFs fall into four general categories: environmental benefits, health and safety benefits, process benefits, and chemical benefits (Table 1.7)

Table 1.7 Advantages of using SCFs rather than conventional organic liquids as reaction medium[76]

Category	**Advantage**	**Which SCF**
Environment	Do not contribute to smog	Most
	do not damage ozone layer	Most
	no acute ecotoxicity	CO_2, H_2O, Argon
	no liquid wastes	CO_2
Health and safety	Non-carcinogenic	Most
	non-toxic	Most
	non-flammable	CO_2, H_2O, Argon
Process	no solvent residues	CO_2
	facile separation of products	CO_2, Ethane, Propane
	high diffusion rates	All
	low viscosity	All
	adjustable solvent power	All
	adjustable density	all
	inexpensive	CO_2, Argon, Hydrocarbons, H_2O
Chemical	high miscibility with gases	All
	variable dielectric constant	The polar SFCs
	high compressibility	All
	local density augmentation	all
	high diffusion rates	all
	altered cage strength	all

1.3.4 Hydroformylation Reaction in $scCO_2$

SCFs have been used in many chemical syntheses and reactions, including homogeneous catalysis[62,76,82-85]. SCFs offer an alternative approach to the problem of catalyst/product separation in homogenous catalysis through their tuneable solvent strength. The most used SCF is CO_2 based on its particular advantages, as seen in Table 1.7 above. Among the advantages of SCFs is the miscibility of gases in these media compared to the very limited solubility of gases in conventional solvents[82]. There is no doubt that this will improve the performance of homogenous catalysts, particularly for those reactions, which depend on the concentration of gases. SCFs can affect the outcome of homogeneous catalysed reactions in a number of ways: They can allow the deliberate control of the phase behaviour, dissolution of the reactants, precipitation of the products or catalysts with a moderate change in reaction conditions i.e. pressure and temperature. They also offer the opportunity to tune reaction rate and selectivity to a certain extent with a small change in reaction conditions. Increasing pressure results in a density increase, which leads to greater solubility of the catalyst precursor, gases and reactants[82]. Most of the SCFs with critical points below 100°C are very non-polar with the exception of CHF_3, CH_3F and CO. By far the most popular choice is $scCO_2$, in which mostly non-polar catalysts will dissolve[82]. Transition metal complexes, which are known to be soluble in $scCO_2$ among many others, are: phosphine complexes[86], porphyrin complexes[87], metallocenes[88], carbonyls[89], and metal oxinates[90]. Polar complexes, charged complexes and even non-polar complexes with many aryl-substituted ligands often have insufficient solubility in $scCO_2$[82]. It simply means that solubilities of complexes can be tuned by modifying the ligand thereof. Another approach used to increase the

solubility of complexes is the addition of co-solvents. This approach has been used and referred to in many instances whereby it is known to increase the solubility of aromatic reagents[91].

Nonetheless, SCFs are not always inert. In fact, almost all SCFs (except argon) will react under certain reaction conditions[82]. For instance $scCO_2$ can be quite reactive, it inserts readily into M-H, M-R, M-OR, or M-NR_2 bonds in transition metal complexes[92] and reacts with secondary or primary amines to form carbamate salts[93,94]. Under this section we will discuss in brief the hydroformylation reaction among many reactions in $scCO_2$.

1.3.4.1 Hydroformylation of alkenes with unmodified (no phosphine ligand) catalyst systems in $scCO_2$

The first homogeneous catalysis reaction to be carried out in $scCO_2$ was the hydroformylation of propene by Rathke *et al*[95]. The catalyst system used was $[Co_2(CO)_8]$ without any phosphine ligand. It was shown that the active catalyst species $[HCo(CO)_3]$ was identical to that in the conventional solvents, the overall reaction rate is similar to that obtained in conventional solvent and the selectivity towards linear aldehyde is almost similar as well. This was attributed to the fact that hydroformylation is not very sensitive to solvent effects.

Koch and Leitner[81] investigated the hydroformylation of 1-octene in $scCO_2$ using [(cod)Rh(hfacac)] as the catalyst precursor and compared it with the reaction carried out in toluene. Isomerisation is one of the predominant side reaction when using

unmodified rhodium catalysis and this was substantiated by the results they obtained where about 40 % of the 1-octene was isomerised to 2, 3 and 4-octene. The catalyst was generally found to be a highly efficient catalyst precursor for the hydroformylation of alkenes in $scCO_2$ even in the absence of any added ligand. The catalyst was found even to hydroformylate 3 and 4-octene in $scCO_2$, hence high conversion to aldehydes (>97 %) as compared to 54 % aldehydes (no 3 and 4-octene hydroformylation detected) when the reaction was done in toluene. The l:b ratios were found to be similar in both toluene and $scCO_2$ (l:b = 1.4) and the hydrogenation in $scCO_2$ was about 2 %. The solubility of solid materials in $scCO_2$ was not a problem as full homogeneity was attained. Nonetheless, the reactivity and selectivity of the catalyst towards linear aldehydes typified those obtained in organic solvents. The difference is that in $scCO_2$, the conversion to aldehydes is high (less hydrogenation and virtually no unhydroformylated alkenes). It was also found that performing the reaction below the critical temperature gave about 5 % conversion of 1-octene. This could be attributed to lower concentration and/or slower mass transfer of the gaseous reactant in liquid CO_2 compared to that in the supercritical phase, although the catalyst precursor was completely soluble in the liquid CO_2.

1.3.4.2 Hydroformylation using soluble alkyl phosphines in $scCO_2$.

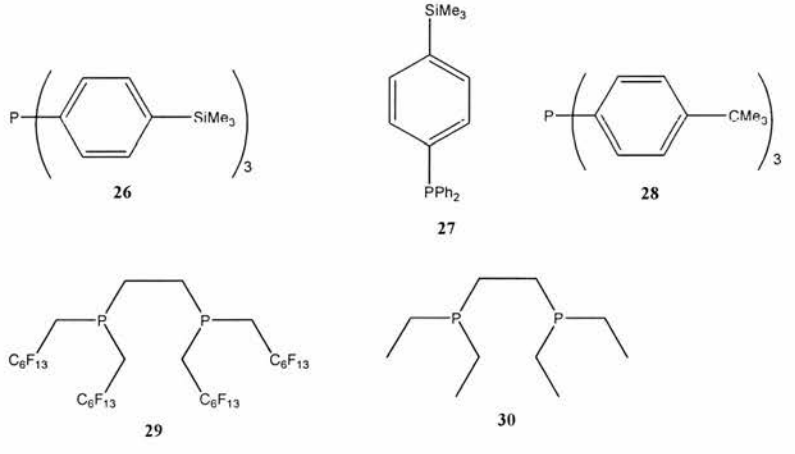
The most popular rhodium hydroformylation catalyst ligands, which have been studied in depth in organic solvents, are aryl and alkyl phosphines. Bach *et al* and Sellin *et al*[83,96] studied the hydroformylation of 1-hexene in $scCO_2$ catalysed by rhodium trialkylphosphine complexes. A catalyst prepared in situ from $[Rh_2(OAc)_4]$ and triethylphosphine (PEt_3) was used. Most triarylphosphines are known to have low

solubility in $scCO_2$[86] but triethylphosphine was found to be soluble as it is reported that only one pale yellow phase solution could be visually observed through a sapphire window[83]. This was also evident from the fact that the reaction rate (TOF = 57 h^{-1}) and l:b ratio of 2.4 are similar to those obtained with the same catalyst under identical conditions using toluene as solvent (TOF = 53 h^{-1}, l:b = 2.1). Nonetheless, it seems as if the catalyst performs slightly better in $scCO_2$. The product was only separated from the solvent not from the catalyst and this was done by just dropping the temperature to -51°C and venting off the CO_2. As a result the catalyst was not recycled. The product would be separated from the product by distillation, which might lead to the decomposition of the catalyst. Using long chain alkyl groups on phosphorus (n-octyl-) seems to cause the ligand to be insoluble in $scCO_2$. This was evident from the two phases observed when using tri-n-octylphosphine. As a result, slow reaction rate (TOF = 6.3 h^{-1}, conversion to aldehydes = 17 %) was observed when compared to the reaction with triethylphosphine (TOF = 27 h^{-1}, conversion to aldehydes = 38 %) under similar conditions. The l:b ratios are similar under identical conditions but at reduced p_{CO} in both cases, the l:b ratio with tri-n-octylphosphine (3.9) is higher than with triethylphosphine (2.6). It has been shown that high l:b ratios can be obtained at low aldehyde conversions.

It has been shown in the past that C_7 alcohols can be produced by hydroformylation of hexene, when using trialkylphosphine rhodium complexes and a protic organic solvent[86]. It has also been shown that C_7 alcohols are produced even in $scCO_2$. The conversion to alcohols was found to be less in $scCO_2$ (2.3 %) as compared to toluene (4.8 %). It has also been reported that adding an alcohol during hydroformylation of 1-hexene in organic solvents enhances the amount of alcohol produced, but adding an

alcohol in $scCO_2$ does not enhance the production of alcohol rather slows down the reaction rate. Alcohol production is higher in CF_3CH_2OH solvent[86].

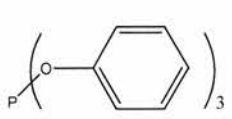
Sellin *et al*[96] also investigated the trimethylsilane containing phosphines **26** and **27**. Trimethylsilyl groups are known to solubilize metal complexes in $scCO_2$. Ligands **26** and **27** gave better activity (conversions = 80 and 82 %, l:b = 4 and 3 respectively) than TPP (conversion = 39, 6 %, l:b = 3.4) for the hydroformylation of 1-octene, whereas ligand **28** gave a system that is almost inactive (conversion = 1.8 %, l:b = 2.7). From visual inspection, it was found that the solubility of silated ligands was rather lower than expected. They also looked at diphosphine ligands (ligand **29** and **30**), where they found that ligand **29** gave superior activity (conversion = 80 %) to ligand **30** (conversion = 20 %).



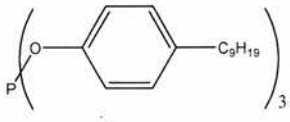
1.3.4.3 Hydroformylation using insoluble metal complexes in $scCO_2$[97]

One of the problems in hydroformylation of long chain alkenes with a rhodium catalyst is the separation of the product from the catalyst and the need to retain the catalyst's performance after distillation. Using $scCO_2$ as a solvent offers efficient

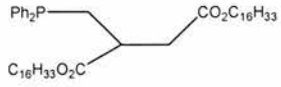
separation of the catalyst from the product simply by decompression of the system. This would be more efficient if the catalyst were to be insoluble in $scCO_2$. Rhodium hydroformylation of long chain alkenes in $scCO_2$ using insoluble metal complexes has been reported in the literature[97]. Ligands **31**, **32** and **33** were reported to be insoluble in $scCO_2$. In the hydroformylation of 1-hexene, it was found that all three ligands give good conversion, just above 50 % and ligands **31** and **32** gave higher l:b ratios (**31**: TOF = 32 h^{-1}, l:b = 6.8; **32**: TOF = 30 h^{-1}, l:b = 5.5) as compared to ligand **33** (TOF = 39 h^{-1}, l:b = 2.8). It is known that phosphites give higher reaction rates and lower l:b ratios than phosphine ligands, but the opposite was observed here. When comparing the reactions in $scCO_2$ and in toluene using ligand **32**, reduced reaction rates but higher l:b ratio were found to characterise the reaction in $scCO_2$ ($scCO_2$: TOF = 30 h^{-1}, l:b = 5.5; toluene: TOF = 49 h^{-1}, l:b = 1.4). This might be due to the difference in solubility of the catalyst in the $scCO_2$ and toluene. The product was extracted with $scCO_2$, leaving the catalyst phase in the reactor. No rhodium leaching was detected after product extraction. The catalyst could be reused but the catalyst died during the second cycle with ligand **31** and during the third cycle with ligand **32**. Ligands **31** and **32** are phosphates, which are known to hydrolyse. This was the reason for the reduction in catalyst activity.



31



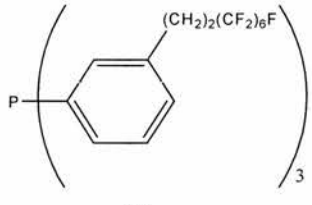
32



33

1.3.4.4 Hydroformylation using functionalised phosphine ligands in $scCO_2$

The catalytic system Rh/TPP, which is well known in organic solvents, was found to be unsuitable for application in $scCO_2$ owing to the low solubility of the active species[81,98]. The system gives 26 % conversion and a l:b ratio of about 3.5 in $scCO_2$. On the other hand, a conversion of 92 % and an l:b ratio of 4.6 were obtained under identical conditions with a catalyst formed in situ from [Rh(hfacac)(η^4-C_8H_{12})] and the TPP-analogue **34**. The perfluoralkyl groups are used as solubilisers. Banet Osuna *et al*[99] also showed that low rates associated with the alkyl ponytail-modified phosphines are primarily due to their low solubility in $scCO_2$. It is also reported that the average TOFs in toluene are markedly lower than those in $scCO_2$.

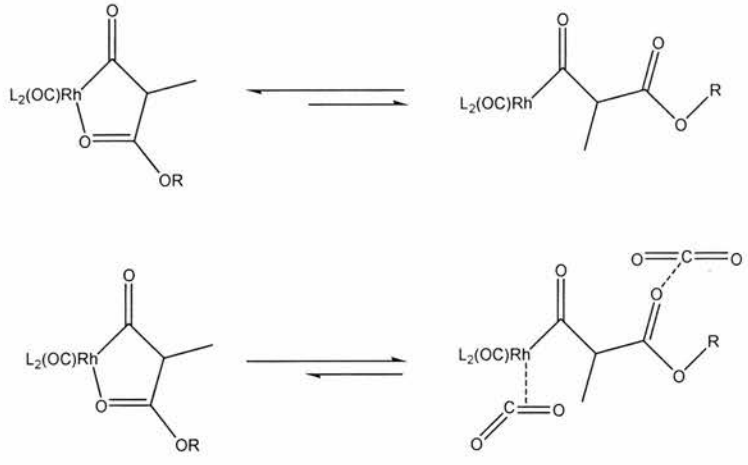


34

It has been reported that even though the perflouralkyl ponytails are meant to solubilise the catalyst in the $scCO_2$, these groups sometimes alter the electron density at the active metal centre. As a result, the catalysis will change. This is evident from results reported in the literature where it has been shown that an increase in reaction rate when perfluoralkyl groups are used is not solely due to the fact that the fluorinated chain improved the solubility of the catalyst but also changed the electron density on the rhodium[81,83,99-101]. It was found that electron withdrawing groups enhance reaction rate as compared to electron donating groups.

Hu *et al*[101] found that CO_2 can also act as an electron acceptor, interacting with and stabilising the key carbonyl intermediates and thus promoting the overall reaction. This was evident during the hydroformylation of alkyl acrylates in $scCO_2$ where the Rh-P(p-$C_6H_4C_6F_{13}$)$_3$ catalyst system was used. It was found that the average TOFs for the formation of aldehydes ranged from 1593 to 1827 h^{-1} in $scCO_2$, whereas in toluene the TOFs were less than 200 h^{-1}. Even though it is reported that $scCO_2$ enhances the syngas concentration, it seemed unlikely that was the primary reason as the pressure was doubled in toluene but the TOFs did not come close to those observed in $scCO_2$. This vast difference in TOFs in the different solvents was explained in terms of solvent-solute interactions. It is believed that the low rates observed in toluene could be a result of the formation of thermodynamically stable five or six membered rings (see Scheme 1.1 below), where only the intermediate leading to the branched product is shown since branched product dominates in this case). The rate determining step in hydroformylation has been suggested to be the dissociation of the chelated carbonyl species to give a co-ordinatively unsaturated intermediate that is active towards

addition of H_2[101]. It was then suggested that, in $scCO_2$, the equilibrium position is shifted in favour of the key unsaturated intermediate as shown in Scheme 1.1.

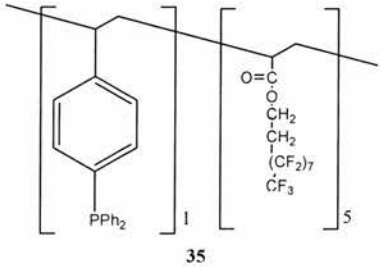


Scheme 1.1[81]**:** Formation of stable five or six membered rings during the hydroformylation of alkyl acrylates in toluene and in $scCO_2$.

Product separation from the catalyst in a system using ponytail fluorinated ligands is usually achieved by changing the pressure and temperature of the system after the reaction is complete. It has been reported that the product collected is a colourless liquid which contains less than 1 ppm Rh under optimum conditions and the catalyst can be reused in about five catalytic runs with overall catalytic TOFs *ca.* 1×10^4 without any noticeable change in activity and selectivity[81].

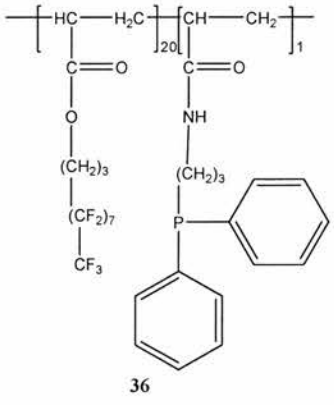
Hu *et al*[102] recently investigated the use of the fluoropolymer ligand **35** for the hydroformylation of ethyl acrylate in the presence of $[Rh(acac)(CO)_2]$ in $scCO_2$. The rate of formation of ethyl-2-formylpropionate varied with $scCO_2$ pressure. The TOF was found to be 1255 h^{-1} (b:l = 206) at 200 bar, but rose to higher to 2066 h^{-1} (b:l = 155) upon reducing the pressure to 150 bar. This behaviour was thought to be due to

the ligand adopting structures that vary with the density of CO_2, as has been shown for poly(vinyl acetate)-block-poly(fluoroacrylate) copolymer at higher pressure[103]. The TOF was found to be affected by the amount of ligand **35**, as it was noted that when the amount of ligand **35** was halved, the TOF dropped to 1251 h^{-1} (linear product was not detected) at 150 bar pressure. In the absence of ligand **35**, no aldehydes were detected. Reducing the pressure further, to 120 bar, led to significant polymerisation of the acrylate. At 120 bar, the acrylate is thought to have separated from the CO_2 phase, thus causing polymerisation. Furthermore, when the reaction was carried out in organic solvents (toluene, hexane and perfluoromethylcyclohexane), the reaction was 5 times slower than in $scCO_2$. Hexane and perfluoromethylcyclohexane are similar to $scCO_2$ in terms of their solubility parameters. The reason for lower rates in organic solvents was found not to be due to mass transport limitation, as increasing the stirrer speed resulted in no significant variations in TOFs of the reaction in toluene. It was found that ligand **35** is chemoselective to mainly acrylates. Under similar conditions in $scCO_2$, 1-decene, 1-hexene, vinyl acetate and styrene did not show any hydroformylation reaction, although allyl alcohol, which was converted to branched and linear aldehydes with a TOF of 118 h^{-1}.



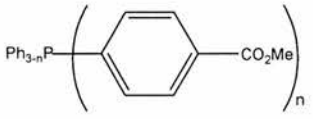
35

Lopez-Castillo *et al*[104] have recently reported on a polymer bound rhodium catalyst **36**, which is said to be the most soluble used in $scCO_2$ to date. The catalyst was recycled about 20 times without any activity loss during the hydrogenation of 1-octene. The activity was also found to increase with the number of cycles. It is believed that during the expansion and depressurisation processes the catalyst grafted in to a polymer undergoes some structural modifications that make the active sites more accessible.

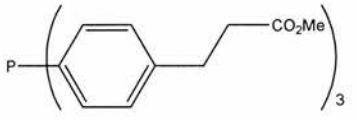


36

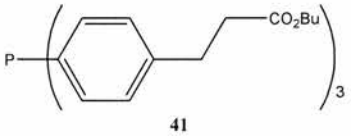
Hu *et al*[105] also investigated the use of ester-modified TPP ligands **37**, **38**, **39**, **40** and **41** for the hydroformylation in $scCO_2$ using $[Rh(acac)(CO)_2]$. It was found that increasing the number of methoxycarbonyl units, lowered the solubility of the ligand in $scCO_2$, which was evident from the TOFs. Ligand **37** gave better results (TOF of 535 h^{-1}) than ligand **38** (TOF = 390 h^{-1}) or ligand **39** (TOF = 4 h^{-1}). The aldehyde selectivity (>99 %) and l:b ratios were similar for all three ligand systems. In order to increase the solubility of the trimethoxy-carbonyl substituted ligands, the rigidity of the ligands was reduced by inserting an ethyl spacer group between the phenyl and the methoxy-carbonyl groups (ligands **40** and **41**). The TOFs were improved from 4 h^{-1} to 61 and 48 h^{-1} respectively, though they were still lower than that of ligand **37**.



n = 1 (**37**), n = 2 (**38**), n = 3 (**39**)

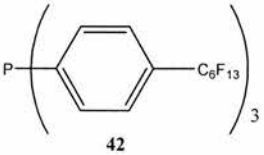


40

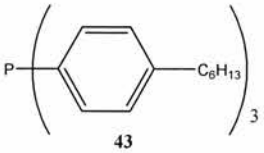


41

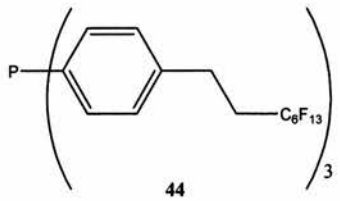
Due to the strong electron-withdrawing effect of the perfluoroalkyl substituents, a spacer group often consisting of methylene units is normally used to insulate the phosphorus from the perfluoroalkylated ponytails[105]. However, Chen *et al*[106] suggest that this is not necessary for hydroformylation in $scCO_2$. They compared ligands **42**, **43**, **44** in the hydroformylation of 1-hexadecene with $Rh(acac)(CO)_2$. The ponytails were found to affect the catalyst activity significantly. Ligand **42**, with no space, gave higher catalyst activity (TOF = 2963 h^{-1}, l:b = 3.6) than ligand **44** (TOF = 957 h^{-1}, l:b = 3.6), with a C_2 spacer. Ligand **43** (no fluorine) showed even lower yield (TOF = 150 h^{-1}, l:b = 4.5), though low ligand solubility in the $scCO_2$ contributes to the low TOF.



42

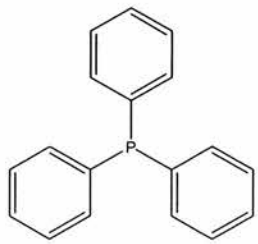


43

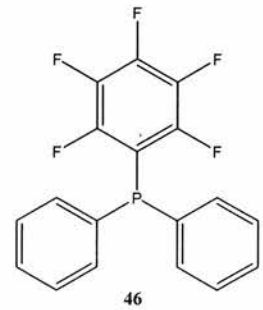


44

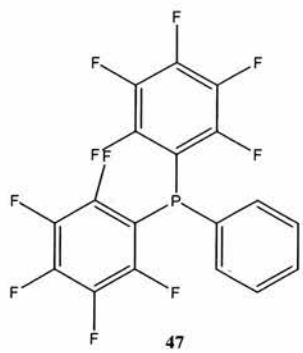
A subsequent study on different perfluorophophine ligands (**45**, **46**, **47**, **48**, **49**, **50**, **51**) was conducted with the aim of investigating the effect of the fluorine positions on the ligand[107]. The effectiveness of the ligands for the yield of aldehydes was found to be **50** ≥ **46**, **47** ≥ **49** > no ligand ≈ **48** > **45** > **51** at 80 bar $scCO_2$. Electron withdrawing groups increase the rate and selectivity of the catalyst system.



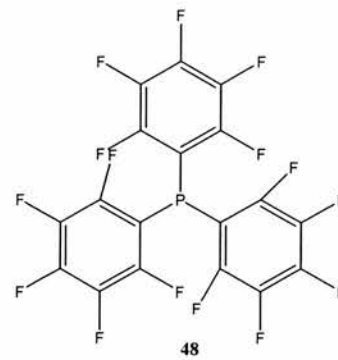
45



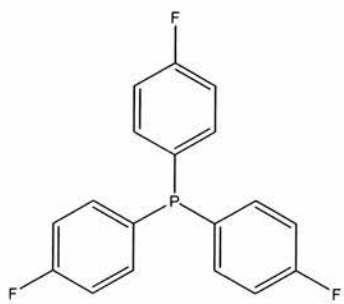
46



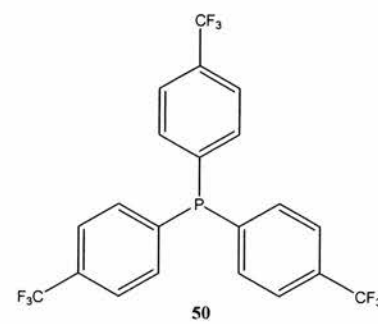
47



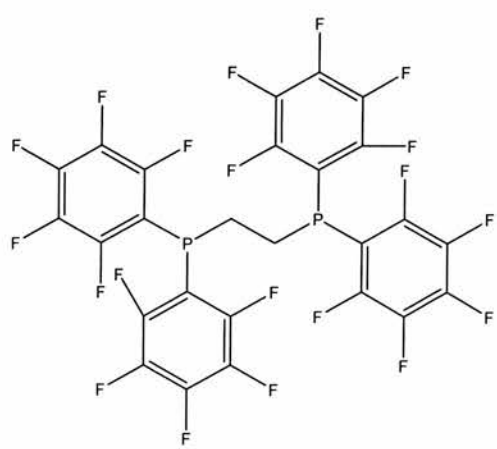
48



49

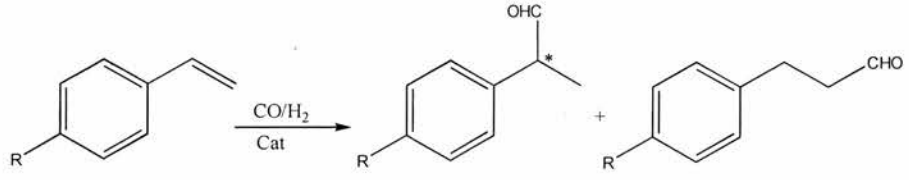


50



51

Asymmetric hydroformylation using chiral transition metal catalysis is an efficient and well established strategy for the synthesis of functionalised no-racemic organic compounds, providing viable routes to important anti-inflammatory drugs starting from simple compounds. The chiral phosphine ligand (R,S)-BINAPHOS 46 allows the hydroformylation of vinyl arenes (Scheme 1.2) resulting in outstanding levels of enantioslectivity[108]. Unfortunately, the regioselectivity towards the chiral branched aldehydes is less satisfactory even under optimised conditions.



1a R = H
1b R = Cl
1c R = isobutyl

(R)-**2a**/(S)-**2a**
(R)-**2b**/(S)-**2b**
(R)-**2c**/(S)-**2c**

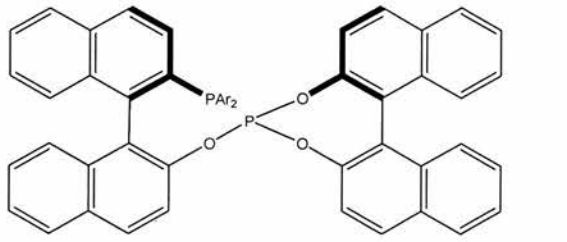
3a
3b
3c

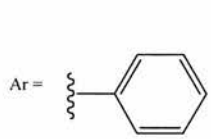
Scheme 1.2 Hydroformylation of vinyl arenes

Francio and Leitner[109] reported the use of new perfluoroalkyl-substituted derivatives of 46, (R,S)-47 in the rhodium hydroformylation of vinyl arenes in $scCO_2$. It was found that ligand **53** gave similar enatioselectivity[109] with higher regioselectivity (93 to 96 % for the case of styrene). The high regioselectivity was said to be due to the ligand structure rather than the use of $scCO_2$, as similar results were found in other solvents. Ojima *et al*[110] investigated the use of the (S,R)-48 in the hydroformylation of styrene. The catalytic activity, regioselectivity and enantioselectivity (b:l = 8-9, ee = 70 –74 %) were found to be comparable to those achieved by BINAPHOS in benzene (b:l = 7.3, ee = 94 %)[108] and (R,S)-48 in $scCO_2$ (b:l = 12.7, ee = 90.6 %) in the

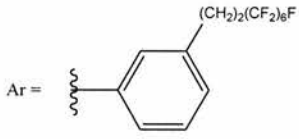
formation of 2-phenylpropanal. The observed reduced enatioselectivity was thought to be due to racemization during the reaction.

Shabahara *et al*[111] supported ligand **52** on a polymer to afford a continuous flow hydroformylation of styrene in $scCO_2$. Despite the insoluble nature of the polymer bound **52** in $scCO_2$, the catalyst gave 90 % conversion, 85 % ee and b:l ratio of 4, although selectivities were a little lower than the ones with **52** (>99 % conversion, 92 % ee and b:l of 9) and the polymer bound analogue of ligand **52** (>99 % conversion, 89 % ee and iso:n of about 5.3).

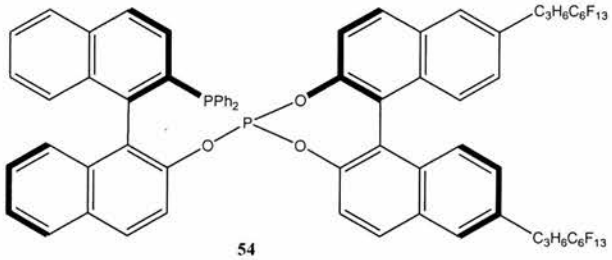




52



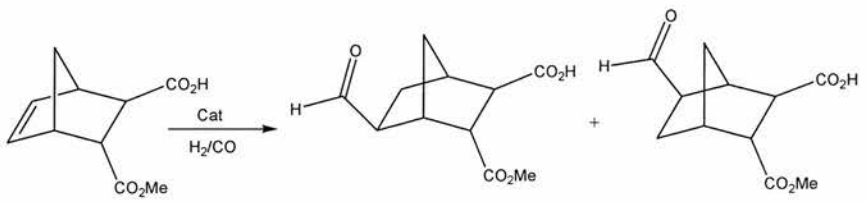
53



54

Hydroformylation of **55** in an inverted $scCO_2$/aqueous biphasic system has been reported using $[Rh(acac)(CO)_2]$ or $[Rh(hfacac)(CO)_2]$ and ligand **44**. The $scCO_2$ is used as a stationary catalyst phase and water as a continuous phase. The reaction was carried out followed by the removal of the water layer, which contained the products. The catalyst was reused. The hydroformylation of **55** using an unmodified rhodium catalyst gave very low conversion of between 4 and 14 %. With modified (ligand **44**) rhodium, complete conversion was obtained. The catalyst was recycled at least three times and metal leaching was minimal

.



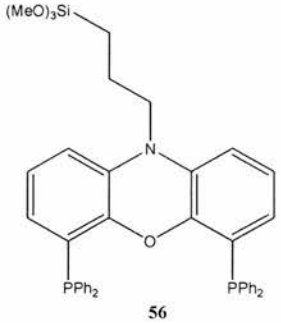
55

1.3.4.5 Hydroformylation with supported phosphine ligands in $scCO_2$

Homogeneous catalysts usually require modification in order to increase the solubility in $scCO_2$ as describe above. Although, unmodified and insoluble catalysts have shown significant activity in $scCO_2$, the use of immobilised homogeneous catalysts may overcome problems associated with the solubility and recovery of the catalyst problems.

Meehan *et al*[112] supported ligand **56** on silica and carried out the hydroformylation of 1-octene in the presence of $[Rh(acac)(CO)_2]$ by transporting the substrates and products over the catalyst in $scCO_2$. The catalyst gave a 14 % conversion (TOF = 160

h^{-1}) and l:b of 40, which is half the rate (TOF = 283 h^{-1}) of the homogeneous analogue. This was nevertheless found to be robust and was used over six days with no loss in activity and selectivity. Other groups have also studied the hydroformylation reaction using a supported catalyst on silica in $scCO_2$[113-115]. They found that the nature of the support affects the reaction



56

Dharmidhikari and Abraham[116] explored the hydroformylation of propene using $RhCl_3.3H_2O$ supported on activated carbon in $scCO_2$. Initial experiments revealed high consumption of propene but little product formation. Once the product was formed, the selectivity to n-butanal was found to be about 1.5 relative to the iso-butanal. The adsorption of the catalyst on activated carbon was found to be significant in as far the rate of reaction was concerned. The reaction was then accelerated by using an activated carbon with a larger than average pore diameter. It was also found that $scCO_2$ pressure affected the adsorption of propene.

1.3.5 Conclusions

It can be concluded that hydroformylation catayst systems in $scCO_2$ and conventional organic solvents generally give similar activity and product selectivity. Solubility of the catalyst system in $scCO_2$ is crucial in order the get the best yields. Most ligands

used in hydroformylation reactions have a low solubility is $scCO_2$, therefore it is important to fine tune the ligand in order to solubilize the catalyst system in $scCO_2$. Some solubilizers also affect the electron density around the metal centre, thus improving the catalyst activity when electron withdrawing groups are used as solubilizers.

1.4 Supercritical fluid/Ionic liquid Biphasic Systems

Homogeneous catalysis offers a number of important advantages over heterogeneous catalysis. In homogeneous catalysis, all the catalytic sites are accessible because the catalyst is a dissolved metal complex, thus giving high turnovers. It is possible to tune the chemoselectivity, regioselectivity and enantioselectivity. Despite all the advantages this brings, many homogeneous catalytic systems have not been commercialised because of one major problem, the difficulty of separating the catalyst from the product and the solvent. This problem arises because the most commonly used methods of separation, like distillation, require elevated temperatures unless the product is volatile and it can be distilled off at the reaction temperature. Most homogeneous catalysts are thermally sensitive and decompose at elevated temperatures, thus losing the expensive metal catalyst. Most commercialised homogeneous systems are either thermally not that sensitive or the products are volatile enough. In most cases, the most active and selective catalysts are thermally sensitive and have not been commercialised.

Researchers have put a lot of time and money into investigating a wide range of separation strategies other than distillation. Biphasic catalysis looks promising for solving the separation problem associated with homogeneous catalysis. It is the most explored among all the processes. Biphasic catalysis involves one solvent, generally polar, which dissolves and retains the catalyst and another solvent, generally non-polar, which dissolves and extracts the products. The success of such a system requires at least two solvents, which have different properties. From sections 1.2 and 1.3 above, it is clear that ionic liquids and supercritical fluids ($scCO_2$) have different

properties though they give similar catalyst performances. Economic advantages of these solvents include potential rate and selectivity increases, facilitated catalyst-product separation, facilitated solvent and catalyst recycling, and reduced waste disposal costs. If such economical advantages drive the industrial adoption of new solvents, then environmental advantages can be expected, including reduced evaporative losses, reduced reliance on petrochemical-derived solvents, reduced liquid hazardous waste, and increased solvent recycling.

The concept of combining these two completely different solvent types was first realized in the batch extraction of naphthalene from [BMIM][PF_6] with $scCO_2$[117]. Under this section, we are going to look at the properties and application of this biphasic system.

1.4.1 Properties of the $scCO_2$/IL biphasic system

1.4.1.1 The interaction of supercritical fluids with ionic liquids

The pioneering work of Brennecke, Beckman and co workers has prompted research into a new field of separation technology[117]. They demonstrated that $scCO_2$ exhibits high solubility in ionic liquids whereas the gas-rich phase remains free of ionic liquid[117]. Ionic liquids have easily modified structures and properties and are often designated as 'designer' solvents. Both ionic liquids and CO_2 therefore represent tuneable solvents, a factor which broadens the scope of their use as a general methodology for biphasic catalyst separation.

An understanding of phase behaviour is key to many chemical processes and biphasic systems involving ionic liquids are no exception. The phase behaviour of CO_2-ionic liquid systems and CO_2-ionic liquid-solute ternary, or higher order systems, governs the feasibility of this technology in effective separations and will therefore be discussed in this chapter. The nature of the interaction between CO_2 and ionic liquids, which gives rise to their remarkable phase behaviour, will also be described.

1.4.1.2 Phase behaviour of CO_2-ionic liquid biphasic systems

Brennecke, Beckman and co-workers paved the way for a new means of biphasic separation with groundbreaking observations that $scCO_2$ dissolves extensively in the ionic liquid [BMIM][PF_6] (BMIM = 1-butyl-3-methylimidazolium) whereas the gas-rich phase remains essentially pure CO_2[117]. Supercritical CO_2 could be used to extract naphthalene as a model compound from an ionic liquid solution without cross-contamination of the gas phase with ionic liquid[117]. Recovery of the organic solute was near-quantitative and brought about by simple expansion of the gas phase downstream. This high gas solubility, coupled with the lack of mutual solubility, is ideal for product separation.

In subsequent work, Blanchard *et al*[118] carried out a systematic study on the phase behaviour of CO_2 with a number of imidazolium and pyridinium-based ionic liquids. The solubility of CO_2 in [BMIM][PF_6] was found to increase with increasing pressure reaching 0.72 mole fraction CO_2 at 40°C and 9.3 MPa as illustrated in Figure 6.4.3.1. Conversely, the solubility of the ionic liquid in CO_2 was determined to be less than 5×10^{-7} mole fraction. Perhaps the best indication of solubility within $scCO_2$ is vapour

pressure, the more volatile a solute the more soluble it will be. The absence of ionic liquid dissolution within the gas-rich phase therefore reflects the vanishingly small vapour pressure of these materials and the inability of CO_2 to solvate charge separated salts. This inherent lack of mutual solubility provides the basis for the use of these systems in biphasic catalysis, which will be discussed below.

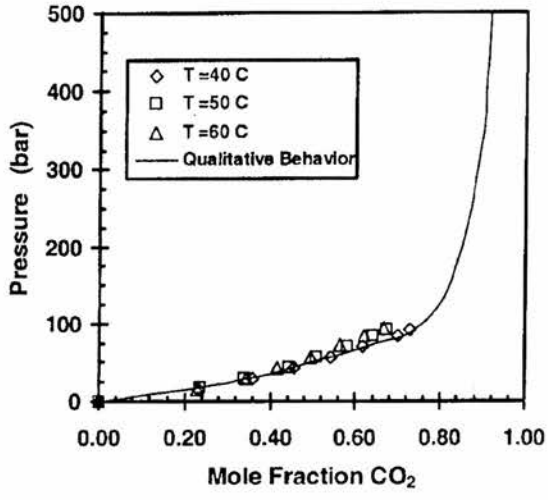


Figure 1.14 Liquid phase compositions of [BMIM][PF_6]-CO_2 at 40, 50 and 60° C.

Two phase immiscibility regions were found to exist for all ionic liquids studied by Blanchard *et al*[118], even at pressures where the phase envelope begins to close in typical organic liquid-CO_2 systems[119]. Figure 1.14, in which the non-linear extrapolation represents a qualitative prediction of phase behaviour to high pressures, clearly illustrates the large immiscibility gap over an extended range. More recently, Shariati and Peters[120] confirmed this qualitative prediction experimentally through measurements of [EMIM][PF_6]-CO_2 phase behaviour at higher pressures. This extended two-phase immiscibility region is an unusual property for liquid-CO_2 systems[119]. When high concentrations of CO_2 dissolve in a liquid at low pressures a

two-phase envelope with a mixture critical point, at moderate pressures, is normally observed. CO_2-ionic liquid phase behaviour is therefore very much different from normal organic liquid-CO_2 phase behaviour and is clearly illustrated in Figure 1.15, which compares the mole fraction solubility of CO_2 in [BMIM][PF_6] and N-methylimidazole[118].

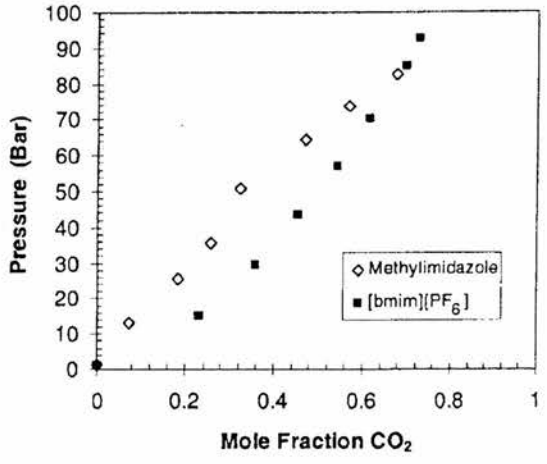


Figure 1.15[118] Liquid phase compositions of the [BMIM]PF_6-CO_2 and N-methylimidazole-CO_2 systems at 40° C.

The shapes of the liquid phase composition curves are seen to differ significantly. The N-methylimidazole curve is concave and typical of many organic liquid-CO_2 systems[119]. This concave correlation implies the presence of a mixture critical point above which a single gas phase exists. Conversely, the ionic liquid-CO_2 system is convex in behaviour and indicates a two-phase region extending to very high pressures and the absence of a mixture critical point.

The solubility of CO_2 in several ionic liquids is listed in Table 1.8[118,120]. In all cases the solubility is found to increase with increasing pressure and although the extent of

dissolution varies significantly, the phase behaviour shown in Figure 1.14 is representative of all ionic liquids studied by Blanchard *et al*[118] and Sheriati and Peters[120]. The extent of CO_2 dissolution is seen to be largely dependent on the degree of fluorination following the general trend [BMIM]PF_6] > [BMIM][BF_4] > [BMIM][NO_3][118]. Subsequent studies by Cadena *et al*[121] revealed further enhancements in solubility when using the triflamide anion. The effect of fluorination is hardly surprising since favourable interactions between C-F and CO_2 have long been exploited in SCF technology for enhancing solubility[122,81].

Table 1.8 Mole fraction solubility of CO_2 in several ionic liquids and the corresponding mixture molar volumes at 50°C and *ca* 9.2 MPa.

Ionic Liquid[a]	**ρ(MPa)**	**X_{CO_2}**	**cm^3/mol**	**Ref**
[OctMIM][PF_6]	9.267	0.705	103.0	116
[BMIM][PF_6]	9.246	0.675	83.9	116
[EMIM][PF_6]	9.260	0.449	------	118
[OctMIM][BF_4]	9.228	0.671	106.1	116
[N-Bupy][BF_4]	9.235	0.581	92.2	116
[BMIM][NO_3]	9.262	0.530	95.0	116
[EMIM][$EtSO_4$]	9.427	0.403	124.6	116

[a] Oct = octyl, EMIM = 1-ethyl-3-methylimidazolium, N-Bupy = N-butylpyridinium.

Welton and co-workers used a series of solvatochromic dyes to determine the Kamlet-Taft parameters of various ionic liquids[123]. The ability of various imidazolium based ionic liquids to hydrogen bond to solutes was found to be greater for ionic liquids possessing a proton (as opposed to methyl) on the C2 carbon of the imidazole ring.

Cadena *et al*[121] studied the effect of the C2 proton on gas solubility by comparing the solubility of CO_2 in [BMIM][PF_6] and its C2-Me analogue ([BMMIM]PF_6]). Although differences in CO_2 solubility were observed, such differences were found to be very small. This is consistent with spectroscopic evidence which demonstrates that the solubility of CO_2 in both [BMIM][PF_6] and [BMIM][BF_4] is governed primarily by interactions with the anion[124]. Using ATR-IR Kazarian *et al*[124] observed a splitting of the ν_2 bending mode of CO_2 when dissolved in [BMIM][PF_6] and [BMIM][BF_4]. This splitting indicates a removal of the double degeneracy of the bending mode and was attributed to specific interactions between CO_2 and the fluorinated anion. The width of the ν_2 mode (determined as an average width of the doublet at half maximum absorbance) was used to provide a qualitative measure of the extent of interaction between CO_2 and the anion (the width increases with the extent of interaction). The broader and more well-defined doublet, observed in the BF_4 ionic liquid, implies that it is a stronger Lewis base in its interaction with CO_2 than the PF_6 analogue. This observation contradicts solubility measurements[118], which suggest that the interaction of CO_2 with PF_6 should be stronger than that with BF_4, although differences in gas solubility may be attributed to differences in their molar volumes. Nonetheless, the anion dominates interactions with CO_2 with the cation playing only a secondary role. The near identical behaviour of [OctMIM][PF_6] and [BMIM][PF_6] (Table 1.8)[118], for example, demonstrates that the length of the alkyl chain has little effect on gas solubility. There does, however, appear to be some correlation between ionic liquid molar volume and CO_2 solubility. Molar volume gives an indication of free volume available in the liquid phase. A higher solubility in liquids with more free volume would be expected and this is exactly what is observed (the solubility of CO_2 in [OctMIM][BF_4] is 20 % greater than that in [N-bupy]BF_4)[118]. Cadena *et al*[121]

performed molecular simulations of the interaction of CO_2 with ionic liquids, the results of which support experimental evidence for the strong association of CO_2 with the PF_6 anion and only a diffuse distribution of the dissolved gas about the imidazole ring. Association of CO_2 about the anion is therefore the best indication of CO_2 solubility in an ionic liquid whereas changes in the alkyl moiety have little influence on gas solubility. The role of the cation in CO_2 solubility appears to be a solely molar volume contribution and not specific chemical interactions with the dissolved gas.

The effect of temperature on gas solubility has also been determined[118,120,125]. Temperature can have a considerable effect on the solubility of a gas within a liquid phase and in general an increase in temperature will cause a drop in gas solubility. Ionic liquids are no exception to this general observation although the temperature dependence was found to be quite small over the temperature and pressure ranges studied[118,120,125].

The presence of water in ionic liquids can have a considerable effect on the solubility of CO_2[118], an important observation considering that ionic liquids can be notoriously difficult to dry. The effect of water can be quite dramatic, for example, the solubility of CO_2 in [BMIM][PF_6] at 5.1 MPa changes from 0.54 mole fraction CO_2 for the dried sample to 0.13 for the water saturated sample. This marked difference in phase behaviour can be attributed to the low mutual solubility of water and CO_2 even at high pressures[118].

Another remarkable property of these biphasic systems is the unusual volumetric behaviour illustrated for [BMIM][PF_6] in Figure 1.16[118]. The volume expansion of the

ionic liquid is comparatively small even at high mole fractions of dissolved CO_2. This phenomenon is represented in Figure 1.16 by a dramatic drop in mixture molar volume, which simply reflects a negligible liquid volume expansion. Similar to the phase behaviour, a weak temperature dependence is observed.

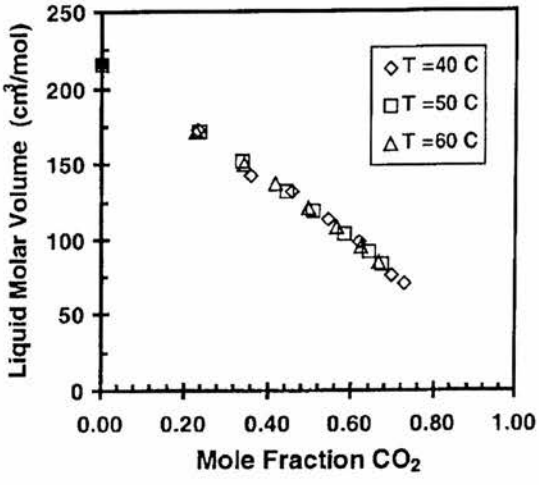


Figure 1.16[118] Liquid molar volumes as a function of CO_2 composition at 40, 50 and 60° C.

This volumetric behaviour is again uncommon to non-ionic organic-CO_2 systems where high gas solubility causes considerable volume expansion of the liquid phase. Blanchard *et al*[118] report a volume expansion of only 18 % (over the pure ionic liquid) for [BMIM][PF_6] with a liquid phase composition of 0.69 mole fraction CO_2. In conventional organic solvent-CO_2 systems the volume expansion is significant as exemplified by the CO_2-toluene system at 40°C and 7 MPa where a liquid phase composition of 0.74 mole fraction CO_2 causes a 134 % increase in liquid phase volume. Such large volume expansions are common and cause a decrease in the solvent strength of the expanded liquid, a phenomenon that is exploited in solute

precipitation technology known as GAS (gas anti-solvent precipitation)[126]. Similar behaviour is demonstrated by other ionic liquids with the largest volume expansion observed for ionic liquids with the largest molar volume[118].

Blanchard *et al*[118] assigned this lack of volume expansion to strong coulombic forces between ion pairs whose separation, and therefore expansion, is thermodynamically unfavourable. The existence of a two-phase region, which extends to high pressures, and the lack of mutual solubility can be attributed to this limited volume expansion. Increasing the CO_2 pressure will cause the pure gas phase to increase in density but since the liquid phase does not expand to any great extent, the two phases will never become identical and a mixture critical point will not be reached.

1.4.1.3 The extraction of organic compounds from ionic liquids using supercritical fluids

For viability as a means of separation it is important that the desirable phase behaviour in ionic liquid-CO_2 systems does not become disrupted by a third component representing the solute. Blanchard and Brennecke[127] performed a systematic study on the recovery of organic solutes from [BMIM][PF_6] with scCO_2 and demonstrated the generality of CO_2-ionic liquid biphasic systems as a new separation technology. Recovery rates of a wide range of aromatic and aliphatic solutes, of varying chemical functionality, were measured by spectroscopic and gravimetric analysis. Of all solutes studied a greater than 95 % recovery was obtained with the ease and rate of extraction corresponding to the relative partition coefficients of the solutes. High volatility and low polarity favours high solubility in CO_2 whereas high polarity and aromaticity will favour solubility in the ionic liquid-rich phase. Not

surprisingly, the more polar the solute the more difficult the extraction becomes reflecting the relative solubility of the solute between the two distinct and very different phases. In terms of biphasic catalysis, however, the ionic liquid, the operating pressure and partial pressures of permanent gases can all be tailored to improve liquid substrate partition coefficients[128]. Blanchard and Brennecke[127] also demonstrated the separation of involatile solutes with the successful extraction of 1,4-butanediol, a solute representative of a high-boiling organic for which separation on the basis of its vapour pressure alone (i.e. distillation) would not be a feasible option.

Scurto *et al*[129] exploited the insolubility of ionic liquids in CO_2 to effect a separation switch in ionic liquid-organic mixtures and demonstrated the complex phase behaviour of ionic liquid-organic-CO_2 ternary systems. Using mixtures of methanol and [BMIM][PF_6], which are miscible in all proportions under ambient conditions, the separation of methanol could be effected by the addition of CO_2 and is illustrated in Figure 1.17.

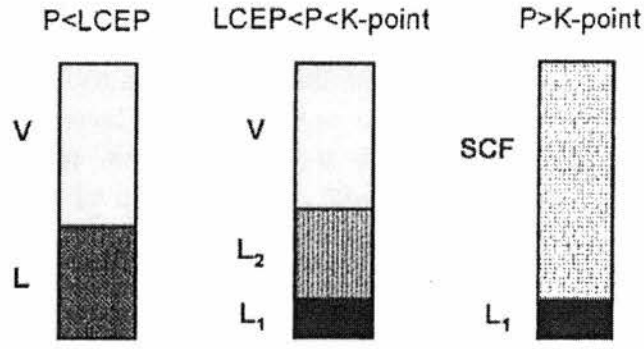


Figure 1.17[129] Schematic illustration of [BMIM]PF_6-methanol-CO_2 phase behaviour with increasing CO_2 pressure.

At low CO_2 pressures, the ionic liquid-methanol mixture exists as a single phase but as the pressure is increased a second liquid phase separates. The system is now comprised of a dense ionic liquid-rich phase (L_1), a methanol rich phase (L_2) and a vapour phase consisting mostly of CO_2. For a given temperature and volumes of methanol and [BMIM][PF_6], the pressure at which the phase transition is induced is termed the lower critical end point (LCEP). At pressures above the LCEP, the methanol rich phase begins to expand significantly while the volume of the ionic liquid-rich phase remains largely unaffected as discussed previously. This expansion reduces the solvating capacity of the methanol rich phase causing further separation of the ionic liquid. As the pressure is increased further a second critical point, the K-point, is reached where the methanol-rich phase merges with the vapour phase, precipitating the remaining dissolved ionic liquid and completing the separation. The vapour phase was found to contain no detectable ionic liquid. The K-point pressure in the ionic liquid-methanol-CO_2 system was found to be identical to the mixture critical point of methanol and CO_2 providing further evidence that the ionic liquid remains absent from the gas-rich phase[129].

At higher ionic liquid concentrations Scurto *et al*[129] report that it is not possible to induce a liquid-liquid separation by the addition of CO_2 i.e. no LCEP is observed. This complex phase behaviour has certain implications for the use of these biphasic systems as reaction/separation media. If large concentrations of reactants and products are present, relative to the ionic liquid itself, an additional liquid phase might occur. A liquid-liquid phase split may then be detrimental in homogeneously catalysed reactions in terms of mass transport limitations.

Care must be exercised, however, when such ternary systems include small, polar solutes. Low molecular weight, polar solvents, in particular methanol, are used extensively as co-solvents in natural products and other extractions employing $scCO_2$[130]. The polar solvent acts as a modifier of gas phase polarity and enhances the solubility of polar species that would otherwise exhibit limited solubility in CO_2. The effect of solvents such as ethanol and acetone was demonstrated by measuring the solubility of [BMIM][PF_6] in CO_2 in the presence of these solvents[125,131]. The solubility data is represented in Figure 1.18 as the mole fraction solubility of [BMIM][PF_6] in CO_2 as a function of the mole fraction of organic in CO_2. In general, the small, polar solutes cause dissolution of the ionic liquid in the gas phase by acting as a modifier whereas n-hexane has no effect even at mole fractions of 30 % in CO_2.

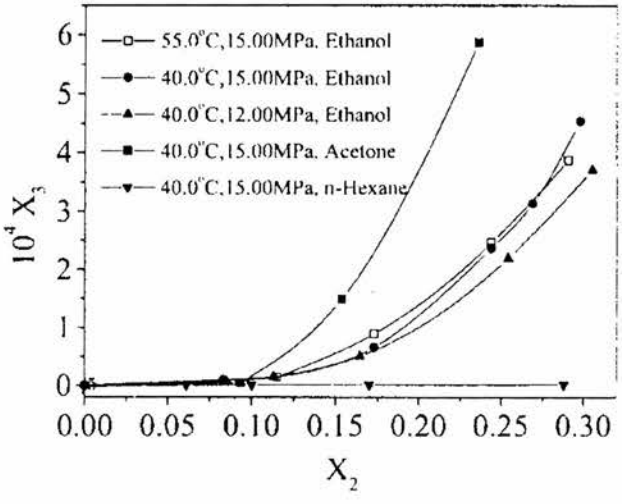


Figure 1.18[125] Mole fraction solubility (X_3) of [BMIM][PF_6] in $scCO_2$-organic mixtures as a function of the mole fraction of organic present in the gas phase (X_2).

The solubility of [BMIM][PF_6] in both CO_2-ethanol and CO_2-acetone mixtures is considerable and strongly dependent on the concentration of the organic solvent.

These experiments serve as an important warning to future practitioners of CO_2-ionic liquid biphasic systems[125,131]. If reactants or products are small, polar solutes, care must be taken to operate under conditions where the mole fraction solubility of the solute is low enough to not disrupt the otherwise mutual immiscibility of the two phases.

1.4.1.4 The Solubility of Gases in Ionic liquids

A number of industrially important reactions, including hydrogenations, hydroformylations, carbonylations and oxidations, involve the reaction of permanent or condensable gases. For reactions in CO_2-ionic liquid biphasic systems, the partial pressure of an additional reactant gas will affect both reaction kinetics and the thermodynamic behaviour. In terms of reaction kinetics, a low gas solubility in the ionic liquid may result in mass transport limitations as a rate-determining factor. The additional gas will also cause expansion of the $scCO_2$ reducing its solvating capacity and its ability to extract reaction products, although the effects on solvent characteristics can be used to an advantage[128]. An understanding of the phase behaviour of CO_2-ionic liquid-solute systems in the presence of reactant gases and the solubility of such gases in the ionic liquid is key to process optimisation. A number of researchers has measured the solubilities of both permanent and condensable gases (other than CO_2) in ionic liquids[132-136] although research into the effects of the additional gas on phase behaviour is limited[128]. Henry's constants for several gases in [BMIM][PF_6] are listed in Table 1.9 in the order of decreasing solubility (i.e. increasing Henry's constant).

Table 1.9 Henry's Constants for Gases in [BMIM][PF_6] at 298K.

Gas	H_1 (MPa)	References.
CO_2	5.34 ± 0.03	133
C_2H_4	17.3 ± 1.7	133
C_2H_6	35.5 ± 3.6	133
CH_4	169 ± 1.8	133
CO	327	135
H_2	538	135
H_2	570	136
O_2	800 ± 540[a]	133

[a]*More accurate measurements are available for [BMIM][BF_4]*[132].

In general, gas solubility is found to be small, compared to the high solubility observed for CO_2. Additionally, and with the exception of CO_2, the solubility of gases in [BMIM][PF_6] is considerably lower than solubilities normally observed in conventional solvents[133]. The trend in gas solubility correlates well with the polarizability of all gases except CO_2. This correlation implies that solubility is governed largely by dispersive forces and not specific interactions with the solvent (as observed in the case of CO_2)[133]. A systematic investigation on the solubility of CO in a series of ionic liquids revealed that ionic liquid structure plays an important role in gas solubility[135]. For the [BMIM] cation the solubility of CO increases according to the series NTf_2 (Tf = CF_3SO_3) > CF_3CO_2 > SbF_6 > PF_6 > BF_4[135], a trend that is identical to that observed for CO_2 solubility[118,121]. CO solubility is also affected by the

chain length of the alkyl substituent in pyridinium and imidazolium ionic liquids; an increase in chain length enhances gas solubility[135].

The solubility of reactant gases in ionic liquids has not yet been determined in the presence of CO_2. High concentrations of CO_2 in the ionic liquid may enhance the solubility of reactant gases although this has only been inferred indirectly by observations that the presence of CO_2 appears to overcome mass transport limitations[62].

The effect of different gas solubilities on reaction rates in different ionic liquids is difficult to predict, because many other things, such as mass transport rates, viscosities, diffusion coefficients, solvation of substrates and transition states, etc. also vary. There are reports where the change in gas solubility does not correlate with changes in reaction rate[134,135] or where homogeneous reactions in a supercritical fluid have similar reaction rates to those in conventional solvents, all else being equal. One example is the hydroformylation of hex-1-ene catalysed by Rh/PEt_3 in toluene or in $scCO_2$. Where the conditions are designed so that the catalyst concentration, the partial pressure of CO and H_2, the temperature, the reaction time and the pressure drop during the reaction are all matched, the conversions after 1 h were only slightly different (72 % in toluene, 84 % in $scCO_2$), despite the very large differences in gas concentration[96].

1.4.2 Continuous flow homogeneous catalysis

1.4.2.1 General considerations

The ideal catalytic reaction would selectively produce a single desired product with 100 % atom economy in a continuous flow process which left the catalyst within the reactor under its optimum operating conditions at all times. There would be no volatile organic compounds, no waste and no by-products. Very few catalytic syntheses of organic compounds meet these criteria, because heterogeneous catalysts, which meet the flow and solvent requirements, are usually rather unselective whilst homogeneous catalysts can approach the selectivity requirements, but can suffer from severe problems associated with the separation of the product from the catalyst and the reaction solvent[137]. Examples of where homogeneous catalysis is carried out as a continuous process is the rhodium/triphenylphosphine catalysed hydroformylation of short chain alkenes such as ethene and propene[8,138]. Here, the product aldehydes are sufficiently volatile that they can be distilled from the reactor at the reaction temperature (100 °C). In the case of ethene, only propanal is formed, whilst for propene, the selectivity to the linear butanal is high (90 %). In both cases, the catalyst solvent is an equilibrium mixture of condensed aldehydes that builds up during the reaction. Although these reactions show the possibility of approaching the ideal situation, the number of processes where this can be realised is very small because, in general, the products are not sufficiently volatile to be distilled from the reactor at temperatures below the decomposition temperature of the catalyst. In most cases, the problem is circumvented by removing some of the reaction mixture and carrying out the separation *ex situ* by low pressure distillation, phase separation etc. However, this

means that, at all times, some of the catalyst is outside the reactor, and is held under conditions for which it has not been optimised. This can lead to precipitation, deactivation or decomposition. In extreme cases, attractive reactions have not been commercialised because the separation problem has not been solved.

A possible alternative, which would exploit the ability of supercritical fluids to dissolve organic compounds and hence impart to them gas like flow behaviour below their boiling points, would involve a catalyst, which is insoluble in a SCF, dissolved in a liquid, which is also insoluble in the SCF. The SCF could be then used to transport substrates into and products out of the reactor and hence systems could be designed which are very close to the ideal described above. The product would be recovered from the SCF by decompression, and the SCF could be recycled.

1.4.2.2 Catalysis in SCF-ionic liquid biphasic systems

Although the results described in section 1.2.6.2 are of interest, the instability of the phosphites makes them unsuitable for continuous operation. However, the very interesting properties of supercritical fluid – ionic liquid biphasic systems described above, specifically the ability of $scCO_2$ to extract organic compounds from ionic liquids and the insolubility of ionic liquids in $scCO_2$, suggests a generic approach to carrying out homogeneous catalytic reactions under continuous flow conditions. All that would be required is that the catalyst dissolves in the ionic liquid, but not in the SCF and that the products be soluble in the SCF. A diagrammatic representation of such a process is shown in Figure 1.19.

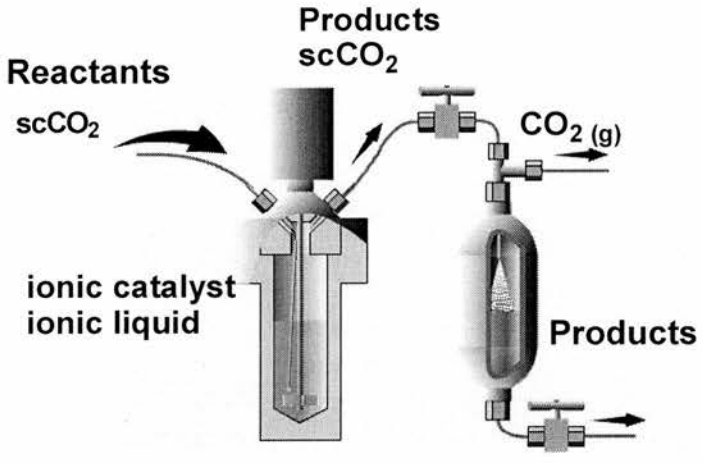


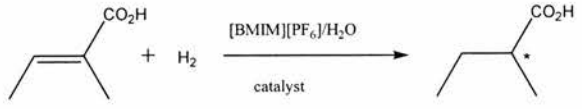
Figure 1.19 Schematic diagram of a continuous flow $scCO_2$-IL catalytic process.

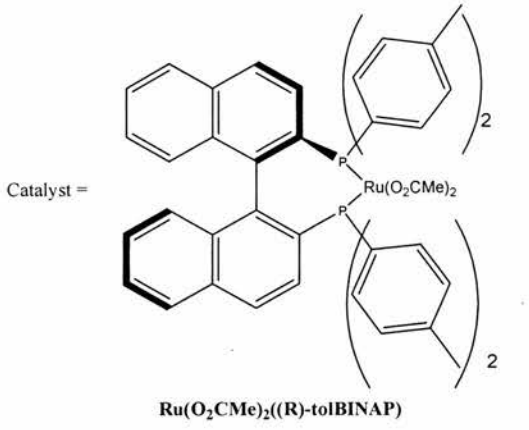
Following the elegant work of Brennecke, Beckman and co-workers[117,127], a number of groups have investigated SCF-ionic liquid biphasic systems. In many cases repetitive batch reactions have been used, or reactions have been carried out in an ionic liquid with subsequent removal of the products by flushing with $scCO_2$, but in some cases genuine continuous flow processing has been demonstrated. The rest of this chapter describes the progress made so far, which has also been included in a variety of reviews[139-143].

1.4.2.2.1 Hydrogenation

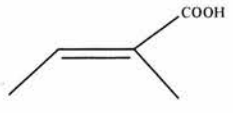
Jessop *et al*[85,144,145] were the first to report on catalytic reactions in SCF-ionic liquid biphasic systems. They investigated asymmetric hydrogenation of tiglic acid catalysed by $[Ru(O_2CMe)_2((R)\text{-tolBINAP})]$ in ([BMIM][PF_6]) with added water (Scheme 1.3). The reaction was performed in the ionic liquid (25 °C, H_2 0.5 MPa, 18 h) followed by

extraction with $scCO_2$ (35 °C. 17.5 MPa, 1 cm^3 min^{-1}, 18 h). The product was recovered by downstream decompression of the CO_2.

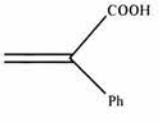




Scheme 1.3[85,144,145] Asymmetric hydrogenation of tiglic acid catalysed by $Ru(O_2CMe)_2$(R)-tolBINAP) in [BMIM][PF_6] with added water



tiglic acid



itaconic acid

The reaction gives high enantioselectivity (85 % e.e.) and conversion (99 %) to 2-methylbutanoic acid. The catalyst could be reused at least five times without losing catalyst activity, which suggests insignificant catalyst leaching, although this was not measured. Interestingly, there was a slight increase in e.e. on the first recycle (to 90 %) and this was retained in later cycles. One advantage of this system over the use of fluorous biphasic or aqueous biphasic reactions is that the ligands, which have been

optimised for organic solvents, do not need to be modified because they are soluble in the ionic liquid but much less so in the SCF. Supercritical carbon dioxide is not present during the reaction because the acidity it generates in the added water deactivates the catalyst.

They recently reported the same reaction in $scCO_2$, [BMIM][PF_6] and an $scCO_2$-[BMIM][PF_6] biphasic system[144]. Ruthenium BINAP complexes catalyse the enantioselective hydrogenation of a range of functionalised alkenes. Some (Class I) give high ee when the availability of H_2 is high, whilst others (Class II) perform better under conditions of hydrogen starvation. The Class I substrate, atropic acid gave high e.e. when the hydrogenation was carried out in $scCO_2$ whilst the class II substrate, tiglic acid gave higher e.e. in ionic liquids. This is because mass transport of hydrogen to the catalyst is favoured in $scCO_2$, with which it is fully miscible, whilst the very low solubility of hydrogen in the ionic liquid makes mass transport slow. Several studies have confirmed that absolute gas concentration does not correlate with reaction rate[96,135,134]. Because $scCO_2$ reduces the viscosity of the ionic liquid (at 50°C the viscosity of [BMIM][PF_6] drops from 60.4 cp to 28.5 cp when CO_2 (0.64 mole fraction) is added[125] and increases the hydrogen mass transport, the SCF-ionic liquid system is better for tiglic acid than the ionic liquid on its own, whilst the e.e. drops for atropic acid when CO_2 is added to the ionic liquid (see Table 1.10).

Although the transport of hydrogen appears to be the dominant factor in determining the outcome of the reaction under different conditions, studies using different ionic liquids show that it is not the only factor. If it were, class I substrates would give higher e.e.'s in less viscous ionic liquids for which H_2 mass transport is better, whilst

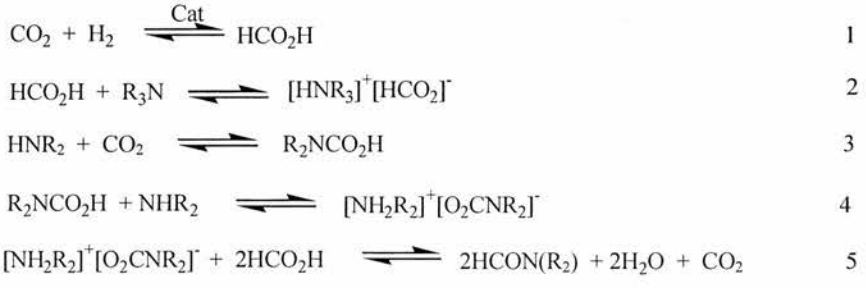
the reverse would be true for class II. In practice, both give higher e.e.'s in the less viscous ionic liquids, although these reactions did not include CO_2[144].

Table 1.10 The effect of CO_2 on the e.e. of products from enantioselective hydrogenation catalysed by **3** in [BMIM][PF_6]

Substrate	**H_2 / MPa**	**CO_2 /MPa**	e.e. %
Tiglic acid	0.5	0	93
Tiglic acid	0.5	7	85
Itaconic acid	5	0	32
Itaconic acid	5	5	57

The hydrogenation of simple alkenes, 1-decene and cyclohexene[146], to decane and cyclohexane respectively has also been investigated in scCO_2-[BMIM][PF_6] using Wilkinson's catalyst [$RhCl(PPh_3)_3$] (50 °C, 4.8 MPa H_2, total pressure 20.7 MPa, 1 h). The catalyst activity was the same in scCO_2-[BMIM][PF_6] as in hexane-[BMIM][PF_6], but the products from 1-decene hydrogenation were removed when using scCO_2 by flushing with scCO_2 at the reactor temperature and pressure and operating repetitive batch reactions. The yield remained at 98 % in each of 5 reactions with the same catalyst. The hydrogenation of CO_2 in the presence of dialkylamines to produce N,N-dialkylformamides was carried out with [$RhCl_2(dppe)_2$] as catalyst (80 °C, H_2 0.5 MPa, total pressure 27.6 MPa, 1 h)[146]. Noyori and coworkers[86,147] reported the hydrogenation of CO_2 in scCO_2 to formamides using scCO_2-soluble $RuCl_2(PMe_3)_2$.

In the $scCO_2$ – [BMIM][PF_6] system, much higher selectivities to formamides were found than when using [$RuCl_2(PMe_3)_4$] in $scCO_2$ alone, probably because the intermediate carbamates and alkyl ammonium formates produced in Equations 2 and 4 of Scheme 1.4 would be expected to be more soluble in the ionic liquid phase than the $scCO_2$ phase. When using Pr_2NH, extraction of the product dipropylformamide with $scCO_2$ was initially poor (5 % recovery), however, the success of the recovery process improved considerably on the second (61 %) and subsequent (almost quantitative) cycles of a series of repetitive batch reactions. Clearly, the partition coefficient of the dipropyl formamide into the $scCO_2$ from the ionic liquid is low, but once the ionic liquid is saturated, successful extraction occurs[146]. This would appear to be a good candidate reaction for continuous processing.



Scheme 1.4[146] Proposed mechanism for the hydrogenation of CO_2 to formamides in the presence of dialkylamines

1.4.2.2.2 Hydroformylation

The first description of a continuous flow reaction being carried out in an SCF-ionic liquid mixture concerned the hydroformylation of medium chain alkenes[128,148,62].

Repetitive batch reactions were carried out using triphenylphosphite modified rhodium catalysts in [BMIM][PF_6] (see sections 1.2.6.2 and 1.2.6.3)

This system was used for continuous processing ([Rh(acac)$(CO)_2$]/[PMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$], 100 °C, total pressure 20 MPa) with a steady rate and l:b ratio being observed for up to 72 h. The rates (5-10 catalyst turnovers h^{-1})[62] of these initial reactions were rather low and product recovery was only about 20 %. In subsequent optimisation studies[128], very significant improvements were realised so that rates comparable to those pertaining in commercial systems have now been achieved.

The product collection efficiency was improved to > 90 by altering the decompression system so that the product was collected after the first decompression valve at a pressure of *ca.* 0.5 MPa rather than after a 2 stage decompression at a pressure of 0.1 MPa.

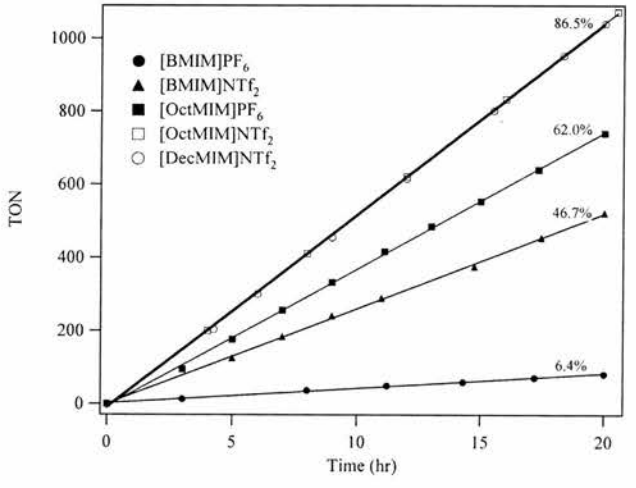


Figure 1.20[128] Hydroformylation of 1-dodecene catalysed by Rh/[PMIM]-[$Ph_2P(3\text{-}C_6H_4SO_3)$] in a variety of ionic liquids. The numbers are conversions of 1-dodecene in the isolated fractions.

The problem of low conversion was largely caused by poor mass transport of the substrate into the ionic liquid, where the catalyst resides. Significant improvements were obtained by increasing the chain length of the 1-alkyl in the imidazolium cations (Figure 1.20) probably because of the known increase in alkene solubility[24]. Conversion efficiencies up to 86.5 %, in the continuous flow system, were obtained using [OctMIM][NTf_2] or [DecMIM][NTf_2] (Dec = decyl,) as the catalyst solvent. 86.5 % was thought to be the maximum obtainable in a one pass flow system. NTf_2 salts gave better rates than PF_6 salts when using the same imidazolium cation (Figure 1.20). This is advantageous because, as indicated above, PF_6^- is sensitive to water, giving HF and $O_2PF_2^-$[62,149] whilst NTf_2^- is stable towards water.

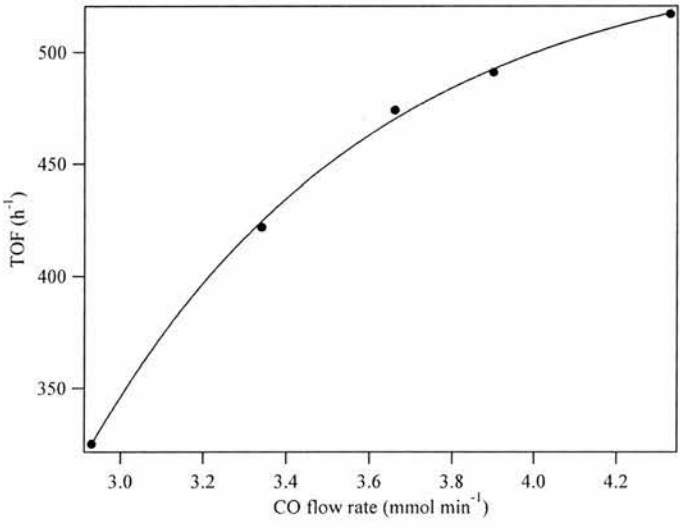


Figure 1.21[128] Effect of CO flow rate on continuous flow hydroformylation of 1-octene catalysed by Rh/[PMIM]-[$Ph_2P(3\text{-}C_6H_4SO_3)$] in the [OctMIM][$NTf_2$]-$CO_2$ biphasic system.

Further rate increases were obtained by changing the reaction parameters, the most important being substrate flow and the partial pressure of the permanent gases.

Increasing the flow rate of CO/H_2, thereby increasing the CO flow rate increases the turnover frequency (Figure 1.21) because the solvating power of the mobile phase decreases and more substrate partitions into the ionic liquid phase where the product resides. At very high CO/H_2 flow rates, the mobile phase cannot solubilise the product sufficiently to remove it at the rate at which it is formed. Nevertheless, turnover frequencies up to 500, comparable to those for the commercial rhodium catalysed hydroformylation of alkenes[137,138], have been observed under the optimum conditions (Figure 1.21). One other advantage of tuning the partition of the substrate and product between the two phases is that the less solubilising the supercritical phase, the less rhodium is extracted[128].

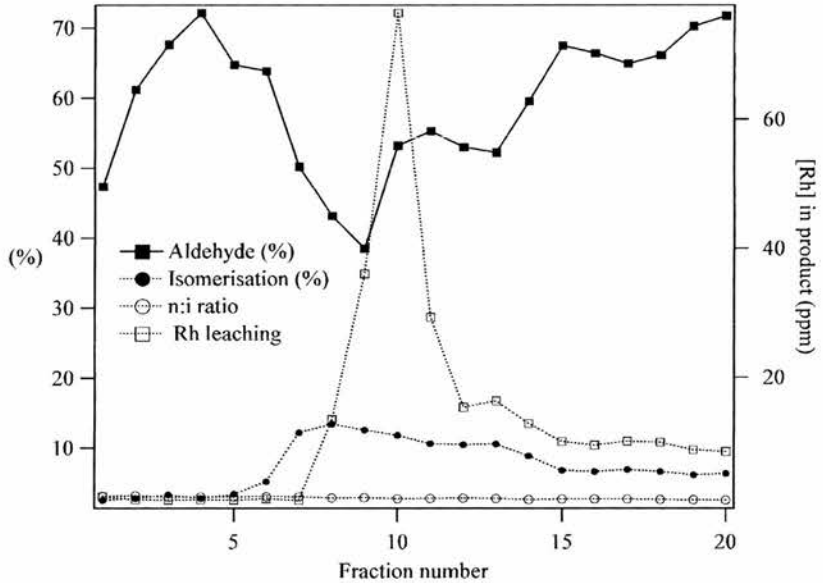
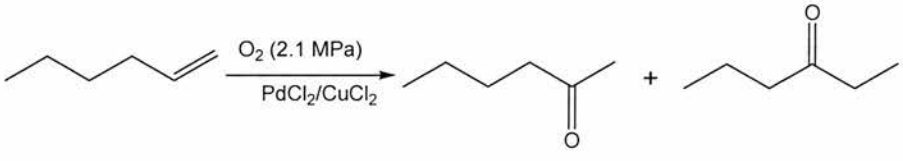


Figure 1.22[128] Effect of changing the partial pressure of CO/H_2 during the continuous hydroformylation of 1-octene in [OctMIM][NTf_2]. The sudden increase in Rh leaching at fraction number 10 is due to an experimental error not the CO flow rate.

Figure 1.22 shows how the rate and rhodium extraction are affected by the partial pressure of CO and H_2. Decreasing the partial pressure of the permanent gases causes a decrease in rate and an increase in rhodium leaching because the supercritical phase is a better solvent for both the substrate and the catalyst. Under the optimum conditions of Figure 1.21, the concentration of rhodium in the collected fractions is 12 ppb. This corresponds to 1 g in 40 tonnes of product aldehyde. The catalyst was very stable, with constant rates and l:b selectivities being observed for up to 72 h, and catalyst still showing good activity after 4 weeks at the reaction temperature and pressure in the presence of product aldehydes[128]. Using [PMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$], (Pr = propyl), the l:b ratio was only modest (l:b ratio = 3-3.5).

1.4.2.2.3 Oxidation of alkenes



Scheme 1.5[150] Wacker oxidation of 1-hexene to 2- and 3-hexanone

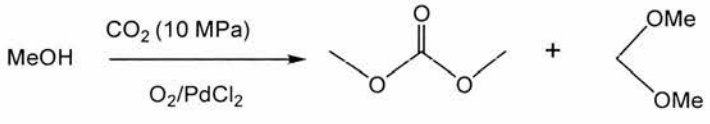
Oxidation of alkenes to methyl ketones using oxygen has been developed in both synthetic organic chemistry and industrial processes. A well-known example is the Wacker process using $PdCl_2$ and $CuCl_2$ as catalysts in acidic water or an organic solvent. Wacker oxidation of 1-hexene has been carried out in an $scCO_2$-ionic liquid biphasic system ($scCO_2$-[BMIM][PF_6]) at 40°C and 12.5 MPa total pressure (2.1 MPa O_2)[150]. The main products for this reaction were 2-hexanone and 3-hexanone (Scheme

1.5), with 2-hexanone being the desired product. The conversion approaches 100 % after 17 hours in all the solvent systems ($scCO_2$ only, [BMIM][PF_6] only, in $scCO_2$-[BMIM][PF_6] as well as in a solventless reaction)[150]. The rate profiles are very similar in $scCO_2$ and in $scCO_2$-[BMIM][PF_6]. It is suggested that this arises because the catalyst is better dispersed (accessible) in the biphasic system, but this is compensated for by poorer mass transport of substrate and oxygen into the ionic liquid.

The selectivity to 2-hexanone was found to be the highest in $scCO_2$-[BMIM][PF_6] biphasic system. 3-Hexanone is the oxidation product from isomerised 1-hexene, which suggests that isomerisation is suppressed in the $scCO_2$-ionic liquid biphasic system. The reaction mostly takes place in the ionic liquid phase since $PdCl_2$ and $CuCl_2$ are insoluble in the $scCO_2$ phase but soluble in the ionic liquid phase. 1-Hexene is soluble in both phases, and thus distributes between them. The improved selectivity in the $scCO_2$-ionic liquid system suggests that the rate of alkene isomerisation is reduced. This has been attributed to the alkene residing preferentially in the $scCO_2$ and not being in contact with the catalyst so isomerisation does not occur[150]. However, this should not only slow the isomerisation, but also the oxidation. If both reactions are catalysed by the same Pd complex, the affect of this partition should be the same on the rate of both reactions. The difference may arise because different species catalyse the two different reactions (oxidation and isomerisation) and the speciation between them is affected by some parameter such as mass transport of oxygen. The reaction could be repeated up to 6 times in repetitive batch mode, with the products being flushed from the reactor using CO_2 at 160 °C and 11 MPa. 100 g of CO_2 were required for complete extraction. The reaction rate and selectivity are reported to decrease over the six cycles[150].

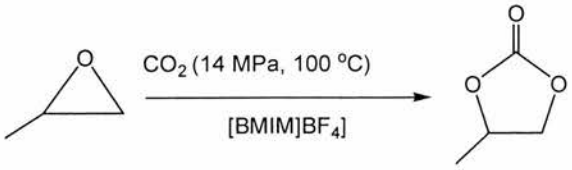
1.4.2.2.4 Carbonate formation

A system has been described[151] for the formation of dimethyl carbonate, a possible phosgene replacement, by the oxidative carbonylation of methanol (110 °C, total pressure 10 MPa, 1 h) catalysed by $PdCl_2$ in [BMIM][PF_6]. Conversions were generally low (< 7 %) and did not improve with increased reaction time, although the selectivity to dimethylcarbonate dropped. Dimethoxymethane was the major product but selectivities of dimethyl carbonate up to 25 % were possible with an O_2:CO_2 ratio of 29:71. Neither the pressure nor the temperature had dramatic effects upon the yield or selectivity, although the reaction was slower at lower temperatures. The reaction was repeated 3 times under the optimum conditions in a repetitive batch process. The rate remained constant, but there was a slight drop in selectivity.



Scheme 1.6[151] Formation of dimethylcarbonate and dimethoxymethane from methanol and CO_2.

Cyclic carbonates, used as a starting monomer to make polymers, can be synthesised by chemical fixation of CO_2, which is a much more environmentally acceptable process compared with that using phosgene.

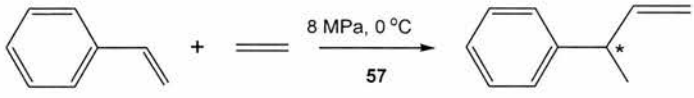


Scheme 1.7[152] Formation of propene carbonate from propene oxide and CO_2.

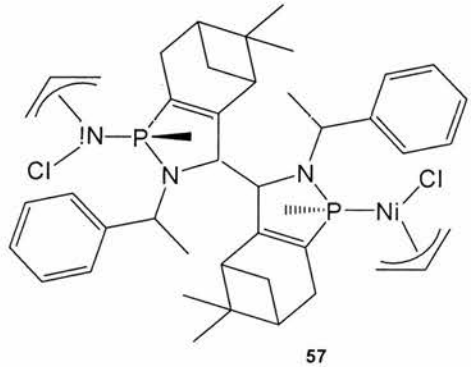
The production of cyclic carbonates has suffered in the past from serious disadvantages of separating the catalyst[153,154], whilst the activity of heterogeneous catalysts is generally very poor[155]. The synthesis of cyclic carbonates from epoxides and CO_2 takes place in $scCO_2$ using small amounts of DMF as a $scCO_2$ soluble acid-base catalyst[156,157]. However, long reaction times (about 12 hours) were required because of the poor catalytic activity of DMF. The reaction time could be reduced to 5 min by replacing the DMF with a catalytic amount of an ionic liquid, which acted as an acid-base catalyst and a solvent[152]. The reaction rate is higher at higher CO_2 pressure, as expected because CO_2 is a reagent, but is still low in imidazolium salts with short alkyl chains ([EMIM][X] (X = NO_3^-, $CF_3SO_3^-$, BF_4^-, or PF_6^-), although it increases in the order $BF_4^- > NO_3^- = PF_6^- > CF_3SO_3^-$. Increasing the chain length to C_4 ([BMIM]BF_4]) gives much better activity and this is again attributed to the better solubility of the epoxide in the ionic liquid. Under these conditions (14 MPa, 100 °C), the reaction was successful at temperatures as low as 60 °C, but not at 40 °C. The reaction medium could be reused at least twice, but the rate of reaction dropped markedly in successive cycles[152].

1.4.2.2.5 Alkene coupling reactions

Hydrovinylation is the transition metal catalysed codimerization of alkenes with ethane to yield 3-sustituted 1-butenes (Scheme 1.8). This is an interesting reaction because there are issues relating to chemoselectivity (dimer vs oligomer formation), regioselectivity and enantioselectivity. The reaction can be achieved with high enantioselectivity using Wilke's complex **57** as the catalyst precursor[158]. The main problem with this reaction in conventional solvents is the fact that the catalyst must be activated by chloride abstraction using highly flammable $Et_3Al_2Cl_3$ and it also requires temperatures below -60°C in dichloromethane[159]. Some of these problems could be overcome by carrying out the reaction in liquid or $scCO_2$ with the catalyst being activated by an alkali salt of a weakly coordinating anion such as Na[BArF] (BArF = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate)[160].



Scheme 1.8[160] Codimerisation of styrene and ethene



57

Further improvements were obtained by using the $scCO_2$-ionic liquid biphasic system[161]. The ionic liquid acts as both solvent and chloride abstractor. It was noted that the effectiveness of the catalyst activation depends on the nature of the anion of the ionic liquid. The conversion drops in the order BArF > $Al[OC(CF_3)_2Ph]_4$ > NTf_2 > BF_4 as anions with EMIM as the cation. This trend is consistent with the nucleophilicity/coordination strength of the anions. In terms of enantioselectivity, the ionic liquid, which most effectively activates the catalyst, also gives the highest e.e. The cation was also found to have an influence on the enantionselectivity of the catalyst with [4-MBP][BF_4] (44.2 %) giving higher e.e. than [EMIM][BF_4] (34.2 %), although the effect is reversed for the bistrifluoromethylsulphonamides, with [4-MBP][NTf_2] giving an ee of 58.4 % and [EMIM][NTf_2] 53.4 %. The best e.e. (89.4 %) was obtained with [EMIM][BArF], but this was at the expense of poor chemo- (10 % oligomers) and regio- (26.2 % of undesired isomers) selectivity. Overall, the best performance was obtained with [EMIM][$Al\{OC(CF_3)_2Ph\}_4$], which allowed 90.5 % conversion with 96.7 % selectivity to the desired 3-phenyl-1-butene (e.e. = 78.2 %)[161]. After optimising the reaction temperature and pressure, the reaction was carried out in a repetitive batch mode, with the product being extracted with $scCO_2$ after the reaction. However, the active species deactivated rapidly after three to four batchwise cycles. This was also observed when using only $scCO_2$ as a solvent[160]. It was suggested that the deactivation is related to the instability of the active species in the absence of substrate, so continuous operation should improve the stability as substrate is always present.

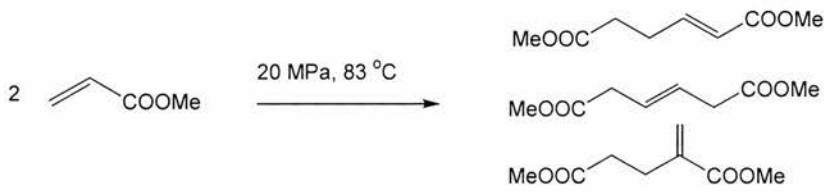
Continuous flow operation was demonstrated in [EMIM][NTf_2][161]. The catalyst was found to be stable for over 61 hours (conversions 75 – 80 %) with the e.e. dropping

slightly 65-58 %) over the long reaction period. This reaction was carried out at 0 °C and 8 MPa with a flow rate of styrene of 0.01 cm^3 min^{-1}. All of the CO_2 will be liquid under these conditions (since it is below the critical temperature), so in some ways this experiment resembles a counter current flow experiment using an ionic liquid and an organic solvent. The great advantages here, however, are that the mobile solvent, CO_2, can easily be separated from the product by simple decompression and it is environmentally much more acceptable than volatile organic solvents, which might otherwise be required.

The head to head dimerisation of methyl acrylate (MA) to dimethyl Δ2- and Δ3-dihydromuconate (DHMs) (Scheme 1.9) leads to an intermediate, which can be transformed to nylon-6,6 via adipic acid.

A $scCO_2$-[BMIM][BF_4] biphasic system for methyl acrylate dimerisation using a complex catalyst consisting of [$Pd(acac)_2$], [Bu_3PH][BF_4] and [Et_2OH][BF_4] in [BMIM][BF_4] has recently been reported[162]. Phase behaviour studies showed that the substrate methyl acrylate is fully miscible with CO_2 in the pressure range 9 – 29.5 MPa, whereas the product dihydromuconates is only fully miscible at the concentrations required above a density of 0.4 g cm^{-3} (15 MPa at 80 °C). The biphasic reactions were therefore carried out at 20 MPa and 83 °C. The conversion (73 %), selectivity (>98 %) and TOF (95 h^{-1}) were found to be similar to those obtained in monophasic (ionic liquid only) conditions. This is somewhat surprising since the concentration of substrate in the ionic liquid is expected to be much lower when the $scCO_2$ is present. The catalyst stability was determined by cooling down the reaction after 6 hours and then after 60 hours, heating the system to the reaction temperature,

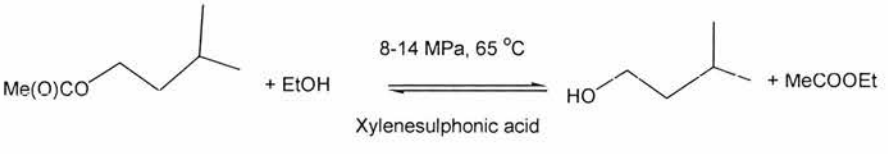
introducing fresh methyl acrylate and re-running the reaction under the same conditions. The results showed that the catalyst was still active, although at a lower rate, and still gave the same selectivity. The product was extracted from the ionic liquid phase by stepwise depressurisation. DHMs precipitate first as they are less soluble in $scCO_2$ than MA[162].



Scheme 1.9[162] Dimerisation of methyl acrylate (MA) to dimethyl Δ^2- and Δ^3-dihydromuconate (DHMs) and the undesired head-to-tail dimer.

1.4.2.2.6 Transesterification

The equilibrium for the transesterification isoamyl acetate by ethanol can be affected by the solvent system. This reaction was studied in $scCO_2$, the ionic liquid, [BMIM][PF_6] and $scCO_2$-[BMIM][PF_6] biphasic system at 65°C using p-xylenesulfonic acid (p-TSA) as a catalyst[163].



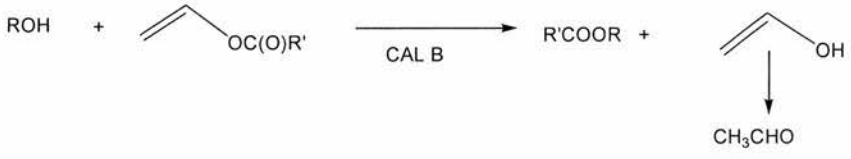
Scheme 1.10[163] Transesterification of isoamyl acetate with ethanol.

It was found that the equilibrium conversion at 65 °C in a $scCO_2$-ionic liquid biphasic system was lower than that in either $scCO_2$ or the ionic liquid alone. In $scCO_2$, the conversion at equilibrium depends on the phase behaviour. When two phases are present (80, 12 MPa), the equilibrium conversion is 45 %, whilst above the critical pressure of the system (14 MPa) the conversion is only 25 %. Similar differences occur when the ionic liquid is present with values of 28 % when no CO_2 is present. At 8 MPa, when three phases are present (predominantly containing ionic liquid, liquid organic compounds and CO_2 respectively), the conversion drops to 20 % whilst at higher pressure (12-14 MPa), where only two phases are present, the conversion drops to only 15 % at equilibrium. It also takes longer for equilibrium to be established in the $scCO_2$-ionic liquid system[163]. Clearly, complex forces are at work here and it is very difficult to deconvolute the effects of different solvation, solubility and fugacity. Although the biphasic system has a negative effect on the equilibrium conversion, in this case, the fact that variations occur depending upon the system may make it possible to design reactions where the equilibrium position can be altered to favour an important and desirable compound.

Transesterification has also been used to demonstrate that enzyme catalysis can be carried out in SCF-ionic liquid biphasic systems. Ionic liquids can stabilise enzymes thereby enabling their use at higher temperatures[164,165], $scCO_2$ on the other hand usually causes reductions in activity for enzymes either because of changes in pH as a result of the acidic CO_2 dissolving in water, or as a result of conformational changes that occur during pressurisation and depressurisation[166]. Many enzyme catalysed reactions suffer from product inhibition, or even inactivation, so continuous flow operation in which the product is continuously removed offers the possibility of

improved performance and/or lifetime. Over reaction might also be avoided in this way.

Lozano *et al*[167-169] and Reetz, Leitner and co-workers[170,171] simultaneously reported $scCO_2$-ionic liquid biphasic biocatalytic systems. Lozano *et al*[167,169] studied the synthesis of butyl butyrate from vinyl butyrate and butan-1-ol (Scheme 1.11, R = butyl, R' = propyl). Vinyl butyrate was used because the product vinyl alcohol tautomerises to ethanal and hence the reaction is irreversible.



Scheme 1.11 Transesterification of vinyl esters with alcohols.

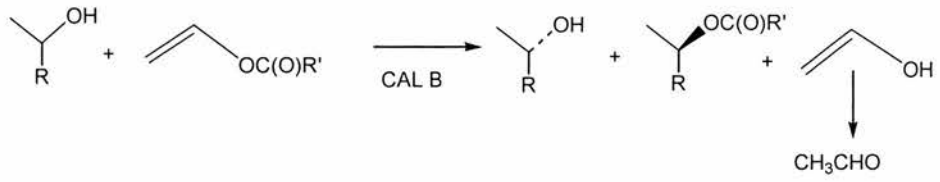
An aqueous solution of *Candida Antarctica* lipase B (CAL B) dissolved in [EMIM][NTf_2] or [BMIM][NTf_2] and then supported on celite was used as a catalyst. The reactions were run continuously at 25 °C and 1.5-15 MPa for 4 h then stored for 20 h at atmospheric pressure before reusing them. They found that the specific activity and selectivity of the enzyme increases with increasing temperature for the synthesis of butyl butyrate from vinyl butyrate and butan-1-ol. This was thought to be due to the reduction in water solubility in the ionic liquid phase, although simple Arrhenius behaviour would be expected to give higher rates at higher temperatures. The increase in specific activity could also be related to a reduction in $scCO_2$ density with temperature, as decreasing the $scCO_2$ density enhances the activity of the enzyme[166]. CO_2 is usually detrimental to enzymes[172] and indeed, the rates in the SCF-ionic liquid system are only about 10 % of those in the ionic liquid alone[165]. The

decrease in gas-phase density will also shift the equilibrium partitioning of the substrate towards the ionic liquid phase, which favours the enzyme action, as has been suggested from comparative work using ionic liquids (see below). The enzyme deactivates with time, the rate of decay increasing with temperature. After 10 cycles at 40 °C, the activity is still 85 % of that initially observed, and even at 100 °C has only dropped to 40 %. Studies in which the ionic liquid is varied show that, for all straight chain alcohol substrates, the activity of the enzyme is higher in [butyltrimethylammonium][NTf_2] than in [4-cyanopropyltrimethylammonium][NTf_2]. The reverse is true in the ionic liquids in the absence of $scCO_2$, an observation that has been attributed to the different viscosities of the ionic liquids. Viscosity cannot explain the results obtained in the presence of $scCO_2$ where the relative rates arise because the substrates are more soluble in [$BuMe_3N$][NTf_2] than in the ionic liquid containing the cyanopropyl group. The observed rate differences are probably then brought about by different rates of mass transport across the SCF-ionic liquid interface[169].

The acylation of octan-1-ol by vinyl acetate catalysed by CAL B in $scCO_2$-ionic liquid biphasic system (Scheme 1.11, R = octyl, R' = methyl) has also been reported[170]. The reactants were added directly to the suspension of the enzyme in [BMIM][NTf_2]. Initially, repetitive batch reactions were carried out at in the absence of CO_2 for 30 minutes and the product was extracted at 39 °C and 9.5 MPa $scCO_2$ over 1 h. Complete conversion was achieved in 4 consecutive cycles and octyl acetate was collected in yields ranging from 92-98 %. With evidence that the enzyme does not lose its activity continuous flow processing was performed. The reactor was charged with [BMIM][NTf_2] and CAL B and flushed with CO_2 at 45 °C and 10.5

MPa[170]. The substrates, octanol and vinyl acetate, were injected using an HPLC pump. After passing through the reactor the CO_2 stream was depressurised and the organic components collected in a cold trap. The system required about 10 minutes to reach a steady state, after which good mass balance was achieved. The total yield of octyl acetate was 93.9 % after 24 hours at a rate corresponding to 0.1 kg (litre of reactor volume)$^{-1}$, and a specific activity of the enzyme of 26 μmol (min g)$^{-1}$.

Both groups also studied the kinetic resolution of *rac*-1-phenyl ethanol by vinyl propanate[167,169], vinyl acetate[170,171] or vinyl dodecanolate[170,171] (Scheme 1.12, R = Ph, R' = Me, Pr or undecyl) The specific activity of the CAL B towards the kinetic resolution of *rac*-1-phenylethanol by vinyl propanoate was lower than for butyl butyrate synthesis because of the lower nucleophilicity of the secondary alcohol, although the activity was found[167,169] to be eight times greater than when the enzyme was immobilised on celite in the absence of an ionic liquid. The enzyme was found to give high enantioselective (>99.9 %) to (*R*)-1-phenylethyl propionate and little difference was observed between [EMIM][NTf_2] and [BMIM][NTf_2] at 50 °C, although the rate was higher for the shorter chain ionic liquid at 100 °C. In both case lower activity was observed at 100 °C than at 50 °C and the activity dropped by half after >20 cycles at 50 °C, but <20 cycles at 100 °C (8 cycles for [BMIM][NTf_2])[167]. The other isomer was not detected.



Scheme 1.12 Kinetic resolution of secondary alcohols by transesterification of vinyl esters.

Reetz, Leitner and co-workers[170,171] observed similar results (about 99 % (*R*)-1-phenylethyl acetate isomer using vinyl acetate and the same), but suspended directly in [BMIM][NTf_2], in repetitive batch mode, although the time to 45 % conversion increased from 1 h to about 12 h on the 4th cycle[170]. Substantial loss of activity appears to have occurred between the 3rd and 4th cycles. Higher yields were obtained with [BMIM][NTf_2] than with [BMIM][PF_6] or [BMIM][BF_4]. The enzyme could be used in free suspension or on a support; supported enzymes being preferred because they do not promote transesterification beyond 50 % making for very high e.e.'s in the recovered alcohol and the product ester. The reaction was also successful with a variety of other secondary alcohol substrates[170].

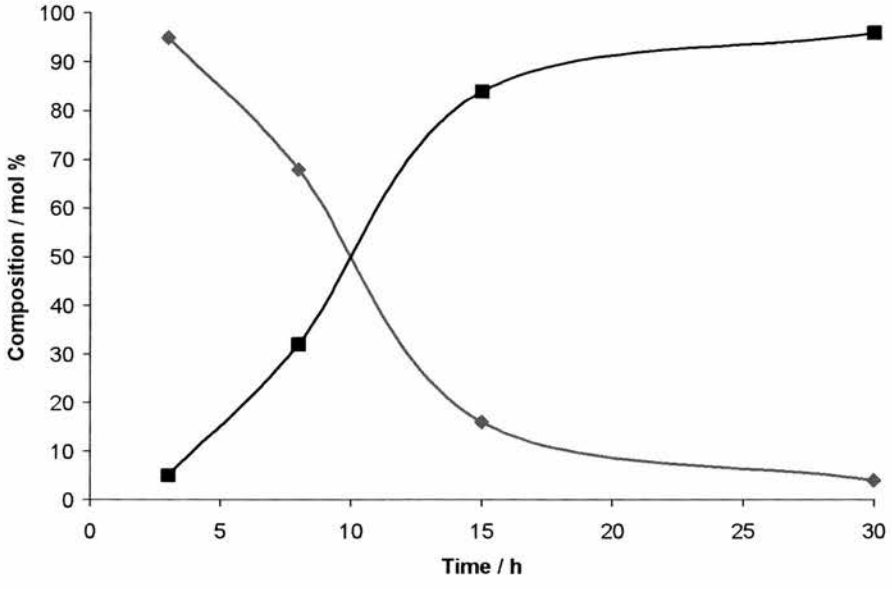


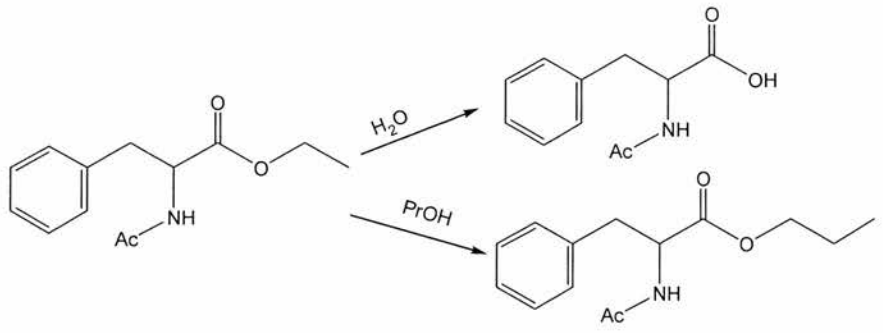
Figure 1.23[171] Separation of (*S*)-2-octanol from vinyl ester from CAL B catalysed kinetic resolution in [BMIM][NTf_2] by extraction with CO_2 (60 °C, 9 MPa)

In an attempt to separate the unreacted (*S*)-alcohol from the product (*R*)-ester, lower pressures were used for the extraction. This gave some enrichment in the ester (1-phenylethyl acetate : 1-phenylethanol = 1.4:1 at 60 °C and 9 MPa). After extraction of 65 % of the ester formed, an alcohol rich fraction was obtained (1-phenylethyl acetate : 1-phenylethanol = 1:3) when the CO_2 pressure was increased to 15 MPa[171]. A more successful separation was achieved when vinyl acetate was replaced by vinyl dodecanoate in the initial reaction and 2-octanol was the substrate (Scheme 1.12, R = 1-hexyl, R' = undecyl). In this case, the high molecular weight ester is less soluble in $scCO_2$ than the alcohol. Extraction at 9 MPa and 60 °C initially gave fractions that were highly enriched in the alcohol (ester: alcohol = 1:18)., whilst the ester was enhanced in later fractions (21:1, see Figure 1.23).

A two step extraction procedure, typically 9-10.5 MPa CO_2 at 60 °C, dropping to 8 MPa in the collector over 90 h to extract the alcohol followed by 20 MPa and 45 °C) also works well for other secondary alcohol substrates so that yields of each of the unreacted alcohol and the recovered ester can be > 90 % with e.e.'s > 90 %. The e.e. is generally lower for the ester than for the recovered alcohol, the exception being $PhCH_2CH_2CH(OH)CH_3$, where only 72.5 % of the ester is recovered (e.e. 88.2 %). The recovered alcohol (92.4 %) has an e.e. of only 65 %[171].

A reaction using 2-phenylethanol and vinyl dodecanoate was operated continuously in a reactor consisting of two consecutive autoclaves containing the enzyme – ionic liquid suspension to ensure high conversion and two decompression chambers with a liquid recycling system and the ability to add further CO_2 independently[171]. The reaction was run at 50 °C and 2 MPa with a mixed substrate flow rate (33 % alcohol) of 0.6 $cm^3 min^{-1}$. The CO_2 stream leaving the reactor was decompressed to 1.3 MPa at 50 °C in a first chamber, where extra CO_2 was added to help remove the alcohol into the second chamber (100 °C, 10 MPa). Finally, the stream was passed into a cryotrap. The liquid collected in the second chamber was periodically recycled to the first so that the alcohol ends up mostly in the cryotrap, whilst the ester is recovered from the first collection chamber. After 112 h of continuous operation, the alcohol (81 %, > 97 % e.e.) containing < 0.1 % of ester was recovered from the cryotrap, whilst the first extraction vessel contained ester (97 %, >97 % e.e.) contaminated by <0.5 % of alcohol. After resuming the substrate and CO_2 flows, identical activities and selectivities were obtained. Acetaldehyde will have been vented from the system because of its high volatility, but the unreacted vinyl laurate, which was used in excess, is of intermediate volatility. It, presumably, is collected with the ester.

As with other substrates, $scCO_2$ also slowed the kinetic resolution (compared with the reaction in pure ionic liquid) of glycidol using vinyl acetate or vinyl butyrate catalysed by *Candida Antarctica* Lipase (CAL) A or B or a lipase from *Mucor miehei*, either suspended in the free ionic liquids or immobilised, when the reactions were carried out in $[EMIM][NTf_2]$[173]. Cal A was inactive, but the other two enzymes showed activity albeit at 10-20 % of that in the absence of CO_2 whether they were free or immobilised. The supported enzymes showed superior performance[173].



Scheme 1.13[174] Hydrolysis or transesterification of N-acetyl phenylalanine catalysed by chymotripsin in $[RMIM][PF_6]$ (R = octyl or butyl) at 45 °C and 13.8 MPa

Chymotripsin, a specific protease for aromatic amino acids, catalyses the hydrolysis or transesterification of the ethyl ester of N-acetylphenylalanine with propanol in $[RMIM][PF_6]$ (R = butyl or octyl) with or without added water (Scheme 1.13). $scCO_2$ improved the reactivity relative to that in the ionic liquid alone or, when chymotripsin was employed in $scCO_2$ without the ionic liquid (Figure 1.24). Addition of 1 % water to the mixture improved the reaction rate, but some hydrolysis was also observed. In this case, $[BMIM][PF_6]$ proved to be superior to $[OctMIM][PF_6]$, whereas the opposite was true for reactions carried out in the absence of $scCO_2$.

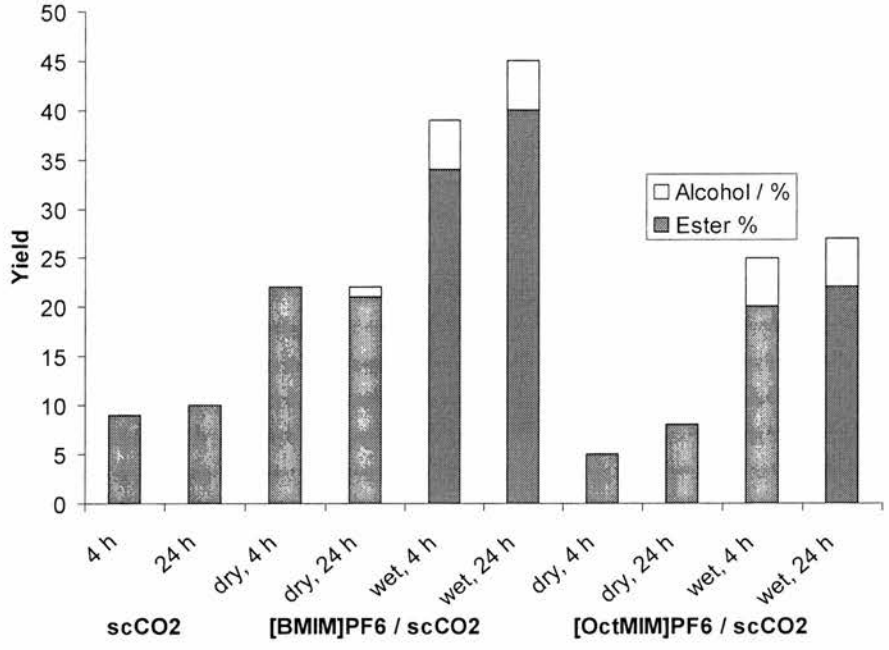


Figure 1.24[175] Influence of solvent, reaction time and the presence of water on the transesterification of N-acetyl phenylalanine catalysed by chymotripsin in $[RMIM]PF_6$ (R = octyl or butyl) at 45 °C and 13.8 MPa. Dry reactions contain < 0.03 % (w/w) water; wet reactions contained 1 % water.

1.4.3 Electrochemistry in SCF-ionic liquid biphasic systems

Electrochemical reactions are usually carried out in polar organic solvents in the presence of large amounts of supporting electrolytes to improve the current densities. The separation of the product from the solvent and supporting electrolytes creates similar problems to those pertaining to homogeneous catalysts. Since ionic liquids are ideal solvents for electrochemistry, providing high conductivities without the need for supporting electrolytes, the SCF-ionic liquid concept should also be applicable in electrosynthesis. An added bonus is that $scCO_2$ increases the conductivity of ionic liquids, presumably because the viscosity is reduced[176]. A recent paper[177] describes

the electrooxidation of benzyl alcohol in [BMIM][PF_6] or [BMIM][BF_4] at 45 °C and 8.8 MPa. Small amounts of water are essential for the successful production of benzaldehyde, otherwise a yellow insulating film grows to cover the electrode. For reactions in the preferred [BMIM][BF_4], the Faradaic efficiency for benzaldehyde production increased with pressure up to 9.3 MPa then reduced again. This behaviour has been attributed to different pressure dependencies of the solubility of benzaldehyde and benzyl alcohol in scCO_2. The reaction was successfully carried out 4 times as a repetitive batch process, with each reaction giving Faradaic efficiencies of 41-44.5 % and selectivities to benzaldehyde > 94.5 %[177].

The full versatility of this type of reaction may be limited somewhat because CO_2 may not be an innocent participant, especially when water is also present. It has been reported that in the presence of water, CO_2 can be electroreduced in [BMIM][PF_6] at 45 °C to CO, hydrogen and traces of formic acid[178]. Oxygen is produced at the anode. The yield of CO increases with the partial pressure of CO_2, because its solubility rises and the viscosity is reduced. The increased availability of CO_2 at the cathode inhibits the adsorption of water so that the hydrogen yield decreases as the pressure is increased. Much lower applied voltages are required for the co-reduction of CO_2 and water (-1.2 V relative to a Pt wire reference electrode than are required for water (< -2 V or CO_2 (-1.8 V) alone[178]. Since the products are largely gaseous, they can be removed easily with the CO_2 and the ionic liquid was recycled 3 times with little or no loss of activity or selectivity[178].

1.4.4 Recent developments

Although the SCF-ionic liquid processes have enormous potential for development and it has been shown that commercially interesting rates, selectivities, catalyst lifetimes and separations can be achieved once optimisation has been carried out,[128,148,171] there is still scope for improvement. Some of the concern centres around the ionic liquids. They are generally considered to be environmentally benign because of their high stability and negligible vapour pressure. However, little attention has been paid to their very long term stability, although a process using one has been running for seven years without any loss or replenishment of the original charge of ionic liquid[179]. There must still be some doubt about their disposal, particularly for those with anions containing fluoride, which can sometimes react with water to give HF.[180,62,128] Although studies show they are generally of very low toxicity, imidazolium salts with long alkyl chains are skin irritants[181] and can be toxic to nematodes, albeit it fairly high dose rates (LD_{50} < 1 mg cm^{-3} for [tetradecyl MIM]Cl between 2.5 and 5 mg cm^{-3} for [OctMIM]Cl and >5 mg cm^{-3} for [BMIM]Cl.[182] The Cost of ionic liquids is currently high, but a major disadvantage of using them in SCF-ionic liquid biphasic systems is that the product must be extracted from the ionic liquid. If the process has been designed to give high rates, this generally means that the ionic liquid has been chosen to dissolve the substrate effectively. Often this will mean that the product is also very soluble so that high rates of extraction require high SCF pressures (typically 20 MPa).[128] This kind of pressure could make the process prohibitively expensive for all but the most valuable products. Consideration is therefore being given to systems in which the ionic liquid is replaced by a liquid polymer, which is insoluble in the SCF, or is omitted altogether.

Polyethylene glycols are readily available at a fraction of the cost of ionic liquids. They have recently been used[144,183] as solvents for the hydrogenation of styrene catalysed by [$RhCl(PPh_3)_3$] (40 °C, H_2 3 MPa, CO_2 5 MPa, 19 h), with the products being removed by flushing with $scCO_2$ (15.5 MPa, 55 °C, 2 cm^3 min^{-1}, 4 h). The reaction was repeated using repetitive batch processing with the yield of > 99 % being maintained for at least five cycles. Small amounts of PPh_3 (0.06 equivalents per Rh atom) and PEG were extracted by the $scCO_2$, with less PEG being extracted for higher molecular weight (ca 0.5 % for PEG 900 and 0.1 % for PEG 1500.[144,183] PEG's are waxy solids but were liquid under the reaction conditions, partly because the $scCO_2$ lowered the melting point. It also caused a favourable reduction in the viscosity of the molten PEG.

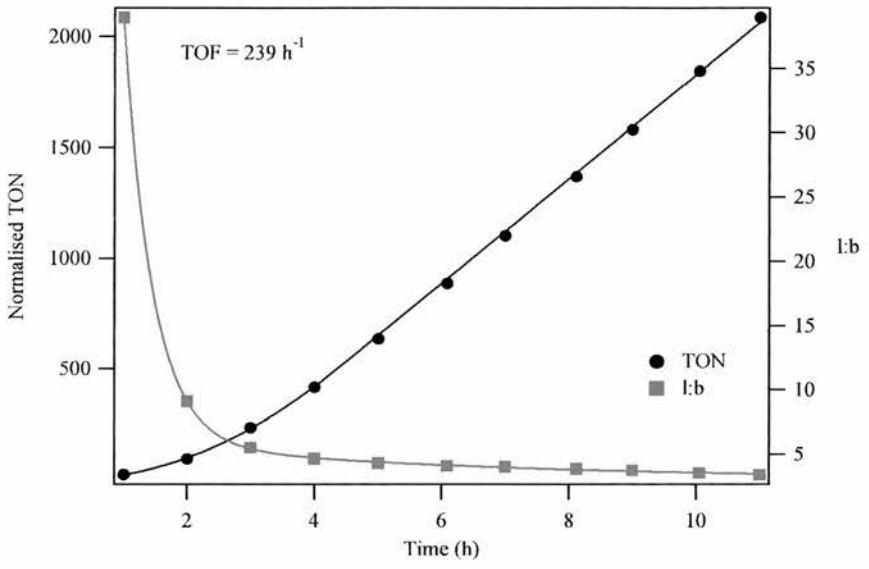


Figure 1.25 Continuous flow hydroformylation of 1-octene in nonanal (initial solvent) with $scCO_2$ as the flowing phase catalysed by Rh / [OctMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$].

Another attempt to obviate the need for the ionic liquid, simply involved dissolving the catalyst in the steady state mixture of reactants and products that develops during the reaction. In reality, the catalyst was dissolved in pure nonanal for a hydoformylation reaction of 1-octene carried out in a flow system, with flow rates balanced so that the rate of product extraction matches the rate of its continuous formation.[184] Figure 1.25 shows the results of one such reaction and illustrates the success of the process. The choice of ligand is very important (Table 1.11), since, if it is too lipophilic ([OctMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$]), significant extraction of rhodium occurs, but if it is too polar ([PMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$]) it is not sufficiently soluble in the product phase, unliganded rhodium complex is formed and the rhodium is rapidly lost from the system. Even with medium polarity ligands ([PentMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$] (Pent = pentyl), the flow rate must be controlled. Too high a flow rate leads to higher levels of 1-octene in the system. This causes some of the catalyst to

precipitate and the conversion to drop. Further catalyst precipitates leading to a negative feed back loop and very poor catalysis. With only preliminary optimisation, the operating pressure for continuous flow operation has been reduced from 20 to 12.5 MPa.

Table 1.11 Hydroformylation of 1-octene at 100 °C catalysed by rhodium complexes of different phosphines, using $scCO_2$ to transport the substrate and gases into and the products out of the reactor[a].[184]

R[b]	[Rh] / mol dm^{-3}	[P] / mol dm^{-3}	CO_2 flow / nL min^{-1}	CO flow[c] / mmol min^{-1}	Octene flow / mmol min^{-1}	p[d] / MPa	TOF[e] / h^{-1}	Conv / %	[Rh] leaching[g] / ppm
Propyl	0.012	0.19	0.47	1.2[h]	0.042	14	22	25	35[i]
Pentyl	0.011	0.16	0.55	2.89	0.32	12.5	80	76	0.1-0.5
Pentyl	0.0057	0.043	0.55	2.78	0.32	12.5	162	77	0.1-0.5
Octyl	0.015	0.22	0.65	1.59	1.27	14	208	50	5-10
Octyl	0.015	0.22	0.65	2.34	1.27	14	239	57	5-10

[a] *Starting solvent is 1-nonanal (16 cm^3), nL = normal litre;* [b] *[RMIM] [$Ph_2PC_6H_4SO_3$];* [c] *$CO:H_2$ = 1:1;* [d] *Total pressure;* [e] *mol product (mol catalyst h)$^{-1}$;* [f] *% aldehyde in recovered product;* [g] *[Rh] in recovered product;* [h] *$CO:H_2$ = 1:2;* [i] *High leaching early in the reaction.*

Although these processes require further optimisation, they do represent interesting new approaches with the potential to be more acceptable for scale-up and commercialisation.

1.4.5 Process considerations.

In principle, the SCF-ionic liquid and related systems could be operated as totally emissionless processes, but this would require recycling of the SCF. This has not been demonstrated in any of the catalytic systems reported so far, but is carried out in e.g. coffee decaffination[130], continuous hydrogenation in SCF's over heterogeneous catalysts[185] and in the conservation of archaeological wood by supercritical drying[186]. In the last process, water in the wood is exchanged for methanol which is then removed by extraction with $scCO_2$, thus avoiding crossing any phase boundaries and avoiding the surface tension forces that lea to collapse of the cells within the wood. The extraction can take several days, so the methanol is precipitated from the $scCO_2$ by decompression before the CO_2 is recompressed and recycled[186].

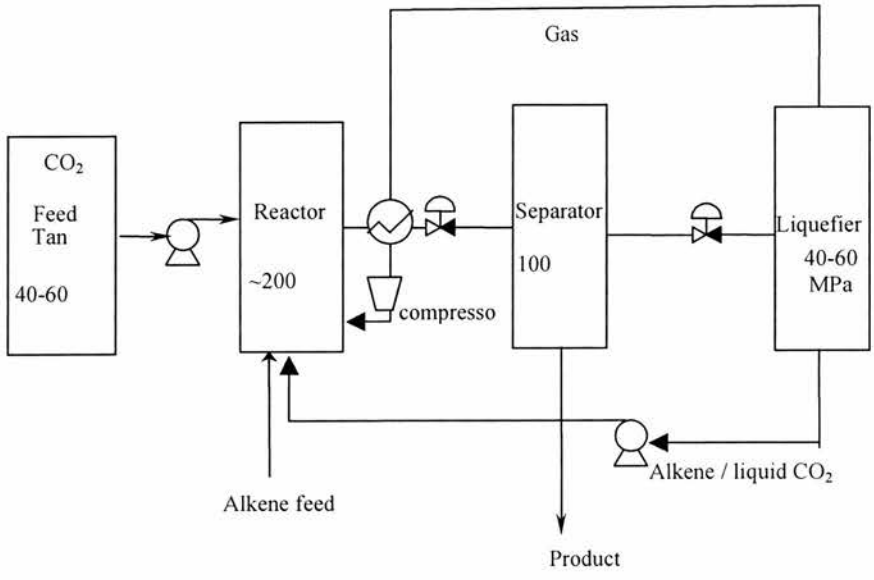


Figure 1.26 Process design for continuous operation with full recycling

A similar procedure could be used when there are no permanent gases involved in the catalytic reaction, but where gases are used, the recycling will be more complex. A possible process design is shown in Figure 1.26. Product recovery is achieved by simple expansion of the gas phase downstream. The remaining gas phase is then cooled or recompressed to liquefy the CO_2 and any remaining organics. This liquid phase can then be recycled to the reactor. The gaseous phase from the liquefier, containing CO_2 and any remaining permanent gases, is heated above its critical temperature (>31.1 ^{o}C, Tc for pure CO_2) and pumped as a gas back into the reactor.

1.4.6 Conclusions

The unusual properties of supercritical fluids and ionic liquids, especially the lack of solubility of ionic liquids in supercritical fluids and the ability of supercritical fluids to extract organic compounds from ionic liquids, makes them excellent candidates for use in continuous flow biphasic catalysis. CO_2-IL biphasic systems differ from other biphasic systems in that one of the phases is a dense gas, enabling reaction and separation under a single set of conditions and the development of continuous processes. The ability to afford reaction and separation under a single set of conditions not only reduces the problems of catalyst deactivation but also has a considerable effect on the size of reactor needed for a given product throughput. Reductions in reactor volumes then offer further advantages in terms of safety (e.g. smaller volumes of inflammable gases) and reduced capital costs.

The low environmental impact of these two very different solvents is also very attractive. A variety of reactions involving homogeneous catalysts have been demonstrated to occur successfully within the ionic liquids and the products can be extracted using supercritical fluids. Often, these reactions have been carried out as repetitive batch reactions and, in these cases, the throughput is probably too low to be of commercial interest. However, in a few cases true continuous flow operation has been demonstrated over prolonged periods with commercially significant rates, good product selectivities, good catalyst stability and very low catalyst leaching[128,171,187]. In one case, which involves the enzyme catalysed kinetic resolution of chiral alcohols by esterification reactions, a sophisticated decompression system has been developed, which allows for the separation of two different enantio pure products[171].

These very exciting initial studies should be developed further, with special emphasis being placed on reducing the overall pressure so that recycling of the SCF can be economically attractive. Some preliminary studies involving cheap polymers such as polyethyleneglycol as the catalyst solvent, or dissolving the catalyst in the steady state mixture of reactants and products, look very interesting as possible further developments of these interesting biphasic systems.

1.5 Aims of this work

The hydroformylation of linear higher alkenes dominates the production of detergent alcohols[8]. It is currently carried out on a commercial scale using cobalt based homogeneous catalyst systems[62]. The disadvantages of this process are that it uses harsh operating conditions, gives relatively poor selectivity to linear aldehydes and has a complex process for catalyst recycling. In general rhodium based catalyst systems have been shown to be superior to cobalt based catalyst systems as they offer milder reaction conditions, high activity and high selectivity to linear aldehydes, but they are not attractive for low volatility products because of the problems associated with the separation of the products and their heavy ends from the catalyst which is thermally sensitive[62]. The "low pressure oxo" technology by Kvaener is the only rhodium based hydroformylation thus far commercialised for long chain alkenes[8]. This process involves the separation of the product from the catalyst by low pressure distillation. It might solve the separation problem but, because it is a continuous batch process, in which the catalyst is in an inactive state outside the reactor, it might result in catalyst deactivation.

There is a need to develop a continuous flow process such that the catalyst remains in the reactor and the products are separated from the catalyst by the flow system. There is a process already operating for rhodium catalysed hydroformylation of ethene and propene[8,62,138], where the solvent is an involatile condensation product of the aldehydes produced and the product aldehydes are sufficiently volatile to be removed by distillation. For long chain alkenes, a different system is required with a very low volatility solvent, and a transport medium for the substrate and the products in and out

of the system. The system we propose to investigate uses an ionic liquid (IL) as the solvent and supercritical carbon dioxide ($scCO_2$) as the transport medium for the substrate and the products into and out of the reactor. It has been reported recently that ionic liquids are insoluble in $scCO_2$ whereas $scCO_2$ is highly soluble in an ionic liquid (up to 0.6 mol fraction)[117], and that $scCO_2$ can extract a large variety of organic compounds from IL, which makes $scCO_2$ a good vector for transporting alkenes and products into and out the reactor in gas-like form[62,127]. Ionic liquids are known to have low vapour pressure[34,33] and this makes them ideal solvents for our proposed system since we need a solvent which will not be extracted with $scCO_2$. We need then, to design a catalyst, which is insoluble in $scCO_2$ but soluble in an ionic liquid for the system to be continuous without losing catalyst during product extraction. Most probably the catalyst should be ionic to dissolve in the ionic liquid.

Cole-Hamilton and co-workers[62,189,185,128] have carried out work on this type of system i.e. $scCO_2$-IL biphasic system, where rhodium complexes of sulphonated triphenylphosphines were used, but they have proven to be ineffective in the $scCO_2$-IL systems since their solubilities in an ionic liquid are not ideal as they are synthesised as their sodium salts. It has been recently reported that using the cation of the ionic liquid as the counterion for the phosphine gives much better results. An immobilised catalyst ($[Rh(acac)(CO)_2]$ and a bidentate phosphite ligand) can be stabilised by the IL under harsh product distillation conditions and can be reused several times without additional regeneration process and without loss in activity and selectivity[56], but $scCO_2$ has not been explored for the extraction process.

Therefore, the aims and objectives of this study are:

i) To further explore the idea of using ionic catalyst systems which will render high solubility of the catalyst in the IL and give high selectivity and activity;

ii) To develop an ionic liquid which will not degrade as it has been reported that degradation of PF_6^- can occur after a few catalyst recycles[2]; and

iii) To develop an ionic liquid in which the solubility properties can be tuned so that the alkene is sufficiently soluble for rapid reaction to occur but the aldehyde partitions well into the $scCO_2$ for removal from the reactor.

1.6 References

1. Roelen, O. *German Patent* **1938,** *849*, 548.
2. Heck, R. F.; Breslow, D. S. *J. Am. Chem. Soc.* **1962,** *83*, 4023.
3. Slaugh, L. H.; Mullineaux, D. *J. Organomet. Chem.* **1968,** *13*, 469.
4. Evans, D.; Osborn, J. A.; Wilkinson, G. J. *J. Chem. Soc. A* **1968**, 3133.
5. Evans, D.; Yagupsky, G.; Wilkinson, G. J. *J. Chem. Soc. A* **1968**, 2660.
6. Brown, C. K.; Wilkinson, G. J. *J. Chem. Soc. A* **1970**, 2753.
7. Jardine, F. H. *Polyhedron* **1982,** *1*, 569.
8. van Leeuwen, P. W. N. M.; Claver, C. *Rhodium Catalysed Hydroformylation*; Kluwer: Dordrecht, 2000.
9. Iwamoto, M.; Yaguchi, S. *J. Org. Chem.* **1966,** *31*, 4290.
10. Pittman, C. U. J.; Hirao, A. *J. Org. Chem.* **1978,** *43*, 640.
11. Sanger, A. R. *J. Mol. Catal.* **1977/8,** *3*, 221.
12. Sanger, A. R. *J. Mol. Catal.* **1977/8,** *3*, 101.
13. Consiglio, G.; Botteghi, C.; Salomon, C.; Pino, P. *Angew. Chem.-Int. Edit.* **1973,** *85*, 665.
14. Hughes, O. R.; Unruh, J., D.;. *J. Mol. Catal.* **1981,** *12*, 71.
15. Unruh, J., D.; Christenson, J. R. *J. Mol. Catal.* **1982,** *14*, 19.
16. Dierkes, P.; van Leeuwen, P. W. N. M. *J. Chem. Soc. Dalton Trans* **1999**, 1519.
17. Devon, T. J.; Phillips, G. W.; Puckette, T. A.; Stavinoha, J. L.; Vanderbilt, J. J. *US Patent*, **1987**; Vol. 4; pp. 109.
18. Devon, T. J.; Phillips, G. W.; Puckette, T. A.; Stavinoha, J. L.; Vanderbilt, J. J. *US Patent*, **1994**; Vol. 5; pp. 846.
19. Casey, C. P.; Whiteker, G. T.; Melville, M. G.; Petrovich, L. M.; Gavney, J. A.; Powell, D. R. *J. Am. Chem. Soc.* **1992,** *114*, 5535.
20. Casey, C. P.; Petrovich, L. M. *J. Am. Chem. Soc.* **1995,** *117*, 6007.
21. Kranenburg, M.; Vanderburgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje. *Organometallics* **1995,** *14*, 3081.
22. van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *Organometallics* **2000,** *19*, 872.
23. Welton, T. *Chem. Rev.* **1999,** *99*, 2071-2083.
24. Wasserscheid, P.; Keim, W. *Angew. Chem.-Int. Edit.* **2000,** *39*, 3773-3789.
25. Hurley, F. H. *US Patent*, **1948**; Vol. 43.
26. Robinson, J.; Osteryoung, R. A. *J. Am. Chem. Soc.* **1979,** *101*, 323.
27. Chum, H. L.; Koch, V. R.; Osteryoung, R. A. *J. Am. Chem. Soc.* **1975,** *97*, 3264.
28. Hitchcock, P. B.; Mohammed, T., J.; Seddon, K. R.; Zora, J. A.; Hussey, C. L.; Ward, E. H. *Inorg. Chim. Acta* **1986,** *113*, L25.
29. Boon, J. A.; Levinsky, J. A.; Pflug, J. L.; Wilkes, J. S. *J. Org. Chem.* **1986,** *51*, 480.
30. Chauvin, Y.; Gilbert, B.; Gidbard, I. *J. Chem. Soc. Chem. Commun.* **1990**, 1715.
31. Carlin, R. T.; Osteryoung, R. A. *J. Mol. Catal.* **1990,** *63*, 125.
32. Wilkes, J. S.; Zaworotko, M. J. *J. Chem. Soc. Chem. Commun.* **1992**, 965.

33. Davis, J. H.; Forrester, K. J.; Merrigan, T. L. *Tetrahedron Lett.* **1998,** *39*, 8955.
34. Davis, J. H.; Forrester, K. J. *Tetrahedron Lett.* **1999,** *40*, 1621.
35. Holbrey, J. D.; Seddon, K. R. *J. Chem. Soc. Dalton Trans.* **1999**, 2133.
36. Zim, D.; de Souza, R. F.; Dupont, J.; Monteiro, A. L. *Tetrahedron Lett.* **1998,** *39*, 7071.
37. Dyson, P. J.; Grossel, M. C.; Srinivasan, N.; Vine, T.; Welton, T.; Williams, D. J.; White, A. J. P.; Zigras, T. *J. Chem. Soc.-Dalton Trans.* **1997**, 3465-3469.
38. Fuller, J.; Carlin, R. T.; de Long, H. C.; Hawort, D. *J. Chem. Soc. Chem. Commun.* **1994**, 299.
39. Ford, W. T.; Hauri, R. J.; Hart, D. J. *J. Org. Chem.* **1973,** *38*, 3916.
40. Poole, C. F.; Kersten, B. R.; Ho, S. S. J.; Coddens, M. E.; Furton, K. G. *J. Chromatogr.* **1986,** *352*, 407.
41. Bolkan, S. A.; Yoke, J. T. *J. Chem. Eng. Data* **1986,** *31*, 194.
42. Bolkan, S. A.; Yoke, J. T. *Inorg. Chem.* **1986,** *25*, 3587.
43. Bonhote, P.; Dias, A. P.; Papageorgiou, N.; Kalyanasundaram, K.; Gratzel, M. *Inorg. Chem.* **1996**, 35.
44. Waffenschmidt, H. *Ph.D Thesis*, Aachen 2000.
45. Wasserscheid, P. *Rehabilitation Dissertation*, RWTH Aachen 2002.
46. Anthony, J. L.; Maginn, E. J.; Brennecke, J. F. Gas solubilities in 1-n-butyl-3-methylimidazolium hexafluorophosphate. In *Ionic Liquids*, 2002; Vol. 818; pp. 260-269.
47. Wilkes, J. S.; Levinsky, J. A.; Wilson, R. A.; Hussey, C. L. *Inorg. Chem.* **1982,** *21*, 1263.
48. Fannin, A. A. J.; Floreani, D. A.; King, L. A.; Landers, J. S.; Piersma, B. J.; Stech, D. J.; Vaughn, R. L.; Wilkes, J. S.; Williams, J. L. *J. Phys. Chem.* **1984,** *88*, 2614.
49. Garcia, M. T.; Gathergood, N.; Scammells, P. J. *Green Chem.* **2005,** *7*, 9-14.
50. Freemantle, M. *Chem. Eng. News* **1999,** *77*, 9-9.
51. Freemantle, M. *Chem. Eng. News* **1998,** *76*, 32.
52. Freemantle, M. *Chem. Eng. News* **2000,** *78*, 37.
53. Karodia, N.; Guise, S.; Newlands, C.; Anderson, J. L.; Rogers, R. D. *Chem. Commun.* **1998**, 2341.
54. Huddleston, J. G.; Willauer, H. D.; Swatloski, R. P.; Visser, A. E. *Chem. Commun.* **1998**, 1765.
55. Dyson, P. J.; Ellis, D. J.; Parker, D. G.; Welton, T. *Chem. Commun.* **1999**, 25-26.
56. Keim, W.; Vogt, D.; Waffenschmidt, H.; Wasserscheid, P. *J. Catal.* **1999,** *186*, 481-484.
57. Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; de Souza, R. F.; Dupont, J. *Polyhedron* **1996,** *15*, 1217.
58. Song, C. E.; Roh, E. J. *Chem. Commun.* **2000**, 837.
59. Parshall, G. W. *J. Am. Chem. Soc.* **1972,** *94*, 8716.
60. Chauvin, Y.; Mussmann, L.; Olivier, H. *Angew. Chem.-Int. Edit. Engl.* **1996,** *34*, 2698-2700.
61. Earle, M. J.; McCormac, P. B.; Seddon, K. R. *Chem. Commun.* **1998**, 2245.
62. Sellin, M. F.; Webb, P. B.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 781-782.

63. Wasserscheid, P.; Waffenschmidt, H. *J. Mol. Catal. A-Chem.* **2000,** *164*, 61-67.
64. Chauvin, Y.; Mussmann, L.; Olivier, H. *Angew. Chem.-Int. Edit.* **1995,** *34*, 2698.
65. Stenzel, O.; Raubenheimer, H. G.; Esterhuysen, C. *J. Chem. Soc.-Dalton Trans.* **2002**, 1132-1138.
66. Deetlefs, M.; Raubenheimer, H. G.; Esterhuysen, W. M. *Organometallics* **2002,** *72*, 29.
67. Favre, F.; Olivier-Bourbigou, H.; Commereuc, D.; Saussine, L. *Chem. Commun.* **2001**, 1360-1361.
68. Brauer, D. J.; Kottsieper, K. W.; Liek, C.; Stelzer, O.; Waffenschmidt, H.; Wasserscheid, P. *J. Organomet. Chem.* **2001,** *630*, 177-184.
69. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Commun.* **2001**, 451-452.
70. Wasserscheid, P.; van Hal, R.; Bosmann, A. *Green Chem.* **2002,** *4*, 400-404.
71. Mehnert, C. P.; Cook, R. A.; Dispenziere, N. C.; Afeworki, M. *J. Am. Chem. Soc.* **2002,** *124*, 12932-12933.
72. Brasse, C. C.; Englert, U.; Salzer, A.; Waffenschmidt, H.; Wasserscheid, P. *Organometallics* **2000,** *19*, 3818-3823.
73. Dupont, J.; Silva, S. M.; de Souza, R. F. *Catal. Lett.* **2001,** *77*, 131-133.
74. Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. *Chem. Commun.* **2002**, 3044-3045.
75. Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc. Dalton Trans* **2004**, 1590.
76. Jessop, P. G.; Leitner, W. *Chemical Synthesis Using Supercitical fluids*; Wiley-VCH: Weinheim, 1999.
77. Morris, C. *Academic Press Dictionary Of Science and Technology; Academic Press*: San Diego, 1992.
78. Webb, P. B. *Ph.D Thesis*, Nottingham, England 2000.
79. Latour, C. C. *Annales de Chimie et de Physique* **1822,** *21*, 127.
80. Andrews, T. *Annales de Chimie et de Physique* **1870,** *21*, 208.
81. Koch, D.; Leitner, W. *J. Am. Chem. Soc.* **1998,** *120*, 13398.
82. Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev.* **1999,** *99*, 475.
83. Bach, I.; Cole-Hamilton, D. J. *Chem. Commun.* **1998**, 1463.
84. Kainz, S.; Brinkmann, A.; Leitner, W.; Pfaltz, A. *J. Am. Chem. Soc.* **1999,** *121*, 6421.
85. Brown, R. A.; Pollet, P.; McKoon, E.; Eckert, C. A.; Liotta, C. L.; Jessop, P. G. *J. Am. Chem. Soc.* **2001,** *123*, 1254-1255.
86. Jessop, P. G.; Hsiao, Y.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1996,** *118*, 344-355.
87. Ashraf-Khorassani, M.; Taylor, L. T. *J. Chromatogr. Sci.* **1989,** *27*, 329.
88. Jentoft, R. E.; Gouw, T. H. *Anal. Chem.* **1972,** *44*, 681.
89. Kreher, U.; Schebesta, S.; Walther, D. *Anorg. Allg. Chem.* **1988,** *624*, 602.
90. Bickmann, F.; Wenclawiak, B. **1985,** *320*, 261.
91. Dobbs, J. M.; Wong, J. M.; Johnston, K. P. *J. Chem. Eng. Data* **1986,** *31*, 303.
92. Dobbs, J. M.; Wong, J. M.; Lahiere, R. J.; Johnston, K. P. *Ind. Eng. Chem. Res.* **1987,** *26*, 56.
93. Jessop, P. G.; Ikariya, T.; Noyori, R. *Chem. Rev.* **1995,** *95*, 259.
94. Wright, H. B.; Moore, M. B. *J. Am. Chem. Soc.* **1948,** *70*, 3865.
95. Rathke, J. W.; Klingler, R. J.; Krause, T. R. *Organometallics* **1991,** *10*, 1350.

96. Sellin, M. F.; Bach, I.; Webster, J. M.; Montilla, F.; Rosa, V.; Aviles, T.; Poliakoff, M.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2002**, 4569-4576.
97. Sellin, M. F.; Cole-Hamilton, D. J. *J. Chem. Soc. Dalton Trans* **2000**, 1681.
98. Kainz, S.; Koch, D.; Baumann, W.; Leitner, W. *Angew. Chem.-Int. Edit.* **1997,** *36*, 1628.
99. Osuna, A. M. B.; Chen, W. P.; Hope, E. G.; Kemmitt, R. D. W.; Paige, D. R.; Stuart, A. M.; Xiao, J. L.; Xu, L. J. *J. Chem. Soc.-Dalton Trans.* **2000**, 4052-4055.
100. Palo, D. R.; Erkey, C. *Organometallics* **2000,** *19*, 81.
101. Hu, Y. L.; Chen, W. P.; Osuna, A. M. B.; Stuart, A. M.; Hope, E. G.; Xiao, J. L. *Chem. Commun.* **2001**, 725-726.
102. Hu, Y. L.; Chen, W. P.; Osuna, A. M. B.; Iggo, J. A.; Xiao, J. L. *Chem. Commun.* **2002**, 788-789.
103. Wells, S. L.; De Simone, J. *Angew. Chem.-Int. Edit.* **2001,** *40*, 518.
104. Lopez-Castillo, Z. K.; Flores, R.; Kani, I.; Fackler, J. P.; Akgerman, A. *Ind. Eng. Chem. Res.* **2003,** *42*, 3893-3899.
105. Hu, Y. L.; Chen, W. P.; Xu, L. J.; Xiao, J. L. *Organometallics* **2001,** *20*, 3206-3208.
106. Chen, W. P.; Xu, L. J.; Hu, Y. L.; Osuna, A. M. B.; Xiao, J. L. *Tetrahedron* **2002,** *58*, 3889-3899.
107. Fujita, S. I.; Fujisawa, S.; Bhanage, B. M.; Ikushima, Y.; Arai, M. *New J. Chem.* **2002,** *26*, 1479.
108. Nozaki, K.; Takaya, H.; Hiayama, T. *Top. Catal.* **1997,** *4*, 175.
109. Francio, G.; Leitner, W. *Chem. Commun.* **1999**.
110. Bonafoux, D.; Hua, Z. H.; Wang, B. H.; Ojima, I. *J. Fluor. Chem.* **2001,** *112*, 101-108.
111. Shibahara, F.; Nozaki, K.; Hiyama, T. *J. Am. Chem. Soc.* **2003,** *125*, 8555-8560.
112. Meehan, N. J.; Sandee, A. J.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Poliakoff, M. *Chem. Commun.* **2000**, 1497.
113. Snyder, G.; Tadd, A.; Abraham, M. A. *Ind. Eng. Chem. Res.* **2001,** *40*, 5317-5325.
114. Tadd, A.; Marteel, A.; Mason, M. R.; Davies, J. A.; Abraham, M. A. *J. Supercrit. Fluids* **2003,** *25*, 183.
115. Hemminger, O.; Marteel, A.; Mason, M. R.; Davies, J. A.; Tadd, A. R.; Abraham, M. A. *Green Chem.* **2002,** *4*, 507-512.
116. Dharmidhikari, S.; Abraham, M. A. *J. Supercrit. Fluids* **2000,** *18*, 1-10.
117. Blanchard, L. A.; Hancu, D.; Beckman, E. J.; Brennecke, J. F. *Nature* **1999,** *399*, 28-29.
118. Blanchard, L. A.; Gu, Z. Y.; Brennecke, J. F. *J. Phys. Chem. B* **2001,** *105*, 2437-2444.
119. Dohrn, R.; Brunner, G. *Fluid Phase Equilib.* **1995,** *106*, 213.
120. Shariati, A.; Peters, C. J. *J. Supercrit. Fluids* **2004,** *29*, 43-48.
121. Cadena, C.; Anthony, J. L.; Shah, J. K.; Morrow, T. I.; Brennecke, J. F.; Maginn, E. J. *J. Am. Chem. Soc.* **2004,** *126*, 5300-5308.
122. Darr, J. A.; Poliakoff, M. *Chem. Rev.* **1999,** *99*, 495.
123. Crowhurst, L.; Mawdsley, P. R.; Perez-Arlandis, J. M.; Salter, P. A.; Welton, T. *Phys. Chem. Chem. Phys.* **2003,** *5*, 2790-2794.
124. Kazarian, S. G.; Briscoe, B. J.; Welton, T. *Chem. Commun.* **2000**, 2047-2048.

125. Liu, Z. M.; Wu, W. Z.; Han, B. X.; Dong, Z. X.; Zhao, G. Y.; Wang, J. Q.; Jiang, T.; Yang, G. Y. *Chem.-Eur. J.* **2003,** *9*, 3897-3903.
126. Field, C. N.; Hamley, P. A.; Webster, J. M.; Gregory, D. H.; Titman, J. J.; Poliakoff, M. *J. Am. Chem. Soc.* **2000,** *122*, 2480.
127. Blanchard, L. A.; Brennecke, J. F. *Ind. Eng. Chem. Res.* **2001,** *40*, 287-292.
128. Webb, P. B.; Sellin, M. F.; Kunene, T. E.; Williamson, S.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *J. Am. Chem. Soc.* **2003,** *125*, 15577-15588.
129. Scurto, A. M.; Aki, S.; Brennecke, J. F. *J. Am. Chem. Soc.* **2002,** *124*, 10276-10277.
130. McHugh, M.; Krukonis, V. *Supercritical fluid extraction: Principles and practice*; Butterworth - Heinemann: Stoneham, 1994.
131. Wu, W. Z.; Zhang, J. M.; Han, B. X.; Chen, J. W.; Liu, Z. M.; Jiang, T.; He, J.; Li, W. J. *Chem. Commun.* **2003**, 1412-1413.
132. Husson-Borg, P.; Majer, V.; Gomes, M. F. C. *J. Chem. Eng. Data* **2003,** *48*, 480-485.
133. Anthony, J. L.; Maginn, E. J.; Brennecke, J. F. *J. Phys. Chem. B* **2002,** *106*, 7315-7320.
134. Dyson, P. J.; Laurenczy, G.; Ohlin, C. A.; Vallance, J.; Welton, T. *Chem. Commun.* **2003**, 2418.
135. Ohlin, C. A.; Dyson, P. J.; Laurenczy, G. *Chem. Commun.* **2004**, 1070.
136. Berger, A.; de Souza, R. F.; Delgado, M. R.; Dupont, J. *Tetrahedron-Asymmetry* **2001,** *12*, 1825.
137. *In Applied Homogeneous Catalysis with Organometallic Compounds*; Herrmann, W. A. Ed; VCH: Weinheim, 1996.
138. Frohling, C. D.; Kohlpaintner, C. W. *In Applied Homogeneous Catalysis with Organometallic Compounds*; Herrmann, W. A. Ed; VCH: Weinheim, 1996; Vol. 1; pp. 27.
139. Leitner, W. *In Recovery and Recycling in Homogeneous Catalysis*; Tooze, R.P. Ed; Kluwer: Dordrecht, 2004; Vol. To be published.
140. Cole-Hamilton, D. J. *Science* **2003,** *299*, 1702-1706.
141. Dzyuba, S. V.; Bartsch, R. A. *Angew. Chem.-Int. Edit.* **2003,** *42*, 148-150.
142. Keim, W. *Green Chem.* **2003,** *5*, 105-111.
143. Tzschucke, C. C.; Markert, C.; Bannwarth, W.; Roller, S.; Hebel, A.; Haag, R. *Angew. Chem.-Int. Edit.* **2002,** *41*, 3964-4000.
144. Jessop, P. G.; Stanley, R. R.; Brown, R. A.; Eckert, C. A.; Liotta, C. L.; Ngo, T. T.; Pollet, P. *Green Chem.* **2003,** *5*, 123-128.
145. Jessop, P. G. *J. Synth. Org. Chem. Jpn.* **2003,** *61*, 484-488.
146. Liu, F. C.; Abrams, M. B.; Baker, R. T.; Tumas, W. *Chem. Commun.* **2001**, 433-434.
147. Jessop, P. G.; Hsiao, Y.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1994,** *116*, 8851.
148. Webb, P. B.; Cole-Hamilton, D. J. GB Patent, 2003, 0300733.3.
149. Smith, G.; Cole-Hamilton, D. J.; Gregory, A. C.; Gooden, N. G. *Polyhedron* **1982,** *1*, 97.
150. Hou, Z. S.; Han, B. X.; Gao, L.; Jiang, T.; Liu, Z. M.; Chang, Y. H.; Zhang, X. G.; He, J. *New J. Chem.* **2002,** *26*, 1246-1248.
151. Jiang, J. C.; Han, B. X.; Zhao, G. Y.; Chang, Y. H.; Gao, L.; Zhang, J. M.; Yang, G. Y. *J. Chem. Res.-S* **2003**, 549.
152. Kawanami, H.; Sasaki, A.; Matsui, K.; Ikushima, Y. *Chem. Commun.* **2003**, 896-897.

153. Paddock, R. L.; Hiyama, Y.; McKay, J. M.; Nguyen, S. T. *Tetrahedron Lett.* **2004,** *45*, 2023.
154. Ji, D. F.; Lu, X. B.; He, R. *Appl. Catal. A-Gen.* **2000,** *203*, 329.
155. Bhanage, B. M.; Fujita, S.; Ikushima, Y.; Arai, M. *Appl. Catal. A-Gen.* **2001,** *219*, 259.
156. Fujita, S.; Bhanage, B. M.; Ikushima, Y.; Shirai, M.; Torii, K.; Arai, M. *Catal. Lett.* **2002,** *79*, 95.
157. Kawanami, H.; Ikushima, Y. *Chem. Commun.* **2000**, 2089.
158. Wilke, G.; Monkiewicz, J. *Ger. Pat.* **1987**, 3,618,169.
159. RajanBabu, T. V.; Nomura, N.; Jin, J.; Radetich, B.; Park, H. S.; Nandi, M. *Chem.-Eur. J.* **1999,** *5*, 1963.
160. Wegner, A.; Leitner, W. *Chem. Commun.* **1999**, 1583-1584.
161. Bosmann, A.; Francio, G.; Janssen, E.; Solinas, M.; Leitner, W.; Wasserscheid, P. *Angew. Chem.-Int. Edit.* **2001,** *40*, 2697-2699.
162. Ballivet-Tkatchenko, D.; Picquet, M.; Solinas, M.; Francio, G.; Wasserscheid, P.; Leitner, W. *Green Chem.* **2003,** *5*, 232-235.
163. Gao, L. A.; Tao, J. A.; Zhao, G. Y.; Mu, T. C.; Wu, W. Z.; Hou, Z. S.; Han, B. X. *J. Supercrit. Fluids* **2004,** *29*, 107-111.
164. Lozano, P.; de Diego, T.; Guegan, J. P.; Vaultier, M.; Iborra, J. L. *Biotechnol. Bioeng.* **2001,** *75*, 563-569.
165. Lozano, P.; de Diego, T.; Carrie, D.; Vaultier, M.; Iborra, J. L. *Biotechnol. Lett.* **2001,** *23*, 1529.
166. Almeida, M. C.; Ruivo, R.; Maia, C.; Freire, L.; de Sampaio, T. C.; Barreiros, S. *Enzyme Microb. Technol.* **1998,** *22*, 494-499.
167. Lozano, P.; de Diego, T.; Carrie, D.; Vaultier, M.; Iborra, J. L. *Chem. Commun.* **2002**, 692-693.
168. Lozano, P.; De Diego, T.; Carrie, D.; Vaultier, M.; Iborra, J. L. *Biotechnol. Prog.* **2003,** *19*, 380-382.
169. Lozano, P.; de Diego, T.; Gmouh, S.; Vaultier, M.; Iborra, J. L. *Biotechnol. Prog.* **2004,** *20*, 661.
170. Reetz, M. T.; Wiesenhofer, W.; Francio, G.; Leitner, W. *Chem. Commun.* **2002**, 992-993.
171. Reetz, M. T.; Wiesenhofer, W.; Francio, G.; Leitner, W. *Advanced Synthesis & Catalysis* **2003,** *345*, 1221-1228.
172. Lozano, P.; Avellaneda, A.; Pascual, R.; Iborra, J. L. *Biotechnol. Lett.* **1996,** *18*, 1345-1350.
173. Lozano, P.; De Diego, T.; Carrie, D.; Vaultier, M.; Iborra, J. L. *J. Mol. Catal. A-Chem.* **2004,** *214*, 113-119.
174. Laszlo, J. A.; Compton, D. L. *ACS Symp. Ser.* **2002,** *818*, 387.
175. Zhao, G. Y.; Jiang, T.; Wu, W. Z.; Han, B. X.; Liu, Z. M.; Gao, H. X. *J. Phys. Chem. B* **2004,** *108*, 13052-13057.
176. Zhang, J. M.; Yang, C. H.; Hou, Z. S.; Han, B. X.; Jiang, T.; Li, X. H.; Zhao, G. Y.; Li, Y. F.; Liu, Z. M.; Zhao, D. B.; Kou, Y. *New J. Chem.* **2003,** *27*, 333-336.
177. Zhang, Z. F.; Wu, W.; Liu, Z. M.; Han, B. X.; Gao, H. X.; Jiang, T. *Phys. Chem. Chem. Phys.* **2004,** *6*, 2352-2357.
178. Zhao, G. Y.; Jiang, T.; Han, B. X.; Li, Z. H.; Zhang, J. M.; Liu, Z. M.; He, J.; Wu, W. Z. *J. Supercrit. Fluids* **2004,** *32*, 287-291.
179. Phillips, G.; W., F. S. *US Patent* **1994**, 5,315,019.

180. Smith, G.; Cole-Hamilton, D. J.; Gregory, A. C.; Gooden, N. G. *Polyhedron* **1982,** *1*, 97-103.
181. Jastorff, B.; Stormann, R.; Ranke, J.; Molter, K.; Stock, F.; Oberheitmann, B.; Hoffmann, W.; Hoffmann, J.; Nuchter, M.; Ondruschka, B.; Filser, J. *Green Chem.* **2003,** *5*, 136-142.
182. Swatloski, R. P.; Holbrey, J. D.; Memon, S. B.; Caldwell, G. A.; Caldwell, K. A.; Rogers, R. D. *Chem. Commun.* **2004**, 668-669.
183. Heldebrant, D. J.; Jessop, P. G. *J. Am. Chem. Soc.* **2003,** *125*, 5600-5601.
184. Webb, P. B.; Cole-Hamilton, D. J. *Chem. Commun.* **2004**, 612-613.
185. Hitzler, M. G.; Smail, F. R.; Ross, S. K.; Poliakoff, M. *Organic Process Research & Development* **1998,** *2*, 137-146.
186. Kaye, B.; Cole-Hamilton, D. J.; Morphet, K. *Studies in Conservation* **2000,** *45*, 233-252.
187. Wasserscheid, P.; Welton, T. *Ionic Liquids in Synthesis*; Wiley VCH: Weinheim, 2003.

2 Rhodium catalysed hydroformylation using known phosphines in $scCO_2$/IL biphasic system

2.1 Introduction

Hydroformylation is an important process in the bulk chemicals industry producing more than 6 M tonnes of aldehydes and alcohols per annum for the manufacture of soaps, detergents, and plasticizers[1,2]. Rhodium catalysts show very high activity and good regioselectivity under mild operating conditions for the hydroformylation of alkenes. Triphenylphosphine modified rhodium catalysts are used commercially for the hydroformylation of short chain alkenes (C_2-C_5) but cannot be used for higher alkenes because the catalyst decomposes at temperatures below the boiling point of the aldehyde product making catalyst separation difficult[1,2]. Commercially, this separation problem is overcome by the use of water-soluble catalysts in aqueous-organic two-phase systems. However, this aqueous biphasic approach is only applied to the hydroformylation of propene because the limited solubility of higher olefins in water results in rates that are simply too slow for the process to be commercially viable[3]. Current technology for the synthesis of detergent range alcohols, which produces over 1M tons per annum, is based on less efficient cobalt catalysts, often modified with tertiary phosphines. Cobalt catalysts require more forcing conditions than their rhodium counterparts, a consequence of their lower catalytic activity, and although separation technologies have been developed for Co systems they are by no means simple[2,4]. The selectivity toward linear products in cobalt systems is also often low, although Shell have developed a process based on a phosphine derived from the addition of $C_{20}H_{42}PH_2$ across 1,5-cyclooctadiene, which can give linear/branched ratios (l/b) as high as 10^5. There are clearly several advantages of working with rhodium compared to cobalt. The development of Rh catalysed processes, for the

hydroformylation of long chain alkenes (C_8-C_{24}), therefore remains one of the biggest challenges in this area.

The catalyst separation problem is not limited to hydroformylation but applies to many homogeneously catalysed reactions. Although heterogeneous systems may provide the obvious answer to the need for separation, homogeneous catalysts can show much higher activity and selectivity than their heterogeneous counterparts. Nevertheless, the need for separation sometimes prevents the commercialisation of otherwise very attractive homogeneous systems. This has prompted extensive research into methods, which combine the ease of catalyst recovery associated with heterogeneous systems with the more desirable activity and selectivity obtained with homogeneous catalysts[6,7]. These approaches can be divided into two main categories involving either (i) anchoring the catalyst to a soluble or insoluble support (heterogenisation), or (ii) dissolving the catalyst in a solvent which is immiscible with the reaction product under certain conditions (biphasic). Cole-Hamilton *et al* have been exploring aqueous biphasic[8], fluorous biphasic[9,10], dendrimer anchored[11-15], and supported catalysts[16,17], as well as the use of supercritical fluids[18-21] as methods for overcoming the separation problem. All of these approaches, however, suffer from the disadvantage that some of the reaction medium must be removed from the bulk before catalyst separation can be effected. As a consequence, not all of the catalyst is involved in the reaction at all times, and perhaps more importantly, the conditions for catalyst separation can be very different from those of the reaction such that catalyst decomposition may still occur. An ideal system would enable continuous operation with separation under conditions identical to those of the reaction itself so that all of the catalyst remains in its active state at all times. The ability to afford reaction and

separation under a single set of conditions would not only reduce the problems of catalyst deactivation but would also have a positive effect on the size of reactor needed for a given product throughput. Reductions in reactor volumes then offer further advantages in terms of safety (e.g., smaller volumes of flammable gases) and reduced capital costs.

Brennecke *et al*[22] reported that the room temperature ionic liquid, 1-butyl-3-methylimidazolium hexafluorophosphate exhibits very interesting phase behaviour with $scCO_2$, where CO_2 can dissolve significantly (up to 0.6 mole fraction) into the IL phase, but no polar IL dissolves in the upper $scCO_2$ phase. Kazarian *et al*[23] provided spectroscopic evidence that $scCO_2$ dissolves in the IL. Brennecke *et al*[24] also reported that $scCO_2$ can extract organic compounds dissolved in an ionic liquid. Thus, the work of Brennecke prompted an increasing interest into the combination of ionic liquid and SCF technologies. Reactions including the hydrogenation of 1-decene[25] and the asymmetric hydrogenation of tiglic acid[26], have both been performed successfully in ionic liquids followed by supercritical fluid extraction of the reaction products. More recently, the continuous flow approach using CO_2 and ionic liquids has been applied to the codimerization of ethene and styrene[27], (although the temperature was below the critical temperature for CO_2), the Wacker oxidation of alkenes[28], the reaction between alkenes and CO_2[29], and reactions using enzymes[30,31]. A short review of the SCF-IL biphasic approach has recently appeared[32].

Following the pioneering work of Brennecke[22,24], Cole-Hamilton *et al* reported an example of a homogeneously catalysed, continuous flow process for products which are of too low a volatility to be removed by direct distillation from the reaction

mixture. The process involved dissolving an ionic catalyst in an ionic liquid and using supercritical CO_2 ($scCO_2$) as a transport vector for both gaseous and liquid substrates and products[33]. The gas-like mass transport characteristics of a supercritical fluid and its complete miscibility with permanent gases coupled with the liquid-like ability to dissolve organic compounds of low to medium polarity makes it an ideal transport vector. The SCF-IL biphasic system enables continuous operation and differs from other biphasic systems in that one of the phases is a dense gas. Thus, unlike many liquid-liquid biphasic systems, the separation of product from catalyst and reaction solvent can be carried out under a single set of conditions with the advantage that all of the catalyst remains in its active state at all times. Furthermore, decompression of the gaseous mixture downstream yields products, which are free from the reaction solvent, thereby removing the necessity for additional purification by distillation.

Cole-Hamilton *et al*[33,34] studied the hydrofomylation reaction of 1-octene catalysed by a $Rh/[PMIM]_2[PhP(3\text{-}C_6H_4SO_3)_2]$ in $scCO_2/[BMIM][PF_6]$ biphasic system. The reaction was run over three days. The catalyst was found to be stable over this period as its activity and l:b ratio of 3.8 were maintained throughout (Figure 2.1). However, conversions (ca. 10 %) and reaction rates (5-10 catalyst turnovers h-1) were very low and the selectivity to the linear product was moderate.

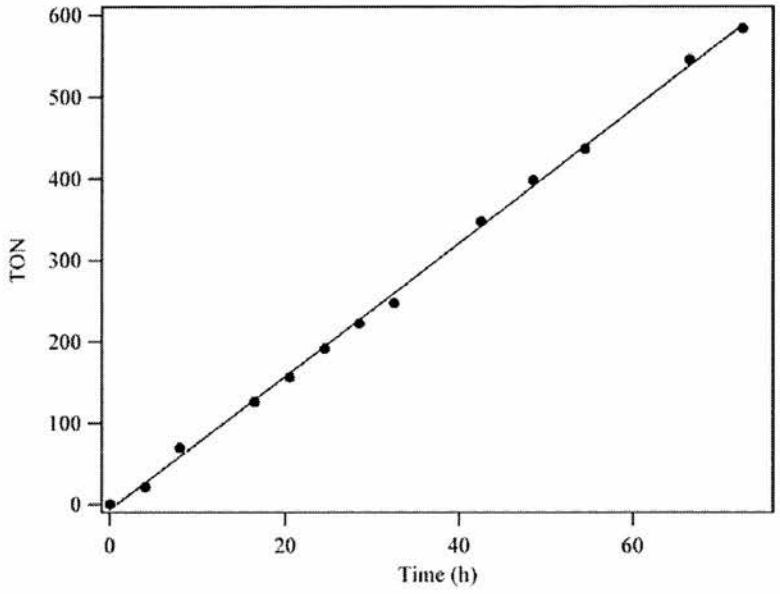
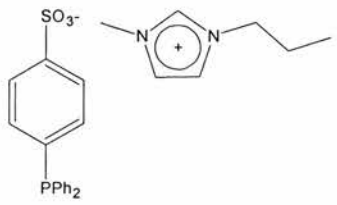


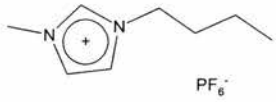
Figure 2.1[34] Continuous flow hydroformylation of 1-octene catalyzed by Rh/$[PMIM]_2[PhP(3\text{-}C_6H_4SO_3)_2]$, over 3 days. l:b = 3.8 throughout. Conditions as in experimental section with a CO flow rate of 1.85 mmol min^{-1} ($CO:H_2$ = 1:1), a 1-octene flow rate of 0.2 mmol min^{-1} and a CO_2 flow rate of 0.78 normal liters per minute (nL min^{-1}).

Lower reaction rates were thought to be, among other things, a result of mass transport limitations, which could be directly linked to the nature of the ionic liquid. The low l:b ratio on the other hand is mainly due to the ligand. In the following section we will be trying to address these two problems.

2.2 Rhodium Catalysed hydroformylation using [PMIM][TPPMS] in $scCO_2$/IL biphasic system – Effect of Alternative Ionic Liquids



[TPPMS][PMIM]



[BMIM][PF_6]

Although [BMIM][PF_6] has been the most used of the ionic liquids for hydroformylation and other catalytic reactions[35-40], the solubility of alkenes within it is not very high and their partition between it and $scCO_2$ may mean that rates in the continuous flow process are determined largely by mass transport limitations. This mass transport limitation is analogous to that found in the aqueous biphasic system described by Cornils, where the limited solubility of higher alkenes in water results in rates that are simply too slow for the process to be commercially viable. It has also been found that [BMIM][PF_6] is water sensitive[33]. Wasserscheid *et al*[10] reported that the solubility of alkenes in ionic liquids can be increased by replacing the butyl group with longer alkyl chains.

We therefore carried out reactions in a range of ionic liquids where the alkyl chain of the imidazolium cation was varied and a different counter anion was used. These ionic liquids were prepared by refluxing N-methylimidazole and the appropriate chloroalkane. At the end of the reaction, the chloride anion is exchanged with the desired anion (e.g. PF_6^-). These ionic liquids were tested in the hydroformylation of 1-octene and 1-dodecene in batch /IL. The reaction profiles using 1-octene and 1-dodecene were monitored by measuring the pressure drop and alkene conversion to aldehyde in batch reactions respectively. Figure 2.2 and Figure 2.3 show the results on 1-octene and 1-dodecene respectively.

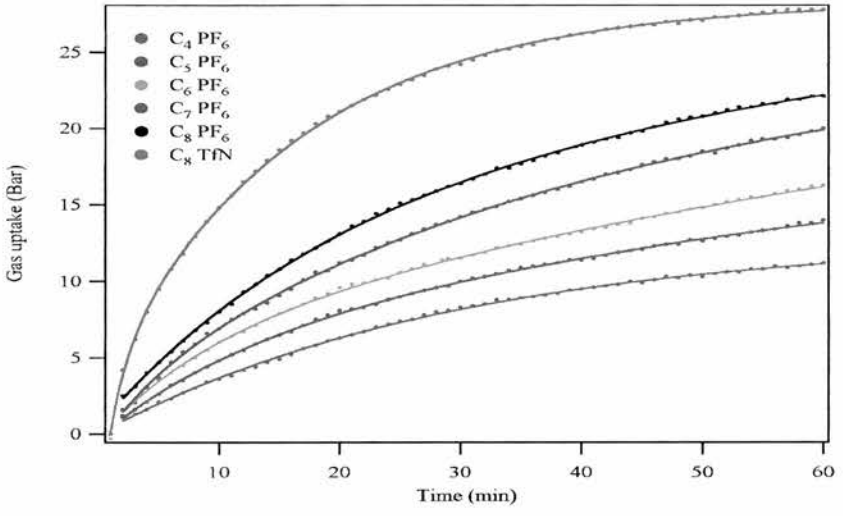


Figure 2.2[34]. Effect of different alkyl groups on the 1-position of 1-alkyl-3-methylimidazolium salts and of the anion on reaction rate for the hydroformylation of 1-octene in a batch reactor using Rh/[PMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$] and $scCO_2$.

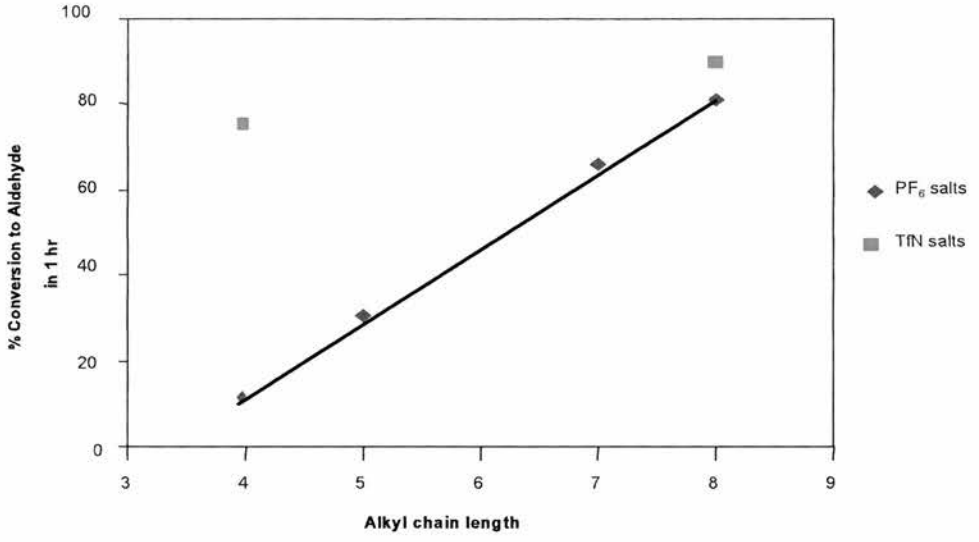
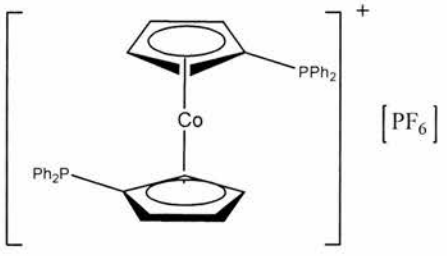


Figure 2.3[34]. Effect of the alkyl group on the 1-position of 1-alkyl-3-methylimidazolium salts and of the anion on reaction rate (conversion in 1 h) for the hydroformylation of 1-dodecene in a batch reactor using Rh/[PMIM][$Ph_2P(3\text{-}C_6H_4SO_3)$] and $scCO_2$.

It is clear from Figure 2.2 that the rate increases dramatically as the alkyl chain length is increased from butyl to octyl. Further rate enhancements are observed if the PF_6 anion is replaced by bis(trifluoromethyl)sulphonamide (NTf_2^-), which has the added advantage that this anion is not sensitive to moisture. Although changes in viscosity may in part be responsible for the increased rates, we believe that increased solubility of the alkene is the dominating factor. Figure 2.3 shows that the increased rate is also observed for the imidazolium salts with longer alkyl chains when 1-dodecene is used as the substrate. Once again dramatic increases in rate are observed and the conversion can be higher than 80 %.

2.3 Rhodium Catalysed hydroformylation using Cobaltocenium based diphosphine in $scCO_2$/IL biphasic system

The use of diphosphines in hydroformylation reactions has recently become an interesting field to explore. This has been due to reports that they can give improved selectivity to linear aldehydes over monophosphines. This was based on the hypothesis that the intermediate which gives high regioselectivity has the two phosphines coordinated on the equatorial plane of the five coordinate intermediate[41-44], hence diphosphines which were thought to favour that type of a coordination should give higher linear selectivities



[DPPCo][PF_6]

Wasserscheid *et al*[45,46] have shown that rhodium complexes using 1,1'-bis(diphenylphosphino)cobaltocenium hexafluorophosphate ([DPPCo][PF_6]), which dissolves in the ionic liquid, can lead to high activity and selectivity in hydroformylation reactions in an IL/organic biphasic system and that the catalyst can be reused. The product was separated from the catalyst by decantation. This type of catalyst system seems to meet the requirements of a continuous flow hydroformylation system proposed for this study. One of the aims of this project is to

develop a catalyst, which will give high activity and selectivity and will dissolve in the ionic phase and not leach to the $scCO_2$ phase, thus avoiding being extracted with the organic compounds. It has been reported that [DPPCo][PF_6] ligand dissolves in the ionic liquid and the Rh leaching was found to be less than 0.2 % of the overall Rh loaded. We reasoned that this cobaltocenium based diphosphine ligand would fulfil the criteria and leaching to the $scCO_2$ phase would be insignificant in the proposed $scCO_2$/IL biphasic system. So, this catalyst system seemed to be a good starting point for our study.

[DPPCo][PF_6] was prepared as outlined by Wasserscheid *et al*[46]. The ligand was successfully synthesised and characterised by ^{31}P and ^{1}H NMR. The ligand was used in the hydroformylation of 1-octene in $scCO_2$/IL biphasic system. The ionic liquid used was 1-buthyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF_6]) which was prepared using methods described by Fuller *et al* and Souza *et al*[47,48]. The system used was a semi continuous system in the sense that the reaction was carried out in a batch autoclave and the product was extracted with $scCO_2$.

2.3.1 Hydroformylation of 1-Octene in $scCO_2$/IL biphasic system using 1,1'-Bis(diphenylphosphine)cobaltocenium hexafluorophosphate ([DPPCo][PF6]) ligand

It has been reported that [DPPCo][PF_6] with [Rh(acac)$(CO)_2$] as a catalyst precursor gives high activity and selectivity (TOF^a = 810 h^{-1}, selectivity to normal aldehyde = 94 %, l:b = 16.2) in the hydroformylation of 1-octene in [BMIM][PF_6].[46] This catalyst system is reported to perform better than TPPTS (TOF = 98 h^{-1}, l:b = 2.6). The hydroformylation reactions showed low hydrogenation of 1-octene to octane (< 2 %) and low isomerisation (< 2 %).

We therefore carried out the hydroformylation of 1-octene in a $scCO_2$/IL biphasic system as as opposed to an organic/IL biphasic system. The reaction was carried out in a semi-continuous mode meaning that the hydroformylation reaction was carried out for 1 hour batchwise at 100°C and 200 bar pressure, followed by the extraction of the product by CO_2. The extraction was done at reaction temperature (100°C) and reaction pressure (200 bar) with the stirrer switched off. Liquid CO_2 was pumped through the HPLC pump at a flow rate of 10 ml/min with the high pressure limit of the pump set at a slightly higher pressure than the reaction pressure (i.e. 201 bar) to keep the pressure constant at 200 bar. The reaction autoclave was linked to a second autoclave (1st collecting vessel) with a pressure regulator to decompress CO_2 from 200 bar to about 5 bar. In that way, CO_2 expands and loses its solvating capacity, thus the product/substrate is precipitated into the 1st collecting vessel. The pressure was subsequently reduced to atmospheric by opening an exit tap on the 1st collecting vessel. In order to trap any product/substrate, which might escape from the 1st

collecting vessel, a 2nd collecting vessel (glass trap) was linked to the 1st collecting vessel. The CO_2 was bubbled through ethanol thereby trapping any organic compounds, which had passed through the 1st collecting vessel. The extraction was carried out for 2 hours; approximately 1 ml of product/substrate was collected in the 1st collecting vessel. The collected sample was then analysed by GC.

Table 2.1 Batch Rhodium catalysed hydroformylation of 1-octene in 5 cm^3 [BMIM][PF_6] using [DPPCo][PF_6] as a ligand[a]

Entry	P/bar	$ScCO_2$	Yield Aldehydes/ %	Isomerisation Products/%	Total Conversion /%	l:b ratio
1A	200[b]	25ml	10.51	38.56	49.07	4
[c]1B	200[b]	25ml	2.95	4.93	7.88	3.5
2	10	no $scCO_2$	6.78	58.47	65.25	4
[d]3	10	no $scCO_2$	6.45	61.6	68.05	3.5
[e,f]4	10	no $scCO_2$	30.41	54.95	85.36	11
[g]5	10	no $scCO_2$	16.67	43.96	60.63	12
[h]6	10	no $scCO_2$	20.25	45.85	66.10	18
[i]7	10	no $scCO_2$	6.84	8.35	15.19	21.8
8	40	no $scCO_2$	14.45	23.49	37.94	5.3
[j]9	200	30 ml	14.12	45.83	59.95	4

[a]*Conditions: ligand/Rh = 2, volume 1-octene = 3.15 cm^3, H_2/CO = 1, t = 1 hour, T = 100°C, Volume BMIM PF_6 = 5 cm^3. The catalyst was not preformed, unless stated.*

[b]*H_2/CO = 40 bar. Catalyst was preformed by heating the system under 40 bar syngas and stirring for 1 hour, cooling down, depressurising and injecting the substrate.*

[c]*Catalyst was recycled once i.e. catalyst used in 1B was recycled from 1A. The product from 1A and B was extracted with $scCO_2$.*

[d]*Run 3 is a repeat of Run 2 except that a different batch of BMIM PF_6 was used and that before starting the reaction, the catalyst/IL solution was stirred for 1 hour at room temperature.*

[e] *cm^3 1-octene was used for reactions other than 1, 2 and 3. Catalyst was preformed and the substrate was introduced through a liquid port*

[f]*15°C temperature overshoot*

[g]*Run 5 is a repeat of Run 4 with no temperature overshoot.*

[h]*Similar to Run 5 except that the catalyst solution was left to form for about 45 under syngas and reaction temperature conditions.*

[i]*Temperature was dropped to 80°C*

[j]*Catalyst was preformed as in Run 4*

After the first reaction, it was found that the total conversion of 1-octene was 49,7 % with the selectivity to aldehydes being 21.4 % and with an l:b ratio of 4 (Table 2.1, reaction 1). A large quantity of isomerisation products was observed (38.6 %). After the autoclave was depressurised, the catalyst was recycled by injecting fresh 1-octene (3.15 cm^3) into the reaction autoclave with the reaction vessel isolated i.e. not opened to the collecting vessels. The autoclave was repressurised and allowed to run for 1 hour, followed by extraction of the product as described above. The same amount of liquid was collected (1 ml) after 2 hours of extraction. The conversion was found to be very low (7.9 %) with a selectivity to aldehydes of 37.4 % and an l:b ratio of 3.5 (Table 2.1, reaction 2). The catalyst seemed to have lost its activity after the first run. This might suggest oxidation of the ligand during the first run or during the product extraction. Unfortunately, the catalyst species at the end of the reaction could not be studied with ^{31}P NMR spectroscopy, as the PF_6 anion phosphorus peak from the ionic liquid ([BMIM][PF_6]) is so intense that the comparatively weak resonances from the ligand itself and its complexes are not visible. As a result, it was not possible to confirm whether the ligand had oxidised or not. The oxidation of the ligand would normally lead to unliganded rhodium i.e. the oxide will decomplex from the metal centre leading to rhodium carbonyl complexes. Metal carbonyl complexes are known to be soluble in CO_2, which could be extracted with the product, and therefore rhodium could be extracted from the reaction vessel and low 1-octene conversions would result.

We also observed substantial alkene isomerisation in both the reactions. Unmodified catalysis and/or mass transport limitations could provide an explanation for this isomerisation.

2.3.1.1. Hydroformylation of 1-octene with an in situ formed [Rh(acac)(CO)$_2$]/[DPPCo][PF$_6$] catalyst

The poor catalyst performance described above, was thought to be a result of a variable, which the scCO$_2$/IL biphasic system might have introduced. As a result of this uncertainty, the organic/IL biphasic system used by Wasserscheid *et al* was studied in order to establish a baseline case for reproducing their results before using the scCO$_2$/IL system.

[Rh(acac)(CO)$_2$] was weighed into the autoclave and the autoclave was flushed three times with CO/H$_2$ before [DPPCo][PF$_6$] dissolved in [BMIM][PF$_6$] was injected into the system under positive CO/H$_2$ pressure. 1-Octene was subsequently injected and the system was pressurised with CO/H$_2$ (10 bar) and heated to 100°C. After the reaction had reached 100°C, it was allowed to run for 1 hour. The reaction was subsequently stopped, the product was decanted and analysed by GC. From Table 2.1 (reactions 2 and 3), it can be seen that the catalyst formed in situ, gives a lower activity with a total conversion of about 66.6 % and an aldehyde yield of 6.6 % and selectivity of 9.9 % (l:b ratio of 3.7) when compared to the results reported by Wasserscheid *et al*. The predominant product was found to be isomerised 1-octene (2-octene). It seems the catalyst is an excellent isomerisation catalyst rather than a

hydroformylation catalyst and this was also noticed with the reactions described in section 2.3. According to ^{31}P NMR, ^{1}H NMR and elemental analysis, the synthesised ligand corresponds exactly with the reported analysis. This result proves that the problem is not with $scCO_2$/IL biphasic system as we initially had thought.

It was considered that something in the IL might be causing catalyst decomposition. [BMIM][PF_6] was prepared from [BMIM][Cl] by ion exchange using HPF_6 as outlined in the experimental section. The product was washed several times with water so as to remove any unreacted [BMIM][Cl] and HCl, but there is a possibility that some unreacted [BMIM][Cl] remains. It is known that chloride anions can block the free co-ordination sites of the catalyst, thus poisoning the rhodium catalyst[49]. Therefore, a test for chloride anions was carried out using $AgNO_3$. The formation of AgCl would suggest the presence of chloride ions in solution. The IL was dissolved in acetone and the formation of AgCl would be observed by the formation of a white precipitate, which is insoluble in acetone. Usually, the presence of chloride anions is tested in water as AgCl is known to be insoluble in water. It turned out that there were no chloride anions present in the IL. Nevertheless, another batch of IL was used, which had been used in $scCO_2$/IL biphasic system using sulfonated triphenylphosphine ligands, and had given good results in the hydroformylation of 1-octene[33]. It is clear that there was nothing wrong with our IL batch (used in reaction 2, Table 2.1), as similar results were obtained with the other batch (reaction 3). Another batch of the same IL was prepared and used in a reaction. Similar results were obtained, which strongly suggested that the problem is not with the IL.

Another possible reason for the observed behaviour was thought to be the decomposition of the ligand with time even though it was kept in the glove box. The ^{31}P NMR spectrum was carried out and it confirmed that the ligand had not oxidised.

The only difference between the work carried out above and that described by Wassercheid's, was that the autoclave was heated under syngas pressure with the substrate already in the system whereas the German Group heated the system first, then pressurise with syngas and added the substrate. This might be the reason why the results could not be reproduced. The next step was to preform the catalyst instead of forming the catalyst in situ.

2.3.1.2. Hydroformylation of 1-octene with a preformed $[Rh(acac)(CO)_2]/[DPPCo][PF_6]$ catalyst

$[Rh(acac)(CO)_2]$ was weighed into the autoclave and the autoclave was flushed three times with CO/H_2 and $[DPPCo][PF_6]$, dissolved in $[BMIM][PF_6]$, was injected into the autoclave under positive CO/H_2 pressure. The catalyst solution was then stirred for an hour and heated to the reaction temperature (100°) for 30 minutes. Once the system reached the reaction temperature, it was charged with 5 bar CO/H_2 and 1-octene was immediately injected through a liquid port. This was achieved by pushing 1-octene into the system with 10 bar CO/H_2. The reaction was run for 1 hour. After an hour, the reaction was stopped and the product was decanted and analysed by GC.

Table 2.1 (reaction 5) shows an increase in conversion to aldehydes of about 44 % and a decrease in isomerised 1-octene of about 16 %. This suggests that 1-octene inhibits the formation of the active catalyst species. There was also an increase in the l:b ratio from about 4 to about 12, although a significant amount of 1-octene is isomerised. The l:b ratio is not necessarily that high if a lot of the substrate is isomerised. 2-Octene, one of the isomerisation products, results from the branched alkyl species (Scheme 2.1). It could be that most of the isomerised products would have given branched aldehydes (iso) if the ß-hydrogen abstraction was slower than CO insertion, leading to lower l:b ratio.

2.3.1.2.1 Effect of preforming time on isomerisation

The reported work on this ligand system could not be reproduced indicating that there was still a missing parameter, which needed optimising. One possibility was that the active catalyst species was not given enough time to form i.e. the catalyst precursor was not stirred under CO/H_2 atmosphere at reaction temperature for long enough to convert all the catalyst precursor to the active species.

Experiment 6 was carried under exactly the same conditions as experiment 5 above, except that the catalyst solution was stirred under 5 bar CO/H_2 pressure at 100°C for 45 minutes and then 1-octene was injected into the system under 10 bar pressure. There was a small improvement in terms of total conversion (reaction 6). The l:b ratio increased from 12 to 18, which is similar to that reported by Wasserscheid *et al*[40], however, the level of isomerisation was still very high. Reactions 5 and 6 suggest that

the time for catalyst performing does not have a significant effect on reaction rate or product distribution.

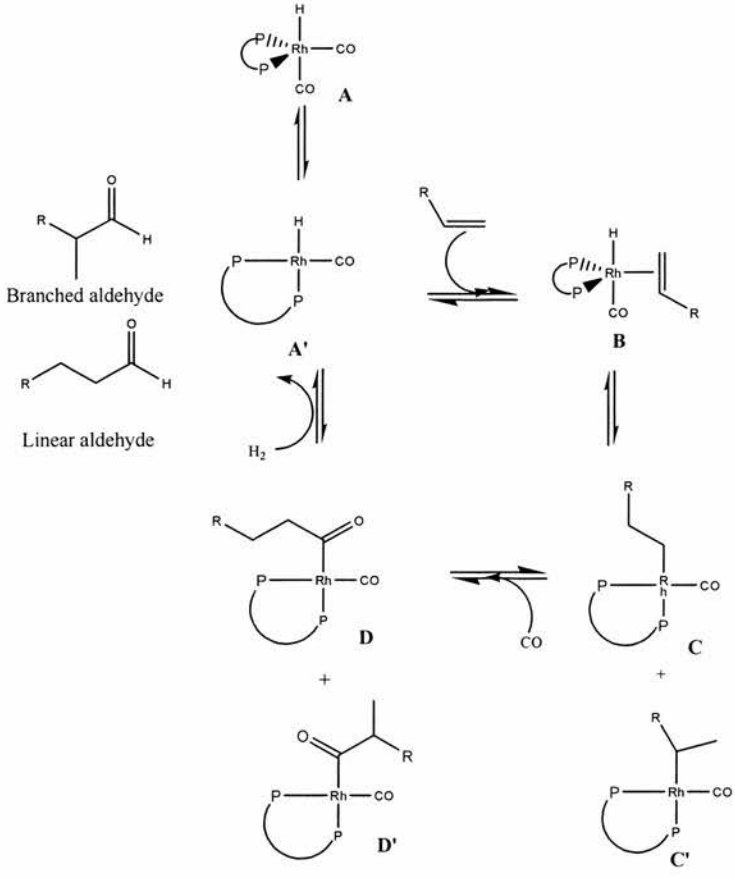
2.3.1.2.2 Effect of temperature on isomerisation

One parameter which can affect the degree of isomerisation is the reaction temperature, thus the higher the temperature, the higher the percentage of isomerisation products. The temperature was then reduced from 100°C to 80°C, which resulted in a significant reduction in isomerisation products (reaction 7). When comparing reactions 6 and 7 from Table 2.1, we observe a 69 % reduction in the levels of isomerisation albeit at the expense of hydroformylation activity (50 %). The selectivity to aldehyde was improved from 30 % (reaction 6) to 45 % (reaction 7). The l:b ratio increased to 21:1.

2.3.1.2.3 Effect of CO partial pressure on isomerisation

The CO partial pressure also affects isomerisation. The total pressure was increased to 40 bar with the p_{CO} increased from 5 to 20 bar. It was thought that by increasing p_{CO}, the equilibrium between the rhodium alkyl species **C** and **C'** and the rhodium acyl species **D** and **D'** would shift towards the rhodium acyl species **D** and **D'** in the hydroformylation catalytic cycle (see Scheme 2.1 below). Reaction 8 shows that increasing the pressure, slows down the reaction rate. Increasing the CO partial pressure, shifts the equilibrium between species **A** and **A'** towards **A**, thus making it difficult for the alkene to coordinate. One other noticeable thing is the drop in l:b ratio

from 18 to 5. It appears that most of the branched alkyl rhodium species were hydroformylated before the ß-hydrogen abstraction took place. This is evident from the drop in l:b ratio and a drop in isomerised 1-alkene, although the overall reaction rate was reduced.



Scheme 2.1 Mechanism of the hydroformylation reaction as proposed by Wilkinson[41]

2.3.1.3 $scCO_2$-IL biphasic hydroformylation

Using $scCO_2$ as a solvent has been shown to improve the catalyst performance in terms of increasing TOFs and selectivities to aldehydes. It is reported that $scCO_2$

mixes with most organic compounds and natural gases[63]. Therefore, introducing $scCO_2$ as a co-solvent is thought to increase the solubility of 1-octene and syngas in the ionic liquid phase, thus improving the reaction rate. Therefore, a reaction using $scCO_2$/IL biphasic system was carried out with a preformed catalyst. $[Rh(acac)(CO)_2]$ was weighed into the autoclave, which was subsequently flushed three times with CO/H_2. [DPPCo][PF_6], dissolved in [BMIM][PF_6], was injected into the autoclave under positive CO/H_2 pressure. The catalyst solution was stirred for an hour in [BMIM][PF_6] and heated to the reaction temperature (100°C). The system was charged with about 40 bar pressure of CO/H_2 and stirred for 5 to 10 minutes. 1-Octene was forced into the autoclave with liquid CO_2, which was pumped using an HPLC pump to make up 200 bar reaction pressure. The reaction was subsequently run for 1 hour. The reaction was stopped and the product was decanted and analysed by GC. The results suggest that there is no improvement in aldehyde yields when using $scCO_2$ as a co-solvent (reactions 8 and 9). Instead the selectivity to aldehydes (more isomerisation products) is poorer than without $scCO_2$.

Overall, the results suggest that [DPPCo][PF_6] favours isomerisation rather hydroformylation under our conditions.

2.3.1.4 Stoichiometric reactions

The catalyst solution in [BMIM][PF_6] was observed through the sapphire window to be darkening as it was heated under syngas pressure. This was thought to suggest that decomposition of the catalyst might be occurring. Unfortunately, the catalyst species at the end of the reaction could not be studied using ^{31}P NMR spectroscopy, as the

PF_6 anion phosphorus peak from the solvent and the catalyst is so intense that the comparatively weak resonances from the phosphine are not visible. This prompted a study of the different catalytic species present under syngas, H_2 and CO conditions.

The study was carried out with 10^{-4} mol/cm^3 Rh in deuterated acetone with L:Rh = 1, under an argon atmosphere. The ^{31}P NMR spectrum showed a doublet at 50 ppm (J_{Rh-P} = 205 Hz), which suggested the formation of a rhodium/ligand complex **A** (Figure 2.4). Syngas was bubbled through a solution of [Rh(acac)$(CO)_2$] and [DDPCo][PF_6] for about 20 minutes. The colour of the solution turned from orange to a darker colour and small black particles were observed. The ^{31}P NMR spectrum showed a doublet at 8 ppm (J_{Rh-P} = 168 Hz), which suggested the presence of either, a dimeric species **B** or hydride species **C** with the black precipitate suggesting rhodium plating. A black solid was also observed whilst unloading the autoclave in most of the reactions described in the sections above. This was thought to be the result of either the ligand decomplexing from the metal possibly via decomposition of the ligand under syngas conditions. To test this hypothesis, H_2 and CO were bubbled through the solution one after the other to observe the effect of each on the rhodium complex.

Carbon monoxide was bubbled through a solution of 10^{-4} mol/cm^3 Rh in deuterated acetone with L:Rh = 1 under an argon atmosphere. The solution turned purple after 20 minutes and a ^{31}P NMR spectrum was obtained. The purple solution contained the same exclusive rhodium species as observed under syngas (doublet at 8 ppm, J_{Rh-P} = 162 Hz). It is possible that this may be a dimer (species **B**). H_2 gas was then bubbled through the purple solution for 20 minutes and a new doublet at 26 ppm (J_{Rh-P} = 191 Hz) appeared. This was attributed to the formation of a hydride rhodium species (**C**).

The solution remained purple. The same chemical shift (26 ppm, J_{Rh-P} = 190 Hz) was observed even when a fresh solution of the complex was used. There were no black precipitates observed when CO and H_2 were bubbled through the complex solution.

White[50] has reported rhodium species present under syngas conditions using (-)-2,3-O-Isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane (DIOP) as a ligand. The results obtained are tabulated below in Table 2.2

Table 2.2 Rhodium/DIOP species present under 1:1 H_2/CO at 25°C as reported by White[50]

Species	δ (^{31}P)/ppm	J_{Rh-P}/Hz
A	39 (50)[1]	188 (205)
B	5.3 (8)	160(162)
C	17.5 (26)	120 (190)

.

From these literature values, we can conclude that the species at 8 ppm corresponds to a dimer of the form **B** and the species at 26 ppm corresponds to a hydride of the form **C**. The difference in chemical shifts could be due to the types of ligands used.

[DPPCo][PF_6] was tested for its stability under H_2 and CO pressures. H_2 and CO gases were bubbled through solutions of the ligand in acetone and the ligand was found to be stable under these conditions. This was verified by no colour change in the solution and by ^{31}P NMR spectroscopy. The ligand was also found to be stable in

[1] Our experimental values (values in brackets)

acetone when exposed to air but when complexed with rhodium, it oxidised after few hours (oxide peak at 19 ppm).

These observations seem to suggest that the dark solution observed when the complex is heated under syngas solution, may contain the dimer and/or hydride species, but this does not explain the black precipitates noticed when the reactor is unloaded.

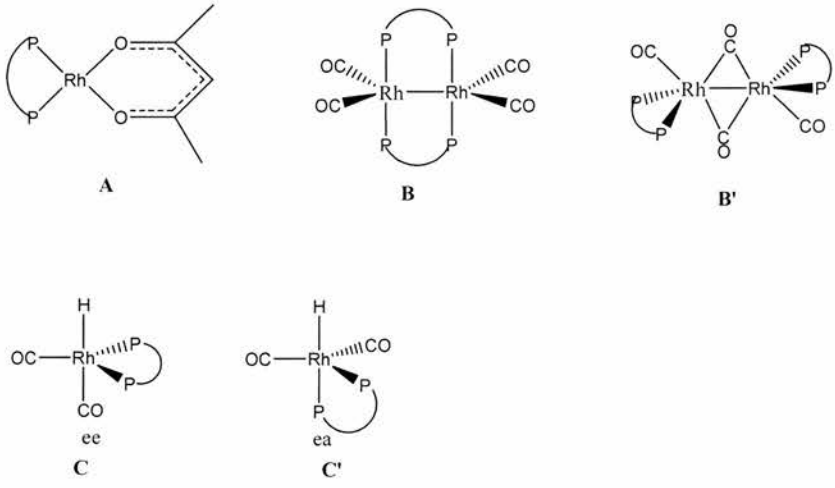


Figure 2.4 Different catalytic species under syngas conditions

2.3.2 Hydroformylation of 1-octene with a preformed [Rh(acac)(CO)$_2$]/[DPPCo][PF$_6$] catalyst in [OctMIM][NTf$_2$]

Based on the results described in section 2.2 above, it was decided that [OctMIM][NTf$_2$] should be used rather than [BMIM][PF$_6$] for hydroformylation reactions, as it seems to give better solubility of the alkene thus eliminating mass transport limitations. Isomerisation and low reaction rates could arise as a result of

slow mass transport of CO into the ionic liquid. From section 2.2 above, it is proposed that [OctMIM][NTf_2] has far better 1-octene solubility as it gives an 88 % olefin conversion (as compared to 10 % for [BMIM][PF_6]) when CO_2 is used as a co-solvent). [DPPCo][PF_6] ligand has been reported to give high activity and selectivity in [BMIM][PF_6] though the result could not reproduced. Trying the reaction in an ionic liquid, where the reaction is not mass transport limited, could improve activity and selectivity of the catalyst.

[$Rh(acac)(CO)_2$] and [DPPCo][PF_6] were weighed into a Schlenk flask. The Schlenk flask was degassed. [OctMIM][NTf_2] was syringed into the flask and the solution was stirred under vacuum at 60°C until all the [$Rh(acac)(CO)_2$] and [DPPCo][PF_6] had dissolved. The catalyst solution was syringed under an argon atmosphere and injected into an autoclave, which had been flushed with CO/H_2, under positive CO/H_2 pressure. The autoclave was then subjected to the appropriate reaction pressure and heated to reaction temperature (100°C). The catalyst solution was stirred for 1 hour to generate the active catalyst species. 1-octene was then injected into the system through an HPLC pump and the reaction was allowed to run for 1 hour. The stirrer and heating were subsequently switched off to allow the system to cool down.

Table 2.3 Batch Rhodium catalysed hydroformylation of 1-octene in 5 cm^3 [OctMIM][NTf_2] using [DPPCo][PF_6] as a ligand[a]

Entry	Pressure/ bar	Total Conversion/%	Conversion to Aldehydes/%	Isomerisation/ %	l:b
1	10	95.6	46.9	48.7	6.1
2	20	99.1	60.3	38.8	5.5
3	20	83.7	59.5	24.2	4.8
4	60	86.3	74.6	11.7	6.1
5	100	92.17	84.98	7.19	5.4

[a]*Conditions: ligand/Rh = 2, volume 1-octene = 3.15 cm^3, H_2/CO = 1, t = 1 hour, T = 100 °C, Volume [OctMIM][NTf_2] = 5 cm^3*

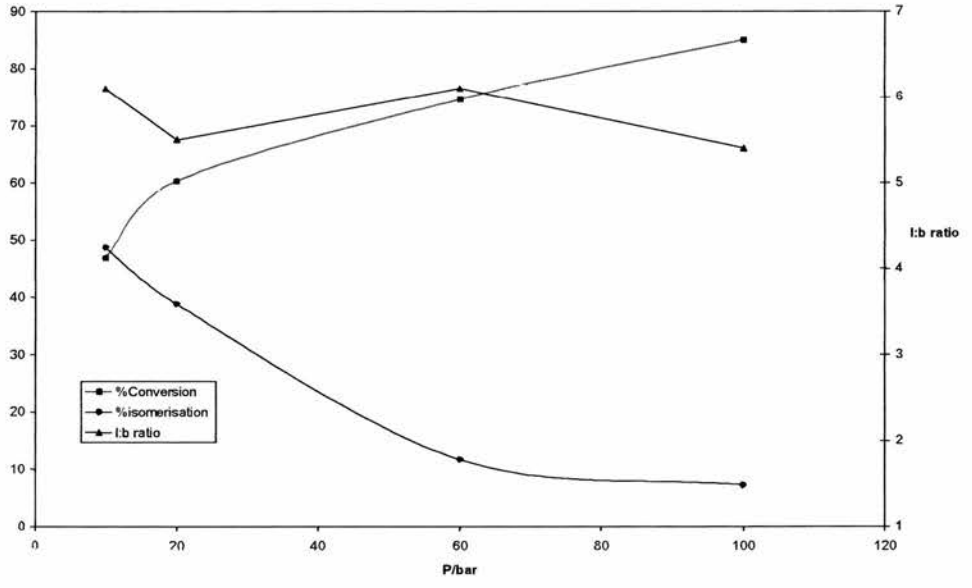


Figure 2.5 Effect of increasing the reaction pressure on conversion, isomerisation and selectivity

It is clear that using [OctMIM][NTf_2] gives better results in terms of conversion to aldehydes though isomerisation is still a problem (Figure 2.5). Conversion to aldehydes increased from 20 % in [BMIM][PF_6] (reaction 2, Table 2.1) to 50 % in [OctMIM][NTf_2] (reaction 1, Table 2.3). This confirms that the reaction in [BMIM][PF_6] probably suffers from greater mass transport limitation than in [OctMIM][NTf_2], although a considerable amount of isomerisation and low l:b ratio are still problematical. From section 2.3.2.3 above, a drop in overall reaction rate was observed when the reaction pressure was increased but the opposite was observed when using [OctMIM][NTf_2]. There was also a reduction in the level of isomerisation when the pressure is increased.

The increase in conversion and the drop in isomerisation suggests that the reaction is being starved of CO (i.e. CO/H_2) at low CO partial pressure i.e. not enough CO to shift the equilibrium from species **C** and **C'** to **D** and **D'** (Figure 2.4). This is in accordance with the high level of isomerisation products observed at low CO partial pressures. At low CO partial pressure, ß hydrogen abstraction competes more effectively, and as a result the degree of isomerisation is increased. It is very interesting to note that even at 60 bar CO/H_2, the reactions seems to be starved of gas although according to our calculations, 30 bar should be sufficient for full conversion. Though increasing the pressure gives better conversion to aldehyde and suppresses isomerisation, the l:b ratio does not seem to be improving as can be clearly seen from Figure 2.5. This is believed to be because the initial hydride migration reaction is not very selective to give the linear alkyl species, so the branched aldehyde forms in place of isomerised alkene.

Usually the l:b ratio is affected by the nature and amount of ligand used. The ligand:Rh ratio was increased from 2 to 5 at 20 bar pressure, in order to try and improve the catalyst selectivity to linear aldehyde. There was no improvement in the linear to branched ratio (l:b ratio of 4.7 as compared to 5.5 from reaction 2 in Table 2.3), even though the conversion to aldehyde was reduced from a 60 to 47 %. Increasing the ligand concentration crowds the Rh centre, making alkene coordination difficult. A drop in isomerisation from about 39 % to 28 % was also observed.

It was decided to carry out the reaction in an organic solvent. THF was found to be a suitable solvent as it dissolves [DPPCo][PF_6]. Exactly the same procedure was followed as outlined above, using 10 bar reaction pressure. Less isomerisation (4 % as compared to 50 % in [OctMIM][NTf_2]) was observed, with 30 % conversion to aldehyde and an l:b ratio of 11. This suggests that the ionic liquids used in this study, promotes isomerisation with the described catalyst system.

2.4 Conclusions

It was found that increasing the alkyl chain length from C4 to C8 on the cation of the ionic liquid improves the turnover frequencies, which could be attributed to better solubility of the alkene. The conversion was further improved by exchanging the PF_6 anion for the $(SO_2CF_3)_2N$ anion. This led to the conclusion that with [BMIM][PF_6], the reaction was mass transport limited because of the low solubility of the substrate in the ionic liquid but with ionic liquids such as [OctMIM][NTf_2], mass transfer limitations are not restrictive under the reaction conditions.

The reported [DPPCo][PF_6] ligand does not seem to give high activity and high linear to branched ratios reported in literature. It does, however, give high levels of isomerisation even with the [OctMIM][NTf_2] where syngas mass transfer limitations do not occur. Nevertheless, increasing the pressure seems to suppress isomerisation but does not improve the l:b ratio.

2.5 References

1. Van Leeuwen, P. N. W. M.; Claver, C. *Rhodium Catalysed Hydroformylation*; Kluwer: Dordrecht, 2000.
2. Frohling, C. D.; Kohlpaintner, C. W. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Ed.; VCH: Weinheim, 1996; Vol. 1, pp 27-104.
3. Cornils, B. In *Applied Homogeneous Catalysis with Organometallic Compounds*; Cornils, B., Herrmann, W. A., Ed.; VCH: Weinheim, 1996; Vol. 1, pp 577-600.
4. Cornils, B. In *New Synthesis with Carbon Monoxide*; Falbe, J., Ed.; Springer-Verlag: Berlin, 1980.
5. Mullineaux, R. D.; Slaugh, L. H. U.S. Patents 3,239,569 and 3,269,570, 1966.
6. Tzschucke, C. C.; Markert, C.; Bannwarth, W.; Roller, S.; Hebel, A.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 3964-4000.
7. Cole-Hamilton, D. J. *Science* **2003**, *299*, 1702.
8. Borowski, A. F.; Cole-Hamilton, D. J.; Wilkinson, G. *Nouv. J. Chem.* **1978**, *2*, 137.
9. Foster, D. F.; Adams, D. J.; Gudmunsen, D.; Stuart, A. M.; Hope, E. G.; Cole-Hamilton, D. J. *Chem. Commun.* **2002**, 916-916
10. Foster, D. F.; Gudmunsen, D.; Adams, D. J.; Stuart, A. M.; Hope, E. G.; Cole-Hamilton, D. J.; Schwarz, G. P.; Pogorzelec, P. *Tetrahedron* **2002**, *58*, 3901-3910.
11. Ropartz, L.; Morris, R. E.; Schwarz, G. P.; Foster, D. F.; Cole-Hamilton, D. J. *Inorg. Chem. Commun.* **2000**, *3*, 714-717.
12. Ropartz, L.; Foster, D. F.; Morris, R. E.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2002**, 1997-2008.
13. Ropartz, L.; Haxton, K. J.; Foster, D. F.; Morris, R. E.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2002**, 4323-4334.
14. Ropartz, L.; Morris, R. E.; Foster, D. F.; Cole-Hamilton, D. J. *J. Mol. Catal. A-Chem.* **2002**, *182*, 99-105.
15. Ropartz, L.; Morris, R. E.; Foster, D. F.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 361-362.
16. De Blasio, N.; Tempesti, E.; Kaddouri, A.; Mazzocchia, C.; Cole-Hamilton, D. J. *J. Catal.* **1998**, *176*, 253-259.
17. De Blasio, N.; Wright, M. R.; Tempesti, E.; Mazzocchia, C.; Cole-Hamilton, D. J. *J. Organomet. Chem.* **1998**, *551*, 229-234.
18. Bach, I.; Cole-Hamilton, D. J. *Chem. Commun.* **1998**, 1463-1464.
19. Sellin, M. F.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2000**, *11*, 1681-1683.
20. Sellin, M. F.; Bach, I.; Webster, J. M.; Montilla, F.; Rosa, V.; Aviles, T.; Poliakoff, M.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2002**, 4569-4576.
21. Sowden, R. J.; Sellin, M. F.; De Blasio, N.; Cole-Hamilton, D. J. *Chem. Commun.* **1999**, 2511-2512.
22. Blanchard, L. A.; Hancu, D.; Beckman, E. J.; Brennecke, J. F. *Nature* **1999**, *399*, 28-29.
23. Kazarian, S. G.; Briscoe, B. J.; Welton, T. *Chem. Commun.* **2000**, 2047-2048

24. Blanchard, L. A.; Brennecke, J. F. *Ind. Eng. Chem. Res.* **2001**, *40*, 287-292.
25. Liu, F. C.; Abrams, M. B.; Baker, R. T.; Tumas, W. *Chem. Commun.* **2001**, 433-434.
26. Brown, R. A.; Pollet, P.; McKoon, E.; Eckert, C. A.; Liotta, C. L.; Jessop, P. G. *J. Am. Chem. Soc.* **2001**, *123*, 1254-1255.
27. Bosmann, A.; Francio, G.; Janssen, E.; Solinas, M.; Leitner, W.; Wasserscheid, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 2697-2699.
28. Hou, Z. S.; Han, B. X.; Gao, L.; Jiang, T.; Liu, Z. M.; Chang, Y. H.; Zhang, X. G.; He, J. *New J. Chem.* **2002**, *26*, 1246-1248.
29. Kawanami, H.; Sasaki, A.; Matsui, K.; Ikushima, Y. *Chem. Commun.* **2003**, 896-897.
30. Lozano, P.; de Diego, T.; Carrie, D.; Vaultier, M.; Iborra, J. L. *Chem. Commun.* **2002**, 692-693.
31. Reetz, M. T.; Wiesenhofer, W.; Francio, G.; Leitner, W. *Chem. Commun.* **2002**, 992-993.
32. Dzyuba, S. V.; Bartsch, R. A. *Angew. Chem., Int. Ed.* **2003**, *42*, 148-150.
33. Sellin, M. F.; Webb, P. B.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 781-782
34. Webb, P.B.; Sellin, M.F.; Kunene, T.E.; Williamson, S.; Slawin, A.M.Z.; Cole-Hamilton, D.J. *J. Am. Chem. Soc.* **2003**, 125,15577
35. Dupont, J.; Silva, S. M.; de Souza, R. F. *Catal. Lett.* **2001**, *77*, 131-133.
36. Favre, F.; Olivier-Bourbigou, H.; Commereuc, D.; Saussine, L. *Chem. Commun.* **2001**, 1360-1361.
37. Brauer, D. J.; Kottsieper, K. W.; Liek, C.; Stelzer, O.; Waffenschmidt, H.; Wasserscheid, P. *J. Organomet. Chem.* **2001**, *630*, 177-184.
38. Brasse, C. C.; Englert, U.; Salzer, A.; Waffenschmidt, H.; Wasserscheid, P. *Organometallics* **2000**, *19*, 3818-3823.
39. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Commun.* **2001**, 451-452.
40. Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3773-3789.
41. Evans; D., Osborn; J.A., Wilkinson, G. *J. Chem. Soc. A* **1968**, 3133.
42. D. Evans; G. Yagupsky; Wilkinson, G. *J. Chem. Soc. A* **1968**, 2660.
43. Brown; C.K., Wilkinson, G. *J. Chem. Soc. A* **1970**, 2753.
44. Jardine, F. H. *Polyhedron* **1982**, *1*, 569.
45. Keim, W.; Vogt, D.; Weffennschmidt, H.; Wasserscheid, P.; *J Catal.* **1999**, 186, 481
46. Brasse, C. C.; Englert, U.; Salzer, A.; Waffenschmidt, H.; Wasserscheid, P. *Organometallics* **2000**, *19*, 3818-3823.
47. Fuller, J.; Carlin, R.T.; De Long, H.C.; Haworth, D. *J. Chem. Soc. Chem. Comm.* **1994**, 299
48. Suarez, P.A.Z.; Dullius, J.E.L.; Einloft, S.; de Souza, R.F.; Dupont, J. *Polyhedron* **1996**, 15, 1217
49. B. Ellis, W. Keim, P. Wasserscheid, *Chem Comm.* **1999**, 337
50. White, D.F.S. *Ph.D Thesis*, University of St-Andrews, Scotland, **2001**

3 Ligand Syntheses

3.1 Introduction

Biphasic catalysis has been established as an effective process for catalyst separation and recycling. One of the biphasic catalytic processes is the IL-$scCO_2$ biphasic system. One of the challenges for this type of system is to retain the catalyst in the ionic liquid. Most of the well known ligands for hydroformylation catalysts e.g. TPP, leach out of the ionic liquid into the organic layer[1,2].

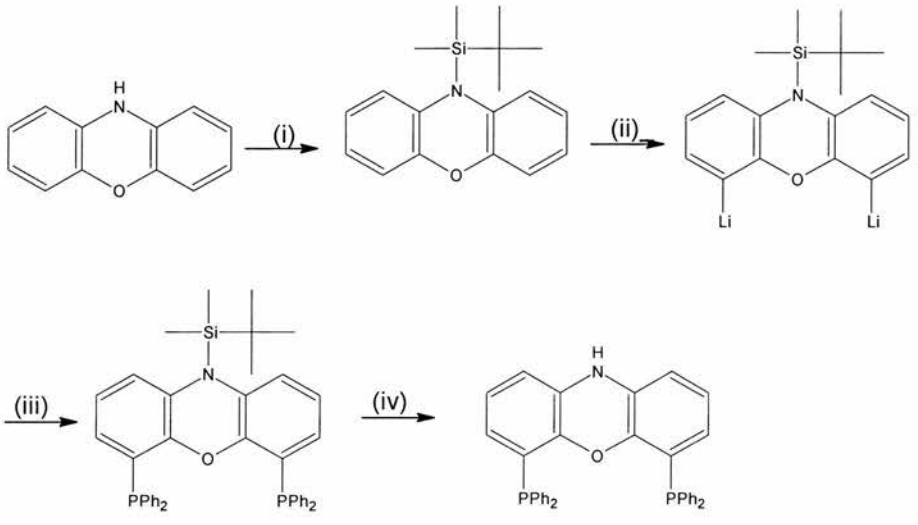
The cobaltocenium based ligands show good solubility in polar solvents owing to their ionic character. Ionic liquids are an alternative polar medium for biphasic hydroformylation. This led Wassercheid and coworkers[3] to synthesize and test functionalised cobaltocenium salts in biphasic (organic / ionic liquid) catalytic reactions.

In order to obtain an IL-$scCO_2$ hydroformylation biphasic system, which combines a high activity, high selectivity and a good retention of the catalyst, the emphasis should be placed upon catalyst (i.e. ligand) design. In this chapter, we will be describing the design and synthesis of new ligands design for hydroformylation in IL-$scCO_2$ biphasic systems.

3.2 Synthesis of Nixantphos ionic analogue

The Nixantphos ligand (Scheme 3.1) has been reported to give high selectivity to linear aldehyde though the reaction proceeds very slowly[4]. Since the $scCO_2$-IL system

seems to need an ionic ligand in order for the system to be continuous without the catalyst leaching and being extracted with the product, the functionality at the nixantphos backbone (N-H) gives us scope to attach an ionic tail, thus making the ligand ionic and rendering Nixantphos suitable for use in IL-scCO_2 biphasic systems, especially continuous flow system. Nixantphos was prepared as reported in literature by van der Veen *et al* (Scheme 3.1).



Nixanthphos

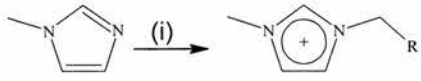
7

Scheme 3.1[4] (i) NaH (THF), tert-Butyldimethylsilyl chloride; (ii) n-BuLi and TMEDA (Diethyl ether); (iii) Chlorodiphenylphosphine; (iv) Tetrabutylammonium fluoride (THF)

The aim was to attach an imidazolium moiety, similar to that present in the ionic liquid onto the nixantphos backbone. An imidazolium group is generally prepared by quartenizing the N-methylimidazole using an alkyl halide (Scheme 3.2). This is usually achieved by refluxing N-methylimidazole and an alkyl halide without any

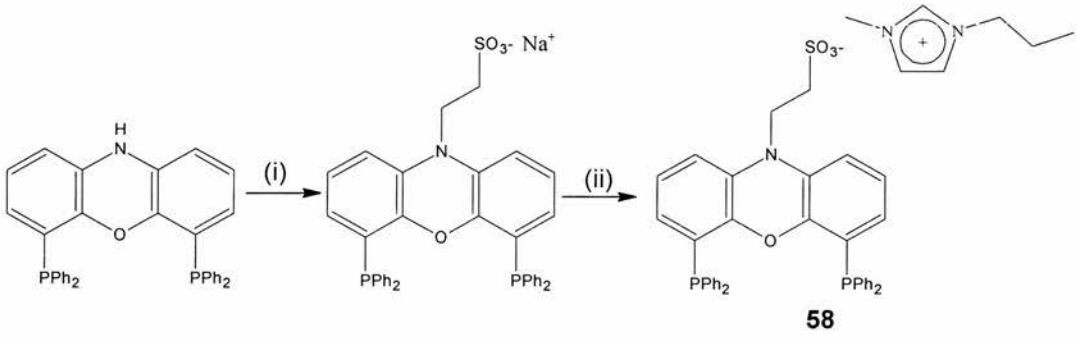
solvent, though sometimes toluene is used as a solvent. The idea was then to employ this concept to functionalise nixantphos with an imidazolium group (Scheme 3.2).

The other way to attach an ionic liquid moiety is to sulfonate the nixantphos ligand at a phenyl ring or attach a sulfonate group through the nitrogen and then exchange the sodium with an imidazolium cation.



Scheme 3.2 (i) Alkyl halide

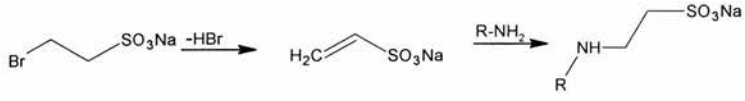
3.2.1 Attempted Synthesis of [Nixantphos$(CH_2)_2SO_3$][PMIM]



Scheme 3.3 (i) NaH (DMF, 2-Bromoethylsulfonate; (ii) 1-Propyl-3-methylimidazolium Chloride

Nixantphos prepared as shown above was dissolved in DMF and NaH was added to deprotonate the N-H proton. 2-Bromoethanesulfonic acid sodium salt was then added

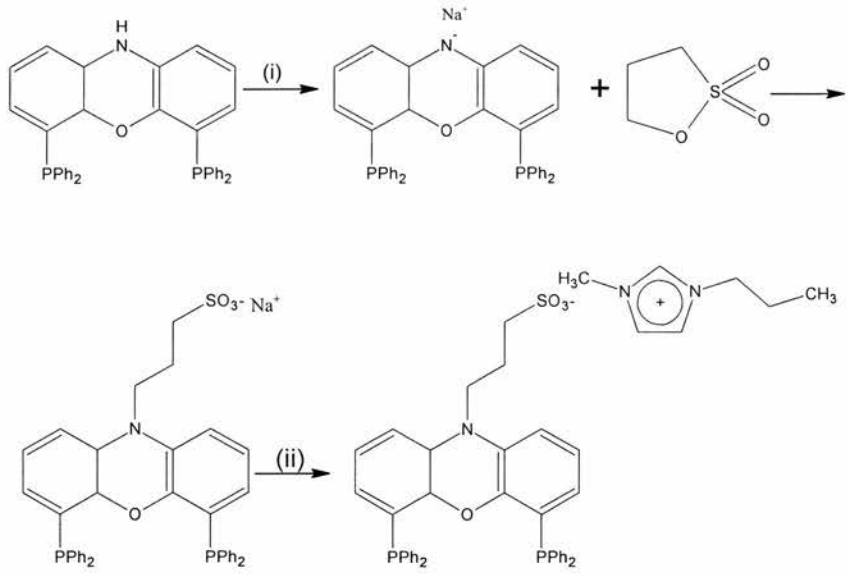
and the reaction was refluxed overnight. 2-bromoethanesulfonic acid sodium salt was found not to dissolve in most organic solvents except the more polar organic solvents like DMSO and DMF, hence the reaction was carried out in DMF as opposed to THF, which is usually the solvent of choice. The reaction was monitored by TLC. After refluxing overnight, the reaction had not taken place according to the TLC. van Ameijde and Liskamp[5] reported that the substitution reaction proceeds via an elimination-addition tandem reaction (Scheme 3.4), when using amines such as dimethylamine



Scheme 3.4 Mechanism of amination of 2-bromoethanesulfonic acid sodium salt

The deprotonated nixantphos is more basic than nucleophilic, so the Michael addition reaction might be difficult. What might also be happening is that the sodium salt of nixantphos just picks up the acidic proton ($CH_2C\underline{H}_2SO_3Na$) from the vinylsulfonate and gives back nixantphos

3.2.2 Attempted Synthesis of [Nixantphos$(CH_2)_3SO_3$][PMIM]



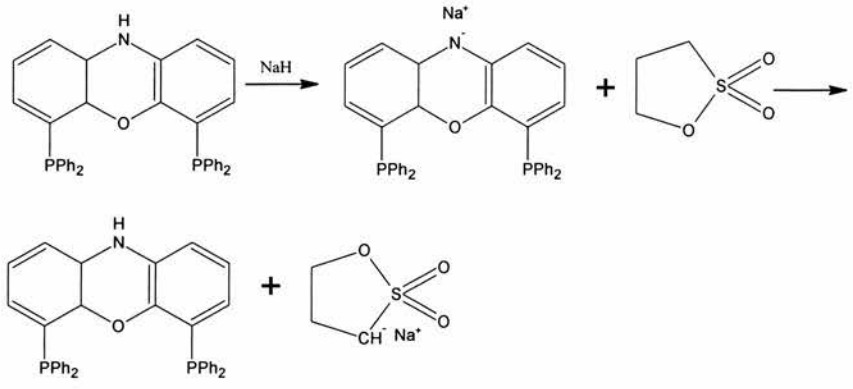
59

Scheme 3.5 (i) NaH (THF); (ii) 1-Propyl-3-methylimidazolium Chloride

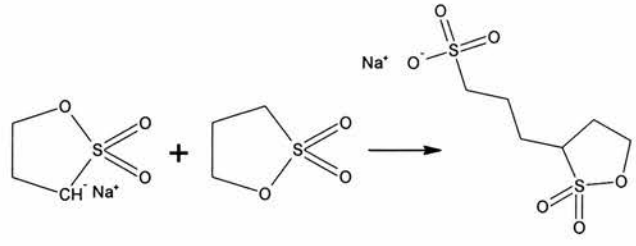
It was thought that sultone might be more reactive since the initial reaction resembles one in which tosyl is the leaving group. It was thought that it would ring open without any problem as it has been reported that the ring opens by nucleophic attack at the C-O bond[6].

The deprotonated nixantphos 'amine' is rather more basic than nucleophilic, so it will readily abstract any acidic proton and goes back to being an amine. It was thought that when reacting the deprotonated nixantphos with sultone, the amine might be simply deprotonating one of the protons on the carbon attached to sulphur (Scheme 3.6, Step i), since they are acidic and then the deprotonated sultone species will ring open another sultone molecule, forming an ionic species which will be very difficult to separate from the desired product. The ^{1}H NMR showed the starting nixantphos.

Step I

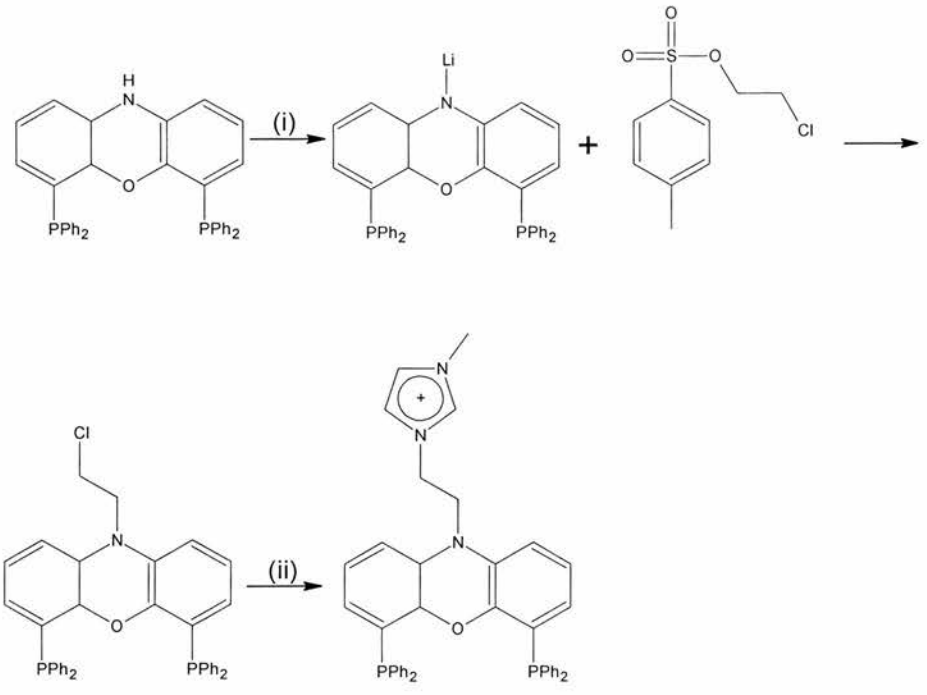


Step II



Scheme 3.6 Possible reaction between sodium salt of nixantphos and sultone

3.2.3 Attempted Synthesis of [NixantphosEMIM][Cl]



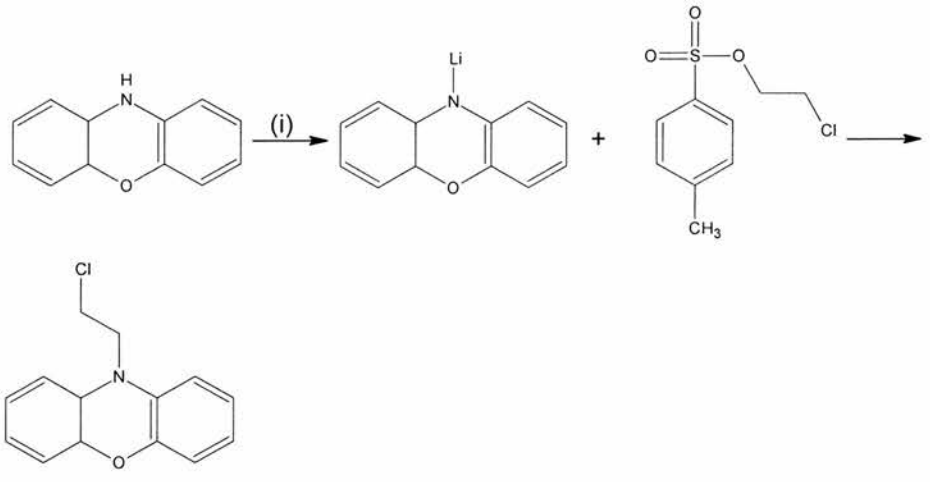
[NixantphosEMIM][Cl]

60

Scheme 3.7 (i) n-Buli (Toluene); (ii) N-methylimidazole

The idea behind this route was to attach an imidazolium salt onto the nixantphos backbone to give a cationic analogue of the ligand rather than an anionic one as in the previous attempts. The principle used to prepared imidazolium salts was followed but first the "alkyl halide" was attached onto xantphos. That was achieved as shown in steps i & ii above. Shirley *et al*[7] reported a similar reaction where phenoxazine was reacted with 2-chloroethyl p-toluenesulfonate to give 10-(2-chloroethyl)phenoxazine. The yields were not impressive which might suggest that there are two competing reactions i.e. nucleophilic attack and deprotonation of the acidic hydrogen on the carbon adjacent to the oxygen atom, since nixantphos is more basic than nucleophilic.

The product obtained from nixantphos was clean i.e. according to ^{1}H NMR spectroscopy.

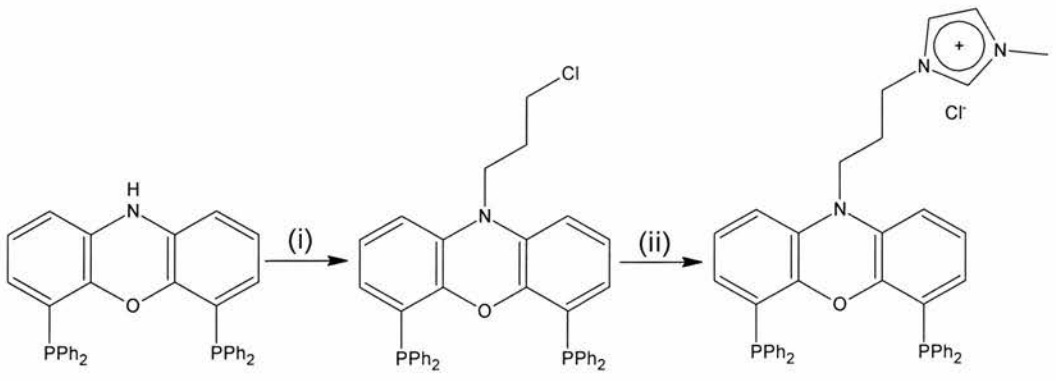


10-(2-Chloroethyl)phenoxazine

Scheme 3.8 (i) n-Buli (Toluene)

10-(2-Chloroethyl)nixantphos was dissolved in acetone and N-methylimidazole was added in excess (Scheme 3.7, step ii). The reaction was then refluxed overnight. The reaction was monitored with TLC. After refluxing overnight, the TLC showed that 10-(2-chloroethyl)nixantphos did not react with N-methylimidazole. In preparing ionic liquids, refluxing overnight is usually enough to obtain reasonable yields, but in this case it seemed as if there was no reaction at all. Among other possible explanations, the problem was thought to be due to steric bulk of the 10-(2-Chloroethyl)nixantphos molecule, which could prevent the reaction, as it was thought the C2 bridge is too short. It was thought that may be by increasing the carbon number on the bridge, the problem could be solved.

3.2.4 Synthesis of [NixantphosPMIM][Cl]



10(3-Chloropropyl)nixantphos [NixantphosPMIM][Cl]

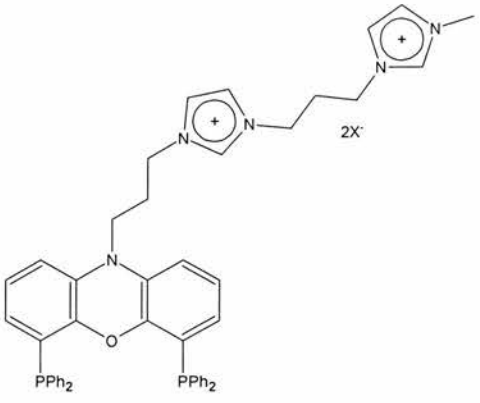
61

Scheme 3.9 (i) NaH (THF), 1-Bromo-3-chloropropane; (ii) N-methylimidazole

The bridge was then increased from C2 to C3. To a solution of nixantphos in THF, NaH was added and then excess of 1-bromo-3-chloropropane (Scheme 3.9, step i). The reason why 1-bromo-3-chloropropane was used, was because bromine is a better leaving group than chlorine, so that would prevent two nixantphos molecules from coupling. The best yield found with step ii was 57 %. The low yield might due to the fact that some deprotonated nixantphos molecules might pick up an acidic proton from 1-bromo-3-chloropropane. The nucleophilic attack could have been helped by the factor that bromine is a better leaving group. The resulting product was dissolved in toluene and N-methylimidazole was added in excess. The reaction was refluxed overnight and the product ([NixantphosPMIM][Cl] precipitated out as it was formed.

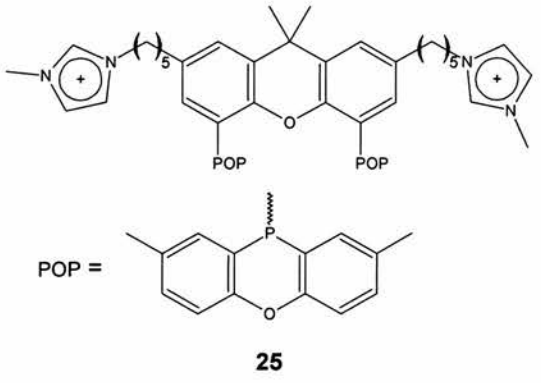
3.3 Attempted Synthesis of ionic Nixantphos with two imidazolium moieties

3.3.1 Introduction



X = halide

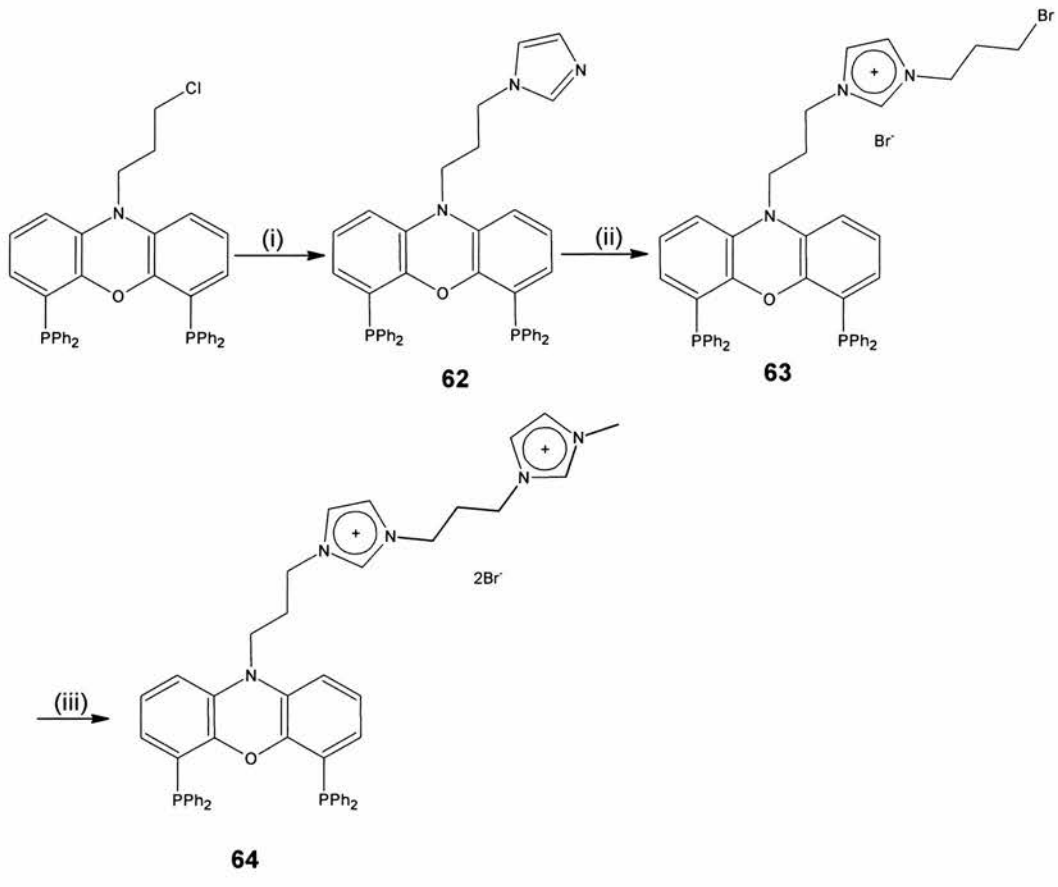
Attaching two or more imidazolium moieties on the nixantphos backbone makes the ligand more ionic in character, thus giving it more affinity to dissolve and be retained in the ionic liquid and lesser affinity to dissolve and be extracted in $scCO_2$. In principle it is possible to attach in series more than two imidazolium moieties. van Leeuwen *et al*[8] recently reported the use of ligand **6** with two imidazolium moieties at the ligand backbone for the hydroformylation of 1-octene at 100°C under 17 bar CO/H_2 (1:1) in [BMIM][PF_6] ionic liquid. No phosphorus (< 100 ppb) or rhodium (< 5 ppb) leaching was detected at all.



25

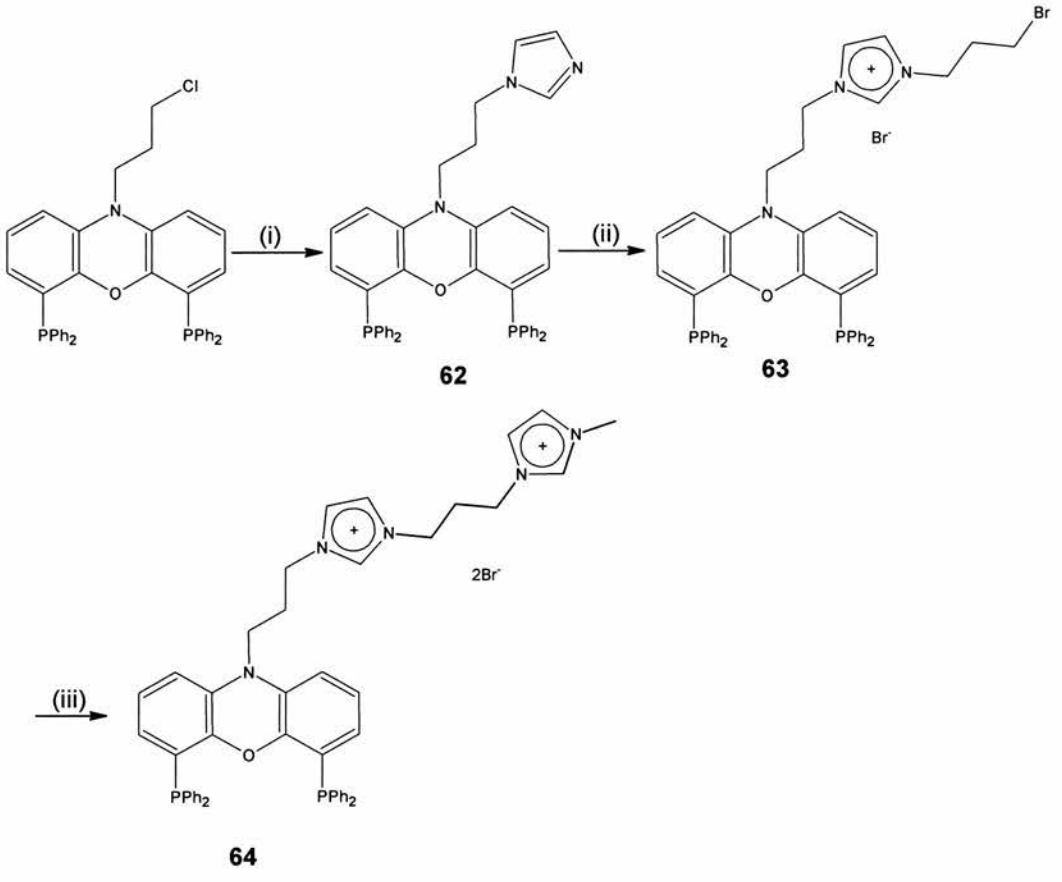
Dicationic phenoxaphosphino – modified Xanthphos[8]

The proposed mechanism for the synthesis of ligand **64** is shown in Scheme 3.10 below.



Scheme 3.10 (i) NaH and Imidazole (THF); (ii) 1,3-Dibromopropane (Toluene); (iii) 1-Methylimidazole

3.3.2 Alkylation of Imidazole



Scheme 3.11 (i) NaH and Imidazole (THF); (ii) 1,3-dibromopropane (Toluene); (iii) 1-methylimidazole

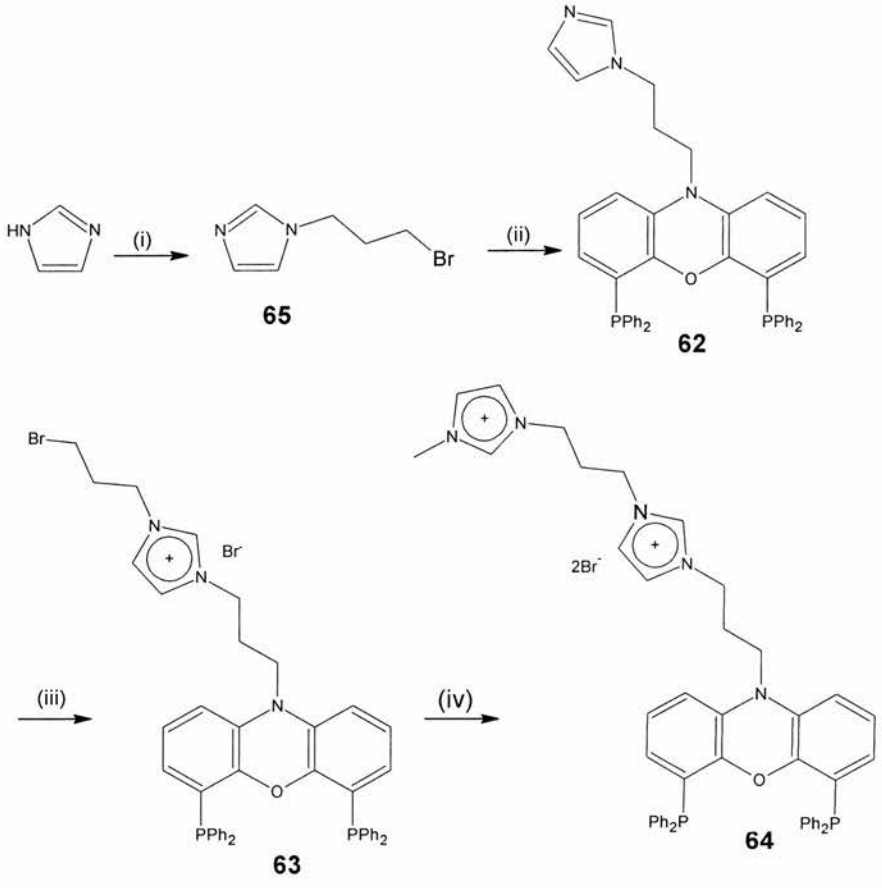
In section 3.2.4 above, [nixantphosPMIM][Cl] was synthesized by reacting 10-(3-chloropropyl)nixantphos with N-methylimidazole. It was then thought that the reaction of 10-(3-chloropropyl)nixantphos with imidazole should yield compound **62** (Scheme 3.11).

Imidazole was dissolved in THF and sodium hydride was added to deprotonate the N-H bond to form a nucleophile. The liberation of H_2 during the addition of sodium hydride with imidazole indicated the abstraction of the proton to form the sodium salt. After refluxing for an hour, 10-(3-chloropropyl)nixantphos was added to the reaction mixture with the hope of forming compound **62**. The reaction was refluxed overnight. The reaction was monitored by TLC but no reaction occurred. This was also evident from the ^{1}H NMR, which showed the starting reagent, 10-(3-chloropropyl)nixantphos.

This could be due to the fact imidazole itself is a base, so the deprotonated imidazole would be even more basic which will make it a very poor nucleophile which might require a better electrophile of which chlorine is not.

It was thought that maybe chlorine was not a better electrophile, so bromine was used in Scheme 3.12 below. Though the reaction is different from Scheme 3.11 above, the reaction protocol is the same.

3.3.3 Alkylation of Imidazole in THF

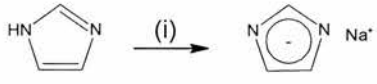


Scheme 3.12 (i)NaH (THF), 1,3-dibromopropane; (ii) NaH (THF), Nixantphos; (iii) 1,3-Dibromopropane (Toluene); (iv) 1-Methylimidazole

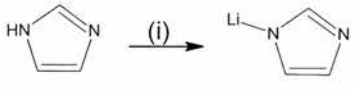
Imidazole was deprotonated successfully in THF with the liberation of H_2 gas being the evidence. 1,3-Dibromopropane was added and the reaction was refluxed overnight. The nucleophilic attack by the imidazolium sodium salt on 1,3-dibromopropane was thought to be relatively simpler but it was not to be the case. Kashima *et al*[9] carried out a similar reaction with a substituted imidazole and they managed to alkylate the nitrogens under basic conditions using NaH. After deprotonation of imidazole, the imidazolium sodium salt was so reactive that it

reacted instantaneously with an alkyl halide. The only difference between our reaction and theirs was the solvent used. They used DMSO as opposed to THF as a solvent. DMSO is more polar and coordinating than THF. This could explain why there was no reaction in our case. The anion formed after deprotonation NaH behaves as shown in Scheme 3.13. The anion is delocalised which might make the nucleophilic attack difficult. So, it's possible that DMSO as a more polar and coordinating solvent, might be stabilizing the anion, thus allowing the reaction to take place. The sodium salt of imidazole could also be insoluble in THF but soluble in the more polar solvent, which might explain the observation.

Despite that Mahoharan and Brown[10] managed to alkylate imidazole in THF but used butyllithium as a base at temperatures below 0°C. What might be happening here is that the lithium forms a Li-N bond (Scheme 3.14) as opposed to just acting as a counter cation like Na in Scheme 3.13 below. The lithium salt is also more reactive than the sodium salt. Therefore, the electrophilic attack by the alkyl halide would be easier and faster.

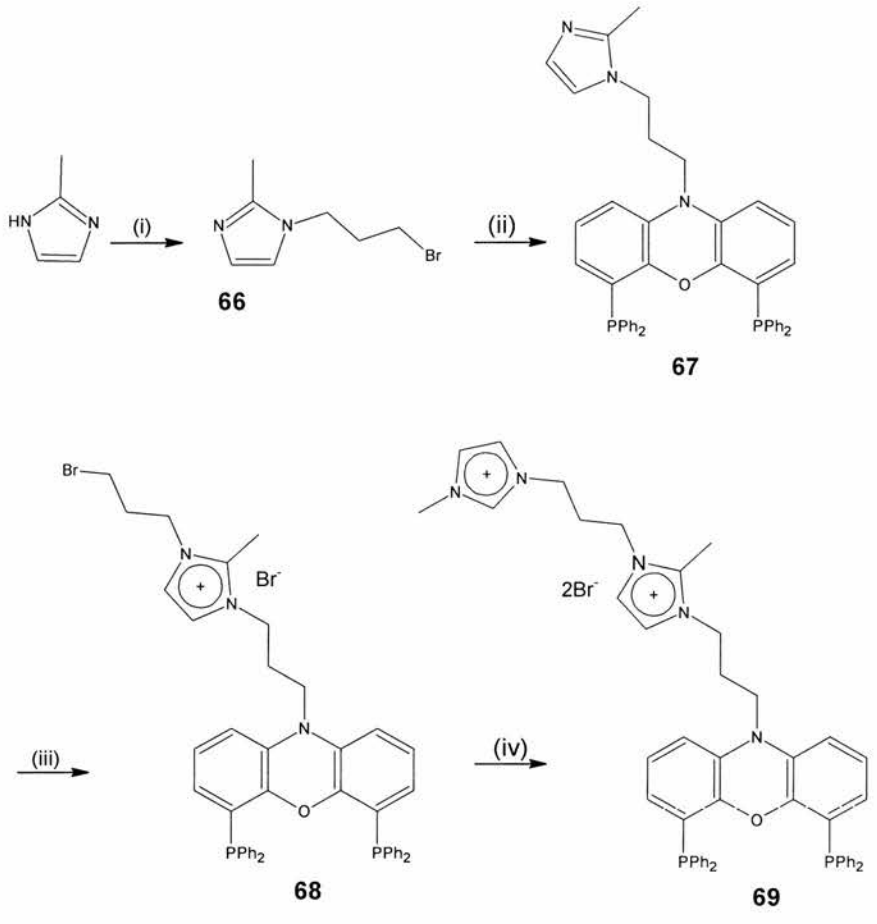


Scheme 3.13 (i) NaH (THF)



Scheme 3.14 (i) n-Buli

3.3.4 Alkylation of 2-methylimidazole in THF

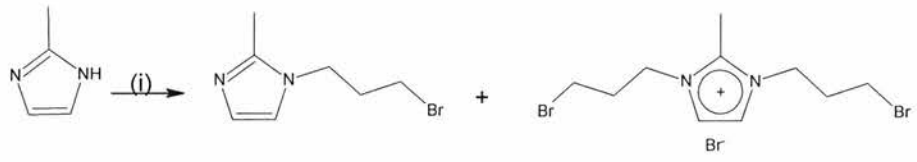


Scheme 3.15 (i) NaH (THF), 1,3-Dibromopropane; (ii) 10-(3-chloropropyl)nixantphos; (iii) 1,3-Dibromopropane; (iv) N-methylimidazole

The reaction of an imidazolium sodium salt with a dihaloalkane was repeated, this time with 2-methylimidazole. The methyl group will have an effect on the reactivity of the imidazolium sodium salt i.e. it pushes electron density into the ring making the 2-methylimidazolium salt more negative, which will make it more nucleophilic and the methyl group also improves the solubility of the sodium salt in THF. Sodium

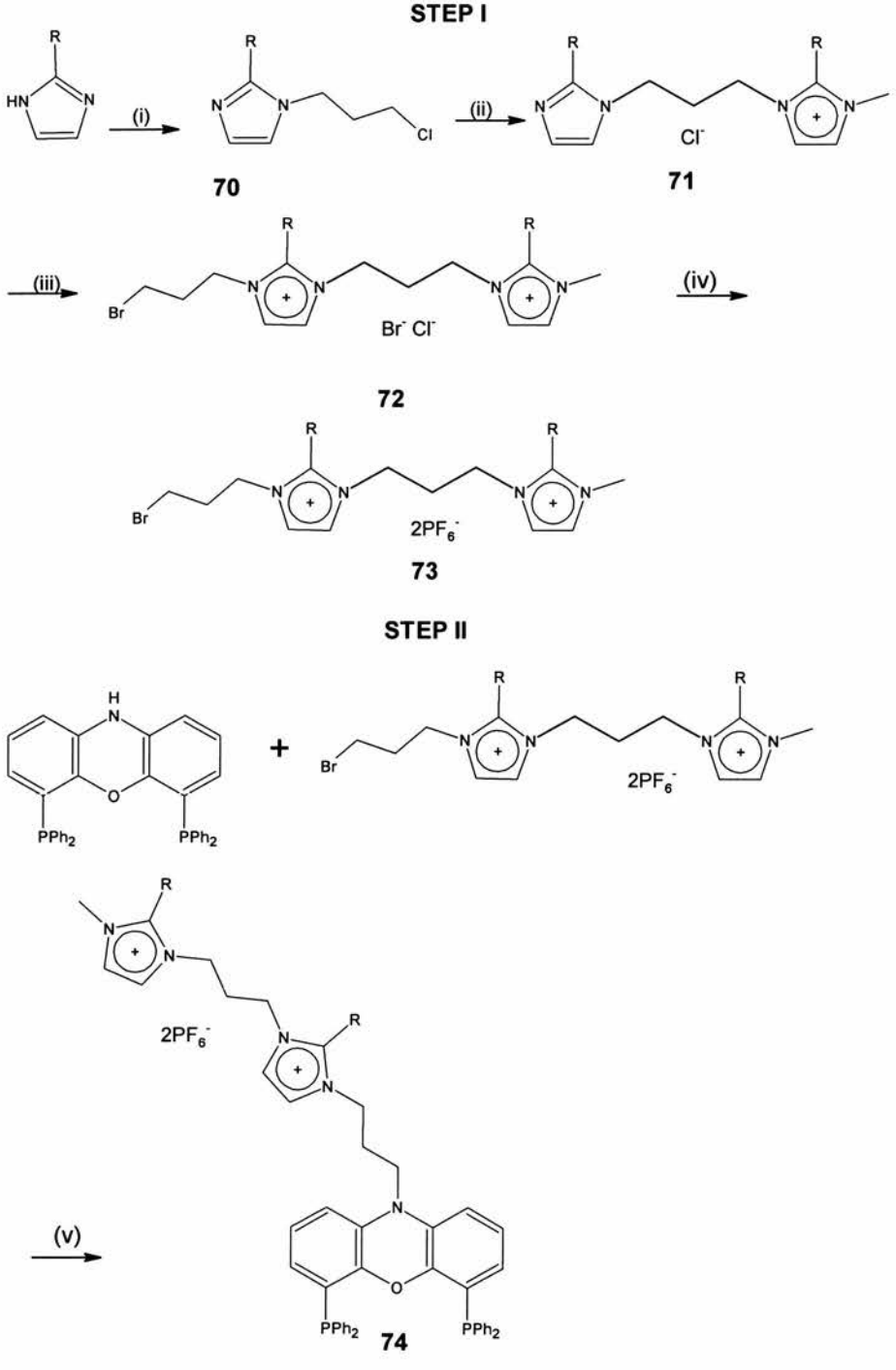
hydride was used to deprotonate 2-methylimidazole and after refluxing for an hour, 0.5 mole equivalent of 1-bromo-3-chloropropane was added. After refluxing overnight, the reaction mixture was poured into water. The product was expected not to be water soluble, but no precipitation occurred. After trying to extract the product with a range of organic solvents (diethyl ether, DCM), sodium hexafluorophosphate ($NaPF_6$) was added to precipitate any ionic compound, which could have formed as side products. The addition of $NaPF_6$ was used as an indication of whether any reaction occurred or not, by exchanging any halide anion with a PF_6 anion. PF_6 salts are insoluble in water, so they would precipitate out of the water solution as soon as they are formed. Immediately after the addition of $NaPF_6$, a white precipitate formed and was collected by filtration. The ^1H NMR spectrum of the precipitate was very complex to interpret, suggesting that more than one imidazolium compound had formed. Possible products formed are shown in Scheme 3.16.

This suggests that the reaction did proceed with 2-methylimidazole. The methyl group could facilitate the solubility of the sodium salt in THF as opposed to the imidazolium sodium salt. The reason for the formation of ionic compounds would be the fact that once one nitrogen on the ring is alkylated, the other one is activated and then reacts further. Again here, the solvent might have been the crucial component as far as the success of this alkylation is concerned. Tanouchi *et al*[11] alkylated one nitrogen selectively with a dihaloalkane in DMF as opposed to THF. DMF as a more polar and coordinating solvent, could be stabilizing the anion as does DMSO.



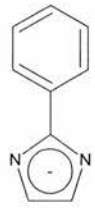
Scheme 3.16 (i) NaH (THF), 1,3-Dibromopropane

3.3.5 Alkylation of 2-phenylimidazole in THF



Scheme 3.17 **R = Phenyl,** (i) NaH (THF), 1-Bromo-3-chloropropane; (ii) 1-methyl-2-phenyl-1*H*-imidazole[12] ; (iii) 1,3-Dibromopropane; (iv) $NaPF_6$; (v) NaH (THF)

Matthews *et al*[13] alkylated 2-phenylimidazole in ethanol using NaOH as base. We tried to react 2-phenylimidazole with 1-bromo-3-chloropropane using NaH as suggested by Kimura *et al*[14]. After refluxing overnight and working up the reaction, the alkylation (step i, Scheme 3.17) was found to be successful. The difference between 2-phenylimidazole, imidazole and 2-methylimidazole is that 2-phenylimidazole has a double bond conjugation which is usually stable, so the conjugation would be difficult to break. Therefore the anion formed would be stabilized and thus making the electrophilic attack easier. The other difference is that 2-phenylimidazole would be the most soluble of the three.

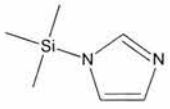


2-Phenylimidazole

1-(3-chloropropyl)-2-phenyl-1*H*-imidazole was then dissolved in toluene and a solution of 1-methyl-2-phenyl-1*H*-imidazole in toluene was added. The solution was refluxed overnight and no reaction occurred after monitoring the reaction with TLC. Also the ^{1}H NMR spectrum only showed the starting material. This could be due to the electron withdrawing effect of the phenyl ring, which renders the lone pairs on the nitrogen less nucleophilic. The other reason could be the fact that the reaction requires the breaking of the double conjugation, which is thermodynamically unfavoured. Usually when quaternizing the nitrogen with an alkyl halide, the reaction is over after

refluxing overnight as it was observed in Chapter 2 when synthesizing ionic liquids from N-methylimidazole.

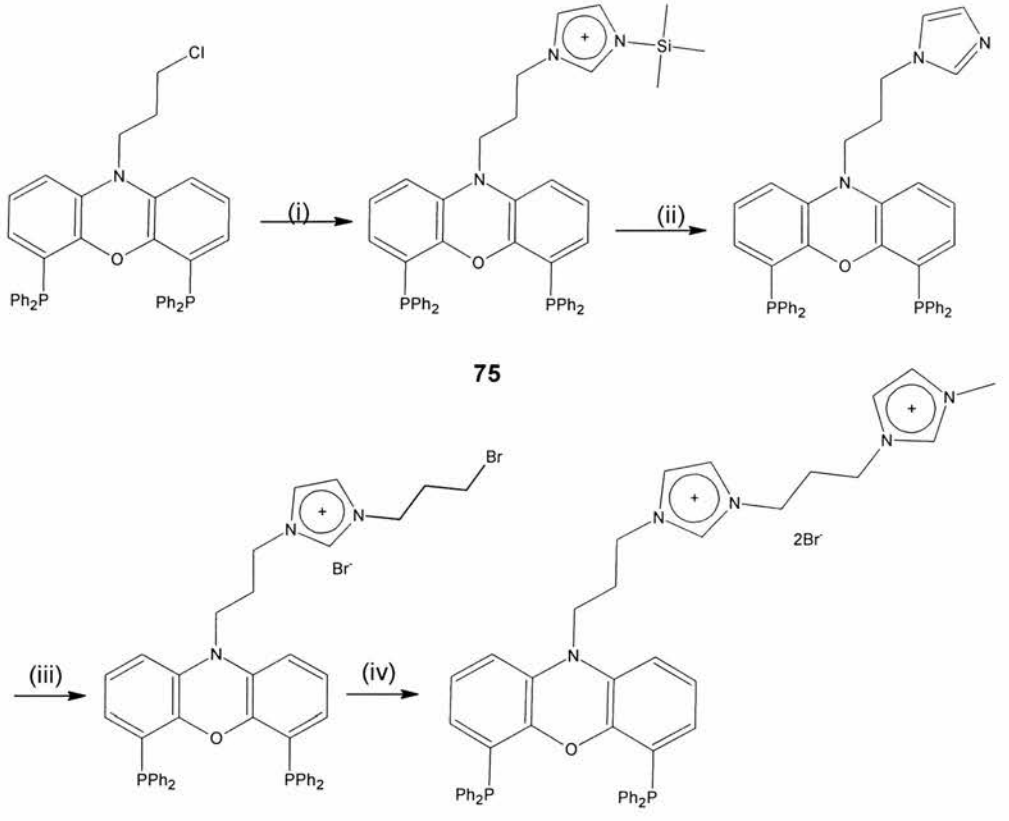
3.3.6 Alkylation of 1-(trimethylsilyl)imidazole



1-(Trimethylsilyl)imidazole

Amine groups are usually protected by silicon containing groups as shown above. Silicon is an element just below carbon on the periodic table, so they have similar properties. Silicon has more electron donating abilities than carbon, so one would expect the silyl group to push more electrons to the imidazole ring than the methyl group in the case of 1-methylimidazole. Therefore, 1-(trimethylsilyl)imidazole should in principle have the same reactivity as 1-methylimidazole towards electrophiles, if not be more reactive. It was, therefore, decided that a similar reaction as in Scheme 3.9 above be carried out with 1-(trimethylsilyl)imidazole (the protected imidazole) . 10-(3-Chloropropyl)nixantphos and 1-(trimethylsilyl)imidazole were dissolved in toluene and refluxed overnight. The reaction was monitored by TLC. The TLC showed no sign of a reaction. The resulting product was expected to be insoluble in toluene, thus precipitating out as it forms as it was observed in the reaction described in Scheme 3.9 above. In this case no precipitation occurred, also indicating that no reaction took place. After the reaction work-up, the ^{1}H NMR spectrum showed the starting material, which was a final confirmation that no reaction had occurred. This

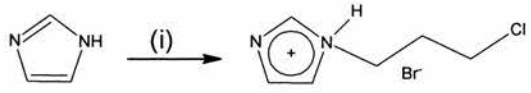
suggested that the silicone group does not behave like the carbon in 1-methylimidazole. The reason for such an observation could have been due to a solvent effect.



Scheme 3.18 (i) 1-(Trimethylsilylimidazole; (ii) Water work-up, NaOH; (iii) 1,3-Dibromopropane; (iv) N-methylimidazole

It was decided that we investigate the solvent effect based on the observations above. The alkylation of imidazole in toluene and acetone was investigated (Scheme 3.18). Two samples of imidazole were dissolved in toluene and acetone respectively and 1-bromo-3-chloropropane was added to each. The two experiments (toluene and acetone) were refluxed overnight. After refluxing overnight, it was found that the alkylation of imidazole in acetone occurred whereas there was no reaction in toluene.

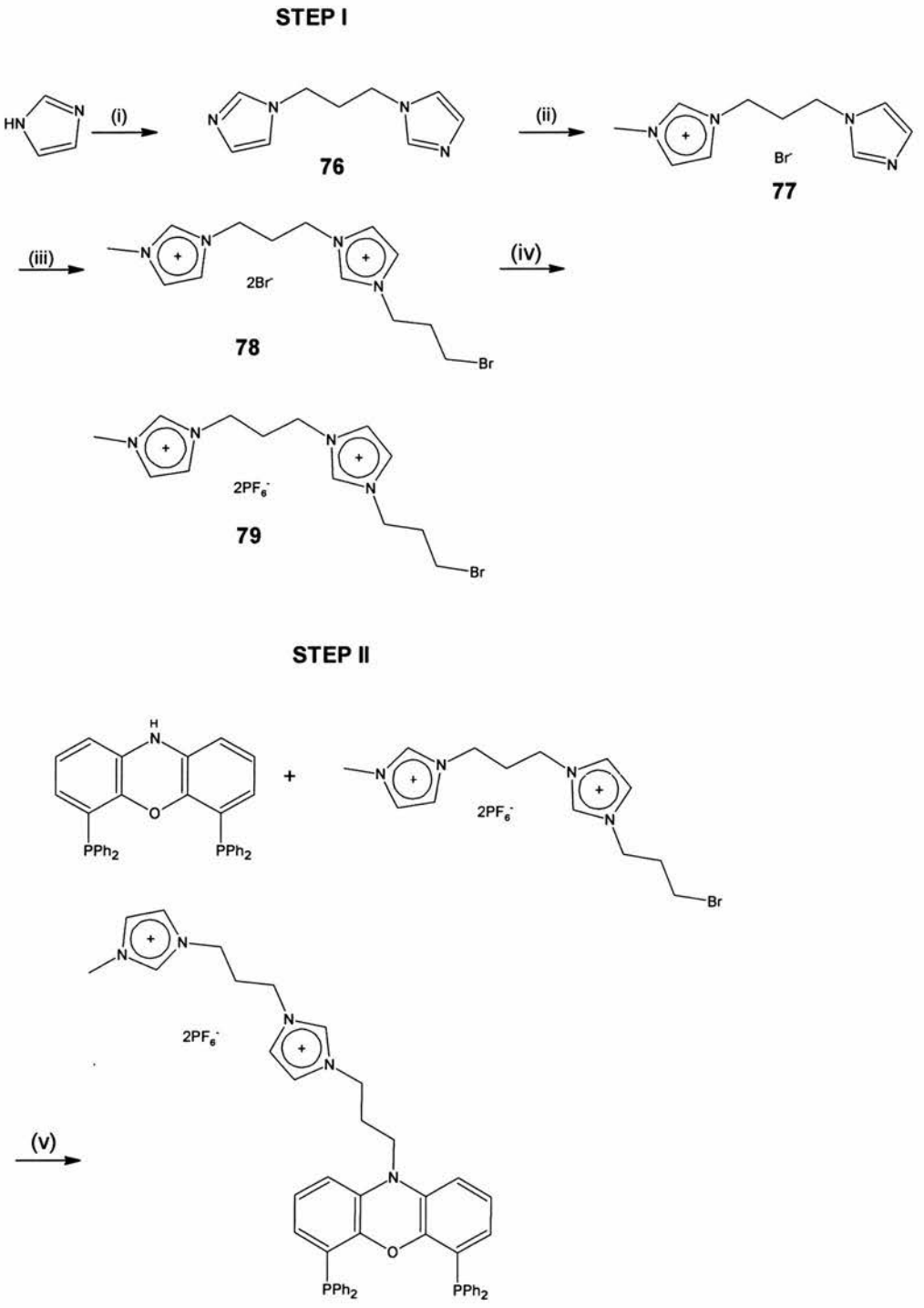
Acetone is more polar than toluene. This confirmed that alkylation of amines (especially imidazole type compounds) usually requires a polar solvent as it was found in sections 3.3.2 and 3.3.3 above.



Scheme 3.19 (i) 1-Bromo-3-chloropropane (Acetone)

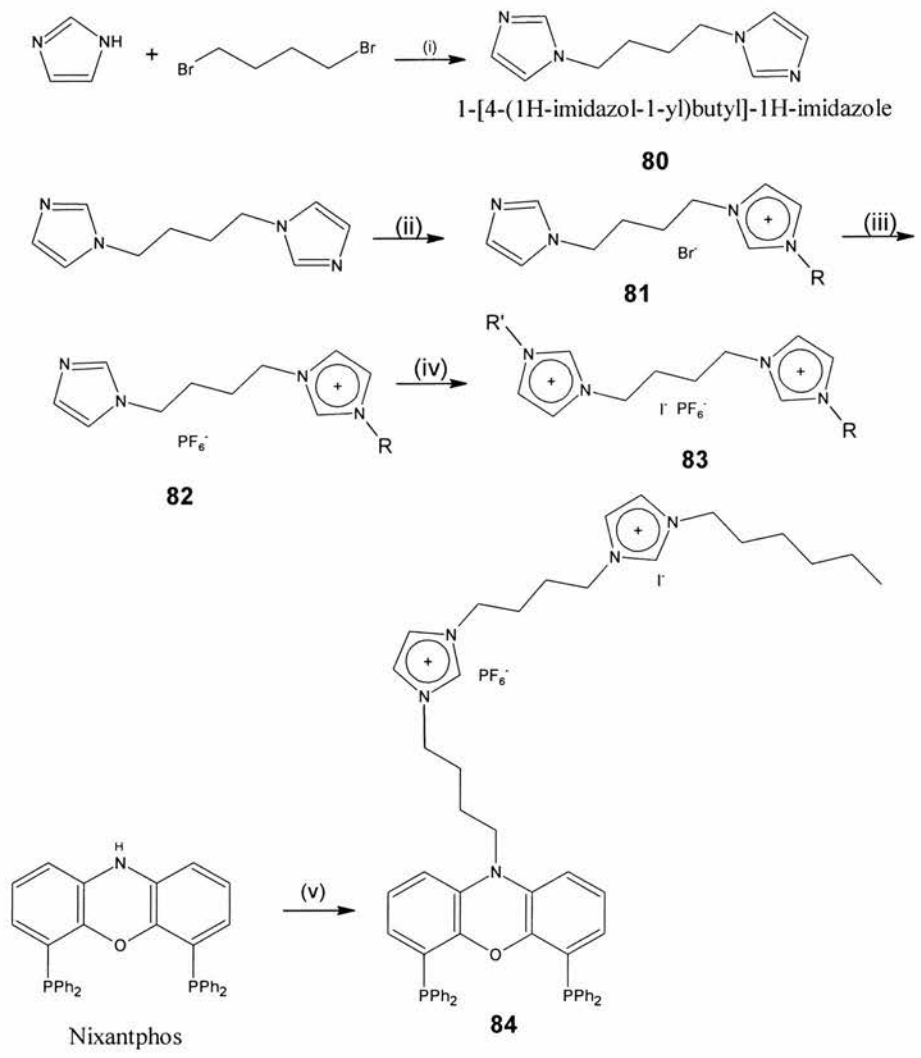
The next step then was to carry out the alkylation of 1-(trimethylsilyl)imidazole in acetone (step i in Scheme 3.18) but 10-(3-Chloropropyl)nixantphos does not dissolve in acetone.

3.3.7 Alkylation of Diimidazole compounds



Scheme 3.20 (i) NaOH, 1,3-Dibromopropane (DMSO); (ii) Methyliodide; (iii), 1,3-Dibromopropane; (iv) $NaPF_6$; (v) NaH (THF)

Ma *et al*[15] reported the reaction of imidazole and dichlorobutane in DMSO to give 1-[3-(1*H*-imidazol-1-yl)propyl]-1-*H*-imidazole. After reaction, the mixture was poured into water to precipitate the product 1-[3-(1*H*-imidazol-1-yl)propyl]-1-*H*-imidazole as it is insoluble in water. In section 3.3.3 above, we tried to couple two imidazole groups without any success. After a literature search, we came across the work of Ma *et al*[15] and we tried to duplicate the reaction using their conditions. It was carried out exactly as outlined by Ma *et al*[15] (scheme 3.20), except that 1,3-dibromopropane was used instead of 1,4-dichlorobutane. To a solution of imidazole and NaOH in DMSO, 1,3-dibromopropane was added. The reaction was refluxed for two hours and after two hours the reaction mixture was poured into water as suggested by Ma *et al*[15] but no product precipitated. The reaction was repeated with refluxing for 6 hours instead of 2 hours without any product precipitation when poured into water. 1,3-Dibromopropane would be expected to be more reactive than dichlorobutane. The carbon chain length could have been the reason why the reaction did not take place as this was the other difference from Ma *et al*'s work.



Scheme 3.21 R = 1-Bromohexane, R' = 1,5-Diodopentane; (i) NaH (THF); (ii) 1-Bromohexane (Acetone); (iii) $NaPF_6$, (iv) 1,5-Diodopentane; (v) NaH

Luo *et al*[16] have also reported the coupling of imidazole groups but using tetra-n-butylammonium iodide as a phase transfer catalyst. in benzene / water.

The solution of imidazole and 1,4-dibromobutane in benzene/water in the presence of NaOH as a base and tetra-n-butylammonium iodide was refluxed for 36 hours. After 36 hours the mixture was filtered and the resulting solid was the desired 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole. The reaction (Scheme 3.21, step i) was

successfully carried out in our laboratories. The formation of 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole was confirmed by ^{1}H NMR spectroscopy.

The solution of 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole and bromohexane in acetone (step ii) was then refluxed overnight. In order to selectively alkylate one of the two nitrogens, which have the same reactivity, 2 mole equivalents of 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole were used. After the reaction, the mixture was poured into water, in order to precipitate out the excess 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole. The resulting compound **81** was thought to have a higher affinity for water compared to 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole, so pouring the mixture into water was expected to precipitate out any unreacted 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole, compound **80,** and dissolve the resulting product, **81**. It was surprisingly found that 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole, **80,** did not immediately precipitate out but rather crystallized out of solution overnight. After crystallizing the 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole compound, it was found by ^{1}H NMR spectroscopy that there were still traces of the -[4-(1H-imidazol-1-yl)butyl]-1H-imidazole left in solution. In order to isolate compound **81** as pure as possible, a solution of ammonium hexafluorophosphate (NH_4PF_6) in water was added into the water solution of the product. The bromide anion (Br^-) was exchanged with hexafluorophosphate anion (PF_6^-) to form compound **82** and ammonium bromide. Compound **82** was instantaneously formed and precipitated, as it is water insoluble. Compound **82** was then collected and washed several times with water.

A solution of compound **82** and diiodopentane in acetone was then refluxed overnight In order to selectively form compound **83** (step iv), 5 mole equivalents of diiodopentane were added. The reaction had to be run overnight to ensure that all of compound **82** was reacted, in order to prevent a situation where there was more than one ionic species in solution, which would lead to separation problems.

Ionic species cannot be separated by column chromatography as they do not move on a silica column. They also dissolve in the same solvent systems, which will make it impossible to precipitate one and not the other. The only separation method could be ion exchange chromatography or crystallization. Selective crystallization usually requires the desired product to be at least 90 % pure, otherwise fractional crystallization can be difficult.

After the reaction, acetone was evaporated and the resulting oil was washed with hexane to remove any excess diiodopentane. The ^{1}H NMR spectroscopy showed only one ionic species, which was the desired product **83**. Product **83** was found to be partially soluble in THF. The reason why long chain alkyl halides (steps ii and iv) were used instead of shorter chains was to try make compound **83** less polar in order to dissolve it in less polar solvents like THF, as nixantphos, the other reagent, dissolves in THF.

To a solution of nixantphos in dry THF, was added NaH (step v) to deprotonate the N-H proton. A solution of compound **83** in THF was then added and the reaction was refluxed overnight. In order to avoid more than one ionic species in solution after the reaction, 2 mole equivalents of nixantphos were used i.e. compound **83** was the

limiting reagent. After an hour of adding compound **83**, there was a colour change to dark brown from a yellowish solution. This was an indication that a reaction was taking place. The reaction could not be monitored by TLC since the product and compound **83** do not move on the TLC plate due to their ionic character and nixantphos was in excess (the TLC method is qualitative rather than being quantitative). The TLC method would only have worked if nixantphos was the limiting reagent because the disappearance of nixantphos would have been a measure of the reaction progress. The disappearance of nixantphos was not going to be visible since it was in excess. After refluxing overnight, the solution was poured into water and extracted with dichloromethane. Dichloromethane was evaporated and the oil residue was washed with diethyl ether to remove all the excess nixantphos. The ^{1}H and ^{31}P NMR spectra were run to check whether the reaction occurred or not. The ^{1}H NMR was found to be complex, so the phosphorus NMR was the next indication. What we were looking for on the ^{31}P NMR spectrum was the phosphorus integration between PPh_2 and PF_6^- signals. The integration was expected to be 2:1 (PPh_2:PF_6^-). The ^{31}P NMR showed only two phosphorus signals at -19 ppm (PPh_2, singlet) and -145 ppm (PF_6^-, septet), but the integration was found to 1:8 PPh_2:PF_6^-. This suggested that not all of compound **83** reacted i.e. the reaction did not go to completion. The other possibility was that no reaction at all occurred. There was no way of separating the product from the reagents, especially the ionic reagent **83**. The best thing was to repeat the reaction and run it for even longer to make sure that all of compound **83** was reacted away.

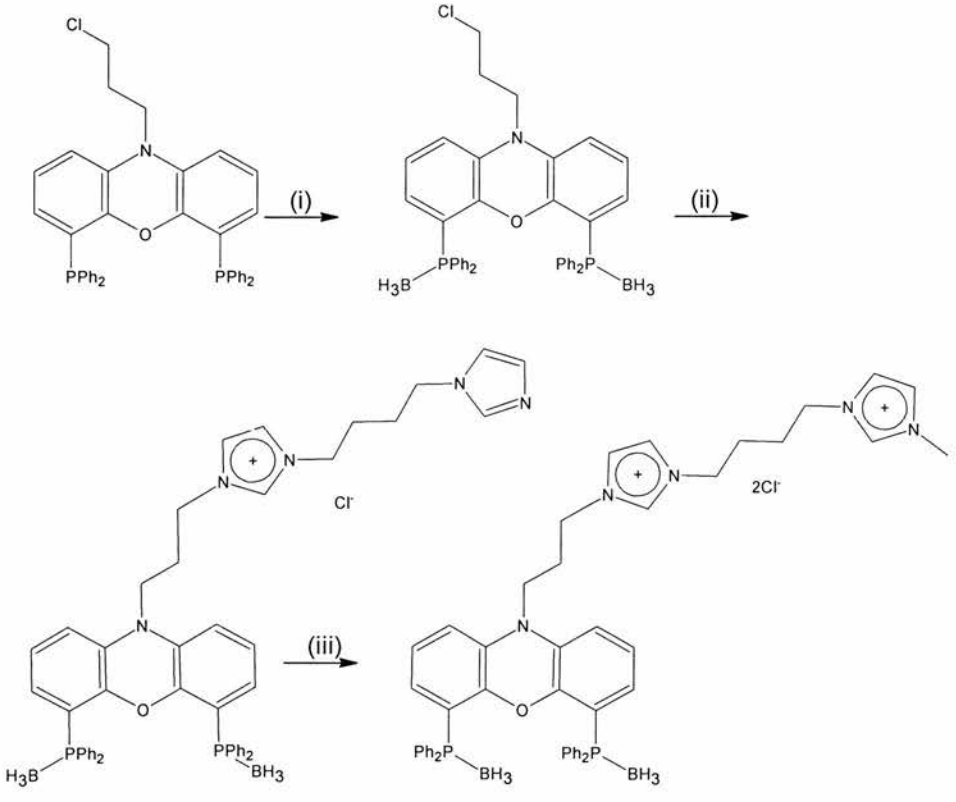
The other reason for the reaction not to go into completion was the fact that maybe the nixantphos was not fully deprotonated in the first instance, though the deprotonation

is expected to be instantaneous. Petrassi *et al* [17] refluxed the deprotonation of the N-H from phenoxazine, which is the starting material for synthesizing nixantphos. They must have realized that carrying the deprotonation at room temperature was not enough to deprotonate all of phenoxazine. The reaction was, therefore, repeated with the deprotonation of the nixantphos using NaH being run for 1 hour under reflux. After refluxing the reaction for 1 hour, a solution of compound **83** in THF was added and the reaction was refluxed for 3 days using 2 mole equivalents of nixantphos. After 3 days, a similar reaction work-up was followed and the ^{31}P NMR spectrum showed four signals with the ones at -19 ppm (PPh_2, singlet) and -145 ppm (PF_6^-, septet) the dominant ones. The integration was about 2:1 PPh_2:PF_6. The integration was not perfectly 2:1, suggesting a little bit more of the PPh_2 signal, which is nixantphos. So, the oily product was dissolved in dichloromethane and diethyl ether was added to only precipitate out the product, leaving excess nixantphos in solution. After two diethyl ether product precipitation, the integration was found to be rather 1:4 PPh_2:PF_6, which suggested that the two signals could have been from two separate compounds, not from the resulting product. The diethyl ether washing was repeated several times and every time the PPh_2 peak was growing small relative to the $PF6^-$. This meant that the oily compound **83** just trapped nixantphos within it and it means that during the diethyl ether wash, the nixantphos was washed out leaving the ionic compound **83**.

The conclusion was that no reaction took place even after 3 days. Most probably the imidazolium cations on compound **83** are interfering with the reaction but the mechanism of interference is not known as yet. That is the only reason, which can be given at this stage. The alkylation of nixantphos was done in section 3.2.3 and 3.2.4

above with bromine as a leaving group and no problems with regards to the reaction were encountered. Iodine was expected to be an even better leaving group, thus the reaction was expected to proceed very fast.

3.3.8 Alkylation of 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole with Borane protected 10-(3-chloropropyl)nixantphos



Scheme 3.22 (i) Borane-THF complex; (ii) 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole; (iii) Methylchloride

In synthesizing 10-(3-chloropropyl)nixantphos (Scheme 3.9), it was noted that one of the side reactions was quaternization at phosphorus by 1-bromo-3-chloropropane

since an excess of 1-bromo-3-chloropropane was used and the reaction was refluxed (THF). Step iii of Scheme 3.22 uses an alkylhalide under reflux of which might lead to quaternization of the phosphine as it was observed during the synthesis of 10-(3-chloropropyl)nixantphos. The alkylation or quaternization of the phosphines would lead to two ionic species in solution, which would lead to separation problems. To avoid the formation of such a side product, we proposed to protect the phosphine groups with borane.

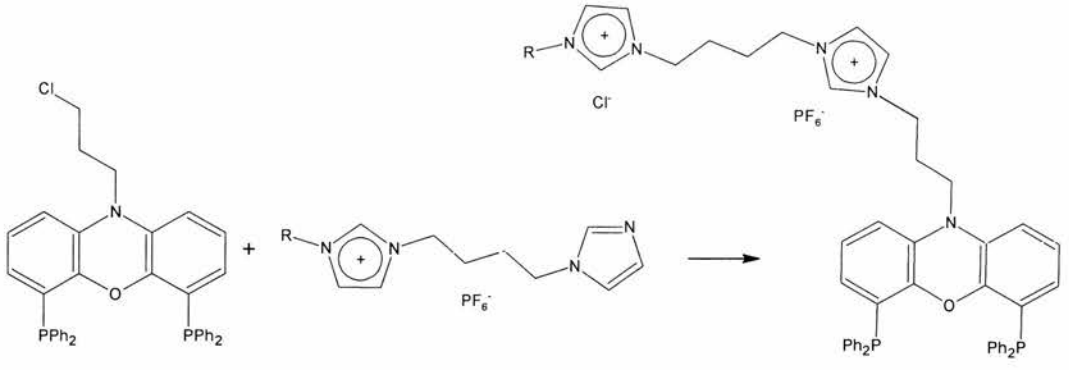
The borane protection was done in THF. 10-(3-Chloropropyl)nixantphos was dissolved in dry THF and a 1.2 mole equivalent of the Borane-THF complex (1M solution in THF) was added. The reaction was monitored by ^{31}P NMR spectroscopy, which showed that the reaction was over instantaneously. There was a phosphorus signal shift from -18 to -24 ppm, which was the evidence that the phosphine groups were successfully protected. The solvent THF was then evaporated. The deprotection step uses diethyl amine under reflux and 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole is a amine as well. It was thought that there was possibility that imidazole and its analogy might deprotect the phosphine groups.

So, we had to do a test reaction using 1-methylimidazole since it has been shown in Scheme 3.9 that the reaction does proceed to give the desired product. The borane protected 10-(3-chloropropyl)nixantphos was used in situ by dissolving it in toluene and 1-methylimidazole was added. The reaction was refluxed overnight. The reaction was monitored by ^{31}P NMR spectroscopy and it was found that at the end of the reaction, there were two phosphorus signals at -18 ppm and -24 ppm. This suggested

that 1-methylimidazole does deprotect the phosphine groups, since the signal at -18 ppm is characteristic of unprotected phosphine groups with a xantphos type backbone.

It was concluded that 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole will behave the same way as 1-methylimidazole by deprotecting the phosphine groups. So, the deprotection will lead to more than one ionic product, which will lead to separation problems.

3.3.9 Alkylation of an ionic diimidazole compound



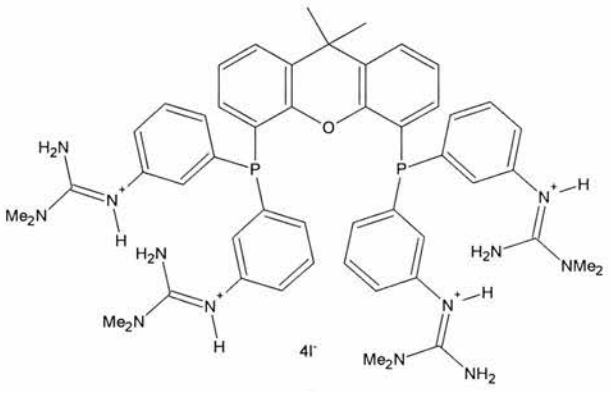
Scheme 3.23 R = Hexyl group

Given that the quaternization of the other imidazole moiety on compound **82** was successfully carried out in acetone to give compound **83** in

Scheme **3.21** above, it was thought that compound **84** could be synthesized in a similar way using 10-(3-chloropropyl)nixantphos together with compound **82** in acetone. It was rather found that 10-(3-chloropropyl)nixantphos does not dissolve in acetone. We then decided to use a two solvent reaction mixture by dissolving 10-(3-chloropropyl)nixantphos in toluene and compound **82** in acetone and then mixing the

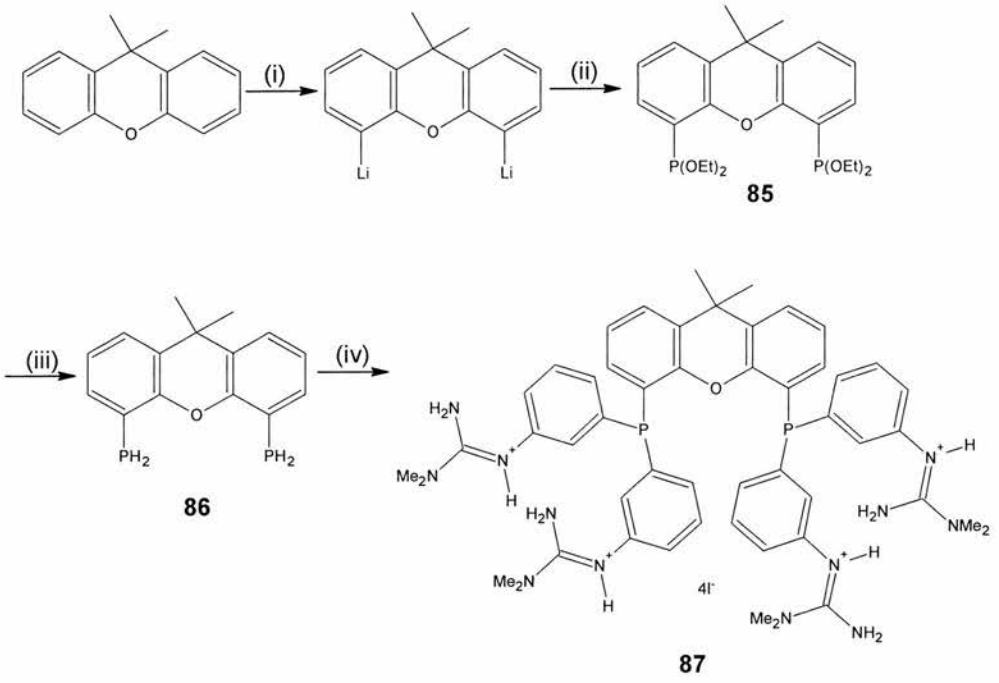
two solutions. 10-(3-Chloropropyl)nixantphos was dissolved in the minimal amount of toluene and then the reaction was carried out in acetone by refluxing overnight. The reaction was monitored by TLC. After refluxing overnight, the reaction had not taken place. This was also confirmed by ^{31}P and ^{1}H NMR studies. Using toluene might have interfered with the alkylation reaction as we have observed that the alkylation of imidazole type compounds prefer more polar solvents.

3.4 Synthesis of a cationic phosphine ligand with phenylguanidininium modified xanthene moiety



87

Ligand **87**, with $[Rh(acac)(CO)_2]$ as a catalyst precursor, has been reported to give high selectivity to linear aldehyde (TOF = 58 h^{-1}, yield = 44 %, n:iso ratio = 18) in the hydroformylation of 1-octene in BMIM PF_6 solvent[18]. The catalyst could be reused at least 4 times. Rhodium leaching was found to be less than 0.07 % of the overall rhodium loading. The guanidinimium moiety attached was reported to be just a solubilizer of the catalyst into the ionic liquid as it was found that the guanidinium does not influence the known positive effect of the xantphos ligand (R = phenyl groups) on regioselectivity of the reaction. It is reported that the steric and electronic properties of arylphosphines are not significantly changed by introducing polar groups like SO_3^-, PO_3^{2-} and guanidinimium in the positions meta or para to the phosphorus[19].

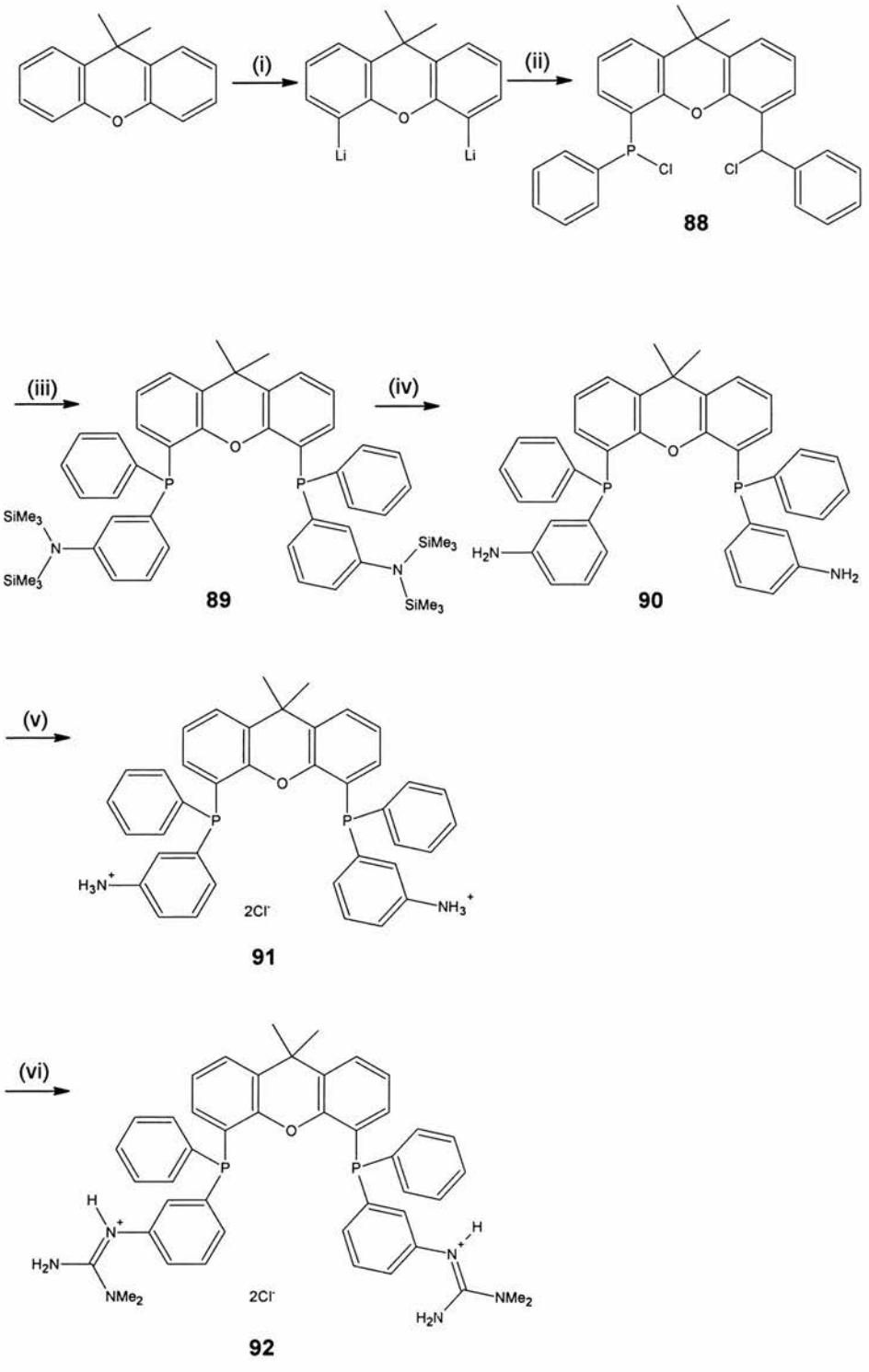


Scheme 3.24 (i) n-BuLi, TMEDA (Diethyl Ether); (ii) Chlorodiethylphosphite; (iii) $LiAlH_4$ (THF); (iv) HCl, Dimethylcynamide

The ligand synthesis procedure is as shown in Scheme 3.24, although details have not been published. We tried to synthesis ligand **87** using the route in Scheme 3.24. The synthesis was tried three times. The first time, the ^{31}P NMR spectroscopy showed four distinct peaks at 151 ppm, 149 ppm, 140 ppm and 132. This suggested that compound xanthene was not fully dilithiated or the dilithiated xanthene was not fully converted to **85**. Steps i and ii were run for 16 hours each. Phosphites (compound 30), like phosphines, are usually air sensitive, so the different compounds could not be easily separated by chromatograph. It was thought rather to proceed with step ii, which was the reduction of the phosphonite to a primary phosphine. After the reduction step, peaks at 150 ppm and 140 ppm disappeared and new peaks appeared at –50 ppm, -100 ppm, –140 ppm and 80 ppm. From the literature, primary phosphines usually have

chemical shifts around –120 ppm and from this, the product was between the peaks at –100 ppm and –140 ppm. The peak at 80 ppm intensified rather than disappearing. It was suggested that we switch off the hydrogen decoupler. Switching the decoupler off means that phosphorus would couple to the directly attached hydrogen atoms to give triplets with large J_{PH} (*ca.* 700 Hz) The decoupler was switched off but no triplet at either –100 ppm or –140 ppm appeared. That was an indication that we do not have the desired primary phosphine. The sec-BuLi used was noticed to contain precipitation, which usually suggests sec-BuLi decomposition. A new batch of sec-BuLi, which did not have any precipitation, was used and the similar procedure was followed. The same was observed.

Again we thought of starting the synthesis afresh but using a different approach. It was decided that we use n-BuLi and reflux for about 1 hour and then stir the solution for about 6 hours. The ^{31}P NMR spectroscopy showed the same results as found previously. It was then decided that more of the chlorodiethylphosphite be added to the solution and stirred overnight. After stirring overnight, no improvement could be seen.



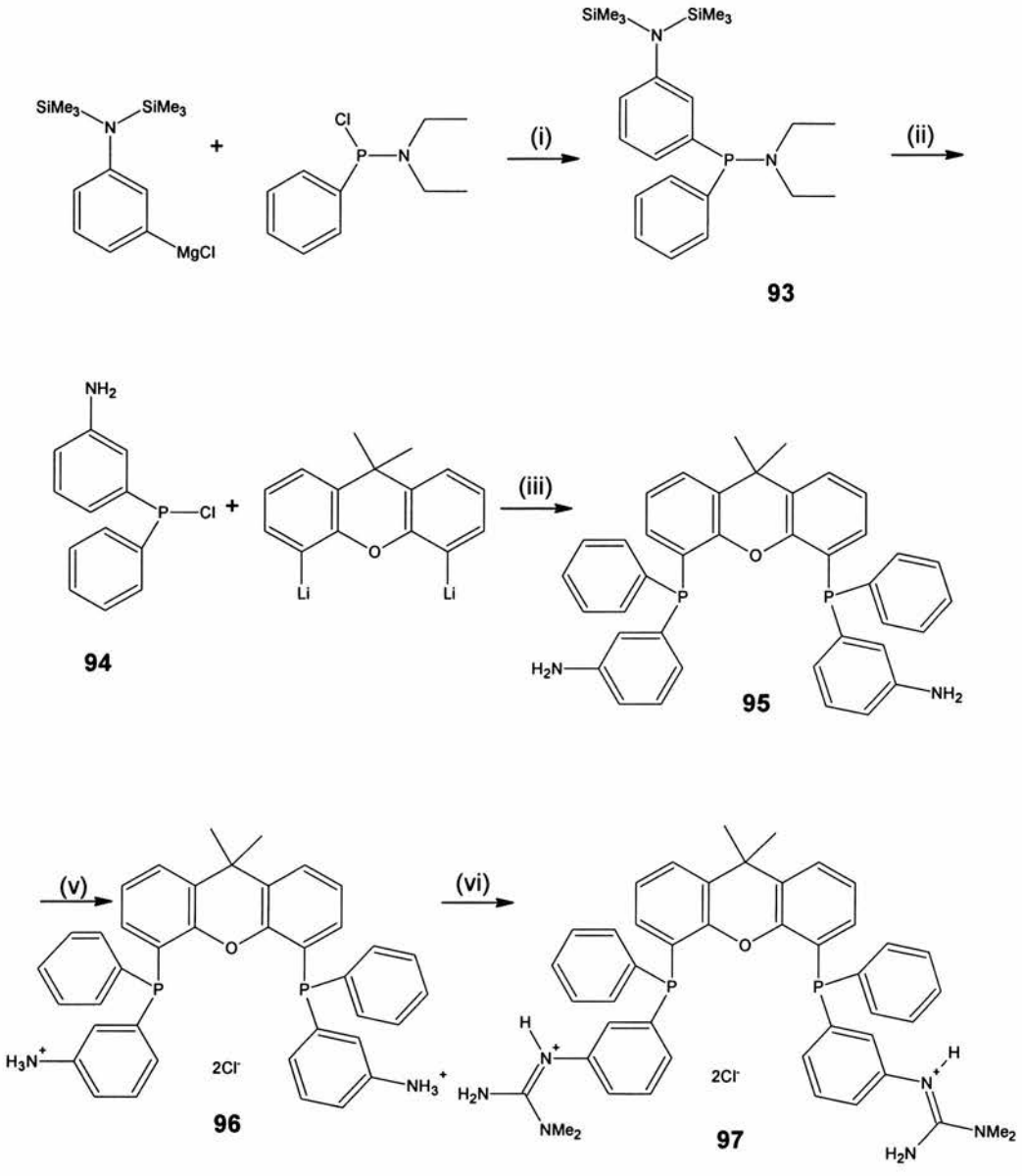
Scheme 3.25 (i) n-Buli, TMEDA (Diethyl Ether); (ii) Dichlorophenylphosphine; (iii) (3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesisium chloride; (iv) Water work-up; (v) HCl solution in diethyl ether; (vi) Dimethylcynamide

After trying the procedure shown in Scheme 3.24 without any success, we tried another route. The route is outline in Scheme 3.25. The idea was to react the dilithiated xanthene species with dichlorophenyl phosphine (step ii) selectively to give compound **88** and then react compound **88** with (3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesisium chloride to give compound **89**. A water work-up would give compound **90**, which when treated with HCl would give compound **91**. Hessler and Stelzer[20] have demonstrated steps iii to vi with a different backbone from xanthene.

Step ii was found to be messy with more than three phosphorus signals i.e. 163 ppm, 160 ppm 25 ppm and many small insignificant peaks between 140 and 150 ppm. The separation was difficult since the desired product was air and moisture sensitive. We had to think about another way of achieving compound **92**.

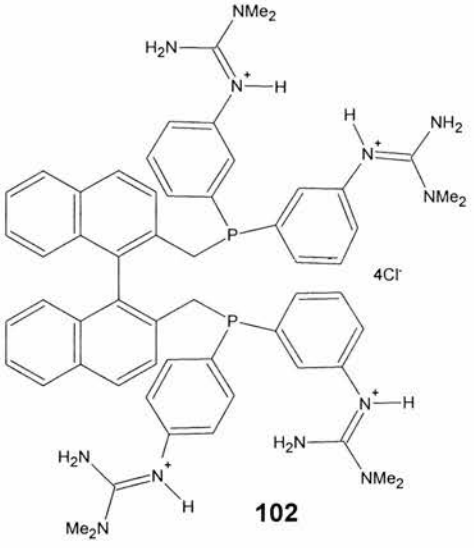
One reactive chlorine of dichlorophenylphosphine can be protected by reacting dichlorophenylphosphine with ½ mole equivalent of dimethyl/ethylamine to give chloro-(dimethyl/ethylamino)phosphine[21]. Then, chloro-(dimethyl/ethylamino)phosphine is reacted with (3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesisium chloride as shown by Hessler and Stelzer[20] to give compound **93**. Compound **93** is then treated with HCl to give compound **94**, which is then reacted with dilithiated xanthene to give compound **95**. Compound **95** is treated with HCl to give the anilinium phosphine **96**, which is then reacted further with dimethylcyanamide to give the guanidium phosphine **97**.

Steps i and ii (Scheme 3.26) were carried out and compounds **93** and **94** were isolated clean. The problem was encountered with step iii, which was found to be messy. More than one phosphorus signals were observed at -13.56 ppm, -13.20 ppm and 24.95 ppm. On the TLC plate, the spots were almost on top of each other, which made it difficult for the product to be purified by column chromatography.



Scheme 3.26 (i) THF; (ii) xanthene, n-BuLi, TMEDA (diethyl ether); (iv) HCl solution in diethyl ether; (v) Dimethylcynamide

3.5 Synthesis of a guanidinium type NAPHOS



102

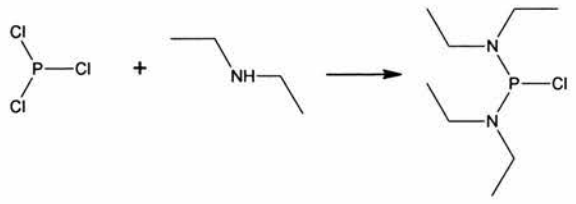
Bahrmann *et al*[22] sulfonated NAPHOS in order to make it water soluble so as to be used in aqueous biphasic hydroformylation of propene. This ligand system was to be compared to TPPTS Ruhrchemie/Rhone-Poulenc process. NAPHOS was found to be the most active, selective ligand for the rhodium hydroformylation of propylene. NAPHOS was found to be 10 times (160 mol aldehyde per mol Rh as opposed to 16 mol aldehyde per mol Rh) more active and 5 times (99:1 as opposed to 20:1 l:b ratio) more selective than TPPTS.

Our group then decided to try this ligand system in IL-scCO_2 biphasic system. Since the main aim of this thesis was to identify or design a catalyst system, which will give high turnover frequencies and high selectivity. This ligand system appealed to us. Dr Paul Webb tried to synthesize BINAS and he encountered problems when coming to the sulfonation of NAPHOS. We decided to rather use guanidinium moiety as opposed to the sulfonate group.

It was thought that lithiating 2.2'-bis(bromomethyl)-1.1'-binaphthyl would be easier than lithiating 2.2'-dimethyl-1.1'-binaphthyl. The latter is more likely to give more than one lithiated species, leading to separation problems.

2.2'-Dimethyl-1.1'-binaphthyl was lithiated as shown in Scheme 3.28 and *N,N,N',N'*-tetraethylphosphorodiamidous chloride was added. The solution was monitored by ^{31}P NMR spectroscopy. The ^{31}P NMR spectrum showed one signal at 88.58 ppm, from compound **98**. The solution of compound **98** in diethyl ether was treated with HCl solution in diethyl ether (step ii). The resulting ^{31}P NMR spectrum of compound **99** showed a signal at 180.23 ppm. There were other small signals between 150 ppm and 180 ppm, which were very insignificant. It was difficult to purify compound **99** except by distillation. Kügelrohr distillation was carried out but compound **99** seemed to decompose. It was decided that compound **99** be reacted in situ (step iii). 3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesisium chloride and compound **99** were reacted and gave compound **100**. Step iii in Scheme 3.29 was found to be cleaner than what was observed in Scheme 3.26 above. There were four phosphorus signals i.e. -13.51, -13.34, 60.01 and 61.20 ppm with a 1:5:1:1 ratio. The prominent one was thought to be the desired product with the one adjacent to it being the monophosphine substituted 2.2'-dimethyl-1.1'-binaphthyl. Compound **100** was then treated with HCl to give compound **101**, which was reacted with dimethylcynamide to give compound **102**. Step v was found to yield a lot of side products and the product separation was found to be difficult since most of the compounds were ionic.

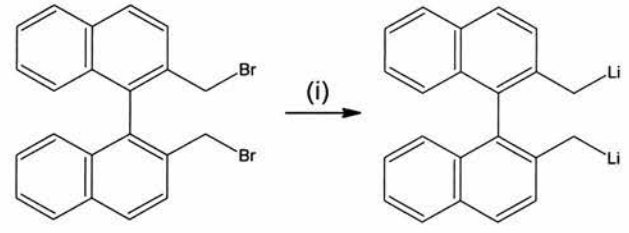
STEP I



N,*N*,*N*',*N*'-tetraethylphosphorodiamidous chloride

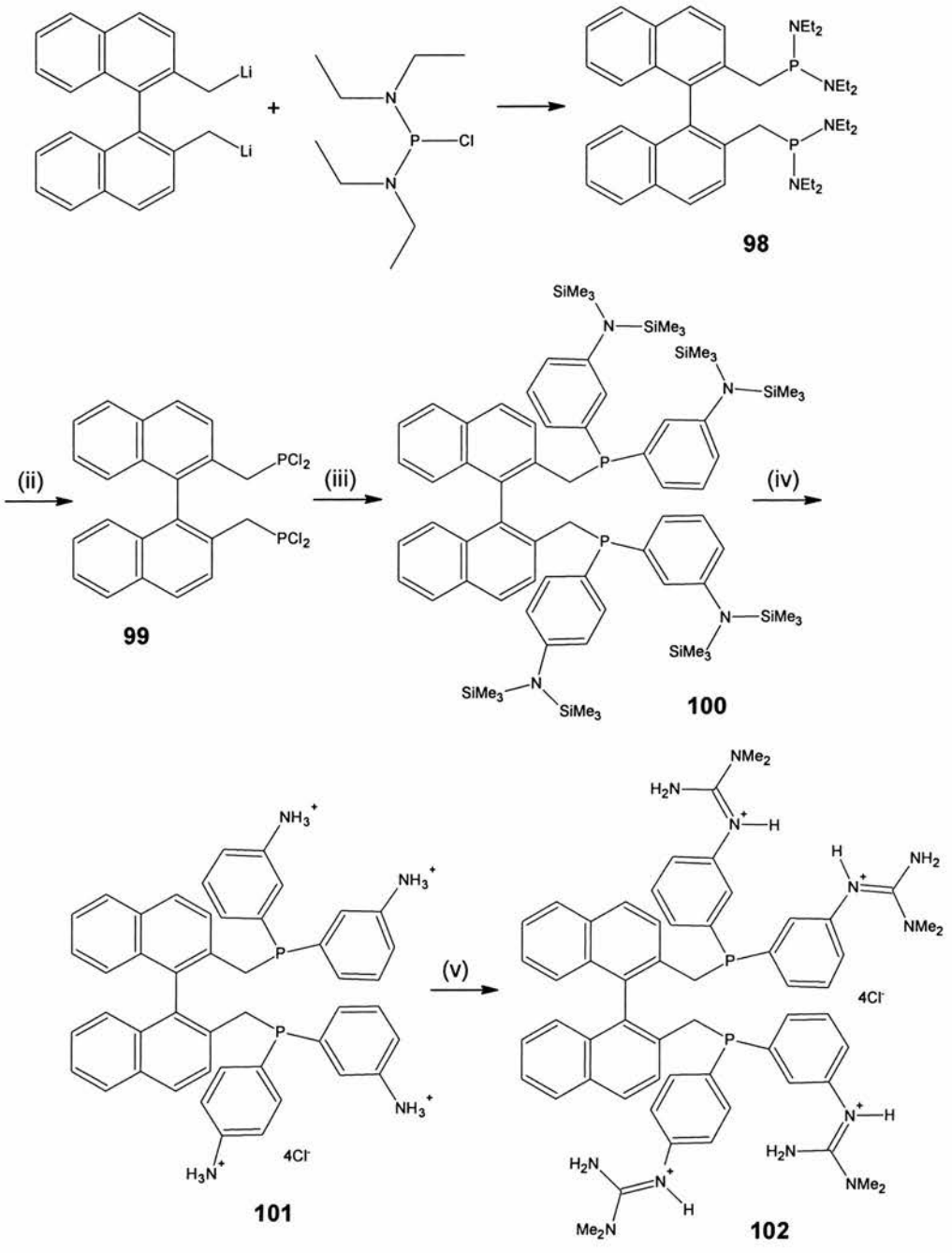
Scheme 3.27 *N*,*N*,*N*',*N*'-tetraethylphosphorodiamidous chloride

STEP II



Scheme 3.28 (i) n-BuLi (diethyl ether)

STEP III



Scheme 3.29 (ii) HCl solution in diethyl ether; (iii) 3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesisium chloride; (iv) HCl solution in diethyl ether; (v) Dimethylcynamide

3.6 Conclusions

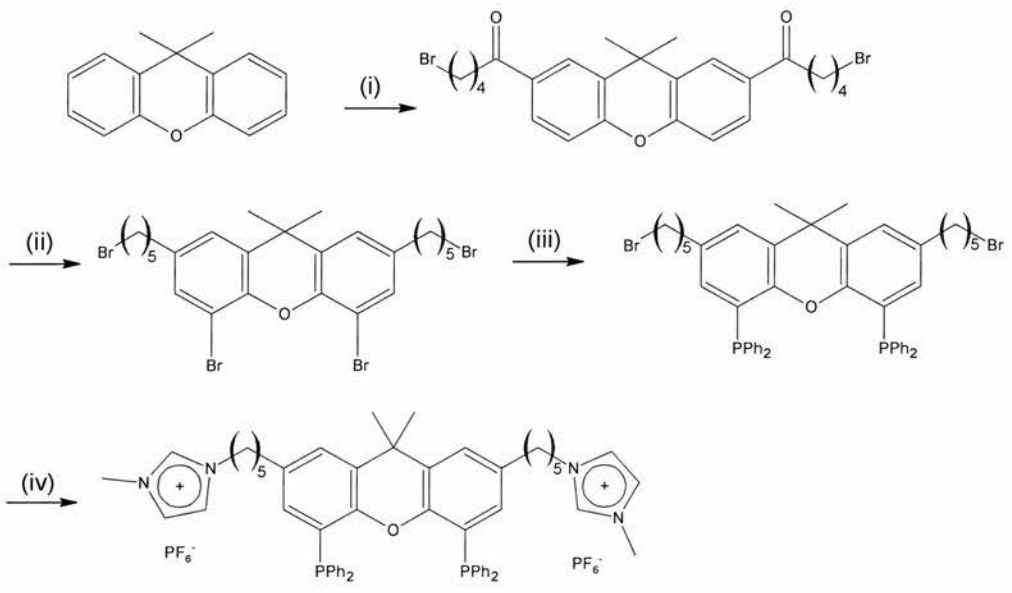
[NixantphosPMIM][Cl] was successfully synthesized and was used in the IL-$scCO_2$ biphasic hydroformylation of 1-octene (See Chapter 4). Rhodium leaching was found to be about 200 ppb which was still high, giving that Webb *et al* reported rhodium leaching as low as 10 ppb with [TPPMS][PMIM]. Rhodium leaching is a function of ligand leaching or ligand affinity to dissolve in $scCO_2$. So, to reduce the rhodium leaching it was felt that a higher ionic character would be required, thus giving less affinity to dissolve in $scCO_2$. We attempted to attach two imidazolium moieties instead of one but a lot of problems were encountered. Some of the problems encountered were solubility of reagents in the same solvent and product purification. Ionic compounds can only be separated easily from one another by crystallization and for a compound to be crystallized out, it needs to be more than 90 % pure. It was also found that alkylation of amines is solvent sensitive, hence the solubility problem.

We also tried to synthesize the cationic phosphine ligand with phenylguanidininium modified xanthene moiety synthesized by Wassercheid *et al*[3]. We could not synthesize it according to the reported experimental procedure, perhaps because key details of the synthesis have not been published The problems encountered included separation and purification of the reaction intermediates. Different routes were explored and the same problem was also encountered.

We also tried to synthesize a guanidinium type NAPHOS and we encountered the same problems.

3.7 Future Work

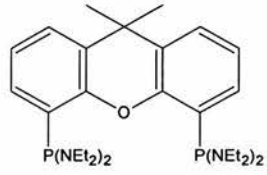
Bronger *et al*[8] reported a dicationic diphosphine type ligand. The next step for our work would be to follow their experimental procedure to synthesize a dicationic xantphos type ligand (Scheme 3.30).



Scheme 3.30 (i) $AlCl_3$/5-bromovaleric chloride; (ii) (a) $InCl_3$/chlorodimethylsilane, (b) Br_2; (iii) (a) n-BuLi and TMEDA, (b) Chlorodiphenylphosphine; (iv) 1-Methylimidazole; (v) $NaPF_6$

The next step in trying to synthesize a cationic phosphine ligand with phenylguanidininium modified xanthene moiety and a guanidinium type NAPHOS is to try and isolate 4,5-(Bis[bis-diethylamino]phosphonito)-9,9-dimethylxanthene and compound **43** (Scheme 3.29) by crystallization. Goertz *et al*[23] managed to isolate 4,5-(Bis[bis-diethylamino]phosphonito)-9,9-dimethylxanthene by crystallization. This

will eliminate side products in the subsequent steps, thus solving the separation and purification problems.



4,5-(Bis[bis-diethylamino]phosphonito)-9,9-dimethylxanthene

3.8 References

1. Wasserscheid, P.; Keim, W. *Ang. Chem.-Int. Ed.Engl.* **2000,** *39*, 3773-3789.
2. Chauvin, Y.; Mussmann, L.; Olivier, H. *Ang. Chem.-Int. Ed. Engl.* **1996,** *34*, 2698-2700.
3. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Commun.* **2001**, 451-452.
4. van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *Organometallics* **2000,** *19*, 872-883.
5. van Ameijde, J.; Liskamp, M. J. *Tetrahedron Lett.* **2000,** *41*, 1103.
6. Zong, K.; Reynolds, J. R. *J. Org. Chem.* **2001,** *66*, 6873.
7. Shirley, D. A.; Sen, K.; Gilmer, J. C. *J. Org. Chem.* **1961,** *26*, 3587.
8. Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Chem. Commun.* **2002**, 3044.
9. Kashima, C.; Haranda, Y.; Hosomi, A. *Heterocycles* **1993,** *35*, 433.
10. Manoharan, T. S.; Brown, R. S. *J. Org. Chem.* **1988,** *53*, 1107.
11. Tanouchi, T.; Kawamura, M.; Ohyama, I.; Kajiwara, I.; Iguchi, Y.; Okada, T.; Taniguchi, K.; Miyamoto, T.; Hayashi, M. *J. Med. Chem.* **1981,** *24*, 1139.
12. Kikugawa, Y. *Synthesis* **1981,** *2*, 124-125.
13. Matthews, D. P.; McCarthy, J. R.; Barbuch, R. J. *J. Heterocyclic. Chem.* **1988,** *25*, 1845.
14. Kimura, T.; Takase, Y.; Hayashi, K.; Tanaka, H.; Ohtsuka, I. *J. Med. Chem.* **1993,** *36*, 1630-1640.
15. Ma, J.; Liu, J.; Xing, Y.; Jia, H.; Lin, Y. *J. Chem. Soc. Dalton Trans.* **2000,** *14*, 2403.
16. Luo, M.; Guo, S.; Zhou, C.; Xie, R. *Heterocycles* **1995,** *41*, 1421.
17. Petrassi, H. M.; Klabunde, T.; Sacchettini, J.; Kelly, J. W. *J. Am. Chem. Soc.* **2000,** *122*, 2178.
18. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Comm.* **2001**, 451.
19. Machnitzki, P.; Tepper, M.; Wenz, K.; Stelzer, O.; Herdtweck, E. *J. Organomet. Chem.* **2000,** *602*, 158.
20. Hessler, A.; Stelzer, O. *J. Org. Chem.* **1997,** *62*, 2362.
21. Bestmann, H. J.; Lienert, J.; Heid, E. *Chem. Ber.* **1982,** *115*, 3878.
22. Bahrmann, H.; Bach, H.; Frohning, C. D.; Kleiner, H. J.; Lappe, P.; Peters, D.; Regnat, D.; Hermann, W. A. *J. Molecular Catal. A* **1997,** *116*, 49.
23. Goertz, W.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Vogt, D. *Chem. Eur. J.* **2001,** *7*, 1614.

4 Continuous flow hydroformylation of long chain alkenes in Supercritical fluid-ionic liquid biphasic systems using [nixantphosPMIM][Cl]

4.1 Introduction

Cole-Hamilton and co-workers[1], for the first time demonstrated simultaneous product extraction in a continuous hydroformylation catalytic reaction using a $scCO_2$/IL biphasic system. By a careful selection of the ionic liquid, the catalyst and the reaction parameters, assisted by reactor design, they have shown that the system can be used for the hydroformylation of long chain alkenes (they have demonstrated up to 1-dodecene) at rates (TOF = 517 h^{-1}) comparable with those found in commercial systems (e.g TOF from 556 to 770 h^{-1} in propene[2] hydroformylation). Using [PMIM][TPPMS] in [OctMIM][NTf_2], rhodium leaching was generally found to be about 0.012 ppm, which is equivalent to 1 g of rhodium in approximately 40 tons of product throughout the steady- state reaction. The long-term stability of the catalyst was tested over 80 hours. The solution was kept at the reaction temperature and pressure throughout this period although the substrate was flowing on and off for about 40 of the 80 hours. After 80 hours, the autoclave was held at temperature and pressure (product, excess CO/H_2 still present) for 4 weeks. The substrate flow and product collection were restarted to give identical rates and product distributions to those that were obtained immediately prior to switching off the flow. After a further 8 hours, the catalyst solution was removed from the autoclave and analysed by ^{31}P NMR spectroscopy. It was found that a significant proportion of the ligand had been oxidised.

Of all the problems associated with this system, low l:b ratios are of key concern. They found l:b ratio of about 3, which translates to a linear aldehyde selectivity of ca. 75 %, whereas, values >80 % are desirable for commercialisation. We tried to address

this problem in chapter 2, by using a cobaltocenium based diphosphine, which is reported to give high selectivities, but without any success. Under this section, we will further address this problem by using an ionic nixantphos complex.

4.2 Hydroformylation reactions with [nixantphosPMIM][Cl] ligand in IL

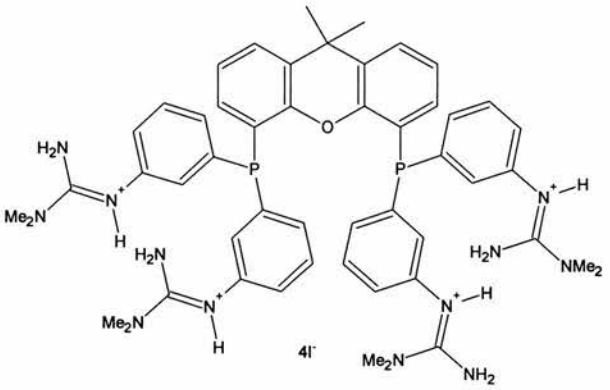
van Leeuwen *et al*[3] have developed a range of ligands based on the xanthene core (xantphos ligands) and shown that they give very high selectivities to linear aldehyde in hydroformylation reactions. Our strategy has been to design a new member of this series such that it retains the high selectivity but is ionic so that it is soluble in the ionic liquid phase. Some researchers have synthesised a variety of ionic analogues of xantphos and carried out hdroformylation reactions in ionic liquids.

Wasserscheid *et al*[4] synthesised a guanidinium-modified xantphos ligand **22** and carried out a hydroformylation reaction of 1-octene in [BMIM][PF_6]. The conversion was found to be steadily increasing as the catalyst was reused (from 10,6 % on the 1st run to 44.3 % on the 7th run) and a much improved l:b ratio of 20:1 was obtained. The increase in conversion was explained to be due to the formation of the active catalyst species with time. Rhodium leaching was found to be less than 0.07 %. Dupont *et al*[5] also investigated the use of xanthene type ligands (sulfonated xanthene **24**) in [BMIM][PF_6] for the hydroformylation of 1-octene. The Rh/sulfonated xantphos could be recycled and almost complete olefin conversion (Yield = 99 %, TOF = 41 h^{-}

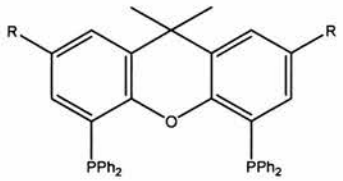
[1], l:b = 1.7) was obtained by increasing the reaction time from 4 to 24 hours. The l:b ratio increased to 42 when the ligand:Rh ratio was increased to 5.

van Leeuwen *et al*[6] recently reported the use of ligand **25** for the hydroformylation of 1-octene at 100°C under 17 bar CO/H_2 (1:1) in [BMIM][PF_6]. At an approximately 30 % conversion, the reaction was stopped, vented, cooled and the product decanted. The IL/catalyst solution was used for seven consecutive recycling experiments. A steady rate was observed from the 4th cycle, which meant that it needed about 4 cycles for the catalyst to be fully activated. The catalyst activity (TOF of about 100 h^{-1} on average) was found to be low, though the l:b ratio (40 on average) was high. A red colour of the ionic solution and the low catalyst activity observed was thought to be due to the formation of a dimeric species. This was overcome by increasing the hydrogen partial pressure, whilst keeping that of CO constant. As a result, the catalytic activity was enhanced threefold, to TOFs greater than 300 h^{-1}, with a l:b ratio of 50. The isomerisation increased from 8 % to about 15 %. No phosphorus (< 100 ppb) or rhodium (< 5 ppb) leaching was observed. The catalyst was found to be extremely air stable. An experiment was carried out after the catalyst solution had been exposed to air for 14 days and it retained its activity albeit with slightly higher isomerisation. The increased in isomerisation was thought to be due to the formation of acidic impurities caused by anion hydrolysis with moisture from air.

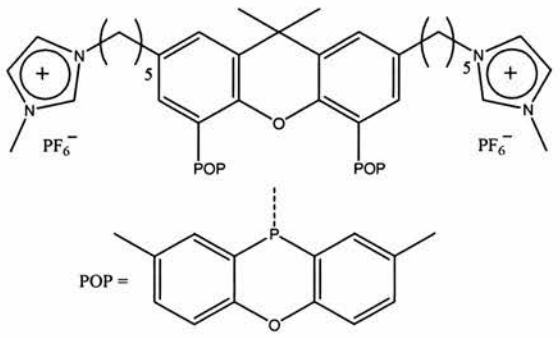
Recently a full paper by Bronger *et al*[7] has been published. They have reported an improved TOF (TOF = 6200 h-1) by increasing the stirring rate and reducing the ligand concentration. The isomerisation was found to be 13 %.



22



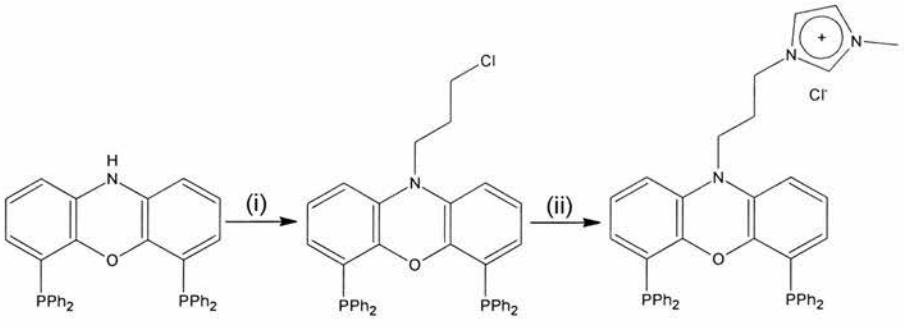
24 R =SO_3Na, Sulfonated Xantphos



25

The ([NixantphosPMIM][Cl]) ligand (as shown in Scheme 4.1), which has the nixantphos core connected to an imidazolium cation by a propyl spacer, was synthesised by the reaction of the sodium salt of nixantphos with 1-bromo-3-chloropropane followed by reaction of the chloroalkyl moiety with N-methylimidazole (refer to chapter 3). This ligand was found to be soluble in ionic liquids. The hydroformylation reaction of 1-octene was carried out in

[OctMIM][NTf_2], as it was found that [OctMIM][NTf_2] is the best ionic liquid when using [PMIM][TPPMS] as a ligand in chapter 2 (Alternative Ionic Liquids section) .



10(3-Chloropropyl)nixantphos [NixantphosPMIM][Cl]

61

(i) NaH (THF), 1-Bromo-3-chloropropane; (ii) N-methylimidazole

Scheme 4.1 Synthesis of an ionic analogue of Nixantphos ([NixantphosPMIM][Cl])

[$Rh(acac)(CO)_2$] was weighed into a 50 cm^3 autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [NixantphosPMIM][Cl] in [OctMIM][NTf_2], was injected into the autoclave with the autoclave under a slight positive syngas pressure. The autoclave was charged with a H_2/CO (1:1) gas mixture to the required reaction pressure and heated up to reaction temperature. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After 1 hour, 1-octene (3 cm^3) was injected through a liquid pump and the reaction was allowed to proceed for 1 hour. The autoclave was then cooled down, opened and the product was extracted from the ionic solution with 40 cm^3 n-hexane. The mixture was analysed by GC and the results are reported in Table 4.1 below.

Table 4.1 Rhodium catalysed hydroformylation of 1-octene in [OctMIM][NTf_2] using [nixantphosPMIM][Cl] as a ligand[a]

Entry	P/bar CO/H_2	Total Conversion/%	Conversion to Aldehydes/%	Isomerisation/%	n:iso
1	10	94.6	41.4	49.2	8
2[b]	20	5.88	3.67	1.92	12
3[c]	20	94.2	83.1	9.9	28
4	40 (200)[d]	60.3	53.4	4.9	37
5	40 (200)[e]	63.3	56.02	5.60	53

[a] *Conditions: [Rh(acac)(CO_2)] (mmol), ligand/Rh = 2, volume 1-octene = 3.15 cm^3, H_2/CO = 1, t = 1 hour, T = 100 °C, Volume OctMIM NTf_2 = 5 cm^3.*

[b] *T = 80 °C, low conversion because of lowering the temperature*

[c] *The pressure was topped up to 20 bar once it had dropped tot 10 bar (almost run at constant 20 bar)*

[d] *Liquid CO_2 was added to make up the reaction pressure to 200 bar*

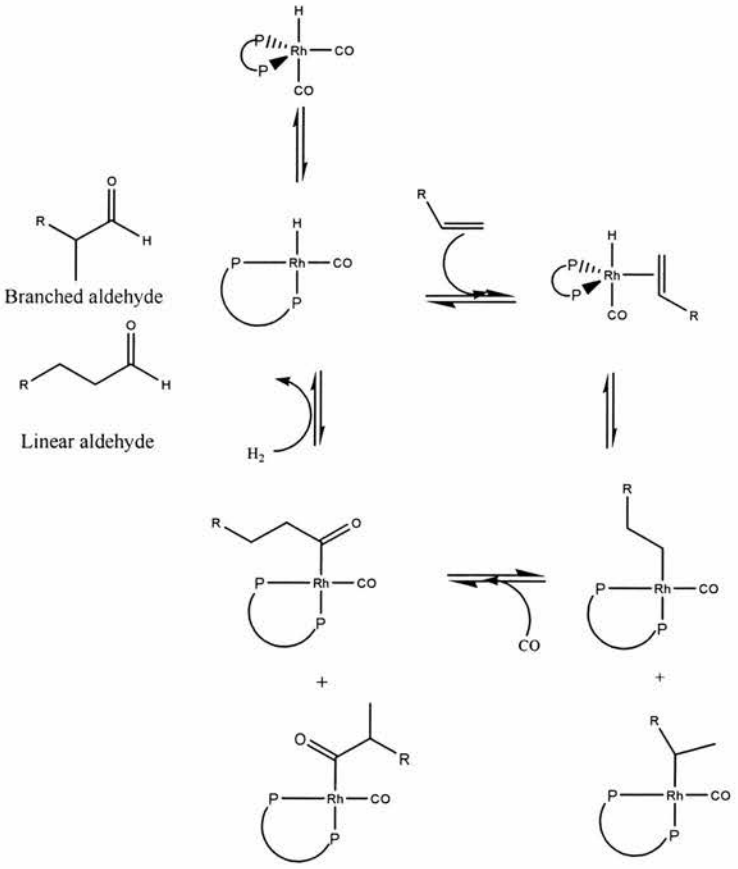
[e] *Repeat of run 4*

At 10 bar pressure, approximately 50 % of 1-octene was isomerised to internal alkenes, whereas only about 10 % 1-octene was converted to internal octenes where the pressure was increased to 20 bar (Table 4.1, experiments 1 and 3). This suggests that the hydroformylation reaction was starved of CO/H_2 at 10 bar. Under reaction conditions the rhodium alkyl complexes (Scheme 4.2) can give either migratory insertion forming the rhodium acyl complexes (Scheme 4.2) or ß-hydride eliminate to either form 1-alkene or 2-alkene. ß-Hydride elimination of the primary rhodium alkyl species is not productive as 1-alkene is reproduced. The branched (secondary) alkyl species, however, can give both the starting 1-alkene and the internal 2-alkenes via ß-

hydride elimination. For both complexes the ß-hydride elimination is competing with the migratory insertion reactions that lead to the product aldehyde. It has been reported that ß-hydride elimination for the branched (secondary) rhodium species is faster than for the primary rhodium species[8]. Thus, isomerisation rates (ß-hydride elimination for the branched rhodium species) will reduce the formation of the branched rhodium acyl species (i.e. branched aldehyde) to a larger extent than the linear rhodium acyl species. As a result the l:b ratio increases with the increase in isomerisation or vice versa, but in our case the decrease in isomerisation (from 50 to 10 %) leads to an increase in l:b (from 8 to 28). The amount of 1-alkene converted to 2-alkenes can be translated as branched aldehyde product since isomerised products seems to mostly result from ß-hydride elimination from the branched alkyl rhodium species. Increasing the reaction pressure increases the CO partial pressure, which forces the alkyl rhodium species to undergo CO insertion to form acyl rhodium species as opposed to ß-hydride elimination. This suggests that if you increase the pressure, one would expect the l:b ratio to drop as most of the branched alkyl rhodium species would be converted to acyl rhodium species, which converts to branched aldehydes.

When the pressure was increased from 10 to 20 bar (experiment 3), a drop in isomerisation rate was observed and an increased in l:b ratio, which is not in line with what Scheme 4.2 suggests in as far as the isomerisation mechanism is concerned. A possible explanation of the observed increase in l:b ratio and reduction in isomerisation as the CO/H_2 pressure is increased is that the linear alkyl forms very selectively through H migration onto the alkene. At high CO pressure it is trapped by migration onto coordinated CO and proceeds to give linear product. At lower CO

pressure, it has a long enough lifetime to undergo reversible β-hydride abstraction, sometimes giving the branched alkyl and moving towards the thermodynamic ratio of linear and branched alkyls. This will lead to an overall increase in the products proceeding down the branched reaction pathway, thus low l:b selectivity and to more isomerisation, since the low CO partial pressure favours β-hydride abstraction to give isomerised alkene over migration onto CO to give branched aldehyde.



Scheme 4.2 Rhodium hydroformylation catalytic cycle

One parameter to control isomerisation is temperature. It was decided to drop the temperature from 100°C to 80°C. Lowering the temperature slows down both isomerisation and hydroformylation as it is evident from experiment 2 in Table 4.1 above.

Table 4.2 Comparing different ionic xantphos analogues in ionic liquids used in the hydroformylation reaction of 1-octene at 100°C[a]

Ligand	Ionic Liquid	L:Rh	P/ bar	Time/ h	TOF[b] /h^{-1}	Isomerisation /%	l:b
22[4]	[BMIM][PF_6]	2	30	8	58	3.9	18
24[5]	[BMIM][PF_6]	4	15	24	32	21	13.1
25[6,7]	[BMIM][PF_6]	4	17	~1	318	13.3	49
61[c]	[OctMIM][NTf_2]	2	20	1	798	9.9	28

[a] *1-octene:Rh ratio is about 1000 for all the reactions.*

[b] *mole aldehydes per mole Rh per hour. Most TOFs have been calculated based on 30% conversion whereas ours is based on almost 100% conversion.*

[c] *[NixanphosPMIM][Cl]*

[NixantphosPMIM][Cl] ligand system (Table 4.2) gives result which are comparable with ligand 3, especially after Bronger *et al*[7] did reaction optimisation where they obtained TOFs of about 6200 h^{-1} in [BMIM][PF_6]. In chapter 2, it was found that [PMIM][TPPMS] performs better in [OctMIM][NTf_2] (conversion of about 80 %) than in [BMIM][PF_6] (conversion of about 10 %). This was attributed to mass transport limitations as arising from the different solubilities of 1-octene in the two ionic liquids. The results in Table 4.2 are may also be examined on a similar basis, as

one would expect at least ligands **22**, **24** and **25** to give similar results since they are similar ligands. The difference might be due to difference in solubilities in the ionic liquid. One would not expect that the different functionalities would dramatically affect the catalysis. The substrate solubility in [OctMIM][NTf_2] is thought to be higher than in [BMIM][PF_6] (chapter 2, section 2.2), hence higher activity with ligand **4** system as compared to the other ligand systems.

The product was extracted with n-hexane and no Rh/phosphine seemed to have leached to the organic layer just from the colour of the organic layer. This suggested to us that the catalyst would not be extracted with $scCO_2$ in the continuous flow system.

4.3 Hydroformylation in supercritical fluid-ionic liquid biphasic systems

Sellin *et al*[1] reported the hydroformylation of long chain alkenes (>C_5) in SCF-IL biphasic systems, which involved rhodium complexes of triarylphosphite ligands. The hydroformylation of 1-hexene was carried out in the ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF_6]) using triphenyl phosphite as the ligand for rhodium. In the absence of $scCO_2$, the rate of alkene consumption was high (conversion>99 %) but the selectivity to the desired aldehyde product was low (15.7 % with l:b ratio of 2.4) on account of the formation of large amounts of aldol condensation products. Carrying out the same reaction in the presence of $scCO_2$ reduced the reaction rate (conversion = 40 %) but increased both the selectivity to the

desired product aldehydes (83.5 %) and the l:b ratio (6.1). Similar linear selectivities have previously been observed using $Rh/P(OPh)_3$ in $scCO_2$ without an ionic liquid[9]. In this case the catalyst is insoluble in $scCO_2$, but still shows high activity. Presumably the reaction takes place in liquid $P(OPh)_3$ as the solvent, but the product is extracted by $scCO_2$. It appears that the main role of the $scCO_2$ in this case is to reduce the residence time of the product aldehyde in the catalyst solution and protect it from further reaction.

Before we carried out continuous flow reactions with [nixantphosPMIM][Cl], we carried out a batch reaction in the IL-$scCO_2$ biphasic system (Experiments 4 and 5 in Table 4.1). $[Rh(acac)(CO)_2]$ was weighed into a 50 cm^3 autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [NixantphosPMIM][Cl] in $[OctMIM][NTf_2]$ was injected into the autoclave with the autoclave under a slight positive syngas pressure. The autoclave was then charged with a 40 bar H_2/CO (1:1) gas mixture and heated up to 100°C. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After an hour, about 30 cm^3 liquefied CO_2 was pumped through an HPLC pump (equipped with a cooled head) to make up 200 bar reaction pressure. The reaction solution was allowed 1 hour to absorb $scCO_2$. Using an HPLC pump, 1-octene (3 cm^3) was pumped into the autoclave. The autoclave was isolated and the reaction was allowed to run for 1 hour. After the reaction was stopped, the autoclave was cooled to about -40°C and the CO_2 was slowly vented off for about 30 minutes. The autoclave was opened and the solution was extracted with 40 cm^3 n-hexane. The sample was analysed by GC.

From Table 4.1 (reactions 4 and 5) above, we notice a drop in conversion from 94.2 % to ~60 % with isomerisation less pronounced (about 5 % as compared 10 %) and n:iso ratio increasing (from 28 to about 40), when $scCO_2$ was introduced as a co-solvent. This was attributed to the fact that $scCO_2$ dilutes the CO/H_2 gas and olefin. The drop in isomerisation could be due to the fact that CO_2 improves the solubility of CO and H_2 in the ionic liquid. By increasing the solubility of CO in the ionic liquid that would have a similar effect to increasing the CO partial pressure. So the explanation given above concerning selectivities and isomerisation would hold. Looking at the two reactions, the selectivities seem to be very different when looking at the l:b ratios whereas the l:b ratio of 37 and 53 gives virtually the same percentage product linearity of about 98 %. So, one should be careful in reading a lot into l:b ratios as that be deceiving, especially when they are high.

The Rh\[nixantphosPMIM][Cl] system gives better l:b and uses far less ligand concentration than Rh\[PMIM][TPPMS] though less active (Table 4.3).

Table 4.3 Comparison between Rh\[PMIM][TPPMS] and Rh\[nixantphosPMIM][Cl] in $scCO_2$/[OctMIM][NTf_2] biphasic systems

Ligand System	L:Rh	%Conv	%Isom	l:b ratio
Rh\[PMIM][TPPMS]	16:1	88	<2	3.6
Rh\[nixantphosPMIM][Cl]	2:1	60	5	37

4.4 Continuous Flow Process

4.4.1 Brief Description of the Continuous Flow Process[10]

All continuous flow reactions were performed in the system shown schematically in Figure 4.1. The continuous flow system comprised a continuously stirred tank reactor (CSTR) (Hastelloy, 30 cm^3) fitted with a thermocouple (T1), pressure transducer (P2), two gas/liquid feed dip-tubes and an outlet port.

Carbon dioxide was delivered into the system to a constant pressure using an air driven liquid pump (LP2). Liquid substrates were delivered at a constant rate through HPLC pump (LP1) and CO/H_2 was delivered through an air driven intensifier (I) coupled to a rheodyne injection unit fitted with a pneumatic actuator (D). The liquid/gas substrates and CO_2 were passed through a check valve and into the CSTR through one of the dip-tubes and into the ionic liquid solution. The gas stream leaving the CSTR was then decompressed from operating pressure to 3-10 bar (PCV1) into a vessel (LCV1) where the majority of liquid fractions were collected. The gas stream was decompressed further to atmospheric pressure (PCV2) into a second collection vessel (LCV2) after which the gas stream was passed through a flow meter.

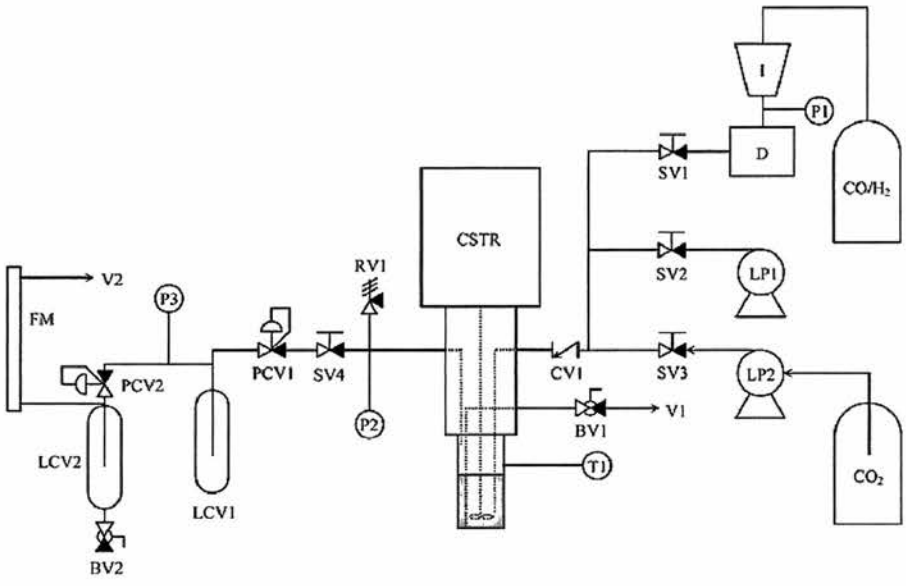


Figure 4.1[10] Reactor for continuous flow hydroformylation. CSTR Continuously stirred tank reactor, CV Check valve, D Dosimeter, FM Flow meter, I Intensifier, LCV Liquid collection vessel, LP Liquid pump, P Pressure transducer, PCV Pressure control valve, RV Relief valve, T Thermocouple, SV Shut-off valve, V Vent.

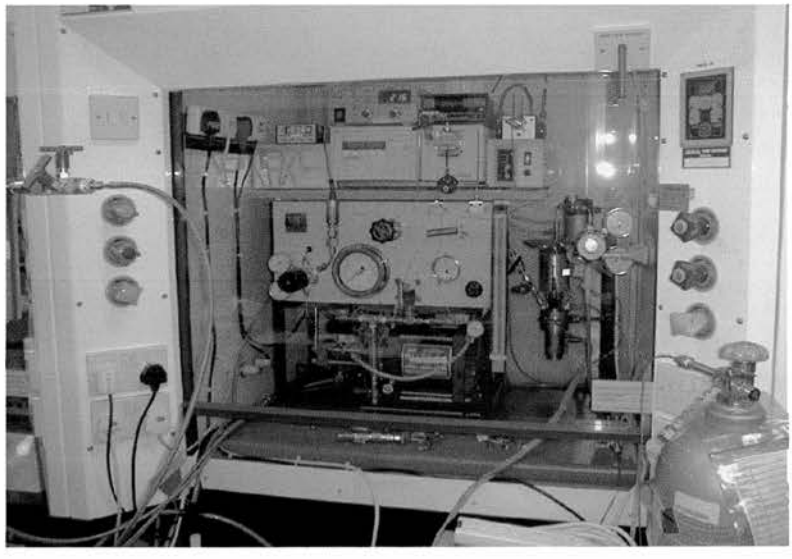


Figure 4.2 Continuous flow system rig

4.4.2 Continuous Flow Hydroformylation with [NixantphosPMIM][Cl]

One of the advantages of this type of process is that the catalyst is always retained in the reactor under the same conditions all the time, reducing the risk of catalyst deactivation and catalyst loss. The main challenge, though with this system is to design the catalyst so as to completely retain it in the reactor. Hence, the ionic analogue of nixantphos was prepared so as to be retained in the ionic phase during extraction with $scCO_2$.

[NixantphosPMIM][Cl] is soluble in ionic liquids and initials studies above indicated that, in the presence of $[Rh(acac)(CO)_2]$, it provided a highly active a catalyst for the hydroformylation of 1-octene in $[OctMIM][NTf_2]$ giving excellent selectivity to linear aldehyde and good retention into the ionic liquid when the product was extracted with hexane. It was therefore tested in the continuous flow system.

In a typical experiment, a solution of $[Rh(acac)(CO)_2]$ and [nixantphosPMIM][Cl] ligand dissolved in the ionic liquid was injected into the reactor through the decompression port of the CSTR under a N_2 purge. The system was then sealed and purged with CO/H_2 (1:1) for several minutes prior to pressurization with CO/H_2 (40 bar). The system was heated with rapid stirring (1100 rpm) to 100°C for ca. 1 h to allow performing of the catalyst. Carbon dioxide (grade N5.5, BOC) was then slowly added to the system to a pressure of 200 bar and the gas mixture was allowed to expand into the decompression stage of the system as far as the first expansion valve (PCV1). The gas expansion valves (PCV 1 & 2) were adjusted to give a fixed total

gas flow through the system, as measured by a flow meter (FM) and a pressure of 3-5 bar at the inlet of the 2nd expansion valve. Synthesis gas (1:1) was then delivered into the system at a predetermined rate. With the temperature of the first expansion valve being maintained at room temperature, the liquid substrate was introduced into the system at a fixed rate by a Gilson 305 HPLC pump (LP1). The system was run continuously with the product stream being sampled and analyzed during the period of substrate injection. Mass balance was checked by weighing the collection vessels before and after the collection of each fraction. Turnover frequencies, for a given set of reactor conditions, were determined from linear regression of turnover number (TON, defined as moles of product (mol rhodium)$^{-1}$) versus time plots with a minimum of 5 data points after equilibration had been reached (2-8 h depending on reactor conditions). The point of equilibration was taken as $t = 0$. Recovered liquid fractions were analyzed by ICPMS and GC. At the end of an experiment the ionic solution was vented under pressure through V1 and analyzed by ^{31}P NMR spectroscopy.

The results obtained over 18 hours of continuous operation are shown in Figure 4.3 and Figure 4.4. The reaction rate is constant for the first 8 hours of the reaction with the turnover frequency (TOF) of 272 mol aldehyde (mol Rh)$^{-1}$ h^{-1}, about half the observed TOF (550 h^{-1}) in the commercial production of butanal in the rhodium catalysed hydroformylation of propene. It is considerably faster than about 85 mol aldehyde (mol Co)$^{-1}$ h^{-1} of the current cobalt process for octene hydroformylation. During this period, the conversion was found to be about 32 % and the l:b ratio to be 41. Both the conversion and the l:b ratio remained constant for this period. This gave a selectivity to linear aldehyde of *ca* 92 % and the degree of isomerisation of 1-octene

to internal octenes was *ca* 2 %. The rhodium content of the collected samples was measured by ICPMS and found to be 170-220 ppb. This was a very promising result though the conversion was found to be low. The conversion could be improved by, among other things, decreasing the flow rate of the substrate, thus increasing the substrate residence time in the autoclave.

From about the 9th hour, the substrate flow rate was reduced from 0.416 cm^{-3}/min to 0.356 cm^{-3}/min (Figure 4.4). The conversion in the recovered fractions remained constant at 32 % but the TOF was slightly reduced to 255 h^{-1}. After 12.75 h, there was a dramatic decrease in l:b ratio, accompanied by an increase in reaction rate and extent of isomerisation, accompanied by an increase in rhodium leaching (Figure 4.4). Examination of the catalyst solution at the end of the reaction showed that all of the phosphine had oxidised to phosphine oxide, which was evident from the ^{31}P NMR spectrum. (only a peak at 29 ppm, which was attributed to oxidised phosphine). When oxidation of the ligands occurs, the ligand is lost from the metal centre and unmodified catalysis is observed. Unmodified catalysis is characterised by high conversion to aldehyde but poor selectivity to linear aldehyde and high isomerisation, which consistent with the behaviour shown in Figure 4.4. The unmodified catalyst is also very soluble in $scCO_2$, thus accounting for the increased rhodium leaching in the later stages of the reaction.

The l:b ratio took about 2 hours to drop from 40 to 10. This was a sudden drop, taking into consideration that the L:Rh ratio used was 2. This then suggests that the effect of ligand oxidation was only felt when there was no excess ligand. This means that the coordinated ligand was oxidised, the free ligand would replace it until there was no

excess free ligand. One would conclude that at about 12.75 hours, the L:Rh was about 1.

The one other interesting observation from Figure 4.4 is that the conversion drops after approximately 16 hours. The decrease in conversion was accompanied by an increase in rhodium leaching, which suggests that most of the unmodified catalyst was extracted with $scCO_2$. Most inorganic carbonyl complexes (unmodified) are soluble in $scCO_2$ and they can be extracted with $scCO_2$.

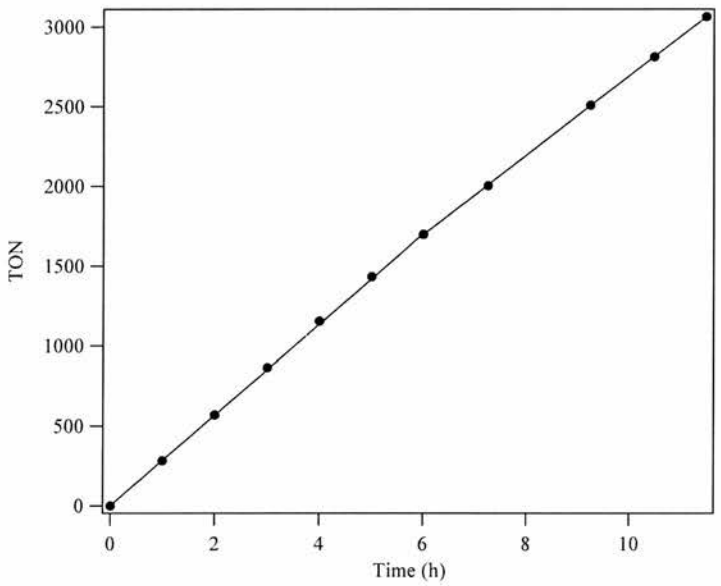


Figure 4.3 Continuous hydroformylation of 1-octene (2.65 mmol min-1 flow 1-octene) catalysed by $[Rh(acac)(CO)_2]$ (47.6 mg, 0.19 mmol) in $[OctMIM][NTf_2]$ (12 cm^3) in the presence of ligand 4 (0.262g, 0.37 mmol) for 8 hours at 100°C and 200 bar. CO/H_2 (1:1, 4.03 mmol min^{-1} of each). Total flow = 1.04 nL min^{-1}. Products collected at 3-4 bar. (Fractions collected while the reaction stabilised have been omitted).

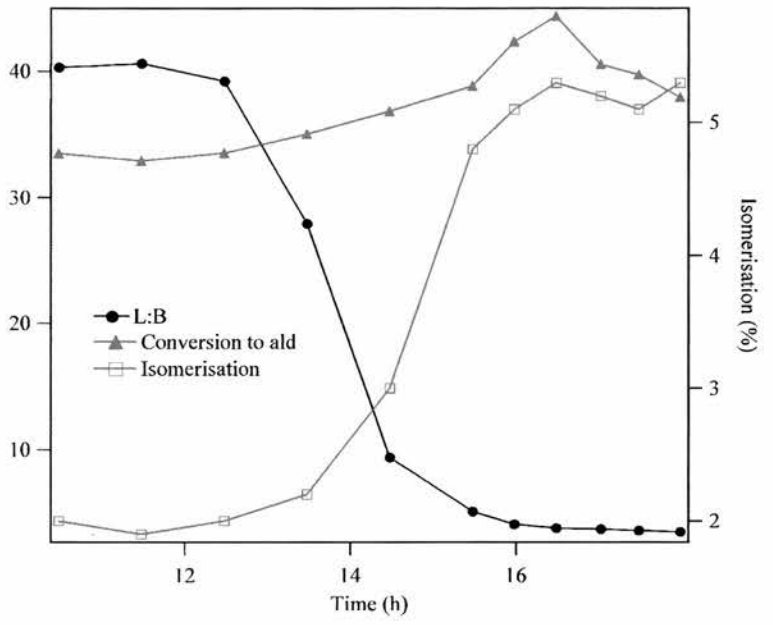


Figure 4.4 Continuous hydroformylation of 1-octene after changing the substrate flow rate from 2.65 mmol min^{-1} to 2.27 mmol min^{-1}.

In our system, the source of oxygen could be CO/H_2 gas mixture, substrate (1-octene) or CO_2 liquid. Investigations into the origin of the oxygen are reported later, after discussion of an experiment aimed at reducing it by use of a sacrificial oxygen scavenger

4.4.3 Continuous Flow Hydroformylation with [NixantphosPMIM][Cl]/[TPPMS][PMIM] Dual ligand system

Webb *et al*[10] were able to run the continuous flow system with [TPPMS][PMIM] for at least 72 hours without observing catastrophic oxidation of the ligand similar to that shown in Figure 4.4 above. The Rh\[TPPMS][PMIM] system used about 16:1 L:Rh ratio (i.e. P:Rh ratio of 16) whereas the Rh\[NixantphosPMIM][Cl] used 2:1 L:Rh

ratio (i.e. P:Rh ratio of 4). This means the Rh\[TPPMS][PMIM] system has 4x mole excess as compared to the Rh\[NixantphosPMIM][Cl] system. It takes about 12 hours for the effect of ligand oxidation to be noticed with the Rh\[NixantphosPMIM][Cl] system, which suggests that in principle it should take at least 4 times the time (about 48 hours) to observe the effect of oxidation with the Rh\[TPPMS][PMIM] system. This was not to be observed with the Rh\[TPPMS][PMIM], but rather a very small amount of ligand was oxidised relative to free ligand at the end of the 72 hour run (^{31}P NMR data). This suggested that the Rh\[TPPMS][PMIM] system or [TPPMS][PMIM] itself was less susceptible to oxidation.

In order to attempt to ameliorate this oxidation problem, we carried out the same reaction using [nixantphosPMIM][Cl], but in the presence of [1-propyl – 3-methyl imidazolium][$Ph_2P(3\text{-}C_6H_4SO_3$] ([PMIM][TPPMS], in the hope that the cheaper phosphine might act as a sacrificial oxygen scavenger.

The catalyst solution was prepared by weighing [$Rh(acac)(CO)_2$] and [nixantphosPMIM][Cl] into a Schlenk tube and adding warm [OctMIM][NTf_2] (12 cm^3) *via* a syringe. The solution was then stirred at 55°C under vacuum until all [NixantphosPMIM][Cl] had dissolved in the ionic liquid. [TPPMS][PMIM] was added into the catalyst solution and the solution was stirred at 55°C under vacuum until all [TPPMS][PMIM] dissolved. The catalyst solution was then syringed, under positive CO/H_2 pressure, into a 50 cm^3 autoclave, which has been flushed with argon and charged with 40 bar CO/H_2. The reaction was carried out as outlined above.

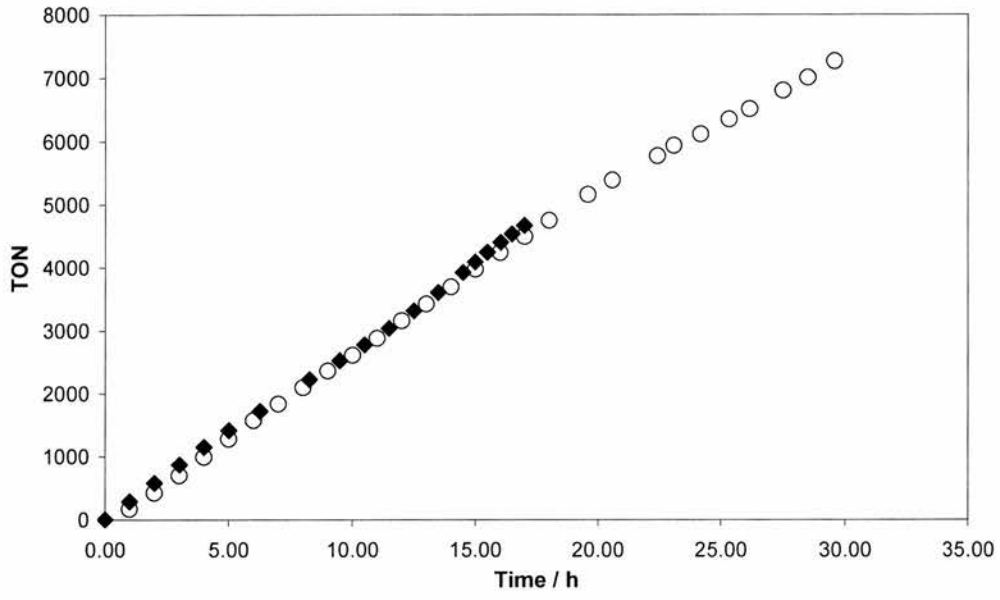


Figure 4.5 Reaction profile for continuous flow hydroformylation of 1-octene (2.65 mmol min^{-1} to) catalysed by $[Rh(acac)(CO)_2]$ (47.6 mg, 0.19 mmol) in $[OctMIM]NTf_2$ (12 cm^3) in the presence of ♦ [nixantphosPMIM][Cl] (0.262g, 0.37 mmol), after 8 h the octene flow rate was dropped to 2.27 mmol min^{-1} or O [nixantphosPMIM][Cl] (0.262g, 0.37 mmol) and [TPPMS][PMIM] (2.85 mmol) at 100°C and 200 bar. CO/H_2 (1:1, 4.03 mmol min^{-1} of each). Total flow = 1.04 nL min^{-1}. Products collected at 3-4 bar. (Fractions collected while the reaction stabilised have been omitted)

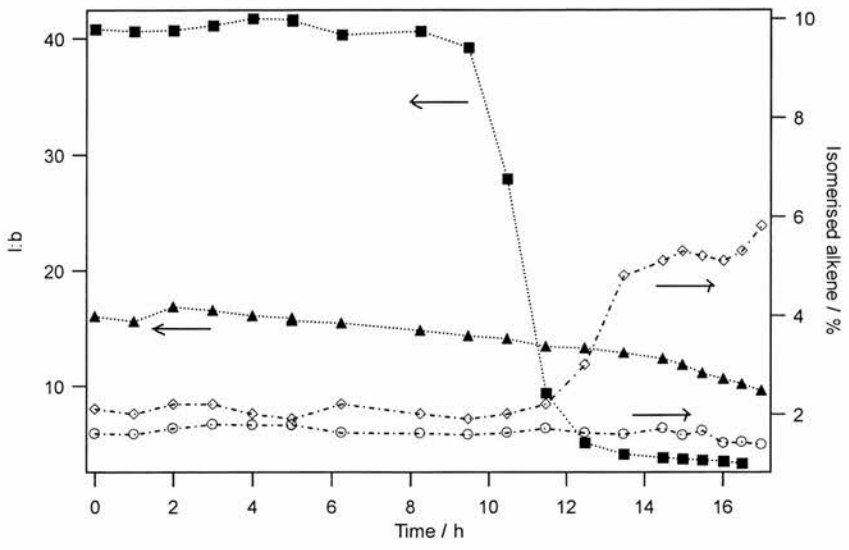


Figure 4.6 l:b ratios (■[nixantphosPMIM][Cl] alone, ▲ [nixantphosPMIM][Cl] and [TPPMS][PMIM]) and isomerised alkene (◈[nixantphosPMIM][Cl] alone, ○ [nixantphosPMIM][Cl] and [TPPMS][PMIM])

The reaction was run for 30 h continuously, with the results shown in Figure 4.3 and Figure 4.6. The two ligands system together showed similar reaction rate (TOF = 272, Conversion = 32 %) to that obtained when using [nixantphosPMIM][Cl] alone (Figure 4.3), but the l:b ratio was found to be 16, corresponding to a nonanal selectivity of 90 %. The rate was constant over the 30 h period and the degree of alkene isomerisation remained very low throughout, whilst the l:b ratio dropped slowly to 6 (nonanal selectivity 83 %) by the end of the reaction. The value of the initial l:b ratio (16) is intermediate between that obtained with [nixantphosPMIM][Cl] alone (l:b = 40) and that obtained with [TPPMS][PMIM] (l:b = 3). This is somewhat surprising and could arise either because a mixed phosphine complex is formed, in which case]NixantphosPMIM][Cl] would probably have to be unidentate in some of the crucial

intermediates, or because both catalysts are present in the reaction. The drop in l:b ratio with continuous use suggests that the contribution from complexes containing [nixantphosPMIM][Cl] diminishes, but no catastrophic loss occurs. It is somewhat surprising that the rate does not increase if [NixantphosPMIM][Cl] is being oxidised. ^{31}P NMR studies on the solution recovered after the 30 h run showed that it contained [NixantphosPMIM][Cl] (-18.65 ppm) and [NixantphosPMIM][Cl] oxide (28.53 ppm) {Figure 4.7}; [NixantphosPMIM][Cl] monophosphine (-22.72 ppm) and its monoxide (28.24 ppm) {Figure 4.8}; and [TPPMS][PMIM] (-3.98 ppm) and its oxide (29.99 ppm).

The spectrum also contained a distinct doublet at δ 31.9 ppm (J_{Rh-P} = 131 Hz), which was identified as the Rh/[TPPMS][PMIM] complex (Figure 4.9). There were also very small peaks at 21.30 ppm and 18.87 ppm, which appeared to be a set of two doublets. In order to assign the two sets of small doublets, a stoichoimetric reaction of $[Rh(acac)(CO)_2]$ and [NixantphosPMIM][Cl] (1:1 mole ratio) in d_4-methanol was carried out and ^{31}P NMR. spectrum was taken. Two doublets at 21.50 ppm (J_{Rh-P} = 137.95 Hz) and 24.53 ppm (J_{Rh-P} = 116.34 Hz) were identified, which could be characteristic of the ee and ea complexes shown in Figure 4.10

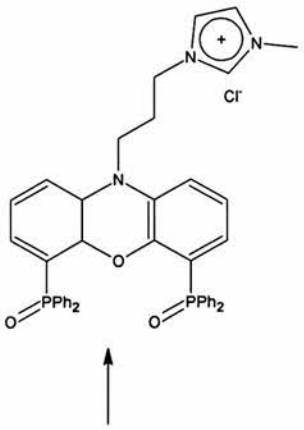


Figure 4.7 [NixantphosPMIM] oxide

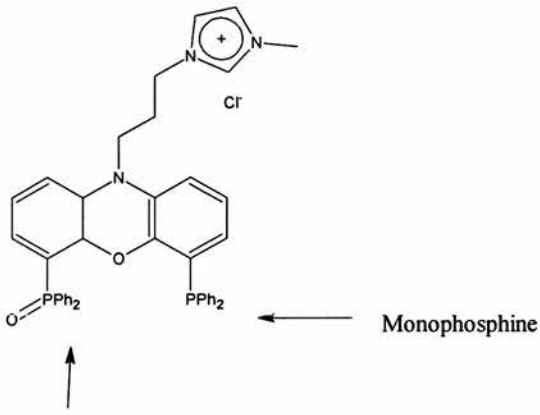


Figure 4.8 [NixantphosPMIM][Cl] monophosphine and its oxide

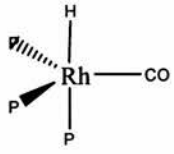


Figure 4.9 Rh/TPP complex in the absence of syngas

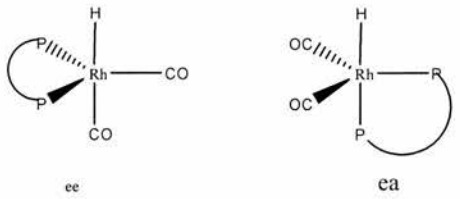


Figure 4.10 Possible Rh/[NixantphosPMIM][Cl] complexes

4.5 Oxygen Scavenger

The dual ligand system gave promising results, although the problem of oxidation was not totally resolved. When accessing the system, there are at least three potential sources of oxygen to the system i.e. CO/H_2 gas mixture, liquid CO_2, substrate (1-octene). CO/H_2 gas mixture and CO_2 used were not 100 % oxygen free. This suggested that there could be traces of oxygen contained in the gases. The accumulation of low levels of oxygen in the system could lead to a significant amount of oxygen, which led to the oxidation of the ligand.

The CO/H_2 and CO_2 gases were first passed through a chromium catalyst bed to trap any traces of oxygen in the gas mixture. Unfortunately there was no difference in catalyst performance with or without the catalyst beds. The results were exactly the same as in Figure 4.3 and Figure 4.4 above. This suggested that any traces of oxygen which could have been contained in the gases was not enough to oxidize the catalyst or that the catalyst beds were not effective enough to scrub all the oxygen.

The other possible source of oxygen in our system was the liquid feed line. For all the reaction, the 1-octene feed was first passed through an alumina column to mostly remove peroxides, which also oxidize the catalyst. The 1-octene was also degassed

with argon before use and continued bubbling argon even during the reaction. This might have not be enough to eliminate oxygen or peroxides from the 1-octene. The next thing was to treat 1-octene with an iron ferrous sulphate catalyst to thoroughly remove peroxides. Unfortunately, lack of time prevented this experiment from being carried out, but it would be an important experiment to try. After the conclusion of this set of experiments, rather similar results were obtained in a totally different system by Dr P Webb. In that case it turned out that the ligand had been extracted and deposited in the decompression line (not oxidised). It is also possible that this happens in our system, although the observation of oxidised [nixantphosPMIM][Cl] in the recovered catalyst solution would appear to argue against this explanation.

4.6 Conclusions

In conclusion, the use of rhodium complexes of ligand [nixantphosPMIM][Cl] dissolved in [OctMIM][NTf_2] in a continuous flow system with $scCO_2$ as the transport medium, provides the first demonstration of a continuous flow hydroformylation process for long chain alkenes in which rates and selectivities to the desired linear aldehyde are of commercial interest. The presence of oxygen in the feed eventually leads to much reduced l:b ratios and increased leaching, but these can be ameliorated to some extent by adding excess [TPPMS][PMIM].

Both the ligands seem not to be very much air sensitive, but once coordinated to the rhodium metal, the oxidation seems to be catalysed. In other words, the ligand is more susceptible to oxidation once coordinated to rhodium metal.

4.7 References

1. Sellin, M. F.; Webb, P. B.; Cole-Hamilton, D. J. *Chem. Commun.* **2001**, 781-782.
2. van Leeuwen, P. W. N. M.; Claver, C. *Rhodium Catalysed Hydroformylation*; Kluwer: Dordrecht, 2000.
3. van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *Organometallics* **2000,** *19*, 872-883.
4. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Commun.* **2001**, 451-452.
5. Dupont, J.; Silva, S. M.; de Souza, R. F. *Catal. Lett.* **2001,** *77*, 131-133.
6. Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. *Chem. Commun.* **2002**, 3044-3045.
7. Bronger, R. P. J.; Silva, S. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *J. Chem. Soc. Dalton Trans* **2004**, 1590.
8. van Leeuwen, P. W. N. W.; Claver, C. *Rhodium Catalysed Hydroformylation*; Kluwer: Dordrecht, 2000.
9. Sellin, M. F.; Bach, I.; Webster, J. M.; Montilla, F.; Rosa, V.; Aviles, T.; Poliakoff, M.; Cole-Hamilton, D. J. *J. Chem. Soc.-Dalton Trans.* **2002**, 4569-4576.
10. Webb, P. B.; Sellin, M. F.; Kunene, T. E.; Williamson, S. M.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *J. Am. Chem. Soc.,* **2003**.

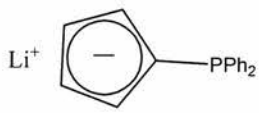
5 EXPERIMENTAL PROCEDURE

All reactions were carried out under an argon atmosphere using standard Schlenk line and catheter tubing techniques with dried solvents, unless otherwise stated. All catalytic reactions were carried out in a batch mode, unless otherwise stated.

5.1 Synthesis

5.1.1 Ligand Synthesis – 1,1-bis(diphenylphosphino)cobaltocenium Hexafluorophosphate[1]

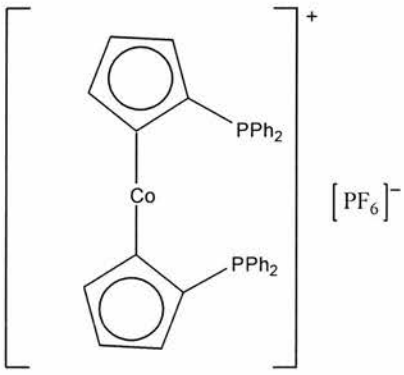
a) Synthesis of Diphenylphosphinocyclopentadienyllithium ($LiC_5H_4PPh_2$)



Sodium cyclopentadienide (NaCp) was prepared by slowly adding cyclopentadiene (50 cm^3) into a flask containing small pieces of sodium (12.5 g) and 1,2-dimethoxyethane (100 cm^3). The mixture was stirred until all the sodium had reacted and the solvent was removed under vacuum. Fresh NaCp (3.63 g, 41.2 mmol) was added to distilled $ClPPh_2$ (9.09 g, 7.4 ml, 41.2 mmol) at -30°C in ether (50 cm^3). The reaction mixture was stirred for about 1.5 hours at room temperature, filtered over celite and the solvent was removed under vacuum. The yield was 7.5 g (72.3%). The residue was then dissolved in THF (50 cm^3), cooled to -78°C. and n-BuLi (18.6 cm^3, 1.6 mol dm^{-3} in hexane, 1.91 g,

29.8 mmol,) was added dropwise. The mixture was stirred overnight at room temperature. The solvent was removed under vacuum and the product was precipitated by the addition of toluene (50 cm^3). The product was filtered using filtering sticks and dried under vacuum. The pale yellow powder product ($LiC_5H_4PPh_2$) was characterised by NMR spectroscopy. ^1H NMR (300 MHz, C_6D_6, 298 K): δ = 7.60-7.71 (m, 4H, CH ortho); 7.42-7.58 (m,6H, CH para/meta); 5.60-5.80 (m, 4H, C_5H_4) ppm, ^{31}P NMR (300 MHz, C_6D_6, 298 K): δ –15.08 ppm

b) Synthesis of 1,1-bis(diphenylphosphino)cobaltocenium hexafluorophosphate ([DPPCo][PF_6])



Anhydrous $CoCl_2$ (0.79 g, 6 mmol) was added to $LiC_5H_4PPh_2$ (3.00 g, 12 mmol) in THF (50 cm^3). The dark solution was stirred overnight and C_2Cl_6 (0.82 g, 3.5 mmol) was added. The resulting solution was stirred at room temperature for about 10 minutes and the volatile substances were evaporated under vacuum. The residue was dissolved in CH_2Cl_2 (25 cm^3) and filtered through celite to remove LiCl. The filtrate was dried under vacuum and the oily brown residue was dissolved in acetone (50 cm^3). Then NH_4PF_6 (0.92 g, 5.6 mmol) in acetone was added. No precipitate was formed. The solution was then added dropwise to distilled water (100 cm^3), producing an oil. The oil

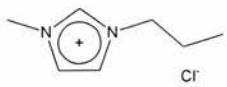
was extracted with CH_2Cl_2 (3×50 cm^3), then added dropwise to diethyl ether (200 cm^3). The solid was collected by filtration and washed with diethyl ether to obtain 2.35 g (78.3%) crude product. The crude product was dissolved in acetone and chromatographed on alumina, eluted with acetone and the solvent was removed under vacuo to obtain 2.0 g (66.7%). Characterisation was by NMR spectroscopy. ^{1}H NMR (300 MHz, Acetone-d_6, 298 K): δ = 7.62 (m, 20H, PH), 5.76, 6,16 (m, 8H, Cp) ppm; ^{31}P {^{1}H} NMR (300 MHz, Acetone-d_6, 298 K) δ = –22.62 (br s, PR_2R'), -145.62 (sept, PF_6) ppm

Literature values: ^{1}H NMR (CD_3NO_2-d_8): δ = 7.47 (m, 20H, PH), 5.51, 5,83 (m, 8H, Cp); ^{31}P {^{1}H} NMR: δ = –22.24 (br s, PR_2R'), -145.13 (sept, PF_6) ppm

5.1.2 Syntheses of 1-Alkyl-3-methylimidazolium Chloride[2]

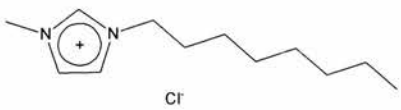
N-Methyl imidazole and a 1.3-fold excess of the corresponding chloroalkane were refluxed at 70 °C for 3 days. After cooling, the upper layer was discarded and the IL was washed with ethyl acetate and then dried in vacuo at 50 °C for 5 h. The product was then dissolved in water and stirred at room temperature in the presence of activated charcoal for 24 h. The solution was filtered through diatomaceous earth (celite), and again dried in vacuo to yield the product as a colorless liquid in all cases except the propyl, butyl, and decyl analogues, which crystallized at room temperature as white solids. The imidazolium chlorides were analyzed by ^{1}H NMR spectroscopy and compared to literature data. NMR data is provided for those compounds, which have not yet been fully characterized. We were unable to obtain accurate microanalysis for the imidazole chlorides because of their hygroscopic nature.

5.1.2.1 1-Propyl-3-methylimidazolium Chloride [PMIM][Cl].



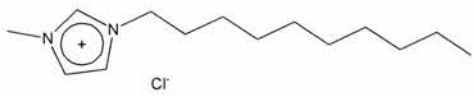
^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 0.67 (3H, t, CH_3), 1.68 (2H, sext, CH_2CH_3), 3.85 (3H, s, NCH_3), 4.09 (2H, t, NCH_2), 7.71, 7.73 (2H, 2 × t, NC(H)C(H)N), 10.29 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 137.2 (s, NCN), 123.4, 122.1 (2 × s, NCCN), 50.6 (s, NCH_2), 35.9 (d, NCH_3), 23.3 (s, CH_2), 10.2 (s, CH_3) ppm.

5.1.2.2 1-Octyl-3-methylimidazolium Chloride [OctMIM][Cl]



^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 0.81 (3H, t, CH_3), 1.21-1.27 (10H, m, CH_2), 1.85 (2H, pent, NCH_2CH_2), 4.03 (3H, s, NCH_3), 4.26 (2H, t, NCH_2), 7.48, 7.63 (2H, 2 × t, NC(H)C(H)N), 10.64 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 138.4 (s, NCN), 123.9, 122.3 (2 × s, NCCN), 50.2 (s, NCH_2), 36.7 (s, NCH_3), 32.0, 30.6, 29.4, 29.3, 26.6, 22.9 (6 × s, CH_2), 14.2 (s, CH_3) ppm.

5.1.2.3 1-Decyl-3-methylimidazolium Chloride [DecMIM][Cl].



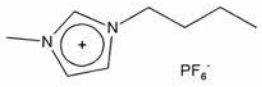
^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 0.87 (3H, t, CH_3), 1.26-1.32 (14H, m, CH_2), 1.88 (2H, pent, NCH_2CH_2), 4.06 (3H, s, NCH_3), 4.28 (2H, t, NCH_2), 7.28, 7.36 (2H, 2 × t, NC(H)C(H)N), 10.39 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 138.7 (s, NCN), 123.7, 122.1 (2 × s, NCCN), 50.6 (s, NCH_2), 37.0 (s, NCH_3), 32.4, 30.8, 30.0, 29.9, 29.8, 29.6, 26.8, 23.2 (8 × s, CH_2), 14.4 (s, CH_3) ppm.

5.1.3 1-Alkyl-3-methylimidazolium Hexafluorophosphate

Preparations of the imidazolium PF_6 salts were carried out as follows: A solution of sodium hexafluorophosphate in water was added to an aqueous solution of the corresponding imidazolium chloride in stoichiometric quantities. After stirring at room temperature for 24 h, the aqueous phase was decanted and the ionic liquid washed with water until the washings were free from chloride. The ionic liquid was then dissolved in acetone and stirred in the presence of activated charcoal for 24 h. The solution was filtered through diatomaceous earth and the solvent removed in vacuo. The ionic liquid was again washed with water and dried in vacuo to yield a colorless liquid. The

imidazole hexafluorophosphates were analyzed by ^{1}H NMR and compared to literature data.

5.1.3.1 1-Butyl-3-methylimidazolium hexafluorophosphate ([BMIM][PF_6])[3,4]



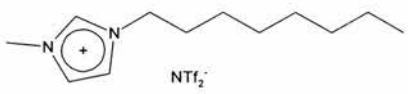
^{1}H NMR (300 MHz, Acetone-d_6, 298 K): δ 8.95 (s, 1H, NCHN); 7.79 & 7.78 (2 x s, 2H, NCHCHN); 4.24 (t, 2H, NCH_2); 4.12 (s, 3H, NCH_3); 2.02 (m, 2H, NCH_2CH_2); 1.52 (m, 2H, $NCH_2CH_2CH_2$); 1.12 (t, 3H, CH_2CH_3) ppm. ^{31}PNMR (300 MHz, Acetone-d_6, 298 K) δ -145.86 (sept, PF_6) ppm.

5.1.4 1-Alkyl-3-methylimidazolium Bis(trifluoromethanesulfonyl)amide[2]

The bis(trifluoromethanesulfonyl)amide salts were similarly prepared using N-lithio bis(trifluoromethanesulfonyl)amide for the salt exchange reaction. Full analysis is provided for the imidazole sulfonyl amides, which have not yet been fully characterized.

5.1.4.1 1-Octyl-3-methylimidazolium

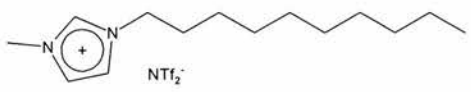
Bis(trifluoromethanesulfonyl)amide [OctMIM][NTf_2]



Elemental analysis calcd. for $C_{14}H_{23}O_4N_3S_2F_6$: C 35.37 H 4.87 N 8.84; found: C 35.00 H 5.52 N 9.16. ^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 0.88 (3H, t, CH_3), 1.27-1.33 (10H, m, CH_2), 1.86 (2H, pent, NCH_2CH_2), 3.92 (3H, s, NCH_3), 4.15 (2H, t, NCH_2), 7.30, 7.31 (2H, 2 × s, NC(H)C(H)N) 8.61 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 136.3 (s, NCN), 124.3, 122.9 (2 × d, NCCN), 120.4 (q, CF_3, J_{CF} = 321 Hz), 50.8 (s, NCH_2), 36.8 (s, NCH_3), 32.2, 30.6, 29.5, 29.3, 26.6, 23.1 (6 × s, CH_2), 14.3 (s, CH_3) ppm.

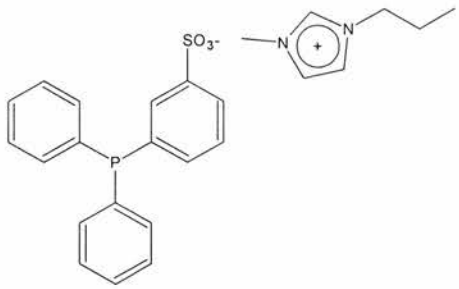
5.1.4.2 1-Decyl-3-methylimidazolium

Bis(trifluoromethanesulfonyl)amide [DecMIM]NTf_2]



Elemental analysis calcd for $C_{16}H_{27}O_4N_3S_2F_6$: C 38.17 H 5.40 N 8.35; found: C 37.87 H 5.84 N 8.88. ^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 1.00 (3H, t, CH_3), 1.40-1.46 (14H, m, CH_2), 1.99 (2H, pent, NCH_2CH_2), 4.05 (3H, s, NCH_3), 4.28 (2H, t, NCH_2), 7.42, 7.43 (2H, 2 × d, NC(H)C(H)N), 8.75 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 136.4 (s, NCN), 124.2, 122.8 (2 × s, NCCN), 120.4 (q, CF_3, J_{CF} = 321 Hz), 50.9 (s, NCH_2), 36.9 (s, NCH_3), 32.4, 30.6, 30.0, 29.9, 29.8, 29.4, 26.6, 23.1 (8 × s, CH_2), 14.4 (s, CH_3) ppm.

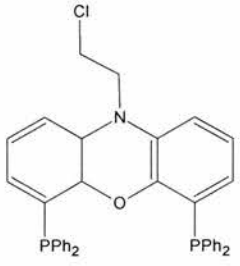
5.1.5 1-Propyl-3-methylimidazolium Diphenyl(3-sulfonatophenyl)phosphine ([PMIM][TPPMS])[2]



[PMIM]Cl (**5.1.2.1**) (14.31 g, 89.1 mmol) was added dropwise to a rapidly stirred solution of sodium diphenyl(3-sulfonatophenyl)phosphine dihydrate (25.74 g, 64.3 mmol) in THF, resulting in immediate formation of a fine white precipitate. The solution was stirred at room temperature for a further 24 h, filtered through diatomaceous earth, and the solvent removed in vacuo. The resulting residue was taken up into dichloromethane, again filtered, and the solvent removed in vacuo. The crude product, which contains an excess of the imidazolium chloride, was left at -10 °C to afford the product as colourless rhomboidal crystals (15.28 g, 32.8 mmol, 50.9%) melting point 88-90 °C. Elemental analysis calcd for $C_{25}H_{27}O_3N_2PS$: C 64.36 H 5.83 N 6.00; found: C 64.42 H 5.64 N 6.14. ^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 0.99 (3H, t, CH_3), 1.92 (2H, sext, CH_2CH_3), 3.97 (3H, s, NCH_3), 4.20 (2H, t, NCH_2), 7.43 (14H, m, $Ph_2PC_6H_4SO_3$), 7.92, 7.96 (2H, 2 × d, NC(H)C(H)N), 9.71 (1H, s, NC(H)N) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): = 148.1 (d, CSO_3, J_{pc} = 6.9 Hz), 138.2 (s, NCN), 138.0 (d, *ipso*-C_6H_5, J_{pc} = 12.7 Hz), 137.5 (d, *ipso*-$C_6H_4SO_3$, J_{pc} = 11.5 Hz), 134.6 (d, *o*-$C_6H_4SO_3$, J_{pc} = 14.9 Hz), 134.2 (d, *o*-C_6H_5, J_{pc} = 19.6 Hz), 131.3 (d, *o*-$CCSO_3$, J_{pc} = 25.3 Hz), 129.3 (s, *p*-C_6H_5), 129.0 (d, *m*-C_6H_5, J_{pc} = 6.9 Hz), 128.8 (d, *m*, $C_6H_4SO_3$, J_{pc} = 5.8 Hz), 126.8 (s, *p*-$C_6H_4SO_3$), 123.8, 122.4 (2 × s, NCCN), 51.6 (s, NCH_2), 36.5 (s,

NCH_3), 23.9 (s, CH_2), 10.9 (s, CH_3) ppm. ^{31}P NMR (121.4 MHz, CD_2Cl_2, 298 K) δ -3.90

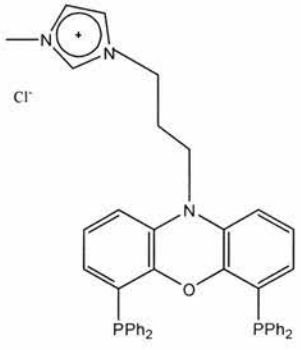
5.1.6 Synthesis of 10-(2-chloroethyl)nixantphos



A solution of nixantphos[5] (1.00 g, 1.813 mmol) in dry toluene was cooled to 0°C and a solution of n-BuLi in hexane (1.6 M, 1.133 cm^3, 1.813 mmol) was added dropwise. The reaction was then allowed to warm to room temperature and was stirred for 30 min. The resulting yellow-red precipitate was added to a solution of 2-chloroethyl p-toluenesulfonate (0.432 g, 1.813 mmol) in toluene. The reaction mixture was stirred at reflux for 16 hours, cooled and washed with water. Evaporation of toluene yielded a brown oily residue. The oily residue was washed with n-hexane and was dissolved in dichloromethane. The solution was layered with methanol. The crystallized white solid (58% yield) was filtered and washed with methanol. Elemental analysis calculated for $C_{38}H_{32}NOP_2Cl$: C 73.60 H 5.20 N 2.26; found: C 73.55 H 5.23 N 2.30. ^{1}HNMR (300 MHz, $CDCl_3$, 298 K): δ 7.30 (m, 12H, Ph), 7.15 (m, 8H, Ph), 6.72 (t, *J*(H,H) = 7.6 Hz, 2H, $Ph_2PCCHC\underline{H}$), 6.70 (d, *J*(H,H) = 7.7 Hz, 2H Ph_2PCCH), 6.02 (d, *J*(H,H) = 7.4 Hz, 2H, $Ph_2PCCHCHC\underline{H}CN$), 4.34 (t, *J*(H,H) = 6.7 Hz, 2H, $NC\underline{H}_2CH_2Cl$), 3.79 (t, *J*(H,H) = 6.8 Hz, 2H, $NCH_2C\underline{H}_2Cl$),. ^{13}C {1H}NMR (300 MHz, $CDCl_3$, 298 K): δ = 146,50 (t,

J(P,C) = 20.6 Hz, CO), 136.35 (t, J(P,C) = 12.5 Hz, Ph_2PC), δ = 133.63 (t, J(P,C) = 21.1 Hz, $Ph_2PC\underline{C}H$), δ = 133.00 (CN), δ = 128.32 (CH), δ = 128.04 (t, J(P,C) = 6.9 Hz, $Ph_2PCCH\underline{C}H$), 125.25 (CH), δ = 123.81 (CH), δ = 112.49 (CH), δ = 35.06 ($N\underline{C}H_2CH_2Cl$), δ = 25.96 ($NCH_2\underline{C}H_2Cl$). ^{31}PNMR (300 MHz, $CDCl_3$, 298 K): δ -18.50 ppm

5.1.7 Synthesis of [Nixantphos PMIMCl].H_2O



Nixantphos[5] (0.100 g, 0.181 mmol) was dissolved in THF (50 cm^3) and NaH (1.5 mole equivalent, 60% in mineral oil) was added at 0°C to the stirring solution. The solution was allowed to warm up to room temperature and was refluxed for 1 hour. The solution was then cooled to room temperature and 1-bromo-3-chloropropane (1.075 cm^3, 6 mole equivalent) was added quickly. After refluxed overnight, the solution was cooled and the solvent was removed under vacuum. The solid residue was dissolved in DCM and filtered through a sintered glass funnel. The solvent was then removed from the filtrate under vacuum and the solid was crystallized from DCM/MeOH mixture. The resulting white product was then dissolved in toluene (50 cm^3) and 1-methylimidazole (3.34 cm^3, 100 mole equivalent) was added and refluxed overnight. The solution was then allowed

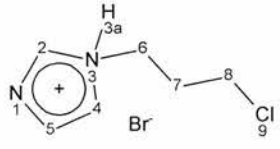
to cool with the stirrer switched off and the product crystallized out. The solution was then filtered off (Yield = 75%). Elemental analysis calculated for $C_{43}H_{40}N_3OP_2Cl$: C 70.92 H 5.54 N 5.77, found: C 67.67 H 5.38 N 5.92. ^{1}HNMR (300 MHz, CD3OD, 298 K): δ 8.81 (s, 1H, NCHN)), 7.57 (s, 1H, NCHC<u>H</u>NCH$_3$), 7.33 (m, 12H, Ph), 7.24 (s, 1H, NC<u>H</u>CHNCH$_3$), 7.20 (m, 8H, Ph), 6.76 (t, *J*(H,H) = 7.8 Hz, 2H, Ph$_2$PCCHC<u>H</u>), 6.73 (d, *J*(H,H) = 7.8 Hz, 2H Ph$_2$PCCH), 6.05 (d, *J*(H,H) = 7.2 Hz, 2H, Ph$_2$PCCHCHC<u>H</u>CN), 4.39 (t, *J*(H,H) = 6.6 Hz, 2H, NC<u>H$_2$</u>CH$_2$CH$_2$NCN), 3.82 (t, *J*(H,H) = 6.6 Hz, 2H, NCH$_2$CH$_2$C<u>H$_2$</u>NCN), 3.70 (s, 3H, NCH$_3$), 2.35 (q, *J*(H,H) = 6.6 Hz, 2H, NCH$_2$C<u>H$_2$</u>CH$_2$NCN). ^{13}C {1H}NMR (300 MHz, CD3OD, 298 K): δ = 147,17 (t, J(P,C) = 20.8 Hz, CO), 136.76 (t, J(P,C) = 12.4 Hz, Ph$_2$PC), 136. 73 (NCN), 133.64 (t, J(P,C) = 21.1 Hz, Ph$_2$PC<u>C</u>H), 133.03 (CN), δ = 128.32 (CH), 128.01 (t, J(P,C) = 6.9 Hz, Ph$_2$PCCH<u>C</u>H), 125.31 (CH), 123.81 (CH), 123.47 (NCH<u>C</u>HNCH$_3$), 122.025 (N<u>C</u>HCHNCH$_3$), 112.49 (CH), 40.67 (NCH$_2$CH$_2$<u>C</u>H$_2$NCN), 35.06 (N<u>C</u>H$_2$CH$_2$CH$_2$NCN), 29.29 (NCH$_3$), 25.14 (NCH$_2$<u>C</u>H$_2$CH$_2$NCN) ppm. ^{31}PNMR (300 MHz, CD3OD, 298 K): δ -18.62 ppm

5.1.8 Synthesis of [NixantphosPMIM][PF$_6$]

[NixantphosPMIM][Cl] (1.00 g, 1.40 mmol) was dissolved in dichloromethane (20 cm^3) and NH_4PF_6 (1.2 mole equivalent) was dissolved in ethanol (20 cm^3). The dichloromethane and ethanol solutions were mixed and stirred at room temperature for 30 minutes. Water (20 cm^3) was added and the organic and aqueous layers were separated. The organic layer was dried with $MgSO_4$ and filtered using a glass sinter funnel. The solvent was removed using a rotary evaporator affording a white solid product (100% yield). Elemental analysis calculated for $C_{43}H_{40}N_3OP_3F_6$: C 63.00 H

4.67 N 5.13; found: C 59.63 H 4.71 N 4.96. ^{1}HNMR (300 MHz, CD3OD, 298 K): δ 8.81 (s, 1H, NCHN)), 7.57 (s, 1H, NCHC<u>H</u>NCH$_3$), 7.33 (m, 12H, Ph), 7.24 (s, 1H, NC<u>H</u>CHNCH$_3$), 7.20 (m, 8H, Ph), 6.76 (t, *J*(H,H) = 7.8 Hz, 2H, Ph$_2$PCCHC<u>H</u>), 6.73 (d, *J*(H,H) = 7.8 Hz, 2H Ph$_2$PCCH), 6.05 (d, *J*(H,H) = 7.2 Hz, 2H, Ph$_2$PCCHCHC<u>H</u>CN), 4.39 (t, *J*(H,H) = 6.6 Hz, 2H, NC<u>H$_2$</u>CH$_2$CH$_2$NCN), 3.82 (t, *J*(H,H) = 6.6 Hz, 2H, NCH$_2$CH$_2$C<u>H$_2$</u>NCN), 3.70 (s, 3H, NCH$_3$), 2.35 (q, *J*(H,H) = 6.6 Hz, 2H, NCH$_2$C<u>H$_2$</u>CH$_2$NCN) ppm. ^{13}C {1H}NMR (300 MHz, CD$_3$OD, 298 K): δ 147,17 (t, J(P,C) = 20.8 Hz, CO), 136.76 (t, J(P,C) = 12.4 Hz, Ph$_2$PC), 136. 73 (NCN), 133.64 (t, J(P,C) = 21.1 Hz, Ph$_2$PC<u>C</u>H), 133.03 (CN), 128.32 (CH), 128.01 (t, J(P,C) = 6.9 Hz, Ph$_2$PCCH<u>C</u>H), 125.31 (CH), 123.81 (CH), 123.47 (NCH<u>C</u>HNCH$_3$), 122.025 (N<u>C</u>HCHNCH$_3$), 112.49 (CH), 40.67 (NCH$_2$CH$_2$<u>C</u>H$_2$NCN), 35.06 (N<u>C</u>H$_2$CH$_2$CH$_2$NCN), 29.29 (NCH$_3$), 25.14 (NCH$_2$<u>C</u>H$_2$CH$_2$NCN) ppm. ^{31}PNMR (300 MHz, CD$_3$OD, 298 K): δ -18.62 ppm

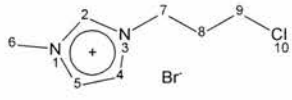
5.1.9 Synthesis of 3-(3-chloropropyl)-1*H*-imidazol-3-ium bromide salt



Imidazole (2.00 g, 29.38 mmol) was dissolved in acetone (50 cm^3) and 1-bromo-3-chloropropane (5 mol equivalent) was quickly added. The reaction mixture was refluxed overnight. The product precipitated out of solution as it formed. The solvent was decanted off and the residue was washed several times with ethyl acetate to remove unreacted 1-bromo-3-chloropropane. The product (100 %) was dried on the rotavapor.

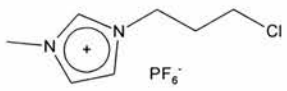
Elemental analysis calcd for $C_7H_{12}N_2ClBr$: C 31.94 H 4.47 N 12.42; found: C 30.35 H 4.76 N 12.10. ^{1}H NMR (300 MHz, D_2O, 298 K): δ 15.86 (s, 1H, H3a) 8.52 (s, 1H, H2), 6.08 (s, 1H, H4), 5.19 (s, 1H, H5), 4.46 (t, 2H, *J*(H,H) = 6.6 Hz, H6), 3.68 (t, 2H, *J*(H,H) = 6.7 Hz, H8), 2.44 (m, 2H, H7) ppm. ^{13}C NMR (300 MHz, D_2O, 298 K): δ 136.40 (s, NCN), 124.01 & 122.55 (2 × s, NCCN), 46.94 (s, NCH_2), 36.12 (s, CH_2Cl), 31.87 (s, $NCH_2\underline{C}H_2CH_2Cl$) ppm.

5.1.10 Synthesis of 3-(3-chloropropyl)-1-methyl-1*H*-imidazol-3-ium bromide salt



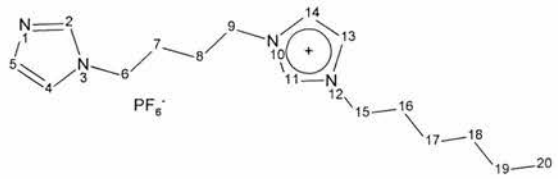
The solution of 1-methylimidazole (2.06 g, 0.025 mol, 2.00 cm^3) and 1-bromo-3-chloropropane (10 mole equivalent) in toluene (30 cm^3) was refluxed for 6 hours. The product precipitated out of solution. The resulting oily product (95% yield) was washed with ethyl acetate. Elemental analysis calcd for $C_7H_{12}N_2ClBr$: C 35.10 H 5.05 N 11.70; found: C 33.35 H 5.38 N 11.9. ^{1}H NMR (300 MHz, D_2O, 298 K): δ 8.50 (s, 1H, H2), 6.00 (s, 1H, H4), 5.10 (s, 1H, H5), 4.45 (t, 2H, *J*(H,H) = 6.5 Hz, H7), 3.96 (s, 3H, H6), 3.67 (t, 2H, *J*(H,H) = 6.8 Hz, H9), 2.41 (m, 2H, H8) ppm. ^{13}C NMR (300 MHz, D_2O, 298 K): δ 136.37 (s, NCN), 123.99 & 122.47 (2 × s, NCCN), 46.83 (s, NCH_2), 41.46 (s, NCH_3), 36.10 (s, CH_2Cl), 31.87 (s, $NCH_2\underline{C}H_2CH_2Cl$) ppm.

5.1.11 Synthesis of 3-(3-chloropropyl)-1-methyl-1H-imidazol-3-ium hexafluorophosphate salt



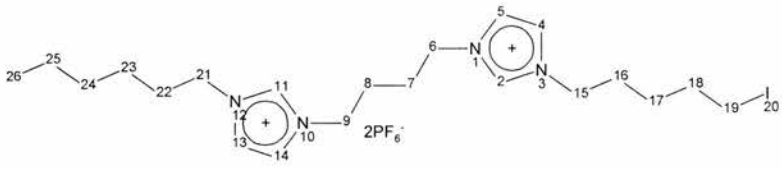
3-(3-Chloropropyl)-1-methyl-1*H*-imidazol-3-ium bromide salt from 5.1.9 was dissolved in water (50 cm^3) and a solution of $NaPF_6$ (1.2 mole equivalent) in water (10 cm^3) was added. The product (100% yield) precipitated out of solution and was washed with water several times. Elemental analysis calcd for $C_7H_{12}N_2ClBr$: C 27.60 H 3.99 N 9.20; found: C 26.20 H 4.31 N 9.40. ^{1}H NMR (300 MHz, CD_2Cl_2, 298 K): δ 8.50 (s, 1H, H2), 6.00 (s, 1H, H4), 5.10 (s, 1H, H5), 4.45 (t, 2H, *J*(H,H) = 6.5 Hz, H7), 3.96 (s, 3H, H6), 3.67 (t, 2H, *J*(H,H) = 6.8 Hz, H9), 2.41 (m, 2H, H8) ppm. ^{13}C NMR (75.4 MHz, CD_2Cl_2, 298 K): δ 136.37 (s, NCN), 123.99 & 122.47 (2 × s, NCCN), 46.83 (s, NCH_2), 41.46 (s, NCH_3), 36.10 (s, CH_2Cl), 31.87 (s, $NCH_2\underline{C}H_2CH_2Cl$) ppm. ^{31}PNMR (300 MHz, CD_2Cl_2, 298 K) δ -145.12 ppm

5.1.12 Synthesis of 3-hexyl-1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazol-3-ium hexafluorophosphate salt



A solution of 1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazole (2.00 g, 0.0105 moll), synthesized as outlined by Luo et al[6], and 1-bromohexane (0.5 mole equivalent) in acetone (30 cm^3) was refluxed for 6 hours. After cooling, the acetone was evaporated and the resulting oily product was dissolved in water. Any excess 1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazole crystallized out of solution and NH_4PF_6 (0.6 mole equivalent) solution in water (20 cm^3) was added. **3**-Hexyl-1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazol-3-ium hexafluorophosphate salt (60% yield) precipitated out immediately. The product was washed with water several times. Elemental analysis calculated for $C_{16}H_{25}N_4F_6P$: C 45.71 H 6.47 N 13.33 found: C 40.68 H 6.51 N 11.68. ^{1}HNMR (300 MHz, Acetone-d_6, 298 K): δ 9.03 (s, 1H, H11)), 8.15 (s, 1H, H2), 7.75 (s, 1H, H13), 7.71 (s, 1H, H14), 7.39 (s, 1H, H4), 7.25 (s, 1H, H5), 4.45 (t, *J*(H,H) = 7.1 Hz, 2H, H15), 4.35 (t, *J*(H,H) = 6.6 Hz, 2H, H9), 4.25 (t, *J*(H,H) = 6.8 Hz, 2H, H6), 2.00 (m, 6H, H7; H8 & H16), 1.37 (m, 6H, H17; H18 & H19), 0.91 (t, *J*(H,H) = 5.9 Hz, 3H, H20) ppm. ^{13}C {1H}NMR (300 MHz, Acetone-d_6, 298 K): δ 136.20 (C11), 135.16 (C2), 122.51 (C13), 122.35 (C14), 120.05 (C4), 119.8 (C5), 51.00 (C15), 49.21 (C9), 47.05 (C6), 31.51 (C16), 29.82 (C8), 27.5 (C7), 27.06 (C17), 25.95 (C18), 23.10 (C19), 15.13 (C20) ppm. ^{31}PNMR (300 MHz, Acetone-d_6, 298 K): δ -144.45 ppm

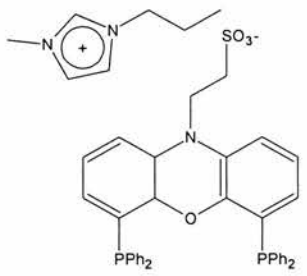
5.1.13 Synthesis of [3-(iodopentyl)-1-[4-(3-hexyl-1*H*-imidazol-3-ium-1-yl)butyl]-1*H*-imidazol-3-ium][iodide][hexafluorophosphate] salt



3-Hexyl-1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazol-3-ium hexafluorophosphate salt (2.00 g, 4.757 mmol) was dissolved in acetone (30 cm^3) and 1,5-diiodopentane (5 mole equivalent) was added. The reaction was refluxed overnight. Acetone was evaporated and the resulting oily product was washed with n-hexane. The oily product was then dissolved in dichloromethane and a solution of NH_4PF_6 (1.2 mole equivalents) in ethanol was added. The solution was stirred for 30 minutes and water was added. The organic layer (DCM layer) and the water layer were then separated yielding the final product (100% yield). Elemental analysis calculated for $C_{21}H_{37}N_4IP_2F_{12}$: C 33.08 H 4.89 N 7.35; found: C 34.45 H 5.93 N 7.56. ^{1}HNMR (300 MHz, Acetone-d_6, 298 K): δ 9.35 & 9.38 (2 x s, 2H, H2 & H11), 7.81 & 7.84 (2 x s, 4H, H4; H5; H13 & H14), 4.52 (m, 8H, H6; H9; H15 & H21), 3.31 (t, 2H, *J*(H,H) = 6.0 Hz, H19), 2.05 (m, 8H, H7; H8; H16 & H22), 1.45 (m, 10H, H17; H18; H23; H24 & H25), 0.95 (t, *J*(H,H) = 6.2 Hz, 3H, H26) ppm, ^{13}C {1H}NMR (300 MHz, Acetone-d_6, 298 K): δ 135.41 & 135.48 (2 x s, C2 & C11), 122.12 & 122.15 (2 x s, C4; C5; C13 & C14), 50.09 (C6 & C9), 50.00 (C21), 49.10 (C15), 32.32 (C24), 31.50 (C18), 29.90 (C23), 28.53 (C17), 27.32 (s, C7 & C8), 26.49 (C16), 25.95 (C22), 22.31 (C19), 13.96 (C20), 6.43 (C25) ppm. ^{31}PNMR (300 MHz, Acetone-d_6, 298 K): δ -144.45 ppm

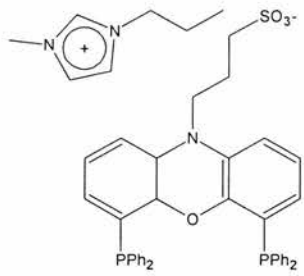
5.2 Attempted Syntheses

5.2.1 Attempted Synthesis of [Nixantphos$(CH_2)_2SO_3$][PMIM]



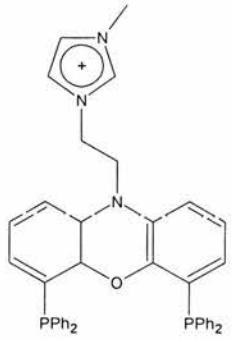
In a solution of nixantphos (1.00 g, 1.81 mmol) in dry DMF (30 cm^3), NaH (1.5 mol equivalent, 60% NaH suspended in mineral oil) was added at 0°C. The reaction was then warmed up to room temperature and stirred at room temperature for 1 hour. A solution of 2-bromoethanesulfonic acid sodium salt (1 mol equivalent) in DMF (10 cm^3) was added. The reaction was allowed to run at 80°C overnight. The reaction was monitored by TLC. No reaction took place i.e. the starting material (nixantphos) was recovered.

5.2.2 Attempted Synthesis of [Nixantphos$(CH_2)_3SO_3$][PMIM]



In a solution of nixantphos (1.00 g, 1.81 mmol) in dry THF (30 cm^3), NaH (1.5 mol equivalent, 60% NaH suspended in mineral oil) was added at 0°C. The reaction was then warmed up to room temperature and the reaction was refluxed for 1 hour. Sultone (1.5 mol equivalent) was added and the reaction was refluxed overnight, monitoring the reaction with TLC. The TLC showed no reaction. The reaction mixture was then poured into water and extracted with diethyl ether (3X10 cm^3). The resulting residue was washed with hexane and ^1H NMR showed the starting material.

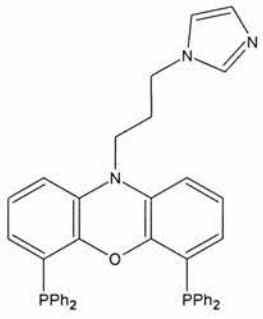
5.2.3 Attempted Synthesis of [NixantphosEMIM][Cl]



10-(2-chloroethyl)nixantphos (0.100 g, 0.161 mmol), as synthesized in section 5.1.6 above, was dissolved in dry toluene (30 cm^3). 1-Methylimidazole (5 mol equivalent)

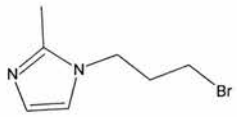
was added and the reaction was allowed to run at 100°C overnight. Toluene was then evaporated under vaccuo and resulting residue was washed with hexane. The ^{1}H NMR showed the starting material

5.2.4 Attempted alkylation of imidazole



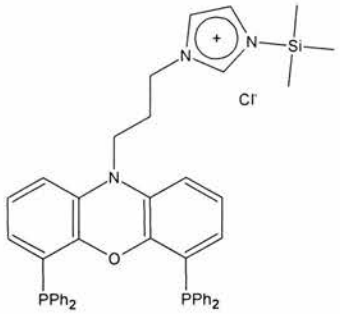
In a solution of imidazole (2.00 g, 29.38 mmol) in dry THF (50 cm^3) , NaH (1.5 mol equivalent, 60% NaH suspended in mineral oil) was added at 0°C. The reaction was then warmed up to room temperature and stirred at room temperature for 1 hour. A solution of 10-(3-chloropropyl)nixantphos (0.5 mol equivalent) in THF (10 cm^3) was added and the reaction was refluxed overnight. The solution was then poured into water and extracted with DCM (3X10 cm^3). The solvent was then evaporated and the resulting ^{1}H NMR showed reagent (10-(3-chloropropyl)nixantphos).

5.2.5 Attempted alkylation of 2-methylimidazole



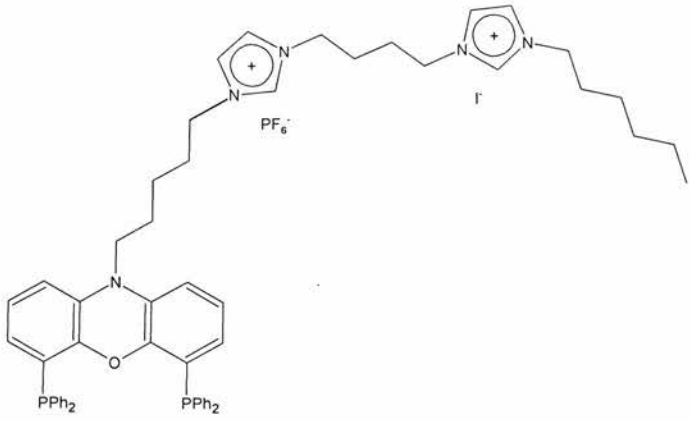
In a solution of 2-methylimidazole (2.00 g, 24.36 mmol) in dry THF (50 cm^3), NaH (1.5 mol equivalent, 60% NaH suspended in mineral oil) was added at 0°C. The reaction was then warmed up to room temperature and stirred at room temperature for 1 hour. 1-Bromo-3-chloropropane (0.5 mol equivalent) added and the reaction was refluxed overnight. The solution was then poured into water and the product was expected to precipitate out of solution. The product was extracted with DCM and diethyl ether without any success. After trying to extract the product with a range of organic solvents (diethyl ether, DCM), sodium hexafluorophosphate ($NaPF_6$) was added to precipitate any ionic compound, which could have formed as side products. The addition of $NaPF_6$ was used as an indication of whether any reaction occurred or not, by exchanging any halide anion with a PF_6 anion. PF_6 salts are insoluble in water, so they would precipitate out of the water solution as soon as they are formed. Immediately after the addition of $NaPF_6$, a white precipitate formed and was collected by filtration. ^{31}P NMR (300 MHz, Acetone d_6, 298 K) δ –145 ppm (septet, PF_6).

5.2.6 Attempted alkylation of 1-(trimethylsilyl)imidazole



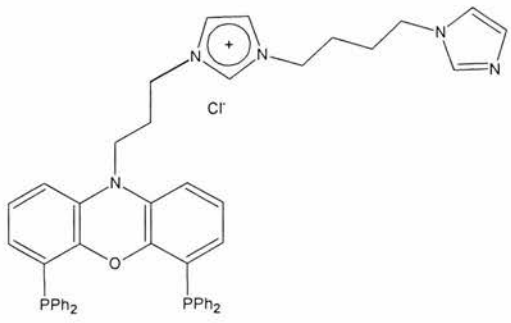
In a solution of 10-(3-chloropropyl)nixantphos (1.00 g, 1.58 mmol) in dry toluene (50 cm^3), 1-(trimethylsilyl)imidazole (2 mol equivalent) was added and the reaction was allowed to stir at 100°C overnight. The product was expected to precipitate out as it forms since the resulting product would be ionic. No precipitation occurred overnight. The solvent was removed in vaccuo and the resulting residue was washed several times with ethyl acetate. TLC and ^1H NMR showed 10-(3-chloropropyl)nixantphos, meaning that no reaction took place.

5.2.7. Attempted synthesis of {nixantphos(3-pentyl-1-[4-(3-hexyl-1*H*-imidazol-3-ium-1-yl)butyl)]-1*H*-imidazol-3- ium)} {][iodide] [hexafluorophosphate} salt



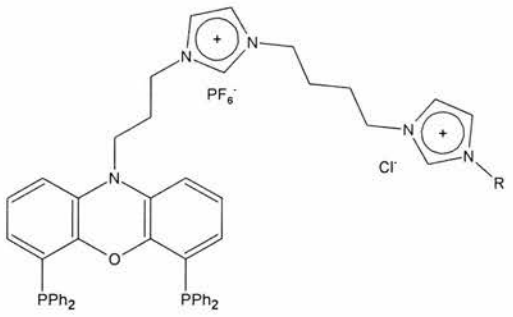
Nixantphos (1.00 g, 1.81 mmol) was dissolved in dry THF (50 cm^3) and NaH (1.5 mol equivalent, 60% NaH suspended in mineral oil) was added at 0°C. The reaction was then warmed up to room temperature and the reaction was refluxed for 1 hour. A solution of [3-(iodopentyl)-1-[4-(3-hexyl-1*H*-imidazol-3-ium-1-yl)butyl]-1*H*-imidazol-3-ium][iodide][hexafluorophosphate] salt (0.5 mol equivalent),as synthesized in section 5.1.13), in dry THF (10 cm^3) was added to the reaction mixture. The reaction mixture was then refluxed for 3 days. The reaction mixture was then poured into water and extracted with DCM (3X20 cm^3). The solvent was removed under vaccuo and the resulting residue was washed several times with diethyl ether to remove any excess nixantphos. After several diethyl ether wash, the ^{31}P NMR only showed [3-(iodopentyl)-1-[4-(3-hexyl-1*H*-imidazol-3-ium-1-yl)butyl]-1*H*-imidazol-3-ium][iodide] [hexafluorophosphate] salt and diethyl ether contained nixantphos. ^{31}P NMR (300 MHz, Acetone d_6, 298 K) δ -145 ppm (sept, PF_6) and δ -18 ppm (s, PPh_2)

5.2.8. Attempted alkylation of 1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazole with Borane protected 10-(3-chloropropyl)nixantphos



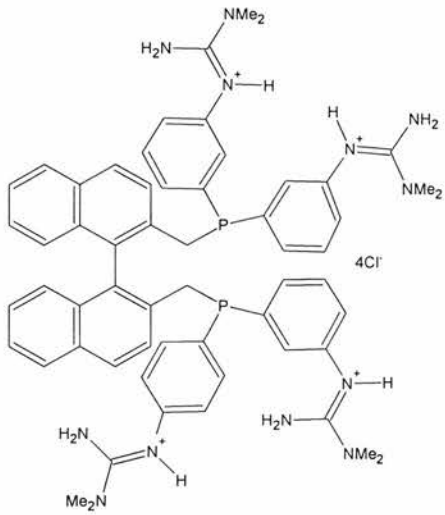
10-(3-Chloropropyl)nixantphos (0.1 g, 0.158 mmol) was dissolved in dry THF (30 cm^3) and borane-THF complex (1,2 mol equivalent, 1M solution in THF) was added. The reaction was monitored by ^{31}P NMR, which immediately showed a shift in chemical shift from –18 ppm to –24 ppm. The solvent was removed under vaccuo and resulting residue was dissolved in toluene (50 cm^3). 1-Methylimidazole (6 mol equivalent) was added and the reaction was stirred at 100°C overnight. 1-Methylimidazole was used as a test reaction before using 1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazole. 1-Methylimidazole was found to deprotect the phosphine. The ^{31}P NMR showed two peaks. The reaction with 1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazole could not carried out since 1-[4-(1*H*-imidazol-1-yl)butyl]-1*H*-imidazole was thought to be similar to 1-methylimidazole. ^{31}P NMR (300 MHz, $CDCl_3$, 298 K) δ -18 ppm (s, PPh_2) and δ –24 ppm (s, BH_3-PPh_2)

5.2.9. Attempted alkylation of 3-hexyl-1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazol-3-ium hexafluorophosphate salt



10-(3-Chloropropyl)nixantphos (0.1 g, 0.158 mmol) was dissolved in dry toluene (10 cm^3) and added to a solution of 3-hexyl-1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazol-3-ium hexafluorophosphate salt (1 mol equivalent) in acetone (20 cm^3). The reaction mixture was refluxed overnight. The solvent was removed under vaccuo and the resulting residue dissolved in DMC and the product was precipitated out by adding diethyl ether. The ^{31}P NMR showed that DCM/diethyl solution contained only 10-(3-Chloropropyl)nixantphos (δ -18 ppm) and residue was found to be only 3-hexyl-1-[4-(1H-imidazol-1-yl)butyl]-1H-imidazol-3-ium hexafluorophosphate salt (δ -145 ppm)

5.2.10. Attempted synthesis of a guanidinium type NAPHOS



2.2'-bis(bromomethyl)-1.1'-binaphthyl (1.00 g, 2.27 mmol) was dissolved in dry diethyl ether and n-BuLi (2.4 mol equivalent, 1.6 M in hexane) was added dropwise at 0°C. The reaction was allowed to warm up to room temperature and stirred for 16 hours. *N*,*N*,*N*',*N*'-Tetraethylphosphorodiamidous chloride (2.4 mol equivalent) was added dropwise at 0°C and the reaction was stirred at room temperature for 4 hours. The reaction was monitored by ^{31}P NMR, which showed one significant peak at δ 88.58 ppm and very small peaks at δ 35 ppm, 36 ppm and 135 ppm with a ratio of 4:1 (significant peak : small peaks). The reaction mixture was the treated with HCl (9.6 mol equivalent, 1 M solution in diethyl ether) and the mixture was filtered off the diethyl ammonium chloride salt. The resulting ^{31}P NMR spectrum of the filtrate showed a signal at δ 180.23 ppm. There were other small signals between δ 150 ppm and δ 180 ppm, which were very insignificant. It was difficult to purify the product except by distillation. Kügelrohr distillation was carried out but the compound decomposed.

It was decided to rather react the resulting compound further in situ. The solvent (diethyl ether) was removed under vaccuo and the resulting residue was dissolved in THF (50 cm^3) 3-[N,N-bis(trimethylsilyl)amino]phenyl)magnesium chloride (2.4 mol equivalent, 1 M solution in THF) was added and the reaction was monitored by ^{31}P NMR. The resulting product showed four peaks at δ -13.51 ppm, -13.34 ppm, 60.01 ppm and 60.20 ppm at 1:5:2:2. The major peak at δ -13.34 ppm is the diphosphine (the desired product) and the peak at δ -13.51 ppm is the monosubstituted phosphine. The reaction mixture was treated with HCl (9.6 mol equivalent, 1M solution in diethyl ether). The peaks at δ 60.01 ppm and 60.20 ppm disappeared and hump appeared at δ 26 ppm, which is characteristic of the phophine oxide. The solvent was removed under vaccuo. The product was crystallized from ethanol without any success.

5.3. Catalysis with [DPPCo][PF_6] in [BMIM][PF_6]

5.3.1. Run 1

A. [Rh(acac)$(CO)_2$] (5.2 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave, which was then flushed 3 times with CO_2. [DPPCo][PF_6] (28 mg, 0.04 mmol) was dissolved in [BMIM][PF_6] (5 cm^3), which had been degassed. For the ligand to dissolve easily, the IL was heated with a hot gun to make it less viscous. The IL-ligand solution was injected into the autoclave while it was still warm for easy handling under inert conditions i.e. the autoclave was under slight positive syngas pressure. It was then pressurised with 40 bar H_2/CO, heated to the reaction temperature and stirred for 1 hour. Afterwards the system was cooled to about room temperature and depressurised slowly. The substrate (3.15 cm^3, 24 mmol 1-octene) was injected under H_2/CO positive pressure, the system was charged with 40 bar H_2/CO and $scCO_2$ (15 cm^3) was added through a cooled head HPLC pump. The system was then heated to 100°C while stirring at 1000 rpm and more $scCO_2$ (about 10 ml) was added to raise the system pressure to 200 bar. The reaction was run for 1 hour.

After an hour, the stirrer was stopped. The HPLC pump high pressure limit was set to 201 bar for the extraction with $scCO_2$. The reaction autoclave was linked to another autoclave with a pressure regulator to regulate the pressure between the two autoclaves. The product recovery was at lower pressure (i.e. pressure in the 2nd autoclave far less than the reaction pressure of 200 bar) in order to strip the product/substrate of CO_2. The temperature was maintained at 100°C during the extraction. The 2nd autoclave was

linked to a gas bubbler to let out the CO_2. The gas bubbler contained ethanol to trap the product/substrate, which escaped the 2nd autoclave. The extraction was carried out by pumping $scCO_2$ continuously into the autoclave at 10 cm^3/min with the pump high pressure limit regulating the flow i.e. as soon as the pressure drops below 201 bar, the pump allows $scCO_2$ to flow again. The extraction was done for 2 hours. About 1 ml of product was recovered.

B. After the extraction in A above was complete, the autoclave was depressurised and the catalyst was reused. Fresh 3.15 cm^3 1-octene was injected into the system under positive syngas pressure. From here a similar procedure was followed as in A above.

5.3.2. Run 2

$[Rh(acac)(CO)_2]$ (5.1 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave, which was then flushed 3 times with H_2/CO. $[DPPCo][PF_6]$ (28 mg, 0.04 mmol) was dissolved in $[BMIM][PF_6]$ (5 cm^3), which had been degassed. For the ligand to dissolve easily, the IL was warmed with a hot gun to make it less viscous. The IL-ligand solution was injected into the autoclave while it was still warm for easy handling under inert conditions i.e. the autoclave was under slight positive syngas pressure. 1-Octene (3.15 cm^3, 24 mmol) was injected into the autoclave, the system was pressurised with 10 bar H_2/CO gas and it was heated to 100°C while stirring at 1000 rpm. The reaction was run for 1 hour, cooled to room temperature and the autoclave was unloaded. The product was decanted and analysed by GC.

5.3.3. Run 3

Runs 2 & 3 are similar in procedure except that a new batch of IL was used in run 3 and that the catalyst/ligand/IL solution was firstly stirred for an hour at room temperature before pressurising with syngas and heating it to 100°C. Fresh catalyst was used i.e. the catalyst was not recycled from Run 2.

5.3.4. Runs 4[a], 5[a], 6[b], 7[c] & 8[d]

[Rh(acac)$(CO)_2$[(5.2 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave with a 2 cm^3 liquid injector (port). The autoclave was then flushed 3 times with H_2/CO. [DPPCo][PF_6] (28 mg, 0.04 mmol) was dissolved in 5 cm^3 [BMIM][PF_6], which had been degassed. For the ligand to dissolve easily, the IL was warmed up with a hot gun to make it less viscous. The IL-ligand solution was injected into the autoclave through the liquid port. The injection was done under inert conditions i.e. the autoclave was under slight positive syngas pressure. The system was stirred for 1 hour meanwhile 1 cm^3 1-octene was injected into the liquid port. The system was then heated up to 100°C, pressurised with about 5 bar syngas just to form the active species and 1-octene was introduced to the system through the liquid port with 10 bar pressure which makes up the system's pressure to 10 bar. The reaction was allowed to run for 1 hour, cooled and unloaded. The product was decanted off.

[a] *Runs 4 and 5 are exactly as described above*

[b] *Run 6 is similar to runs 4 and 5 except that the catalyst was given 45 minutes preforming time under 5 bar pressure*

[c] *Similar to runs 4 and 5 except the temperature was reduced to 80°C*

[d] *Similar to runs 4 and 5 except that the system's total pressure was increased to 40 bar*

5.3.5. Run 9

[Rh(acac)$(CO)_2$] (5.2 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave with a 2 cm^3 liquid port and was flushed 3 times with H_2/CO. [DPPCo][PF_6] (28 mg, 0.04 mmol) was dissolved in 5 cm^3 [BMIM][PF_6], which had been degassed. For the ligand to dissolve easily, the IL was warmed up with a hot gun to make it less viscous. The IL-ligand solution was injected into the autoclave through the liquid pot. The injection was done under inert conditions i.e. the autoclave was under slight positive syngas pressure. The system was stirred for 1 hour meanwhile 1 cm^3 1-octene was injected into the liquid port. The system was then heated up to 100°C, pressurised with 40 bar and the system was left to stabilise at the reaction temperature for about 5 minutes. 1-Octene (1 cm^3) was introduced to the system through the liquid port with 30 cm^3 liquid CO_2, which raised the system's pressure to 200 bar. The reaction was let to run for 1 hour, cooled down to -40°C and CO_2 gas was released. The product was extracted from the ionic phase with toluene (5 cm^3) and analysed by GC.

5.4 Hydroformylation of 1-octene with a preformed [Rh(acac)$(CO)_2$]/[DPPCo][PF_6] catalyst in [OctMIM][NTf_2]

[Rh(acac)$(CO)_2$] (5.2 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [DPPCo][PF_6] (28.2 mg, 0.04 mmol) in an ionic liquid (5 cm^3), was injected into the autoclave with the autoclave under slight positive syngas pressure.

The autoclave was charged with H_2/CO (1:1) gas mixture and heated to 100°C. The pressure was varied from 10 to 60 bar H_2/CO. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After an hour, 1-octene (3 cm^3) was injected through a liquid pump and the reaction was let to run for I hour. The autoclave was the cooled, opened and the product was extracted from the ionic solution with n-hexane (40 cm^3). The product was analysed by GC.

5.5 Batch hydroformylation reaction of 1-Octene with [TPPMS] [PMIM] in an Ionic Liquid – $scCO_2$ biphasic system

$[Rh(acac)(CO)_2]$ (46.8 mg, 0.181 mmol) was weighed into a 50 cm^3 autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [TPPMS][PMIM] (1.31 g, 2.81 mmol) in an Ionic Liquid (12 cm^3), was injected into the autoclave with the autoclave under slight positive syngas pressure. The following different ionic liquids were tested:

The autoclave was charged with 40 bar H_2/CO (1:1) gas mixture and heated to 100°C. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After an hour, about 30 cm^3 liquefied CO_2 was pumped through an HPLC pump (equipped with a freezer) to make up 200 bar reaction pressure. The reaction solution was allowed 1 hour to absorb $scCO_2$. Using an HPLC pump, 1-dodecene/1-octene (2 cm^{-3}) was pumped through and the reaction was isolated and run for 1 hour. The gas uptake was monitored every minute for 1 hour for 1-octene.

After the reaction was stopped, the autoclave was cooled to about -40°C and the CO_2 was slowly vented over about 30 minutes. The autoclave was opened and the solution was extracted with n-Hexane (40 cm^3).

5.6 Batch hydroformylation reaction of 1-Dodecene with [TPPMS] [PMIM] in an Ionic Liquid – $scCO_2$ biphasic system

$[Rh(acac)(CO)_2]$ (46.8 mg, 0.18 mmol) was weighed into an autoclave (30 cm^3) fitted with a magnetically driven stirrer. The autoclave was purged with CO/H_2 and then charged with a solution of [PMIM][TPPMS] (1.31 g, 2.81 mmol) in the ionic liquid (12 cm^3), again under a CO/H_2 purge. The autoclave was pressurized with CO/H_2 (1:1, 40 bar) and heated to 100 C with rapid stirring. The catalyst solution was stirred for 1 h at 1100 rpm to allow for the formation of active catalyst. The autoclave was then filled with CO_2 from an HPLC pump (Gilson 304 fitted with a cooled pump head) to a total pressure of 200 bar. The reaction solution was left for 1 h to allow the ionic liquid to absorb $scCO_2$. 1-Dodecene (2 cm^3, 9.01 mmol) was injected into the autoclave by an HPLC pump and the reaction solution was stirred at temperature and pressure for 1 h. The autoclave was then cooled to ca. -40 C and the CO_2 was slowly vented over a period of approximately 30 min. The ionic liquid solution was extracted with hexane (3 × 15 cm^3). The hexane extract was analysed by GC.

5.7 Batch hydroformylation of 1-octene with [NixantphosPMIM][Cl] in [OctMIM][NTf_2]

[$Rh(acac)(CO)_2$] (5.2 mg, 0.02 mmol) was weighed into a 50 cm^{-3} autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [nixantphosPMIM][Cl (28.6 mg, 0.04 mmol) in an ionic liquid (5 cm^{-3}), was injected into the autoclave with the autoclave under slight positive syngas pressure.

The autoclave was charged with 10/20 bar H_2/CO (1:1) gas mixture and heated to 100°C. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After an hour, 1-octene (3 cm^3) was injected through a liquid pump and the reaction was run for I hour. The autoclave was the cooled, opened and the product was extracted from the ionic solution with n-hexane (40 cm^3). The product was analysed by GC.

5.8 Batch hydroformylation of 1-octene with [NixantphosPMIM][Cl] in an ionic liquid – $scCO_2$ biphasic system

[$Rh(acac)(CO)_2$] (5.2 mg, 0.02 mmol) was weighed into a 50 cm^3 autoclave and the autoclave was flushed 3 times with H_2/CO. A ligand solution, which was prepared by dissolving [nixantphosPMIM][Cl] (0.0286 g, 0.04 mmol) in [OctMIM][NTf_2] (5 cm^3), was injected into the autoclave with the autoclave under slight positive syngas pressure.

The autoclave was charged with H_2/CO (40 bar, 1:1) gas mixture and heated to 100°C. The catalyst solution was stirred for 1 hour at 1100 rpm in order to form the active catalyst species. After an hour, liquid CO_2 (about 30 cm^3) was pumped through an

HPLC pump (equipped with a cooled head) to make up 200 bar reaction pressure. The reaction solution was allowed 1 hour to absorb $scCO_2$. Using an HPLC pump, 1-octene (3 cm^{-3}) was pumped through and the reaction was isolated and run for 1 hour.

After the reaction was stopped, the autoclave was cooled to about -40°C and the CO_2 was slowly vented over about 30 minutes. The autoclave was opened and the solution was extracted with n-hexane (40 cm^3). The sample was analysed by GC.

5.9 Continuous Flow Hydroformylation with [NixantphosPMIM][Cl]

The catalyst solution was prepared by weighing $[Rh(acac)(CO)_2]$ (46.8 mg, 0.181 mmol) and [NixantphosPMIM][Cl] (262,3 mg, 0.362 mmol, L:Rh = 2) into a Schlenk tube and syringing in $[OctMIM][NTf_2]$ (12 cm^3). The solution was then stirred at 55°C under vacuum until everything dissolved in the ionic liquid. The catalyst solution was then syringed, under positive CO/H_2 pressure, into a 50 cm^{-3} autoclave, which had been flushed by Argon and charged by CO/H_2 (40 bar). The autoclave was stirred gently while heated up to 50°C and eventually to 100°C. The stirrer speed was then increased to 1000 rpm and stirred for 1 hour to preform the catalyst. Liquid CO_2 was added, through an air driven liquid pump, to make up 200 bar reaction pressure and $scCO_2$ was allowed to saturate the ionic phase over 1 hour. The reaction was started by pumping 1-octene at 0.416 cm^3 min^{-1} flow rate via a liquid pump and feeding CO/H_2 via the dosimeter continuously. CO_2 was also pumped into the system continuously to maintain a 200 bar reaction pressure while continuously extracting. Total flow = 1.04 nL min^{-1}.

Products collected at 3-4 bar. Sampling was done at regular intervals and analysed by GC. The reaction was run for about 8 hours before changing the 1-octene flow rate to 0.356 cm^3 min^{-1} and the reaction was then continued for another 16 hours before it was stopped. The system was allowed to cool and was depressurised and cleaned with acetone.

5.10 Continuous Flow Hydroformylation using a dual ligand system ([NixantphosPMIM][Cl] and[TPPMS][PMIM])

The catalyst solution was prepared by weighing [Rh(acac)$(CO)_2$] (46.8 mg, 0.181 mmol) and [NixantphosPMIM][Cl] (262.3 mg, 0.362 mmol, L:Rh = 2) into a Schlenk and warm [OctMIM][NTf_2] (12 cm^{-3}) was syringed in. The solution was then stirred at 55°C under vacuum until everything dissolved in the ionic liquid. [PMIM][TPPMS] (1.31 g, 2.81 mmol) was added and the solution was stirred again at 55°C under vacuum until all the [PMIM][TPPMS] had dissolved. The catalyst solution was then syringed, under positive CO/H_2 pressure, into a 50 cm^{-3} autoclave, which had been flushed with argon and charged by 40 bar CO/H_2. The autoclave was stirred gently while heated up to 50°C and eventually to 100°C. The stirrer speed was then increased to 1000 rpm and stirred for 1 hour to preform the catalyst. Liquid CO_2 was added, through an air driven liquid pump, to make up 200 bar reaction pressure and $scCO_2$ was allowed to saturate the ionic phase over 1 hour. The reaction was started by pumping 1-octene at 0.416 cm^3 min^{-1} flow rate via a liquid pump, feeding CO/H_2 (1:1 at 4.03 mmol min^{-1} of each) via the dosimeter continuously. CO_2 was also pumped into the system continuously to maintain a 200 bar reaction pressure while continuously extracting. Total flow = 1.04 nL min^{-1}. Products collected at 3-4 bar. Sampling was done at regular intervals and

analysed by GC. The reaction was run for about 30 hours. The system was allowed to cool and was depressurised and cleaned with acetone.

5.11 Reference

1. Wasserscheid, P.; Waffenschmidt, H.; Machnitzki, P.; Kottsieper, K. W.; Stelzer, O. *Chem. Commun.* **2001**, 451-452.
2. Webb, P. B.; Sellin, M. F.; Kunene, T. E.; Williamson, S.; Slawin, A. M. Z.; Cole-Hamilton, D. J. *J. Am. Chem. Soc.* **2003,** *125*, 15577-15588.
3. Fuller, J.; Carlin, R. T.; de Long, H. C.; Hawort, D. *J. Chem. Soc. Chem. Comm.* **1994**, 299.
4. Suarez, P. A. Z.; Dullius, J. E. L.; Einloft, S.; de Souza, R. F.; Dupont, J. *Polyhedron* **1996,** *15*, 1217.
5. van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *Organometallics* **2000,** *19*, 872.
6. Luo, H.; Guo, S.; Zhou, C.; Xie, R. *Heterocycles* **1995,** *41*, 1421-1424.