Synthesis and studies of the coordination chemistry with catalytic applications of tripodal ligands based on nitrogen, oxygen and sulfur donors

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With Love
And
Heartiest Thanks

Your love and devotion towards your family doesn't stop growing. You are understanding, friendship, someone to count on who will always be there. You've never stopped caring, you've never stopped giving, always putting us before yourself. Your warm words of wisdom have shaped my perspective on life and your courage in tough times has been my strength through the years. Every time I turn around I find you standing there with open arms and a heart full of love. For your family you become a shield that weathers all storms. You are the epitome of love, the acme of being and a paragon in my eyes. Even though I might not say what I really feel inside, how much your endless love means to me but today I would like to say how very proud and fortunate I am to have you in my life.

Thank you

I dedicate this thesis to

Babaji Puran Singh Ji
(founder of GNNSJ-Birmingham),
Babaji Norang Singh Ji,
Babaji Mohinder Singh Ji ~ Mataji Baldev Kaur Ji,
Mum and Dad,

without whom I would not have accomplished
all that I have.

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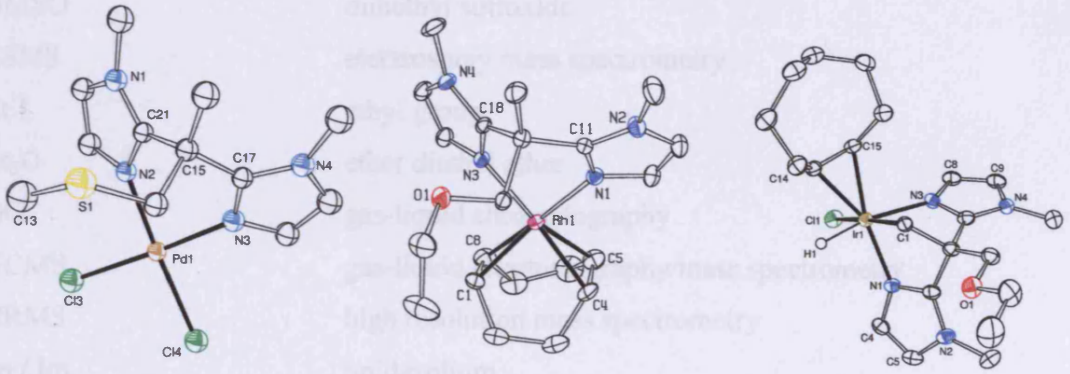
Abstract

This thesis describes the synthesis of a series of mixed N,O,S donor ligands, their co-ordination chemistry using palladium, rhodium and iridium metal precursors and their catalytic behaviour.

First synthesised were a series of potential tripodal oxygen donor ligands mimicking the synthesis of meTAM but incorporating a fourth additional group that was hoped to preferentially co-ordinate to a metal centre. A variety of synthetic pathways were unsuccessfully employed to synthesise mixed donor ligands using aliphatic bidentate backbones. This work was followed by the synthesis, structure and co-ordination chemistry of novel tripodal ligands containing bis(1-methylimidazol-2-yl)methyl methane in combination with an ether or sulfide functionality. These N,N,O and N,N,S ligands were expected to demonstrate properties intermediate of those of the Trofimenko and Klaui ligands.



As expected these ligands found application in both co-ordination chemistry and organometallic chemistry, as a series of metal complexes of the N,N,O and N,N,S hemilabile ligands were isolated and fully characterised; crystal structures of Pd, Rh and Ir complexes are illustrated above. The Pd(II) complexes were found to be active catalysts in the Heck coupling of alkenes with aryl halides.

Abbreviations

Acac	pentane-2,4-dione
$Acac^-$	acetylacetonate ion
Ar	aryl group
BA	*n*-butylacrylate
BAP	4-bromoacetophenone
BIM	bis(*N*-methylimidazol-2-yl)methane
BPM	bis(pyrazol-1-yl)methane
Bpy	bi-pyridine
^nBu	*n*-butyl group
^tBu	*tert*-butyl group
COD/cod	1,5-cyclooctadiene
DCM	dichloromethane
DMAc	N,N-dimethylacetamide
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
ESMS	electrospray mass spectrometry
Et	ethyl group
Et_2O	ether diethyl ether
GC	gas-liquid chromatography
GCMS	gas-liquid chromatography/mass spectrometry
HRMS	high resolution mass spectrometry
im / Im	imidazolium
iPr	*iso*-propyl group
IR	infra red spectroscopy
LSIMS	liquid secondary ion mass spectrometry
M	metal
MAO	methylaluminoxane
Me	methyl group
MeTAM	1-methyltris[acetyl]methane

MS	mass spectrometry
N	nitrogen (donors)
NHC	nucleophilic heterocyclic carbene
NMR	nuclear magnetic resonance
NaOAc	Sodium acetate anion
O	oxygen (donors)
OTf	trifluoromethanesulfonate (triflate) anion
Ph	phenyl group
Py	pyridyl group
Pz/pyz	pyrazole group
R	alkyl group
S	sulfur (donors)
SHOP	shell higher olefin process
THF	tetrahydrofuran (solvent and/or ligand)
TOF	turnover frequency (molProduct / molPd)
Tol	toluene
TON	turnover number (molProduct / molPd / hr)
UV	ultraviolet visible (spectroscopy)
X	halogen

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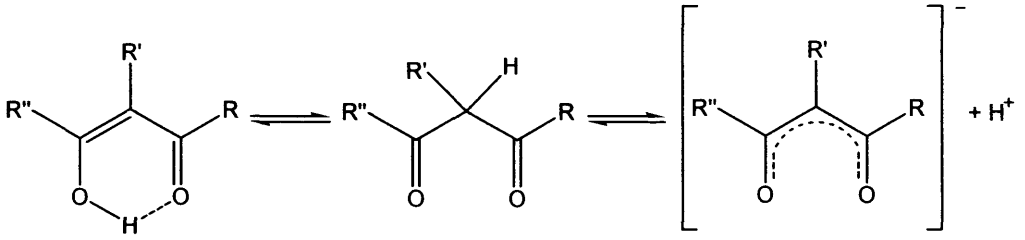
CHAPTER ONE

Introduction

1.1 1,3-Diketones

Chelating ligand systems such as 1,3-diketones typically form six-membered metal containing rings and are widely used in modern co-ordination chemistry.[1] 1,3-Diketones can exist in solution as a mixture of enol **I** and keto **II** forms, related by a 1,3 hydrogen shift and this equilibrium has been measured by nuclear magnetic resonance (NMR) techniques.[2] The methine proton in the keto form and the hydroxyl proton in the enol form are acidic and their removal generates 1,3-diketonate anions **III**, which are the source of a broad class of co-ordination compounds referred to generically as diketonates or acetylacetonates (acac's). The most common ligand of this class is the acetylacetonate ion $(acac)^-$, in which R = R" = CH_3 and R' = H.

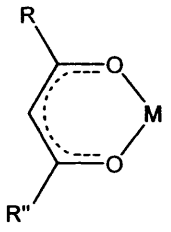
Figure 1.1 *β*-Diketones and their anions



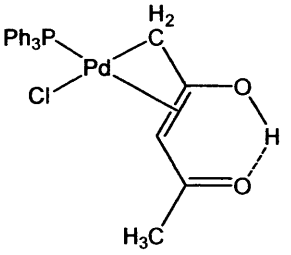
I enol form **II** 1,3-dicarbonyl **III** enolate anion

Diketonate anions are strong chelating ligands and form stable complexes with virtually every transition and main group element, as reported in several extensive reviews.[3-7] However, the co-ordination chemistry of β-diketones is not limited to the formation of

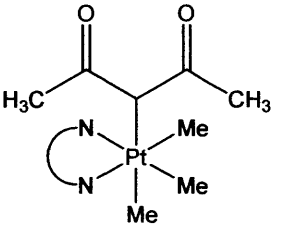
chelates but extends to alternative, e.g. bridging co-ordination modes, forming mono, di and polynuclear β-diketonate complexes; these may be divided on a structural basis into several broad classes: (1) Oxygen bonded diketonates **IV**; (2) semi-chelating β-diketonate bonding, in which one oxygen is in an axial position below the co-ordination plane of the molecule and has a significantly longer M-O bond length compared to the bond in the plane; (3) monodentate oxygen bonded; (4) acetylacetonates in which the metal is σ-bonded to a terminal CH_2 and π-bonded to the C=C double bond in the enolic form of the ligand **V**;[8] (5) η^1-diketonate ligands bonded to the central carbon atom **VI**;[9] (6) tridentate bonding involving both oxygen atoms and the apical carbon atom **VII**.[10] An unusual bonding type eluding formal description was found in the complex $Ag\text{-}Ni(acac)_3.2AgNO_3.H_2O$.[11] In this compound the octahedral Ni was co-ordinated to three acetylacetonate ligands and the Ag was surrounded by three oxygen atoms and was in close proximity to the acetylacetonate methine carbon; thus the diketonate ligand could loosely be considered to be tridentate and bridging.



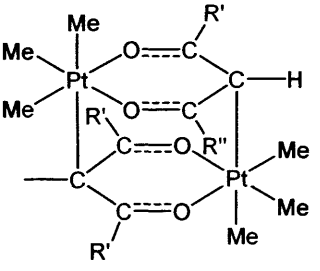
IV



V



VI

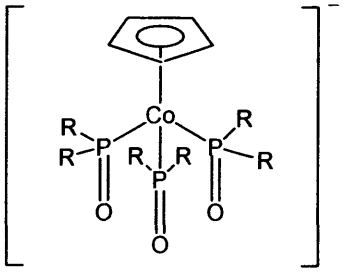


VII

There has been an increase in the trend to use tridentate ligands over bidentate examples as they have structural and electronic properties that allow the stabilisation of many metallic centres with varying oxidation states and geometries. This has been exemplified by polydentate phosphane ligands, triazacyclononane (TACN) and trispyrazolylborate (Tp) ligands. Complexes of these tripodal ligands have been successfully used as catalysts for the hydrogenation of alkynes, alkenes and nitriles, hydroformylation and isomerisation reactions of alkenes and oligomerisation and polymerisation of alkynes. More recently the use of triols with C_3 symmetry in place of chiral C_2-symmetric diols in catalytic

asymmetric alkylation of aldehydes has been found advantageous in several respects. The introduction of chiral C_3-symmetric triols as ligands for vanadium and titanium complexes gave complexes with greater structural stability due to stronger chelating effects. Facial co-ordination of tridentate ligands possessing C_3 symmetry rendered vacant cis-oriented co-ordination sites equivalent thus catalytic reactions proceeded via octahedral intermediates.[12] The increased rate of reaction was complemented by the presence of three stereo centres which led to better asymmetric induction.

Klaui reported the synthesis of a tripodal oxygen ligand, based on a phosphito donor system **VIII**. This ligand was nearly as hard as fluoride[7] according to the HSAB principle (see p22) and chemically extremely robust as it dissolves without decomposition in aqueous sulphuric acid. The stability extends further such that it is not oxidised by atmospheric oxygen but can be, with difficulty, using nitric acid. The phosphorus ligand in complex **VIII** complexes in a 2:1 ratio with a wide variety of main group and transition di- and tri-valent metal ions. Complex **VIII** is a mono-anionic half-sandwich complex $[(C_5H_5)Co(P(O)R_2)_3]^-$ (L_R^-), which can co-ordinate as a tridentate ketone ligand by means of three P=O units. The steric and electronic properties of L_R^- can be controlled by varying the R substituents (-alkyl, -O-alkyl, -O-phenyl).

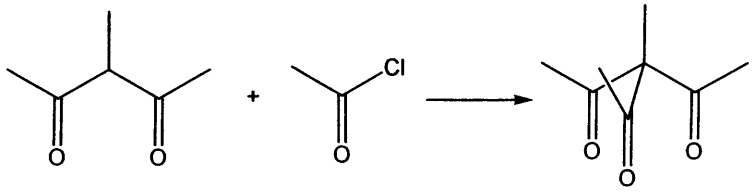


(Cyclopentadienyl)tris[diorganylphosphito-P]cobaltate(**VIII**)

In a previous note the Cavell group reported the synthesis and catalytic behaviour of chromium(III) complexes bearing a tridentate triketone ligand, 1-methyltris[acetyl]methane, also known as MeTAM.[13] MeTAM was first described in a

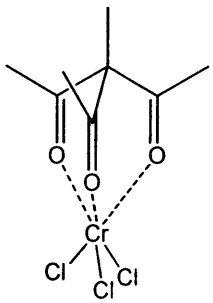
patent by M^{C}Killop in 1968, synthesised using thallous salts and acyl chlorides.[14] The reaction was hazardous and expensive as the waste products from the reaction were extremely toxic and costly to remove. For that reason the use of MeTAM in catalysis was restricted until an alternative safer and easier synthesis from pentan-2,4-dione was developed.[13]

Scheme 1.1 Synthesis of MeTAM



MeTAM

MeTAM is a tripodal oxygen ligand that donates three pairs of electrons to the metal centre to which it complexes. When complexed to Cr(III) and activated with MAO, MeTAM was reported to give a very active system for ethylene oligomerisation giving a high yield of 1-alkenes. [13] Complex **IX** was postulated as a neutral, homogeneous mimic for the hard oxygen environment in heterogeneous supporting materials.[13]



(IX)

MeTAM is an oxophilic ligand with high affinity for hard, oxophilic metals such as $Cr^{3+}$and Zr^{4+}, thus its ability to bind to softer metals is somewhat depleted. Therefore an

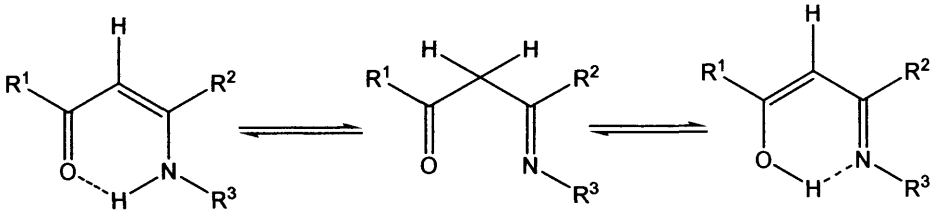
interest arose in designing a nitrogen equivalent of the MeTAM ligand, combining the softer donor properties of the Tp system with the geometry of Klaui's ligands to give ligands that could open up an unexplored area of co-ordination chemistry and catalysis. Notably, the electron-donating nitrogen atoms are able to accommodate an additional substituent, allowing manipulation of steric and electronic factors in the resulting metal complexes.

1.2 β-Aminoketone ligands

β-Aminoketone ligands (also referred to as enaminones, vinylogous amides, β-ketiminates or nacac) have demonstrated importance as organic intermediates with interesting biological activity. For example enaminones of β-dicarbonyl compounds are quite stable and have been employed as prodrugs; Edafiogho *et al.* reported several enaminone type species to exhibit anticonvulsant activity with very low neurotoxicity.[15] Early transition metals prefer hard donors whereas late transition metals prefer softer donor ligands. Thus ligands of the type O-Y where O are hard donors atom and Y are soft donors, for example N or S, are particularly interesting ligands across the transition series. In early transition metals, the oxygen provides a site for strong co-ordination whereas the other donor, Y, is likely to be less strongly bound and hence may lead to ligand hemilability and subsequently to interesting catalytic behaviour. These β-aminoketones provide a donor atom set [NO] which can be good for both early and late transition metals and on co-ordination would typically form a delocalized chelate ring including the metal centre.

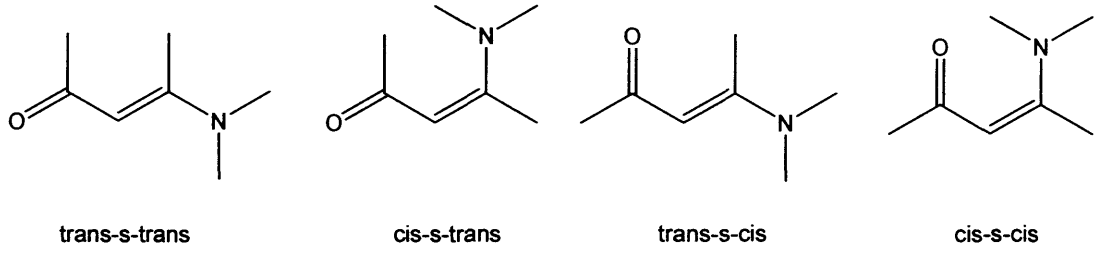
Free β-aminoketone ligands may be prepared from the condensation of primary amines with the corresponding β-diketones. There are three different tautomeric forms that are possible for such ligands as illustrated in Figure **1.2** and it is well established that enaminones of all types exist predominantly in the carbonyl form **X**,[16] however Dudek *et al.* concluded that tautomer **XII** predominates in non-polar solvents.

Figure 1.2 Possible β-aminoketone tautomers



In β-aminoketones the atoms comprising the π system lie in the same plane allowing maximum resonance stability, thus four geometric isomers (*trans-s-trans*, *cis-s-trans*, *trans-s-cis* and *cis-s-cis*) possible. These isomers can be distinguished by U.V. spectroscopic data, although the distinction between the *cis-s-cis* and *cis-s-trans* is difficult.

Figure 1.3 Four possible β-aminoketone isomers



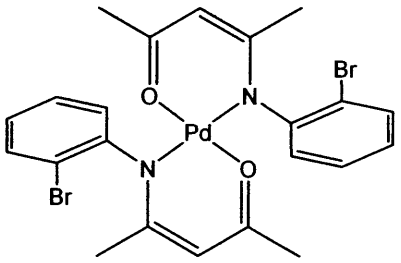
1.2.1 Complexes of β-aminoketone ligands

The synthesis of transition metal complexes containing nitrogen based chelates has received much attention in recent years, most notably with the preparation by Brookhart and Gibson of new Ni, Pd,[17,18] Co[19] and Fe[20] catalyst systems incorporating bidentate α-diimine and tridentate bisiminopyridine environments. Examples of these systems were found to be highly active catalysts for olefin polymerisation.[17,18,20]

Nickel, palladium and zirconium complexes of β-aminoketones have been extensively explored and found to possess interesting catalytic behaviour in the oligomerisation of ethylene,[21] for methyl methacrylate polymerisation[22] and as intermolecular Heck arylation catalysts.[23]

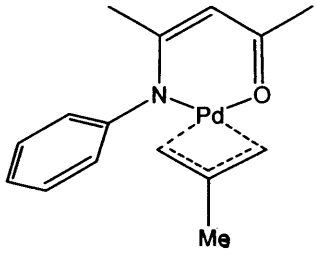
1.2.1.1 Palladium complexes bearing β-aminoketone ligands

Lida *et al.* reported the first palladium complex of a β-aminoketone ligand Pd(II) 4-(2-Bromoanilino)pent-3-en-2-one, **XIII**.[23] Their study demonstrated that β-aminoketones derived from β-diketones and primary amines with the *cis-s-cis* structure were suitable bidentate ligands for Pd(II) and gave stable, yellow, crystalline complexes. The same group reported intramolecular Heck arylation reactions and some ring closing reactions using these palladium complexes.[23]



XIII

Chi *et al.* reported η^3-allyl(β-ketoiminato) palladium(II) complexes which served as precursors for the chemical vapour deposition of thin palladium films attractive for the manufacture of various electronic devices.[24] More recently, Bouquillon *et al.* described the simultaneous, one pot generation of anionic and neutral Pd(II) complexes **XIV** from the reaction of η^3-allylpalladium chloride and β-aminoketones.[25] No catalysis with these complexes has been reported thus far, however similar systems have been used as highly active catalysts for Suzuki and Heck reactions.[26]



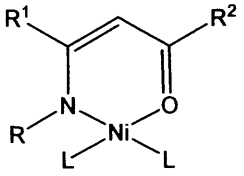
XIV

1.2.1.2 Nickel complexes bearing β-aminoketone ligands

There has been a significant interest in the catalytic behaviour of nickel complexes based on N,O donor chelate ligands. Nickel(II) complexes bearing S,S, S,O, and O,O chelating ligands have demonstrated high catalytic activity for olefin oligomerisation; however, the product distribution was difficult to control therefore commercialisation could not be achieved. The introduction of a nitrogen group into the bidentate O containing chelate Ni systems allowed the steric properties to be varied and resulted in almost 100% selectivity for linear hexenes with a high proportion (60-80%) being α-olefins.[27]

Nickel(II) complexes bearing N,O chelating ligands have been extensively studied. A series of four co-ordinate Ni(II) complexes derived from β-ketoamines were reported by Everett *et al.*[28] followed by work by He *et al.*[22] describing Ni(II) complexes bearing mixed β-aminoketone ligands that proved to be good precursors for methyl methacrylate polymerisation catalysts following activation with methylalumoxane (MAO).

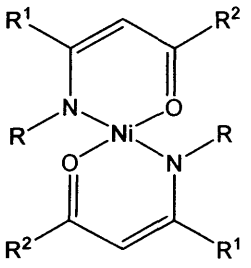
Figure 1.4 Nickel complexes bearing β-aminoketone ligands



(1) General formula

$L_2Ni[R_1COCH(NHR)R_2$

XV



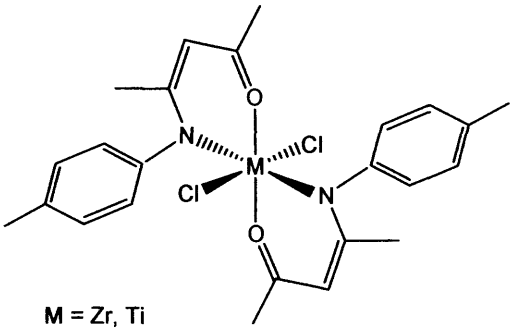
(2) $R^1 = R^2 = Me$, R^3 = 2,6-diisopropylphenyl

(2a) $R^1 = Me$, $R^2 = C_6H_5$, R^3 = 2,6-diisopropylphenyl

XVI

1.2.1.3 Zirconium and titanium complexes bearing β-aminoketone ligands

Complexes of early transition metals bearing softer mixed donor chelating ligands have been reported. Although weaker than the M-O bond, co-ordination of the nitrogen atom to both Zr and Ti has been documented.[21,29] Kakaliou *et al.* were able to isolate and characterise β-ketiminate titanium and zirconium complexes bearing two tolnacac as illustrated by **XVII** and two tolnacnac ligands by X-ray crystallography;[29] however, no catalysis was reported.

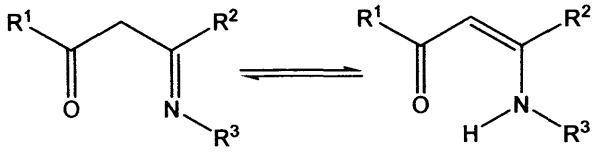


M = Zr, Ti

XVII

Interest in β-aminoketone ligands was pursued within the Cavell group and Figure **1.5** illustrates a series of nacac ligands for zirconium and titanium complexes that were investigated as catalysts for oligomerisation reactions.[30]

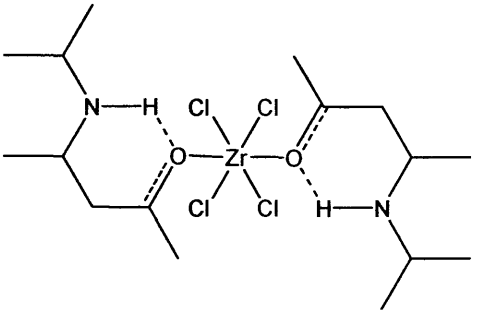
Figure 1.5 Bis β-aminoketone



XVIII

$R^1 = R^2 = Me$, $R^1 = R^2 = Ph$
$R^1 = Me$, $R^2 = CF_3$
$R^1 = Me$, $R^2 = Ph$
$R^3 = Pr^i$, Bu^t, hexyl-, cyclohexyl, Ph, *p*-MeOPh, *p*-ClPh- or 2,4,6-trimethylphenyl

Jones *et al.* reported the reaction of $ZrCl_4$ with iPr-nacac to give an unexpected octahedral co-ordination mode, as illustrated by **XIX**.[21] Crystal structure determination confirmed a six co-ordinate Zr^{4+} species with *trans* monodentate N-O ligands bound through the oxygen only and the co-ordination sphere was completed by chlorine atoms. In this case the β-aminoketone behaves as a monodentate ligand co-ordinating to the early transition-metal through the harder oxygen donor. This complex was reported to be highly effective catalysts for the conversion of ethylene into linear α-olefins. *In situ* reactions using zirconium tetrachloride, β-aminoketone and an alkylaluminium chloride Lewis acid cocatalyst gave turnover frequencies (TOFs) of up to 54,000 /hr.[21]

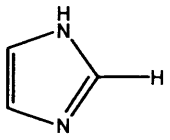


$ZrCl_4.2Pr^iHNCMe{=}CHCMe{=}O$

XIX

1.3 Imidazole Ligands and their Complexes

The imidazole group occurs naturally in the amino acid residue histidine and can bind to metal centres through the sp^2-hybridised nitrogen. Imidazole is the aromatic heterocycle responsible for binding to metals within many enzymes and is intimately involved in catalytic biological processes requiring proton transfers. For example, carbonic anhydrases and alkaline phosphatases contain Zn^{2+} bound by three imidazole residues and in thermolysin and carboxypeptase Zn^{2+} is bound by two imidazole residues.[31] Imidazole containing ligands were first synthesised as models to mimic the active sites of such metalloenzymes.[32,33]



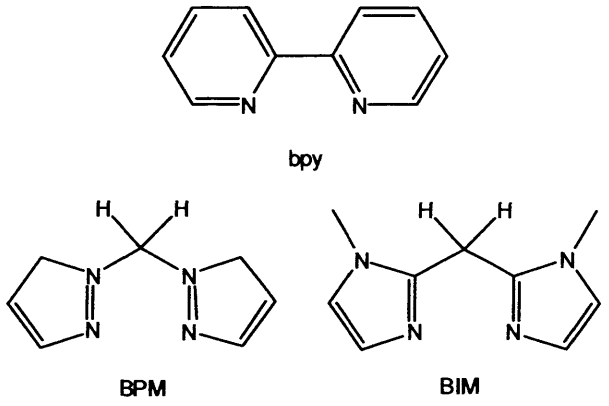
Imidazole

1.3.1 Bidentate Ligands

It was reported that there was a direct correlation between the basicity and s-donor capacity of a ligand which could determine the overall strength with which it could bind to a metal.[34] The basicity of the sp^2-N donor atoms of the five membered heterocycles pyrazole and imidazole (or their bidentate counterparts bis(pyrazol-1-yl)methane [BPM] and bis(*N*-methylimidazol-2-yl)methane [BIM], Figure **1.6**), are markedly different compared to pyridine based donors with respect to the relative degree of electron donation to the metal centre.[34] This difference in basicity directly affects the degree to which electrons are donated to the metal centre. Stronger ability to donate electrons to the metal centre leads to more stable complex formation and Byers *et al.* reported the order of donor ability to be BIM > py > pz. Byers *et al.* demonstrated that *N*-substituted imidazole

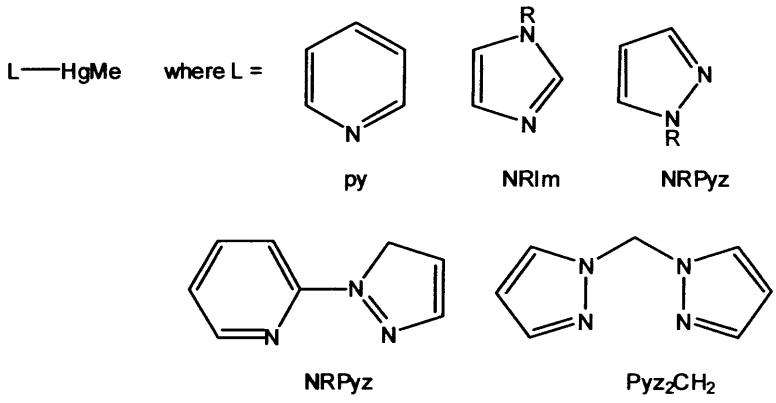
ligands were better s-donors than pyrazole and pyridine ligands and therefore more likely to form stable complexes.[35]

Figure 1.6



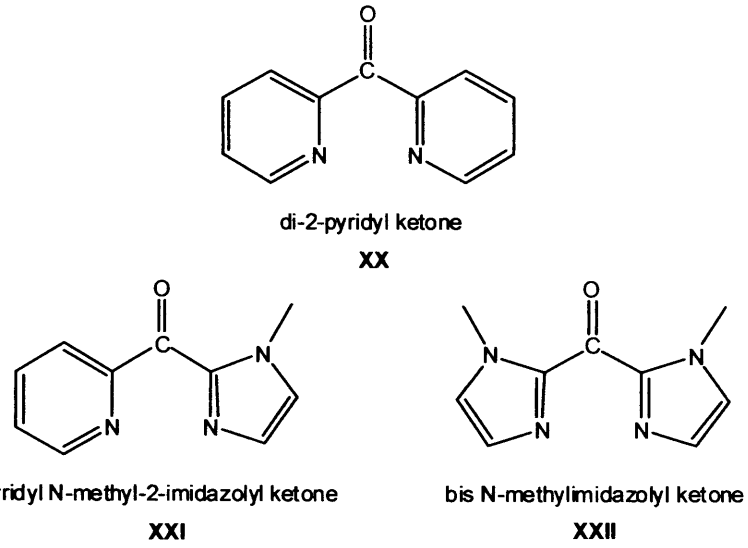
Extensive study of the interactions of pyridine, imidazoles and pyrazoles with mercury(II), one of the simplest Lewis acids, provided significant information on the s-donor ability of each of the ligands investigated. The Me-Hg $^{2}J(^{1}H\text{-}^{199}_{Hg})$ coupling constant gives an estimated order of the strength with which a ligand can co-ordinate to the metal and the measured $^{2}J(^{1}H\text{-}^{199}_{Hg})$ coupling constants for the complexes illustrated in Figure **1.7** decreased with increasing basicity of nitrogen donor heterocycle. Thus the imidazole containing ligands demonstrated most superior binding ability. For mixed heterocyclic donors containing both an imidazole and a pyridyl ring, it has been observed that binding takes place via the imidazole ring only.[36]

Figure 1.7 Methylmercury(II) complexes of N-substituted heterocycles



Extensive studies have been conducted involving bidentate ligands with imidazole as one or both potential donors. The first bis-*N*-methylimidazolyl species, composed of two imidazole rings bridged by a ketone was synthesised in 1977 by Regel and Büchnel.[37]

Figure 1.8



Byers *et al.* compared the co-ordination chemistry of di-2-pyridyl ketone **XX**, 2-pyridyl-*N*-methyl-2-imidazolyl ketone **XXI** and bis *N*-methyl-2-imidazolyl ketone **XXII**. They found that substituting the imidazole rings for pyridyl groups subtly altered the co-ordination chemistry of the resulting complex by increasing the tendency toward hydration of the ketone in the ligand, only observed on complexation to a metal centre. Hydration was reported on complex formation of **XX** with $Au^{III}Me_2$ and nickel nitrate in water. However, under the same conditions hydration of the complexes of **XXII** was not observed. The complex of **XX** readily hydrates to form a six-membered chelate ring with a stable boat conformation, however without hydration the complex would be too constrained and would decompose. Additionally the five-membered imidazolyl rings show smaller intra-ring angles thus increasing the distance between the nitrogen donor atoms and giving a larger bite angle.[38]

1.3.2 Complexes of nitrogen containing bidentate N-heterocyclic ligands

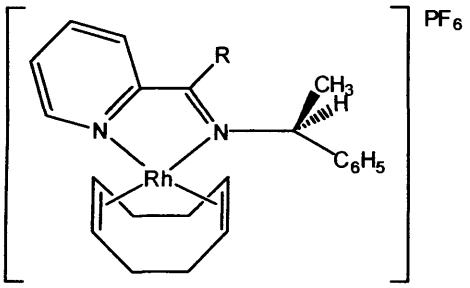
Over the past three decades bidentate nitrogen-based ligands containing sp^2-hybridised nitrogen donors have been successfully complexed to a variety of transition metals, many of which have been isolated and found to possess useful catalytic behaviour.

Complexes containing bidentate ligands can be divided into two sets based on the geometry about the metal centre, either square planar or octahedral. Similar co-ordination modes are displayed by the bidentate ligands across all examples with the fundamental difference in the number of bidentate ligands able to co-ordinate to the metal centre.

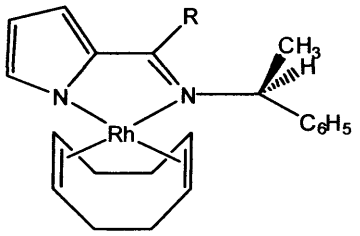
1.3.2.1 Square planar complexes

Rh(I) and Ir(I) complexes of nitrogen-based bidentate ligands 1,10- phenanthroline (phen) and 2,2-bipyridyl (bpy)[39] are well studied and have demonstrated biological activity[40] as

well as being active precatalysts for reactions such as hydrogenations,[41-43] hydroformylations and hydrosilylations.[44] Brunner *et al.* detailed the synthesis of Rh and Pt complexes of a range of novel chiral bidentate ligands derived from primary amines, amino acids and amino acid derivatives, as illustrated by **XXIII** and **XXIV**; these complexes were active catalysts for the enantioselective hydrosilylation of ketones.[44,45]



XXIII



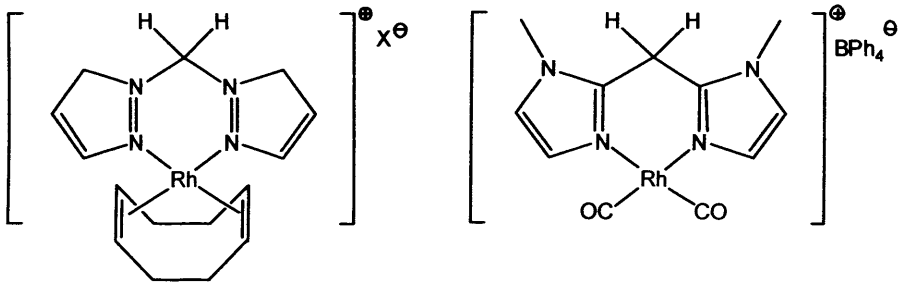
XXIV

Rhodium complexes of both pyrazolyl and pyridyl containing bidentate nitrogen donors have been detailed extensively, however there are fewer reports on Rh complexes of imidazolyl containing ligands. The first was a patent reporting a neutral Rh complex containing N-methylimidazolyl, as well as analogues containing a variety of N-donor heterocyclic ligands (phenazine, quinoxaline and 1,3,4-triazole),[46] that were active catalysts for hydrosilation reactions in the formation of siloxane polymer gels.

Messerle reported an extensive study of both neutral and cationic rhodium and iridium complexes of five-membered nitrogen donor bidentate ligands.[47,48] As illustrated in Figure **1.9**, all complexes were reported to be square planar about the metal centre, with similar bond lengths of approximately 2 Å and relatively small bite angles ranging between 86-89°. It is known that nitrogen ligands are in general more labile than the more strongly bound phosphine or carbene donors. The lability of BIM and bpm was tested by adding free ligand to $[Rh(BIM)(CO)_2]^+[BPh_4]^-$ with the reactions followed by NMR.[48] It was discovered that BIM bound more strongly to the rhodium and iridium centres than bpm and the complexes and the more labile bpm containing complexes produced superior

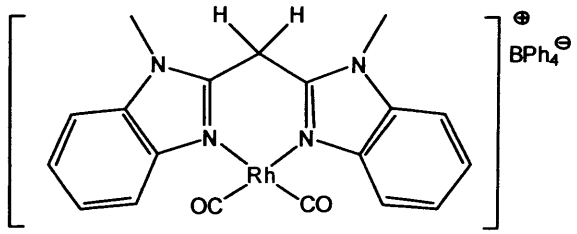
conversions and turnover numbers in hydroamination reactions.[48] In general it was observed that the iridium catalysts demonstrated longer lifetimes than their rhodium counterparts.[48]

Figure 1.9 Rhodium complexes bearing bidentate nitrogen ligands

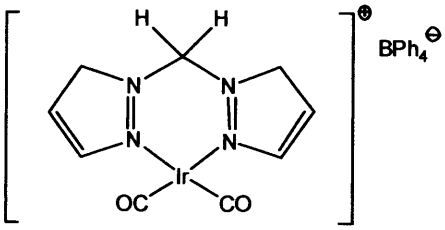


XXV

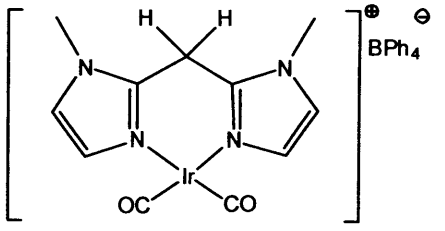
XXVI



XXVII



XXVIII

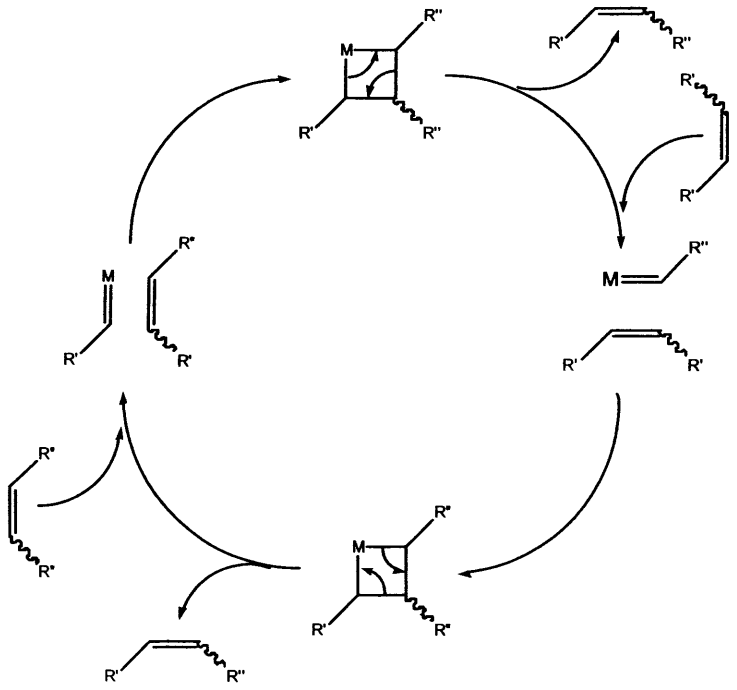


XXIX

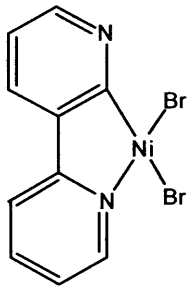
In the past decade Brookhart's discovery of (a-diimine)nickel(II) catalysts for high molecular weight polyethylene formation has led to a continued interest in olefin polymerisation.[17,49,50] The use of soluble, nickel-based catalysts was first initiated commercially by Dimersol (Institut Français du Pétrole) and the Shell Higher Olefin

Process (SHOP). The SHOP process consists of three steps: Ethylene oligomerisation; double bond isomerisation and olefin metathesis, Figure **1.10**.

Figure 1.10 The SHOP Process

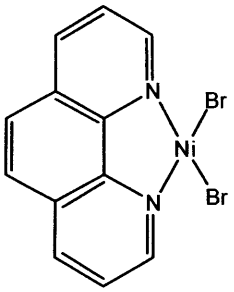


The SHOP catalysts contain a bidentate [P-O]$^-$ ligand co-ordinated to Ni(II) and show exceptionally high selectivities for linear a-olefins. Nickel dichloride is renowned for its activity towards styrene polymerization however the addition of bidentate ligands such as phen and substituted bpys form soluble $NiCl_2$ catalysts with significantly altered catalytic activity.



$Ni(bpy)Br_2$

XXX



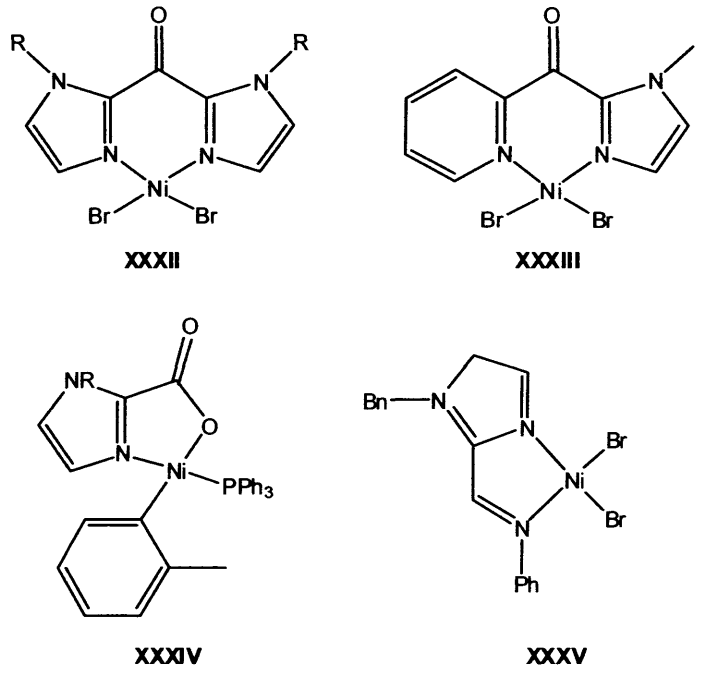
$Ni(phen)Br_2$

XXXI

Using **XXX** and **XXXI**, Bialek reported that increasing the steric bulk of the ligand in precatalysts can reduce the reactivity, the conversion and the molar mass of the product.[51] Therefore the extraordinary selectivity of the product formed from the SHOP process is believed to be due to the presence of chelating ligands.[52,53] Brookhart reported that the molecular weight of the polymer formed was dependent on the steric bulk of the ligand, since increasing bulk hinders the termination step (ß-elimination) of the growing polymer chain, increasing the length of the alkane chain.[18,54] Brookhart's nickel complexes have a high degree of tolerance for heteroatoms, allowing copolymerisation of olefins with substrates such as acrylate, vinylacetate and pyrimidone-functionalised olefins.[55] Conversely, early transition metal catalysts are oxophilic in nature and therefore are limited to non-polar olefins as substrates.

Batten *et al.* reported an extensive study of nickel complexes of neutral mixed imidazole and a-imine ligands, allowing comparisons with Brookhart's diimine chemistry.[56] The catalytic activity of nickel complexes containing bidentate ligands with mixed nitrogen donors, imidazole, pyridine and imine ligands as illustrated in Figure **1.11**, were investigated in order to compare with the results of the SHOP process.

Figure 1.11

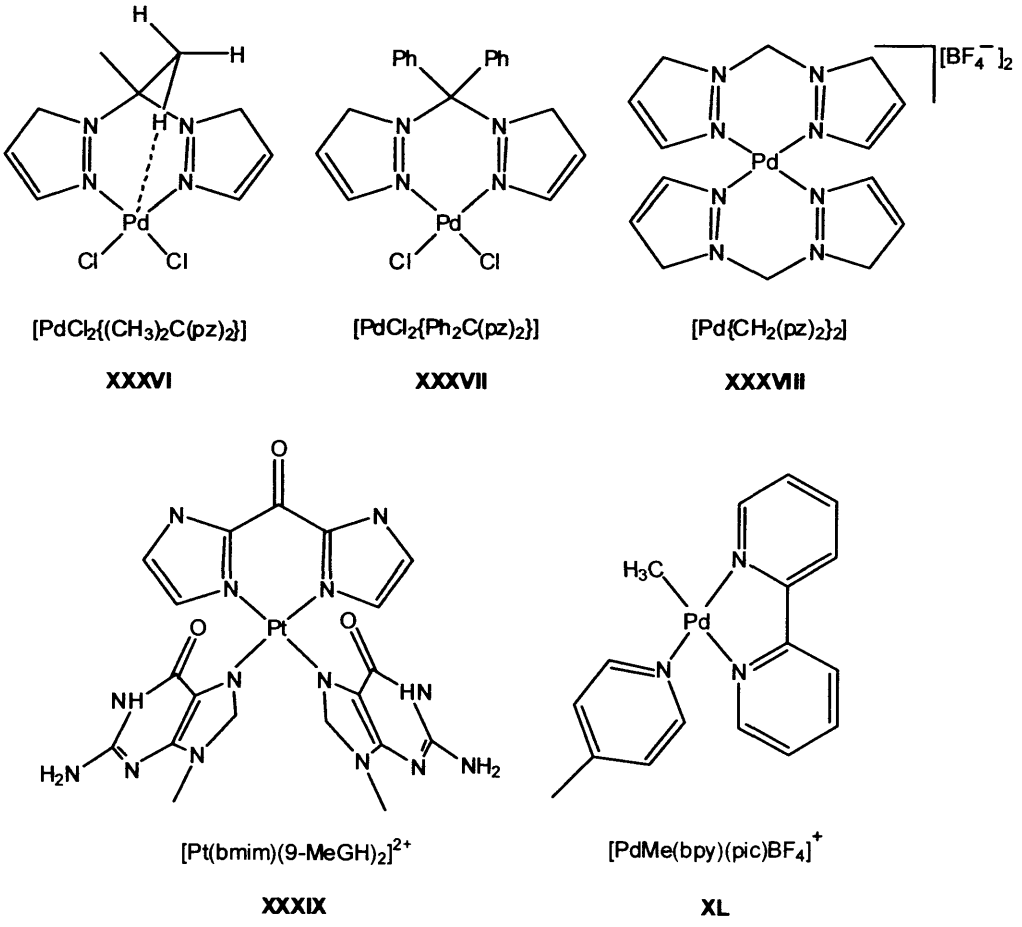


The catalysis results of the complexes in Figure **1.11** demonstrated that ligands forming five-membered chelate rings on co-ordination generate catalysts that behave like typical low steric bulk a-diimine systems and yield predominantly oligomeric products. However, the BIM ligands form six membered chelates and are stronger s-donors; catalysts dervived from them generate a mixture of oligomers with significant amounts of high molecular weight polymer. Within the series of bis(heterocycle)methanone precatalysts studied, Figure **1.11**, increasing the p-acidity of the chelating ligand resulted in a decrease of the overall activity, while the ratio of polymer to oligomer increased.

Research into the co-ordination chemistry of BIM ligands began when Canty *et al.* compared the co-ordination chemistry and behaviour of copper(II), nickel(II) and dimethyl gold(III) complexes of imidazole containing ligands to those of the related pyridyl ligands.[38] This work was followed by reports of a series of novel bidentate nitrogen donor ligands containing pyridine and imidazole groups and their complexes with Pd(II).[57]

A number of palladium and platinum complexes containing BIM, BPM and bpy ligands have been successfully isolated and characterised using X-ray crystallography, Figure **1.12**. In all of the four co-ordinate complexes the nitrogen donor rings are coplanar, although Minghetti's $[Pd\{CH_2(pz)_2\}_2][BF_4]_2$ complex was slightly distorted towards tetrahedral from the ideal square planar geometry.[58]

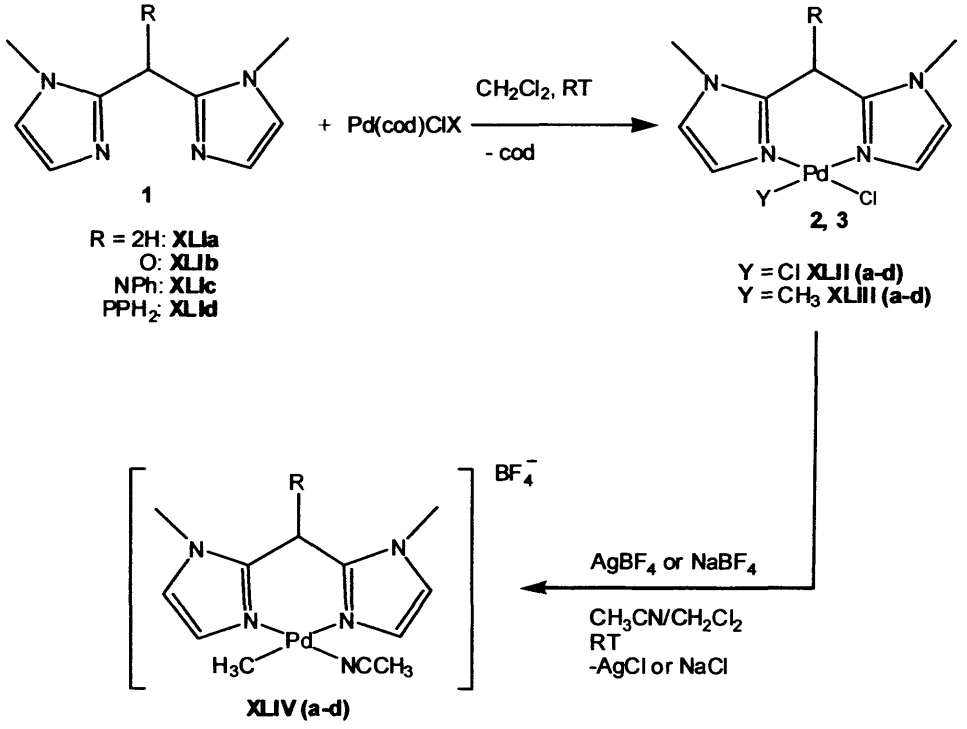
Figure 1.12 Examples of palladium complexes bearing bidentate nitrogen ligands



The complex **XXXVI** also shows a Pd···H-C agostic interaction; no strain, or buckling of the ligand was evident in the complex. Replacing the apical protons and methyl groups on the bidentate backbone with larger electron donating groups, such as ketones, methyl and phenyl groups had little effect on the M-N bond lengths and N-M-N bond angles,[59-61]

however Done *et al.* showed that introduction of a third donor function across the bridging backbone could lead to improved catalyst activity.[62,63]

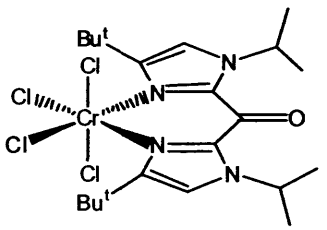
Scheme 1.2 Bis(1-methylimidazol-2-yl) based chelate ligands used in the preparation of palladium complexes



The dichloro complexes $PdCl_2\{(bim)CO\}$ (**XLIIb**) and $PdCl_2(bim)PPh_2$ (**XLIId**) were found to be relatively air and temperature stable compounds.[63] Complex **XLIIb** was soluble in DMSO and **XLIId** was soluble in DCM and $CDCl_3$. The mass spectrum of complex **XLIIId** suggested a dimeric compound formed possibly by bridging of the apical R groups and NMR analysis showed the presence of only one isomer. Crystal structures of $PdCl_2\{(mim)_2C{=}NPh\}$ (**XLIIc**) and $PdCl(CH_3)\{(bmim)_2CO\}$ (benzyl substituted imidazoles in **XLIIIc**) demonstrated square planar geometry around the Pd(II) centre with the ligands co-ordinated to the metal via the ring nitrogen donors and the chelate ring bridge protruding above the co-ordination plane.

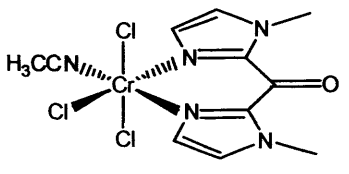
1.3.2.2 Octahedral complexes of bidentate imine ligands

Cavell and co-workers published several papers on bi- and tri-dentate ligands based on a bim framework containing additional functional groups with different electronic properties and chemical hardness, hard soft acid base concept (HSAB). This empirical classification by Pearson stated that early transition metals denoted as hard acids prefer to react with hard ligands (or hard bases) and the opposite is true for later transition metals denoted as soft acids.[64] This work allowed improved understanding of how variations of the ligand system within a class of catalysts influences the electronic properties of the co-ordinated metal centre and impacts on its catalytic performance. The co-ordination chemistry and catalytic behaviour of Cr(III),[13,65] V(III)[13] and Pd(II)[62] complexes of bim based systems linked to additional, varying, donor sets was reported. It was demonstrated that subtle changes in the electronic and steric properties of the ligand system could control the reactivity of the complexes in the catalytic oligmerisation of ethylene.[65] Theoretical studies on Ni(II), Pd(II) and Co(II) catalysts containing sterically demanding nitrogen ligands have revealed that placing bulky substituents on the ligand blocks the axial co-ordination sites on the metal, thus suppressing ß-hydride transfer, the termination step in a catalytic cycle. Cavell *et al.* demonstrated that pre-catalysts lacking steric bulk gave 1-alkenes with a maximum production of C_8. However, they also reported complex **XLV** that contained bulky t-butyl groups where 1-alkenes ranging from C_4-C_{30} rather than polyethylene were produced. It was concluded this was due to the t-butyl group not being able to reach across the co-ordination plane to block the axial sites, therefore bulky substituents were important but more so their position in the ligand.



$[CrCl_3\{(fBupim)_2CO\}]_2$

XLV

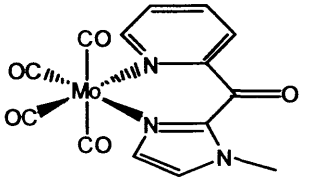


$[Cl_3Cr(bim)CO(NCCH_3)]$

XLVI

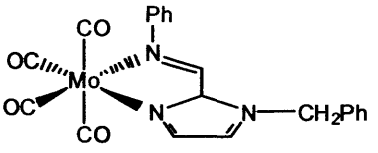
The chromium complex **XLVI** demonstrated quasi-octahedral geometry, with three chlorine atoms disposed *mer* in the co-ordination sphere, with the planar bim ligand and a MeCN completing the ligand set. The slight difference in Cr-N bond lengths was explained in terms of *trans* influence; the MeCN group exhibits a greater *trans* influence than the chloride ligand. This enforces a shorter M-N bond length opposite the MeCN group than the M-N bond length opposite the chloride ligand.

Canty and Cavell *et al.* reported molybdenum bim complexes, **XLVII** and **XLVIII**. These Mo complexes were synthesised in order to define the co-ordination behaviour of the bidentate nitrogen donor ligands.[66] Distorted octahedral geometries around the Mo(0) centres were observed with *cis*-bidentate ligand configuration.



[Mo(CO)$_4${(py)(mim)CO}]

XLVII



[Mo(CO)$_4$(PhN=CHbim)]

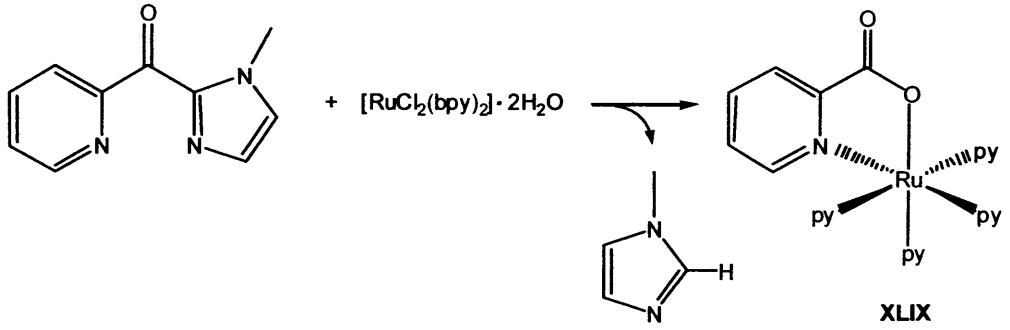
XLVIII

The crystal structure of Mo(CO)$_4${(py)(mim)CO} showed that the ligand had adopted a *quasi*-boat conformation. Comparisons of the Mo-N bond lengths of **XLVII** and **XLVIII** showed the most significant difference; in both complexes the imidazole nitrogen-Mo bond being considerably shorter than that of the other nitrogen donors. When compared to literature reports of similar complexes bearing symmetrical, heterocyclic, five and six membered ligands, both bond lengths and bite angle in **XLVII** and **XLVIII** were smaller than the values reported for {FerrocenylCH=C(py)$_2$}Mo(CO)$_4$ (six membered donor ring) and {3,5-dimethyl-1,2,4-triazol-1-yl)$_2$CH$_2$}Mo(CO)$_4$ (five membered donors). The bond lengths and angles reported for Mo(CO)$_4$(PhN=CHbim) were comparable to known compounds, in particular six membered 2-pyridyl donor systems; however the imidazole-Mo bond length is relatively shorter.[66]

Recently Zhou *et al.* reported oxidative condensation reactions of (diethylenetriamine)cobalt(III) complexes with substituted bis(pyridine-2-yl) ligands yielding mixtures of octahedral *fac* and *mer* isomers.[67]

Ruthenium(II) complexes of nitrogen ligands containing a mixture of py and bim groups have been reported.[68] Canty observed that the reaction of (py)(bim)C=O with the ruthenium containing precursor yielded an unexpected, hydrolysed product in which the ligand degraded to form a pyridine-2-carboxylate Ru(II) complex, Scheme **1.3**.[69] To overcome the degradation of (py)(mim)C=O the ketone group was replaced with an ethene group, to give the $[Ru(bpy)_2\{(bim)C=CH_2\}][PF_6]_2$ complex. Canty *et al.* reported longer bond lengths of 0.037 Å and a bite angle 8.32° greater than found in the analogous $[Ru(bpy)_2(pyCO_2)][PF_6]_2$ complex.

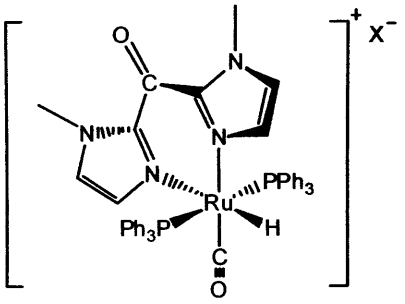
Scheme 1.3 Pyridine-2-carboxylate complex of ruthenium



XLIX

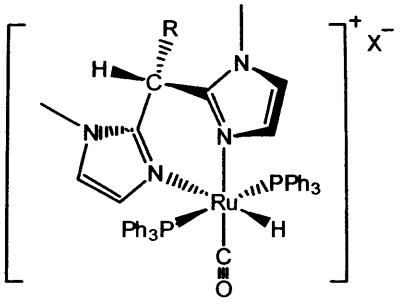
Elgafi *et al.* synthesised two novel ruthenium complexes containing bidentate imidazole-based ligands **L** and **LI**, that have a distorted octahedral geometry around the metal centre; this was assumed to be due to the steric effects of the phosphine and the small bite angle of the bidentate ligand.[70] Relatively small N-Ru-N bond angles were reported as 83.2(1)° for complex **L** and 84.7(2)° for complex **LI**. The Rh-N bond lengths were indistinguishable for these complexes at 2.18(3) and 2.14(3) Å, for the bonds trans to the hydride and the carbonyl group, respectively. Deviation from coplanarity is greater in **L** probably driven by the interaction of the carbonyl group with the adjacent methyl groups,

giving C···O bond lengths of approximately 2.8 Å; the same bond lengths in complex LI are notably longer at approximately 3.3 Å.



X = Cl
X = BF_4

L



R = OH, X = Cl
R = H, X = Cl

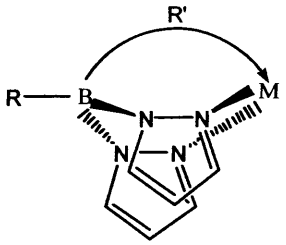
LI

Three ruthenium complexes of BPM, bis(3,5-dimethylpyrazol-1-yl)methane (dmBPM) and BIM, this time free of phosphane co-ligands, were reported.[68] Infra-red characterisation of these complexes revealed a shift in ?(C=O) frequencies towards lower wave numbers in the order BPM > dmBPM > BIM, consistent with the four additional electron donating methyl groups increasing the electron donating ability of dmBPM compared to BPM. This trend confirms that BIM is a better electron donator than pyrazole groups, as observed by Canty *et al.*

In conclusion, classical heterocyclic nitrogen donor ligands have played a key role in the development of diverse areas of co-ordination and organometallic chemistry and catalysis. An important early development for bidentate ligands was the introduction of alternative bridging groups (CO and NH) to replace the bridging methylene. In the case of pyrazole, a major impetus in their development was Trofimenko's early work on poly(pyrazolyl)borate ligands.

1.3.3 Tripodal Ligands

Tripodal ligands are facially co-ordinating, tridentate, chelating ligands, that continue to receive considerable attention in both co-ordination and organometallic chemistry. Over the past 25 years there have been numerous publications on metal complexes of tripodal ligands, many of which involve poly(pyrazolyl)borate ligands, **LII**.[71]



Poly(pyrazolyl)borate

LII

Where R and R' can be H, alkyl, aryl, NR_2, ArS or Pz*.

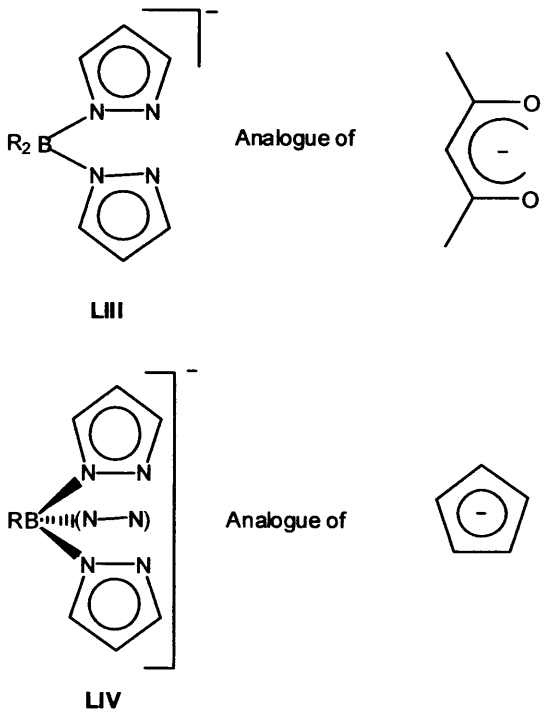
The hydrotris(pyrazolyl)borate anion (Tp) was introduced as a ligand in co-ordination chemistry in 1966 by Swiatoslaw Trofimenko and complexes of these ligands with most metals of the periodic table have been prepared.{Trofimenko, 1993 #24} For the purpose of co-ordination chemistry it is important to note that Tp ligands have a tendency to adhere to octahedral co-ordination by binding facially to the metal centre giving rise to tripodal geometry (with N-M-N bite angles close to 90°).[72] Notably, any modifications made to the 3- and 5-positions of the pyrazolyl rings have relatively little influence to the overall donor ability of the ligand but allow significant steric tuning. The sp^2-N donor poly(pyrazol-1-yl)methane and poly(imidazole-2-yl)methane ligands, BPM[73] and BIM,[57] are neutral ligands, closely related to Trofimenko's poly(pyrazolyl)borate ligands.[2]

Bidentate Tp ligands [R_2B-$(pz)_2$ = **LIII**] and [RB-$(pz)_3$ = **LIV**], Figure **1.13** have been compared to ß-diketonates and to cyclopentadienyls (Cp') for tridentate comparisons. Tp ligands are isolobal with Cp and share steric and electronic properties both are formally monoanionic and cap three metal co-ordination sites in octahedral complexes. For electron

counting purposes, both these ligands act as 5- or 6-electron donors in covalent or ionic models, respectively. However, the analogy with Cp ligands is not as close as once thought as there are significant differences between the Tp and Cp ligands as listed below:

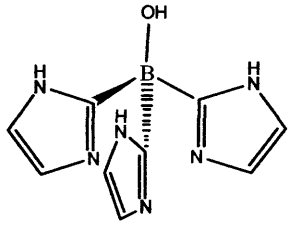
1. Cp ligands form p bonded complexes rather than s bonded complexes like Tp.
2. Tp ligands have a lower field strength than Cp.
3. Tp_2Fe is paramagnetic unlike Cp_2Fe.
4. Tp ligands are bulkier than Cp as illustrated the values of some of the respective cone angles: Tp 262°; Cp 150°; Tp* 276° and Cp* 182°.
5. Tp ligands are hard nitrogen donor ligands as opposed to the soft Cp ligands.

Figure 1.13



Breslow and co-workers reported the first tris(imidazolyl)borate species in 1978.[31] The tris(imidazolyl) ligand is a close analogue of the Tp ligand.[33] Ligands of the type **LV** type

ligands were synthesised as models of metal binding sites in zinc enzymes and have continued to yield advances in the study of antitumor activity.[59,74]



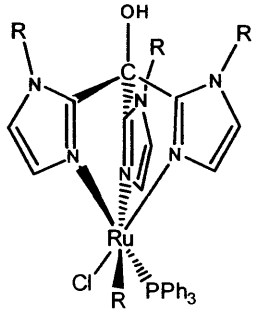
Breslow's Tris Imidazolyl borate

LV

1.3.4 Complexes of tridentate ligands

1.3.4.1 Group 8

Elgafi *et al.* reported the preparation and characterisation of ruthenium(II) and osmium(II) complexes with tris(imidazolyl) ligands tris(*N*-methylimidazol-2-yl)methanol {$(mim)_3COH$} and tris(*N*-ethoxymethylimidazol-2-yl)methanol {$(emim)_3COH$}, as illustrated by **LVI**.[75]



LVI

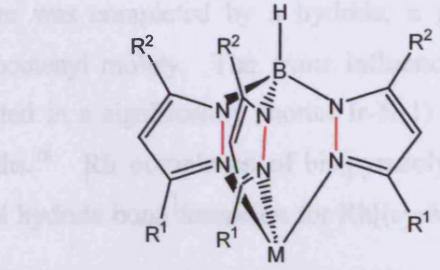
Crystal structures of ruthenium complexes of type **LVI** showed a slightly distorted octahedral geometry about the central metal atom due to constraints imposed by the tris(imidazole) architecture.

1.3.4.2 Group 9

The activation of unfunctionalised alkanes to proceed in chemical reactions is a fundamental area of organometallic chemistry. This is effective method of inducing controlled selective reactions in unfunctionalised alkanes to give a new field of chemistry and allow the use of petroleum cracking products and/or vegetable oils as feed stocks in the chemical industry. One of the most successful approaches to this challenge is the C-H activation of alkanes with late transition metals and in particular with complexes of rhodium and iridium.[72,76-78] Recently there have been rapid developments in the fields of catalytic C-H activation and the related area of alkane dehydrogenation, with rhodium and iridium featuring prominently in both systems. The most active catalysts for alkane dehydrogenation are rhodium and iridium phosphine and phosphinite complexes, with pincer complexes being particularly useful in this context. These complexes are capable of dehydrogenation of unactivated alkanes with the conversion of cyclooctane to cyclooctene being the standard comparison of activity.

Facial co-ordination of ligands to give complexes with octahedral geometry is particularly favourable for the d^6 systems rhodium(III) and iridium(III), as illustrated in Figure **1.14**. ^{103}Rh NMR spectroscopy can be useful to determine the environment about the Rh metal centre, indirectly inferring whether the Tp ligand is bi- or tridentate. For example, in 4-co-ordinate Rh-Tp-compounds the ^{103}Rh chemical shift can be found at approximately 1350 ppm, whereas for a penta-co-ordinated complex it is shifted upfield to approximately 1130 ppm.[72]

Figure 1.14

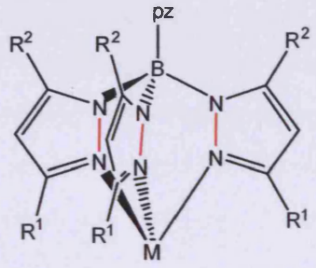


R^1 = ^{i}Pr, R^2 = ^{i}Pr : Tp^{iPr2}

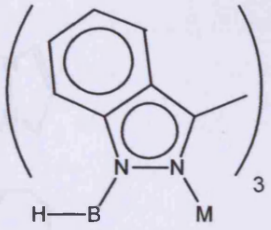
R^1 = Ph, R^2 = H : Tp^{Ph}

R^1 = Me, R^2 = Me : Tp^{Me2}

M = Rh or Ir



pzTp



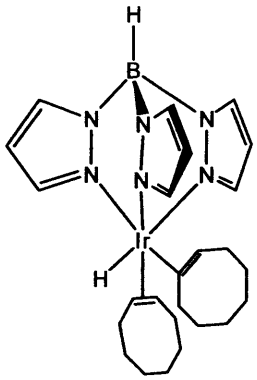
Tp^{Mei}

The most common oxidation state of iridium is (+3), typically with a low spin $(t_{2g})^6$ electronic configuration. Most Ir(III) compounds have a co-ordination number of six with octahedral geometry and tend to be colourless or pale yellow. The second most common oxidation state is Ir(I), which is d^8, usually square planar and susceptible to oxidative addition reactions to give Ir(III) species. The oxidative addition of a C-H bond usually requires a highly unsaturated metal centre, therefore mechanistic studies on this process have often involved 14 or 16 electron d^8 metal complexes of rhodium(I), iridium(I) and platinum(II).

Alvardo *et al.* reported tris(pyrazolyl)borates as useful compounds to stabilise different transition metal complexes in the homogenous hydrogenation of quinoline. Catalysis by complexes formed *in situ* by reacting $[Rh(cod)Cl]_2$ with Tp gave the highest activity followed by use of $[Ir(cod)Cl]_2$, then $[Ir(coe)_2Cl]_2$ as metal precursors.[79]

Fernández *et al.* reported a reaction between $Na[HB(pz)_3]$ and $[Ir(coe)_2Cl]_2$ to afford a Ir(III)(vinyl)(hydrido) complex **LVII** as the sole product. The hydride ligand was

observed at -18.30 ppm in the ^1H NMR spectrum. The structure displayed a pseudo-octahedral geometry around the metal centre with a *fac* Tp ligand and the co-ordination sphere was completed by a hydride, a p-bonded cyclooctene molecule and s-bonded cyclooctenyl moiety. The *trans* influence of the p-accepting coe ligand *trans* to N(1) resulted in a significantly shorter Ir-N(1) distance compared to the other two Ir-N bond lengths.[78] Rh complexes of bis(pyrazolyl)borates have also been published, showing metal hydride bond formation for Rh[(cyclooctane-1,5-diyl)bis(pyrazol-yl)borate)(cod)].[80]

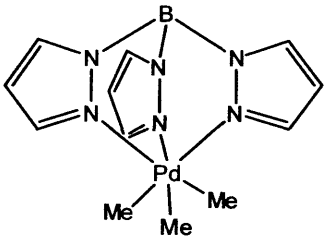


$IrH\{HB(pz)_3\}(C_8H_{13})(C_8H_{14})$

LVII

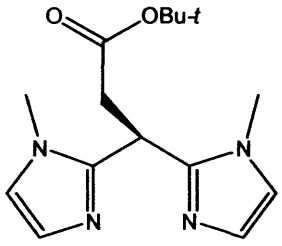
1.3.4.3 Group 10

The first reported palladium(II) complexes of poly(pyrazol-1-yl) ligands were the $Pd(C_3H_5)\{(pz)_3BR\}$ (where R can be H, Et, pz or Ph) complexes of $(pz)_3BH$? and $(pz)_4B$?, obtained on reaction of the dimer $[PdCl(C_3H_5)]_2$ with $K[(pz)_3BR]$.[81] In 1987 Byers *et al.* reported a facially co-ordinated tris(pyrazol-1-yl)methane ligand that gave Pd(IV) and Pt(IV) complexes with octahedral geometry. Byers followed this work with reports on series of analogous tripodal complexes containing py and bim ligands.[82]



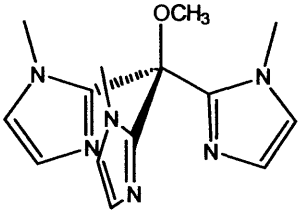
LVIII

As discussed previously, neutral and cationic palladium complexes of the bidentate imidazoles have demonstrated interesting catalytic activity with tunable electronic and steric properties. Rüther *et al.* reported some novel methylpalladium(II) complexes bearing tridentate imidazole-based ligands, **LIX**, **LX** and **LXI**, following the reactions illustrated in Scheme **1.4**. These ligands constituted a bridged bis(1-methylimidazol-2-yl) framework and incorporated a range of third donors with hard to soft character.[62]



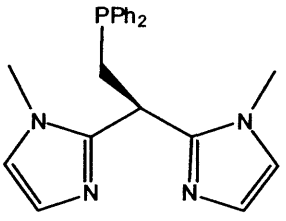
(bim)CHCH$_2$COOBu-*t*

LIX



(mim)$_3$COCH$_3$

LX

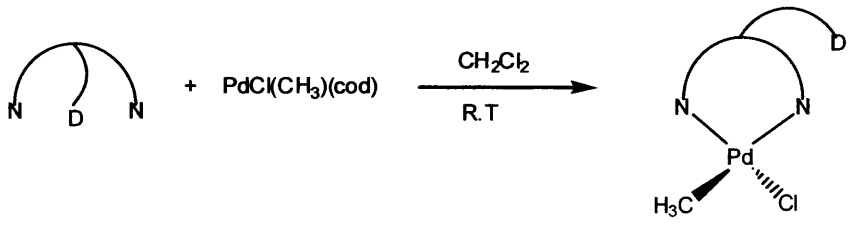


(bim)CHCH$_2$PPh$_2$

LXI

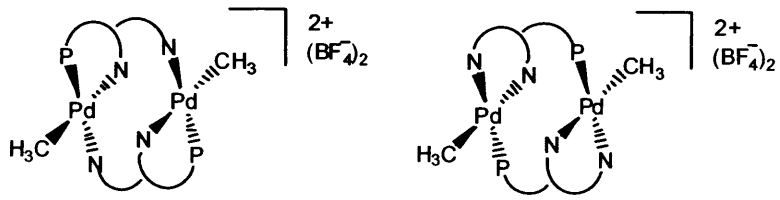
The Pd complexes PdClMe[**LIX**], PdClMe[**LX**] and PdClMe[**LXI**] were prepared by substitution from PdClMe(cod). Canty *et al.* have previously demonstrated tridentate ligands exhibiting fluxional behaviour however palladium complexes of the type PdClMe[**LXI**] demonstrate zero fluxional co-ordination behaviour at room temperature in $CDCl_3$ and CD_2Cl_2. ^1H NMR spectra of this complex gave sharp peaks demonstrating the presence of one product in which the imidazole rings were inequivalent, Scheme **1.4**.

Scheme 1.4

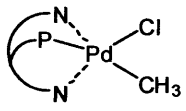


The phosphorous group on ligand **LXI** was found to be a better donor than the oxygen group on **LIX** and co-ordinated to the soft palladium centre, resulting in an N,P co-ordination mode. Analysis by NMR spectroscopy at room temperature showed that complex PdClMe[**LXI**]was fluxional in solution in a process involving alternate association and dissociation of the donor groups with respect to the metal centre. Dissolving complex PdClMe[**LXI**] in methanol gave two possible isomers of dicationic dimeric geometry, in which it was proposed that two Pd centres were bridged by the PPh_2 or imidazole group, Scheme **1.5**. A five-co-ordinated species at ambient temperature was postulated by ^{1}H and ^{31}P NMR analysis at varying temperatures.

Scheme 1.5



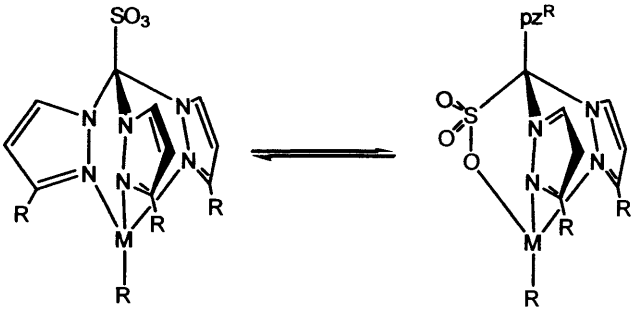
Possible isomers for the palladium centred N,P complex



Probable 5 co-ordinate species

Ligands **LX** and **LXI** display a strong tendency to co-ordinate in a tridentate fashion, leading to the formation of dinuclear complexes and fluxional behaviour, respectively. Under metathetical conditions, even in the presence of a co-ordinating solvent, the third imidazole donor occupies the vacant co-ordination site forming a dimeric isomer with s[3] N,N,N co-ordination.

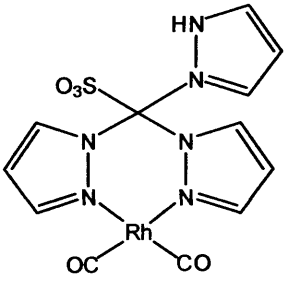
Similar competitive, preferential co-ordination was observed by Klaui in the mixed donor tris(^{tBu}pyrazolyl)methanesulfonate (Tpms^{tBu}) ligand, which is a variant of the well known Tp ligands that incorporates a hard oxygen donor. In common with Tp, Tpms is a facially co-ordinating monoanionic six-electron donating ligand, the sulfonate group makes the Tpms^{tBu} ligand more hydrophilic. Although the sulfonate group is regarded as weakly co-ordinating in comparison to nitrogen donors, the preferential co-ordination of the pyrazolyl rings compared with the sulfonate group, to cobalt, copper and zinc metal centres was observed.[83] In solution a 1:1 ratio of ligand to metal precursor gave isomers **LXII** and **LXIII** observed in equilibrium (N,N,N and N,N,O co-ordinated). Using diethyl zinc as precursor gave a dinuclear complex with a N,O bonding mode. Crystals suitable for X-ray crystallography were isolated for the zinc and cobalt complexes, **LXII** and **LXIII**.



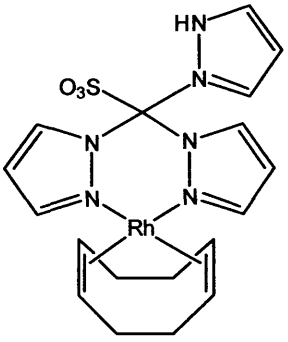
LXII **LXIII**

Klaui's Tp style ligand Tpms^{tBu}

Klaui reported rhodium(I) complexes, TpmsRh(CO)$_2$, **LXIV** and TpmsRh(cod), **LXV** as active catalysts for the hydroformylation of 1-hexene.[84] The addition of phosphine ligands (PPh_3, PMe_3, PCy_3) was reported to negatively effect the activity.



LXIV

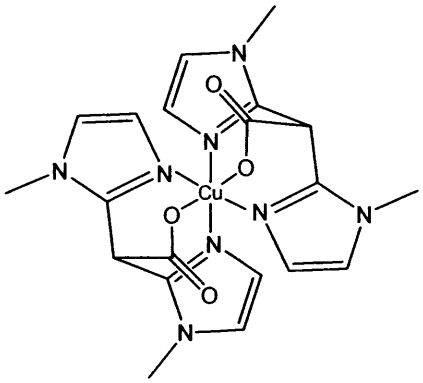


LXV

Nickel and rhodium complexes of the Tpms^{tBu} ligand exhibited N,N,N and N,N co-ordination bonding modes. The range of complexes isolated by Klaui *et al.* proved that Tpms^{tBu} can act as a tripodal N,N,N or N,N,O ligand or as a bipodal N,O ligand. Importantly, this variable demonstrates that Tpms^{tBu} is a structurally flexible ligand capable of accommodating the requirements of different metal centres and exemplifies the benefits of having mixed nitrogen and oxygen donor combinations.

1.3.4.4 Hemilabile ligands

Bruijnincx reported tripodal N,N,O ligands bis(1-methylimidazol-2-yl) propionate and bis(1-methylbenzimidazol-2-yl) propionate bearing one carboxylate group and two biologically relevant imidazole moieties.[85] These ligands were designed to mimic enzymes exhibiting the 2-His-1-carboxylate motif by facially co-ordinating one carboxylate and two imidazole groups to metal centres. The ligand in the Cu(II) complex **LXVI** facially co-ordinates and yields a 2:1 ligand:metal complex with tetragonally distorted octahedral co-ordination geometry. However no catalytic applications were reported for complexes such as **LXVI**.



LXVI

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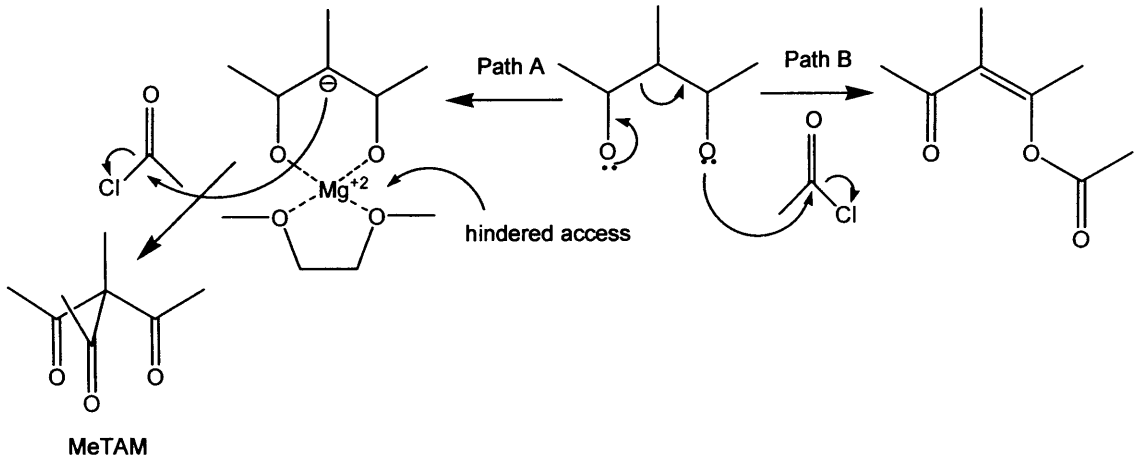
CHAPTER TWO

Synthesis of some novel oxygen containing ligands and attempted complexes

2.1 Introduction

The chemistry described in this chapter is primarily influenced by Rüther *et al.*'s reports of a chromium(III) complex bearing the podand ligand 1-methyltrisacetylmethane (MeTAM), demonstrating superior catalytic activity for ethylene oligomerisation reactions compared to its imidazole chelated counterparts.[1] MeTAM is a neutral tripodal oxygen ligand that is well suited to complex hard, earlier transition metals. This chapter describes the attempts to introduce a soft nitrogen donor into the MeTAM system, in an attempt to synthesise mixed N,O donor tripodal ligands capable of accommodating softer metals like palladium, platinum and nickel.

Attempted syntheses of imine substituted MeTAM were modelled on the synthesis of MeTAM. There are two parts to the MeTAM synthesis. First, the deprotonation of the 3-methylpentane-2,4-dione creating a negative charge, delocalised between the two carbonyl groups and the bridging carbon atom, followed by the addition of an acetyl group. A mixture of two products is probable due to possible competitive acylation of carbon and oxygen, Scheme **2.1**. The required *C*-acylated product was obtained by blocking the attack of the oxygen atoms using the Grignard reagent methyl magnesium bromide (MeMgBr). The Grignard deprotonates the Meacac and the Mg molecular species is able to co-ordinate the oxygen atoms. However, coordination of Mg alone is insufficient as the spatial arrangement around the oxygen atoms and the coordination plane would nonetheless allow electrophilic attack at the oxygen atoms. Therefore a bulky bidentate chelating solvent i.e. dimethyl ethylene glycol ether (DME) was utilised and coordination to the metal successfully hindered electrophilic attack of the oxygen atoms.



Scheme **2.1** Path A shows *C*-acylation giving the required product MeTAM and Path B illustrates possible *O*-acylated product.

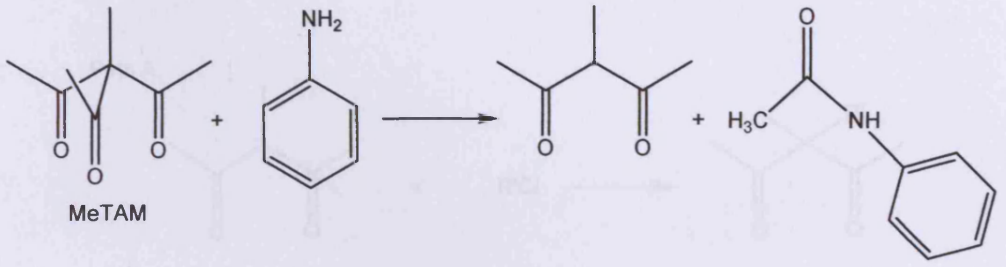
2.2 Results and Discussion

2.2.1 Organic Synthesis

Synthesis of the required nitrogen substituted N,O tripodal compounds were attempted using three potential pathways. The first involved reacting MeTAM itself in a condensation reaction or using the Wittig process, to substitute one or more of the ketones with an imine, Scheme **2.2** and **2.3**. The remaining methods followed the procedure used to synthesise MeTAM and required either the syntheses of alternative electrophiles incorporating a nitrogen donor or the syntheses of substituted bidentate imine ligands as potential nucleophiles as summarised in Scheme **2.4**.

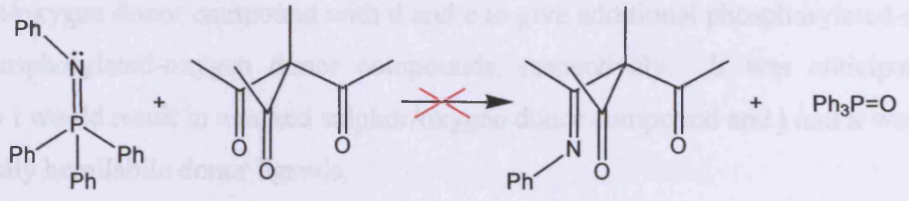
Condensation reactions of one or more of the ketone groups of MeTAM to give an imine were attempted by stirring a solution of MeTAM in DCM with aniline over sodium sulphate as a drying agent, overnight. The crude ^{1}H NMR spectrum showed that the MeTAM had cleaved to give Meacac and acetanilide. Formation of acetanilide suggests

that attack by the nucleophile takes place but cleavage of the C-C bond takes preference over the loss of water. This is probably due to the expected product from this reaction being less stable than the starting materials, resulting in the preferential loss of Meacac which is also a stable leaving group.



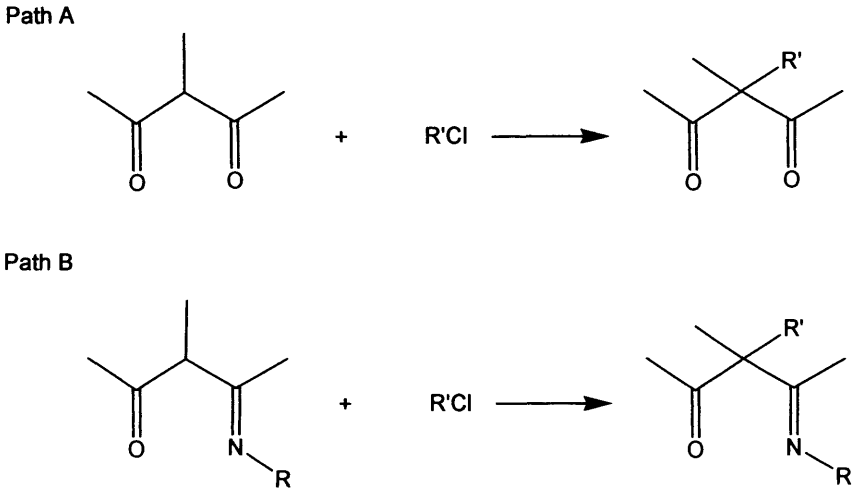
Scheme **2.2** Reaction of MeTAM to give Meacac and acetanilide.

Using an alternative approach following the failure of the condensation reaction led to an attempt of the Wittig reaction. *N*-(Triphenylphosphoryanylidene) was used to substitute one of the ketones with an imine, Scheme **2.3**. Only starting material was detected by NMR and TLC analyses, even after several days of heating at 120 °C. Most literature references involve the use of more reactive trifluoro substituted ketones or aldehydes, which are more reactive than MeTAM. Trifluoro substituted ketones are able to polarise the carbonyl groups, rendering them more susceptible to nucleophilic attack by the nitrogen of *N*-(Triphenylphosphoryanylidene). Aldehydes, in general, are more reactive and less sterically hindered than ketones.



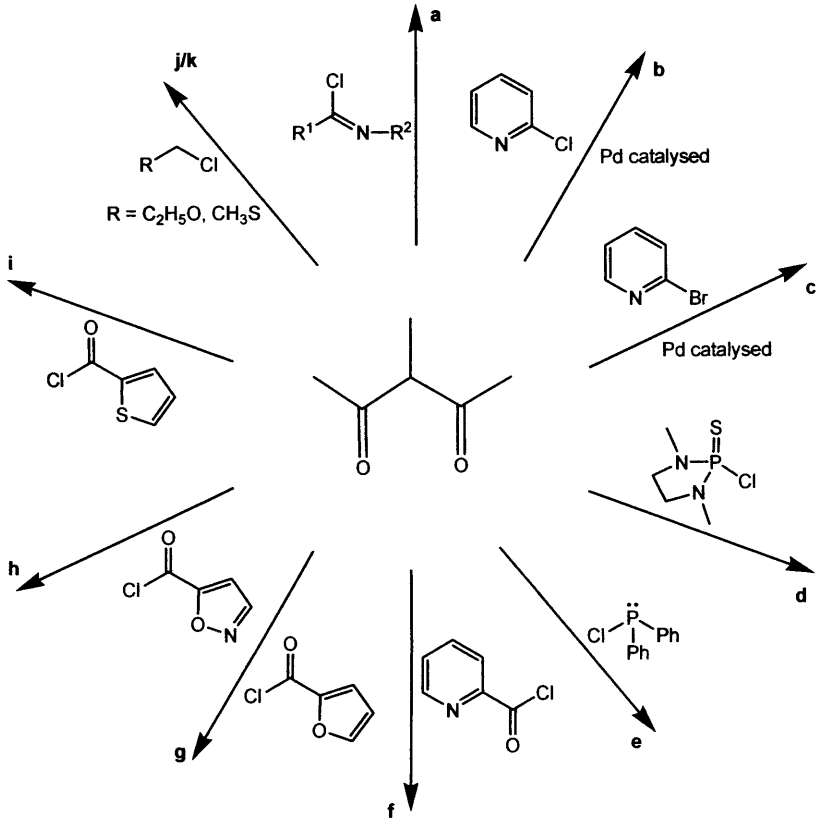
Scheme **2.3** Attempted synthesis of a mixed nitrogen/oxygen containing organic compound using the Wittig process.

Illustrated in Scheme **2.4** are the two remaining pathways by which the syntheses of a mixed tripodal nitrogen/oxygen compound were attempted. Pathway A involves the use of alternative electrophiles to acetyl chloride and hence requires the synthesis of imidoyl chlorides. Path B requires the syntheses of different bidentate ligands as potential nucleophiles for acylation, to give mixed N,O,O donor species.



Scheme **2.4** Two pathways illustrating the synthetic methods attempted to synthesise mixed N,O ligands.

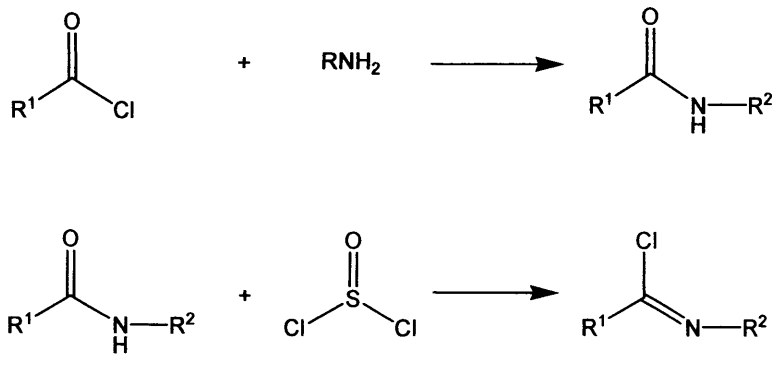
Many electrophiles were employed in path A, some commercially available and others were synthesised for this work. Scheme **2.5** summarises twelve different attempts at synthesising the desired products. The results of a, b and e-h were expected to give mixed nitrogen/oxygen donor compound with d and e to give additional phosphorylated-sulphide and phosphorylated-oxygen donor compounds, respectively. It was anticipated that reaction i would result in a mixed sulphur/oxygen donor compound and j and k would give potentially hemilabile donor ligands.



Scheme **2.5** A summary of the attempts to synthesise mixed N,O,O species utilising different potential electrophiles used for Path A in Scheme **2.4**. All reactions were conducted under the same conditions unless stated otherwise. MeMgBr was the base chosen to be used under reduced temperatures for the deprotonation step and DME was the reaction solvent.

The synthesis of imidoyl chlorides for reaction **a** in Scheme **2.5** was first reported by Braun *et al.* in 1930, using 2-methylacetanilide and phosphorus penta-chloride.[2] Later Roche *et al.* reported a similar reaction using benzene as a solvent.[3] However, the synthetic methods followed by Chandler *et al.* gave significantly improved yields and safer reaction conditions compared to the previous two literature reports, using thionyl chloride both as reagent and solvent with acetanilide, as illustrated in Scheme **2.6**.[4]

Chandler's method was employed and a range of imidoyl chlorides were synthesised, all with reasonable yields ranging from 50-65%. The imidoyl chlorides with less bulky substituents, **1** and **2** in Scheme **2.6**, were found to be extremely volatile and very susceptible to decomposition. Attempted reactions of such chlorides with Meacac resulted in hydrolysed starting material. It was postulated that this was primarily due to the instability of the imidoyl chlorides, thus the synthesis of phenylbenzimidoyl chloride **3** in Scheme **2.6**. The introduction of two phenyl rings in the imidoyl chloride resulted in increased stability compared to the less bulky counterparts, as it decomposed more slowly at room temperature and was easier to handle under the required reaction conditions. Analysis by NMR demonstrated possible product peaks suggesting a reaction had taken place between phenylbenzimidoyl chloride and Meacac however it was not possible to isolate any clean product from the crude reaction mixture.



1. R^1 = H, R^2 = Me
2. R^1 = Me, R^2 = Me, Ph, t^{me}Ph
3. R^1 = R^2 = Ph

Scheme **2.6** Syntheses of required anilides and their reaction with thionyl chloride to give the respective imidoyl chlorides.

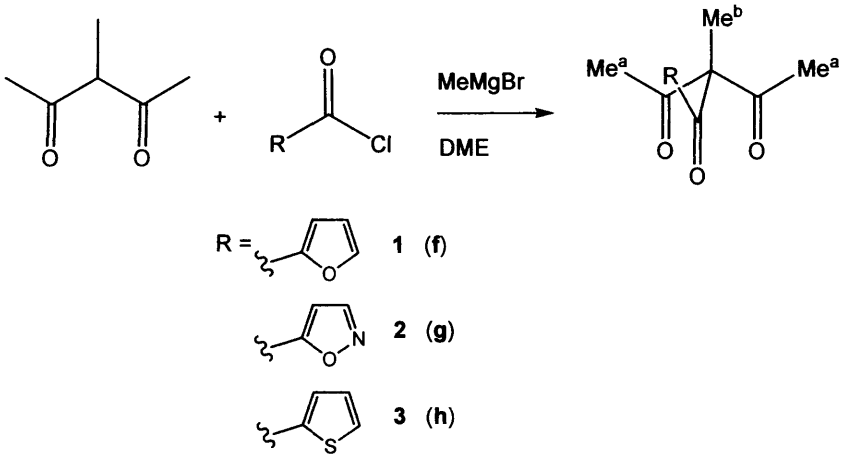
Less reactive and more stable reagents were utilised for reaction **b** and **c** in Scheme **2.5**, 2-chloropyridine and 2-bromopyridine. In both cases no product was formed when using MeMgBr as the base and DME the solvent and starting material was recovered. The aromatic C-Cl and C-Br bonds are strong bonds that require 402, 339 kJ/mol of energy to

be broken, therefore an alternative route was sought to reduce the amount of activation energy the reaction required, i.e the use of palladium catalysts. Palladium tetra-triphenylphosphine and palladium dichloride bis-acetonitrile were used for reactions **b** and **c** respectively. These reactions were repeated under Pd catalysed conditions but no reaction was detected by the ^{1}H NMR spectra and only starting materials were recovered.

For reactions **d** and **e** phosphorus containing reagents were also used to give an alternative to nitrogen donors. Thiophosphoryl-*N,N*-dimethylethylenediamine chloride used for reaction **d** was synthesised from thiophosphoryl chloride and *N,N*-dimethylethylenediamine. After several hours of reflux in DME with deprotonated Meacac, there was no indication of product formation by ^{1}H NMR and mass spectroscopy and only unreacted Meacac was recovered. However analysis by ^{31}P NMR of the crude mixture demonstrated reduction in the intensity of the phosphorus starting material signal and appearance of three different phosphorus species, that did not correspond to any starting materials used, thiophosphoryl chloride and thiophosphoryl-*N,N*-dimethylethylenediamine chloride or their hydrolysed counterparts. These unknown species comprised approximately 10% of the crude reaction mixture however they could not be isolated and identified and only starting materials were recovered. Reduction in the phosphorus starting material was assumed by comparing to the new phosphorus signals in the ^{31}P NMR spectrum, suggesting one or more reactions had taken place. It is possible that under the reaction conditions thiophosphoryl-N,N-dimethylethylenediamine chloride may not be stable and therefore decomposes to give different phosphorus species. Alternatively, the supposed P,O,O product from this reaction may not be as stable as expected thus also decomposing and resulting in different phosphorus species. No reaction was observed when using chlorodiphenylphosphine in reaction **e** and again only unreacted starting materials were isolated.

Preferential binding of alternative donor atoms in a ligand is observed when co-ordination to different metals is attempted, illustrated by Klaui's Tp style ligands.[5] Klaui observed rotation in the ligand such that the apical sulphonate group otherwise regarded as a weakly co-ordinating ligand, preferentially interacted over the nitrogen donor, with late transition

metals, cobalt, copper and zinc, as discussed in chapter 1 (**LXIII** and **LXIV**). As the replacement of oxygen for nitrogen in MeTAM was unsuccessful, an attempt was made to replicate Klaui's result by introducing a fourth potential donor that may inadvertently give rise to a X,O,O system (where X can be a different donor), reaction **g**, **h** and **i** in Scheme **2.5**. One of the methyl groups in MeTAM was replaced by another donor group when reacting Meacac with either furoyl-2-carbonyl chloride, isoxazole-5-carbonyl chloride or thiophene-2-carbonyl chloride giving three ligands, Ligands **1**, **2** and **3** respectively, Scheme **2.7**.



Scheme **2.7** Synthesis of three mixed nitrogen, oxygen and sulfur donor compounds.

In this family of ligands, in addition to the three hard oxygen donor atoms there is an alternative fourth donor available for co-ordination to a metal centre, in the case of ligands **2** and **3** a softer donor, nitrogen or sulfur, respectively. The ^{1}H NMR spectra clearly showed the formation of one product for each reaction, with all the organic compounds exhibiting similar spectral features. The axial methyl groups Me^a from the Meacac backbone were equivalent and remained unchanged at 2.2 ppm compared to the Meacac starting material. The apical Me^b between 1.7 and 1.8 ppm for the ligands was shifted downfield by 0.4 ppm and the quartet representing the apical proton as for Meacac was no longer present. The signals in the ^{1}H NMR spectra representing the heterocyclic rings were shifted upfield by 0.1-0.3 ppm for all the ligands, compared to the carbonyl chloride

starting materials. Crystals suitable for X-ray crystallography were obtained by slow recrystallisation from DCM and hexane at -20 °C of the organic compound from the crude reaction mixture, to give **2** and **3**.

Figure 2.1 Molecular structure of the isoxazole containing tripodal triketone, Ligand 2

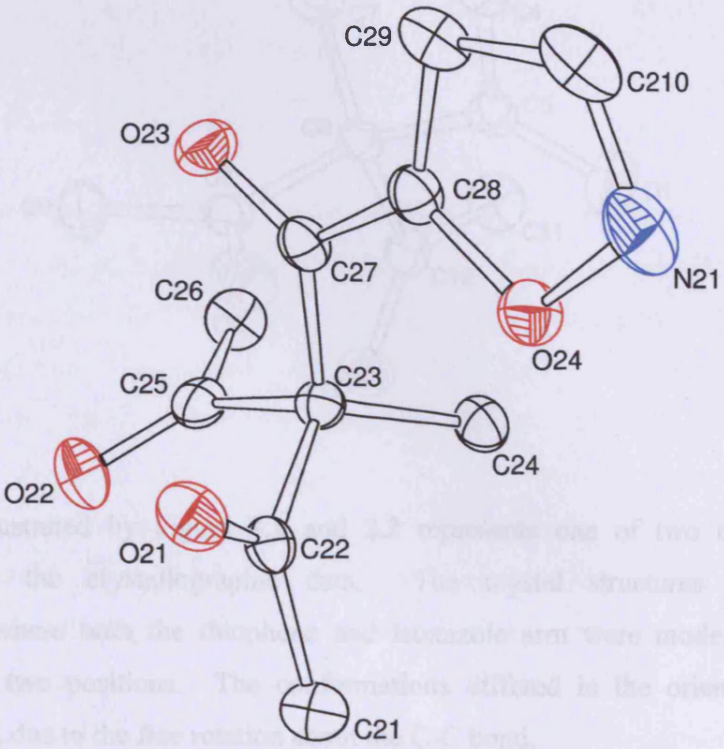
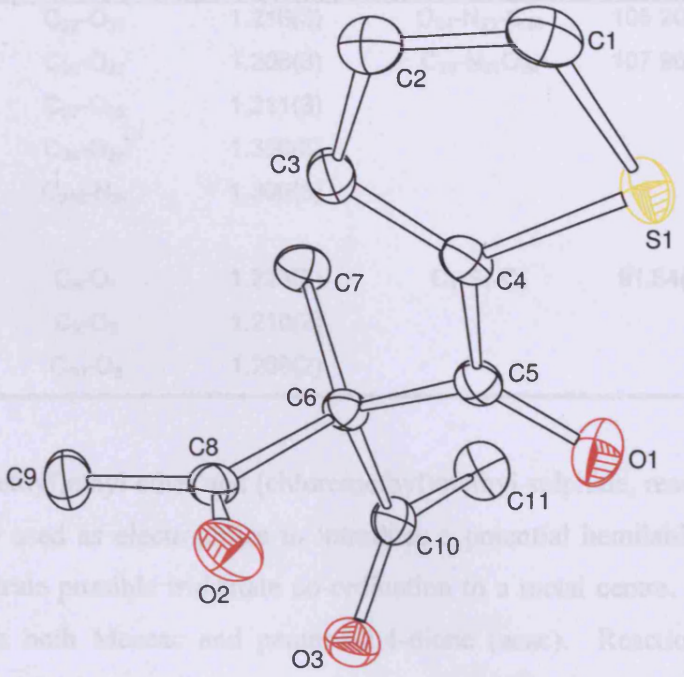


Figure 2.2 Molecular structure of the thiophene containing tripodal triketone, Ligand 3

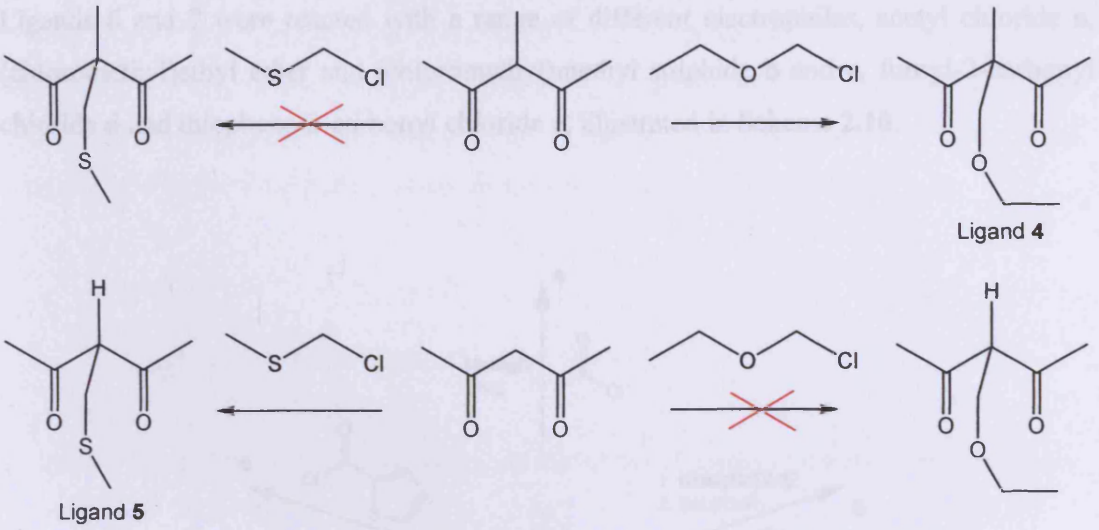


The ORTEP illustrated by Figure **2.1** and **2.2** represents one of two conformations calculated from the crystallographic data. The crystal structures showed two conformations, where both the thiophene and isoxazole arm were modelled as being disordered over two positions. The conformations differed in the orientation of the heterocyclic arm, due to the free rotation about the C-C bond.

Table 1 Selected bond lengths (Å) and bond angles (°) for ligands 2 and 3

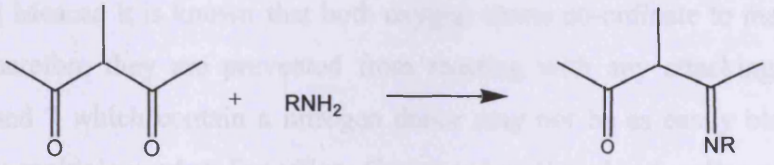
		Bond Length (Å)		Bond Angles (°)
Ligand 2	C_{22}-O_{21}	1.216(3)	O_{24}-N_{21}-C_{28}	105.20(18)
	C_{25}-O_{22}	1.208(3)	C_{28}-$N_{21}O_{24}$	107.90(18)
	C_{27}-O_{23}	1.211(3)		
	C_{28}-O_{24}	1.356(3)		
	C_{210}-N_{21}	1.300(3)		
Ligand 3	C_5-O_1	1.223(3)	C_1-S_1-C_4	91.84(10)
	C_8-O_2	1.210(2)		
	C_{10}-O_3	1.208(2)		

Finally, (chloromethyl)ethyl ether and (chloromethyl)methyl sulphide, reactions **j** and **k** in Scheme **2.5** were used as electrophiles to introduce a potential hemilabile donor group, that may demonstrate possible tridentate co-ordination to a metal centre. These reagents were trialled with both Meacac and pentane-2,4-dione (acac). Reaction with Meacac successfully gave ligand **4** however following several distillations and column chromatography the sulfide containing ligand could not be purified. From the ^{1}H NMR spectrum product signals were evident however the impurity present could not be identified or removed. The opposite was true for the reactions with acac in which crystals of pure product containing the sulfide moiety were attained from slow recrystallisation from DCM and hexane at -20°C to give ligand **5**. Both ligands **4** and **5** have been synthesised previously and are available from Strem, however no co-ordination chemistry has been reported, searched by Scifinder and the CCDC. In order to draw comparisons with similar nitrogen containing systems and to investigate the possible coordination chemistry of these ligands, synthesis of complexes were attempted using $ZrCl_4$, $TiCl_3(THF)_3$ and $CrCl_3(THF)_3$ metal precursors. However in all cases no product was formed, even under more forcing conditions by refluxing for several hours in THF.



Scheme **2.8** The reactions of Meacac and acac with (chloromethyl)ethyl ether and (chloromethyl)methyl sulphide.

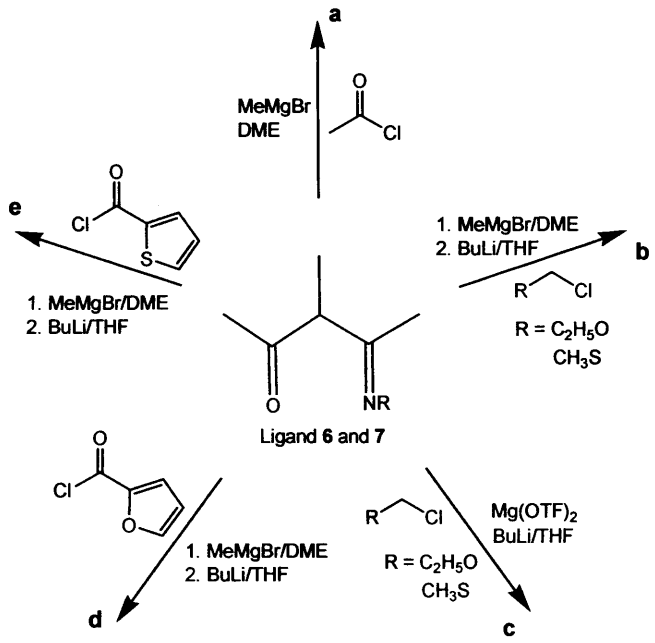
Path B in Scheme **2.4** requires the synthesis of bidentate nucleophiles incorporating a nitrogen donor atom, in place of Meacac. Hence the synthesis of two β-aminoketones, Scheme **2.9**, here in referred to as Menacac. These compounds have been synthesised previously and their chemistry extensively explored.[6,7] These ligands were reproduced following the condensation reaction of Meacac and isopropylamine and aniline.



R = $CH(CH_3)_2$ **6**
or
C_6H_5 **7**

Scheme **2.9** Syntheses of two Menacac ligands from the condensation reaction of Meacac with isopropylamine and aniline.

Ligands **6** and **7** were reacted with a range of different electrophiles, acetyl chloride **a**, (chloromethyl)ethyl ether and (chloromethyl)methyl sulphide **b** and **c**, furoyl-2-carbonyl chloride **d** and thiophene-2-carbonyl chloride **e**, illustrated in Scheme **2.10**.



Scheme **2.10** A range of potential electrophiles trialled with ligands **6** and **7**.

When using Meacac it is known that both oxygen atoms co-ordinate to magnesium from the base, therefore they are prevented from reacting with any attacking electrophiles. Ligands **6** and **7** which contain a nitrogen donor may not be as easily blocked and this could lead to multiple product formation, *C*-acylated or *N*-acylated and/or even both. This was probably the case for each reaction described in Scheme **2.10**, the crude NMR was very messy and no product was isolated. An alternative route to encourage N,O co-ordination to magnesium was to allow *in situ* magnesium complexes of ligands **6** and **7** to form as for reaction **c**. Allowing a solution of the $Mg(OTF)_2$ and the ligand in THF to stir for 30 minutes, followed by deprotonation with BuLi and addition of the appropriate electrophiles, made little difference to the result of the reaction. Following several distillations of the crude product for reaction **a**, the anticipated product was not isolated.

Fractions analysed by ^{1}H NMR spectrum showed the presence of starting material and other organic species that could not be identified. Analysis by mass spectroscopy of one such fraction suggested the presence of acylated product however it could not be determined whether the product or products were *C*-acylated, *N*-acylated or both.

2.3 Attempted synthesis of complexes

Ligands **2**, **3** and **4** were reacted with a variety of metal precursors in an attempt to form complexes: $TiCl_3(THF)_3$, $VCl_3(THF)_3$, $CrCl_3(THF)_3$, $ZrCl_4$, $Mo(CO)_6$, $FeCl_2$, $Cu(OTF)_2$, $Mn(CO)_6$, $CoCl_2$, $PdCl_2(MeCN)_2$, $PdCl_2cod$, $PtCl_2cod$ and $Ni(cod)_2$. The reaction temperatures were varied from -40 °C to 100 °C, solvent systems used were changed and different procedures were followed. In most cases a solution of the precursor (cooled for more reactive and temperature sensitive metal precursors $TiCl_3(THF)_3$, $VCl_3(THF)_3$ and $CrCl_3(THF)_3$) was added dropwise to the ligand in the same solvent (also cooled if required). Reactions were analysed primarily by ^{1}H NMR spectroscopy, in the cases of paramagnetic species mass spectrometry was used. If no reaction took place after stirring at room temperature for 48 hours, the mixtures were gradually heated, in some cases for several days.

No reactions were detected for the precursors used except for titanium and vanadium. Dropwise addition of a solution of the ligand to the turquoise titanium precursor gave an immediate colour change to dark purple, consistent with literature references. The vanadium reaction gave a dark black emerald mixture from the bright red/orange solution of the precursor. The possible titanium (III) complexes that could form would be paramagnetic and analysis by NMR spectroscopy would be difficult. Thus crystals of the product were required for the identification of the product by x-ray crystallography. Reducing the mixture *in vacuo* resulted in isolating starting material and cooling resulted in crystal growth of the metal precursor. Reactions with vanadium gave a black/emerald product almost immediately with black insoluble solid deposited soon after. This suggested decomposition was taking place therefore the reaction was slowed down by

repeating both the Ti and V reactions using a layering technique in which a solution of the ligand was allowed to diffuse slowly at ~4 °C, into a solution of the appropriate metal precursor over a period of several days. In neither case was product isolated nor crystals of the metal precursor were grown.

No complexations were attempted for ligands **6** and **7** however *in situ* Heck catalysis was performed (see Chapter 4).

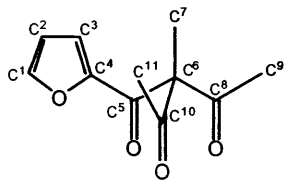
2.4 Conclusions

In this study a family of the required target molecules have been successfully synthesised and a range of tridentate oxygen donor organic compounds are reported, with the concurrent development of suitable synthetic methods. All organic compounds reported in this chapter demonstrated a high level of stability, both to air and moisture. The stability of these compounds could be the predominant factor resulting in a lack of complex formation.

Although spectral analysis suggested the possibility of some product formation for tripodal ligands incorporating one or more nitrogen donors, the synthesis was less successful and an alternative approach was required to successfully synthesise nitrogen containing ligands. This was the fundamental concept behind the chemistry described in chapter 3.

2.5 Experimental

2.5.1 Synthesis of ligand 1

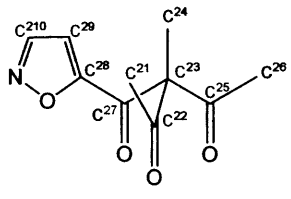


Prepared under a nitrogen atmosphere in a Schlenk. To a solution of 3-methylpentane-2,4-dione (3.06 ml, 0.13 mol) in dry

degassed DME (40 ml), methyl magnesium bromide in 3 M ether (10.5 ml) was added drop wise, via a dropping funnel, under the cooling action of an ice bath. The addition of the Grignard took 10 minutes and the mixture was allowed to stir for 40 minutes. While still under the influence of an ice bath, 2-furoyl carbonyl chloride (3.4 ml) was added drop wise, to the cloudy white solution, from a syringe via a septum over 5 minutes to give a deep yellow mixture. The solution was allowed to stir for 20 hours outside the ice bath. The reaction mixture was diluted with saturated ammonium chloride (50 ml) and allowed to stir for 5 minutes and the mixture was transferred to a separating funnel. The water layer was extracted with DCM (3 x 50 ml). The organic layer was then dried over sodium sulphate, transferred to a round bottom flask and the solvent was removed on a rotary evaporator, resulting in a viscous brown oil. The crude product was distilled under vacuum at 110-115^{0}C to give a pale coloured oil, in a 70% yield.

Found: δ_H (400MHz:$CDCl_3$) 1.71(3H, s, Me), 2.21(6H, s, 2 x Me), 6.53(1H, m, H-*Ar*), 7.21(1H, m, H-*Ar*) and 7.54(1H, m, H-*Ar*); ^{13}C δ (100MHz:$CDCl_3$) 17.8(C^7), 28.5($C^{9,11}$), 77.6(C^6), 113.4(C^2), 119.4(C^3), 147.5(C^1), 151.6(C^4), 185.8(C^5) and 204($C^{8,10}$); MS: (ESMS): 207 $[M + H]^+$ 100%.

2.5.2 Synthesis of ligand 2

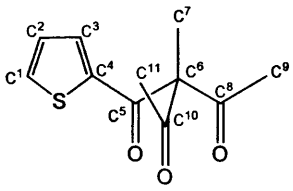


Prepared under a nitrogen atmosphere in a Schlenk. To a solution of 3-Methylpentane-2,4-dione (0.35 ml, 0.13mol) in dry degassed DME (20 ml), methyl magnesium bromide in 3 M ether (1.1 ml) was added drop wise, via a dropping funnel, under the cooling action of an ice bath. The addition of the Grignard took 10 minutes and the mixture was allowed to stir for 40 minutes. While still under the influence of an ice bath, isoxazole-5-carbonyl chloride (0.5 ml) was added drop wise, to the cloudy white solution, from a syringe via a septum over 5 minutes to give a pale orange mixture. The solution was allowed to stir for 20 hours outside the ice bath. The reaction mixture was diluted with saturated ammonium

chloride (50 ml) and allowed to stir for 5 minutes and the mixture was transferred to a separating funnel. The water layer was extracted with DCM (3 x 50 ml). The organic layer was then dried over sodium sulphate, transferred to a round bottom flask and the solvent was removed on a rotary evaporator, resulting in a yellow solid. The crude product was distilled in a glass oven under vacuum at 68-73 ^{0}C, affording large colourless crystals in yields of 68%.

Found: δ_H (400MHz:$CDCl_3$) 1.78(3H, s, Me), 2.23(6H, s, 2 x Me), 6.95(1H, s, H-*Ar*) and 8.29(1H, s, H-*Ar*); ^{13}C δ (100MHz:$CDCl_3$) 17.0 (C^{24}), 27.7($C^{21,26}$), 109.2(C^{23}), 150.7(C^{29}), 164.4(C^{210}), 185.6(C^{27}) and 202.4($C^{25,27}$); MS: (ESMS): 223 $[M + H]^+$ 100%; Anal. Calcd for $C_{11}H_{12}O_3S$: C, 57.42; H, 5.3; N, 6.69. Found C, 57.23; H, 5.29 and N, 6.56.

2.5.3 Synthesis of ligand 3



Prepared under a nitrogen atmosphere in a Schlenk. To a solution of 3-methylpentane-2,4-dione (3.06 ml, 0.13 mol) in dry degassed DME (40 ml), methyl magnesium bromide in 3 M ether (10.5 ml) was added drop wise, via a dropping funnel, under the cooling action of an ice bath. The addition of the Grignard took 10 minutes and the mixture was allowed to stir for 40 minutes. While still under the influence of an ice bath, 2-thiophene carbonyl chloride (3.65 ml) was added drop wise, to the cloudy white solution, from a syringe via a septum over 5 minutes to give a deep yellow mixture. The solution was allowed to stir for 20 hours outside the ice bath. The reaction mixture was diluted with saturated ammonium chloride (50 ml) and allowed to stir for 5 minutes and the mixture was transferred to a separating funnel. The water layer was extracted with DCM (3 x 50 ml). The organic layer was then dried over sodium sulphate, transferred to a round bottom flask and the solvent was removed on a rotary evaporator, resulting in a yellow solid. The crude product was distilled in a glass oven under vacuum at 70-75^{0}C, affording large colourless crystals in high yields, 78%.

Found: δ_H (400MHz:$CDCl_3$) 1.75(3H, s, Me), 2.20(6H, s, 2 x Me), 7.03(1H, m, H-*Ar*), 7.35(1H, m, H-*Ar*) and 7.62(1H, m, H-*Ar*); ^{13}C δ (100MHz:$CDCl_3$) 18.8 (C^7), 28.4($C^{9,11}$), 77.4(C^6), 128.5(C^2), 133.4(C^3), 135.0(C^1), 141.8(C^4), 189.3(C^5) and 204.3($C^{8,10}$); MS: (ESMS): 210 $[M + H]^+$ 100%; Anal. Calcd for $C_{10}H_{11}NO_4$: C, 58.91; H, 5.39. Found C, 58.88 and H, 5.35.

2.5.4 Synthesis of ligand 4

To a solution of 3-methylpentane-2,4-dione (0.34 ml, 2.9 mmol) in DME (20 ml) cooled in an ice bath, MeMgBr (1.12 ml, 3.4 mmol) was added dropwise. The mixture was allowed to stir for 40 minutes at room temperature. On cooling the reaction mixture chloromethyl ethyl ether (0.34 ml, 3.7 mmol) was added dropwise. The reaction mixture was allowed to stir overnight. Ammonium chloride (30ml) was added to the mixture to give 2 clear layers. The aqueous layer was further extracted with DCM (3x20ml). The organic layers were combined, washed with water (20ml), dried over Na_2SO_4 and evaporated *in vacuo*. The residual yellow oil (0.37 g, 73%) was distilled at 55 ^0C to give almost colourless oil.

Found: δ_H (400MHz: $CDCl_3$) 1.10(3H, t, *J* 7.0, Me-*ether*), 1.35(3H, s, Me-*apical*), 2.11(6H, s, 2 x Me), 3.45(2H, q, *J* 7.0, CH_2 - *ether*) and 3.72(2H, s, CH_2); ^{13}C δ (100MHz:$CDCl_3$) 14.2(Me-*apical*), 16.3(Me-*ether*), 25.1(*2 x* Me-*axial*), 66.7(CH_2), 72.9(CH_2), 76.4(C_q) and 205.4(C=O)

2.5.6 Synthesis of ligand 5

3-Methylpentane-2,4-dione (0.8 ml, 7.0 mmol), chloromethymethylsulphide (0.77 ml, 8.0 mmol), anhydrous potassium carbonate (1 g), a catalytic amount of tetrabutylammonium iodide and acetone (20 ml) was placed in a 100 ml round bottom flask fitted with a reflux condenser. The reaction mixture was allowed to reflux under nitrogen for 20 hours. The insoluble material was removed by filtration and washed with dry DCM. The combined

filtrate and acetone washing were concentrated and dried under vacuum the residual oil was distilled at 55 ^{0}C to give pale yellow solid (0.72 g, 61%)

Found: δ_H (400MHz: $CDCl_3$) 1.33(3H, s, *J* 7.0, Me-*apical*), 2.16(9H, s, 2 x Me-*axial*, Me-*s*) and 2.91(2H, s, CH_2); ^{13}C δ (100MHz:$CDCl_3$) 17.2(Me-*apical*), 25.9(Me-*axial*), 40.1(Me-*s*), 67.4(CH_2), 76.3(C_q) and 205(C=O).

2.5.7 Synthesis of ligand 6

3-Methylpentane-2,4-dione (4.0 ml, 0.03 M), isopropylamiine (18. 0 ml) and Na_2SO_4 was placed in 100ml round bottom flask and allowed to stir for 5 days. DCM (50 ml) was added followed by more Na_2SO_4 and mixture was allowed to stir for one hour. The reaction mixture was filtered and excess solvent was removed removed on the rotary evaporator and further dried under vacuum to yield a pale yellow oil in a .

(Found: δ_H (500MHz:$CDCl_3$) 1.15(6H, d, *J* 6.4 2 x me) 1.75(3H, s, Me), 1.85(3H, s, Me), 2.05(3H, s, Me), 3.73(1H, s, J 6.4, H); ^{13}C δ (125MHz:$CDCl_3$) 13.7 (Me- *apical*), 14.1(Me- *axial*), 22.9(2 x ^{ipr}Me), 27.4(Me- *axial*), 43.7 (C-N), 96.6(C_q), 160.2(C=N) and 193.0(C=O); MS: (ESMS): 155 $[M + H]^+$ 100%.

2.5.8 Synthesis of ligand 7

3-Methylpentane-2,4-dione (4.1ml, 0.03 M), Aniline (16.3ml) and $MgSO_4$ was placed in 100ml round bottom flask and allowed to stir for 6 days. DCM (50ml) was added followed by more $MgSO_4$ and mixture was allowed to stir for one hour. The reaction mixture was filtered and excess solvent was removed. Distillation between 67-73 ^{0}C gave a yellow oil (3.03 g, 44%).

Found: δ_H (400MHz:$CDCl_3$) 1.85(3H, s, Me) 1.95(3H, s, Me), 2.10(3H, s, Me), 6.93(2H, m, *Ar*-H), 7.11(1H, m, *Ar*-H) 7.25(2H, m, *Ar*-H) and 13.41(1H, s, N-H); ^{13}C δ (125MHz:$CDCl_3$) 14.9(Me-*apical*), 17.0(Me-*axial*), 28.7(Me-*axial*), 77.1(C_q), 101.0(C_{Ar}), 125.1(2 x C_{Ar}), 129.4(2 x C_{Ar}), 139.5(C-N_{Ar}), 158.3(C=N) and 196.6(C=O).

2.6 References

(1) T. Ruther; K. Cavell *Journal of the Chemical Society; Dalton Transactions* **2002**, 4684.

(2) J. V. Braun; H. Silbermann *Eingegangen* **1930**, 498.

(3) E. B. Roche; D. W. Stansloski *Journal of Heterocyclic Chemistry* **1970**, 139.

(4) A. Chandler; A. Hegarty; M. McCormack. *Journal of the Chemical Society; Perkins II* **1980**, 1318.

(5) W. Klaui; M. Berghahn; W. Frank; G. J. Reib; T. Schonherr; G. Rheinwald; H. Lang *European Journal of Inorganic Chemistry* **2003**, 2059.

(6) H. Lida; Y. Yuasa; C. Kibayashi *Journal of Chemical Society, Daltons Trans* **1981**, 2212.

(7) J. V. Greenhill *Chemistry Society Reviews* **1977**, *6*, 277.

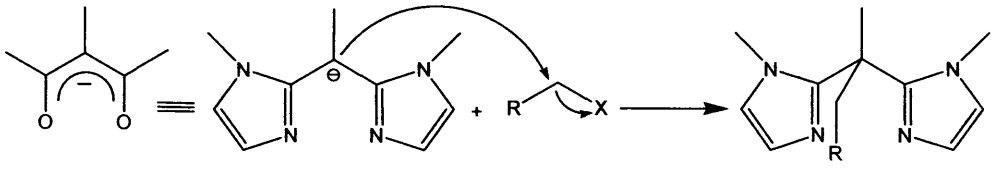
CHAPTER THREE

Synthesis of some novel imidazole containing ligands and their complexes

3.1 Introduction

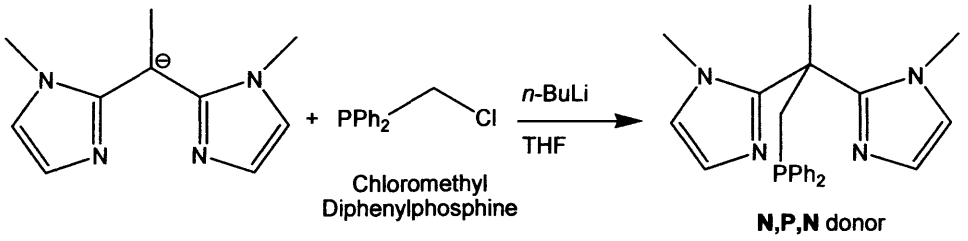
Following the concept described in chapter two, a potential bidentate alternative to meacac was sought for the synthesise of mixed N,O tridentate donor ligands.

Scheme 3.1



Cavell *et al.* reported a family of bridged bis-imidazole containing ligands in which the apical carbon atom is susceptible to deprotonation followed by electrophilic attack.[1] These ligands have been successfully used as building blocks for the synthesis of bi- and tridentate mixed donor ligands, N,P; N,N; N,O,N and N,P,N.[1] As illustrated in Scheme **3.2**, an alkylating phosphine reagent was used by Cavell *et al.* when synthesising an N,P,N tridentate ligand.

Scheme 3.2



Palladium complexes of bis(1-methylimidazol-2-yl)methane (BIM) ligands have been isolated and reported as successful precatalysts in the Heck reaction.[2,3] Ligands with more exotic combinations of these types of functional groups are sought for the synthesis of precatalysts,[4] in particular in the synthesis of hemilabile ligands for their ability to stabilise catalytic intermediates and possibly affect product distribution. As a part of ongoing interest in functionalised ligand systems BIM ligands became the backbone for the family of tridentate ligands reported in this Chapter.

3.2 Results and Discussion

Bis(1-methylimidazol-2-yl)ketone (**8**) (see Scheme **3.3**) has been made via several different synthetic routes, with reported yields ranging from 30 to 76%. Although all methods are similar and involve the deprotonation of imidazole followed by the addition of an electrophile, the procedures vary in the way in which the crude product is isolated from the reaction mixture. As Braussaud *et al.* has observed,[1] we found that prolonged exposure of the product to the reaction mixture led to its decomposition to 1-methylimidazole, presumably via hydrolysis and therefore the method described by Elgafi[5] and Gorun[6] was adopted. The synthesis of bis(1-methylimidazol-2-yl)methane (**9**) was taken from a modified preparation published by Cavell *et al.*[1]

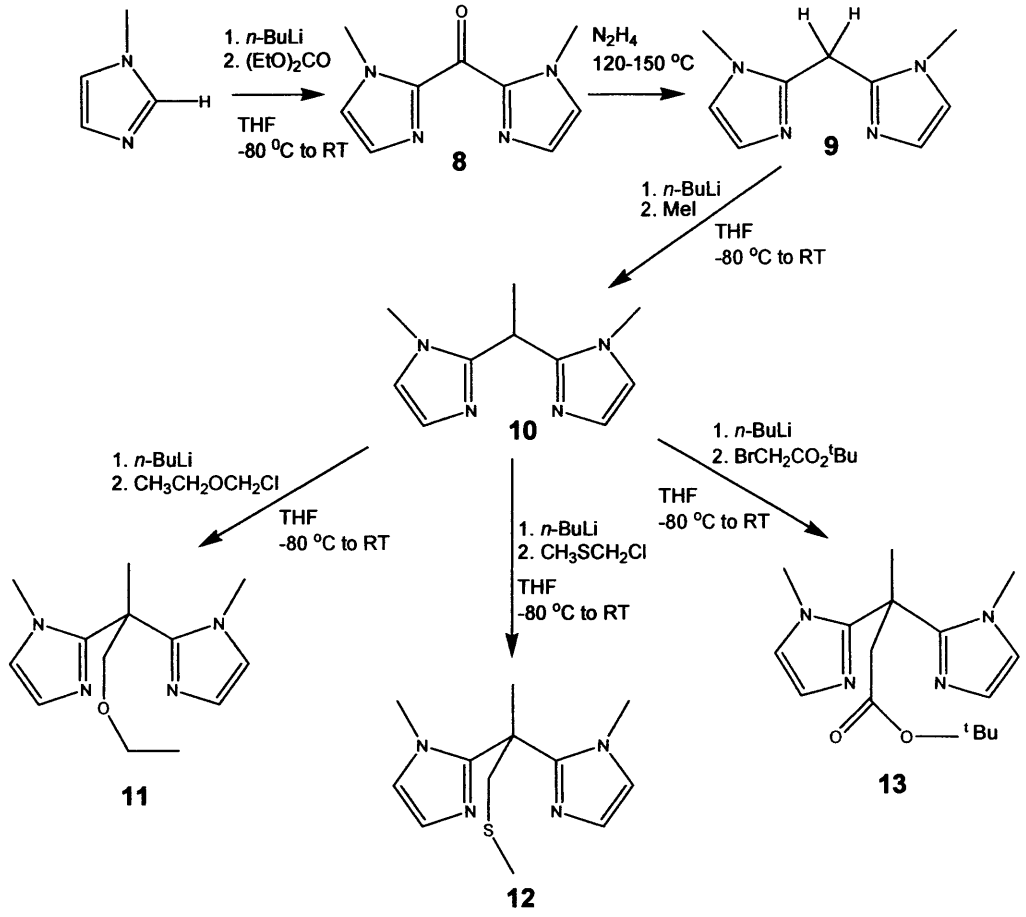
3.2.1 Ligand Synthesis

A general synthesis of the imidazole-based ligands described in this chapter is outlined in Scheme **3.3**. Deprotonation of 1-methylimidazole with *n*-butyllithium followed by the addition of diethyl carbonate at low temperatures gave the bis(1-methylimidazol-2-yl)ketone [(BIM)CO] **8**. Bis(1-methylimidazol-2-yl)methane [(BIM)CH_2] **9** was formed by heating a mixture of **8** with hydrazine and sodium hydroxide and all apart from **8** and **9** are novel ligands that have not previously appeared in the literature.

Methylation of **9** using MeI/BuLi gave the parent compound for all the tridentate ligands in this chapter, bis(1-methylimidazole-2-yl)methylmethane **10**, a bidentate ligand analogous to meacac. It was essential to optimise the conditions for this synthesis such that the maximum yield could be obtained.

The crude reaction mixture from the synthesis of compound **10** contains the protonated (N-H) bis-imidazolium and must be basified using $NaHCO_3$ before extracting the required product with DCM. The ^1H NMR spectrum of the crude protonated product showed a characteristic singlet at 6.7 ppm due to the two pairs of inequivalent protons on the imidazole rings representing a coincidental unresolved coupling, rather than the expected two singlets. The two equivalent N-methyl groups were shifted downfield by 0.4 ppm and the apical H and methyl group were both shifted by 0.1 ppm, the former downfield and latter upfield, compared to product **9**.

Scheme 3.3 A general scheme describing the synthesis of four novel imidazole-based ligands

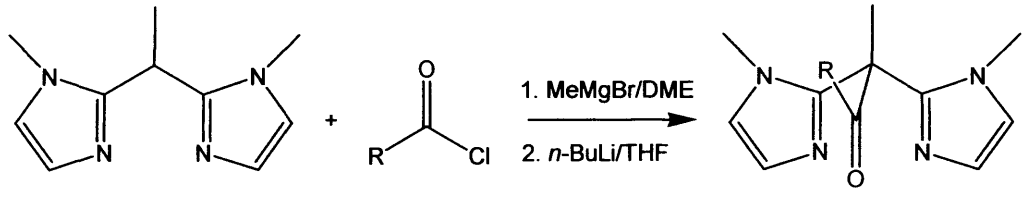


Prolonged exposure of the product to the crude reaction mixture was kept to an absolute minimum extracting the product as soon as possible, increasing the yield, while storing the product under an inert atmosphere at room temperature maximised its shelf life, no decomposition is detected for at least six months; **10** was observed to be more susceptible to decomposition by hydrolysis than either **8** and **9**.

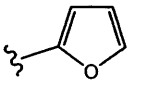
As illustrated in Scheme **3.4**, acylation of the bisimidazole **10** using a variety of different electrophiles was attempted. These reactions were conducted under two different conditions, using MeMgBr as the base and DME as the reaction solvent in which the

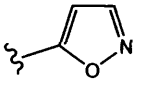
deprotonation step was conducted at 0 °C, alternatively *n*-BuLi and THF were utilised and deprotonation was achieved at -70 °C. Acyl chlorides were added maintaining the respective low temperatures and the reactions were allowed to warm gradually to room temperature whilst stirring for 24 hours. Each reaction was analysed by NMR spectroscopy and a mixture of compounds was observed however only starting material was identified and recovered.

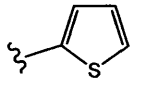
Scheme 3.4 Attempted acylation reactions of the bis(1-methylimidazole-2-yl)methylmethane substrate

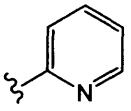


R = Me Acetyl chloride


Isoxazole-5-carbonyl chloride


2-thiophene carbonyl chloride

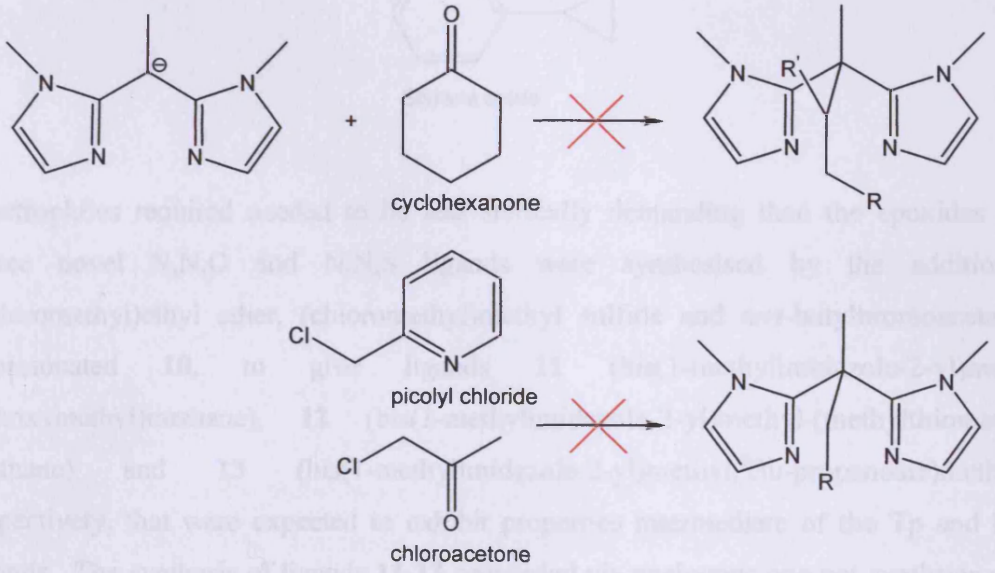

2-furoyl carbonyl chloride


Picolyl carbonyl chloride

Alkylation of BIM type ligands was proved by the synthesis of **10** and the mixed donor ligands reported by Cavell *et al.* Acylating reagents are more reactive than comparative alkylating reagents therefore it is expected that the reactions illustrated in Scheme **3.4** should have worked. It is speculated from the observed NMR spectra that product formation took place however acyl groups are susceptible to cleavage therefore the C-C bond must have broken as soon at it formed. Therefore alternative less reactive

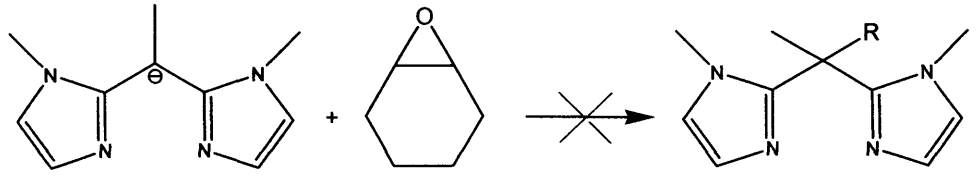
electrophiles; cyclohexanone, picolyl chloride and chloroacetone were considered suitably milder electrophiles, Scheme **3.5**. In these cases no reaction took place with only starting material visible in the NMR. Inevitably this was an extreme case of the other spectrum and the electrophiles chosen demonstrated a higher than required stability resulting in no reaction.

Scheme 3.5 Acylation attempts using lesser reactive electrophiles

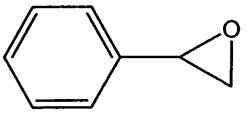


The epoxides of cyclohexene oxide and styrene oxide were then trialled, Scheme **3.6**, however no reaction took place again and starting material was retrieved. In addition to the reduced electrophilicity/reactivity of the epoxide reagents, their larger bulk may have had a negative effect on the reactivity due to steric bulk.

Scheme 3.6 Attempted reactions of ligand 10 using epoxides as electrophiles



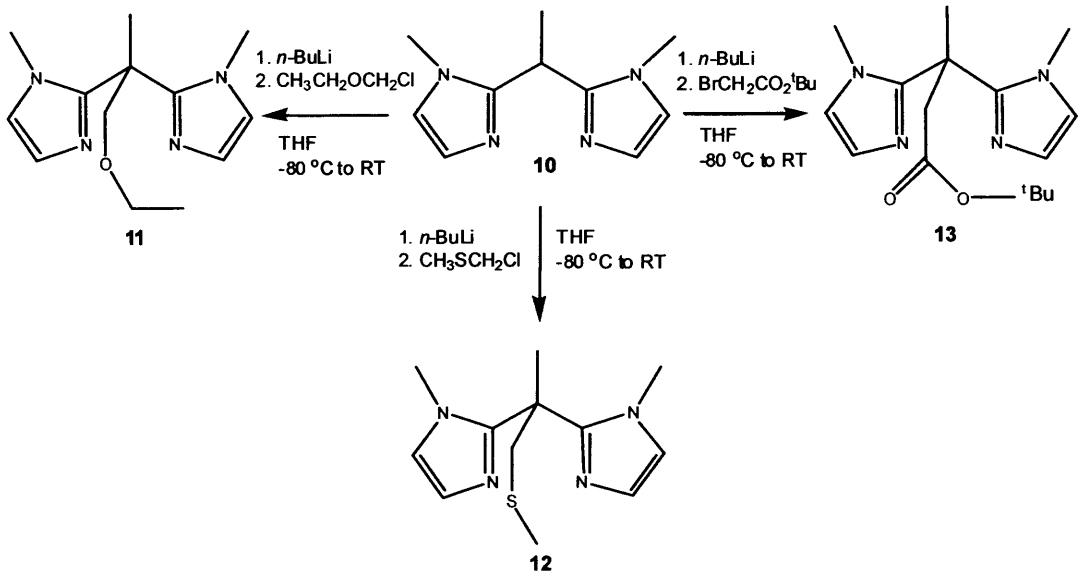
Cyclohexene oxide



Styrene oxide

Electrophiles required needed to be less sterically demanding than the epoxides used. Three novel N,N,O and N,N,S ligands were synthesised by the addition of (chloromethyl)ethyl ether, (chloromethyl)methyl sulfide and *tert*-butylbromoacetate to deprotonated **10**, to give ligands **11** (bis(1-methylimidazole-2-yl)methyl-(ethoxymethyl)methane), **12** (bis(1-methylimidazole-2-yl)methyl-(methylthiomethyl)-methane) and **13** (bis(1-methylimidazole-2-yl)methyl(^{t}Bu-propanoate)methane), respectively, that were expected to exhibit properties intermediate of the Tp and Klaui ligands. The synthesis of ligands **11-13** proceeded via analogous one pot synthesis as for **10** and involved metalation at the bridging methylene group with *n*-BuLi at low temperatures, forming a nucleophile for further *in situ* reactions with the respective electrophiles, Scheme **3.7**. Significantly higher yields of **11-13** were obtained when the deprotonation step and addition of the electrophiles was performed dropwise at -45 °C and -80 °C, respectively.

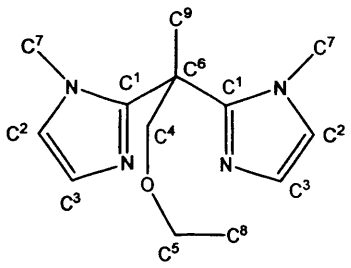
Scheme 3.7 Synthesis of ligands 11, 12 and 13



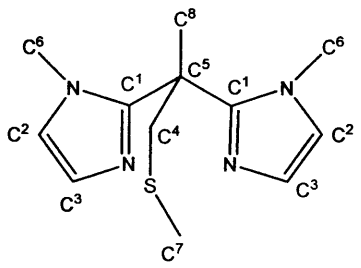
Ligands **11** and **12** are water soluble and more hygroscopic than **10** and **13** therefore methanol was used to quench unreacted *n*-BuLi and the products extracted into dry ethyl acetate. Ligand **11** was isolated as a very pale yellow solid and **12** as an off-white powder. All ligands were stored under an inert atmosphere to prolong their shelf life. Ligands **11**, **12** and **13** were fully characterised by NMR spectroscopy, mass spectrometry and elemental analysis. For **11**, **12** and **13** the ^{1}H NMR spectra clearly showed the formation of only one compound. Compared to the spectrum of the starting material **10**, the most obvious feature is the loss of the quartet at 4.5 ppm corresponding to the apical proton, due to its replacement with the hemilabile arm. As a result, the apical methyl group can no longer couple to anything and is represented by a singlet at 1.8 ppm. In each case the methyl groups on the imidazole rings were shifted upfield by 0.4 ppm on addition of the O or S moiety but no change for the imidazole proton signals was observed. New peaks, singlets integrating to two protons, appeared at 4.15, 3.5 and 3.2 ppm for ligands **11**, **12** and **13**, respectively and were assigned to the CH_2 groups adjacent to the apical carbon atom. The greater electronegativity of the oxygen ether donor induced a greater deshielding effect on the apical protons in **11**, thus pushing this signal further upfield than in **12** or **13**. The alkyl groups on the newly introduced heteroatoms in ligand **11**, gave two

additional peaks, a triplet and quartet, for the CH_2 and CH_3 attached to the ether group introduced. Ligand **12** showed an extra singlet for the methyl group adjacent to the sulfide and ligand **13** demonstrated the presence of tertiary butyl group also adjacent to a heteroatom.

The ^{13}C NMR spectra for ligands **11** and **12** showed the correct number of peaks, 9 and 8, respectively. The aromatic C-N signals remained unchanged for both ligands, with the quaternary carbon C^1 peak at 148 ppm and C^2 and C^3 at 127 and 123 ppm, respectively. The saturated carbon atoms and the apical quaternary carbon signals also remained the same. The most obvious difference in the spectra from ligand **10** was the additional signals representing the carbons attached to the O and S groups. In **11**, peaks at 76 and 67 ppm represented C^4 and C^5, these signals were significantly higher than the alphiphatic carbons due to the greater electronegativity of the oxygen atom. The signals for C^4 and C^7 in **12** were observed at 44 ppm and 23 ppm, respectively. Mass spectroscopy and elemental analysis both supported product formation with the elemental analysis demonstrating accuracy for ligand **11** within 0.5% for C, 0.1% for H and 0.03% for C, 0.1% for H for **12**.



11



12

3.2.2 Synthesis and Characterisation of Complexes

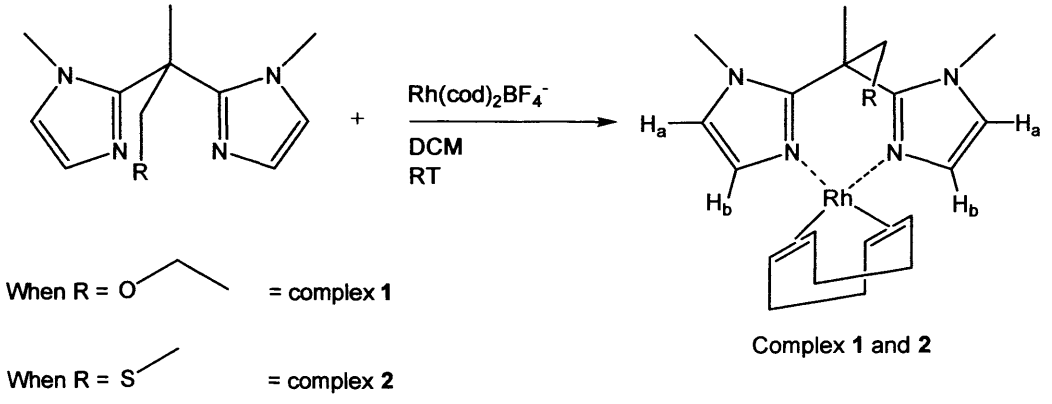
As a part of an ongoing investigation, ligands **11** and **12** have been used to develop neutral complex systems that may be able to switch between tridentate and bidentate binding

modes in catalytic reactions, as a result of a kinetically inert chelating system combined with a hemilabile third donor. Syntheses of the neutral rhodium (Rh), iridium (Ir) and palladium (Pd) complexes are outlined in Schemes **3.7**, **3.8** and **3.9**, respectively. Displacement of the labile 1,5-cyclooctadiene (cod), cyclooctene (coe) or acetonitrile (MeCN) ligands from the respective metal precursors by one equivalent of ligands **11** or **12**, gave the corresponding products in high yields. The products were characterised using NMR spectroscopy, mass spectrometry and elemental analysis.

3.2.2.1 Rhodium(I) complexes

Dropwise addition of colourless solution of ligand (**11** or **12**) in DCM to deep orange Rh precursor solution also in DCM gave an almost immediate colour change to yellow, the reaction mixture was allowed to stir at room temperature overnight to ensure completion. The reaction mixture was reduced *in vacuo* to give a pale yellow waxy solid which was washed with hexane and ether to give a fine yellow solid.

Scheme 3.7 Synthesis of rhodium complexes 1 and 2 bearing imidazole containing ligands



The NMR spectra for complexes **1** and **2** clearly demonstrated the formation of only one compound from each of the reactions. Co-ordination of the ligand to the metal centre was confirmed by shifts in the ligand signals and through broadening in the NMR spectra.

The ^{1}H NMR spectra of both complexes **1** and **2** exhibit similar features and compared to free ligand certain signals had moved significantly. The apical methyl group resonance shifted downfield from its free base form, by 0.5 ppm for **1** and by 0.2 for **2**. The H_b protons were shifted very slightly upfield compared to the free ligand and the CH_2 and CH_3 groups α to the ether and sulfide groups were shifted downfield by 0.1 ppm. Both N-Me groups remained equivalent and shifted downfield by 0.9 ppm in the complexes. The most significant difference was that of the CH_2 group attached to the apical carbon atom shifting downfield by 1.0 and 2.0 ppm in **1** and **2**, respectively. This suggested that the hemilabile donors may have co-ordinated to the metal centre. However, if the O or S moiety were bonded to the metal centre then a more significant shift of the CH_2 and CH_3 groups adjoining the third donor atom would be expected. Four co-ordinate species in which two sites are taken up by the cod ligand, render only two other sites for co-ordination. O or S co-ordination at the expense of an imidazole group would destroy the symmetry of the square planar Rh^I(bis-imid)(cod) complexes giving four peaks in the aromatic region of the NMR and two signals for each of the inequivalent N-Me. However two peaks are observed in the aromatic region with one singlet representing the equivalent N-Me groups suggesting N,N′ co-ordination in symmetrical square planar complexes. Confirmation of the suggested structures of **1** and **2** by x-ray crystallography was desired.

Large, colourless, rhombic crystals were afforded by recrystallisation of the yellow solid of complexes **1** and **2** from DCM and hexane at -5 °C. The results of the low temperature single-crystal x-ray studies showed square planar Rh complexes, with two co-ordination sites on Rh taken up by the imidazole nitrogen donor and the remaining two sites by the cod co-ligand. The larger than expected resonance shift for the CH_2 group α to the apical carbon atom, in the NMR spectra, is proposed to be a result of fluxional character the complex exhibits in solution. This behaviour would allow the hemilabile donors to adopt

a conformation that puts them in close proximity to the rhodium centre, leading to deshielding of the CH_2 group, relative to the free ligand.

Table **3.1** lists selected bond lengths and chelate angles of rhodium complexes containing imidazole donors or other nitrogen heterocyclic donor groups.

Table 3.1 Bond lengths and angles for selected rhodium complexes

Compound	M-N1 (Å)	M-N2 (Å)	N-M-N (°)	References
Rh(pzTp)(cod)	2.099(2)	2.099(2)	86.1(3)	7
$RhTp^{Ph}$(cod)	2.091(3)	2.096(3)	84.6(24)	8
$RhTp^{Mei}$(cod)	2.105(6)	2.120(6)	82.3(2)	9
$[Rh\{(pz)_2CH_2\}(cod)ClO_4]^-$	2.111(8)	2.097(7)	88.4(3)	10
$[Rh\{(mim)_2CH_2\}(CO)_2BF_4]^-$	2.071(3)	2.048(3)	87.6(1)	11
$[Rh\{(mBenzim)_2CH_2\}(CO)_2BF_4]^-$	2.069(6)	2.066(5)	85.8(2)	11
$[Rh\{(mim)_2CH_2OCH_2CH_3\}cod]BF_4^-$	2.089()	2.087()	84.2()	Complex 1
$[Rh\{(mim)_2CH_2SCH_3\}cod]BF_4^-$	2.104(2)	2.080(2)	84.2(9)	Complex 2

Complexes **1** and **2** deviated from the square planar geometry with nitrogen chelate bite angles almost identical at 84.85 and 84.20°, respectively. Rh-N bond lengths in **1** of 2.089 and 2.087 Å were similar to those in **2**, 2.104 and 2.080 Å. However on of the bond lengths in **2** was slightly longer and this may be due to the presence of more electronegative oxygen relative to sulfur, affecting the electronics of the complex. Another factor could be the presence of a larger sulfur atom preventing a closer approach of the N,N′ system to the metal centre. The tight N_1-Rh-N_3 bite angles and the Rh-N bond lengths found for these complexes, revealed in Table **3.2**, are comparable to previously reported complexes listed in Table **3.1**. However complexes **1** and **2** showed the bis-imidazole ligand deviating further out of the coordination plane, with the two imidazole rings inclined at 131.1 and 126.64°, to each other.[12]

Figure 3.1 Molecular structure of $[Rh\{(mim)_2CH_2OCH_2CH_3\}cod]BF_4$, (1)

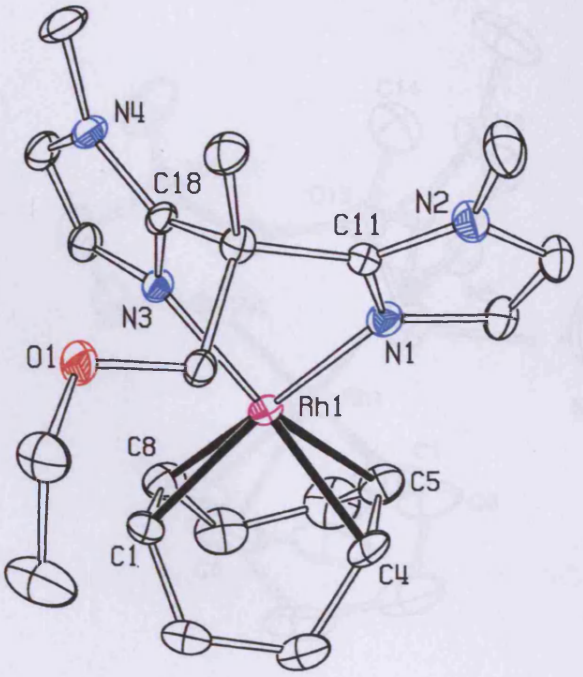
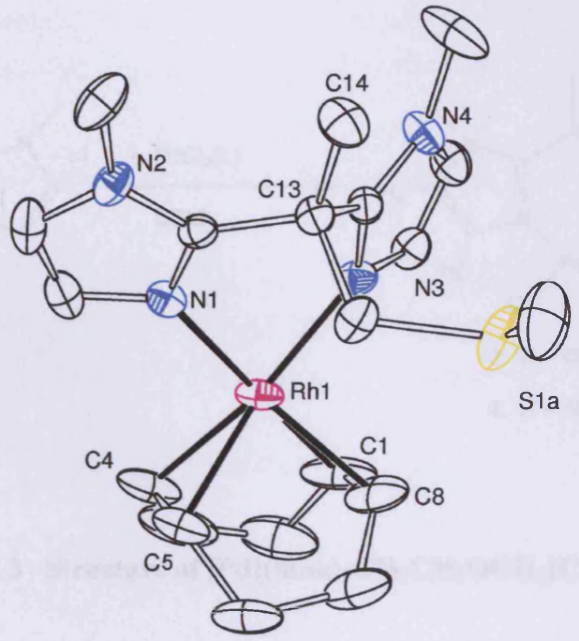


Table 3.2 Selected bond lengths (Å) and bond angles (°) for complex 1 and 2

	Bond Length (Å)		Bond Angles (°)	
Complex 1	$Rh\text{-}N_1$	2.089(3)	$N_1\text{-}Rh\text{-}N_3$	84.85(18)
	$Rh\text{-}N_3$	2.087(3)	$C_1\text{-}Rh\text{-}C_4$	82.08(18)
	$Rh\text{-}C_1$	2.113(4)	$C_5\text{-}Rh\text{-}C_8$	81.42(19)
	$Rh\text{-}C_4$	2.145(4)		
	$Rh\text{-}C_5$	2.135(4)		
	$Rh\text{-}C_8$	2.150(4)		
Complex 2	$Rh\text{-}N_1$	2.104(2)	$N_1\text{-}Rh\text{-}N_3$	84.20(9)
	$Rh\text{-}N_3$	2.080(2)	$C_1\text{-}Rh\text{-}C_4$	81.69(17)
	$Rh\text{-}C_1$	2.155(3)	$C_5\text{-}Rh\text{-}C_8$	81.89(15)
	$Rh\text{-}C_4$	2.127(3)		
	$Rh\text{-}C_5$	2.139(2)		
	$Rh\text{-}C_8$	2.129(3)		

Figure 3.2 Molecular structure of $[Rh\{(mim)_2CH_2SCH_3\}cod]BF_4$, (2)



In rhodium complexes C-H activation is commonly observed and occurs at sites that are electronically favoured. Although such activation is not observed in complexes **1** and **2**, the significant yet larger than expected shift of the signal representing the CH_2 group adjacent to the apical carbon atom suggests a slight interaction with the metal centre. It can be proposed the steric properties of the molecule prevent co-ordination of the CH_2 group.

3.2.2.2 Palladium(II) complexes

Dropwise addition of a colourless solution of ligand (**11** or **12**) in DCM, to a solution containing the palladium precursor in DCM (($PdCl_2$(cod) yellow, $PdCl_2(MeCN)_2$ orange gave no obvious colour change. The reaction mixtures were stirred at room temperature overnight, reduced *in vacuo* and the residue washed with ether to give an orange micro-crystalline product. Crystals suitable for X-ray crystallography were afforded on slow recrystallisation of Pd complexes **3** and **4** from DCM and hexane at -20 °C.

Scheme 3.8 Synthesis of palladium complexes 3 and 4 bearing imidazole containing ligands

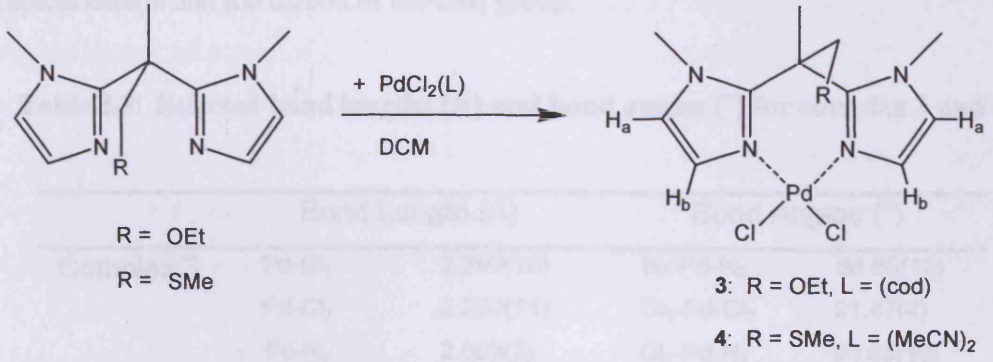
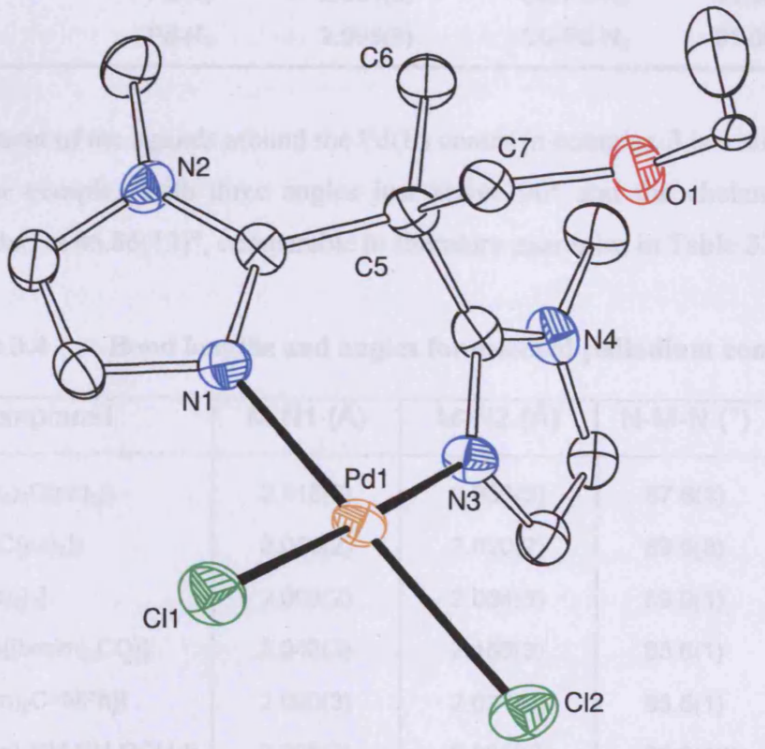


Figure 3.3 Structure of $[Pd\{(mim)_2CH_2CH_2OCH_3\}Cl_2]$, (3)



The ORTEP of **3**, Figure **3.3** shows one of the two conformations of the disordered ether arm which was modelled as being disordered over two positions. The conformations differed in the orientation of the hemilabile arm, by rotation about the C-C bond between the apical carbon and the carbon of the CH_2 group.

Table 3.3 Selected bond lengths (Å) and bond angles (°) for complex 3 and 4

	Bond Length (Å)		Bond Angles (°)	
Complex 3	Pd-Cl_1	2.299(10)	N_1-Pd-N_3	86.86(13)
	Pd-Cl_2	2.290(11)	Cl_1-Pd-Cl_2	91.47(4)
	Pd-N_1	2.003(3)	Cl_1-Pd-N_1	90.65(10)
	Pd-N_3	2.035(3)	Cl_2-Pd-N_1	91.04(10)
Complex 4	Pd-Cl_3	2.289(17)	N_2-Pd-N_3	85.69(2)
	Pd-Cl_4	2.299(19)	Cl_3-Pd-Cl_4	90.34(7)
	Pd-N_2	2.004(6)	Cl_3-Pd-N_2	91.33(18)
	Pd-N_3	2.995(6)	Cl_4-Pd-N_3	91.65(18)

The arrangement of the ligands around the Pd(II) centre in complex **3** is a slightly distorted square planar complex with three angles just above 90° and the chelate ligand angle slightly smaller, at 86.86(13)°, comparable to literature examples in Table **3.4**.

Table 3.4 Bond lengths and angles for selected palladium complexes

Compound	M-N1 (Å)	M-N2 (Å)	N-M-N (°)	References
$[PdCl_2\{(CH_3)_2C(pz)_2\}]$	2.018(3)	2.030(3)	87.8(1)	13
$[PdCl_2\{Ph_2C(pz)_2\}]$	2.018(2)	2.020(2)	89.5(8)	14
$[Pd\{CH_2(pz)_2\}_2]$	2.003(2)	2.004(3)	89.0(1)	13
$[PdCl(CH_3)\{(bmim)_2CO\}]$	2.042(3)	2.156(3)	85.6(1)	3
$[PdCl_2\{(mim)_2C{=}NPh\}]$	2.020(3)	2.031(2)	88.5(1)	3
$[PdCl_2\{(mim)_2CH_2CH_2OCH_3\}]$	2.003(3)	2.035(3)	86.9(13)	Complex 3
$[PdCl_2\{(mim)_2CH_2SCH_3\}]$	1.998()	2.004()	85.7()	Complex 4

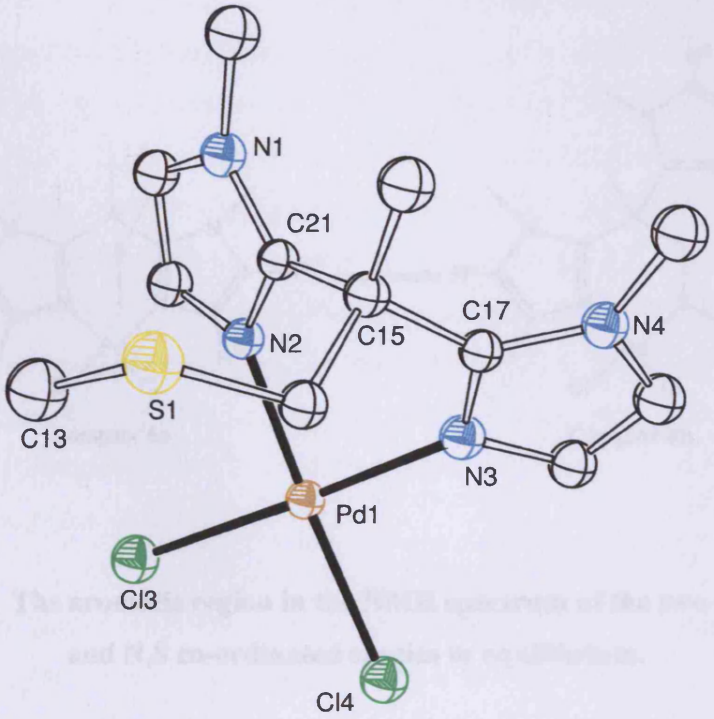
Crystal structures of metal complexes bearing bis-imidazole containing ligands have been reported, by Done *et al.* who found that the bite angle of the fused benzimidazole ligand in the square planar $PdCl(CH_3)\{(bmim)_2CO\}$ **XLIIIb**, was significantly diminished at 85.6(1)° versus 88.5(1)° for $PdCl_2\{(mim)_2C{=}NPh\}$ **XLIIc**. This resulted in a distortion of the square planar structure of **XLIIIb**, however **XLIIc** deviated only slightly from ideal values.[3] Increasing the steric bulk on the ligand giving smaller chelate bite angles was also observed by Jordan *et al.*[15] when comparing the bis(pyrazolyl) complexes, $[PdCl_2\{Ph_2C(3\text{-}^tBu\text{-}pz)_2\}$ (83.63(8)°) and $PdCl_2\{Ph_2C(pz)_2\}$ (89.51(8)°) and also by Canty *et al.* in tris(pyrazolyl)Pd(IV) complexes.[16-18]

The bis-imidazole ligand in complex **3** is coplanar however the chelating imidazole ligand is bent out of the co-ordination plane and the two imidazole rings within this ligand are inclined at an angle of 126.16° to each other. The imidazole rings are bent further out of the co-ordination plane compared to reports on Done's structurally similar ligand.[2,3] This is probably due to the restriction of spatial arrangement around the ligand due to the free rotation of the mobile hemilabile donor about the apical carbon to which it is bonded, in solution, forcing the imidazole rings closer together. Palladium complexes containing chelating nitrogen ligands typically show bite angles between 88.4(2)-94.0(5)°,[19-23] with Pd-N bond lengths around 2.0 Å. Done *et al.* observed that one Pd-Cl bond length was common to both complexes **XLIIc** and **XLIIIb** and one divergent Pd-Cl bond length across these two complexes which was longer in **XLIIIb**, by ~ 0.03 Å, due to the replacement of the CNPh in **XLIIc** with a carbonyl group in **XLIIIb**. The greater *trans*-effect of the methyl group in **XLIIIb** versus chloride co-ligands is reflected in the Pd-N bond lengths, in **XLIIIb** (2.042(3) and 2.156(3) Å) and **XLIIc** (2.020(3) and 2.031(2) Å). The longest bond length representing the bond *trans* to the methyl group the remaining Pd-N bond lengths are all *trans* to chlorine atoms. In the case of complex **3** both co-ligands in the square planar complex were identical and the Pd-N bond distances were indifferent at approximately 2.0 Å and comparable to literature values.

Consistent with the co-ordination of two imidazole rings, the $N\text{-}CH_3$ resonance was found at 0.9 ppm downfield from the free ligand in the ^1H NMR. The CH_3 group of the ether

arm in complex **3**, at 1.1 ppm in the ^{1}H NMR spectra and the imidazole H_a protons at 6.7 remained unchanged upon complex formation; however H_b at 6.95 ppm in the free ligand was shifted down field to 7.4 ppm in the complex. The sharp singlets for the apical methyl resonance and the CH_2 attached to the apical carbon were all shifted down field by ~0.5 ppm in complex **3**. The most significant feature of the ^{1}H NMR of this complex was the singlet at 5.1 ppm representing the CH_2 group adjacent to the apical methyl group, shifted 1 ppm downfield from the free ligand. From the orientation of the ether arm in the crystal structure and the rather large shift downfield of the CH_2 observed in the ^{1}H NMR spectrum, suggests that deshielding of the CH_2 is a result of the spatial orientation of the hemilabile donor arm in close proximity to the metal centre. NMR data retrieved demonstrates a symmetrical spectrum, this is only plausible on N,N′ co-ordination to give a symmetrical square planar complex. Co-ordination of the ether arm to the metal centre would have given a very different pattern in the NMR, as discussed for the rhodium complexes.

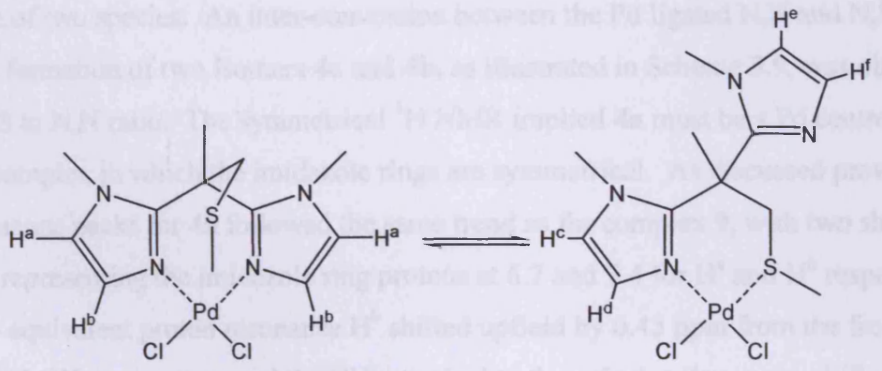
Figure 3.4 Molecular structure of $[Pd\{(mim)_2CH_2SCH_3\}Cl_2]$, (4)



The ORTEP of **4**, Figure **3.4** shows one of the two conformations of the disordered sulfide arm which was modelled as being disordered over two positions. The conformations differed in the orientation of the hemilabile arm, by rotation about the C-C bond between the apical carbon and the carbon of the CH_2 group.

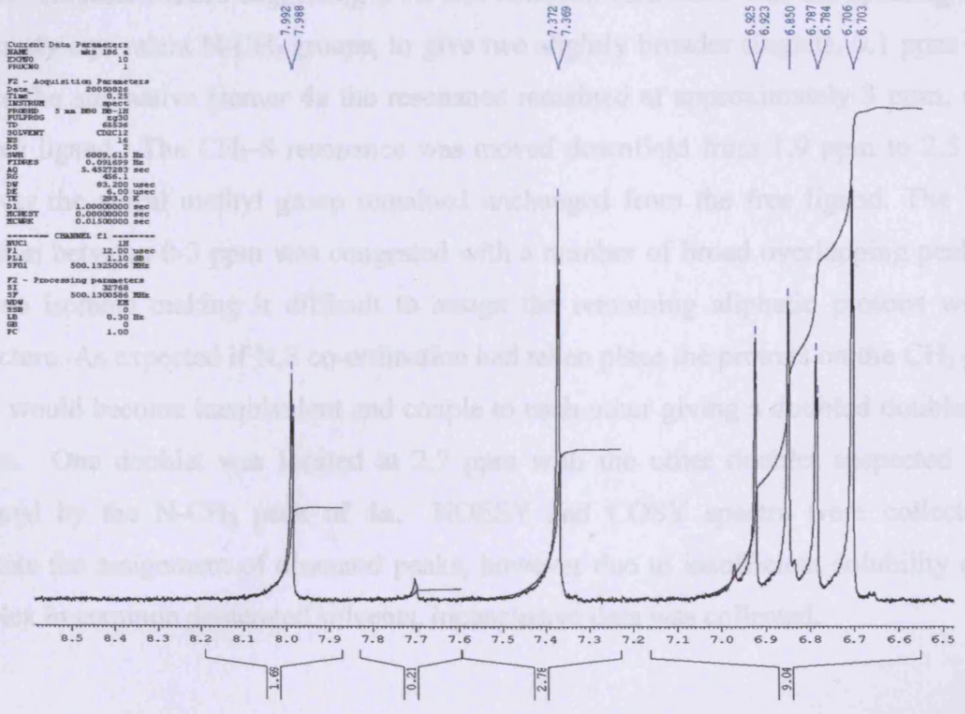
Radiating orange crystal clusters were grown from a mixture of DCM and hexane at -5 °C and represented the symmetrical isomer **4a**, as illustrated in Figure **3.4**. A low temperature single-crystal X-ray crystallographic determination of complex **4**, found a Pd-centred slightly distorted square planar complex. Two of the sites around the Pd were taken up by the bis-imidazole chelating ligand, with a bite angle of 85.69°, the remaining two occupied by chlorine atoms. The imidazole ligand was bent out of the co-ordination plane and the two imidazole rings are inclined at an angle of 124.14° with respect to each other.

Scheme 3.9 [Pd(bimsulfide)Cl_2] in equilibrium, giving two different N,N and N,S co-ordinated species



Complex **4a** Complex **4b**

Diagram 3.1 The aromatic region in the NMR spectrum of the two different N,N and N,S co-ordinated species in equilibrium.



The appearance of multiple signals in the aromatic region of the ^{1}H NMR, as opposed to the two expected for the N,N ligated square planar complex and the presence of two CH_2 groups in the ^{13}C NMR, when only one is present in the expected complex, suggested the presence of two species. An inter-conversion between the Pd ligated N,N and N,S modes with the formation of two isomers **4a** and **4b,** as illustrated in Scheme **3.9**, was observed in a 6:5 N,S to N,N ratio. The symmetrical ^{1}H NMR implied **4a** must be a Pd centred N,N ligated complex in which the imidazole rings are symmetrical. As discussed previously the resonance peaks for **4a** followed the same trend as for complex **9**, with two sharp singlets representing the imidazole ring protons at 6.7 and 7.4 for H^a and H^b respectively. The two equivalent proton resonance H^b shifted upfield by 0.45 ppm from the free ligand. The two N-CH_3 resonances and the CH_2 attached to the apical carbon were shifted 1.0 ppm downfield from the free ligand. The CH_2 group moved downfield by 0.3 ppm and the apical methyl group was unshifted.

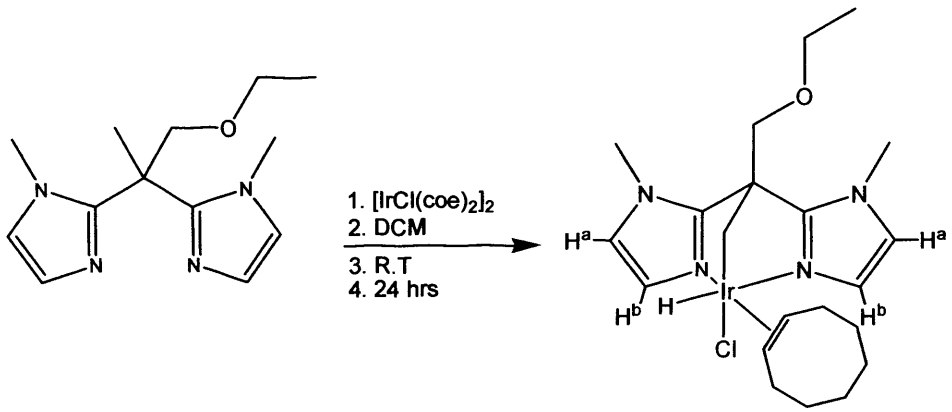
The asymmetrical part of the NMR implied that complex **4b** was a Pd centred N,S ligated complex in which the imidazole rings were asymmetrical thus represented in the ^{1}H NMR spectrum by four inequivalent resonance peaks, H^c, H^d, H^e and H^f, each integrating to one proton. Another feature suggesting a Pd-N,S complex formation was the splitting of the previously equivalent N-CH_3 groups, to give two slightly broader singlets, 0.1 ppm apart. Unlike the alternative isomer **4a** the resonance remained at approximately 3 ppm, as for the free ligand. The CH_3-S resonance was moved downfield from 1.9 ppm to 2.5 ppm, however the apical methyl group remained unchanged from the free ligand. The NMR spectrum between 0-3 ppm was congested with a number of broad overlapping peaks for the two isomers making it difficult to assign the remaining aliphatic protons without conjecture. As expected if N,S co-ordination had taken place the protons on the CH_2 group of **4b** would become inequivalent and couple to each other giving a doubled doublet spin system. One doublet was located at 2.7 ppm with the other doublet suspected to be obscured by the N-CH_3 peak of **4a**. NOESY and COSY spectra were collected to facilitate the assignment of obscured peaks, however due to insufficient solubility of the complex in common deuterated solvents, inconclusive data was collected.

Crystals grown from the reaction mixture of complex **4** gave the symmetrical N,N co-ordinated complex **4a**. The crystals of **4a** were re-dissolved in CD_2Cl_2 and characterised by NMR spectroscopy to give the identical mixture of isomers, replicated in the same 6:5 ratio. This suggested that the two compounds were in equilibrium in solution and the least soluble product, the N,N chelated palladium complex, **4a** preferentially crystallised.

3.2.2.3 Iridium(III) complexes

Reactions of ligands **11** and **12** were initially attempted with $[IrCl(cod)]_2$ under a variety of conditions, using DCM, $CDCl_3$ and THF as reaction solvents however no reaction was observed. Even under forcing conditions such as heating at 60°C for 48 hours only starting materials were recovered. The more reactive $[IrCl(coe_2)]_2$ (coe = cyclooctene) dimer was then trialled, as cyclooctene is more labile than cyclooctadiene and readily displaced by stronger ligands. The reaction of ligand **11** with $[IrCl(coe_2)]_2$ in dichloromethane at room temperature, as illustrated in Scheme **3.10**, gave a colour change from deep orange to a pale yellow which proceeded to completion overnight. Complex **5** was the major product in the crude reaction mixture, obtained as a white solid in 80% yield.

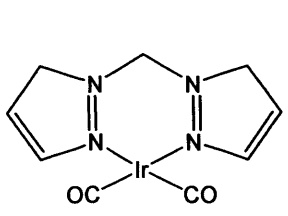
Scheme 3.10 Reaction of ligand 11 with $[IrCl(coe)_2]_2$ to give an iridium hydride complex



Complex **5**

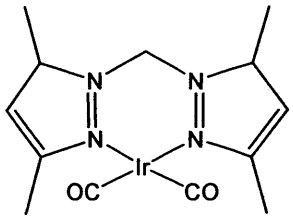
The spectral evidence was not consistent with the expected product of a simple displacement of a single coe ligand and the break up of the dimer to form a square planar N,N-Ir-Cl(coe). The reaction of ligand **4** with $[IrCl(coe_2)]_2$ resulted in the isolation of a facially co-ordinated Ir(III) hydride complex. In both ^1H and ^{13}C NMR spectra it was clear that the symmetry of the ligand had been breached in complex formation. This could be expected in square planar complexes but the presence of a signal at -17 ppm, characteristic of an iridium hydride was clearly incompatible with the expected structure of the complex. Following the observed patterns for rhodium and palladium complexes (**1**, **2**, **3** and **4**), the imidazole proton resonance H^a was unchanged and H^b was shifted downfield from 6.7 to 7.3 ppm. The resonance of the methylene group α to the apical carbon and the oxygen atom did not shift and remained at 4.15 ppm however the protons were no longer equivalent and were represented by a doublet of doublets, owing to geminal coupling in the Ir-CHH′ caused by the different environments. Signals due to the ether group remained unchanged. The coe peaks in the ^1H NMR were broader than in the precursor and overlapped the CH_2 derived from the activated methyl group. The methyl groups on the imidazole ligands were slightly overlapped by the coe signals however were identifiable as two singlet peaks shifted downfield to 3.6 and 3.7 ppm from 3.0 ppm in the free ligand.

Recently more crystal structures of Ir complexes containing bidentate nitrogen donors and one structure containing a bidentate bis-imidazole donor have been reported. Ir(I) complexes IrXYL (in which L = bis(1-pyrazolyl)methane (BPM), bis(3,5-dimethyl-1-pyrazolyl)methane (dmBPM)[24] and bis(1-methylimidazol-2-yl)methane (BIM)[25] and the co-ligands X and Y are CO, cod and/or Cl) have recently been reported.



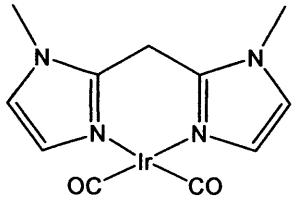
$[Ir(BPM)(CO)_2]^+[BF_4]^-$

LXVII



$[Ir(dmBPM)(CO)_2]^+[BF_4]^-$

LXVIII



$[Ir(bim)(CO)_2]^+[BF_4]^-$

LXIX

These complexes were prepared in high yields from the iridium precursor $[Ir(cod)Cl]_2$ and were isolated as air stable cationic complexes and found to be square planar with N-Ir bond lengths between 2.057(5)- 2.079(6) Å and N-Ir-N angles ranging from 85.9(2) - 86.8(2)°. The tris(pyrazolyl)borate iridium(III) hydride complex reported by Fernández *et al*, displayed pseudo-octahedral geometry around the metal with a *fac* Tp, a hydride ligand and two sites occupied by cyclooctene molecules. The N-Ir-N bond angles in this complex ranged between 81.3 - 87.4(3)° and Ir-N bond lengths between 2.079 - 2.224 Å, with the ligand *trans* to the hydride typically longer.[26]

To clarify the nature of the product, crystals of **5** suitable for X-ray crystallography were afforded on slow recrystallisation from DCM and hexane at -5 °C. Figure **3.5** shows that complex **5** has a slightly distorted octahedral iridium co-ordination sphere, with two nitrogen donors and a CH_2 group occupying one face of the metal, while coe, chloride and hydride ligands occupy the other. The interaction of the apical methyl group of the bis-imidazole ligand, with the iridium centre has resulted in a tripodal *fac* ligand.

Figure 3.5 Molecular structure of $[IrH(mim)_2CH_2OCH_2CH_3\}(coe)(Cl)]$, (5)

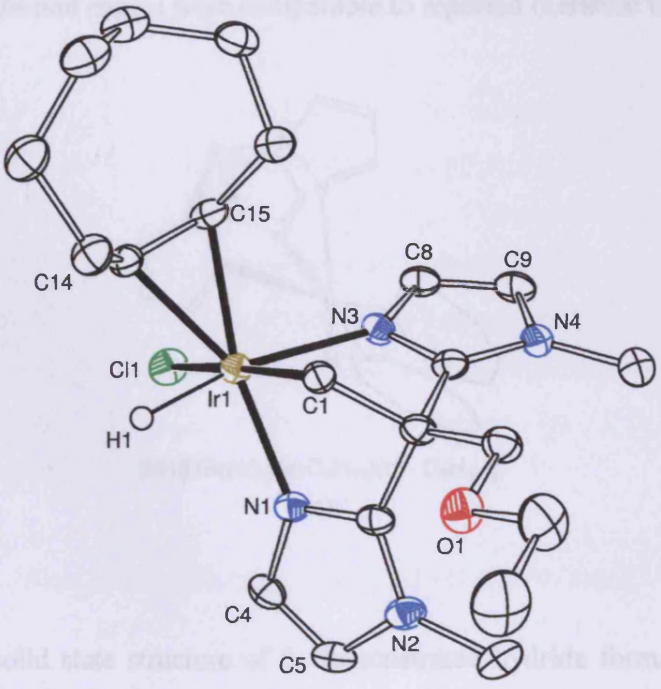
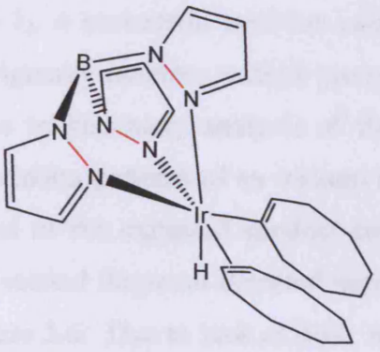


Table 8 Selected bond lengths (Å) and bond angles (°) for complex (5)

Complex 5	Bond Length (Å)		Bond Angles (°)
$Ir\text{-}N_1$	2.087(4)	$N_1\text{-}Ir\text{-}N_3$	83.28(14)
$Ir\text{-}N_3$	2.149(3)	$C_1\text{-}Ir\text{-}N_1$	76.98(16)
$Ir\text{-}C_1$	2.080(4)	$C_1\text{-}Ir\text{-}N_3$	77.98(15)
$Ir\text{-}C_{14}$	2.174(4)	$C_1\text{-}Ir\text{-}Cl_1$	170.95(11)
$Ir\text{-}C_{15}$	2.175(5)	$N_1\text{-}Ir\text{-}C_{14}$	167.69(16)
		$N_1\text{-}Ir\text{-}C_{15}$	153.31(16)

The bidentate imidazole rings were significantly bent with respect to the co-ordination plane, at an angle of 108.20°, adopting a butterfly conformation. The Ir-N_1 bond length at 2.087 Å was notably shorter than Ir-N_3 at 2.149 Å, likely due to the π accepting cyclooctene ligand forcing a stronger electron release from the *trans* nitrogen, N_1, causing a stronger shorter N_1-Ir bond to form, also observed by Fernández for their

tris(pyrazolyl)borate iridium(III) hydride complex. Alternatively, the hydride ligand causes lengthening of the bond *trans* to it. The N_1-Ir-N_3 angle was found to be 83.28(14)°, both the bond lengths and angles were comparable to reported literature values.



$[IrH\{HB(pz)_3\}(\sigma\text{-}C_8H_{13})(\eta^2\text{-}C_8H_{14})]$

LXX

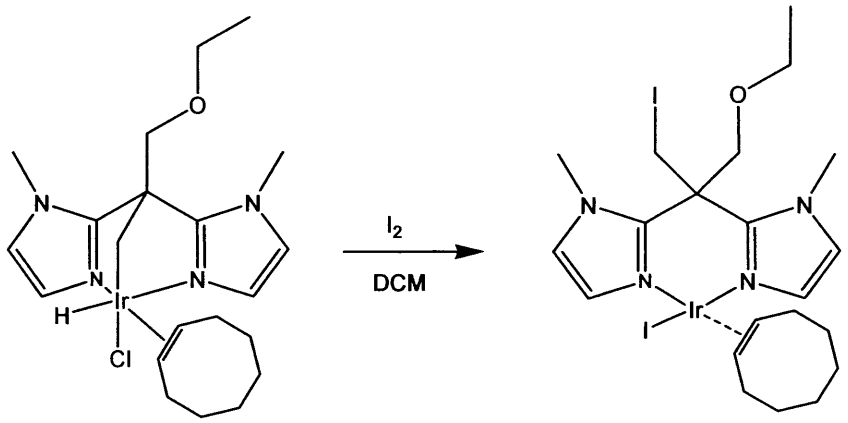
Inspection of the solid state structure of **5**, demonstrated hydride formation through the activation of what was thought to be a relatively inactive methyl group, a direct result of steric constraints within the molecule. Ligand conformation, when N,N-co-ordinated, determined the subsequent reaction. The *cis*-position of the hydride and the CH_2 moities suggests that the two nitrogen donors complexed first, locking the ligand conformation such that the pendant arm was not in a suitable position for C-H activation and the metal centre could only interact with the apical methyl group. Therefore, it can be proposed that the apical methyl group must then have oxidatively added across the metal centre to give a hydride cis to the CH_2 co-ordinated group.

Although C-H activation is common with rhodium and iridium complexes[27,28] of amines, imines and nitrogen heterocycles, it almost invariably occurs at sites which are either electronically activated or stereoelectronically favoured. The geometry of the complex directs the cyclometallation to occur with activation of a C-H bond in the ligand which is preorganised for interaction with the metal centre. The controlled activation of remote or electronically unfavoured sites in iridium complexes of N-donors is unreported and has potential implications for the C-H activation of unfunctionalised alkanes and other

unreactive species. In this context the C-H activation and characterisation of the cyclometallation product, at an electronically disfavoured site whilst in the presence of a more reactive methyl group in an iridium bis-imidazolemethane complex, is reported.

Complex **5** was reacted with I_2, a successful addition reaction across the Ir-CH_2 bond would demonstrate that an originally inactive methyl group is able to undergo reactions otherwise not possible. Mass spectrometry analysis of the product obtained from this reaction demonstrated fragmentation patterns of an iridium and iodine containing species. Fragmentations were identified as the expected product containing one iodine molecule but absent of the hydride. A second fragment detected corresponded to the loss of a coe molecule, as illustrated in Figure **3.6**. Due to lack of time, no further investigations of the reactivity of this complex could be conducted.

Figure 3.6 Reaction of complex 5 with iodine



Complex **5**

3.2.2.4 Attempted synthesis of complexes with functionalised bis-imidazole ligands

Synthesis of complexes of ligands **11** and **12** were trialled with chromium, cobalt and nickel precursors. Dropwise addition of a colourless solution of ligands **11** and **12** in DCM, was added dropwise to solutions of corresponding metal precursors in the solvent.

Reaction of the ligands with $CrCl_3(THF)_3$ in DCM gave an immediate colour change giving a pale green solid precipitated. An octahedral chromium centred complex was expected in which the ligand would occupy two or three sites of one face of the metal and the remaining sites would be taken up by the co-ligands Cl and/or THF. Three different Ni precursors, $NiCl_2DME$ (yellow solid), $NiCl_2(PPh_3)_2$ (blue/black solid) and $Ni(cod)_2$ (pale yellow solid) were used in an attempt to synthesise an octahedral nickel chelate complex. In each case a turquoise/blue solid precipitated almost immediately. The same pattern was observed on addition of the ligands to a transparent blue solution of $CoCl_2$, a blue insoluble solid precipitated. In each case the product was insoluble in most NMR solvents and therefore no NMR data was obtained. The chromium reaction would yield a paramagnetic complex therefore the NMR data would not reward and micro analysis was attempted but no product was identified.

The products formed in each of the above cases were found to be air stable but insoluble in all common NMR solvents, this led to speculation that the reactions had yielded polymeric products. The reactions were repeated at lower temperatures with the dropwise addition of ligands to slow down the reaction and prevent polymer formation however identical results were obtained. Lack of solubility resulted in limited data collection and inconclusive identification of all Cr, Ni and Co products.

3.3 Conclusions

This chapter reports a family of neutral novel imidazole based ligands and their complexes with rhodium, iridium and palladium. The aim of this investigation was to assess the effect if any of the introductions of third donor atoms to a rigid imidazole based bidentate nitrogen ligand, in the form of a hemi-labile arm.

Complexes **1-3** all showed co-ordination of two nitrogen atoms from three possible donors. Complex **5** demonstrated tripodal geometry but co-ordination of the third site took place via the C-H activation of the inactive apical methyl group, the ether arm remained unbound. Although complexes with the hemilabile donors co-ordinated to the metal centre were not isolated, the NMR spectrum of complex **4** clearly showed interaction of the sulfur donor rather than the oxygen atom. Sulfur is a softer donor than oxygen and able to compete with N-donors with a soft metal like palladium, therefore co-ordination of sulphur is more probable than oxygen in complexes **3** and **4**.

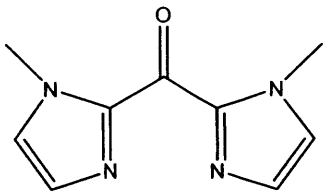
When designing these types of ligands for co-ordination chemistry the most important feature is the presence of nitrogen donors as demonstrated by the co-ordination observed in the Pd, Rh and Ir-N,N ligated complexes. The second fundamental point to consider is the metal to which the ligand must co-ordinate. Soft metals prefer co-ordination to soft donors therefore the properties of the third donor in the ligand must be such that it can compete with the nitrogen donors for co-ordination to the metal centre, as observed for complex **4**.

The functional groups in ligands **11-13** are weak donors and potentially hemilabile; the O and S donors are expected to be capable of weak interactions with metal centres thus can have subtle influence on reaction behaviour, especially in catalysis. Both the ether and sulfide arm have minimal steric requirements and are potentially hemilabile donors. Therefore it is expected that these weakly co-ordinating could interact with the metal centre and have an influence in catalysis, see chapter four.

3.4 Experimentals

The precursor complexes used in this part of the project were synthesised following literature preparations, $PdCl_2(cod)$, $PdCl_2(MeCN)_2$,[29] $[RhCl(cod)]_2$, $[Rh(cod)_2]BF_4$, $[IrCl(cod)]_2$ and $[IrCl(coe)_2]_2$.[30] The Pd precursors are air stable and can be stored without any special provisions, while $[RhCl(cod)]_2$ and $[IrCl(cod)]_2$ (although not too air sensitive) are better stored in a vacuum dessicator. The $[IrCl(coe)_2]_2$ and $[Rh(cod)_2]BF_4$ precursor have the greatest sensitivity to moisture and air, therefore were stored in an inert atmosphere in the glove box.

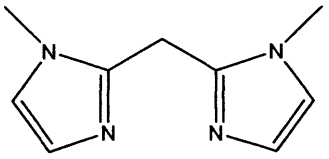
3.4.1 Synthesis of ligand 8



A solution of 1-methylimidazole (5.35 g, 65 mmol) in dry THF (50 ml) was cooled to – 45 °C and n-BuLi (1.6 M in hexane) (40.6 ml, 65 mmol) was slowly added. The bright yellow solution was stirred at – 45 °C for 30 minutes and then cooled to – 80 °C. Diethylcarbonate (3.85 g, 32.5 mmol) was then added drop wise. The solution changed colour from yellow to purple and thickened. The reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was cooled to – 20°C again before being quenched by water (5 ml). After warming to room temperature, THF was removed *in vacuo* and the residue was extracted with DCM (3 x 50 ml). The pooled DCM layers were dried ($NaSO_4$), filtered and evaporated to give a brown oil. The pure product was obtained as pale yellow crystals (3.7 g, 60%) from the recrystallisation from acetone.

Found: δH (400MHz: $CDCl_3$) 4.03(6H, s, *2 x* Me), 7.05(2H, s, *imidazole*) and 7.25(2H, s, *imidazole*); MS: (ESMS): 191 $[M + H]^+$ 100%.

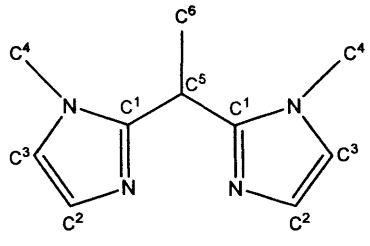
3.4.2 Synthesis of ligand 9



Bis(1-methylimidazol-2-yl)ketone (3.0 g, 15.8 mmol) and ground KOH (3.0 g, 53.6 mmol) were placed into a round bottom flask fitted with a reflux condenser. Hydrazine hydrate (28 ml, 0.56 mol) was added and the flask immersed into an oil bath. On heating a yellow solid began to form at 60 °C. The reaction became clear and almost colourless at 120 °C at which temperature stirring was continued for 1 hour. The temperature was increased to 150 °C and stirring was allowed to continue for 3 hours. The reaction mixture was allowed to cool down to room temperature during which time a white solid precipitate formed. At this point all operations were carried out in air; CH_2Cl_2 (40 ml) was added and the solution was transferred to a separatory funnel. The CH_2Cl_2 layer was separated and remaining light brown liquid was extracted with CH_2Cl_2 (2 x 40 ml). The pooled CH_2Cl_2 layers were washed with H_2O twice to remove the excess hydrazine hydrate. The combined H_2O were extracted with CH_2Cl_2 (12 x 20 ml; crucial to obtain a good yield). The pooled CH_2Cl_2 extracts were dried over $NaSO_4$, filtered and rotary evaporated to give off white crystalline solid (2.1 g, 78%). The product was pure enough by NMR to use in the next step.

Found: δH (400MHz: $CDCl_3$) 3.63(6H, s, *2 x* Me), 4.25(2H, s, Me-*apical*), 6.72(2H, s, *imidazole*) and 6.92(2H, s, *imidazole*); MS: (ESMS): 174 $[M + H]^+$ 100%.

3.4.3 Synthesis of ligand 10

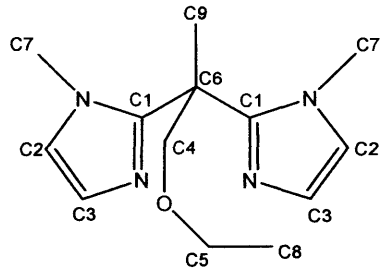


Bis(1-methylimidazol-2-yl)methane (3.09 g, 17.5 mmol) in dry THF (200 ml) was cooled to – 45 °C and n-BuLi (2.5 M in hexane) (8.5 ml, 21.0 mmol) was slowly added. The bright yellow solution was stirred at – 45 °C for 45 minutes and then cooled to – 80 °C. Methyl iodide (1.35 g, 21.0 mmol) was then added dropwise. The transparent solution changed

colour from yellow to white and thickened white solid precipitated. The reaction mixture was allowed to warm to room temperature overnight. The reaction mixture was cooled to – 20 ^{0}C again before being quenched by water (5 ml). After warming to room temperature; THF was removed *in vacuo* and the residue was extracted with DCM (3 x 50 ml), dried over $NaSO_4$, filtered and rotary evaporated to give cream solid (2.73 g, 82%) which by NMR did not require any further purification for the next reaction.

Found: δ_H (400MHz: $CDCl_3$) 1.8(3H, d, *J* 4.0, Me-*apical*), 3.38(6H, s, *2 x* Me), 4.52(1H, q, *J* 4.0), 6.72(2H, s, *imidazole*) and 6.89(2H, s, *imidazole*); ^{13}C δ_H (100MHz:$CDCl_3$): 16.0(C^5), 32.0(C^3), 33.0(C^4), 121(C^3), 120.9(C^2), 125.8(C^1) and 146.2(C^6); MS: (ESMS): 191.1290 $[M + H]^+$ 100%.

3.4.4 Synthesis of ligand 11

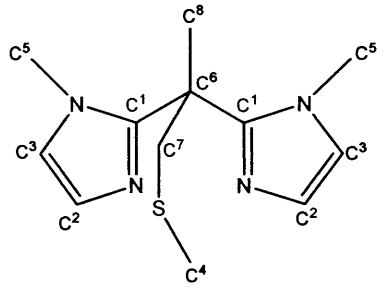


To a solution of bis(imidazol-2-yl)methyl methane (0.3 g, 1.6 mmol) in THF (20 ml) cooled to – 45 °C, n-butyl lithium (1.6 M in hexanes) (1.2 ml) was added drop wise affording a dark yellow transparent solution. The mixture was allowed to stir for 40 minutes maintaining this temperature. On cooling the reaction mixture to – 80 °C chloromethyl ethyl ether (0.19 ml, 2.06 mmol) was added drop wise. The mixture was gradually allowed to warm to room temperature overnight. Methanol (5 ml) was added and the reaction mixture was reduced *in vacuo*. DCM was added and the organic layer was extracted and again reduced *in vacuo*. Finally the product (0.23 g, 60%) was extracted with diethyl ether.

Found: δ_H (500MHz: $CDCl_3$) 1.03(3H, t, *J* 7.0, Me-*ethyl*), 1.78(3H, s, Me-*apical*), 3.00(6H, s, *2 x* Me), 3.40(2H, q, *J* 7.0, CH_2-*ethyl*), 4.15(2H, s, CH_2), 6.72(2H, s, *imidazole*) and 6.93(2H, s, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 14.9(C^9), 23.1(C^8), 32.9(C^7), 42.3(C^6), 67.0(C^5), 75.7(C^4), 122.5(C^2), 126.7(C^3) and 148.5(C^1); MS: (ESMS):

249 $[M + H]^+$ 100%. Anal.Calcd for $C_{13}H_{20}N_4O$: C, 62.88; H, 8.12; N, 22.56 %. Found: C, 62.31; H, 8.23; N, 21.60%.

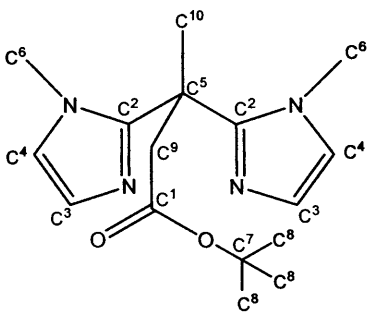
3.45 Synthesis of ligand 12.



To a solution of bis(imidazol-2-yl)methyl methane (1.41 g, 7.4 mmol) in THF (200 ml) cooled to – 45 °C, n-butyl lithium (1.6 M in hexanes) (5.2 ml) was added drop wise affording a dark yellow transparent solution. The mixture was allowed to stir for 40 minutes maintaining this temperature. On cooling the reaction mixture to – 80 °C chloromethyl methyl sulfide (0.78 ml, 8.5 mmol) was added drop wise. The mixture was gradually allowed to warm to room temperature overnight. Methanol (20 ml) was added and the reaction mixture was reduced *in vacuo*. DCM was added and the organic layer was extracted and again reduced *in vacuo*. Finally the product (1.11g 59 %) was extracted with diethyl ether.

Found: δ_H (500MHz: $CDCl_3$) 1.78(3H, s, Me-*apical*), 1.84(3H, s, Me-*sulfur*), 3.01(6H, s, *2 x* Me), 3.52(2H, s, CH_2), 6.72(2H, s, *imidazole*) and 6.95(2H, s, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 16.8(C^8), 24.6(C^4), 33.0(C^5), 41.8(C^7), 44.5(C^6), 122.8(C^3), 126.(C^2) and 148.8(C^1); MS: (ESMS): 251 $[M + H]^+$ 100%. Anal.Calcd for $C_{12}H_{18}N_4S$: C, 57.57; H, 7.25; N, 22.38 %. Found: C, 57.60; H, 7.36; N, 21.44%.

3.46 Synthesis of ligand 13.

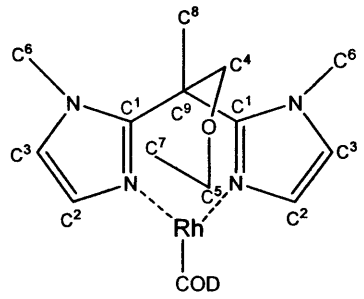


To a solution of bis(imidazol-2-yl)methyl methane (0.86 g, 4.5 mmol) in THF (100 ml) cooled to – 45 °C, n-butyl lithium (1.6 M in hexanes) (2.0 ml) was added drop wise affording a dark yellow transparent solution.

The mixture was allowed to stir for 40 minutes maintaining this temperature. On cooling the reaction mixture to – 80 °C *tert*-butylbromoacetate (0.85 ml, 5.8 mmol) was added drop wise. The mixture was gradually allowed to warm to room temperature overnight. Methanol (5 ml) was added and the reaction mixture was reduced *in vacuo*. DCM was added and the organic layer was extracted and again reduced *in vacuo*. Finally the product was extracted with diethyl ether to give a cream coloured solid (1.1g, 80%).

Found: δ_H (500MHz: $CDCl_3$) 1.18(9H, s, ^tBu), 1.82(3H, s, Me-*apical)*, 3.04(6H, s, *2 x* Me), 3.22(2H, s, CH_2), 6.74(2H, s, *imidazole*) and 6.91(2H, s, *imidazole*); ^{13}C δ_H (100MHz:$CDCl_3$): 25.4(C^{10}), 28.1(C^8), 33.4(C^6), 40.3(C^5), 45.3(C^9), 81.0(C^7), 123.4(C^4), 126.8(C^3), 148.9(C^2) and 170.0(C^1); MS: (ESMS): 305.1973 $[M + H]^+$ 100%.

3.47 Synthesis of complex 1

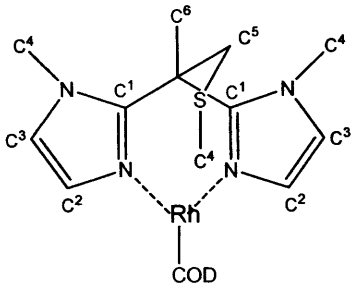


Ligand 11 (0.02 g, 0.08 mmol) in DCM (10 ml) was added slowly to a solution of $Rh(COD)_2$ BF_4^- (0.04 g, 0.09 mmol) in DCM (3 ml). A colour change from a deep orange to yellow was visible almost immediately. The mixture was allowed to stir overnight. The transparent yellow solution was reduced *in vacuo* to give a yellow wax. The waxy solid was washed with dry degassed hexane (1 x 5 ml) and once with dry degassed diethyl ether (5 ml), to remove any displaced COD. The resulting fine, yellow solid (80%) was recrystallised from dry DCM and Hexane to afford large, pale yellow rhombic crystals.

Found: δ_H (500MHz: $CDCl_3$) 1.13(3H, t, *J* 6.9, Me-*ether*), 1.94(4H, bs, *cod*),2.28(3H, s, Me-*apical*), 2.42(2H, bs, *cod*), 2.58(2H, bs, *cod*), 3.59(2H, q, *J* 6.9, *ethyl*), 3.89(6H, s, *2 x* Me), 4.09(2H, bs, *cod*), 4.21(2H, bs, *cod*), 5.13(2H, s, CH_2), 6.68(2H, s, *imidazole*) and 6.79(2H, s, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 15.0(C^8), 20.5(C^7), 30.2(cod), 30.9(cod), 38.7(C^6), 47.3(C^9), 67.4(C^5), 81.8(cod), 82.9(cod), 83.0(C^4), 125.3(C^3), 125.7(C^2) and

145.7(C^1); Anal.Calcd for $C_{21}H_{32}N_4OBF_4Rh$: C, 46.18; H, 5.90; N, 10.26 %. Found: C, 45.91; H, 6.06; N, 9.84 %.

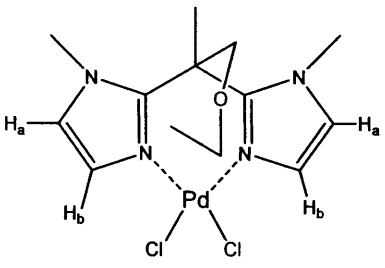
3.48 Synthesis of complex 2



Ligand 12 (0.1g, 0.4mmol) in DCM (10 ml) was added slowly to a solution of $Rh(COD)_2BF_4^-$ (0.2 g, 0.9 mmol)in DCM (3 ml). A colour change from a deep orange to very pale yellow was visible immediately. The mixture was allowed to stir overnight. The transparent yellow solution was reduced *in vacuo* to give a yellow wax. The waxy solid was washed with dry degassed hexane (1 x 5 ml) and once with dry degassed diethyl ether (5 ml), to remove any displaced COD. The resulting fine, pale yellow solid in yields of up to 78%, was recrystallised from dry DCM and Hexane to afford pale green crystals.

Found: δ_H (500MHz: $CDCl_3$) 1.52(3H, bs, Me-*sulfur*), 2.11(3H, bs, Me -*apical*), 2.35(4H, bs, *cod*), 2.43(4H, bs, *cod*) 3.96(6H, s, *2 x* Me), 4.15(2H, bs, *cod*), 4.32(4H, bs, *cod*), 5.56(2H, s, CH_2), 6.82(2H, bs, *imidazole*) and 6.91(2H, bs, *imidazole*); MS: (ESMS): 546.1585 $[M + H]^+$ 100%; Anal.Calcd for $C_{21}H_{32}N_4OBF_4Rh$: C, 43.82; H, 5.52; N, 10.22 %. Found: C, 43.58; H, 5.48; N, 9.97 %.

3.49 Synthesis of complex 3

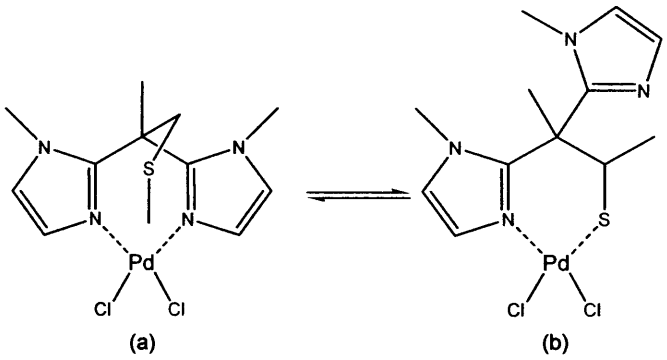


Ligand 11 (0.1 g, 0.42 mmol) in DCM (10 ml) was added slowly to a solution of $PdCl_2(MeCN)_2$ (0.1 g, 0.42 mmol) in DCM (5 ml). No colour change was visible therefore the orange mixture was allowed to stir overnight. Some fine solid precipitated, and was

separated. The transparent orange solution was reduced *in vacuo* to give an orange solid. The waxy solid was washed with dry degassed hexane (1 x 5 ml) and once with dry degassed diethyl ether (5 ml), to remove any displaced COD. The resulting fine, yellow solid was recrystallised from dry DCM and Hexane to afford large, pale, orange, rhombic crystals (0.1 g, 60%).

Found: δ_H (500MHz: $CDCl_3$) 0.95(3H, t, *J* 7.0, Me *-ether*), 2.22(3H, s, Me-*apical*), 3.56(2H, q, *J* 7.0, CH_2), 3.84(6H, s, *2 x* Me), 4.87(2H, s, CH_2), 6.73(2H, s, *imidazole*) and 7.33(2H, s, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 14.9(C^8), 20.5(C^7), 38.8(C^6), 47.6(C^9), 67.4(C^5), 80.0(C^4), 124.2(C^3), 128.3(C^2) and 143.4(C^1); Anal.Calcd for $C_{13}H_{20}Cl_2N_4OPd$: C, 36.70; H, 4.70; N, 13.20%. Found: C, 36.64; H, 4.72; N, 12.99%.

3.50 Synthesis of complex 4

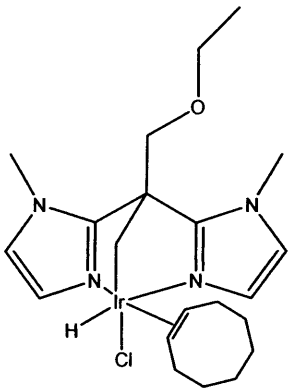


Ligand 12 (0.1 g, 0.42 mmol) in DCM (10 ml) was added slowly to a solution of $PdCl_2(MeCN)_2$ (0.1 g, 0.42 mmol) in DCM (5 ml). No colour change was visible therefore the orange mixture was allowed to stir overnight. Some fine solid precipitated, and was separated. The transparent orange solution was reduced *invacuo* to give an orange solid. The waxy solid was washed with dry degassed hexane (1 x 5 ml) and once with dry degassed diethyl ether (5 ml), to remove any displaced COD. The resulting fine, yellow solid was recrystallised from dry DCM and Hexane to afford large, pale orange rhombic crystals (0.08 g, 55%).

Found: δ_H (500MHz: CD_2Cl_2) [For complex 4 (a)] 1.82(3H, s, Me-*apical*), 2.23(3H, s, Me-*sulfur*), 3.91(6H, s, *2 x* Me), 4.53(2H, s, CH_2), 6.72(2H, s, *imidazole*) and 7.36(2H, s, *imidazole*); [For complex 4 (b)] 2.01(3H, s, Me-*apical*), 2.51(3H, s, Me-*sulfur*), 3.04(3H,

s, *me*), 3.12(3H, s, Me), 6.82(1H, s, *imidazole*), 6.85(1H, s, *imidazole*), 6.97(1H, s, *imidazole*), and 8.01(1H, s, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 122.4(C^{Ar}), 123.3(C^{Ar}), 126.2(C^{Ar}), 128.2(C^{Ar}), 151.4($C^{C\text{-}N(a)}$) and 154.3($C^{C\text{-}N(b)}$); Anal.Calcd for $C_{12}H_{18}Cl_2N_4SPd$: C, 33.70; H, 4.20; N, 13.10%. Found: C, 34.13; H, 4.24; N, 12.09 %.

3.51 Synthesis of complex 5



Ligand 11 (0.2 g, 0.80 mmol) in DCM (10 ml) was added slowly to a solution of $Ir(ClCOE_2)_2$ (0.25 g, 0.36 mmol) in DCM (3 ml). A colour change from a deep orange to pale yellow was visible overnight. The mixture was allowed to stir overnight. The transparent yellow solution was reduced *invacuo* to give a pale yellow wax. The waxy solid was washed with dry degassed hexane (1 x 5 ml) and once with dry degassed diethyl ether (1 x 5 ml), to remove any displaced COE. The resulting fine, white solid (80%) was recrystallised from dry DCM and Hexane to afford colourless crystals.

Found: δ_H (500MHz: CD_2Cl_2) -17.01(1H, s, H-*hydride*), 1.1-1.8(11H, bm, Me-*ether*, *coe*), 2.12(3H, s, Me-*apical*), 3.43(2H, m, CH_2), 3.62(4H, m, *coe*), 3.71(3H, s, Me), 3.75(3H, s, Me), 4.13(2H, d, *J* 10, CH_2), 4.28(2H, d, *J* 10, CH_2), 5.32(2H, bm, *coe*), 6.74(2H, d, *J* 7.0, *imidazole*) and 7.32(2H, d, *J* 7.0, *imidazole*); ^{13}C δ_H (125MHz:$CDCl_3$): 15.1(C^{api}), 26.7, 32.9, 34.9, 60.9, 63.1, 67.8, 69.7, 122.4(C^{Ar}), 123.3(C^{Ar}), 126.2(C^{Ar}), 128.2(C^{Ar}), 151.4(coe) and 154.3(CN); MS: (ESMS): 549.2331 $[M + H]^+$ 100%.

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CHAPTER FOUR

Palladium-catalysed C-C coupling reactions

4.1 Introduction

4.1.1 Catalysis-Definition and uses

A catalyst can be defined as a substance that increases the rate at which a chemical reaction approaches equilibrium; therefore catalysts affect the kinetic properties of a reaction rather than the thermodynamics.[1] Different catalysts are able to preferentially accelerate one reaction over another, therefore they are able to influence product selectivity.[2]

The practical importance of catalysts is illustrated by the fact that many chemical reactions will not proceed to the required extent until a catalyst is present. Therefore catalysts are not only vitally important for the economy but have a significant biological impetus. All living organisms would not exist if not for the presence of catalysts in the form of enzymes. In the chemical industry 75% of all chemicals are produced with the presence of a catalyst, at some point in the reaction. If current processes are considered alone, this number increases to 90%.[2]

Catalytic reactions may be divided into three categories: i) Heterogeneous – where the catalyst is a solid in contact with the regents; ii) Homogeneous – in which the catalyst is dissolved in the reaction solution and iii) Enzymatic – a biological process involving enzymes. For the purpose of this study, homogeneous catalysis was considered, which comprises approximately 15% of all industrially catalysed processes. Examples include, hydroformylation reactions which produce around 6.2 million tonnes of aldehydes

worldwide per annum and the Shell Higher Olefin Process (SHOP) producing 868 thousand tonnes of α-olefins per year.[3]

Major advantages of homogeneous catalysis are that the precatalyst i.e. the precursor to the reactive catalytic species is dispersed in the same phase as the reactants. The active catalyst is often suited to mechanistic study and can be analysed spectroscopically, therefore can be synthesised in a reproducible manner, allowing new and improved catalysts to be designed. The key disadvantages of homogeneous catalysis are more difficult product/catalyst separation and lower thermal stability relative to heterogeneous systems.

Catalytic reactions take place at the metal centre however the activity of the catalyst is also dependent upon the ancillary ligands attached to the metal. The ligands have four primary roles i) to keep the metal in a state of low-nuclearity (prevention of aggregation); ii) to stabilise intermediates; iii) to provide vacant co-ordination sites via dissociation equilibria and iv) to effect the activity and selectivity by causing electronic and steric changes to the metal.[4]

Catalysts are regenerated during the catalytic cycle but remain unchanged unless deactivation proceeds from the degradation or poisoning by side reactions. Transition metal mediated phosphorus-carbon bond cleavage is a major cause of catalyst deactivation for phosphine based homogeneous catalysts[4] and an excess of phosphine is required to combat this. Despite the fact that the economics of such procedures are controlled by the price of ligands, rather than the price of the metal, phosphines remain one of the most common ligands used in homogeneous catalysis.

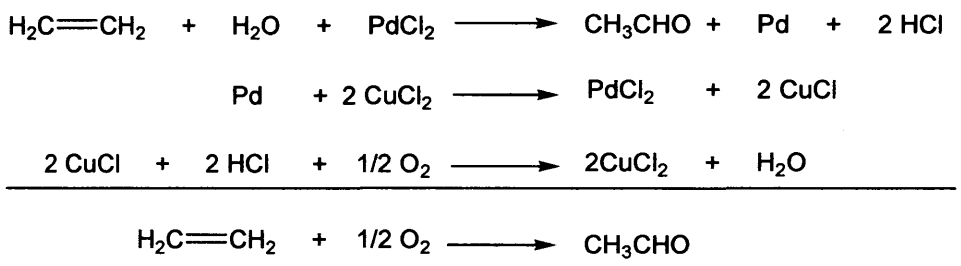
There is still a requirement to develop new catalytic systems both to combat some of the problems in existing processes and for the development of new systems in which cheaper ligands and catalyst systems can be used. Catalyst precursors used need to have a greater stability, with the aim of a greater catalyst lifetime. Catalysts with increased activity and

selectivity need to be synthesised, in addition to improving the catalyst separation so that the catalyst may be recycled and a cleaner product may result.

4.1.2 Palladium in catalysis

In particular this study investigates the activity of homogeneous systems incorporating palladium complexes as precursors. Originally, palladium was used predominantly in heterogeneous catalysis. During the 1950's the Wacker process was the first large scale commercial process catalysed by palladium as a homogeneous catalyst. This process involved the synthesis of acetaldehyde by the oxidation of ethene using palladium(II) chloride and copper(II) chloride.

Figure 4.1 The Wacker process for the production of acetaldehyde



Reactions catalysed by palladium can be divided into two main categories. The first are oxidation reactions catalysed by Pd(II) salts. These mainly involve the oxidation reactions of olefins and aromatic compounds and oxidative carbonylation reactions e.g. the Wacker process; production of oxamides, oxalates and isocyanates. These reactions can be carried out in both liquid and gas phases, using both homogeneous and heterogeneous systems.

The second category of palladium catalysed reactions are those that are apparently catalysed by Pd(0) complexes or at least an intermediate between Pd(0) and Pd(II). The foremost of these is the Heck reaction for the production of substituted olefins. Other

reactions include telomerisation and carbonylation reactions of olefins which were originally developed by Reppe using nickel catalysts.

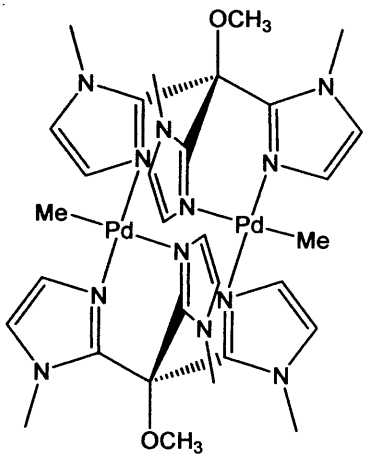
Another important reaction catalysed by palladium is the copolymerisation of carbon monoxide and ethene. This reaction is best described as a migratory insertion reaction resulting in the formation of polyketones.

4.1.3 Nitrogen containing ligands in palladium catalysed reactions

Following the extensive success and problems of mondentate, bidentate phosphine[5] and tridentate ligands in catalysis, attention turned to the use of bidentate nitrogen donor species. Some of the earlier work produced by Consiglio and Brookhart reported the use of bidentate nitrogen ligands, 1,10-phenanthroline, 2,2-bipyridine and diazabutadienes in copolymerisation reactions.[6-9] Cabri *et al.* demonstrated that using palladium complexes of the ligand 1,10-phenanthroline compared to the use of bulky bidentate triphenyl phosphine ligands, allowed the reaction to proceed under milder conditions. They argued that the flat nature of the ligand allowed the olefin to approach the catalyst from both above and below the co-ordination plane, alternatively the presence of a bulky tertiary phosphine would hinder olefin co-ordination. Asselt observed that bidentate nitrogen ligands have good σ-donor and π-acceptor abilities that stabilise both higher and lower oxidation states, formed in alternating oxidative addition and reductive elimination steps. Palladium (II) systems reported by Brookhart and coworkers based on square planar cationic alkyl compounds supported by bulky diimine N,N ligands, were the first examples of late transition metal catalysts capable of polymerising higher α-olefins as well as ethylene to higher molecular weight polymers.[10,11] Feldman and coworkers also reported the synthesis of a β-diimine palladium complex as an active olefin polymerisation catalyst.[12]

There are now a number of mixed donor ligands used in both catalysis and for studying reaction mechanisms. Cavell *et al.* reported in-depth mechanistic studies of the

copolymerisation of carbon monoxide and ethene using N,O ligands, in the form of substituted picolinates and picolinamides.[13,14] Mixed donor studies were developed to investigate tridentate ligands in the form of N,N,N and mixed donors P,N,N and P,O,N. Gibson and coworkers published extensive work incorporating N,N,N ligands, including the tridentate 2,6-bis(imino)pyridine ligand.[15] Cavell *et al.* reported an excellent TON of 808000 with good conversion in a relatively short time for their dimeric tridentate palladium complex **LXXI**.[16]



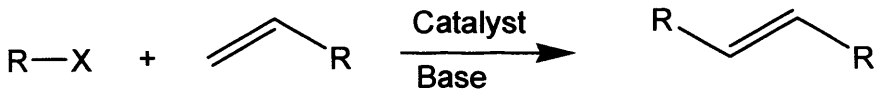
$[Pd(CH_3)\{(mim)_3COCH_3\}]$ LXXI

This result was similar to that of the donor-functionalised carbene complexes $[PdCl(CH_3)\{3\text{-methyl-1(methylacetyl)imidazolin-2-ylidene})_2]$ and $[PdCl(CH_3)(3\text{-methyl-1-picolylimidazolin-2-ylidene})_2 \cdot 0.7AgI]$, reported to give very high TON's for the Heck reaction. This exemplified the importance of nitrogen chelated Pd complexes, which have received little attention in the Heck reaction but can serve as highly active catalysts in this reaction and provide a new entry into the development of non phosphine based late metal homogeneous catalysis.

4.1.4 The Heck Reaction

In 1968 Heck reported palladium catalysed olefination of aryl and vinyl halides, using arylmercury substrates, a reaction now referred to as the Heck reaction, illustrated in Scheme **4.1**.[48]

Scheme 4.1 The Heck Reaction



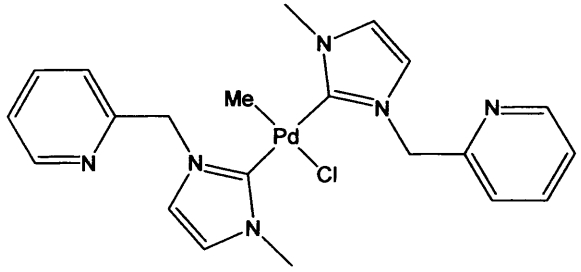
X=I, Br, Cl, triflate

Problems related to the availability, stability and toxicity of organomercury compounds were eliminated as Mizoroki[17] and Heck[18] independently discovered that the olefination of aryl iodides in the presence of base could be catalysed by simple Pd(II) salts in the absence of mercury. The reaction received little attention during the seventies and early eighties due to the expense of aryl iodide substrates. However, since then the Heck reaction has become one of the most well known and widely used transition metal catalysed organic synthetic method. Benefits of this reaction include its chemoselectivity, regioselectivity, stereoselectivity, mild reaction conditions, low toxicity and cost of reagents required. The Pd-catalysed Heck reactions have been applied to the industrial synthesis of fine chemicals such as the analgesic Naproxen, the pesticide Prosulfuron and the UV-B sunscreen octyl methoxycinnamate.[19] High activities have been obtained with more reactive bromides and iodides, however applications on an industrial scale until more recently have been rare, primarily due to the expense of aryl iodide substrates. Aryl chlorides are preferred due to their availability, low cost and stability. Conversley, the stability of these compounds, which is a result of the strength of C_{aryl}-Cl bond compared to C_{aryl}-Br and C_{aryl}-I bonds (402, 339 and 272 kJ/mol in PhCl, PhBr, and PhI, respectively)[20] has hindered industrial applications of this reaction. Industry requires turnover numbers (TON's) exceeding 10000 $mol_{Product}/mol_{Pd}$ and turnover frequencies (TOF's) exceeding

500 $mol_{Product}/mol_{Pd}/hr$ before the classical methods to synthesis fine chemicals can be replaced. The activity of industrially attractive aryl chlorides remained low, until Littke *et al* reported using activated electron deficient aryl chloride substrates efficiently in the Heck reaction at room temperature.[21] However further improvement is necessary before the Heck reaction can become the most fundamental tool in industry for the production of fine chemicals.

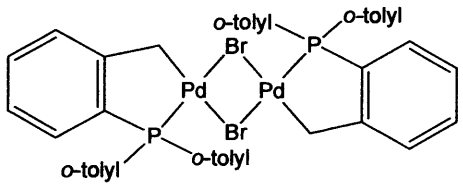
The use of heterocyclic carbenes as ligands for active catalysts was a significant discovery for the Heck process.[22] In 2000 Heck coupling reactions carried out using bromoacetophenone and η-butylacrylate with heterocyclic carbene type catalysts, Figure **4.2**, containing an alkyl group gave TON's of 1 700 000 with conversion rates of up to 85%.[23] In 1998 Herrmann reported the first palladacycle used as a catalyst in the Heck reaction, Figure **4.3**, giving TON's of 5 750 000,[24] under the same conditions.

Figure 4.2 Active known Pd(II) catalyst for the Heck reaction.



LXXII

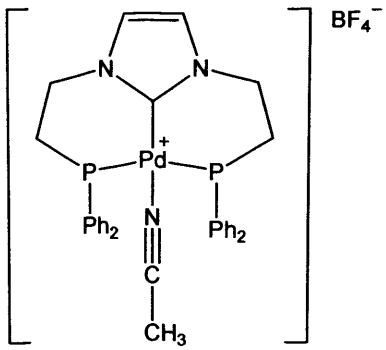
Figure 4.3 The first palladacycle Carbene catalyst for the Heck reaction



LXXIII

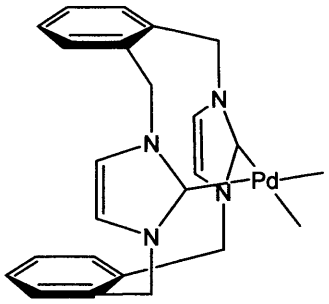
During the last five years interest in the Heck reaction has led to the synthesis of particularly higher active Heck catalysts.[25] The coupling of iodobenzene using a cationic Pd PCP-pincer, illustrated in Figure **4.4** has given the highest turnover number reported to date at 56000000.[26] In related studies Baker *et al.* achieved high turnover numbers, up to 7100000, for Heck reactions of iodobenzene using a PdX_2 complex(X = Br, I) with a cyclophane embedded chelating NHC ligand, Figure **4.5**.[27,28]

Figure 4.4 Most active Pd(II) PCP-pincer catalyst for the Heck reaction.



LXXIV

Figure 4.5 Baker's cyclophane-carbene catalyst for the Heck reaction



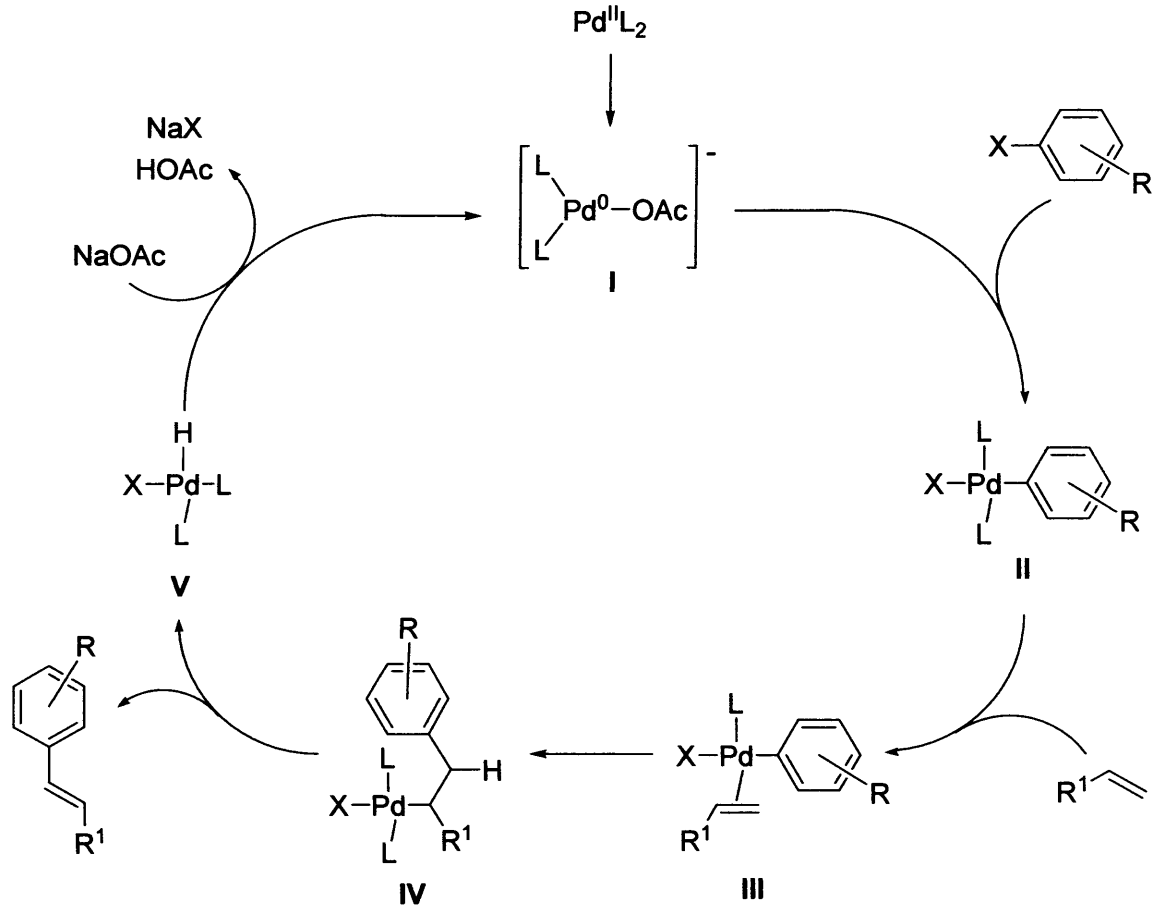
LXXV

4.1.5 Mechanistic aspects of the palladium-catalysed Heck reaction

The Heck reaction is general fairly well investigated, Scheme **4.2**. Research is still ongoing into understanding the formation of the possible intermediates and oxidation state of the active Pd species, however it seems certain that the reaction proceeds via oxidative addition, insertion and product elimination/reduction.[29-31]

If the catalyst is added as a palladium(II) complex or salt, it is first reduced to the active catalyst, thought to be a 14-electron, palladium(0) species. However, Amatore and Jutand demonstrated that under catalytic conditions, an excess of halide or acetate in solution, allows these anions to co-ordinate to unsaturated Pd(0) species giving anionic Pd(0) species **I** that are the actual active catalysts for these types of reactions.[32,33] This is of relevance to this work as NaOAc is employed as base in all of the Heck reactions discussed in this chapter.

Scheme 4.2 Mechanism of the Heck Reaction



The initial step of the catalytic cycle is the oxidative addition of a haloarene or haloalkene to a Pd(0) compound to yield an aryl Pd(II) halide complex, **II**, in which the *trans*-isomer is the thermodynamically stable product. Fitton observed the rate of oxidative addition to aryl halides is of the order I>Br>Cl.[34] The oxidative addition step in the cycle can be considered as the rate determining step, with complex **II** reported to be the catalyst resting state and in equilibrium with **I** type species.[35] The next step involves the co-ordination of an alkene molecule, **III**, concomitantly with the dissociation of L or X^-, **IV**. In the latter case a cationic species is formed. The need for free co-ordination sites for the oxidative addition step and the olefin complexation is consistent with the observation that high concentrations of phosphines retard the reaction rate.[36,37] This is followed by the migratory insertion of the alkene into the Pd-C bond via a four centre transition state. In

cases where the neutral ligands are strongly co-ordinating and cannot dissociate, as is often the case for chelated ligands, it has been demonstrated that dissociation of the anionic ligand can occur to give a cationic Pd intermediate from which insertion can take place.[38,39] Subsequently β-hydride elimination generates the product olefin and a Pd(II) hydride complex, **V**. The final step involves the reductive elimination of HX, which is a reversible process but is driven by the presence of a base and the Pd(0) catalyst is regenerated, **I**.

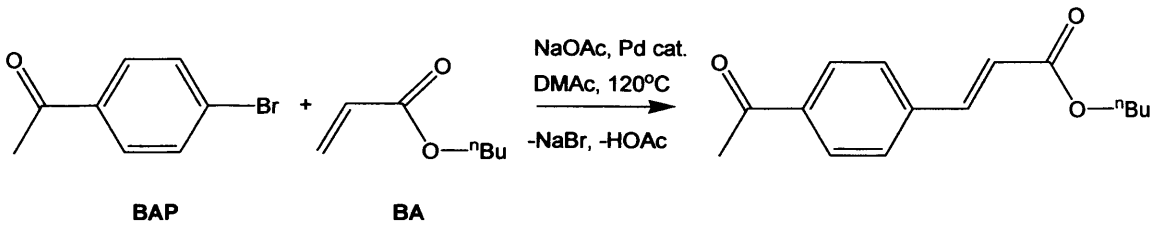
The mechanism illustrated above has a number of shortcomings. Acceleration of the reaction by addition of certain additives and the effects of using different ligands and solvents are not accounted for. A number of alternative pathways have been proposed. Amatore *et al.* used electrochemical techniques to show that the Pd(II) precatalyst was reduced by the phosphine to give an anionic Pd(0) complex, which is the active catalyst.[32,33] Herrmann and coworkers invoked a Pd(II) and Pd(IV) sequence for the palladacycle catalysts, although this was negated in due course.[40,41]

While all intrinsic details of the Heck cycle are still to be established, it is certain the reaction proceeds via a process of oxidation addition, insertion and product elimination. Therefore, when designing precatalysts it is essential that the supporting ligands attached to the metal centre is able to stabilise the different oxidation states in the cycle.

4.1.6 Conditions for the Palladium catalysed Heck reaction

This chapter describes the testing of precatalysts in the Heck reaction, focussing on the coupling of activated aryl bromide, 4-bromoacetophenone (BAP) with η-butylacrylate (BA), under standardised conditions, to give *n*-butyl-4-acetylcinnamate. This coupling reaction could feasibly produce two isomers, the *E* and *Z* conformer. The conformers can be detected by GCMS techniques and distinguished between by NMR spectroscopy. However, all the Heck experiments conducted gave a single product and for the purpose of these reactions, no further analysis was required. Sodium acetate was the choice base,

previously proven to be suitable for Heck reactions using a variety of substrates and catalyst precursors.

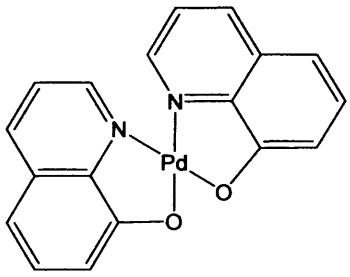


Scheme **4.3**: The Heck reaction of 4-bromoacetophenone and *n*-butyl acrylate catalysed by Pd(II) complexes of bis imidazole (bim) type ligands or Menacac bidentate species.

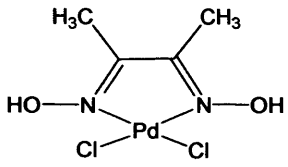
4.2 Results and Discussion

4.2.1 Heck reaction with Pd(II) complexes of Menacac type ligands

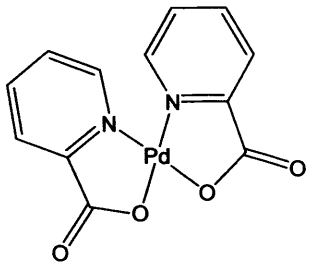
The β-aminoketones (menacac) tested in the Heck reaction in this chapter were synthesised as a possible backbone from which novel hemilabile bidentate and tridentate ligands could be synthesised but these procedures were unsuccessful. These ligands and their palladium complexes have been previously reported[42,43] however there are no reports on such complexes tested as active Heck catalysts. Iyer *et al.* reported five membered four co-ordinate Pd(II) complexes bearing N,O ligands, **LXXVI**, **LXXVII** and **LXXVIII**, as active Heck catalysts with reasonable conversions, however the TON's were not reported.[44]



LXXVI



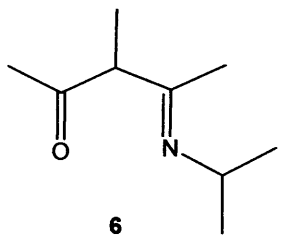
LXXVII



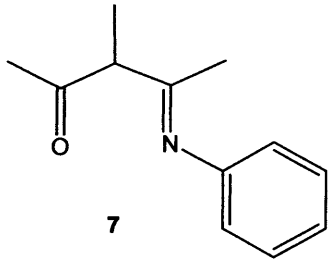
LXXVIII

All tests were conducted using *in situ* generated systems starting from $PdCl_2(MeCN)_2$ and ligands **6** and **7**. The precatalyst was formed by allowing the Pd precursor and the respective ligand to stir in the reaction vessel for 30 minutes. Figure **4.8** illustrates the ligands **6** and **7** used to form the proposed precatalysts tested in the Heck reactions.

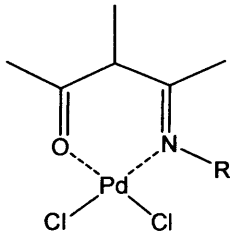
Figure 4.8 Ligands synthesised from chapter 2 and possible Pd system generated under *in situ* conditions.



6



7



R = C_3H_7, C_6H_5

Proposed complex 6 and 7

Table 4.2: Results of the *in situ* Heck coupling of 4-bromoacetophenone and *n*-butyl acrylate catalysed by Pd(II) complexes of menacac ligands.

Run	Ligand *In situ* $(PdCl_2(MeCN)_2$	Pd (mmol%)	Arylhalide	Conversion (%)	TON[a]	TOF[b]
1	6	0.5	BA	> 99	10643	665
2	7	5.0	BA	> 99	4001	250

Reaction condtions: NaOAc (0.459 g, 5.6 mmol), DMAc (5 ml), 120 °C, 16 hours.

[a] Turn over number in moles product per mole catalyst.

[b] Turn over frequency: $TON.hr^{-1}$.

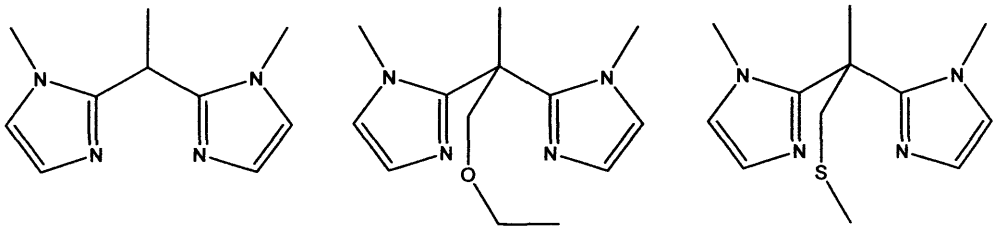
The palladium complex of the aniline substituted ligand **7** demonstrates a greater than two fold catalytic activity than the corresponding palladium complex of the isopropyl containing ligand **6**. It can be proposed that the aromaticity of the aniline ring may stabilise the Pd complex in the Heck reaction resulting in higher TON's, however the data set of two ligands alone is insufficient to draw any conclusions. Although the *in situ* complexes are active Heck catalysts, the TON's are quite low by industrial standards.

4.2.2 Heck reaction with Pd(II) complexes of bis imidazole type ligands

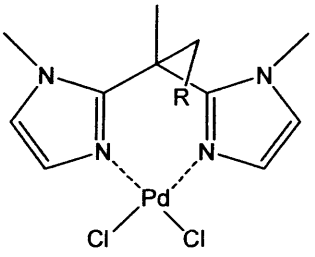
Catalytic testing of Pd(II) complexes bearing bis-imidazole type ligands reported in chapter three was required to assess whether the hemilabile donor motif attached to the bis-imidazole backbone would have any influence in the catalytic cycle. Figure **4.6** summarises the ligands/complexes tested in the Heck reactions. The addition of ligand **11** and **12** to an appropriate Pd precursor resulted in complexes **3** and **4** that have been isolated and characterised by x-ray crystallography (see chapter three). Palladium complexes bearing ligand **10** have not been isolated however it is assumed for the purpose of catalytic testing that under *in situ* conditions, (allowing a solution of the ligand and the

metal precursor to stir for 30 minutes prior to the addition of the substrates) ligand **10** would give a similar four co-ordinate N,N ligated Pd(II) centred complex as observed for complexes **3** and **4**.

Figure 4.6 Ligands and complexes tested in the Heck reaction



10 **11** **12**



Complexes **3** R = O-CH_2CH_3, **4** R = S-CH_3

It is known that Heck reactions are dependent on vacant sites at the metal centre,[3] therefore dissociation of the ligand from the metal centre is fundamentally important. Thus the competitive co-ordination or lack of, as discussed in chapter three, between the N,O and N,S to the Pd centre in complexes **3** and **4**, respectively, may be an elementary contribution in the Heck reaction. Comparing the catalytic activity of complex **3** and **4**, to similar precursors with ligands absent of such hemilabile donors (ligand **10**), could indicate the influence, if any, of the labile third donor.

Tests were started using preformed catalysts, however due to shortage of product and to obtain a fair result, all tests were repeated with *in situ* catalysts. This would eliminate discrepancies arising from using different batches of product containing different levels of impurities, thus all reactions were performed utilising the same batch of ligand and

precursor. It is known that in certain cases the reaction rates *in situ* can be lower than those for preformed, isolated complexes. However in this case the difference between test results for preformed and *in situ* catalytic runs was negligible. The precatalyst was formed by allowing the Pd precursor and the respective ligand to stir in the reaction vessel for 30 minutes. The results of the *in situ* catalysis of $PdCl_2(MeCN)_2$ with ligands **10-12** are summarised in the Table **4.1**. The extent of reaction completion and product identification was monitored using gas chromatography with mass spectrometry (GC-MS). Due to the low boiling point of DCM the catalysis reactions could not be conducted in this medium and dimethylacetamide (DMAc) was the solvent of choice. DMAc is a co-ordinating solvent and may compete with the hemilabile donors to co-ordinate to the Pd centre. However this should not affect the comparative results of catalysis as all reactions were conducted in the same solvent. Standard conditions were used for all catalysis runs, using activated Ar-Br except for the use of an activated Ar-Cl for runs **6** and **7**.

Table 4.1: Results of the *in situ* Heck coupling of 4-bromoacetophenone (BA), 4-chloroacetophenone (CA) and *n*-butylacrylate catalysed by Pd(II) complexes of the bis- imidazole ligands **11** and **12**.

Run	Ligand *In situ*	Pd (mol%) ($PdCl_2(MeCN)_2$)	Arylhalide	Conversion[a] (%)	TON[b]	TOF[c]
3	10	10×10^{-3}	BA	> 99	11030	689
4	11	0.2×10^{-3}	BA	> 99	117843	7365
5	12	0.2×10^{-3}	BA	> 99	367300	22956
6	11	0.5	CA	-	0	0
7	12	0.1	CA	-	0	0

Reaction condtions: NaOAc (0.459 g, 5.6 mmol), DMAc (5 mL), 120 °C, 16 hours.

[a] The conversion calculation was a result of the amount of starting material consumed in the reaction and not related to the amount of desired product formed.

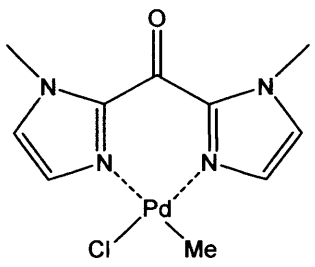
[b] Turn over number in moles product per mole catalyst.

[c] Turn over frequency: $TON.hr^{-1}$.

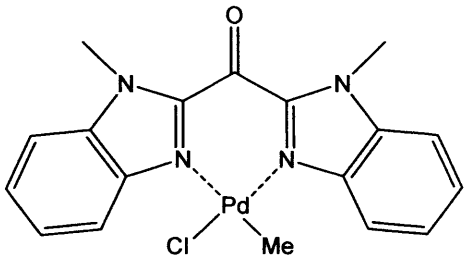
Turnover numbers and conversions quoted were those obtained when the reactions were terminated after set times and do not necessarily represent maximum values, nor do they indicate that the catalyst had ceased to operate.

Run 1 representing the Pd(II) complex bearing ligand **10**, gave a poor TON of 11030 $mol_{product}/mol_{Pd}$ however under the same conditions, the Pd(II) complex of ligand **11** was 10 times more active, run **3**. The Pd(II) complex of ligand **12**, run **5**, was most active with an approximately 35 times greater rate of reaction at 367300 $mol_{product}/mol_{Pd}$.

Done's investigation of two similar complexes, absent of a third potential donor, **LXXIX** and **LXXX** in the Heck reaction have been reported to give TON's of 100 000 and 53 000, respectively.[45] The importance of incorporating a hemilabile donor into a precatalyst design to increase the rate of catalysis for Heck type reactions was exemplified when comparing both run **3** and Done's results with the superior rate of reaction, run **4** and **5** in Table **4.1**.



LXXIX

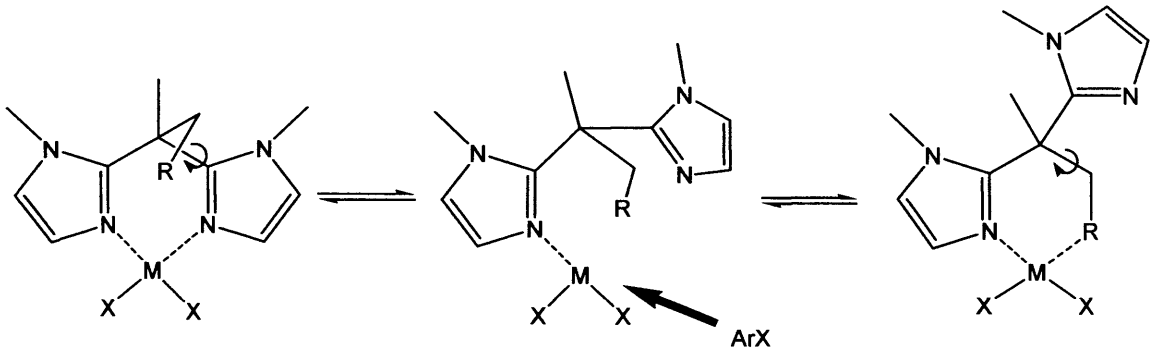


LXXX

An interesting observation was the sulfur containing catalyst, run **5**, giving a three fold increase in the rate of reaction compared to the oxygen counterpart, run **4**. Sulfur is a softer donor than oxygen and able to compete with nitrogen donors on a soft metal like palladium. In solution, complex **10** is fluxional and competition of the N,S donors for co-ordination to the metal was evident by NMR spectroscopy (as discussed in Chapter three). Dissociation of a ligand from the metal centre in a catalytic cycle creates a vacant site for the co-ordination of a substrate molecule. It is proposed that competition of donors can cause temporary vacant sites at the metal centre inadvertently causing less

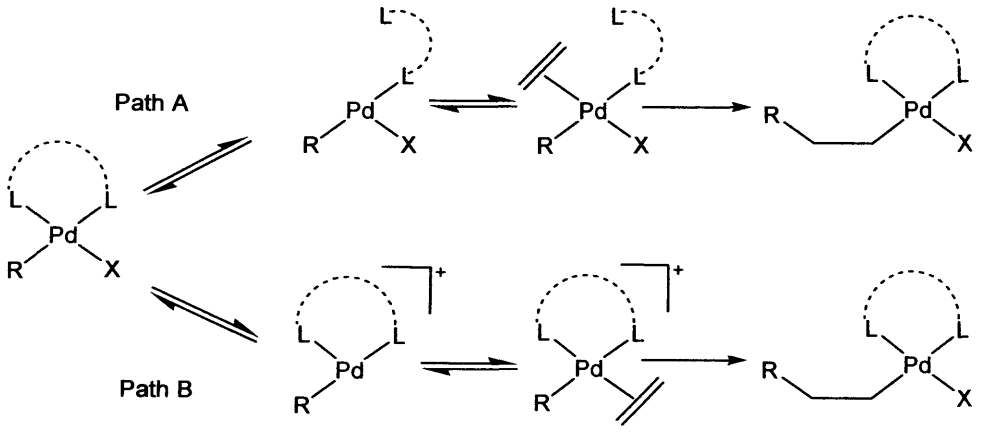
steric hindrance about the Pd centre and ease of co-ordination for the substrate molecules. This could be the cause of the highest catalytic activity for the coupling reaction of bromoacetophenone with butyl acrylate.

Figure 4.5 Rotation about the C-C bond, giving N,N and N,R donor ligands.



Run **4** also shows high catalytic activity with a relatively high turnover number compared to the precatalyst absent of any hemilabile donors, run **3**. Oxygen is a harder donor than sulfur therefore is unable to compete as strongly as sulfur with N-donors on a soft metal like palladium. Thus, the exchange of donors in complex **3**, may be enforced under catalytic conditions and not as easily as observed for complex **4**. The lack of competitive co-ordination to the soft palladium centre compared to the sulfur donor is a proposed rationale for the reduced catalytic reactivity observed.

The mechanism of this reaction has not been investigated therefore the nature of the active catalyst is unknown. As discussed earlier a traditional mechanism is expected, this would require the Pd(II) starting complex to undergo a reduction to form a Pd(0) species. There are two reaction pathways by which this can occur; path A involves co-ordination of the olefin *via* dissociation of one neutral ligand; path B involves the co-ordination of the olefin *via* dissociation of one anionic ligand. It is assumed that path B is a more plausible route as Cabri *et al.* and Beletskaya *et al.* have reported that path B was the more probable pathway for catalysts incorporating bidentate ligands, Scheme **4.4**.[30,31]



Scheme 4.4: Two proposed pathways of the co-ordination-insertion step in the Heck reaction for Pd complexes containing bidentate ligands.

Pd complexes of ligands **11** and **12** were also tested in the Heck coupling of 4-chlorobenzaldehyde and *n*-butylacrylate. However no Heck products were produced under these conditions, even when using catalytic loading over 2000 times higher. The precatalysts tested are unable to activate the stronger Ar-Cl bonds as they require greater activation energy compared to the weaker Ar-Br bonds.

4.3 Conclusions

All Pd(II) precatalysts formed from the ligands described in Chapters 2 and 3 are active catalysts for Heck reactions. Heck reactions were conducted to benchmark these precatalysts relative to existing catalyst systems and as an attempt to discern trends in reactivity related to their structural and electronic properties.

The Heck reaction was the fundamental tool used to investigate the influence of the pendant arms on the potentially hemilabile ligands by comparing the reactivity of the Pd complexes **9** and **10** to the Pd complex of bis(imidazol-2-yl)methylmethane. The catalytic results clearly demonstrated that the oxygen and sulfide arm were involved in the catalytic

pathway, increasing the rate of reaction and resulting in an increased turnover number. These complexes demonstrated superior catalytic activity compared to bidentate complexes reported in the literature, [45] It is proposed that competative co-ordination of donor atoms in ligand **12** is the behaviour directly responsible for the increased activity. Therefore it is imperative that the properties of the donor suit the metal centre to which it co-ordinates, i.e soft donors are able to better co-ordinate to soft metals than harder donors, when considering catalyst design. Thus the precatalyst incorporating ligand **12**, with the soft sulfide donor, gave the greatest activity with the highest turnover number.

There is still scope for optimizing catalyst design and further investigation into the catalytic activity of bis-imidazole containing precatalyst systems. The maximum TON's and catalyst life times are yet to be determined as the reactions were terminated after 16 hours, this could be done by increasing the reaction time and varying the Pd catalyst loading. The catalytic activities observed across this range of test reactions conducted were well below the currently most active systems. However, investigations by synthesising similar ligands incorporating for example phosphorus and nitrogen hemilabile substituents and testing their behaviour as catalysts are yet to be conducted; this would give a broader understanding of the effect of ligands on precatalyst design.

4.4 Experimental

For all catalytic Heck reactions using Pd(II) precatalyst complexes, the yields of coupled products were determined by GC based on the amount of aryl halide remaining after reaction, using internal standard quantitation methods. Complete conversion to the desired product was assumed. GC-MS analysis of reaction mixtures was used to confirm the identity of the desired product and the approximate amount and nature of any by-products. GC calibrations were performed by preparing a series of solutions with varying amounts of aryl halide and a constant amount of the internal standard. Each solution was run in duplicate and the result from the two injections averaged. A linear plot of the peak are

ratio *vs.* amount of aryl halide was produced; thus an experimentally determined peak area ratio was able to be converted to the amount of aryl halide in the sample.

4-Bromoacetophenone (0.995 g, 5.00 mmol) and NaOAc (0.459 g, 5.60 mmol), were suspended in DMAc (5 mL) and *n*butyl acrylate (1.1 mL, 7.7 mmol) added, followed by the precatalyst as a solution in DMAc. The mixture was immediately put into an oil bath and heated to 120 °C. After stirring for the desired time, 16 hours, the reaction was cooled to room temperature and naphthalene (0.339 g, 3.11 mmol) added as internal standard, followed by DCM (5 mL) and Petroleum ether 40/60 (30 ml) to precipitate inorganic salts. The resulting suspension was allowed to stand then filtered and the resulting filtrate injected on the GC.

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