Palladium Complexes of (Benzoimidazol-2-ylmethyl) amine Ligands: Synthesis and Applications as Catalysts in Methoxycarbonylation of olefins

By

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Thesis

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Supervisor: Dr Stephen O. Ojwach

DECLARATION

I declare that the thesis, (Benzoimidazol-2-ylmethyl) amine ligands: synthesis and applications as catalysts in methoxycarbonylation of olefins, is my original work and has never been presented for the award of any degree at any other university before and that all the information, references and sources I have used and or quoted have been indicted and acknowledged by means of complete physical references.

Name: Thandeka Adelinah Tshabalala

Signature:…………………………….. Date:……………………………

Supervisor: Dr Stephen Ojwach

Signature:…………………………….. Date:……………………………

DEDICATION

DEDICATED TO MY PARENTS MR AMOS

AND MRS THEMBENI

TSHABALALAAND MY SON, ASAVELA

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ABSTRACT

Compounds N-(1H-benzoimidazol-2-ylmethyl)-2-aniline(**L1**), N-(1H-benzoimidazol-2-ylmethyl)-2-methoxyaniline (**L2**), N-(1H-benzoimidazol-2-ylmethyl)-2-thioaniline (**L3**) and N-(1H-benzoimidazol-2-ylmethyl)-2-bromoaniline (**L4**) were prepared by reaction of 2-(chloromethyl) benzimidazole with the appropriate aniline. Ligands **L1**– **L4** were reacted with either [PdCl$_2$(COD)] or [PdClMe(COD)] to form palladium complexes [PdCl$_2$(**L1**)], [PdClMe(**L1**)], [PdCl$_2$(**L2**)],[PdClMe(**L2**)], [PdCl$_2$(**L4**)] and [PdClMe(**L4**)].

Treatment of the neutral complexes **C1 – C6** with one equivalent of PPh$_3$ in the presence of the halide abstractor NaBAr$_4$ (Ar = 3,5-(CF$_3$)$_2$C$_6$H$_3$) led to the formation of the cationic species [(PdCl(**L1**)]Bar$_4$, [(PdMe(**L1**)]Bar$_4$, [(PdCl(**L2**)]BAr$_4$, [(PdMe(**L2**)]BAr$_4$ and [(PdMe(**L4**)]BAr$_4$. All the new compounds were characterized by combination of ^{1}H and ^{31}P NMR spectroscopy, mass spectrometry, X-ray crystallography of complexes **C8**, **C9** and **C11** and elemental analysis (for complexes).

The palladium complexes were investigated as catalyst in methoxycarbonylation of olefins. Methoxycarbonylation of 1-hexene using **C2**, **C4**, **C6**, **C8-C11** was studied in order to investigate the effect of catalyst structure and PPh$_3$ ligand on activity and selectivity. Complex **C10** bearing electron donating OCH$_3$ substituent on phenyl group was the most active, while the corresponding analogue containing the Br substituent on phenyl group was the least active. Complex **C9** with Pd-Cl showed lower catalytic activity, compared complex **C10** with Pd-Me. Addition of PPh$_3$ to the

palladium complexes resulted in higher catalytic activities and high regioselectivity towards the linear esters. The activity also dependent in the identity of acid promoter where HCl gave highest active system while no activity was observed with *p*-TsOH. The effects of pressure, temperature, catalysts concentration, identity of the olefin and time was also investigated. Increasing the catalysts concentration, chain length and time resulted in higher catalytic activities and higher regioselectivity towards the branched ester.

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ABBREVIATIONS

COD	Cyclooctadiene
GC	Gas chromatography
GC-MS	Gas chromatography-mass spectrometry
MS	Mass spectrometry
NMR	Nuclear magnetic resonance
p-TsOH	*para*-toluene sulfonic acid
L	Ligand
DCM	Dichloromethane
ESI-MS	Electrospray ionization
PPh₃	Triphenyl phosphine
LAB	Linear alkyl benzene
LABS	Linear alkyl benzene sulfonates
CM	Cross metathesis
ADMET	Acyclic diene metathesis polymerization
ROMP	Ring-opening metathesis polymerization

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Synthesis and applications of olefin and the role of transition metal catalysts

1.1.   General Introduction

Olefins are a family of organic compounds with a chemical formula C_nH_{2n} containing at least one double bond. The reactivity of the olefin is controlled by the location of the double bond (terminal or internal) and this makes the olefins useful for a number of applications. The olefins can either be branched or linear and this significantly influences their physical and chemical properties. Originally thermal cracking of waxes and chlorination/dehydrochlorination of linear paraffin's was used for the manufacturing of linear α-olefins and linear internal olefins.[1] Linear olefins can also be manufactured by dehydration of alcohols in the vapor phase. Olefins are used as substrates in a variety of catalytic reactions such as polymerization, oligomerisation, carbonylation and hydrogenation.

1.2.   Synthesis of α-olefins

Linear α-olefins are very significant from an industrial perspective; examples include C_4 – C_{12} linear α-olefins and higher blends of C_{20} – C_{24}, C_{24} – C_{30} and C_{20} – C_{30} ranges.[1] Oligomerisation of ethylene and Fischer Tropsch synthesis are the two main routes used for the preparation of the α-olefins industrially.[1]

1.2.1. Ethylene oligomerisation

Oligomerisation is by far the most widely used in the conversion of lower olefins (C_2 – C_4) into industrially significant higher olefins (C_8 – C_{30}).[2] The use of organometallic complexes in the oligomerisation process has been studied.[3] In the oligomerisation of ethylene, straight and branched chain olefins are produced. The straight chain olefins have been found to be more useful than branched olefins; because of high biodegradability of the products.[4] The α-olefins can be produced by the oligomerisation of ethylene in a non-selective manner. Such processes (non-selective) typically generate amathematical distribution (Poisson) of olefins.[5] Non-selective ethylene oligomerisation reactions include the Shell Higher Olefin Process, Albemarle and Chevron Processes, and the Idemitsu process.[6]

1.2.2. Fischer Tropsch synthesis

Fischer- Tropsch synthesis converts biomass, coal and natural gas to hydrocarbon products which are used as transportation fuels. Fischer- Tropsch synthesis is, however, also known for producing chemicals such as olefins, which are of much higher value than low value fuels.[7] The total olefin content and α-olefin selectivity depends on the ratio of hydrogen to carbon monoxide, pressure and catalysts.[8] A higher operating pressure gives more α-olefins. [8]

Sasol (South Africa) produces α-olefins through Fischer- Tropsch synthesis and has recently built a large scale commercial plant for the synthesis of 1-pentene and 1-hexene

from fluid bed Fischer- Tropsch synthesis reactors. [9] The purification method employed by Sasol involves a number of distillation steps to separate the olefins from other products.[10] To reduce the cost of product separation, Fujimoto and co-wokers[11, 12] have demonstrated that it can be accomplished by Fischer- Tropsch synthesis in supercritical fluids. They studied Fischer- Tropsch synthesis on silica supported cobalt – lanthanum and /or alumina supported ruthenium catalyst, in a supercritical n-hexane and they showed advantages of this operation, including higher olefin selectivity, relative to gas phase and liquid phase operation.[11, 12]

1.3.   Applications of olefins

Imagine life today without packaging, detergents, sun creams or lubricants. Products would not be as fresh and crisp, clothes would not be protected and our cars would under perform. α-olefins and internal olefins help to provide all of these benefits. Linear α-olefins are valuable commodity chemicals used as precursors in many areas of industry, such as detergents (C_{10} – C_{30}), synthetic lubricants, plasticizer alcohols, as well as co-monomers in the synthesis of linear low-density polyethylene (LLDPE), as is depicted in figure 1.1.[13 - 14]

Among the α-olefins, 1-hexene and 1-octene are particularly pleasing as they allow the formation of co-polymers displaying excellent chemical and physical properties.[14] The lower linear α-olefins C_4- C_8 can be used for the synthesis of linear aldehyde through

oxo-synthesis by a process known as hydroformylation. The linear aldehydes can be used for the synthesis of a carboxylic acid or linear alcohols.[15]

Linear α-olefins		
1-Butene	→	PE comonomers
1-Hexene	→	Plasticizer Alcohols
1-Octene	→	Polyalpha Olefins
1-Decene	→	Alkylbenzene
1-C_{12}	→	Detergent Alcohols
1-C_{14}	→	Amine / Sulfonates
1-C_{16}	→	Alkenyl Succinates
$C_{16} - C_{18}$ LIO fractions		
1-C_{18}	→	Oil field Chemicals
1-C_{20}+	→	Lubricant Waxes
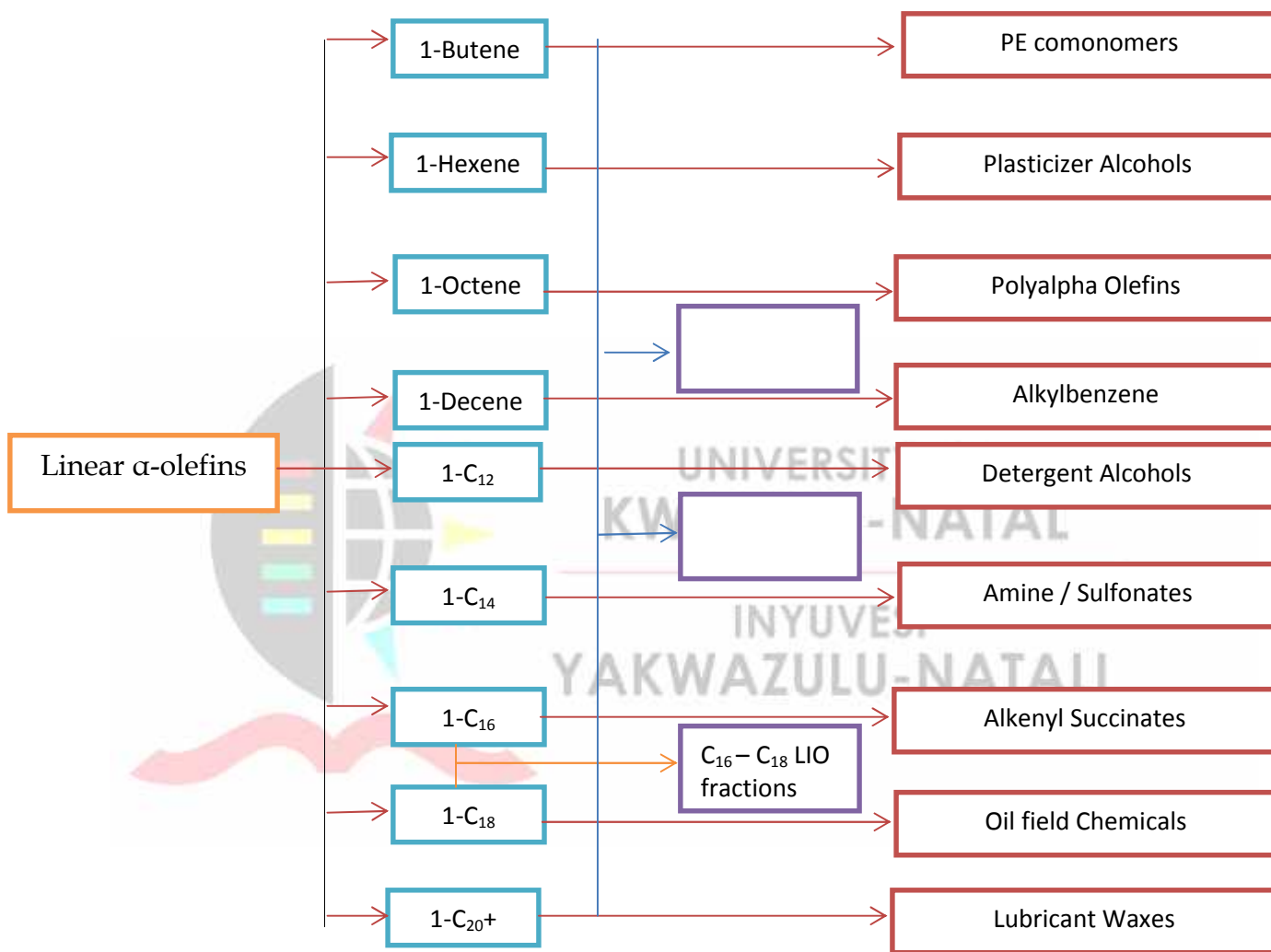
Figure 1.1: Chart depicting the various uses of linear olefins in the chemical and petrochemical industries.[13]

1.3.1. Application of α-olefins as detergents

Detergents have shown slower growth than plasticizers with less biodegradable surfactants, but growth is occurring as biodegradable surfactants are being replaced by α-olefins. The application of 1-decene is in the synthesis of lubricant base stock and it can be used to make surfactants.[16] C_{16}–C_{18} linear α-olefins are applied as hydrophobes in oil-soluble surfactants.[16] The α-olefins are used as intermediates for the production of olefin sulfonate surfactants. C_{14}–C_{16} α-olefin sulfonate blends are used in liquid hand soaps.[16] C_4- C_8 linear α-olefins may be reacted with benzene via Lewis acid catalysis to produce linear alkyl benzene (LAB). LAB is then sulfonated and neutralized to produce linear alkyl benzene sulfonates (LABS), which are employed in laundry detergents, dishwashing soaps and all-purpose cleaner.[16]

α-olefins can also be used for the manufacturing of alkyl dimethyl amines. Hydrogen peroxide oxidation of alkyl dimethyl amines produces amine oxide which is used in dishwashing detergents, shampoos and bubble baths. α-olefins can be used to produce alkane sulfonates by reacting them (α-olefins) with sodium bisulfate via free-radical mechanism.

1.4.   Conversion of α- olefins to fine chemicals and pharmaceutical products

There are a number of applications of linear α-olefins; these include their use in the conversion to fine chemicals and pharmaceutical products. Transition metal catalysts have played a major role in the conversion of linear α-olefins to fine chemicals and pharmaceutical products. These involve: oxidation of α-olefins to olefin derivatives such as epoxy compounds, aldehyde, and ketone and metathesis of olefins to fine chemicals. The α-olefins can also be converted to aldehydes, alcohols, carboxylic acids and methyl esters via the reaction of α-olefins with carbon monoxide.

1.4.1.   Oxidation of olefins

Oxidation of olefins to olefin derivatives such as epoxides, aldehydes and ketones is one of the significant chemical productions. In the oxidation of olefins; oxygen is used as an oxidant to produce the corresponding epoxide. For example, the world production capacity of ethylene oxide is currently about 17.1 Mt/a. At low temperatures, dilute $KMnO_4$ olefins are oxidized to glycols (Scheme 1.1).[17] There is 75% production of glycols i.e. ethylene glycol used in making polyesters and antifreeze, triethyl glycol (solvent, plasticizer and gas dehydration) and higher glycols.[17]
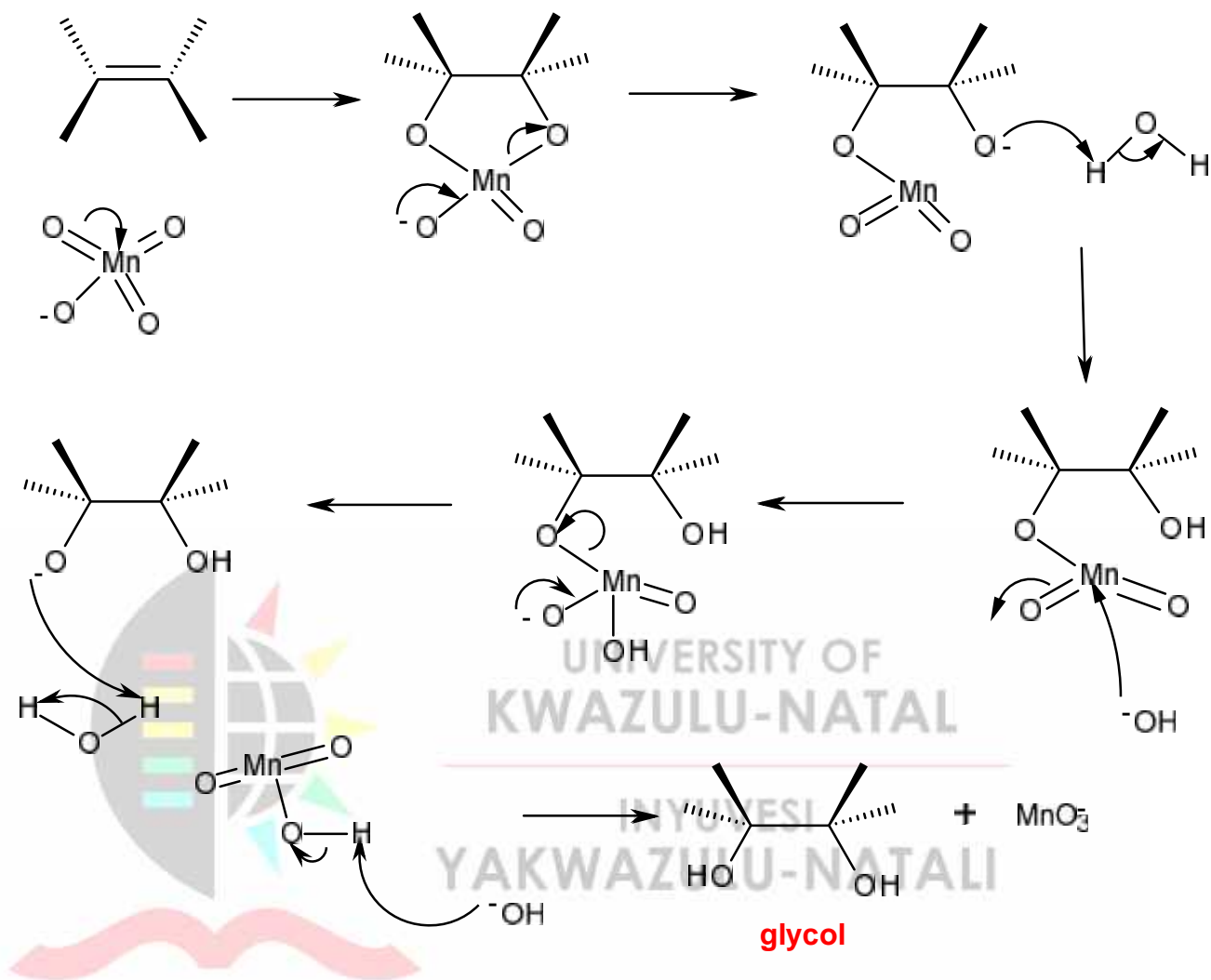
Scheme 1.1: Oxidation of olefins to glycols.

The catalytic oxidation methods employing silver based catalysts such as Ag /Al$_2$O$_3$ discovered in the 1940's (Scheme 1.2)[18] has been used by developed countries instead of non-catalytic oxidation methods such as chlorohydrin process; this is done in order to prevent pollution.[19]
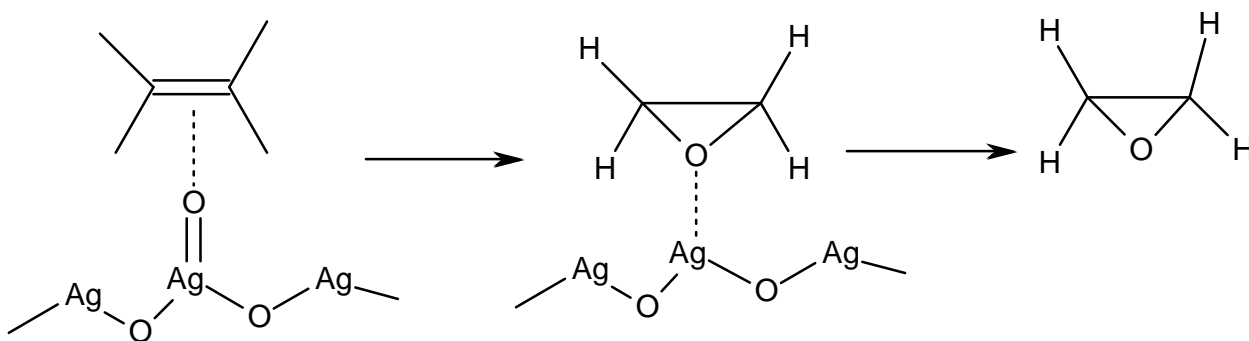
Scheme 1.2: Silver based catalyst, catalytic oxidation method.

The oxidation of olefins to ketones and aldehydes can be achieved by a process known as the Wacker oxidation. This process was discovered for the first time by Smidt and co-workers.[20,21] The Wacker oxidation has been applied in many areas of industry[22] i.e. plants with production capacity of 15 000 tons of acetaldehyde per year have been developed.[21] Recently the Wacker oxidation has been used for conversion of terminal olefins to methyl ketones via the for the production of natural and non-natural products.[23]

1.4.2. Metathesis of olefins

Olefin metathesis is the exchange of substituent's between different olefins by the scission and regeneration of carbon-carbon double bonds (Scheme 1.3).[24] The catalysts used for the olefin metathesis are the Grubbs[24] and Schrock catalysts[25] (Scheme 1.3). Olefin metathesis can be applied in the production of pharmaceutical drugs, monocyclic compounds and the production of propylene.[26]
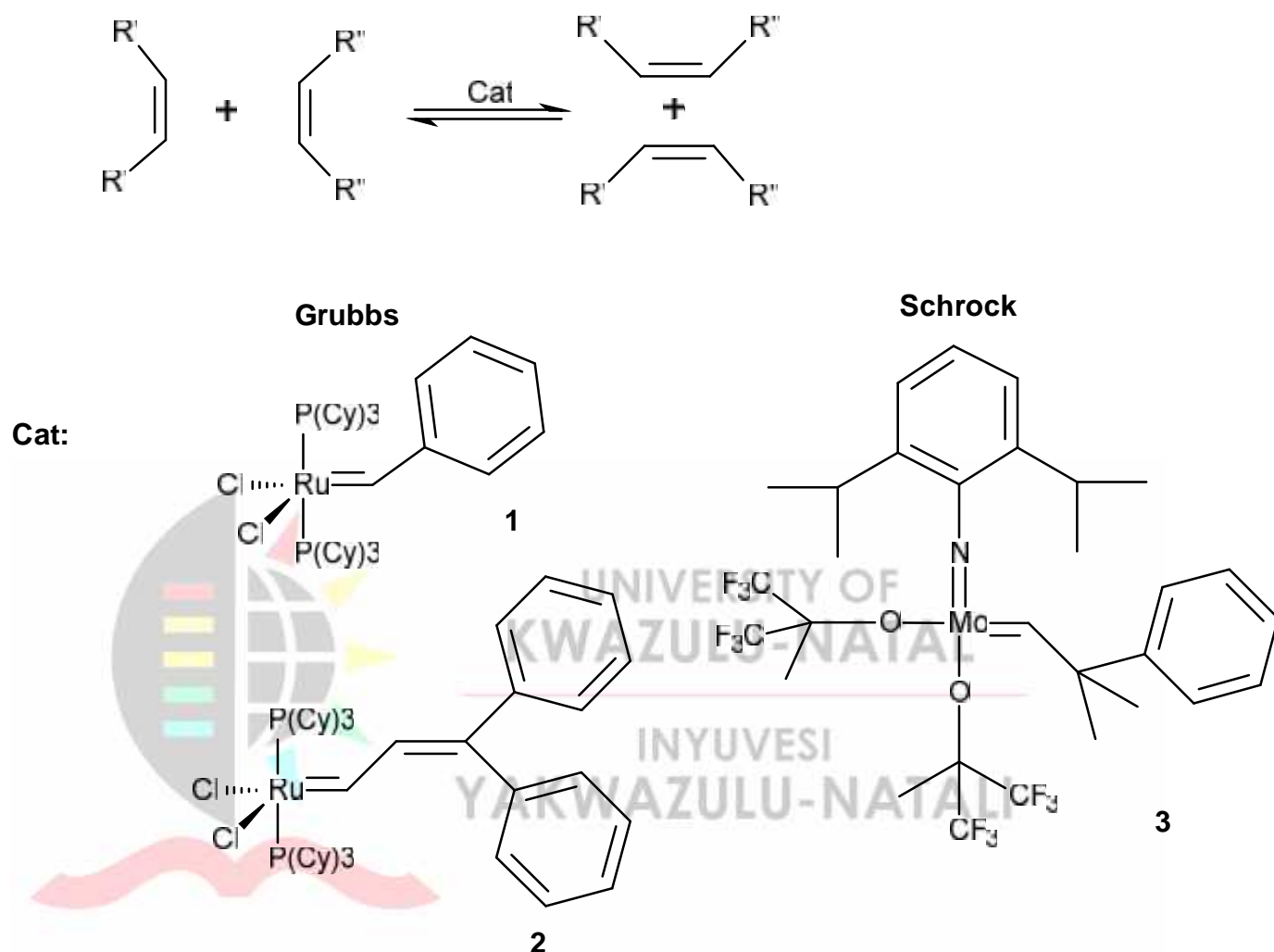
Scheme 1.3: Grubbs and Schrock catalysts used for olefin metathesis.

There are six types of olefin metathesis: cross metathesis (CM), ring-closing metathesis (RCM), acyclic diene metathesis polymerization (ADMET), ring-opening cross metathesis (ROCM), ring-opening metathesis polymerization (ROMP) and intermolecular enyne metathesis.[27,28] All of these methods are employed in the production of small, medium and polymeric molecules as well as novel materials.[27,28]

1.4.3. Reaction of alpha olefins with carbon monoxide

The reactions of carbon monoxide with olefins fall into two main categories: methoxycarbonylation which is the addition reaction of carbon monoxide to the double bond of the olefin to produce an ester respectively and hydroformylation which converts α-olefins to aldehydes and alcohols.

1.4.3.1. Hydroformylation

Hydroformylation is an important industrial process for the synthesis of aldehydes, alcohols, carboxylic acids and esters. Figure 1.2 summarizes some of the possibilities for hydroformylation reactions.

$$RHC=CH_2 \xrightarrow{\substack{CO/H_2 \\ CAT}} RCH_2CH_2CHO \ + \ RCH(CH_2)CHO$$

Aldehydes

H_2/CAT

$$\xrightarrow{\substack{CO/2H_2 \\ CAT}} RCH_2CH_2CH_2OH \ + \ RCH(CH_2)CH_2OH$$

Alcohols

Caustic Fusion

$$\xrightarrow{\substack{CO/H_2O \\ CAT}} RCH_2CH_2CO_2H \ + \ RCH(CH_2)CO_2H$$

Carboxylic Acids

Methanol Water

$$\xrightarrow{\substack{CO/CH_2OH \\ CAT}} RCH_2CH_2CO_2CH \ + \ RCH(CH_2)CO_2CH$$

Methyl Esters
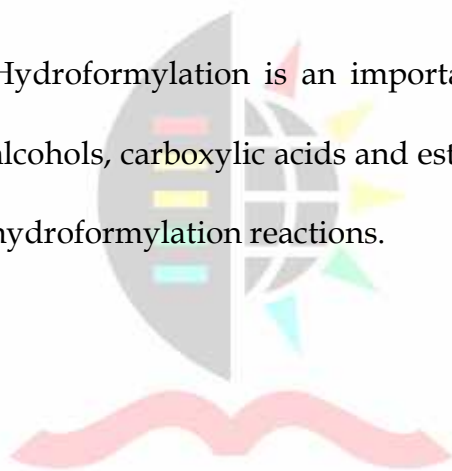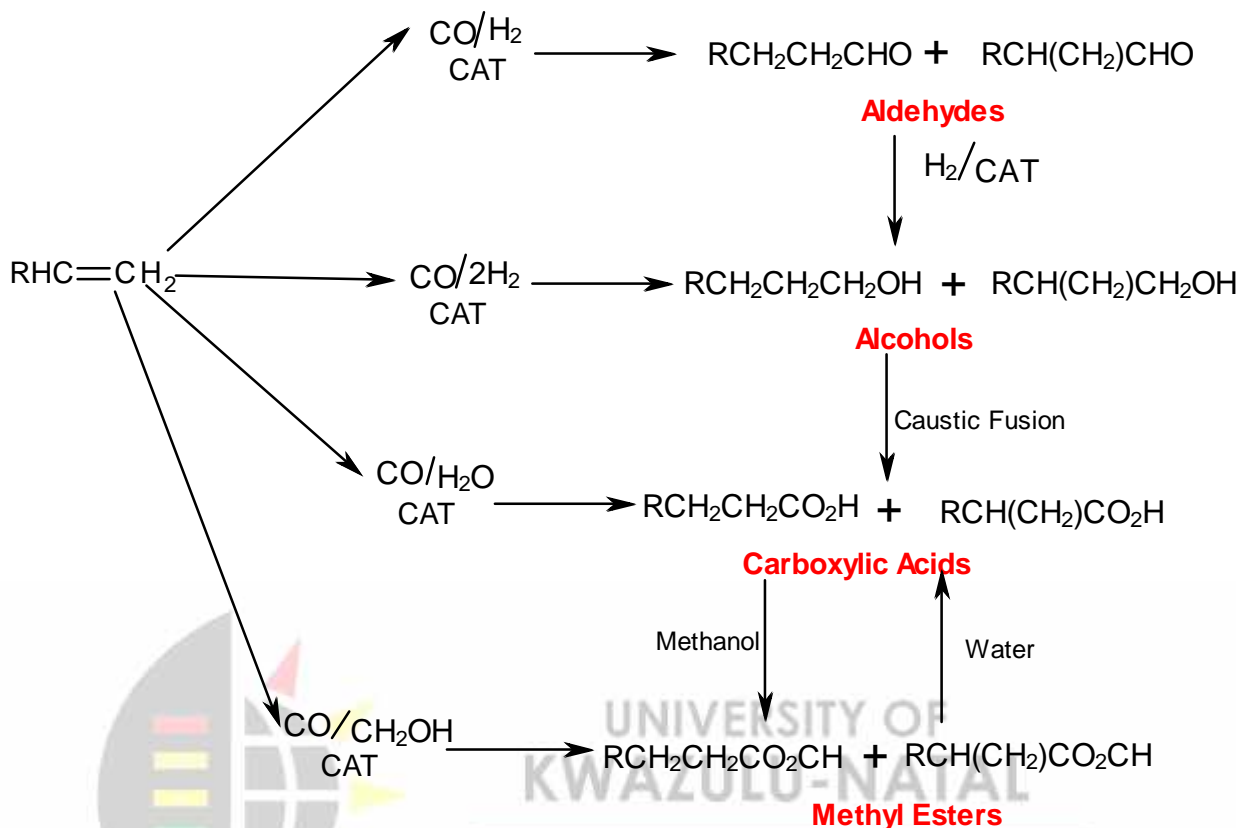
Figure 1.2: Hydroformylation of alkenes to aldehyde and associated products.

Otto Roelen was the first person to discover hydroformylation in 1938.[29] Roelen was able to observe that ethylene, H_2 and CO can be converted into propanal at higher pressures. The production of $HCo(CO)_4$ as an active catalysts for the hydroformylation under H_2/CO pressure using cobalt salts was discovered by Roelen.[30] The general mechanism for the hydroformylation was proposed in 1960 and 1961 by Heck and Breslow.[31] Hydroformylation of olefins can be used for the manufacturing of $C_3 - C_{40}$ aldehydes and alcohols. The resulting aldehydes are converted to detergents. Hydroformylation of ethylene can lead to the formation of propionaldehyde and n-

propanol as major products. Propionaldehyde and n-propanol can be applied as solvent precursors in the manufacture of pharmaceuticals, pesticides and perfumery products.[31]

1.4.3.2. Methoxycarbonylation

Methoxycarbonylation is the addition reaction of CO and an alcohol (methanol) to the double bond of the olefin to produce an ester. The methoxycarbonylation of olefins can be achieved in several appropriate ways. The first example is the methoxycarbonylation of olefins in the presence of a palladium (II) salt for example $PdCl_2$ and methanol (Scheme 1.4).[32]
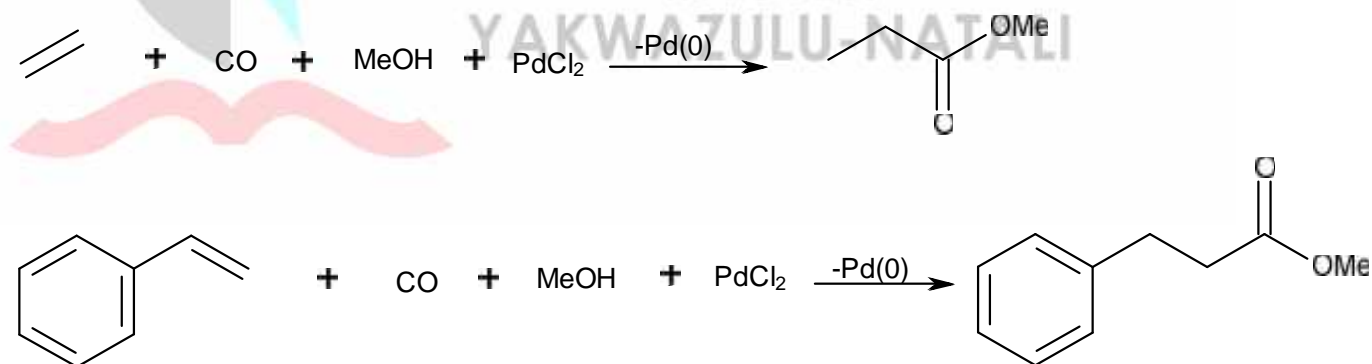
Scheme 1.4: Methoxycarbonylation of olefins in the presence of a stoichiometric amount of PdCl₂ and methanol.

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In the absence of a suitable oxidant the methoxycarbonylation of alkenes with Pd(II) salts and methanol (or other alcohols) is designated methoxycarbonylation (Scheme 1.5).[32] Both the branched and linear products in Scheme 1.5 can be used as valuable building blocks for other functionalized olefins, such as carboxylic acid, aldehydes and many more.

L = donor ligand
N^N or P^P
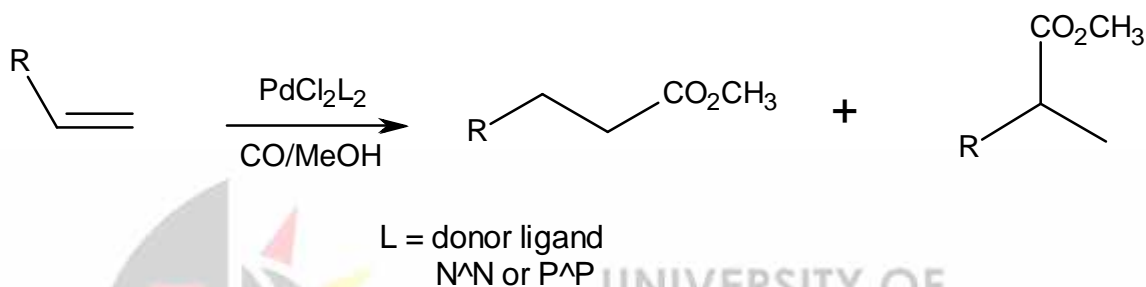
Scheme 1.5: Methoxycarbonylation of alkenes in the absence of a suitable oxidant

Seayad *et al.* have proposed a mechanism of methoxycarbonylation of styrene employing Pd(OAc)$_2$ and *p*-TsOH as a promoter in methanol solution.[33] Several years later, a mechanism for the methoxycarbonylation of 1-(4-isobutylphenyl) ethanol employing a homogeneous PdCl$_2$ (PPh$_3$)$_2$/TsOH/LiCl catalyst system was also proposed.[34] An anionic Pd(0) species containing coordinated Cl$^-$ has been suggested as the likely species in the catalytic cycle in the presence of TsOH and LiCl. Liu *et al.*[35] also reported the hydride and methoxycarbonyl cycles using [Pd(dipp)CH$_3$)(TsOH)] for Pd-catalyzed reactions.

1.4.3.2.1   Mechanism of palladium (II) catalyzed methoxycarbonylation reactions

Scheme 1.6 represents a proposed hydride cycle for the methoxycarbonylation of olefins using nitrogen donor palladium-based catalysts and HCl as an acid promoter in methanol solution. The hydride cycle (Scheme 1.6, ligands ommitted) starts with the addition of PPh$_3$ as a stabilizer and HCl (acid promoter) to **A**, resulting in a cationic species **B** which upon reduction with methanol results in intermediate **C** and forms **D**. Coordination of the substrate, followed by insertion into the Pd-H bond then leads to the formation of Pd-alkyl complex **F** or **K**, which is converted into an acyl complex **H** or **M** by migratory insertion of CO. Nucleophilic attack of methanol on the acyl carbonyl leads to the formation of **I** (linear ester) or **N** (branched ester) depending on regioselectivity.
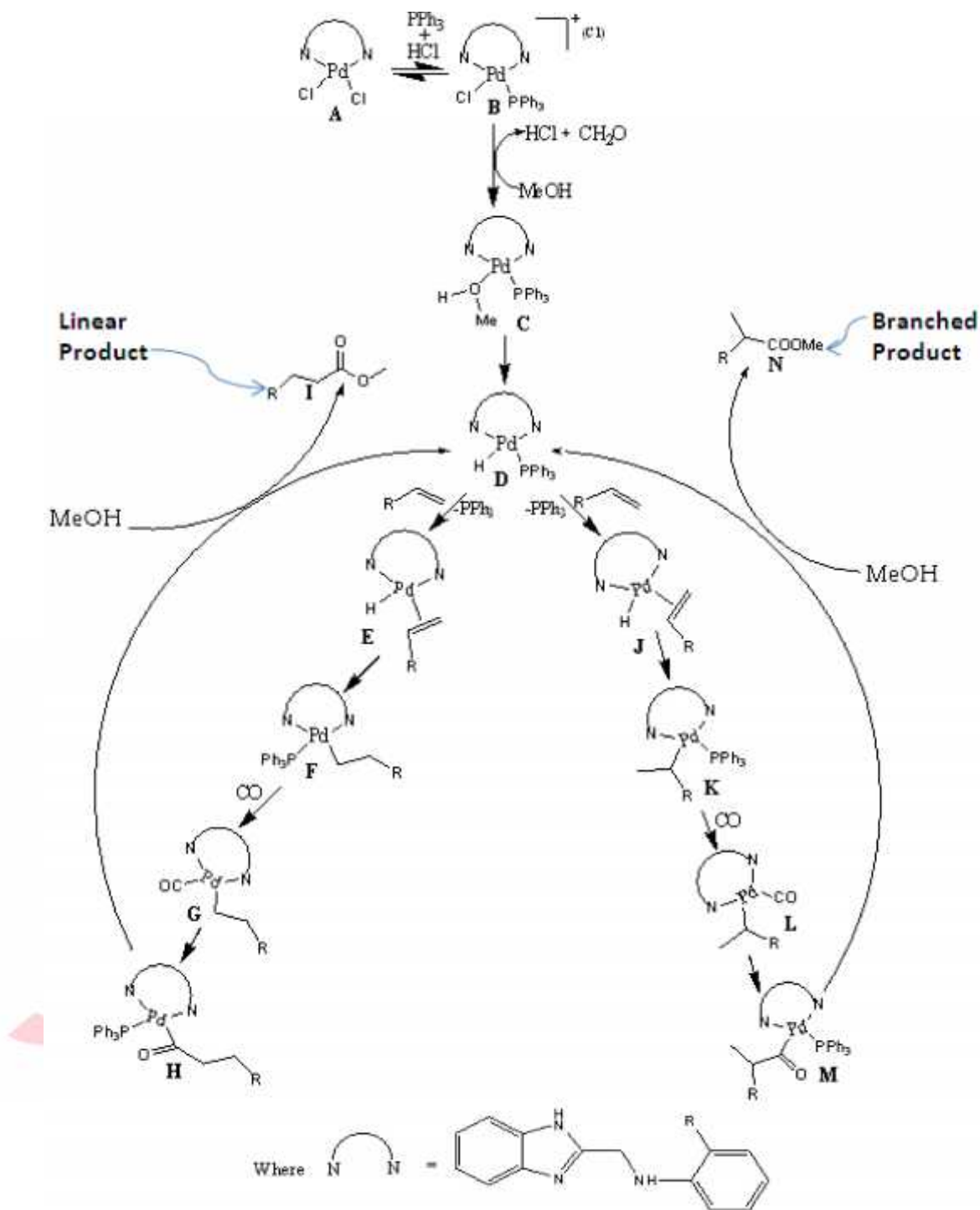
Scheme 1.6: Hydride cycle for palladium catalyzed methoxycarbonylation reactions

Scheme 1.7 represents a proposed methoxycarbonyl cycle for the methoxycarbonylation of olefins using nitrogen donor palladium-based catalysts. The methoxycarbonyl cycle starts with a Pd-OMe complex **O**. Then, the insertion of CO into the Pd-OMe leads to the production of methoxycarbonyl complex **P** or **T**. Coordination and insertion of the

appropriate substrate followed by methanolysis to produce the products **S** (linear ester) or **W** (branched product) depending on regioselectivity and regenerate the catalysts.
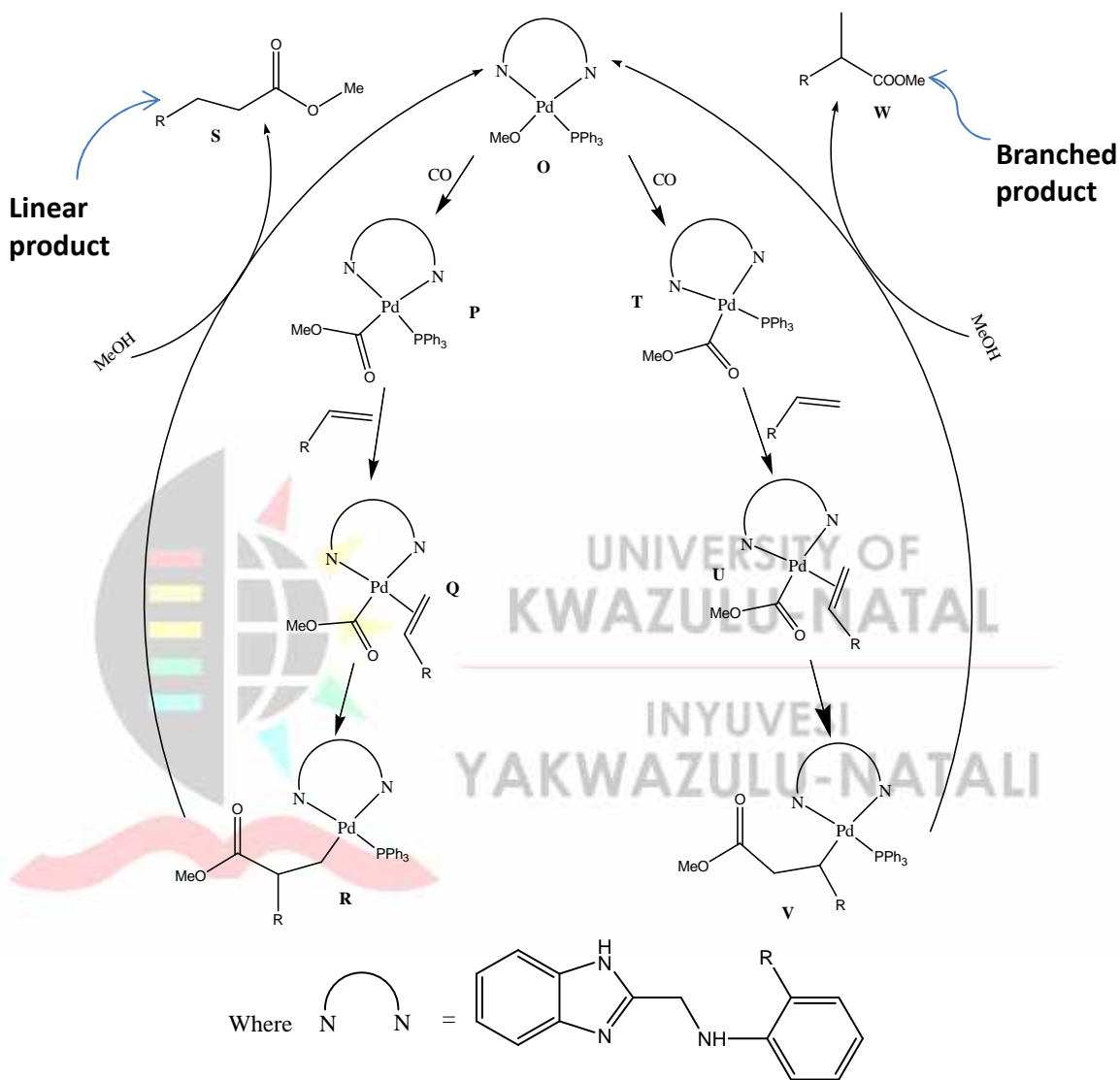
Scheme 1.7: Carbomethoxy cycle for palladium catalyzed methoxycarbonylation reactions.

1.4.3.2.2   Significance of the methoxycarbonylation products

The ester products obtained from the methoxycarbonylation reactions can be used for the formation of detergents, surfactants as well as perfumes. Scheme 1.8 is a representation of a possible route for the formation of detergents from esters.[36] Addition of sulfur trioxide to the linear ester **X** results in the formation of **Y** which upon addition of NaOH to the olefin sulfonate **Y** results in the formation of methyl ester sulfonate (MES). MES is used as an anionic surfactant in liquid soaps and detergents to clean wool.[36]
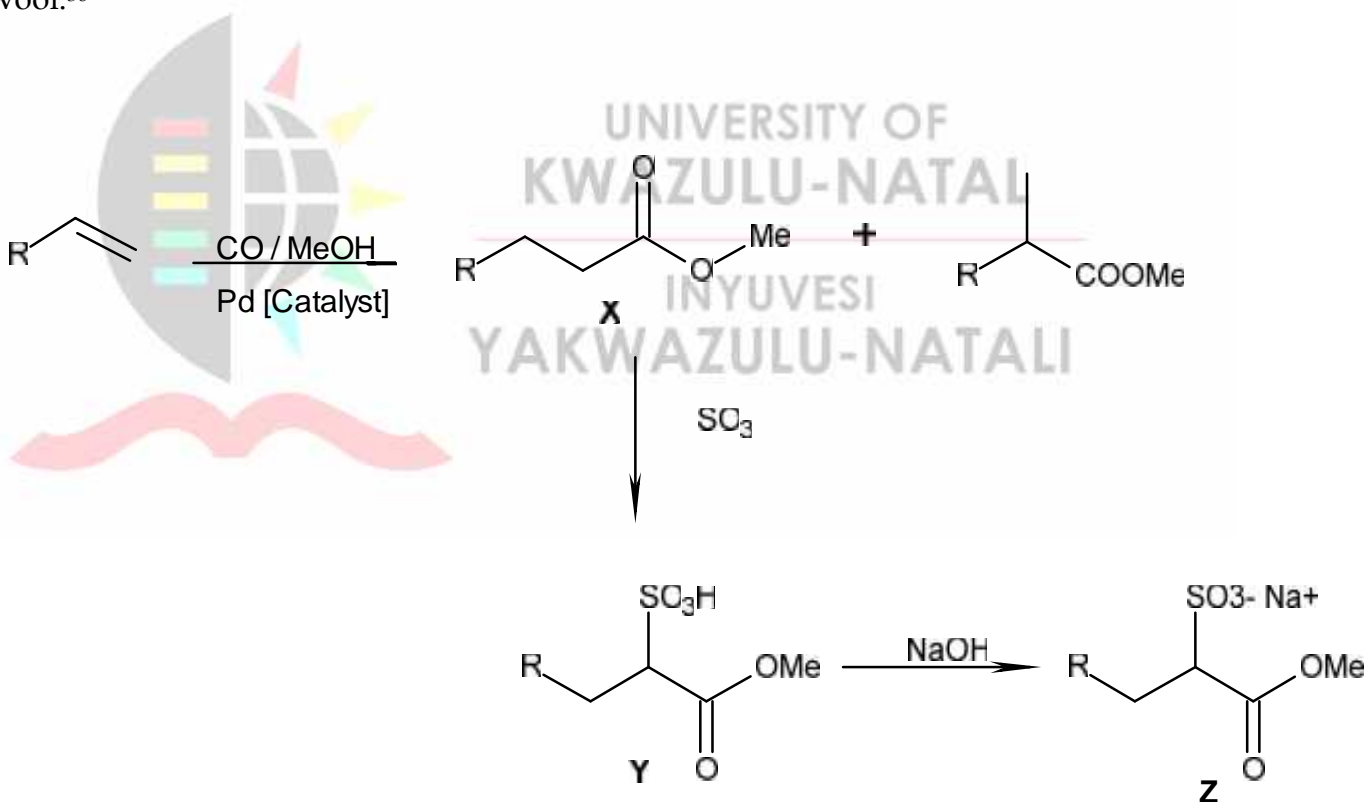
Scheme 1.8: Formation of detergents from esters.

From this chapter, it is clear that the significance of α-olefins from the academic and industrial point of view is clearly evident. This therefore justifies current research efforts being spent in the design of transition metal catalysts active for the methoxycarbonylation of higher α-olefins such as 1-octene, 1-nonene, 1-decene, 1-dodecene, 1-tetradecene and 1-octadeceneto produce esters (branched and linear). This is mainly aimed at designing and developing active, stable and selective catalysts. In the next chapter, a review of Pd(II) complexes as olefin methoxycarbonylation catalyst is described.

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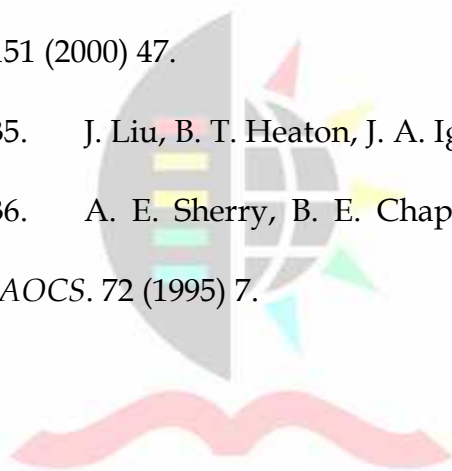
<div align="center">**CHAPTER TWO**</div>

Review of palladium complexes as alpha olefin methoxycarbonylation.

2.1.   General Introduction

Transition –metal complexes such as Pd[1-5], Rh[6], Ru[7], Co[8]and Ni[9] complexes have been used along with phosphine ligands in most methoxycarbonylation reactions. To date palladium-catalysts were found to be most active and have generated the most interest in the methoxycarbonylation of olefins. This is due to the fact that the electrophilicity of the palladium metal centers results in rapid rates of olefin insertion and coordination.[10] The high regioselectivity towards the branched or linear products can be obtained, depending on the catalytic system used and reaction conditions employed. In the next sections, we review a range of palladium complexes supported by different donor ligands that have been used as catalysts in the methoxycarbonylation reactions.

2.2   Palladium – based catalystsin methoxycarbonylation reactions

Palladium has been extensively and successfully used as catalysts in methoxycarbonylation reactions. The palladium can either be Pd^0 (Pd metal and PdL_4) or Pd(II) (PdX_2 and PdX_2L_2) species.[2] It has been established that palladium catalysts tend to decompose to palladium black[11,12] or form dinuclear complexes[13] if not stabilized. This transformation renders the systems inactive.[14]

Substances such as acid promoters play a major role in the stabilization and activity of palladium catalysts.[15] The role of acid promoters is to transform the Pd(0) to Pd(II) which is very active and then form palladium-hydride species (Scheme 2.1).[16,17]

$$Pd^0 \ + \ HX \longrightarrow HPdX$$

$$HPdX \ + \ HX \longrightarrow \ PdX_2 + H_2$$
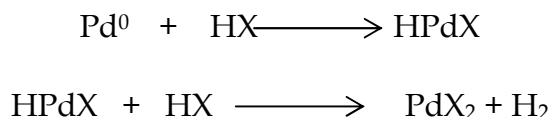
Scheme 2.1: Generation of the hydride intermediate using an acid promoter.

The hydride intermediate from scheme 2.1 initiates the catalytic cycle by reacting with the hydrocarbon substrates[18,19,20] leading to an increase in the reaction rates.[21,22,23]

The choiceof Brønsted acid in the methoxycarbonylation reaction is significant because it is able to determine the type of the counterion available for the palladium species.[24] Strongly coordinating anions reduce the rate of the addition of CO to an olefin, whereas weakly coordinating or non-coordinating anions increase the rate of the addition of CO.[25,26] Strong Brønsted acids such as methanesulfonic acid (MSA) and *p*-toluenesulfonic acid (*p*-TsOH) are used to achieve the required reaction rates[27] and they contain weakly coordinating anions.

Although the counterion plays an important role in achieving the required reaction rates, a substrate also plays a significant role in determining which promoter would allow most reaction activity. Therefore the order of activity has been determined when

different Brønsted acids are used and the order varies with the substrate used. For instance if styrene is used as a substrate, the activity decreases in the order *p*-toluene sulfonicacid (*p*-TsOH) > methane sulfonic acid (MSA) > trifluoro methanesulfonic acid > trifluoro acetic acid > hydrochloric acid.[28] However when propene is used the series differs, trifluoro methanesulfonic acid > sulfuric acid > *p*-toluene sulfonic acid (TSA) > hydrochloric acid.

2.2.1 Phosphine-donor palladium based catalysts in methoxycarbonylation reactions

The ligand plays a critical role in catalyst stability (by preventing the formation of palladium black[29]), activity as well as selectivity in methoxycarbonylation reactions. The steric and electronic effects of the ligand affect the reaction outcome.[30] Various ligands such as phosphine systems have been used in the methoxycarbonylation reactions to improve or direct reactivity.

The methoxycarbonylation of ethene has been studied both experimentally[31] and theoretically[32], catalyzed by phosphine ligands of types **1** and **2**. It was found that monodentate phopshines (Figure 2.1) favor methoxycarbonylation of ethene to methyl propanoate, while bidentate phosphines (Figure 2.2) switch selectivity to polyketones.[33]

1

2
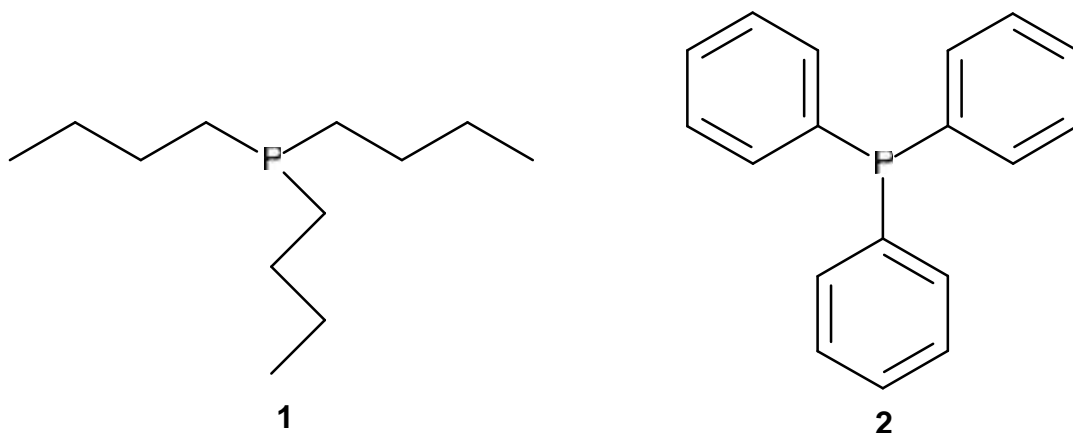
Figure 2.1: Monodentate alkyl phosphine ligand (P(*n*Bu)₃) ( ) and monodentate aryl phosphine ligand (PPh₃) ( ).

3

4
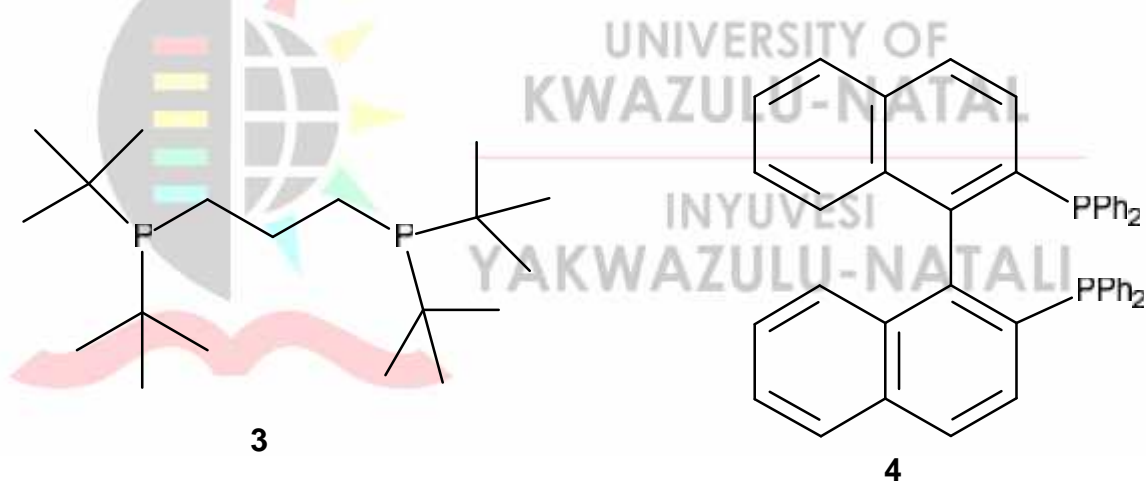
Figure 2.2: Bidentate alkyl phosphine ligand (dtbpp) ( ) and bidentate aryl phosphine ligand (BINAP) ( ).

Fine–tuning the ligand is essential in regulating the performance of methoxycarbonylation reactions. For example, 2-Pyridyl ligands work best for all alkyne conversions but are inactive in the conversion of alkenes.[34,35] The bulky bidentate alkyl phosphinesare preferred for alkenes.[36,37] It has also been discovered that the

increased basicity and steric bulk of the bidentate alkyl phosphine ligands alters the selectivity of Pd catalysts from polyketones to esters.[2] Recent computational studies also confirmed that methoxycarbonylation prevails over polymerization when bidentate alkyl phosphine ligands are used.[2]

Drent's group at Shell[38] carried out extensive ligand screening for the methoxycarbonylation of olefins using [Pd(AOc)$_2$L$_2$/L] system in the presence of acid promoters such as p-TsOH and HCl.[38] Drent's group at Shell[38] established that trialkyl monodentate phosphine ligands such as P(nBu)$_3$ are more effective than aryl monodentate phosphine ligands like PPh$_3$ in the methoxycarbonylation of olefins in the [Pd(AOc)$_2$L$_2$/L] catalyst system. In the presence of an acid promoter (HCl), the aryl monodentate phosphine (PPh$_3$) are more effective than trialkyl monodentate phosphine ligands (P(nBu)$_3$) in the methoxycarbonylation reactions.[39]

Palladium complexes of the type Pd(OTs)$_2$(PPh$_3$)$_2$ (**5**) and [(Pd(MeCN)$_2$(PPh$_3$)$_2$](Bf$_4$)$_2$ (**6**) (Figure 2.3) are well known to give high catalytic activities as well as selectivity in the methoxycarbonylation of styrene and ethene under mild conditions.[40,41] Rio and co-workers[42] discovered that the palladium catalysts containing mono-phosphine ligands favour the formation of branched esters, while palladium catalysts containing diphosphine ligands lead to the formation of linear esters.[42] In a further study, Guiu and co-workers[43] observed that both the bite angle of the chelate and electronic effects

of the ligand influence strongly the selectivity of the reaction towards the branched esters.[43]
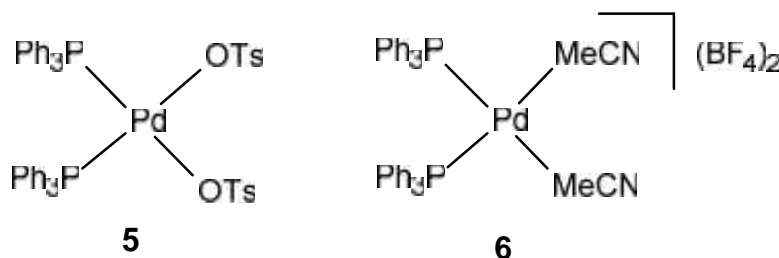
Figure 2.3: Palladium complexes providing high activity and selectivity for methoxycarbonylation of styrene and ethene under mild conditions.

2.2.2 Chiral phosphine-donor palladium catalysts in asymmetric methoxycarbonylation reactions

Asymmetric methoxycarbonylation of styrene has been studied to obtain 2-arylpropionic acids, which are used as non-steroidal anti-inflammatory drugs.[44] Palladium-based systems containing bidentate diphosphine ligands have been used for this reaction and they afford low regio- and enantioselectivity to the branched product[45] whereas palladium catalysts containing monodentate phosphine ligands provide high regioselectivities to the branched ester. Commetti and Chiusoli[46] reported the use of neomentyldiphenyl phosphine **7** (Figure 2.4), later Nozaki and co-workers[47] used phospholane ligand **8** and recently the same authors reported on the application of palladium complexes with binaphthol–derived phosphine **9** in the

methoxycarbonylation of vinylarenes achieving 53 % ee and 100 % regioselectivity to the branched esters.[48] A similar behaviour was observed by Rio and co-workers for related palladium-catalysed methoxycarbonylation of styrene, where they observed that palladium complexes containing monodentate ligands result in higher regioselectivity towards the branched esters, but low enantioselectivity, while palladium systems bearing bidentate ligands result in higher regioselectivity towards the linear esters.[42]
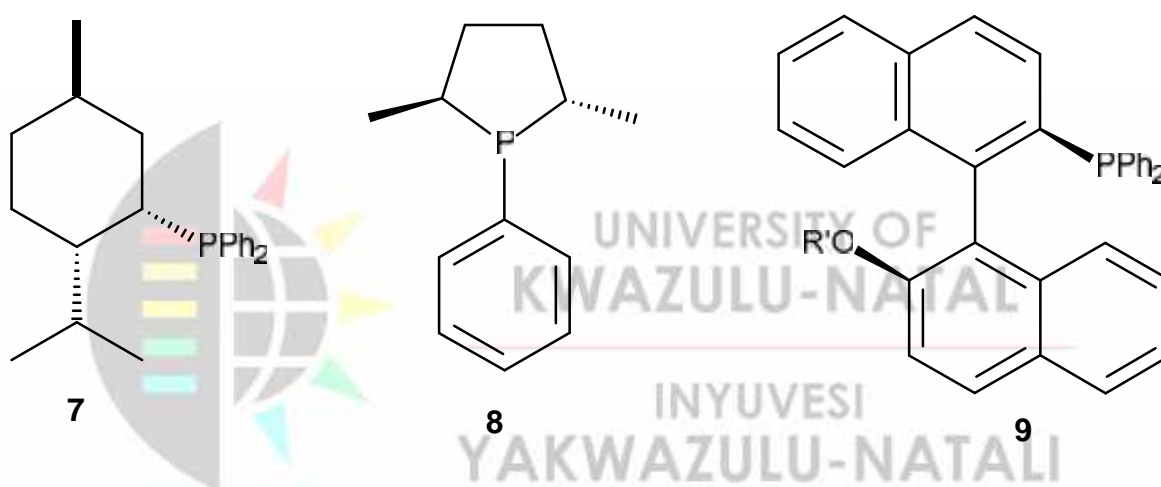
Figure 2.4: Monodentate phosphines used in asymmetric methoxycarbonylation of styrene.

In another related study, Mufioz and co-workers[49] reported the asymmetric methoxycarbonylation of styrene catalysed by palladium complexes containing monodentate chiral phosphetane ligands (Figure 2.5).[49] From their study, they discovered that, under mild conditions, the chemo- and regioselectivity towards the branched esters was higher.[49]
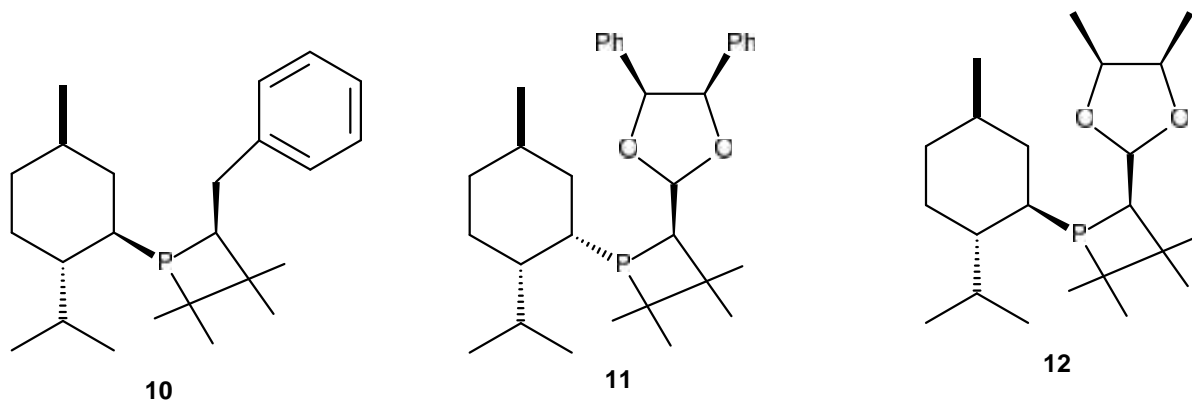
Figure 2.5: Chiral phosphetanes

2.2.3 Metallocene and non-metallocene diphosphine palladium catalysts in methoxycarbonylation reactions

Several chelating diphosphine ligands have been studied with those containing metallocenic fragments due to the fact that mono- and bidentate diphosphine ligands display low-regio - and enantioselectivity. Bianchini and co-workers[50], have proven in their study that palladium complexes with 1,1-bis(diphenylphosphino) ferrocene(ddf) **13** (Figure 2.6), 1,1-bis(diphenylphosphino) octamethylferrocene (dppomf) **14** (Figure 2.6), 1,1-bis(diphenylphosphino) ruthenocene(ddpr) **15** and 1,1-bis(diphenylphosphino) osmocene (dppo) **16** (Figure 2.6) can catalyse the methoxycarbonylation of styrene, with high regioselectivity(up to 85%) towards the linear esters.[50] The selectivity to linear esters was proven by Gusev and co-workers[51], whereby they stated that the steric and electronic properties of these mellocenes containing phosphine ligands should form M-

Pd (M = Fe, Ru and Os) bonds during the catalytic cycle thus favouring the formation of linear products.[51] however, the branched ester is the most desirable ester.
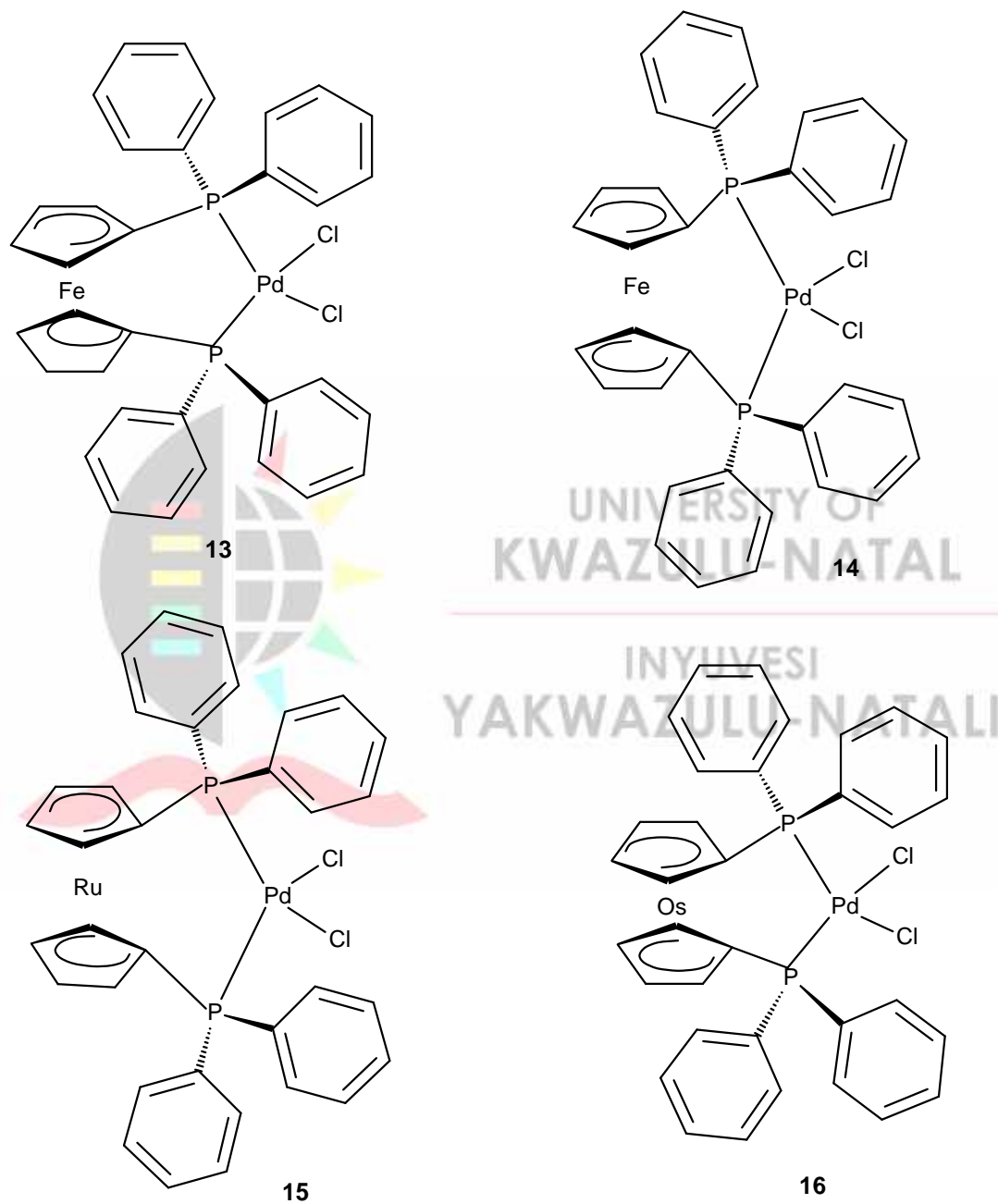
Figure 2.6: Diphosphine ligands containing metallocenic fragments.

Recently Zuniga and co-workers[52] reported palladium-catalysed methoxycarbonylation of vinylarenes using *trans*-[η^5-C$_5$H$_4$PPh$_2$)Re(CO)$_3$]PdCl$_2$(NCMe) **17** (Figure 2.7), a non-metallocenic organometallic ligand. They observed that the catalytic system *trans*-[η^5-C$_5$H$_4$PPh$_2$)Re(CO)$_3$]PdCl$_2$(NCMe) **17** (Figure 2.7) in the presence of HCl and methanol gave good catalytic activity, as well as high regioselectivity towards the branched esters (94 %).[52]

17
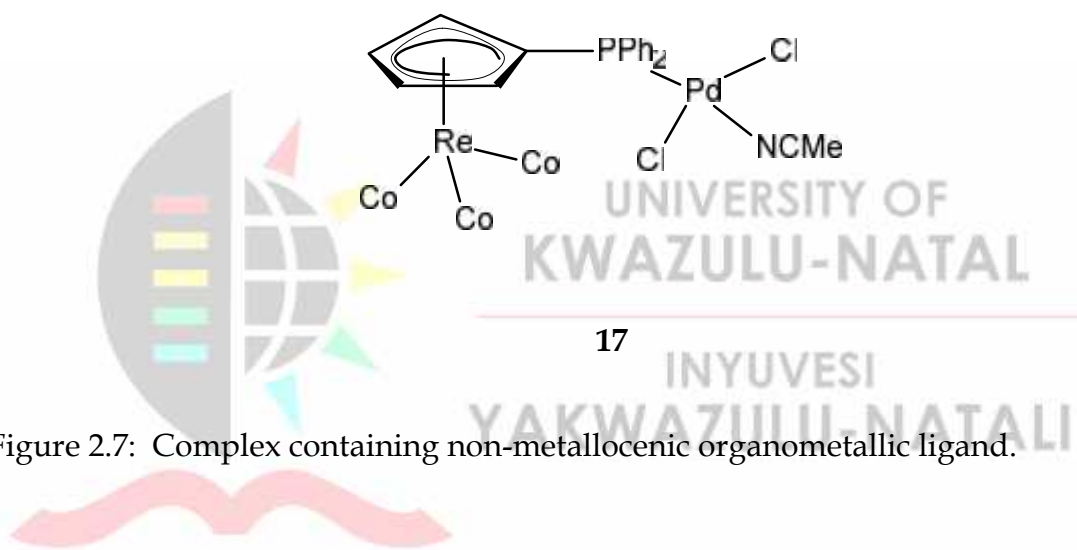
Figure 2.7: Complex containing non-metallocenic organometallic ligand.

2.2.4 Mixed nitrogen and phosphine–donor palladium catalysts in methoxycarbonylation reactions

Heterobidentate *P,N*-donor ligands have been used in metal-catalyzed methoxycarbonylation of olefins.[53] Pd (II) complexes containing these types of ligands were observed to be active in methoxycarbonylation reactions. Their activity in the methoxycarbonylation reactions results from the ease of substitution of the *N*-donor

fragment by CO ligand. In 2007, Aguire *et al.*[53] reported the methoxycarbonylation of olefins catalysed by palladium complexes bearing *P, N*-donor ligands (Figure 2.8).

18

R = H: Ph₂PNHpy
R = Me: Ph₂PNMepy

19

20
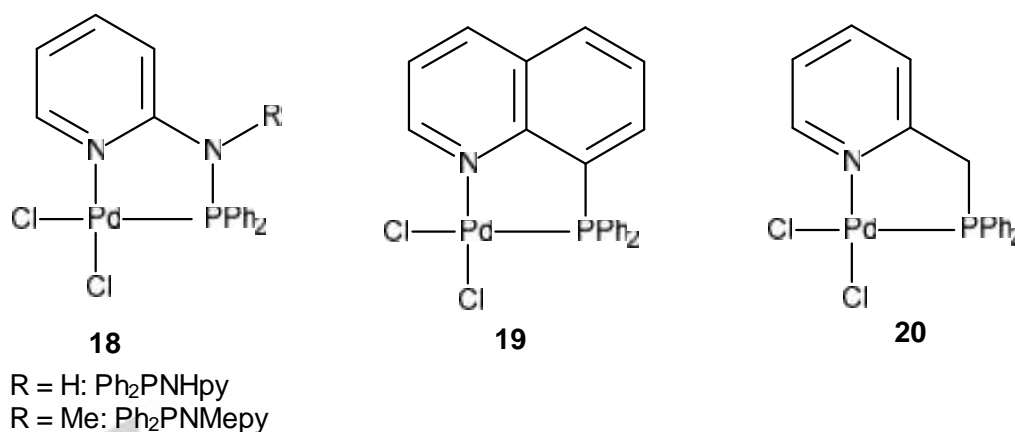
Figure 2.80:Pd-catalysts with*P, N*-donor ligands.

Aguire *et al*[53] observed that (Ph₂PNHPh) or (Ph₂PNMepy) catalytic system increases activity.[53] It was also observed that neutral complex **21** (Scheme 2.3) affords low conversions and selectivities towards the branched product. In addition, extensive decomposition of the neutral complexes to palladium black was observed.[53] Addition of PPh₃ to the neutral complexes (Scheme 2.3) dramatically improves the catalytic activities up to 99%, as well as higher regioselectivity (90%) towards the branched ester.[53] No decomposition was observed upon addition of PPh₃ indicating that PPh₃ enhances stability of the relevant cationic species.[53]

21   **22**
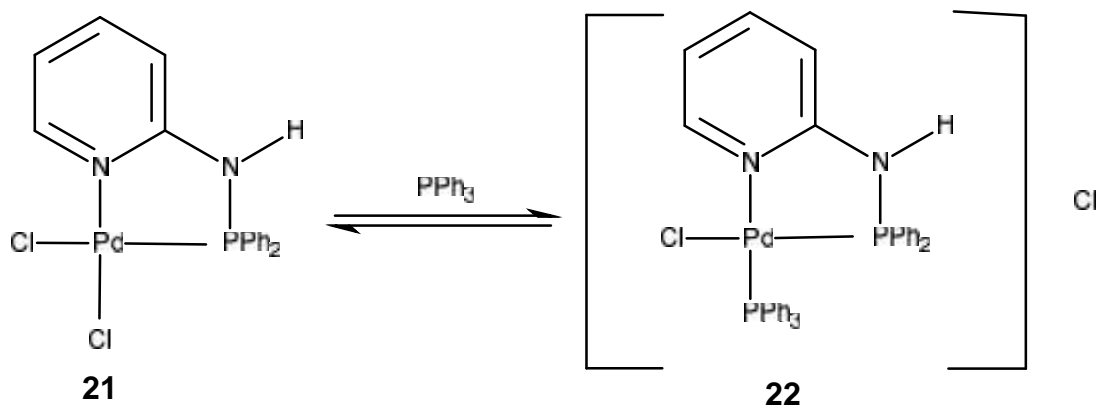
. . . . *et al.*[53]

Based on the literature review, the current work is aimed at producing a balance
between catalysts stability and activity. Our ligand design (benzoimidazol-2-yl) methyl
amines . . (Figure 2.9) is hemilabile in nature and should impact stability. The
palladium complexes used for methoxycarbonylation reaction will be the cationic
complexes . . (Figure 2.9). They were chosen due to the fact that the neutral complexes
are not stable. The cationic complexes have metal-phosphine bonding which can be
described by σ donation from the phosphorus lone pair to the metal center and π back
bonding from a filled metal orbital to the σ* P-R orbitals. Thus the π back bonding
capabilities of the triphenylphosphine ligand will result in a more positive Pd-metal
center which will promote coordination of substrates for the methoxycarbonylation
reaction. It has been reported that the diphosphine ligands have the disadvantage to

produce products in low-regio and enantioselectivity,[53] therefore in this study the phosphine (PPh₃) ligand will be used instead of the diphosphine ligand. Triphenylphosphine (PPh₃) also acts as a stabilizer.
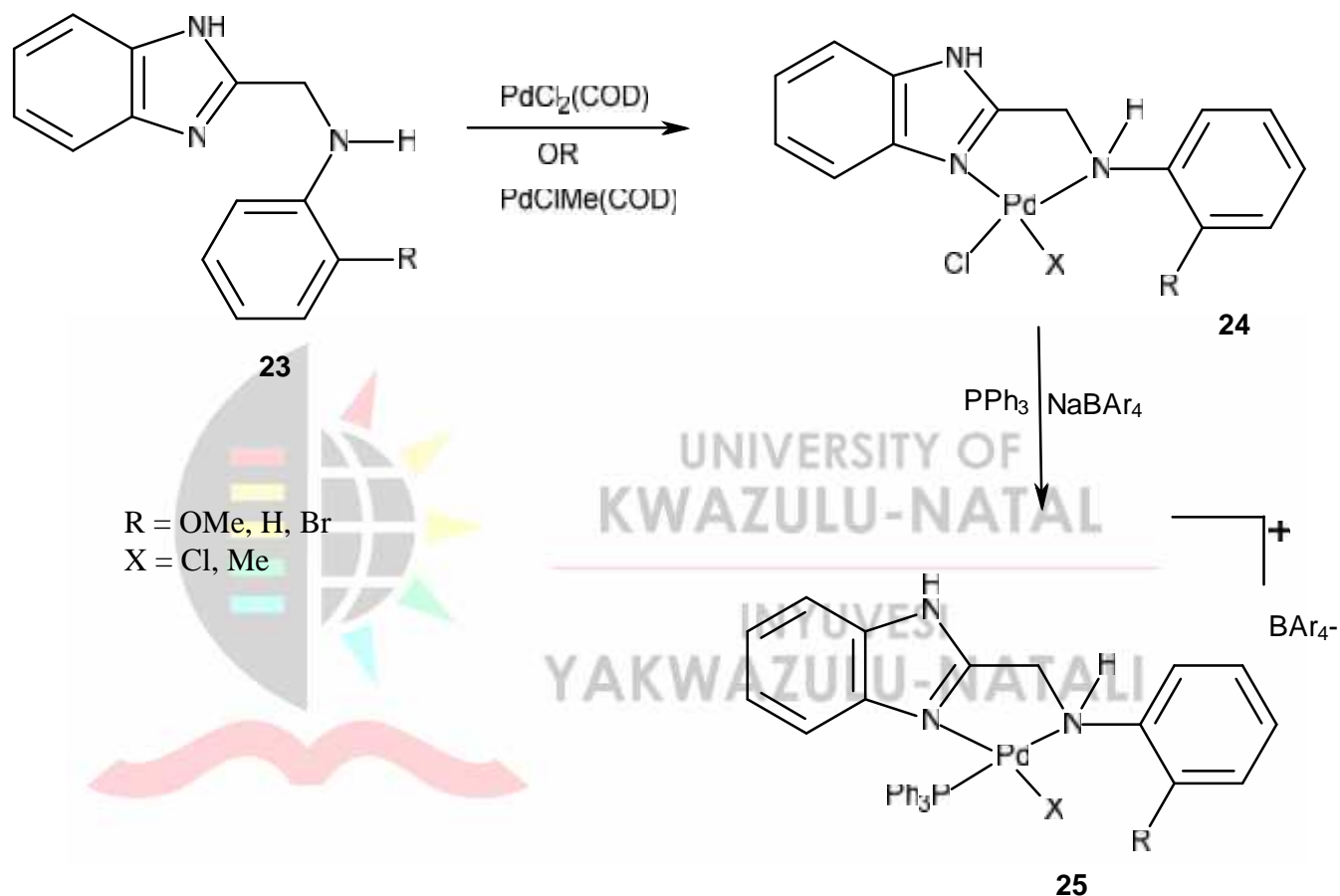
Figure 2.9: (Benzoimidazol-2-yl) methyl amine ligands that will be used for this study.

2.4   Aims and Objectives of the Study

General objective

- ❖ To develop efficient palladium catalysts for the methoxycarbonylation of higher olefins and fully understand the catalytic reactions.

Specific objectives

- ❖ To synthesize the (benzoimidazol-2-ylmethyl) amine ligands and their palladium complexes.

- ❖ To apply the palladium complexes as catalysts in the methoxycarbonylation of olefins.

- ❖ To investigate the effects of catalyst structure and reaction conditions in methoxycarbonylation reactions.
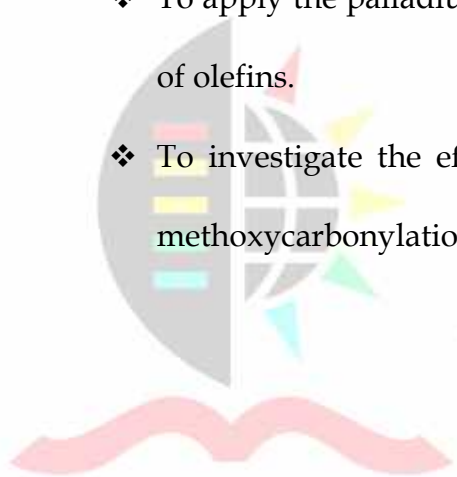
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Palladium(II) complexes of (benzoimidazol-2-ylmethyl) amine ligands: Synthesis,

Characterization and Molecular Structures

3.1.   Introduction

From the literature review in chapter 2, it is evident that the stability and activity of palladium catalysts in methoxycarbonylation reactions of olefins depend on the nature of the ligand coordinated to the metal center. Hemi-labile ligands discovered by Jeffery and Rauchfuss[1] in 1979 have the ability to occupy the vacant coordination site and hence stabilize active species during a catalytic cycle. The other classes of ligands that have been employed in methoxycarbonylation reactions are the phosphine type ligands. Bidentate phosphine ligands are reported to lead to co-polymer formation while monodentate phosphine ligands result in ester formation in the presence of methanol.[2] An illustration is the use of Pd(OTs)$_2$(PPh$_3$)$_2$ and [Pd(MeCN)$_2$(PPh$_3$)$_2$](BF$_4$)$_2$ which, when combined with HCl an acid promoter gives high activities and selectivities for the methoxycarbonylation reactions,[3,4] resulting in the formation of branched and linear esters respectively.

In this chapter, the synthesis of hemilabile ligands is reported.[5] These have been utilized in the production of neutral and cationic palladium complexes. The aim was to make a range of cationic(benzoimidazol-2-yl) methyl amine Pd(II) complexes for application as

potential catalysts in the methoxycarbonylation of olefins. The methoxycarbonylation of a range of olefins by these catalysts will be discussed in chapter four.

3.2. Experimental section

3.2.1 Materials and instrumentation

All moisture and air sensitive reactions were performed under dry nitrogen positive pressure conditions. Methanol, acetone, diethyl ether, dichloromethane, absolute ethanol, ethyl acetate, DMSO-d_6, potassium iodide (KI), sodium hydroxide (NaOH) and potassium hydroxide (KOH) were purchased from Merck. Chloroform ($CDCl_3$) was purchased from Sigma Aldrich. The chemicals, 2-chloromethylbenzimidazole, aniline (≥99.5%), 2-methoxyaniline (≥99.5%), 2-aminothiophenol (≥99%), and 2-bromoaniline (98%) were purchased from Sigma Aldrich and were used without further purification. $NaBAr_4$ (Ar = 3,5-$(CF_3)_2C_6H_3$) was obtained from Boulder Scientific and used as received. Starting materials [PdCl$_2$(COD)][6] and [PdClMe(COD)][7] were synthesized following literature methods. Thin-layer chromatography analysis was carried out on silica gel 60 F_{254} plates, eluting with the solvents indicated and visualized using a UV light. Column chromatography was performed using silica gel 60 PF_{254}.

 Nuclear magnetic resonance spectra (NMR spectra) were acquired at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 162 MHz for ^{31}P on a Bruker avance spectrometer equipped with Bruker magnet (9.395 T). All the spectra were obtained at 25℃. The abbreviations s, d, t, q and m denote singlet, doublet, triplet, quartet and multiplet. The chemical shift in

nuclear magnetic spectroscopy are all in ppm relative to $CHCl_3$ δ^1_H: 7.26 ppm and δ^{13}_C: 77.6 ppm and DMSO-d_6 δ^1_H: 2.50 ppm. Coupling constants are measured in Hertz, Hz. Elemental analyses were carried out using CHNS-O Flash 2000 Thermoscientific analyzer. Mass spectral analyses were conducted using micromass LCT premier mass spectrometer with Thermo LTQ XL.

3.2.2 Synthesis of (benzoimidazol-2-ylmethyl) amine ligands

3.2.2.1 *N*-(1*H*-benzoimidazol-2-ylmethyl)-2-aniline(L1)
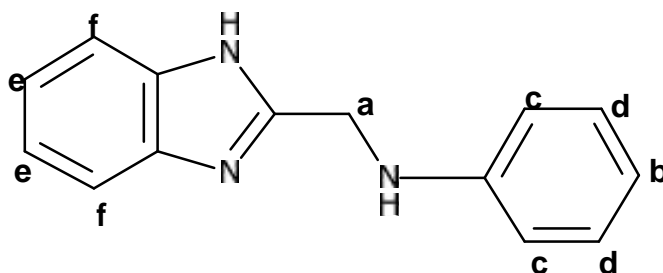
2-(chloromethyl) benzimidazole (1.66 g, 10.0 mmols) was dissolved in ethanol (20 ml) before adding aniline (0.94 g, 10.0 mmols) and KI (1.66 g, 10.0 mmols). The solution was then refluxed at 80°C for 6 h. A solution of NaOH (0.40 g, 10 mmols) in a 1:1 water/ethanol mixture was added to the mixture and the reaction was further refluxed for 2 h, the solution was cooled to room temperature and poured into ice/water to give a pale yellow precipitate. The mixture was filtered and the solvent removed *in vacuo* to afford **L1** as a brown solid. Yield = 1.25 g (56%). ^{1}H NMR (CDCl$_3$): $_H$ (ppm): 4.65 (s, 2H, H$_a$); 6.61 (t, 1H, $^3J_{HH}$= 7.20 Hz, H$_b$); 6.70 (d, 2H, $^3J_{HH}$ = 7.90 Hz, H$_c$); 6.98 (t, 2H, $^3J_{HH}$ = 7.70 Hz, H$_d$); 7.38 (dd, 2H, $^3J_{HH}$ = 7.13 Hz, H$_e$); 7.68 (dd, 2H, $^3J_{HH}$= 7.50 Hz, H$_f$). 8.30 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d$_6$): δ 42.38; 112.92; 116.93; 121.73; 129.34; 129.93; 138; 148.92; 154.17. MS (ESI) m/z (%) 224 (M$^+$, 100). HRMS-ESI ([M$^+$-H$^+$]): m/z calc: 223.1; found: 222.1.

3.2.2.2 *N*-(1*H*-benzoimidazol-2-ylmethyl)-2-methoxyaniline (L2)
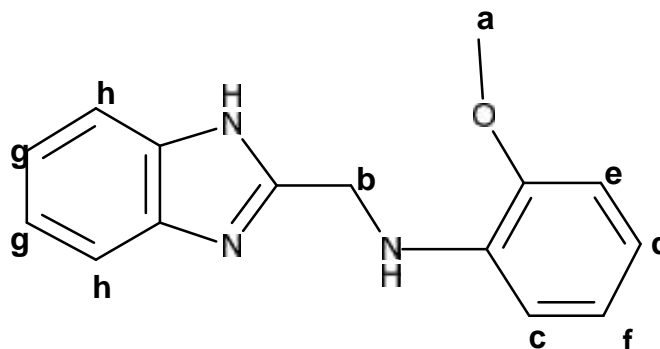
2-(chloromethyl) benzimidazole (1.68g, 10.3 mmol), 2-methoxyaniline (0.86 ml, 7.26 mmol) and KI (1.67g , 10.0 mmol) were dissolved in 50.0 ml of absolute ethanol and refluxed at 80°C for 6 h. KOH (0.44 g, 7.88 mmol) was dissolved in water and ethanol and was added to the mixture and refluxed for 2 h at 80 °C. The resultant solution was poured into ice/water and filtered. The sticky brown product was dissolved in methanol and evaporated *in vacuo*. The resultant brown product was purified by column chromatography using ethyl acetate: hexane (5: 3) to give **L2** as an analytically pure solid. Yield = 0.99 g (48%). ^{1}H NMR (CDCl$_3$): δ_H (ppm): 3.80 (s, 3H, H$_a$); 4.65 (s, 2H, H$_b$); 6.58 (d, 1H, $^3J_{HH}$= 6.90 Hz, H$_c$); 6.76 (m, 4H, H$_d$, H$_e$ and H$_f$); 7.24 (dd, 2H, $^3J_{HH}$= 5.40 Hz, H$_g$); 7.54 (dd, 2H, $^3J_{HH}$= 2.00 Hz, H$_h$). 8.75 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d$_6$): δ 42.20; 55.77 ; 110.00 ; 110.26 ; 116.88 ; 121.44 ; 138.08 ; 147.07; 154.06. MS (ESI) m/z (%) 254 (M$^+$, 100). HRMS-ESI ([M$^+$ + Na$^+$]): m/z calc: 276.3; found: 276.1.

3.2.2.3 *N*-(1*H*-benzoimidazol-2-ylmethyl)-2-thioaniline (L3)
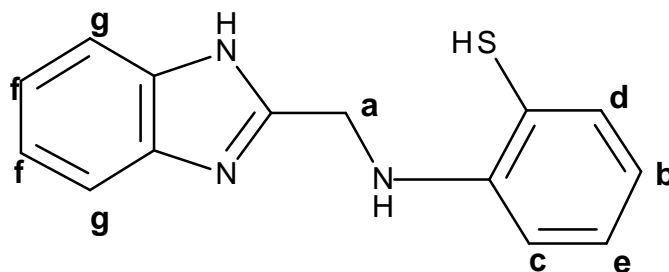
Compound **L3** was prepared according to the procedure described for **L1** using 2(chloromethyl) benzimidazole (0.93 g, 5.58 mmol), 2-aminothiophenol (0.60 ml, 5.58 mmol), KI (0.92 g, 5.59 mmol) and KOH (0.32 g, 7.88 mmol). The crude product was dissolved in CH_2Cl_2 (20 ml), filtered off and the solvent removed to afford **L3** as a yellow solid. Yield = 1.39 g (89%). ^{1}H NMR (CDCl$_3$): $_H$ (ppm): 4.20 (s, 2H, H$_a$); 5.56 (s, 1H, *S-H*); 6.53 (t, 1H, $^3J_{HH}$ = 7.88, H$_b$); 6.64 (d, 1H, $^3J_{HH}$ = 6.30, H$_c$); 6.72 (d, 1H, $^3J_{HH}$ = 8.93, H$_d$); 7.01 (t, 1H, $^3J_{HH}$ = 7.35, H$_e$); 7.24 (dd, 2H, $^3J_{HH}$= 7.88, H$_f$); 7.52 (dd, 2H,$^3J_{HH}$= 5.25, H$_g$). 8.25 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d$_6$): δ 32.06; 114.95; 115.48; 116.54; 130.23; 131.59; 135.46; 135.86; 149.75; 150.20; 151.93. MS (ESI) m/z (%) 257 (M$^+$, 100). HRMS-ESI ([M$^+$- H$^+$]): m/z calc: 254.33; found: 254.12.

3.2.2.4   *N*-(1*H*-benzoimidazol-2-ylmethyl)-2-bromoaniline (L4)
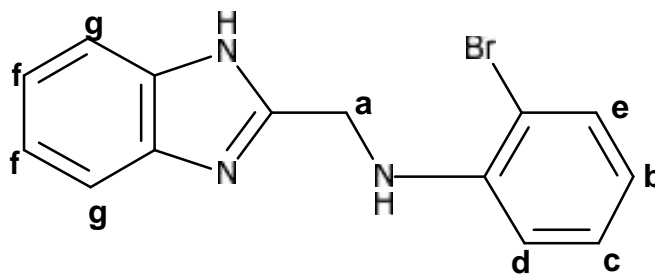
Compound **L4** was prepared according to the procedure described for **L1** using 2(chloromethyl) benzimidazole (1.08 g, 6.45 mmol), 2-bromothiophenol (1.11 ml, 6.45 mmol), KI (0.73 g, 6.45 mmol) and KOH (0.37 g, 6.45 mmol). Mixture was poured into ice/water; this resulted in the formation of a bright yellow precipitate. The precipitate was dissolved in methanol and filtered. The resultant filtrate was evaporated *in vacuo*. The product was purified by column chromatography using 5:1 diethyl ether: hexane solvent system to yield **L4** as a pale yellow precipitate. Yield = 1.53 g (79%). H NMR (DMSO-d): δ 4.60 (s, 2H, H); 5.94 (t, 1H,$^3J_{HH}$= 7.11, H); 6.66 (t, 1H, $^3J_{HH}$= 8.29, H); 6.67 (d, 1H, $^3J_{HH}$= 1.50, H); 7.12 (d, 1H, $^3J_{HH}$ = 2.81, H); 7.14 (d, 2H, $^3J_{HH}$ = 3.43, H); 7.44 (d, 2H, $^3J_{HH}$= 1.70, H). 8.75 (s, 1H, *N-H*). C NMR (DMSO-d): 55.36; 109.26; 112.08; 118.31; 121.90; 129.09; 132.73; 145.22; 153.34. MS (ESI) m/z (%) 302 (M + H, 100). HRMS-ESI ([M]): m/z calc: 302.22; found: 302.01.

3.2.3 Synthesis of neutral and cationic complexes

3.2.3.1 Syntheses of neutral complexes

3.2.3.1.1   [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-aniline}PdCl₂] (C1)
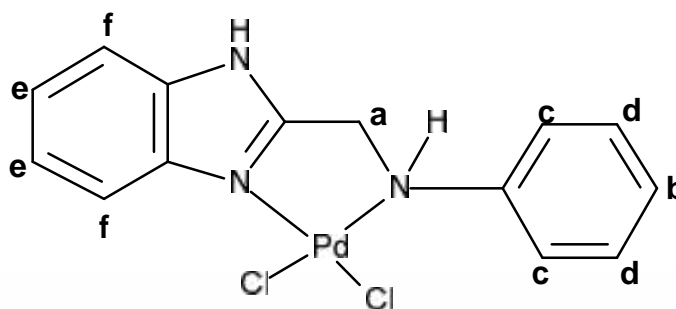
To a solution of **L1** (0.10 g, 0.45 mmol) in CH_2Cl_2 (10 ml) was added a solution of [Pd(COD)Cl₂] (0.13 g, 0.45 mmol) in CH_2Cl_2 (10 ml). The mixture was stirred overnight under nitrogen, filtered and the material isolated recrystallized from CH_2Cl_2- hexane to give a light yellow solid. Yield = 0.13 g (80%). ¹H NMR (DMSO): $_H$ (ppm): 4.58 (s, 2H, H_a); 6.62 (t, 1H, $^3J_{HH}$= 4.70, H_b); 6.78 (d, 2H, $^3J_{HH}$ = 7.50, H_c); 7.26 (t, 2H, $^3J_{HH}$= 5.09, H_d); 7.38 (dd, 2H, $^3J_{HH}$ = 7.83, H_e); 7.46 (dd, 2H, $^3J_{HH}$ = 8.22, H_f); 13.28 (s, 1H, *N-H*). ¹³C NMR (DMSO-d₆): 42.31; 113.56; 115.33; 117.20; 123.00; 129.65; 137.91; 138.90; 143.50. MS (ESI) m/z (%) 224 (M+- Cl₂ - Pd, 92%). Anal. Calc. for $C_{14}H_{13}N_3PdCl_2$: C, 41.97; H, 3.27; N, 10.49. Found: C, 41.92; H, 3.88; N, 10.99.

3.2.3.1.2 [{N-(1H-benzoimidazol-2-ylmethyl)-2-aniline}PdClMe] (C2)
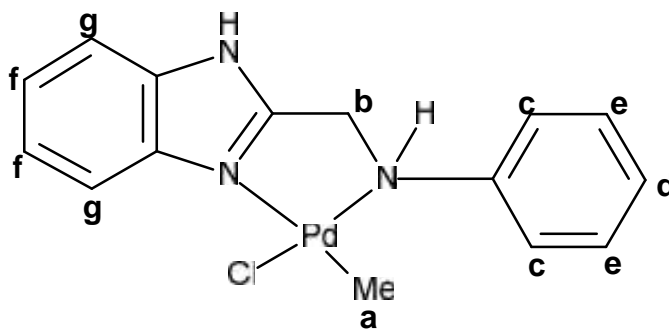
Complex **C2** was synthesized following the procedure described for **C1. L1** (0.20 g, 0.89 mmol) in Et$_2$O (10 mL) and [PdCl(COD)Me] (0.21 g, 0.89 mmol) in Et$_2$O (10 mL). The material was isolated, recrystallized from CH$_2$Cl$_2$- hexane to give a light yellow solid. Yield = 0.218 g (87%). ^{1}H NMR (CDCl$_3$): δ$_H$ (ppm): 0.82 (s, 3H, H$_a$); 5.50 (s, 2H, H$_b$); 6.63 (d, 2H, $^3J_{HH}$= 6.74, H$_c$); 6.78 (t, 1H,$^3J_{HH}$= 7.58, H$_d$); 7.07 (t, 2H, $^3J_{HH}$= 3.21, H$_e$); 7.33 (dd, 2H, $^3J_{HH}$= 5.90, H$_f$); 7.50 (dd, 2H, $^3J_{HH}$= 7.75, H$_g$); 13.15 (s, 1H, *N-H*). MS (ESI) m/z (%) 224 (M+- Cl$_2$- Pd, 85%). Anal. Calc. for C$_{15}$H$_{16}$N$_3$PdCl: C, 47.39; H, 4.24; N, 11.05. Found: C, 48.93; H, 4.04; N, 10.99.

3.2.3.1.3   [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-methoxyaniline}PdCl$_2$] (C3)
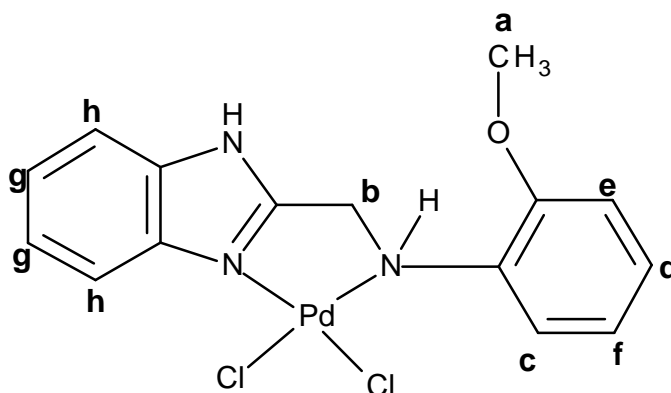
Complex **C3** was synthesized following the procedure described for **C1** using **L2** (0.20 g, 0.83) and[Pd(COD)Cl$_2$] (0.22 g, 0.83 mmol) in CH$_2$Cl$_2$ (10 mL). Yield = 0.27 g (77%). ^{1}H NMR (DMSO): $_H$ (ppm): 0.78 (s, 3H, H$_a$); 4.90 (s, 2H, H$_b$); 6.48 – 6.57 (d, 1H,$^3J_{HH}$ = 7.60, H$_c$); 6.59 (t, 1H, $^3J_{HH}$ = 5.36, H$_d$,); 6.61(d, 1H, $^3J_{HH}$ = 4.98, H$_e$,); 6.69 (d, 1H, $^3J_{HH}$ = 6.51, H$_f$,); 6.84 (dd, 2H, $^3J_{HH}$= 4.80, H$_g$); 7.07 (dd, 2H, $^3J_{HH}$= 7.66, H$_h$). 13.18 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d$_6$): 36.50; 55.99; 114.10; 115.40; 118.25; 121.95; 123.01; 129.10; 137.93; 138.65; 141.55; 144.77. MS (ESI) m/z (%) 254 (M+-Cl$_2$–Pd, 100%). Anal. Calc. for C$_{15}$H$_{13}$N$_3$PdCl$_2$.0.75CH$_2$Cl$_2$: C, 38.97; H, 3.06; N, 8.66. Found: C, 39.01; H, 3.66; N, 8.76.

3.2.3.1.4 [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2methoxyaniline}PdClMe] (C4)
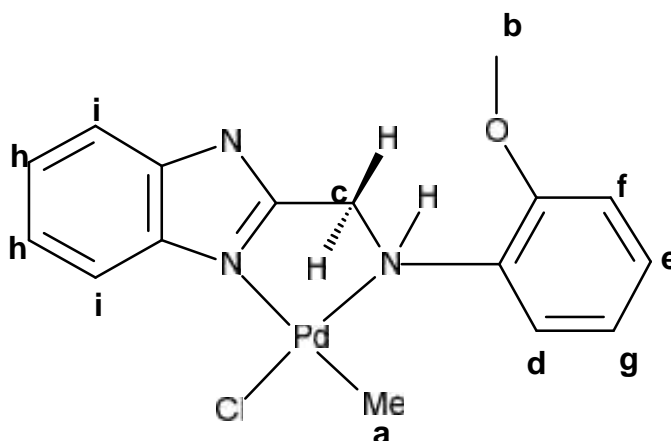
Complex **C4** was synthesized following the procedure described for **C1** using **L2** (0.10 g, 0.41 mmol) and [PdCl(COD)Me] (0.10 g, 0.350 mmol) in Et$_2$O (10 mL). Yield = 0. 09 g (63%). ^{1}H NMR (DMSO-d$_6$): $_H$ (ppm): 0.78 (s, 3H, H$_a$); 3.84 (s, 3H, H$_b$); 4.91 (s, 2H, H$_c$); 5.17 (s, 2H, H$_c$); 6.50 (d, 1H, $^3J_{HH}$= 3.74, H$_d$); 6.58 (t, 1H, $^3J_{HH}$= 3.21, H$_e$); 6.69 (d, 1H, $^3J_{HH}$= 3.34, H$_f$); 6.81 (t, 1H, $^3J_{HH}$ = 5.23, H$_g$); 7.35 (dd, 2H, $^3J_{HH}$= 6.86, H$_h$); 7.51 (dd, 2H, $^3J_{HH}$= 7.77, H$_i$). 13.05 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d$_6$): 28.30; 45.88; 55.99; 114.30; 115.10; 115.35; 118.20; 121.90; 123.00; 129.10; 137.85; 138.70; 141.50; 144.70. MS (ESI) m/z (%) 254 (M+ - Cl2 – Pd, 97%). Anal. Calc. for C$_{16}$H$_{18}$N$_3$PdClO: C, 46.85; H, 4.42; N, 10.24. Found: C, 47.11; H, 4.11; N, 8.58.

3.2.3.1.5 [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-bromoaniline}PdCl₂] (C5)
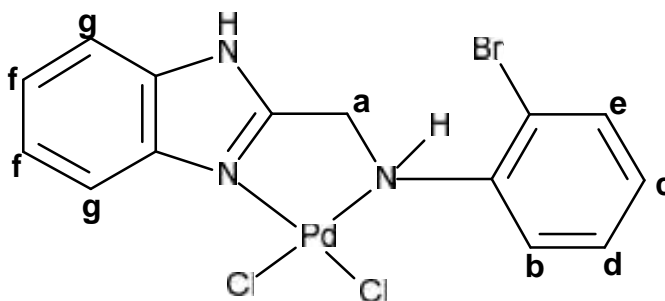
Complex **C5** was prepared according to the procedure for **C1** using **L4** (0.10g, 0.33mmol) and [Pd(COD)Cl₂] (0.086 g, 0.33 mmol) CH₂Cl₂ (10 mL). Yield = 0.08 g (51%).

^{1}H NMR (DMSO-d₆): $_H$ (ppm): 5.11 (s, 2H, H$_a$); 6.30 (d, 1H, $^3J_{HH}$ = 5.56, H$_b$); 6.61 (t, 1H, $^3J_{HH}$ = 8.70, H$_c$); 7.02 (t, 1H, $^3J_{HH}$ = 7.67, H$_d$); 7.32 (dd, 1H, $^3J_{HH}$ = 7.63, H$_e$); 7.38 (dd, 2H, $^3J_{HH}$ = 7.53, H$_f$); 7.48 (d, 2H, $^3J_{HH}$ = 7.98, H$_g$); 13.25 (s, 1H, *N-H*). ^{13}C NMR (DMSO-d₆): 37.33; 114.85; 115.30; 115.99; 119.48; 123.00; 128.88; 132.50; 137.90; 138.86; 141.55; 146.90. MS (ESI) m/z (%) 482 (M$^+$- 2H, 12%). Anal. Calc. for C₁₄H₁₂N₃BrPdCl₂.0.25 CH₂Cl₂: C, 34.18; H, 2.52; N, 8.39. Found: C, 34.37; H, 2.51; N, 8.05

3.2.3.1.6 [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-bromoaniline}PdClMe] (C6)
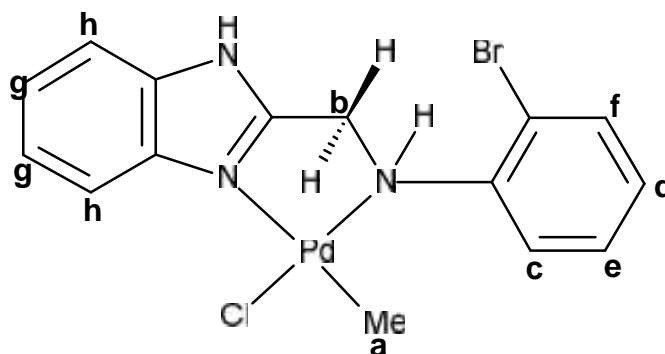
Complex **C6** was prepared according to the procedure for **C2** using **L4** (0.10 g, 0.34 mmol) and [PdCl(COD)Me] (0.10 g, 0.34 mmol). Yield = 0.09 (58%) ^{1}H NMR (DMSO-d$_6$): δ$_H$ (ppm): 0.80 (s, 3H, H$_a$); 4.61 (s, 2H, H$_b$); 5.01 (s, 2H, H$_b$); 6.27 (d, 1H, $^3J_{HH}$ = 6.67, H$_c$); 6.56 (t, 1H, $^3J_{HH}$ = 5.64, H$_d$); 7.06 (t, 1H, $^3J_{HH}$ = 6.77, H$_e$); 7.15 (d, 1H, $^3J_{HH}$ = 7.89, H$_f$); 7.31 (dd, 2H, $^3J_{HH}$ = 6.78, H$_g$); 7.48 (dd, 2H, $^3J_{HH}$ = 7.33, H$_h$); 13.01 (s, 1H,). MS (ESI) m/z (%) 482 (M$^+$- Cl, 22%). Anal. Calc. for C$_{15}$H$_{15}$N$_3$BrPdCl: C, 39.24; H,3.29; N, 9.15. Found: C, 38.94; H, 3.87; N, 8.99.

3.2.3.2 Syntheses of cationic complexes

3.2.3.2.1 [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-aniline}PdCl(PPh₃)] BAr₄ (C7)
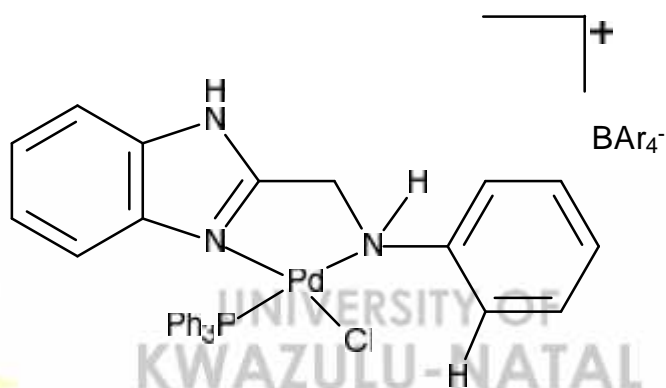
To a suspension of **C1** (0.036g, 0.090 mmol) in CH_2Cl_2 (10 mL), PPh₃ (0.023g, 0.09 mmol) and NaBAr₄ (Ar₄ = 3,5-$(CF_3)_2C_6H_3$) (0.080g, 0.090 mmol) were added and stirred under inert atmosphere for 24 h. The reaction mixture was filtered to remove NaCl and the filtrate concentrated to approximately 3 mL and recrystallized from hexane: CH_2Cl_2. **C7** was obtained as a yellow crystalline solid. Yield = 0.060 g (83%). ¹H NMR (CDCl₃): H (ppm): 5.61 (s, 2H, CH₂), 6.51 (d, 2H, Ph-aniline), 6.57 (t, 1H, Ph-aniline), 6.59 (d, 2H, Ph-aniline), 7.17 (6H, PPh₃), 7.25 (d, 2H, Bzim), 7.37 (8H, BAr₄), 7.56 (9H, PPh₃), 7.71 (4H, BAr₄), 7.74 (d, 2H, Bzim). 9.52 (s, 1H, *N-H*). ³¹P NMR (CDCl₃): δ(ppm): 35.1, 29.6. Anal. Calc. for $C_{64}H_{43}BClF_{24}N_3PPd$: C, 51.50; H, 2.90; N, 2.80. Found: C, 51.41; H, 2.98; N, 3.01.

3.2.3.2.2   [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-aniline}PdMe(PPh₃)] BAr₄ (C8)
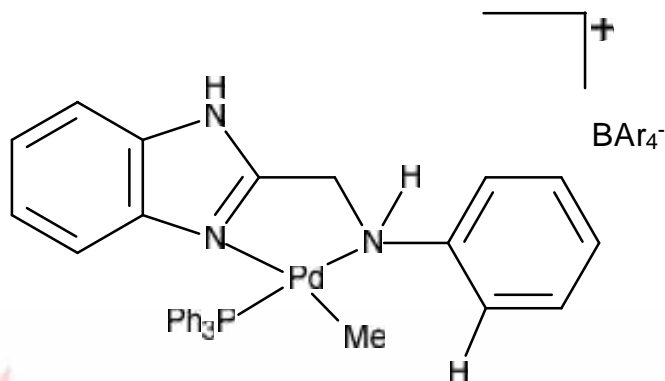
Complex **C8** was prepared following the same procedure described for **C7**. **C2** (0.034g, 0.09 mmol), PPh₃ (0.023g, 0.090 mmol) and NaBAr₄ (Ar₄ = 3,5-(CF₃)₂C₆H₃) (0.080g, 0.090 mmol) were used. Yield = 0.050 g (71%). ¹H NMR (CDCl₃): ᵤ (ppm): 1.29 (s, 3H, CH₃), 5.61 (s, 2H, CH₂), 6.12 (t, 1H, Ph-aniline), 6.27 (d, 2H, Ph-aniline), 7.08 (d, 2H, Ph-aniline), 7.19 (6H, PPh₃), 7.35 (d, 2H, Bzim), 7.44 (8H, BAr₄), 7.50 (9H, PPh₃), 7.71 (4H, BAr₄), 7.73 (d, 2H, Bzim). 9.75 (s, 1H, *N-H*). ³¹P NMR (CDCl₃): δ(ppm): 37.8. Anal. Calc. for C₆₅H₄₃BF₂₄N₃PPd: C, 53.10; H, 2.95; N, 2.86. Found: C, 53.26; H, 2.65; N, 2.81.

3.2.3.2.3 [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-methoxyaniline}PdCl(PPh₃)]BAr₄ (C9)
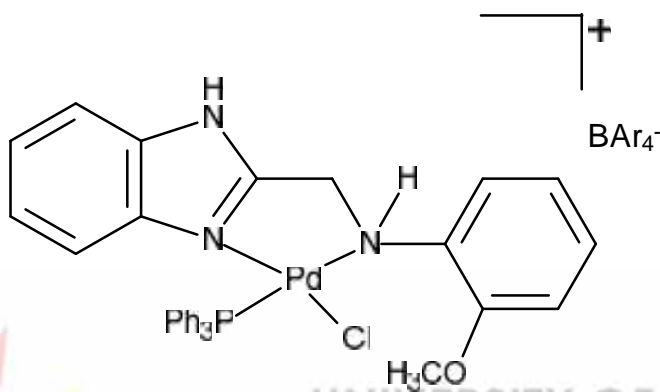
Complex **C9** was prepared according to the procedure for **C7** using **C3** (0.038 g, 0.090 mmol), PPh₃ (0.023 g, 0.090 mmol) and NaBAr₄(Ar₄ = 3,5-(CF₃)₂C₆H₃) (0.08 g, 0.090 mmol). Yield = 0.062 g (83%). ^{1}H NMR (CDCl₃): δ_H (ppm): 3.40 (s, 3H, CH₃), 5.49 (s, 2H, CH₂), 6.60 (d, 1H, Ph-aniline), 6.73 (t, 1H, Ph-aniline), 6.83 (d, 1H, Ph-aniline), 6.89 (t, 1H, Ph-aniline), 7.21 (6H, PPh₃), 7.29 (d, 2H, Bzim), 7.43 (8H, BAr₄), 7.52 (9H, PPh₃), 7.73 (4H, BAr₄), 7.74 (d, 2H, Bzim). 10.02 (s, 1H, *N-H*).^{31}PNMR (CDCl₃): H (ppm): 38.6, 30.7. Anal. Calc. for C₆₅H₄₂BClF₂₄ON₃PPd:C, 51.37; H, 2.42; N, 2.77. Found: C, 50.95; H, 2.42; N, 2.41.

3.2.3.2.4   [{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-methoxyaniline}PdMe(PPh$_3$)]

BAr$_4$ (C10)
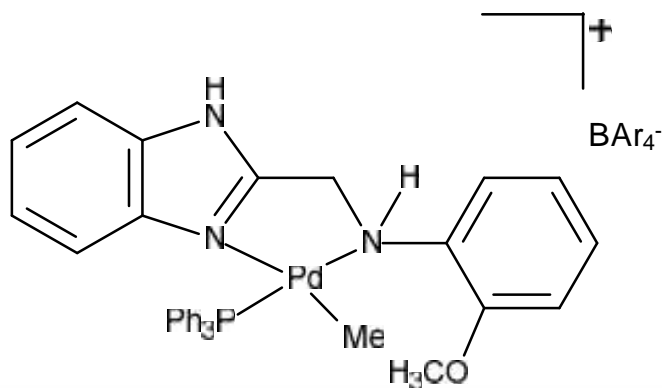
Complex **C10** was prepared according to the procedure for **C7** using **C4** (0.018 g, 0.09 mmol), PPh$_3$ (0.011 g, 0.090 mmol) and NaBAr$_4$(Ar$_4$ = 3,5-(CF$_3$)$_2$C$_6$H$_3$) (0.037 g, 0.09 mmol). Yield = 0.082 g (81%). ^{1}H NMR (CDCl$_3$): $_H$ (ppm): 0.95 (s, 3H, CH$_3$), 3.43 (s, 3H, OCH$_3$), 5.52 (s, 2H, CH$_2$), 6.47 (d, 1H, Ph-aniline), 6.69 (t, 1H, Ph-aniline), 6.75 (d, 1H, Ph-aniline), 6.98 (t, 1H, Ph-aniline), 7.21 (6H, PPh$_3$), 7.34 (d, 2H, Bzim), 7.36 (8H, BAr$_4$), 7.50 (9H, PPh$_3$), 7.71 (4H, BAr$_4$), 7.72 (d, 2H, Bzim), 9.06 (s, 1H, *N-H*). ^{31}P NMR (CDCl$_3$) δ_H (ppm): 30.7. Anal. Calc. for C$_{66}$H$_{45}$BF$_{24}$ON$_3$PPd:C, 52.46; H,3.05; N, 2.82. Found: C, 52.94; H, 1.39; N, 3.09.

3.2.3.2.5 **[{*N*-(1*H*-benzoimidazol-2-ylmethyl)-2-bromoaniline}PdMe(PPh₃)] BAr₄**

(C11)
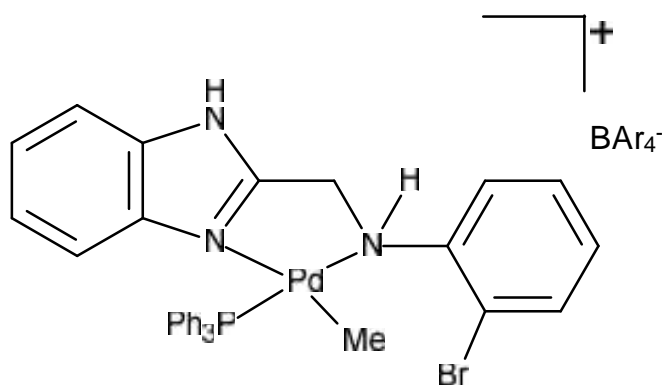
Complex **C11** was prepared according to the same procedure for **C7** using **C6** (0.041 g, 0.09 mmol), PPh₃(0.023 g, 0.090 mmol) and NaBAr₄ (Ar₄ = 3,5-$(CF_3)_2C_6H_3$) (0.08 g, 0.09 mmol). Yield = 0.06 g (76%). ^1H NMR (CDCl₃): $_H$ (ppm): 0.98 (s, 3H, CH_3), 5.65 (s, 2H, CH_2), 6.33 (d, 1H, Ph-aniline), 6.60 (t, 1H, Ph-aniline), 7.10 (d, 1H, Ph-aniline), 7.20 (t, 1H, Ph-aniline), 7.25 (6H, PPh₃), 7.38 (d, 2H, Bzim), 7.40 (8H, BAr₄), 7.59 (9H, PPh₃), 7.63 (d, 2H, Bzim), 7.74 (4H, BAr₄); 9.03 (s, 1H, *N-H*) ^{31}P NMR (CDCl₃): 30.6. Anal. Calc. for $C_{65}H_{45}BBrF_{24}N_3PPd$: C, 50.30; H, 2.92; N, 2.70. Found: C, 50.61; H, 2.72; N, 2.87.

3.3. Results and discussion

3.3.1. Synthesis and characterization of Pd complexes

Compounds **L1 – L4** were prepared by reaction of 2(chloromethyl) benzoimidazole with the appropriate aniline derivative and was obtained in low to good yields (48 – 89%) Scheme 3.1 following the literature procedure.[5,8] **L2** was obtained in low yields (48%) possibly due to purification by column chromatography. **L1** and **L3** did not require any purification and were thus obtained in high yields.

R = H (**L1**); R = OCH$_3$ (**L2**)

R = SH (**L3**); R = Br (**L4**)

Scheme 3.1: Synthesis of the (benzoimidazol-2-ylmethyl) amine ligands.

Reactions of compounds **L1 - L4** with either [PdCl$_2$(COD)] or [PdClMe(COD)] produced the corresponding neutral complexes **C1-C6** in low to good yields (38-87%), Scheme 3.2.[9]

R = H (**L1**); R = OCH₃ (**L2**)   R = H, X = Cl (**C1**); R = H, X = Me (**C2**)

R = SH (**L3**); R = Br (**L4**)   R = OCH₃, X = Cl (**C3**); R = OCH₃, X = Me (**C4**)

R = Br, X = Cl (**C5**); R = Br, X = Me (**C6**)

To generate the cationic species, that could be readily used as methoxycarbonylation catalysts . . – . . were treated with 1 equivalent of NaBAr₄ (Ar = 3,5-(CF₃)₂C₆H₃) in the presence of triphenylphosphine (PPh₃) to afford complexes . . . . . in good to high yields (66 – 97%), Scheme 3.3.

R = H, X = Cl (**C1**); R = H, X = Me (**C2**)   R = H, X = Cl (**C7**); R = H, X = Me (**C8**)

R = OCH₃, X = Cl (**C3**); R = OCH₃, X = Me (**C4**)   R = OCH₃, X = Cl (**C9**); R = OCH₃, X = Me (**C10**)

R = Br, X = Cl (**C5**); R = Br, X = Me (**C6**) R = Br, X = Me (**C11**)

All the new compounds synthesized were characterized by ^{1}H, ^{13}C (for all the ligands and some of the complexes) and^{31}P NMR spectroscopies, mass spectrometry (for some of the complexes), elemental analyses and single X-ray crystallography for **C8a**, **C9a** and **C11a**.^{1}H NMR spectra of **L1**, **L2**, **L3** and **L4** gave signature peaks of the CH_2's protons as singlets at 4.86, 4.65, 4.20 and 4.60 ppm respectively. For **L2**, an upfield peak at 3.86 ppm was observed in the ^{1}H NMR spectrum which was assigned to the OCH_3 protons. The aromatic protons for **L1, L2**, **L3** and **L4** were observed further downfield between 5.94 – 7.69 ppm. ^{13}C NMR spectra of **L1 – L4** were consistent with ^{1}H NMR data. For instance **L1 – L4** showed upfield peaks at 42.38, 42.20, 55.77 and 55.36 ppm assigned to the CH_2 carbon. In addition, **L2** gave a signal at 55.77 ppm corresponding to the OCH_3 carbon.

The CH_2 peaks were demonstrative in the next step to verify complexation of the (benzoimidazol-2-ylmethyl) amine ligands to the palladium salts. For example, the ^{1}H NMR spectra of **L4** and corresponding complex **C5** (Figure 3.1) showed downfield shift of CH_2 protons at 5.11 ppm in complex **C5** compared to 4.60 ppm in **L4** indicating that complexation has occurred. Similar trends were observed for all the complexes and their corresponding ligands.
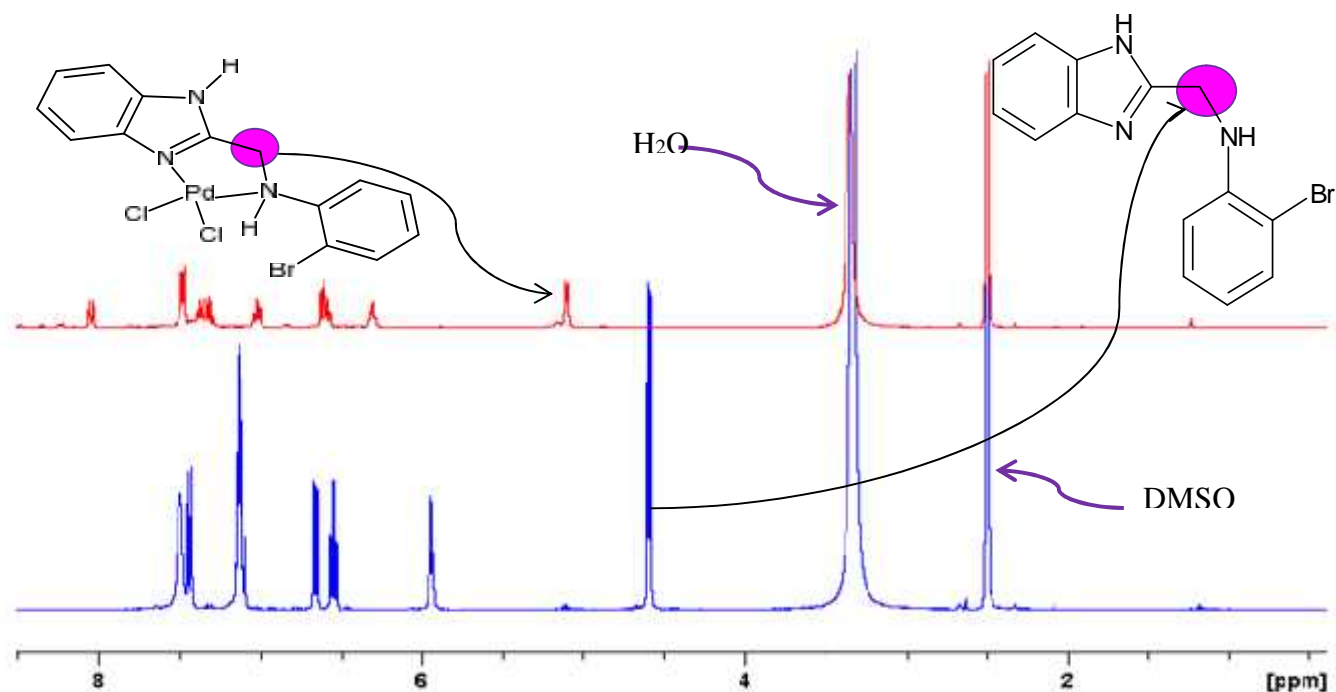
Figure 3.1: ^{1}H NMR spectrum of **L4** and complex **C5** showing a shift in the CH$_2$ and aromatic protons in the respective compounds.

One interesting observation in the ^{1}H NMR data was the appearance of broad signals for CH$_2$ at 4.61 ppm and 5.01 ppm for complex **C6** (Figure 3.2). Similar trend was recorded for complex **C4.** In addition, two sets of aromatic protons were also reported. This reveals the presence of two isomers, which may arise from unsymmetrical nature of complexes **C4** and **C6** due to Pd-Me bond as opposed to the symmetric PdCl$_2$ in complex **C5**. This observation was also reported by Ojwach and co-workers[10] using (pyrazol-1-ylmethyl)pyridine palladium complexes, where two signals for the CH$_2$ linker protons were discovered at about 5.28 and 5.58 ppm.[10] Figure 3.2 shows ^{1}H NMR spectrum of complex **C6** respectively that illustrates the above discussion.
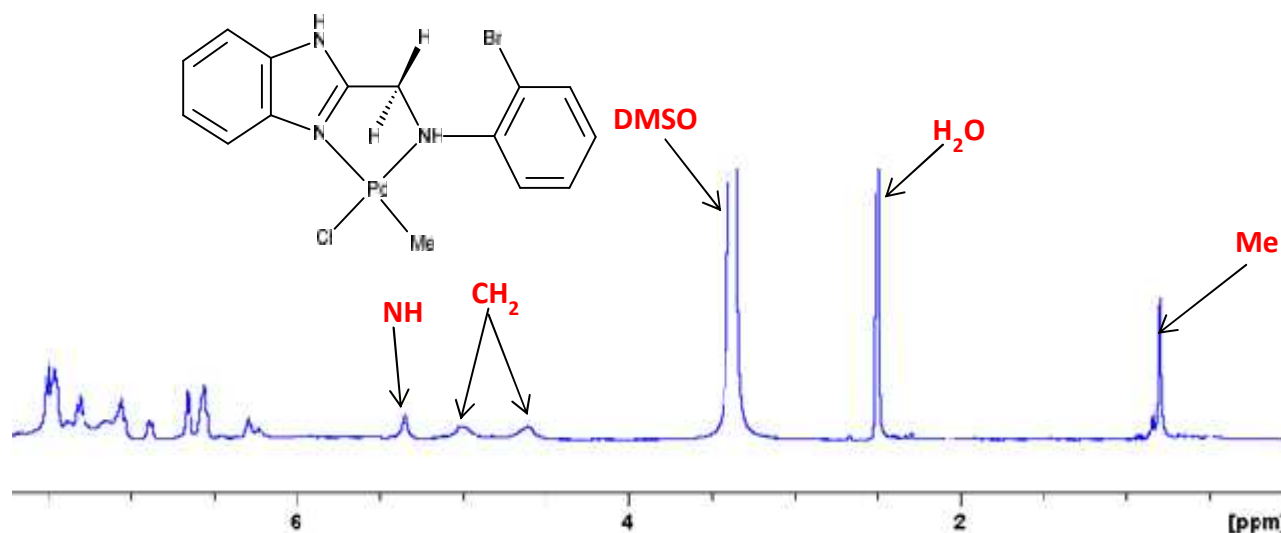
Figure 3.2: ^{1}H NMR spectrum of complex **C6** showing CH$_2$ protons as broad peaks.

^{1}H NMR spectroscopy was also used to deduce the formation of the cationic complexes. For instance; the CH$_3$ and CH$_2$ signals for complex **C8** were recorded at 1.28 ppm and 6.22 ppm respectively, compared to upfield signals at 0.81 ppm and 5.12 observed in the corresponding neutral complex **C2** (Figure 3.3). In addition aromatic signals at 7.15 & 7.50 ppm and 7.44 & 7.71 ppm confirmed the presence of PPh$_3$ and BAr$_4^-$ groups.[11]
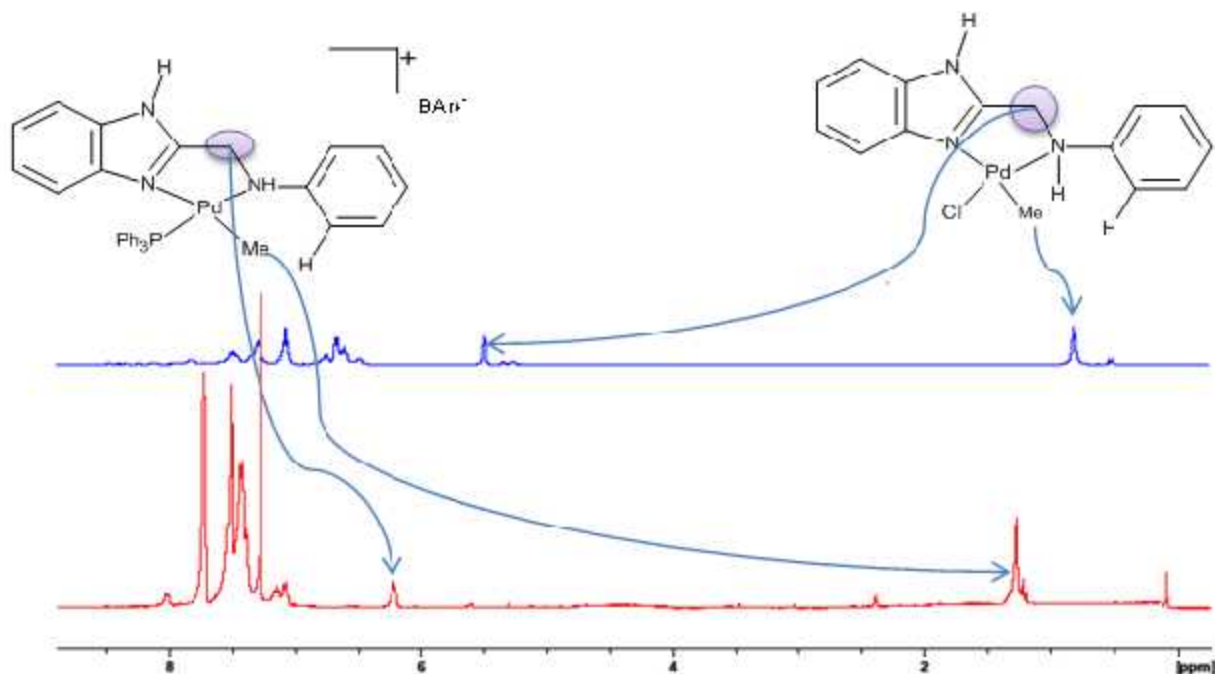
Figure 3.3: ^{11}H NMR spectrum of **C8** and **C2** showing a signal shift in the CH$_2$ and CH$_3$ protons.

The cationic complexes **C7– C11** were further characterized by ^{31}P NMR in order to determine the presence and nature of the coordination of PPh$_3$ ligand upon chloride abstraction. Complexes **C8, C10** and **C11** containing Pd-Me bonds displayed singlets between 30.6 – 37.8 ppm. This data was consistent with typical values of between 30.59 - 35.70 ppm observed for a range of mono-coordinated PPh$_3$ compounds. [12-18]Figure 3.4 shows the ^{31}P NMR spectrum for complex **C8**.
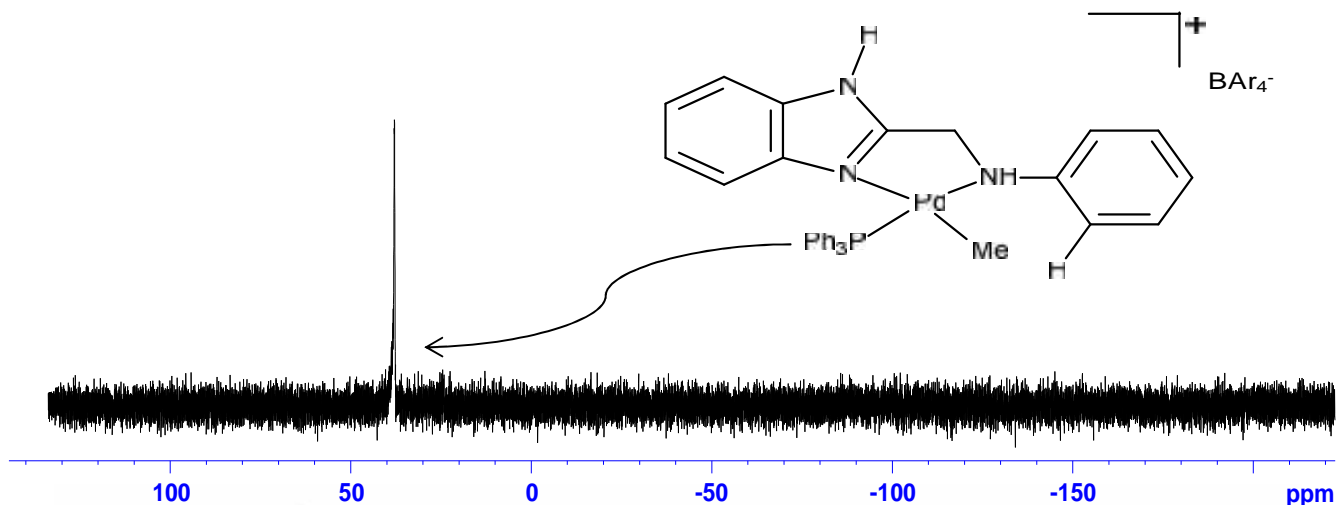
Figure 3.4: ^{31}PNMR spectra of **C8** in CDCl$_3$ solution showing a singlet peak.

Interestingly, instead of a single signal, the ^{31}PNMR spectrum of the cationic chloride-coordinated Pd compounds **C7** and **C9** (Figure 3.5) showed two signals at about 29.60 – 38.60 ppm. From Figure 3.5, the ^{31}P NMR spectra of complex **C9** gave two signals at 30.69 and 38.62 ppm. This observation might be due to the existence of *cis* (P *cis* N) and *trans* (P *trans* N) isomers in the CDCl$_3$ solvent used to acquire the NMR data. The reason why this phenomenon was not observed for the Pd-Me complexes is still unclear to us.
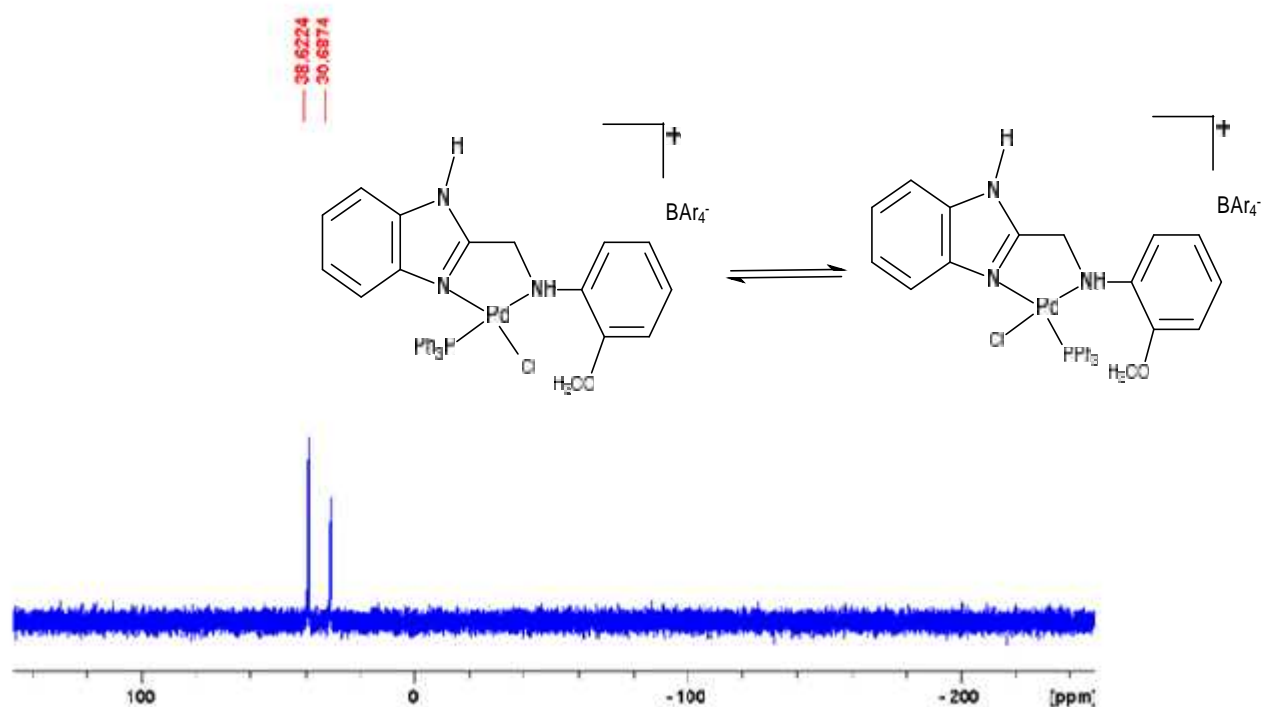
Figure 3.5: ^{31}PNMR spectra of **C9** in CDCl$_3$ solution showing two peaks.

The compounds were also characterized by electron-spray ionization mass spectrometry (ESI-MS). For example complex **C6** showed fragmentation pattern consistent with the loss of Cl$^-$ ion (m/z = 423.96) (Figure 3.6). This was followed by the loss of PdMeCl fragment to produce a peak at m/z = 304 corresponding to **L4** (Figure 3.6). However, **C1 – C4** showed the fragment peak corresponding to the ligand (M$^+$-Cl$_2$-Pd). Even though the presence of the ligand does not confirm complex formation but does indicate complexation (complex = ligand + metal).
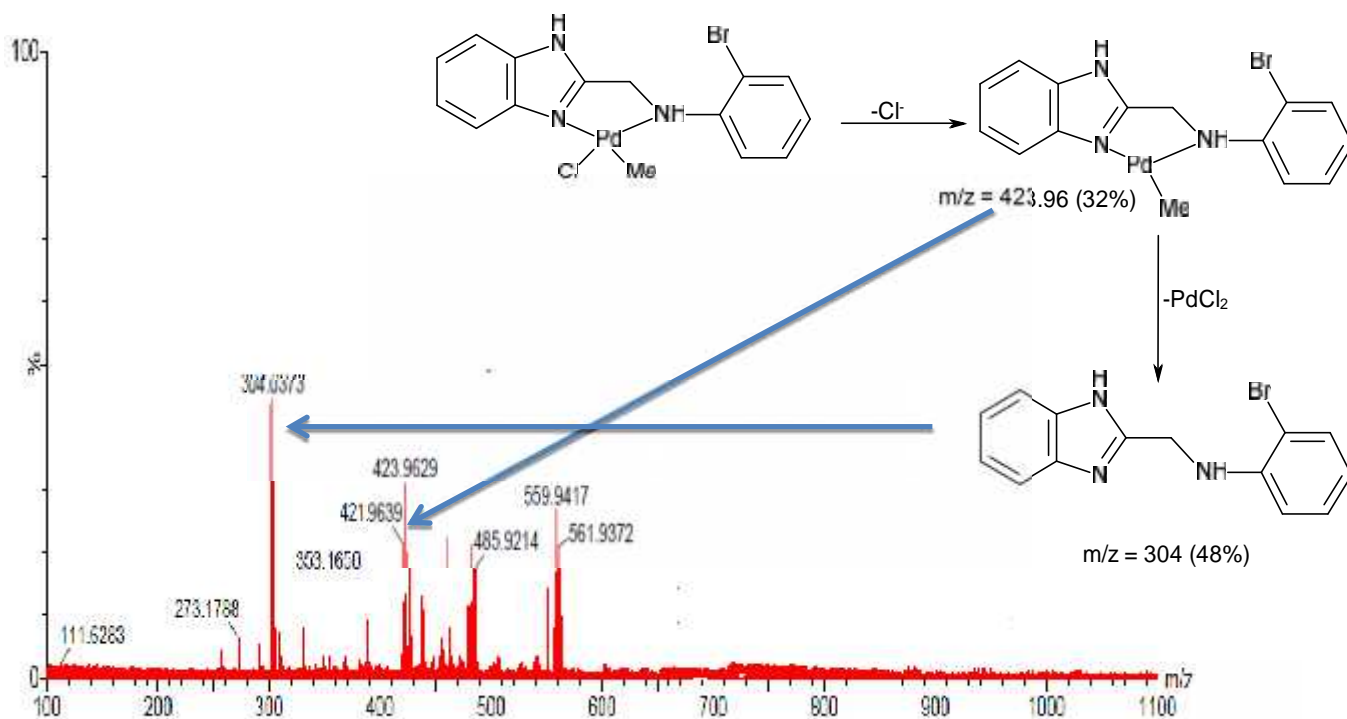
Figure 3.6: ESI-MS for **C5** showing the fragmentation pattern.

Complexes **C1 – C11** were also characterized by elemental analysis. Micro-analyses results were found to be in satisfactory agreement with the calculated data for the proposed structures of **C1 – C11** shown in Scheme 3.2 and proved the purity of the compounds. However, elemental analysis for **C2** did not meet the anticipated purity standards even after further purification. The micro-analyses data for **C7 – C11** were consistent with one ligand unit and one PPh$_3$ per Pd-metal in the coordination sphere. This rules out the possible presence of two phosphine ligands within the complex coordination sphere [Pd(L)X(PPh$_3$)$_2$] (X = Cl or Me) in the bulk material.

3.4 Solid state structure of complexes C8a, C9b and C11c

In order to verify the proposed coordination modes of (benzoimidazol-2-ylmethyl) amine ligands, solid state structures of complexes **C8a**, **C9** and **C11a** were determined. A summary of crystallographic data and structure refinement parameters for **C11a** is represented in Table 3.1, while Table 3.2 contains selected bond lengths and angles for **C11a**. Solid state structures of **C8a**, **C9a** and **C11a** are shown in Figures 3.7– 3.9 respectively. Complex **C11a** crystallizes in the triclinic space group P-1 with Z = 2. The structure of **C11a** (Figure 3.7) showed that the (benzoimidazol-2-ylmethyl) amine ligand is coordinated to Pd in a monodentate fashion via Bzim-Nitrogen N(2). Also, two triphenylphosphines are coordinated to Pd (II) center and are trans to each other. The distorted square geometry is completed by a CH_3 ligand *trans* to N(2) of the benzoimidazolylmethyl amine ligand. The bond length of Pd(01)-N(2) of 2.1290 (19)Å, is very similar to that observed in other palladium (II) complexes.[19-20] In addition, Pd(01)-P(003) and Pd(01)-P(004) bond lengths of 2.3003 (8) and 2.3311 (8) Å, respectively are in agreement with other structurally characterized palladium phosphine complexes.[20-22] Significant distortions for the ideal square planar geometry were evident both in bond angles of N(2)-Pd(01)-P(003) of 94.19(5)° and C(1)-Pd(01)-P(004) of 87.54(7)°, respectively, arising from the steric demands of the two bulkier PPh_3 groups.

The quality of the crystals data and refinement parameters for **C8a** (Figure 3.8) and **C9a** (Figure 3.9) were not good enough for discussion of bond parameters. The coordination chemistry and atom connectivity was however, not in doubt.

Table 3.1. Crystal data and structure refinement parameters for **C11a**

Empirical formula	C83 H57 B Br F24 N3 P2 Pd	
Formula weight	1811.38	
Temperature (K)	100	
Crystal system , space group	Triclinic, P-1	
Unit cell dimensions	a = 14.006(5) Å	α= 106.116(5)°.
	b = 14.701(5) Å	β= 99.021(5)°.
	c = 19.868(5) Å	δ= 94.595(5)°.
Volume	3848(2) Å^3	
Z	2	
Crystal size (mm^3)	0.12 x 0.07 x 0.05	
Absorption coefficient (mm^{-1})	0.908	
Theta range for data collection	1.09 to 26.03°.	
Index ranges	-17<=h<=16, -18<=k<=18, -24<=l<=24	
Reflections collected	57888	
R$_{(int)}$	0.0321	
Completeness to theta = 25.00°	99.3 %	
Max. and min. transmission	0.9560 and 0.8989	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	15010 / 0 / 1045	
Goodness-of-fit on F^2	1.026	
R1^a, wR2^b [I>2σ(I)]	0.0351, 0.0782	
Largest diff. peak and hole	1.027 and -1.643 e.Å^{-3}	

^{a}R1 = $\sum \left| F_0 \right| - \left| F_c \right| / \sum F_0$. ^{b}wR2 = $\left[\sum [w(F_0{}^2 - F_c{}^2)^2] \right| / \sum [w(F_0{}^2)^2] \right]^{1/2}$.

Table 3.2. Selected bond lengths [Å] and bond angles [°] for **C11a**

Pd(01)-C(1)	2.069 (2)	Pd(01)-P(003)	2.3003(8)
Pd(01)-N(2)	2.1290(19)	Pd(01)-P(004)	2.3311(8)
C(1)-Pd(01)-N(2)	178.97(9)	C(1)-Pd(01)-P(004)	87.54(7)
N(2)-Pd(01)-P(004)	93.16(5)	C(1)-Pd(01)-P(003)	85.13(7)
P(003)-Pd(01)-P(004)	172.61(8)	N(2)-Pd(01)-P(003)	94.19(5)
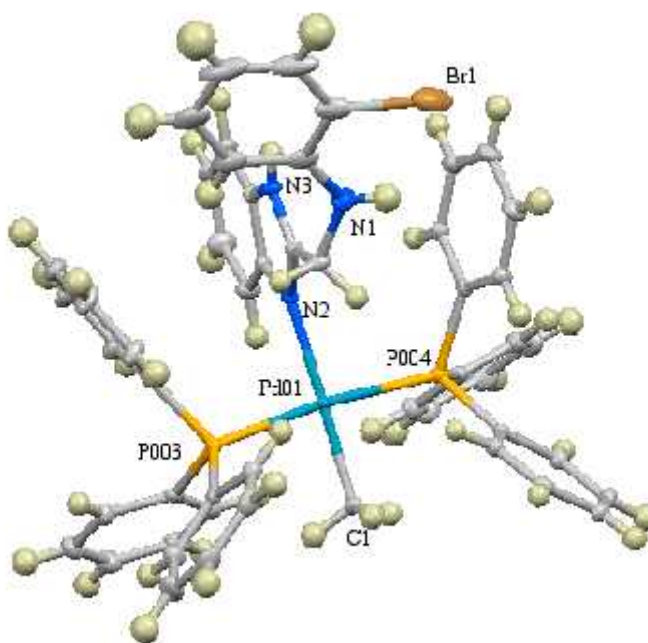
Figure 3.7: Crystal structure for [{N-(1H-benzoimidazol-2-ylmethyl)-2-bromoaniline} [PdMe(PPh₃)₂] BAr₄ (**C11a**).
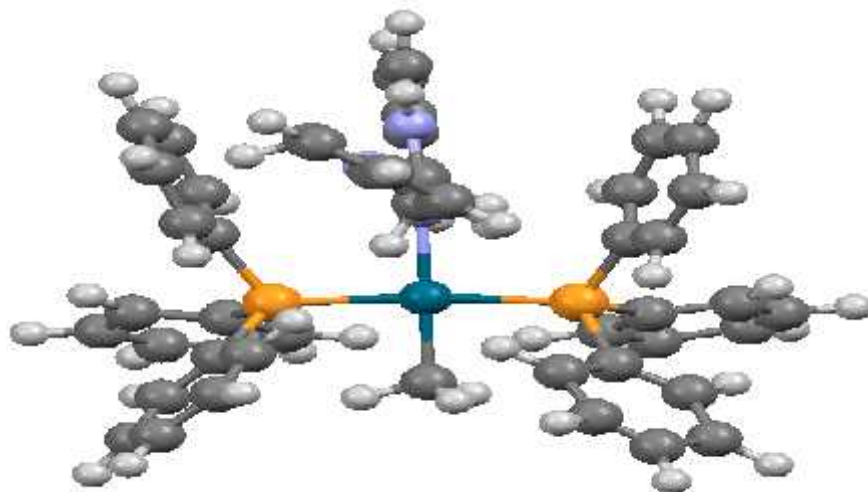
Figure 3.8: Crystal structure for [{N-(1H-benzoimidazol-2-ylmethyl)-2-aniline} [PdMe(PPh₃)₂] BAr₄ (**C8a**).
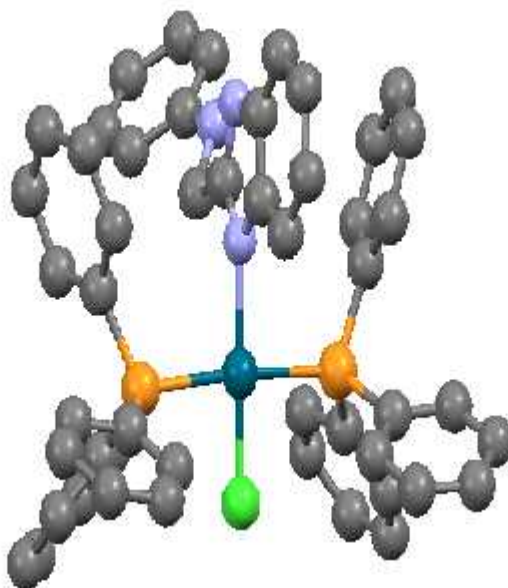
Figure 3.9: Crystal structure for [{N-(1H-benzoimidazol-2-ylmethyl)-2-methoxyaniline} [PdCl(PPh₃)₂] BAr₄ (**C9a**).

The hemilability nature of the benzoimidazolyl amine ligands resulted in one coordinating group of the secondary amine *N–H* functionality linking the aromatic ring

being easily displaced from the palladium metal center during crystallization, while the other *N* atom remained firmly bound. Similar results were obtained by Attandoh *et al.*[5] using the same benzoimidazolyl amine ligands. However these results are in disagreement with the elemental analyses and ^{31}P NMR data which correspond to one PPh$_3$ group in the proposed structures. Thus it is reasonable to deduce that the change in coordination chemistry occur during crystallization process.

3.5   Conclusion

In conclusion, four benzoimidazolyl amine ligand derivatives (**L1–L4**) were synthesized and fully characterized by NMR techniques and high resolution mass spectroscopy. Reactions of benzoimidazolyl amine ligands (**L1–L4**) with either [PdClMe(COD)] or [PdCl$_2$(COD)] gave the corresponding Pd(II) complexes (**C1–C6**) in good yields. Treatment of palladium complexes (**C1–C6**) with one equivalent of PPh$_3$ in the presence of NaBAr$_4$ (Ar$_4$ = 3,5-(CF$_3$)$_2$C$_6$H$_3$), afforded   the cationic complexes (**C7–C11**) respectively, in good yields, respectively. The solid state structures of **C8a**, **C9a** and **C11a** showed that the benzoimidazolyl amine ligands are coordinated to Pd(II) in a monodentate fashion via Bzim-Nitrogen donor. The presence of two PPh$_3$ groups in trans-position and monodentate coordination of ligands **L1–L4** confirmed the hemilability of the potentially bidentate ligands **L1–L4**.

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Methoxycarbonylation of olefins catalyzed by (Benzoimidazol-2-yl) methyl amine Pd complexes.

4.1   Introduction

The literature review presented in Chapter 2 indicates that Pd catalysts are among the best candidates for methoxycarbonylation of olefins. In recent years, a number of palladium complexes containing varied ligand architectures have been reported to show high activity as well as selectivity for methoxycarbonylation of olefins such as styrene[1], 1-hexene[2] or ethene[3] under mild reaction conditions. Under low partial pressures of carbon monoxide and moderate temperatures, some of these catalyst systems show high regioselectivity (>90 ˚) to branched isomers.[4-12] Toniolo and Cavinato employed [PdCl$_2$(PPh$_3$)$_2$][13-14] in the presence of HCl as an acid promoter[15-16] and PPh$_3$ to enhance stability and avoid catalyst decomposition to palladium black. Other palladium based catalysts of the type [PdCl$_2$(Ph$_2$PNHpy-k^2 P,N)] and [PdCl(Ph$_2$PNHpy-k^2 P,N)(PPh$_3$)]Cl in the presence of PPh$_3$ and p-TsOH as an acid promoter were found to be active in the methoxycarbonylation of styrene. However, they were less active in 1-hexene and cyclohexene reactions.[2]

In this Chapter, experimental results on the catalytic evaluation of some of the palladium complexes synthesized in chapter 3 (Scheme 4.1) in the methoxycarbonylation of styrene, 1-hexene, 1-octene, 1-nonene and 1-decene are

discussed. The effects of catalyst design, identity of substrate, reaction conditions such as temperature, pressure and nature of acid promoter have been systematically studied and are herein reported.
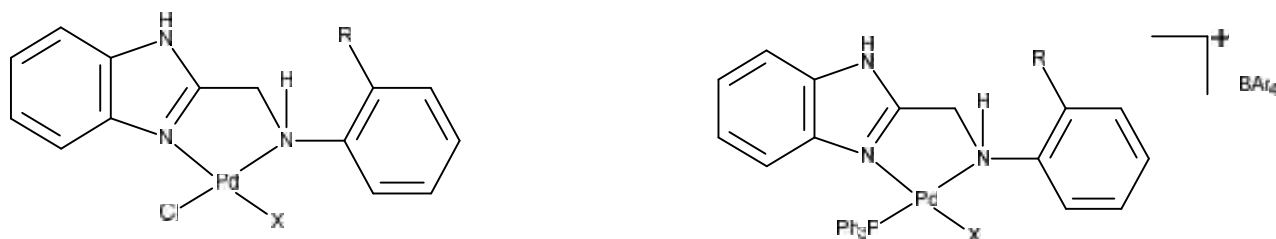
R = H, X = Me (**C2**)   R = H , X = Me(**C8**)

R = OCH$_3$, X = Cl (**C3**); R = OCH$_3$, X = Me (**C4**)   R = OCH$_3$, X = Cl (**C9**); R = OCH$_3$ X, Me(**C10**)

R = Br, X = Me (**C6**)   R = Br, X = Me (**C11**)

Scheme 4.1: Palladium complexes used for the methoxycarbonylation reactions.

4.2   Experimental

4.2.1   Materials and instrumentation

The catalytic methoxycarbonylation of olefins were performed in a stainless steel autoclave equipped with a temperature control unit and a sampling valve. Styrene, C$_6$ – C$_{10}$ α-oleifns, *p*-TsOH, hydrochloric acid (HCl), oxalic acid, sulfuric acid (H$_2$SO$_4$), HBr and PPh$_3$ were obtained from Sigma Aldrich. Toluene and methanol were purchased from Merck chemicals. The palladium complexes used were prepared in chapter 3. GC-MS analyses were run under the following standard chromatography conditions: -25 m CPSil 19 capillary column, 1.2 mm film thickness, Helium carrier column gas 5 psi,

injector temperature 250 ˚C, oven program 50 ˚C for 4 minutes rising to 200 ˚C at 20 ˚C/ min and holding at 200 ˚C.

4.2.2   General procedure for the methoxycarbonylation reactions

The catalytic methoxycarbonylation reactions were performed in a stainless steel autoclave equipped with temperature control unit and a sample valve. In a typical experiment, **C10** (48.78 mg, 0.0799 mmol), PPh_3 (41.95 mg, 0.160 mmol), HCl (0.0247 mL, 0.799 mmol) and 1-hexene (2 mL, 15.93 mmol) were dissolved in a mixture of methanol (20 mL) and toluene (40 mL). The reactor was evacuated and the catalytic solution was introduced to the reactor. The reactor was purged three times with CO, and then set at the required pressure, heated to the desired temperature and the reaction initiated by stirring at 500 rpm. At the end of the reaction time, the reaction was cooled, CO was vented off and the samples were taken for GC analysis to determine the changes in concentration of reactants and products. GC-MS was also used to determine the molecular weights and identity of the resulting esters. The branched and linear esters were assigned using authentic samples.

4.3 Results and discussion

4.3.1 Catalytic screening of palladium complexes in methoxycarbonylation reactions

Preliminary evaluation of complexes **C2**, **C4**, **C6**, **C8-C11** in the methoxycarbonylation of 1-hexene were performed at 60 bar of CO, 90 °C and [1-hexene]: HCl: [Pd] = 200 : 10 : 1 (Scheme 4.2). The major products were methyl heptanoate (linear product **1**) and methyl 2- methylhexanoate (branched product **2**).
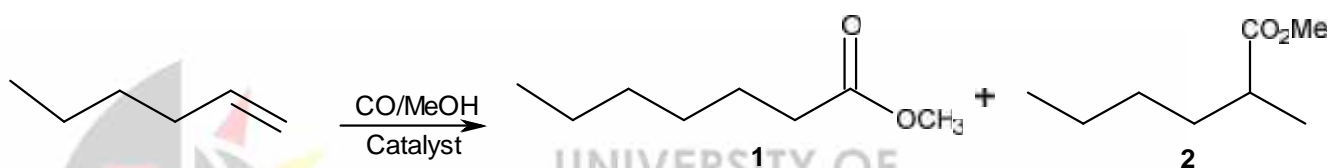
Scheme 4.2: Major products obtained in the methoxycarbonylation of 1-hexene.

The methoxycarbonylation products were characterized by gas chromatography and GC–MS. Figures 4.1 and 4.2 represent a typical GC and GC–MS trace for 1-hexene respectively. From Figure 4.2, m/z peak at 145.12 was observed at 4.70 and 5.19 minutes corresponding to both methyl heptanoate (linear product) and methyl 2-methylhexanoate (branched product). Similar GC-MS spectra were observed for all the substrates, acid catalysts.
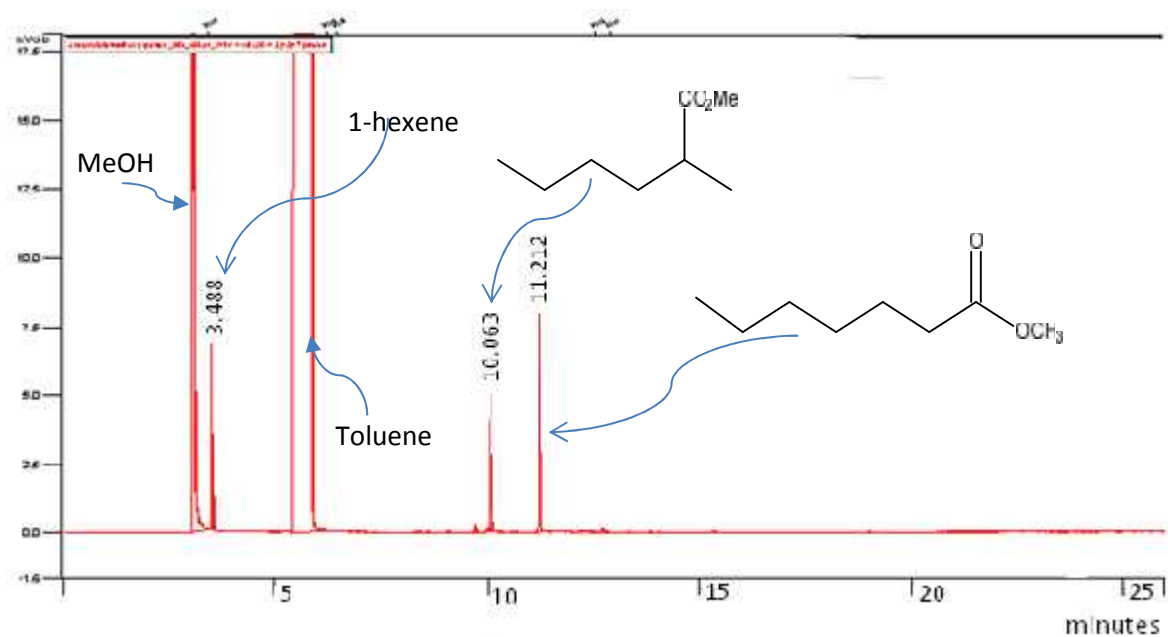
Figure 4.1: GC spectra of methoxycarbonylation product obtained from 1-hexene using complex **C10** (0.07 mmol), solvent: toluene (40 mL) and methanol (30 mL); Pd/1-hexene ratio, 200:1, Pd/ HCl ratio; 1:10; $P_{(CO)}$ = 60 bar; temperature; 90°C; time 24 h.
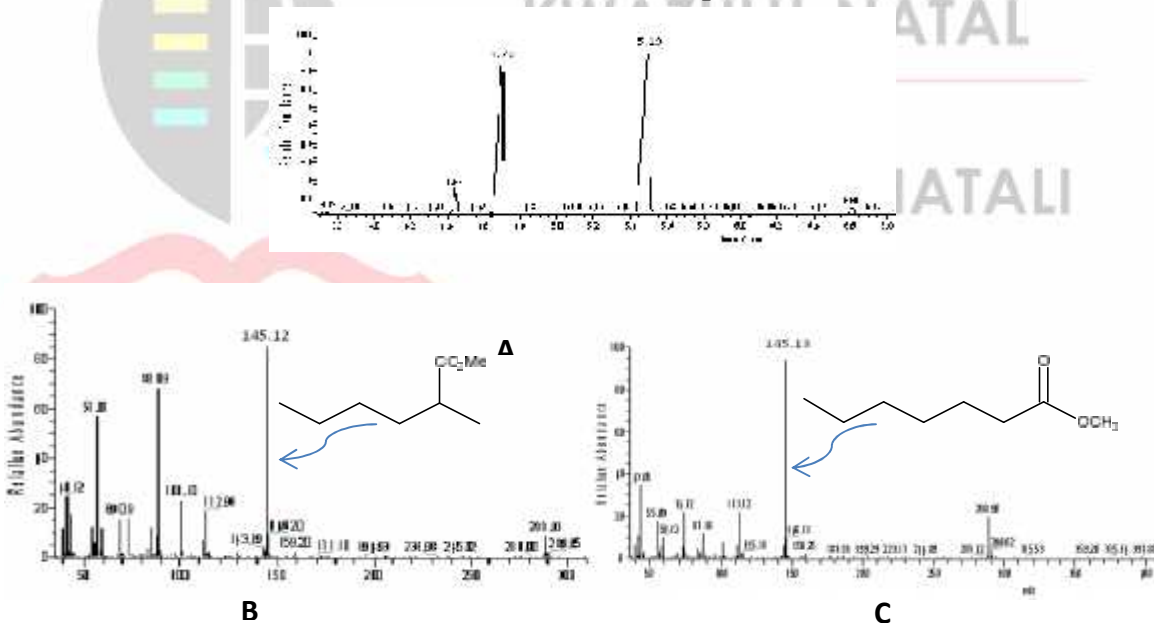
Figure 4.2: GC spectra (**A**) and MS spectra for the branched ester (**B**) at a retention time of 4.70 min and linear ester (**C**) at a retention time of 5.19 min for 1-hexene using complex **C10**.

4.3.2 Effect of catalysts structure on methoxycarbonylation of 1-hexene

The catalytic activities of complexes **C2**, **C4**, **C6**, **C8-C11** in the methoxycarbonylation of 1-hexene were studied in order to investigate the effect of complex structure on catalytic activity. The effect of ligand substituent in the phenyl group was observed to influence the catalytic activity. For example, complex **C10** bearing electron donating OCH_3 group was the most active (Table 4.1, entries 7 and Figure 4.3), while the corresponding complex **C11**, containing the electron withdrawing Br substituent was the least active (Table 4.1, entry 8). This trend is consistent with OCH_3 resulting in very stable Pd(II) complexes while the Br substituent is likely to form unstable Pd(II) complexes and promotes the reduction of the catalytically active Pd(II) to less active Pd(I) / Pd(0) species.[17-20]

Another factor that affected the catalytic activity was the Pd-Cl/Me bond on the complex structure. Complex **C9** containing Pd-Cl bond showed lower catalytic activity (Table 4.1, entry 6, Figure 4.3) compared to **C10** bearing Pd-Me bond which gave higher catalytic activity (Table 4.1, entry 7, Figure 4.3). The possible reason might be the ease of CO coordination and insertion into Pd-Me bond. Another reason would be the high stability exhibited by the $PdCl_2$ complexes hence not highly reactive towards the alkene substrate (do not easily dissociate to create a vacant site for substrate coordination).

We also compared the behavior of the neutral versus cationic palladium complexes. From the results obtained it was evident that the catalytic activity was higher for the neutral complexes. For example, the neutral complex **C2** (78%) was the more active

(Table 4.1, entries 1), compared to the corresponding cationic complex **C8** (47%), Table 4.1, entries 5. However, the neutral complex **C4** (Table 4.1, entries 3) was comparable with its cationic analogue **C10**. This might be due to the higher activities of the methoxy containing complexes.

Table 4.1: Effect of catalyst structure in the methoxycarbonylation of 1-hexene.[a]

Entry	Catalyst	PPh$_3$	Conversion (%)[b]	b/l ratio (%)[c]	TOF(h^{-1})
1	C2	2	78	41/59	6.5
2	C3	2	52	43/57	4.5
3	C4	2	80	40/60	6.7
4	C6	2	39	40/60	3.1
5	C8	2	47	32/68	3.9
6	C9	2	47	45/55	3.9
7	C10	2	86	37/63	7.1
8	C11	2	29	40/60	2.4
9	C8	-	15	55/45	1.2
10	C10	-	37	52/48	3.1
11	C11	-	10	68/32	0.8

[a]Reaction conditions: Pre-catalysts (0.07 mmol), solvent: toluene 40 mL and methanol 30 mL; Pd/1-hexene ratio 200:1, Pd/ HCl ratio; 1:10; P (CO) = 60 bar; temperature: 90°C; time 24 h; [b]% of 1-hexene converted after 24 h reaction, [c]branched/linear ester ratio.
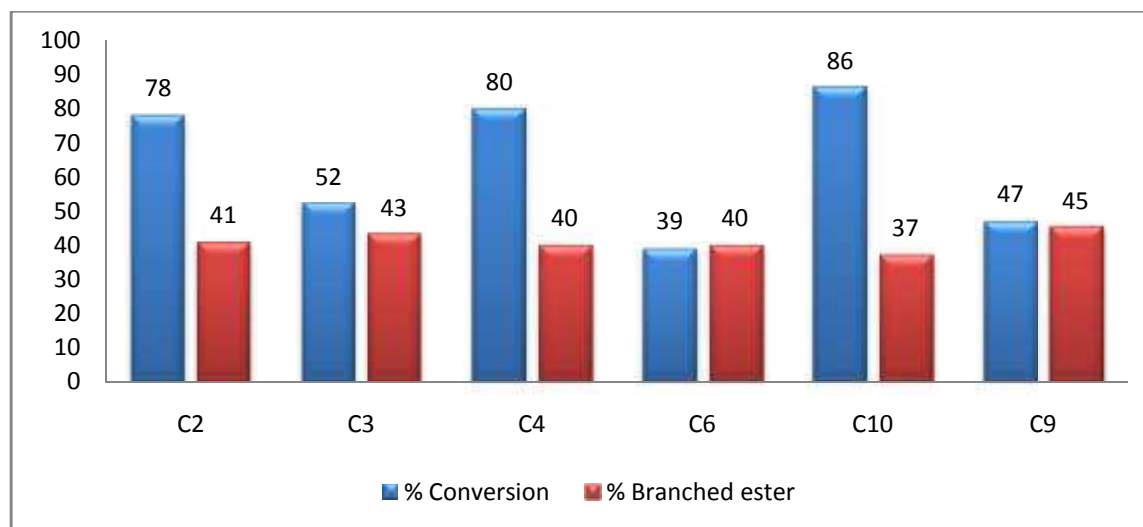
Figure 4.3: Plot of percentage conversion and regioselectivity for complexes **C2 – C11** in the methoxycarbonylation of 1-hexene.

The nature of the complex structure was seen to also affect the regioselectivity of the esters produced. From Table 4.1, it is apparent that, the cationic complexes bearing the PPh$_3$ ligand gave lower percentages of the branched esters compared to their respective neutral complexes. For example, while the neutral and cationic complexes **C2** and **C8** produced 41% and 32% of the branched esters respectively (Table 4.3, entries 1 vs 5). This is expected due to the presence of the bulkier PPh$_3$ groups in the cationic complexes which may hinder the isomerization process to give the branched esters. However, the cationic complex **C9** showed relatively higher regioselectivity towards the branched ester (45%) for reasons not clear to us

4.3.3 Effect of triphenyl phosphine (PPh₃) on the methoxycarbonylation of 1-hexene

The catalytic performance of complexes **C8**, **C10** and **C11** in the methoxycarbonylation of 1-hexene was studied upon addition and absence of PPh$_3$ in order to evaluate the effect of triphenyl phosphine (PPh$_3$) on their catalytic activities and selectivity. We observed that addition of PPh$_3$ to the palladium complexes (Table 4.1, entries 5, 7 and 8) resulted in higher catalytic activity. From literature reports,[21-23] it is believed that the presence of PPh$_3$ improves the stability of the resultant catalyst by limiting decomposition to Pd(0). Indeed, extensive decomposition of the complexes to palladium black was observed in the absence of PPh$_3$. The same observations have also been extensively reported by Aguirre and coworkers.[2]

It was also found that addition of PPh$_3$ played a significant role in product regioselectivity. For instance, it was seen that addition of PPh$_3$ to the palladium complexes decreased the amount of the branched ester (37 – 40%) formed during the reaction (Table 4.1, entries 5, 7 and 8). In the absence of PPh$_3$ (Table 4.1, entries 9 - 11) high regioselectivity towards the branched products was observed (52 - 68%). This trend could largely be attributed to steric factors. Therefore this observation can be explained by the steric hindrance caused by the addition of the bulky PPh$_3$ ligand thus disfavors the formation of more sterically hindered branched isomer.[22] Similar results were obtained by Zuniga *et al*[24] and Seayad *et al*[22] for the palladium catalyzed methoxycarbonylation of styrene. Where they observed that in the absence of PPh$_3$ there

was high regioselectivity towards the branched ester (45– 86) and the addition of the presence of PPh$_3$ to the palladium complexes decreased the amount of the branched ester (21 – 34%).[24]

4.3.4   Effect of acid promoters on methoxycarbonylation reactions

The nature of the acid promoter is another important feature to consider in the methoxycarbonylation reactions. The key function of the acid promoter is to stabilize the active Pd(II) species by limiting decomposition to Pd(0) black.[25-26] This is achieved by coordination of the Pd(II) to the anions from the acid.[25-26] The catalytic activity of **C10** was studied in the methoxycarbonylation of 1-hexene in order to investigate the effect of the acid promoters on activity. Table 4.2, entry 12 showed that there was no activity in the existence of weakly coordinating anions, such as TsO$^-$, derived from the addition of *p*-TsOH. When HCl was used as an acid promoter (Table 4.2, entry 13), high catalytic activity (86%) and activity (TOF = 7.1) was observed. These results are not surprising since Zuniga *et al*[27] and Claver *et al*[28] have reported similar observations (but *p*-TsOH showed lower activity) for the methoxycarbonylation of styrene by using other Pd – catalytic systems and HCl as the acid source. When sulfuric acid was used as the acid promoter (Table 4.2, entry 14), the activity was lower (TOF = 3.5) and low conversion (47%) to the products was observed (Table 4.2, entry 19). This observation was expected because both *p*-TsOH and H$_2$SO$_4$ are non- or weakly coordinating anions and when used in the presence of monodentate phosphine ligands in this case PPh$_3$ results in

rapid alkylation. This loss of phosphine inevitably leads to unstable palladium species.[29] Compared to HCl (coordinating anion) this confirmed the stabilizing effect of additional chloride anions[13] and hence no loss of phosphine.

The acid promoter also plays an important role in product selectivity. For example, when HCl was used as an acid promoter high regioselectivity towards the linear ester was observed (Table 4.2, entry 13, 63%), while high regioselectivity towards the branched ester was obtained (Table 4.2, entry 14, 47%) when H_2SO_4 was used.

Table 4.2: Effect of reaction conditions in the methoxycarbonylation of 1-hexene using **C10**.[a]

Entry	Acid	P_{CO}/ bar	T/°C	[substrate]/[Pd]	Time	Conv (%)[b]	b/lratio(%)[c]
12	*p*-TsOH	60	90	200:1	24	--	--
13	HCl	60	90	200:1	24	86	37/63
14	H_2SO_4	60	90	200:1	24	42	47/53
15	HCl	50	90	200:1	24	50	38/62
16	HCl	60	60	200:1	24	86	36/64
17	HCl	60	90	400:1	24	55	31/69
18	HCl	60	90	100:1	24	89	50/50
19	HCl	60	90	200:1	12	49	28/72
20	HCl	60	90	200:1	32	92	47/53
21	HCl	60	90	200:1	36	99	55/45

[a] Reaction conditions: Solvent: toluene 40 mL and methanol 30 mL; Pd/ acid ratio; 1:10; time 24 h; [b] % of hexene converted after 24 h reaction; [c] Molar ratio between branched and linear ester.

4.3.5   Effect of reaction conditions in methoxycarbonylation reactions

The effect of carbon monoxide pressure on the performance of complex **C10** was investigated. Complex **C10** was chosen for further of the reaction conditions on catalyst performance due to higher catalytic activity shown initially (Table 4.1, entry 7). Carbon monoxide pressure substantially influences the catalytic activity. For example, at higher pressures (Table 4.2, entry 13), the catalytic activity increases (86%), while at lower

pressures (Table 4.2, entry 15) lower catalytic activity was observed. This observation might be due to the faster insertion of CO at higher pressures which results in higher conversion to the products. A temperature study of the methoxycarbonylation of 1-hexene with **C10** as the catalysts showed that at higher temperatures (90 $^{\circ}$C), there is large decomposition of the catalysts at the end of the reaction. However, similar conversions were observed at a temperature of 90 $^{\circ}$C (Table 4.2, entry 13) and 60 $^{\circ}$C (Table 4.2, entry 16). Similar results were observed by Aguirre *et al.*[2] The catalyst concentration is another important parameter to consider. It was observed that at higher catalyst concentration of 1:100 (Table 4.2, entry 18), higher catalytic activity (89%) was obtained, while at lower catalyst concentration of 1:400 (Table 4.2, entry 17), lower catalytic activity (55%) was observed. Similar observations were also made by Vavasori and cowokers.[30] We also investigated the effect of time on catalytic activity. It was evident from the results that the reaction time influences the catalytic activity. At 12 h (Table 4.2, entry 19) lower conversion to the products (49%) was observed, while increasing the reaction time to 36 h (Table 4.2, entry 21) resulted in higher percentage conversions of 99% (Figure 4.4).

The regioselectivity towards the branched/linear was also investigated using the reaction conditions. Changing the carbon monoxide pressure from 50 to 60 bar (Table 4.2, entries 13 and 15) resulted in no effect in regioselectivity. Increasing the temperature from 60 to 90 $^{\circ}$C (Table 4.2, entries 13 and 16) resulted in no effect in

regioselectivity. However, the reaction time and catalyst concentration affected the regioselectivity. For instance, increasing reaction time from 12 h to 36 h resulted in high regioselectivity towards the branched ester from 28% to 55% (Figure 4.4). It was also observed that increasing the catalyst concentration from 1:100 to 1:400 (Table 4.2, entries 13, 17 and 18) resulted in high regioselectivity towards the branched from 31% to 50%.
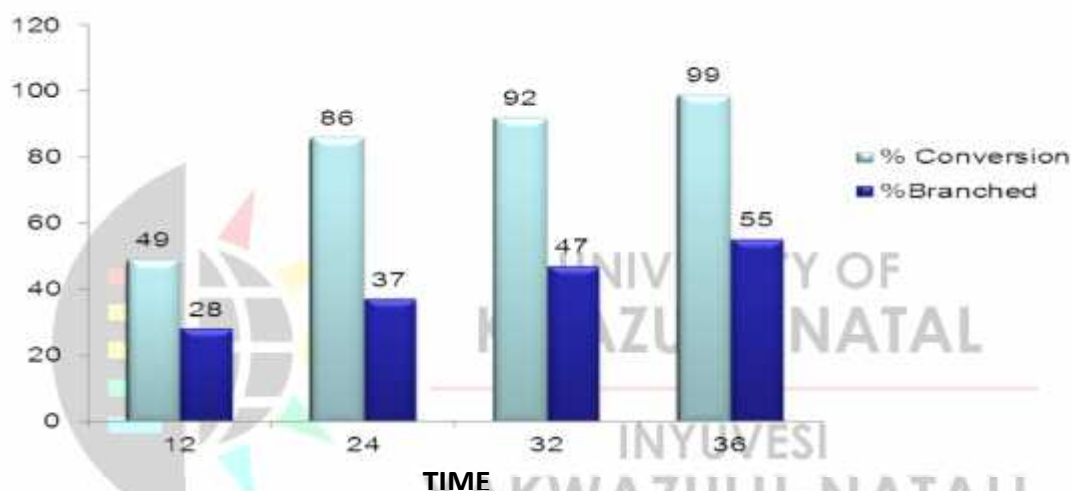
Figure 4.4: Graph of % conversion and regioselectivity using complex **C10** showing the influence of time on the methoxycarbonylation reactions.

4.3.6   Effect of olefin substrate on methoxycarbonylation using C10

Complex **C10** was used to investigate the effect of substrates such as; styrene, 1-octene, 1-nonene and 1-decene on the methoxycarbonylation reactions (Table 4.3). It was clear from the results obtained that the catalytic activity was significantly affected by the nature of the substrate. For example, when 1-hexene was used, higher catalytic activity of up to 86% compared to conversions of 26% recorded for 1-decene (Table 4.3, entries 23 vs 26). It is therefore apparent that increasing the chain length from 1-hexene to 1-

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decene resulted in lower catalytic activities. The lower catalytic activity when the chain length is increased might be due to the increased steric hindrance.

The regioselectivity towards the branched/linear esters was also affected by the nature of the alkene substrate. It was generally observed that with increase in chain length, the regioselectivity towards the branched ester was favored. For instance, while 37% of the branched ester was obtained for 1-hexene, 67% branched esters were obtained using 1-decene as the substrate (Table 4.3, entries 23 vs 26). This phenomenon could be partly apportioned to the higher number of possible isomers present in the higher alkenes compared to lower alkenes. For example, while 1-hexene has four internal isomers, 1-decene contains eight possible internal isomers.

Table 4.3: Effect of olefin in the presence of PPh$_3$ with **C10** as catalyst

Entry	Substrate	Conversion (%)	b/lratio(%)[a]	TOF(h^{-1})
22	Styrene	88	18/82	7.3
23	1-Hexene	86	37/63	7.1
24	1-Octene	36	54/46	3.0
25	1-Nonene	24	58/42	2.0
26	1-Decene	10	67/33	0.8

Reaction conditions: Solvent: toluene 40 mL and methanol 30 mL; Pd/substrate ratio 200:1, Pd/ HCl ratio; 1:10; P (CO) = 60 bar; temperature: 90°C; time 24 h; [a]Molar ratio between branched and linear ester.
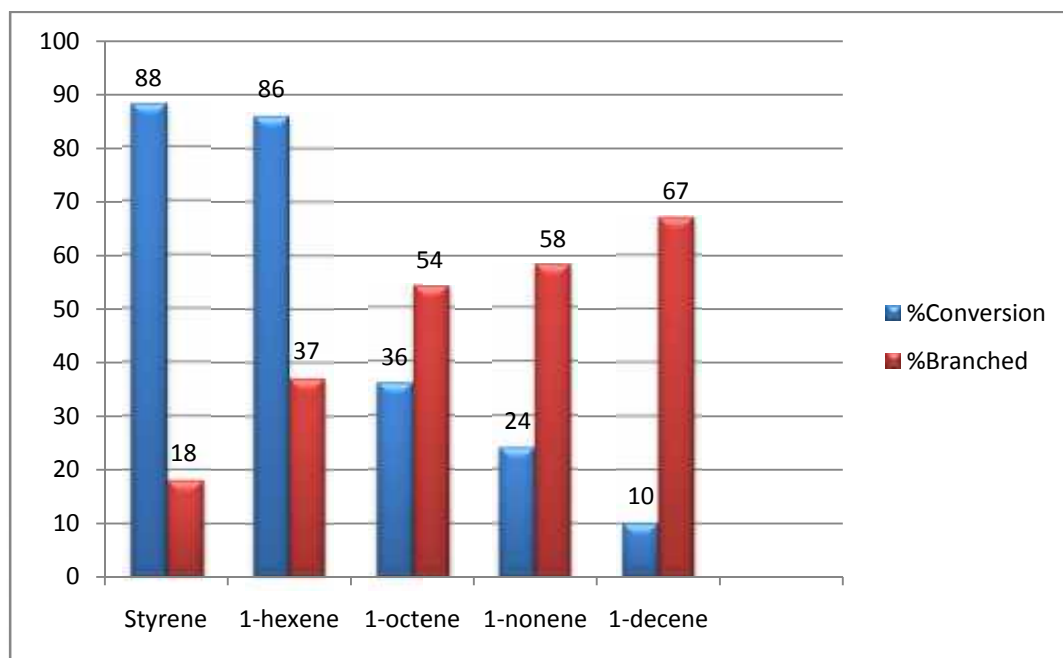
Figure 4.5: The effect of substrate on percentage conversion and regioselectivity towards branched product using catalyst **C10**.

4.4 Conclusion

In conclusion, the synthesized complexes were all active in the methoxycarbonylation reactions. Both the electronic and steric factors affected the catalytic behavior of the catalysts. Complexes bearing electron donating groups were found to be more active than those bearing electron-withdrawing groups. Thus stability of the resultant catalytically active species could be said to play a major role in determining activity. Addition of PPh$_3$ to the complexes gave higher catalytic activities and high regioselectivity towards linear esters. The use of HCl as an acid promoter resulted in higher catalytic activity compared to non- or weakly-coordinating acids p-TsOH and H$_2$SO$_4$. High reaction temperatures, pressure and catalyst concentration resulted in higher catalytic activities. The reactivity and selectivity of the substrates were largely affected by the chain length. Increasing the olefin chain length resulted in lower catalytic activities and high regioselectivity towards the branched ester.

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CHAPTER FIVE

General concluding remarks and future prospects

5.1   General conclusions

In summary, this thesis has presented a systematic investigation of (benzoimidazol-2-ylmethyl) amine palladium complexes as potential methoxycarbonylation catalysts. The synthesized benzoimidazolyl amine palladium complexes were characterized by ^{1}H NMR, elemental analysis, ^{31}P NMR (**C7 – C11** cationic complexes) and X- ray analyses for some cationic complexes. The solid state structures of **C8a**, **C9b** and **C11c** showed that the (benzoimidazol-2-ylmethyl) amine ligands are coordinated to Pd(II) in a monodentate fashion via Bzim- nitrogen atom. However these results were in disagreement with the elemental analysis data. The elemental analyses showed one ligand unit and one PPh$_3$ per-metal ion. The ^{31}P NMR for complexes **C8**, **C9** and **C11** confirmed the presence of mono-coordinated PPh$_3$ ligand.

The palladium complexes bearing electron donating groups were most active and most stable, while the palladium complexes containing electron withdrawing groups were least active and less stable. Addition of PPh$_3$ to the palladium complexes resulted in higher catalytic activities and higher regioselectivity towards the linear esters. No activity was observed in the presence of weakly coordinating anions, such as TsO$^-$ derived from p-TsOH. While H$_2$SO$_4$ (weakly coordination anion) as the acid promoter

resulted in lower catalytic activity. The use of HCl (strongly coordinating anion) gave higher catalytic activity. The effect of reaction conditions such as pressure, temperature, catalyst concentration and time were also investigated. It was observed that at high pressure there was high conversion to the products. No effect on catalytic activity was observed when the temperature was decreased. Increasing the catalysts concentration, chain length and time resulted in an increase in conversion to products and higher regioselectivity towards the branched ester was observed. Therefore the performance of the palladium complexes in methoxycarbonylation of olefins depends on catalysts structure, olefin substrate, acidic medium and reaction conditions. The key attribute of these palladium complexes is the 100% chemoselectivity towards the formation of esters.

5.2   Future prospects

This study revealed that the benzoimidazolyl Pd(II) complexes were active towards the methoxycarbonylation of olefins. However, one needs to modify the catalysts structure to improve selectivity towards the branched esters. This is due to the fact that branched esters are essential in pharmaceutical industries as they are applied in non-steroidal anti-inflammatory drugs such as aspirin, ibuprofen, naproxen and ketoprofen. This could be achieved by synthesizing palladium complexes that contain less bulky ligands to reduce steric hindrance around the metal atom as shown in Figure 5.1.
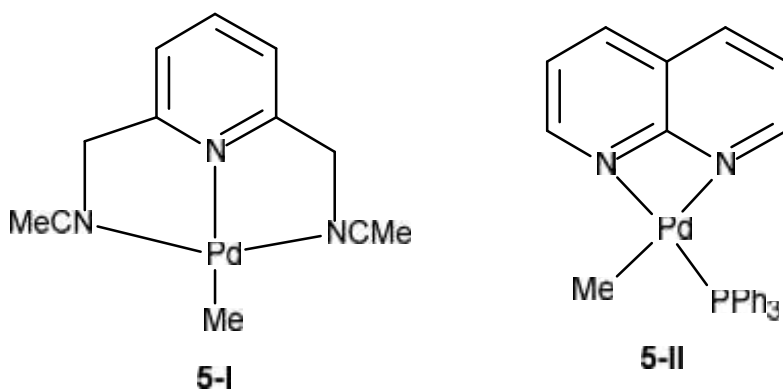
Figure 5.1: palladium complexes containing less bulky ligands.

Another way of obtaining branched esters would be to investigate the methoxycarbonylation of internal olefins. Furthermore one needs to investigate the effects of other acidic medium. An example will be to investigate the effect of oxalic acid because it has been observed in literature that it provides high regioselectivity towards the branched esters. We will also use HBr and HI to investigate the effect of HX with X = Cl⁻, Br⁻, I⁻, which will show us the acid conversion.

The major setbacks of homogeneous catalysts are product separation from the reaction mixture and catalyst recovery. This can be achieved by heterogenizing the catalysts and the product into two immiscible, separate phases. Therefore the biphasic reactions offer a possible answer to the problem. Therefore we will design water soluble catalyst for biphasic catalysis and an example of such catalysts is shown in Figure 5.2. The triphenyl

phosphine tri-sulfonate ligand in the complexes in **5-III** and **5-IV** could be used as water
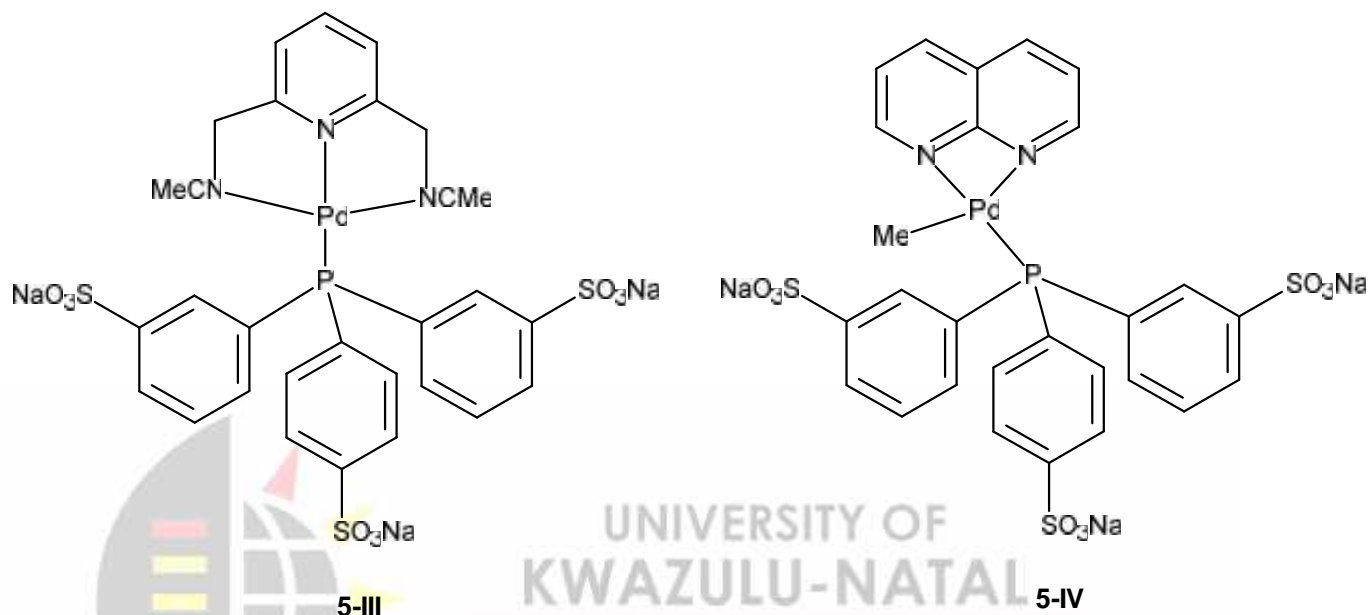
soluble phosphines.

Figure 5.2: Water soluble catalyst for biphasic catalysis.