CHIRAL (IMINO)PYRIDINE AND (IMINO)PHOSPHINE PALLADIUM (II) COMPLEXES: SYNTHESIS, MOLECULAR STRUCTURES AND APPLICATIONS AS CATALYSTS IN METHOXYCARBONYLATION OF OLEFINS

by

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Thesis

Submitted in fulfilment of the academic requirements

for the degree of Master of Science in Chemistry

College of Agriculture, Engineering and Science,

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Pietermaritzburg

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DECLARACTION I

I, **Nondumiso Lean Ngcobo** declare that;

1. The research reported in this thesis, "CHIRAL (IMINO)PYRIDINE AND (IMINO)PHOSPHINE PALLADIUM (II) COMPLEXES: SYNTHESIS, MOLECULAR STRUCTURES AND APPLICATIONS AS CATALYSTS IN METHOXYCARBONYLATION OF OLEFINS" except where otherwise specified, is my original research.

2. This thesis has not been submitted for any degree or examination at any other university.

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Signed:  Date: 13th November, 2020

As the candidate's supervisor, I have approved this thesis/dissertation for submission.

Signed:  Name: Prof. Stephen Ojwach Date: 16th November, 2020

DECLARATION II – CONFERENCE PRESENTATION AND PUBLICATION

Some segments of this research have been presented in the following conferences:

1. Nondumiso L. Ngcobo & Stephen O. Ojwach, DST-NRF Centre of Excellence in Catalysis: Centre for Catalysis Research Conference (November 2018), Shanghai resort; Limpopo. Oral presentation. Chiral (iminopyridine) and (imino)phosphine palladium(II) complexes: synthesis, molecular structures and application as catalysts methoxycarbonylation of olefins.
2. Nondumiso L. Ngcobo & Stephen O. Ojwach, DST-NRF Centre of Excellence in Catalysis: Centre for Catalysis Research Conference (November 2019), Krystal Beach Hotel - Gordon's Bay, Western Cape. Oral presentation. Chiral (iminopyridine) and (imino)phosphine palladium(II) complexes: synthesis, molecular structures and application as catalysts methoxycarbonylation of olefins.

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ABSTRACT

The chiral (imino)pyridine and (imino)phosphine ligands, (*S*)-1-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine **(L1),** *(R)-1*-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine **(L2),** (*S*)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine **(L3)** and (*R*)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine **(L4)**, (*S*)-N-(2-(diphenylphosphino)benzylidene)-1-phenylethanamine (**L5**) and (*R*)-N-(2-(diphenylphosphino)benzylidene)-2-methoxyethanamine (**L6**) were prepared by condensation of one mole equivalents of either (*S*)- or (*R*)-methylbenzylamine with the appropriate aldehyde: acetylpyridine, 2-pyridinecarboxaldehyde or 2-(diphenylphosphino)benzaldehyde. Reactions of ligands **L1-L6** with either [Pd(COD)Cl_2] or [PdClMe(COD)] metal precursors, afforded the respective palladium(II) complexes [Pd(**L1**)Cl_2] (**C1**), [Pd(**L2**)Cl_2] (**C2**), [Pd(**L3**)Cl_2] (**C3**), [Pd(**L4**)Cl_2) (**C4**), [Pd(**L4**)MeCl] (**C5**), [Pd(**L5**)Cl_2] (**C6**) and [Pd(**L6**)Cl_2] (**C7**) in moderate to high yields. The ligands and complexes were characterized by ^{1}H-NMR, ^{13}C NMR, ^{31}P NMR spectroscopy, mass spectrometry, elemental analysis, FT-IR spectroscopy, and single X-ray crystallography. Molecular structures of complexes **C1-C4, C6** and **C7** established bidentate coordination of ligands **L1-L6** to give distorted square planar geometries. All the complexes **C1- C7** displayed low to moderate catalytic activities in the methoxycarbonylation of 1-hexene and styrene, although with high regio-selectivity towards the branched esters. Only racemic mixtures of the branched ester products were obtained, indicating very low enantio-selectivities of the complexes. *In situ* NMR studies pointed to possible decomposition of the active species, *via* ligand dissociation, to be responsible for the lower catalytic activities observed.

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DEDICATION

Dedicated to my parents Mr Bhekuyise Richard Ngcobo and Mrs Delisile Frota Ngcobo, and my whole family at large.

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CHAPTER 1

Catalytic transformation of olefins: Industrial significance and the role of transition metal catalysts

1.1. Introductory remarks

Olefins are defined as a family of organic compounds which are characterized with at least one carbon-carbon double bond and a chemical formula C_nH_{2n}.[1, 2] In the chemical industry, olefins are amongst the most important building blocks for conversion of many valuable products and are categorized as light and heavy olefins.[3] The light olefins constitute as precursors for oligomers and polymers, whilst the heavier olefins ($\geq C_{10}$) are precursors for surfactants, coatings, paints, varnishes, etc.[4] Olefins can also form naturally in living things for example as nutrient beta carotene found in carrot and ethylene which aids the ripening of fruits.[5] And can also be industrially synthesized using steam cracking, propane dehydrogenation[6, 7] and other refinery catalytic cracking processes to afford light olefins[8, 9], whilst the heavier olefins can be synthesized from lower olefins (ethylene and propylene) and *syn* gas through the oligomerization reaction.[10]

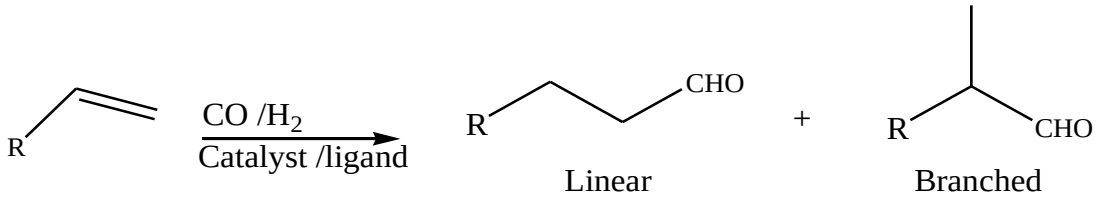
Catalyst design and development is one of the multi-disciplinal approaches which has played a vital role in the advancement of the chemical industry, permitting the conversion of olefin feedstock into industrially valuable products such as the transformations to oligomers and the polymers conversion to alkanes and other functionalized fine products.[11, 12] The application of transition metal complexes as catalysts in various organic transformation has grown to be of interest due to its success.[13, 14]

1.2. Olefins reactions, transformations and applications

The conversion of olefins has been employed by using various reactions and transformations namely, oligomerization, polymerization, metathesis and carbonylation.[15-19] Over the years, these olefin transformations have been proved to be a resourceful tool in organic synthesis. Many biologically active molecules and natural products have been synthesized using these reactions.[1-5, 15, 19, 36, 39, 51] A high deal of olefin transformations resulted in their recurrent applications in industrial processes. The industrial applications of these reactions and transformations is highly influenced by type of catalyst.

1.2.1. Hydroformylation reactions of olefins

This is an atom-efficient industrially applied process which was first discovered in 1938 by Otto Roelen when he was developing the Fischer-Tropsch reaction at the Ruhrchemie Industry.[15, 16, 20] This reaction involves the *cis*-addition of hydrogen and carbon monoxide (also known as syngas) to the characteristic double bond of the olefin to produce aldehydes in the presence of a catalyst. (Scheme 1).[15, 20] Transition metal-based catalysts consisting of Fe, Co, Ru, Rh, Pd, Pt, and Os metal centres have been extensively studied but currently Rh- and Co-based catalysts are most widely used for hydroformylation due to their selectivity toward linear aldehydes, their affordability and abundancy.[15, 21] Chiral and aliphatic aldehydes are mostly applied in the pharmaceutical, agrochemical and cosmetic industries due to their application as precursors in the synthesis of anti-inflammatory drugs such as ibuprofen and naproxen, and in yielding detergents, plasticizers, solvent or surfactants.[5]

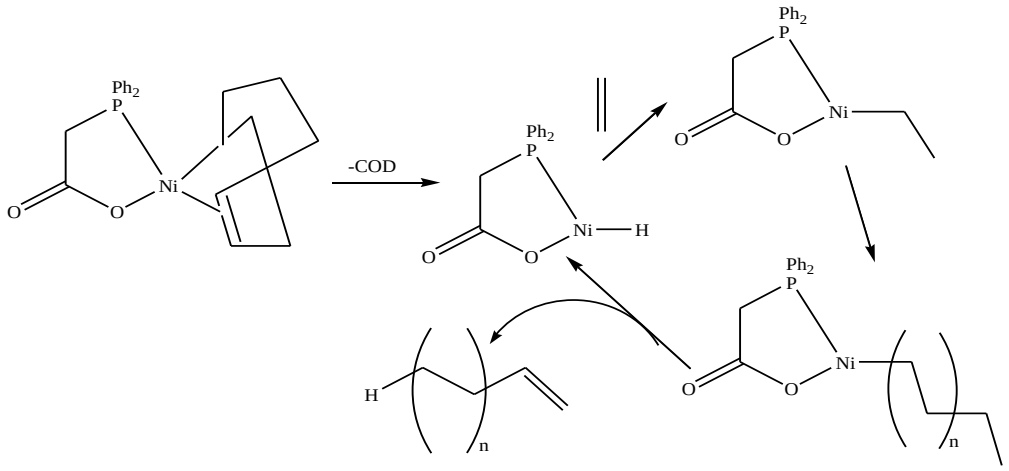


Scheme 1.1. Hydroformylation reactions of olefins.[16]

1.2.2. Oligomerization reactions

Oligomers are low molecular weight products of α-olefin transformations, and are also of interest for the chemical industry.[22] The zirconocene catalysts activated with minimal amounts of methylalumoxane (MAO) can be employed for the preparation of these oligomeric products.[23- 26] Oligomerization reactions involves the conversion of low molecular weight monomers into macromolecules whose applications are significantly influenced by the length of chain and nature of repeating unit of monomers.[27] For instance, short chain linear olefins C_2-C_4 and C_5-C_9 olefins give rise to liquefied petroleum gas (LPG) and naphtha respectively.[15] The mono-olefins of these light olefins can be promoted to produce fuel components (such as gasoline and intermediates for the manufacture of many types of products in the petrochemical industry, Sasol) via oligomerization.[15] Synthesized oligomers of α-olefins (C_{14}-C_{16}) form the basis for lubricating oils.[16] Oligomerization is by far the most extensively used reaction in the conversion of lower olefins (C_2 –C_4) into industrially significant higher olefins (C_8 – C_{30}).[3, 17]

A well-defined and most commonly used non-selective ethylene oligomerization industrial process is the Shell Higher Olefin Process (Scheme 2), whereby ethylene is used as feedstock to manufacture diesel, petrol, lubricants and surfactants[17] , using the mostly studied nickel metal catalyst.[28, 29]



Scheme 1.2. Typical example of catalytic cycle for the Shell Higher Olefin Process (SHOP) oligomerization step.[29]

1.2.3. Olefin Polymerization reactions

Oligomers are essential intermediates in the polymerization reaction. Polymerization is a chemical reaction that is usually performed with a catalyst, heat or light and pressure in which enormous number of relatively simple olefins combine to form a high molecular weight product.[30] In the early 1950s, Karl Ziegler and Giulio Natta introduced the Ziegler-Natta catalyst which allowed the production of polyethylene at low temperatures and pressures.[31, 32] Later in the 1980s, the Ziegler-Natta catalyst (Figure 1.1) was modified by the addition of metallocene ligands which upgraded and expanded the properties of polyolefin materials.[18]

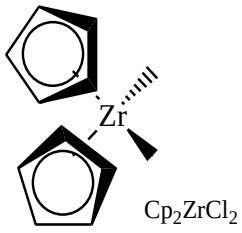


Figure 1.1. Example of Metallocene catalyst for olefin polymerization.[33]

Polyolefins can be functionalized with acids or esters, which tend to transform them to polymers consisting monomeric cross links. These are useful in applications towards products that require extreme toughness involving golf ball covers or superior sealing properties such as bacon packaging.[17]

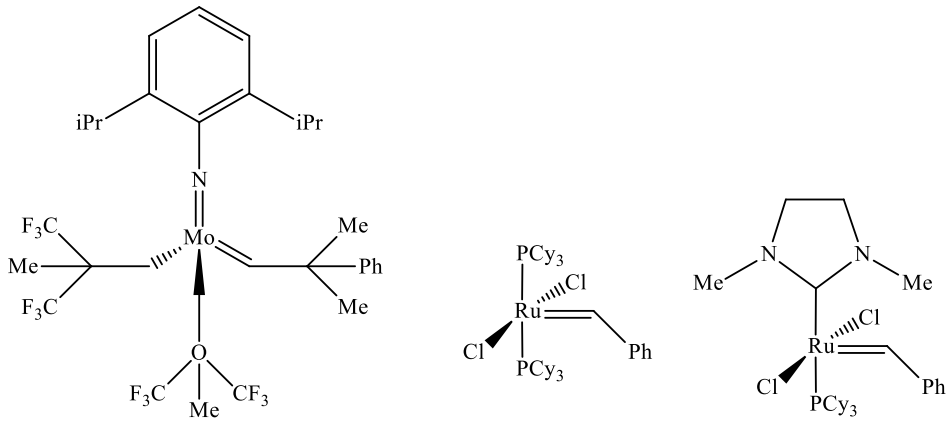
Table 1.1. Classification of polyethylene and applications

Polyethylene	**Definition**	**Preparation**	**Applications**	**Ref.**
LDPE (Low-density polyethylene)	characterized as a branched ethylene homopolymer	prepared in a high-temperature and high-pressure free-radical process hence it is a very cost-effective process	Heavy duty bags, industrial sacks, packaging of pharmaceuticals, power cables	[1, 3]
LLDPE (Linear low-density polyethylene)	random copolymer of ethylene and terminal olefins (C_4-C_8)	commercially prepared using Ziegler Natta, chromium, and metallocene catalysts	Lamination, film	[1, 4]
HDPE (High-density polyethylene)	characterized as linear, semi crystalline and consisting ethylene homopolymer	Ziegler-Natta and chromium-based coordination polymerization technology are employed for the preparation of these polyethylene	Pipes, thin walled food containers, toys, houseware	[5]

1.2.4. Metathesis reactions

Olefin metathesis is a chemical reaction that was accidentally discovered during the investigation of Ziegler-Natta polymerization using alternative metal systems.[19] It involves scission and regeneration of C-C double bonds of olefins whereby the substituents among the different olefins are exchanged to generate new olefins.[19, 20] The olefin metathesis reaction is considered to be a well-defined and useful process in synthetic organic chemistry.[34] Transition metal carbenes are used as catalysts and/or as initiators to aid in propagation process of metathesis catalytic cycle.

The major breakthrough in the evolution of this reaction was the use of tungsten carbenes $Ph_2C=W(CO)_5$, discovered by Katz and co-workers as initiators in the alkene metathesis in the absence of coactivators.[35, 36] This discovery has led to the development of the modern mostly employed Grubbs and Schrock complexes (Figure 1.2).[34, 37-39]

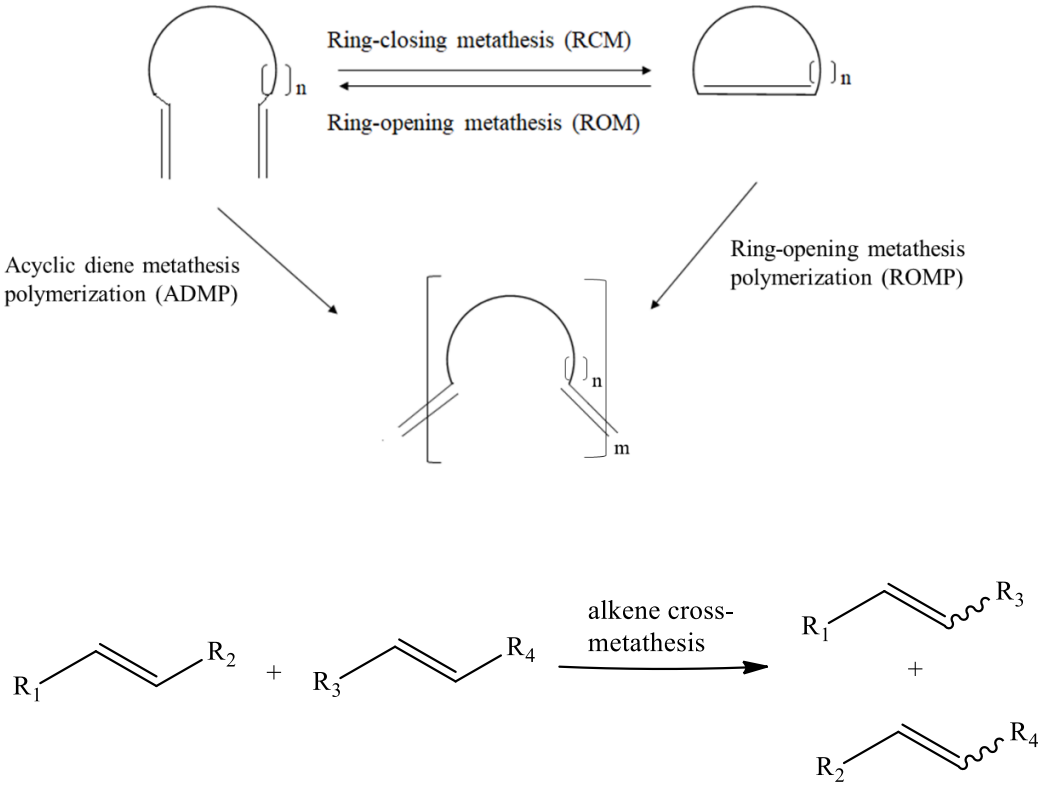


a **b** **c**

Figure 1.2. Schrock and Grubbs transition metal anchored carbenes as catalysts in olefin metathesis.[34, 40]

There are six known types of olefin metathesis namely cross metathesis (CM) for the production of light olefins and bulk chemicals such as pesticides, ring-closing metathesis (RCM) to

manufacture fine chemicals such as drugs, perfumes, acyclic diene metathesis polymerization (ADMET), ring-opening cross metathesis (ROCM), ring-opening metathesis polymerization (ROMP) for production of specialty polymers such as polyclooctene, and lastly intermolecular enzyme metathesis (Scheme 1.3).[20, 35]

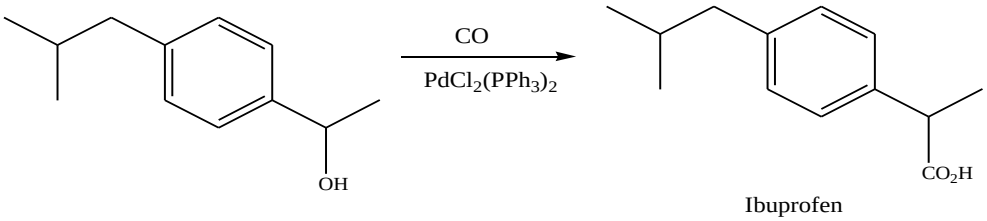


Scheme 1.3. Selected types of olefin metathesis reactions.[34, 41]

1.2.5. Carbonylation reactions

Carbonylation reactions involves the C=O functional unit being inserted into different organic molecules as substrates.[42] These reactions are accelerated by catalysts based on transition metal complexes. The first well-established catalytic carbonylation reaction was discovered by Roelen

using the cobalt-catalysed Fischer-Tropsch mechanism for the synthesis of hydrocarbons from carbon monoxide and hydrogen.[12, 43] This was further extended by Reppe and co-workers who synthesized unsaturated carbonyls from alkenes and alkynes in the presence of $Ni(CO)_4$ catalyst. [11] Since the 1990s, this process has been utilized commercially by the Boots-Hoechst-Celanese Company in Bishop, Texas.[44] Significance of this reaction is highly influenced by the reactivity and versatile functionalities of the carbonyl group which favours good products and high selectivity.[45] Non-steroidal anti-inflammatory drugs (2-arylpropanoic acid known as ibuprofen) can be synthesized using substituted benzyl alcohols *via* the carbonylation reaction (Scheme 1.4).[44]



Scheme 1.4. Formation of ibuprofen *via* carbonylation reaction.[44]

There are various types of carbonylation reactions namely, alkoxy carbonylation (Reaction 1), alcohol carbonylation such as methanol carbonylation (Reaction 2) as well as heck carbonylation which has been used as an important method for the synthesis of aromatic esters.[46] Traditionally, this method requires the use of gaseous carbon monoxide to introduce the carbonyl functionality.[47]

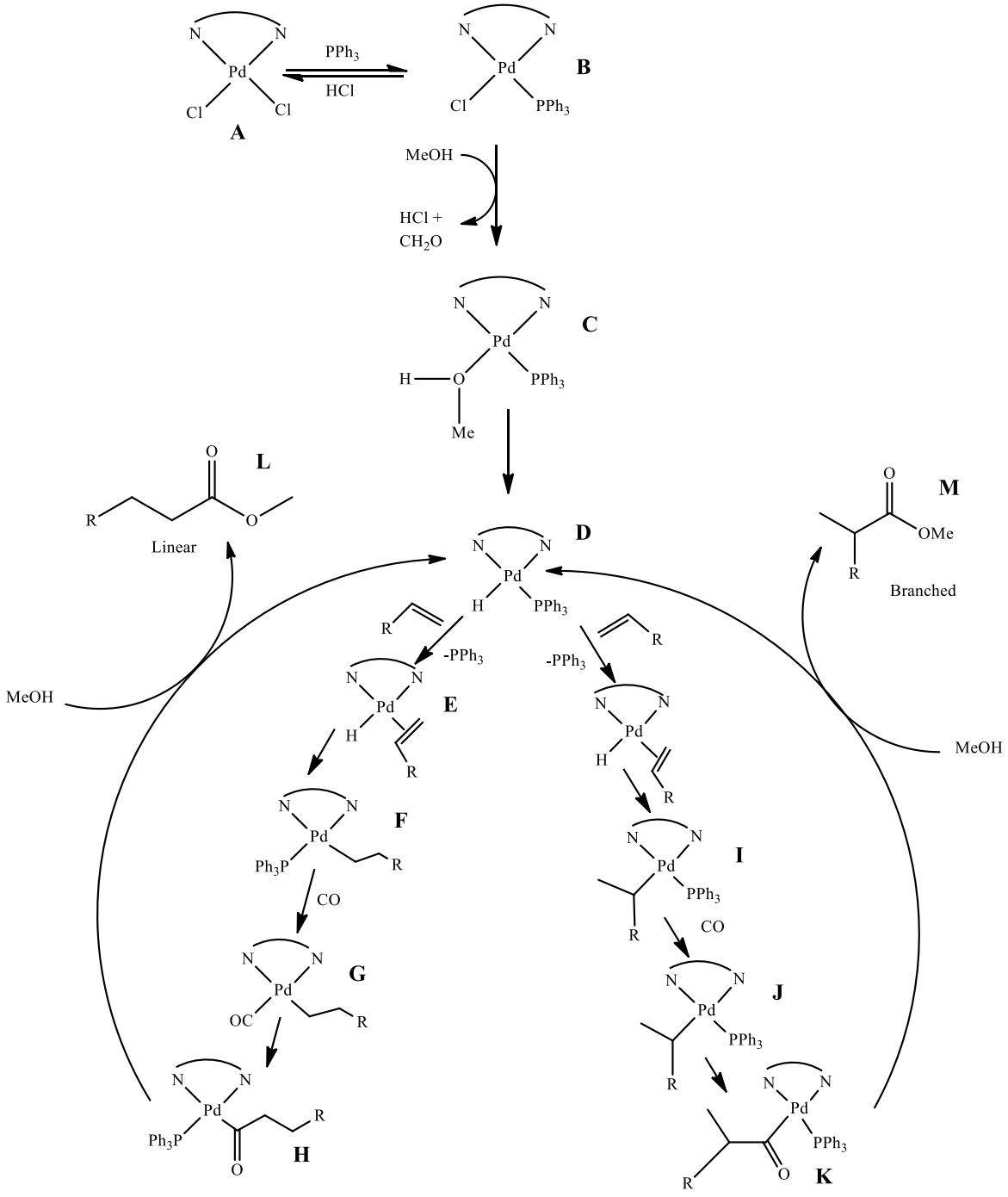
Reaction 1. $RCH{=}CH_2 + CO + R'OH \longrightarrow RCH_2CH_2CO_2R' + RCH(CO_2R')CH_3$

Reaction 2. $MeOH + CO \longrightarrow MeCO_2H$

1.3. Methoxycarbonylation reactions

Methoxycarbonylation, also known as hydroesterification, is a form of carbonylation reaction whereby methanol is used as the alcohol reagent.[12, 48] In methoxycarbonylation reactions, different alcohols may be utilized to afford different esters for example ethanol which yields out ethyl esters. One limitation of this reaction is that the more complex the alcohol is, the slower the rates of reaction as well as higher possibility of more complications.[12] So, in this case, methanol will be used to yield out methyl ester products. The methanol reagent allows for good solubility of catalysts in methoxycarbonylation reactions and assists in the reductive elimination step of the reaction mechanism in the proposed catalytic cycle.[12, 20, 49-50]

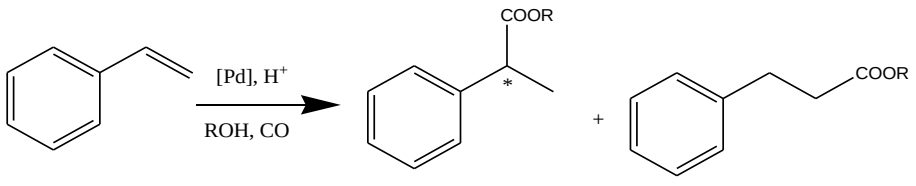
The methoxycarbonylation mechanism of olefins using nitrogen donor palladium (II) based catalysts is proposed to be the hydride cycle immersed in HCl as the acid promoter and methanol solution (Scheme 1.5).[20] The hydride cycle begins with the addition of PPh_3 (stabilizer) and HCl to **A**, resulting in a cationic species **B** which upon reduction with methanol results in intermediate **C** and subsequently forms **D**. The coordination of the substrate occurs, afterwards insertion into the Pd-H bond which leads to the formation of Pd-alkyl complex **F** or **G**, then is converted into an acyl complex **J** or **K** by migratory insertion of CO gas introduced.[20, 49] Finally, there is a nucleophilic attack of methanol upon the acyl carbonyl forming product **L** (linear ester) and/or **M** (branched ester) depending on regioselectivity.[20]



Scheme 1.5. Diagrammatic representation of the proposed mechanism for the methoxycarbonylation reaction catalysed by palladium complexes.[20, 50-53]

1.4. Asymmetric methoxycarbonylation reactions of olefins

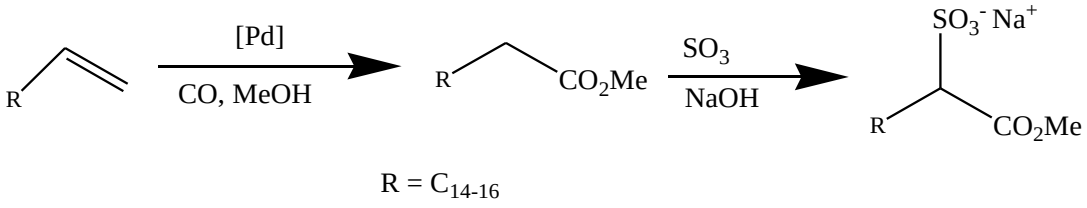
Numerous ligands are chiral, they exist in two auxiliary shapes (enantiomers) that are non-superimposable reflect pictures of each other and can easily be identified by their lack of a plane of symmetry. Moreover, the receptors, proteins, and other cellular components made from these particles are chiral and tend to be associated specifically with one or two enantiomers of a given substance.[54] For several drugs, customary research synthesis brings about a blend of enantiomers - one enantiomer ordinarily has the specified effect whereas the other enantiomer may be dormant or cause undesirable side effects. This matter has stirred researchers to seek after chiral catalysts, which drive chemical reactions towards one of two possible results.[55] Asymmetric methoxycarbonylation is a type of methoxycarbonylation reaction that gives rise to chiral ester compounds (Figure 1.6). In 1974, William Knowles was the first to discover a direct commercial synthetic route of an optically active material (called the L-dopa) using Rh coupled with chiral phosphine ligands, which subsequently resulted in the treatment of Parkinson disease.[12, 56] Kegl and Kollar, reported that the enantioselectivity of chemical reactions can be induced most effectively by an enantiomerically pure catalyst whereby a small quantity of chiral catalyst can transmit or transfer its chirality to a large quantity of substrate to afford chiral compounds.[42] Molecular chirality is an important characteristic within the pharmaceutical, agrochemical, flavour and fragrance industries.[42]



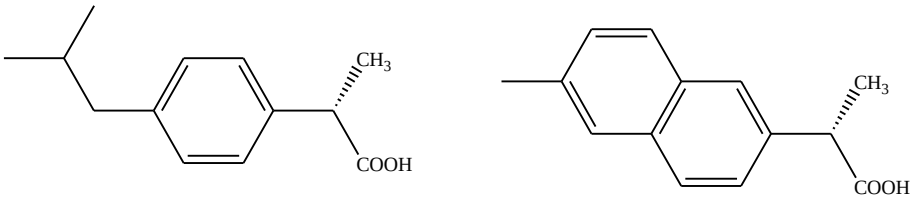
Scheme 1.6. Typical asymmetric methoxycarbonylation reaction.[48, 52, 57-59]

1.4.1. Industrial application of asymmetric methoxycarbonylation reactions

This reaction has been found to be exceptionally valuable in the class of unsaturated carbohydrates, from starting materials for the synthesis of detergents, surfactants as well as in the manufacture of several other industrial products such as solvents, perfumes, drugs and flavourings.[52, 59-61] For instance, the reaction in Scheme 1.7, shows the addition of sulphur trioxide to the linear ester product giving rise to the formation of an olefin sulfonate upon which the addition of sodium hydroxide resulting to the formation of methyl ester sulfonate.[63] The vinyl aromatics produce branched carboxylic acid esters, in the asymmetric methoxycarbonylation reactions of olefins, that serve as precursors for the synthesis of non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and naproxen (Figure 1.3).[62, 63] These NSAIDs are used in both sport medicine and prescription, assist in reducing pain and inflammation.[57]



Scheme 1.7. The production of surfactants from ester intermediates.[63]



(S)-Ibuprofen (S)-Naproxen

Figure 1.3. Non-steroidal anti-inflammatory drugs produced *via* asymmetric methoxycarbonylation reactions.[12, 64]

1.5. References

1. Bruice P.Y., Organic Chemistry (4th Ed.). Irene Lee Case Western Reserve University Cleveland, OH. Prentice Hall, 2004, Ch. 03, 111-112.
2. Sadeghbeigi, R. FCC Feed Characterization. Fluid Catalytic Cracking Handbook, 2000, 42.
3. Galvis H. M.T. and de Jong K. P., Catalysts for Production of Lower Olefins from Synthesis Gas: A Review. ACS Catal., 2013, 2130-2149.
4. Ferreira L.A., Sokolovicz Y. C. A., Couto J. L. and Schrekker H. S., Tandem olefin isomerization/metathesis and volatiles capture: Accessing light olefin blends and broadening the scope to higher olefins. Mol. Catal., 2018, 460, 36-39.
5. Hathaway B.A., Organic Chemistry the Easy Way. Barron's Educational Series, Inc., New York, 2006, Ch. 04, 61-86.
6. Yang L., Powell D. R. and Houser R. P., Structural variation in copper(I) complexes with pyridylmethylamide ligands: structural analysis with a new four-coordinate geometry index. Dalton Trans., 2007, 955-964.
7. Schmidt F., The importance of Catalysis in the Chemical and Non-Chemical industries. Basic Principles in Appl. Catal., 2004, 7-8.
8. Yılmaz M. K., Keleş H., İnce S. and Keleş M., Iminophosphine palladium catalysts for Suzuki carbonylative coupling reaction Appl. Organometal Chem., 2018, 32, 1-8.
9. Rodriguez C. J., Foster D. F., Eastham G. R. and Cole-Hamilton D. J., Chem. Commun., 2004, 1720.
10. Gnanasoundari V.G. and Natarajan K., Synthesis, Characterisation and Catalytic Studies of Iron(III), Cobalt(II), Nickel(II) and Copper(II) Complexes Containing N,O Donor Ligands and Triphenylphosphine. Transition Metal Chemistry, 2004, 29, 511-515.

11. Amghizar I., Vandewalle L. A, Van Geem K. M and Marin G. B., New Trends in Olefin Production. Engineering, 2017, 3, 171-178.
12. Makume B.F., Pd-catalysed methoxycarbonylation reactions of alkynes. University of Johannesburg, 2013, Ch. 01, 1-30.
13. Esmeraldo M.A., Gonçalves N. S., Rios, M. A. S., Mele G, Vasconcellos L. C. G. and Mazzetto S. E., Thermal and photochemical behavior of trans-ruthenium (II) dichloride tetraphosphite complexes. J. Photochem. and Photobiol. A: Chem., 2006, 184, 265-272.
14. Köhn R., 6.06 - Oligo- and Polymerization of Olefins A2 - Reedijk, Jan, in Comprehensive Inorganic Chemistry II (2nd Ed.), K. Poeppelmeier, Editor. Elsevier: Amsterdam. 2013, 127-154.
15. Sharma, D., V. Ganesh, and A. Sakthivel, Rhodium incorporated monometallic cobalt hydrotalcite-type materials: Preparation and its applications for the hydroformylation of alkenes. Appl. Catal. A: Gen., 2018, 555, 155-160.
16. Neves Â. C. B., Calvete M. J. F., Pinho e Melo T. M. V. D. and Pereira M. M., Immobilized catalysts for hydroformylation reactions: A versatile tool for aldehyde synthesis. Eur. J. Org. Chem., 2012, 32, 6309-6320.
17. Ittel S.D., Johnson L. K., and Brookhart M., Late-Metal Catalysts for Ethylene Homo- and Copolymerization. Chem. Rev., 2000, 100, 1169-1204.
18. Damavandi S., Ahmadjo S., Sandaroos R. and Zohuri G. H., FI Catalyst for Polymerization of Olefin, in Polymerization, A.D.S. Gomes, Editor. InTech: Rijeka, 2012, Ch. 06.
19. Grubbs R.H., Olefin metathesis. Tetrahedron, 2004, 60, 7117-7140.
20. Tshabalala T.A., Ojwach S. O., and Akerman M. A., Palladium complexes of (benzoimidazol-2-ylmethyl) amine ligands as catalysts for methoxycarbonylation of olefins. J. Mol. Catal. A: Chem., 2015, 406, 178-184.

21. de la Fuente V., Waugh M., Eastham G. R., Iggo J. A., Castillon S. and Claver C., Phosphine ligands in the palladium-catalysed methoxycarbonylation of ethene: insights into the catalytic cycle through an HP NMR spectroscopic study. Chem. Eur. J., 2010, 16, 6919-6932.

22. Janiak C. Coord. Chem. Rev. 2006, 250, 66.

23. Christoffers J., Bergman R. G., J. Am. Chem. Soc. 1996, 118, 4715.

24. Christoffers J., Bergman R. G., Inorg. Chim. Acta. 1998, 270, 20.

25. Fujikawa S., Okamoto T., Yokota K., US Patent 8119850, Filed 15 Feb 2006, Issued 21 Feb 2012.

26. Nifant'ev I. E., Vinogradov A. A., Vinogradov A. A., Ivchenko P. V., Catal. Commun., 2016, 79, 6.

27. Sato I., Urabe H., Ishii S., Tanji S. and Soai K., Asymmetric Synthesis with a Chiral Catalyst Generated from Asymmetric Autocatalysis. Org. Lett., 2001, 3, 3851-3854.

28. Ankersmit H. A., Veldman N., Spek A. L., Vrieze K. and van Koten G., Methyl-, acetyl-and allyl-palladium and-piatinum complexes containing the novel chiral phosphorus-imine 2-(diphenylphosphino)-benzylidene-S (−)-α-methyl-benzylamine ligand. Inorg. Chim. Acta, 1996, 252, 141-155.

29. Cavell R.G., Metal complexes of di-phosphorus imines. An exploration of multifunctional phosphorus–nitrogen ligand–metal chemistry. Current Sci., 2000, 440-451.

30. Speight J.G., Environmental Organic Chemistry for Engineers, Butterworth-Heinemann, 2016, Ch 03, 87-151.

31. Patel R.M., 2 - Polyethylene, in Multilayer Flexible Packaging (2nd Ed.), J.R. Wagner, Editor. William Andrew Publishing, 2016, 17-34.

32. Ronca S., Polyethylene, in Brydson's Plastics Materials (8th Ed.), M. Gilbert, Editor. Butterworth-Heinemann, 2017, Ch. 10, 247-278.

33. Kaminsky W., Highly active metallocene catalysts for olefin polymerization. J. Chem. Soc., Dalton Trans., 1998, 1413–1418.
34. Nicolauo K. C., Bulger, P. G., & Sarlah, D. Metathesis Reactions in Total Synthesis. Ange. Chem. Int. Ed., 2005, 44, 4490–4527.
35. Katz T. J., McGinnis J., Katz T. J., Hurwitz S., J. Am. Chem. Soc. 1976, 98, 605 – 606
36. Astruc D., New J. Chem., 2005, 29, 42-56
37. Schrock R. R., Olefin Metathesis by Well-Defined Complexes of Molybdenum and Tungsten. In: Fürstner A. (eds) Alkene Metathesis in Organic Synthesis. Topics in Organometallic Chemistry. Springer, Berlin, Heidelberg, 1998, 1, 1-36..
38. du Toit J.I., P. van der Gryp, Loock M. M, Tole T. T., Marx S., Jordaan J. H. L. and Vosloo H. C. M., Industrial viability of homogeneous olefin metathesis: Beneficiation of linear alpha olefins with the diphenyl-substituted pyridinyl alcoholato ruthenium carbene precatalyst. Catal. Today, 2016, 275, 191-200.
39. Balcar, H. and Čejka J., SBA-15 as a support for effective olefin metathesis catalysts, Catalysts, 2019, 9, 743.
40. Anderson D. R., Hickstein D. D., O'Leary D. J. and Grubbs R. H., Model compounds of ruthenium−alkene intermediates in olefin metathesis reactions. J. Am. Chem. Soc., 2006, 128, 8386–8387.
41. Bhawal B. N. and Morandi B. Catalytic isofunctional reactions - expanding the repertoire of shuttle and metathesis reactions. Ange. Chem. Int. Ed., 2018.
42. Kégl, T. and L. Kollár, Chiral Phosphorous Ligands in Asymmetric Catalysis A2 - Reedijk, Jan, in Comprehensive Inorganic Chemistry II (2nd Ed.), K. Poeppelmeier, Editor. Elsevier: Amsterdam, 2013, Ch. 6.11, 271-308.

43. Eastham G.R., Heaton B. T., Iggo J. A., Tooze R. P., Whyman R. and Zacchini S., Synthesis and spectroscopic characterisation of the intermediates in the Pd-catalysed methoxycarbonylation of ethene. Chem. Commun., 2000, 609-610.
44. Haynes A., Carbonylation Reactions A2 - Reedijk, Jan, in Comprehensive Inorganic Chemistry II (2nd Edition), K. Poeppelmeier, Editor. Elsevier: Amsterdam, 2013, Ch. 6.01, 1-24.34.
45. Godard C., Perandones B. F., Gual A., Claver C., Asymmetric Carbonylations: Jan Reedijk, Kenneth Poeppelmeier, Comprehensive Inorganic Chemistry II (2nd Ed.), Elsevier, 2013, Ch. 6.13, 383-411.
46. Schoenberg A., Bartoletti I, and Heck R. F., Palladium-catalyzed carboalkoxylation of aryl, benzyl, and vinylic halides. J. Org. Chem., 1974, 39, 3318-3326.
47. Hegedus L.S., Organopalladium chemistry. Organometallics in synthesis: a manual (2nd Ed.), 2002, 1123-1217.
48. Nozaki K., Kantam M. L., Horiuchi T. and Takaya H., Hydroesterification of styrene catalyzed by montmorillonite-diphenylphosphinepalladium(II) chloride in the presence of chiral phosphines. J. Mol. Catal. A: Chem., 1997, 118, 247-253.
49. Blanco C., Godard C., Zangrando E., Ruiz A. and Claver C., Room temperature asymmetric Pd-catalyzed methoxycarbonylation of norbornene: highly selective catalysis and HP-NMR studies. Dalton Trans., 2012, 41, 6980-6991.
50. Arderne C., Holzapfel C. W., and Bredenkamp T., Branched selectivity in the pd-catalysed methoxycarbonylation of 1-alkenes. ChemCatChem, 2016, 8, 1084-1093.
51. Roth J.F., Some adventures and innovations in industrial catalysis. Catal. Today, 1992, 13, 1-12.

52. Wang L., Kwok W. H., Chan A. SC, Tu Tao, Hou X., D. L. Asymmetric hydroesterification of styrene using catalysts with planar-chiral ferrocene oxazoline ligands. Tetrahedron: Asymmetry, 2003, 14, 2291-2295.
53. Dong K., Sang R., Wei Z., Lui J., Duhren R., Spannenberg A., Jiao H., Neumann H., Jackstell R., Franke R. and Beller M., Chem. Sci., 2018, 9, 2510.
54. Cunningham J. M. and Das D., William S. Knowles, Encyclopaedia Britannica Inc., 2020
55. Knowles W. S., Application of Organometallic Catalysis to the commercial production of L-Dopa, J. Chem. Ed., 1986, 63, 222-225
56. García-Suárez E. J., Khokarale S. G van B., Olivier N, Fehrmann R., Riisager A. Pd-catalyzed ethylene methoxycarbonylation with Brønsted acid ionic liquids as promoter and phase-separable reaction media. Green Chem., 2014, 16, 161-166.
57. Oi S., Nomura M., Aiko T., Inoue Y d, Regioselective hydroesterification of styrene catalysed by cationic palladium (II) complexes under mild conditions. J. Mol. Catal. A: Chem., 1997, 115, 289-295.
58. Zhou H., Hou J., Cheng J., Lu S., Fu H., Wang H., Asymmetric hydroesterification of styrene by $PdCl_2$-$CuCl_2$-chiral phosphine catalyst systems. J. Organomet. Chem., 1997, 543, 227-228.
59. Zolim D., de Souza R. F., Dupont J., Monteiro A. L., Regioselective synthesis of 2-arylpropionic esters by palladium-catalyzed hydroesterification of styrene derivatives in molten salt media. Tetrahedron Lett., 1998, 39, 7071-7074.
60. Yamamoto H. and Tsuji H., Palladium-catalysed asymmetric hydroesterification of alkenylphenols. Synfacts, 2015, 11, 1161-1161.

61. Sherry A. E., Chapman, Benjamin E, Creedon, Michael T, Jordan, James M, Moese, Rosa L, Nonbleach process for the purification of palm $C_{16–18}$ methyl ester sulfonates. J. Am. Oil Chem. Soc., 1995, 72, 835-841.
62. Godard C, A.R., and Carmen Claver, Systematic study of the asymmetric methoxycarbonylation of styrene catalysed by palladium systems containing chiral ferrocenyl diphosphine ligands. Helv. Chim. Acta, 2006, 89, 1610-1622.
63. Diez V., C.J.V., Garcia-Herbosa G., Allon G., Charmant J. P. H., Carbayo A. and Munoz A., ^{1}H NMR Direct observation of enantiomeric exchange in palladium(II) and platinum(II) complexes containing N, N' bidentate aryl-pyridin-2-ylmethyl-amine ligands, Inorg. Chem., 2007, 46, 568-577.
64. Hertel J., The role of nonsteroidal anti-inflammatory drugs in the treatment of acute soft tissue injuries, J. Athletic Training, 1997, 32, 350-358.

CHAPTER 2

Literature review of asymmetric methoxycarbonylation of olefins catalyzed by palladium(II) complexes

2.1. General introduction

Palladium-catalyzed methoxycarbonylation is one among the foremost studied reactions amongst the carbonylation catalysis reactions and has been applied to varied alkene substrates to afford intermediates in organic synthesis thus playing a key role within the pharmaceuticals, agrochemicals and detergents industries.[1-3] The demand and application of enantiomeric compounds as building blocks in both fine chemical and pharmaceutical industries is ever increasing. One of the main ways of producing these compounds is through asymmetric catalysis over transition metal catalysts. For example, asymmetric methoxycarbonylation of alkenes is commonly used to produce the chiral carbonyl compounds which some of them serve as intermediate for non-steroidal anti-inflammatory drugs.[4] This reaction gives an extension to drug development and discovery.[5]

Some of the early chiral catalysts reported in this reaction are dated from 1982, for instance the monodentate phosphine donor ligands supported by palladium(II) based precursor.[6] Then over the years, more attempts have been made to achieve regiospecific, good ester yields with high enantiomeric excess percentages whilst broadening the scope of ligand donors and denticity.[7-9] In 1990, Alper *et al.*, reported the synthesis of 2-aryl propionic acids in good optical purity (91% ee) using a chiral ligand (BNPPA) and palladium chloride to catalyse the reaction.[10] In recent years, Li Jingfu and co-workers reported on asymmetric methoxycarbonylation of styrene

catalysed by palladium(II) P-O donor ligands which achieved excellent enantioselectivities and regioselectivities up to 95% ee and 15:1 b/l ratio under mild reaction conditions.[11] The use of chiral complexes in this reaction has attracted great attention over the years, hence numerous works has been reported on this reaction using various donor ligands and supported with palladium(II) precursor. Although, there are a limited number of isolated palladium(II) complexes.

2.2. Chiral palladium(II) catalysts employed as catalysts in the asymmetric methoxycarbonylation of olefins

2.2.1. Phosphine donor palladium(II) complexes

Various palladium(II) complexes bearing phosphine donor ligands have been reported in the asymmetric methoxycarbonylation of styrene which afforded high regioselectivities to the branched esters and low enantioselectivity.[3-6] For instant, Cometti and Nozaki reported the use of phosphines in asymmetric methoxycarbonylation of styrene achieving 52% ee (at 50 ^{o}C, below 2 atm CO gas within 4 h) and 2.4% ee (at 120 ^{o}C, 45 atm, 24 h) respectively, both with excellent regioselectivities 94% and 98% favouring the formation of branched esters (Figure 2.1).

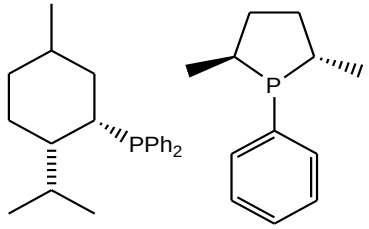
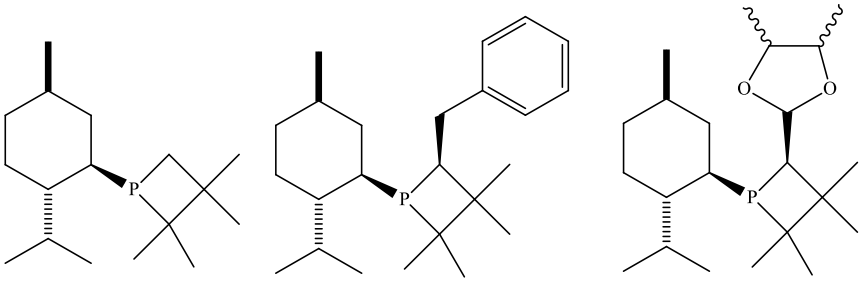


Figure 2.1. Monodentate phosphines employed in asymmetric methoxycarbonylation of styrene giving **a** 52% ee (b/l = 94/6)[6] and **b** 2.4% ee (b/l = 98/2)[7] respectively.

Munoz *et al.*, reported on the use of chiral phosphetanes in asymmetric methoxycarbonylation of styrene and afforded enantioselectivity of 0% ee, 6% ee and 29% ee for **a**, **b** and **c** $PdCl_2$ complexes.[8] Phosphetanes systems afforded excellent regioselectivity 92%, 99% and 97% to the branched ester respectively. However, when oxygen donor alkyl substituent was added onto ligand **a** to give ligand **c**, the product yield is reduced from 82% to 26% but the enantioselectivity increased from zero to 26%, which was highest ee amongst the phosphetanes reported in Munoz's work. It was noteworthy that when **a** 4-methoxystyrene was used instead of styrene as a substrate, the enantioselectivity of the reaction was found to increase up to 50% ee but with compromised product yield of 71%.



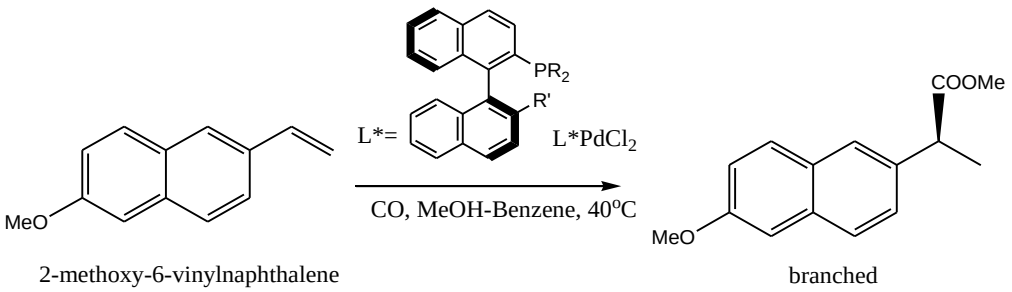
a **b** **c**

Figure 2.2. Chiral phosphetanes ligands, **a** gave 82% yield, 92:8 b/l ratio 0% ee; **b** gave 99% yield, 99:1 b/l ratio and 6% ee and **c** gave 26% yield, 97:3 b/l ratio and 29% ee (~35 atm CO gas, 70 ^{o}C within 24 h).[8]

The catalytic activity as well as the enantioselectivity of the ester products is controlled by the steric bulkiness of ligand. For instance, monophosphine ligands (L) were investigated in the asymmetric hydroesterification of vinylarene bearing cyclohexane as first R-group and methoxy group as the second R'-group afforded a 99% yield with 34% ee towards branched products whereas the one bearing cyclohexane and an isopropyl group respectively produced 17% yield

with 30% ee towards branched ester product. The 2-methoxy-6-vinylnaphthalene as substrate and monophosphine ligand (L) consisting cyclopentane and methoxy group afforded 53% ee of (S)-naproxen methyl ester but with low catalytic conversions when (S)-2-dicyclopentylphosphino-20-methoxy-1,10-binaphthyl was employed for the asymmetric methoxycarbonylation reaction.[9]

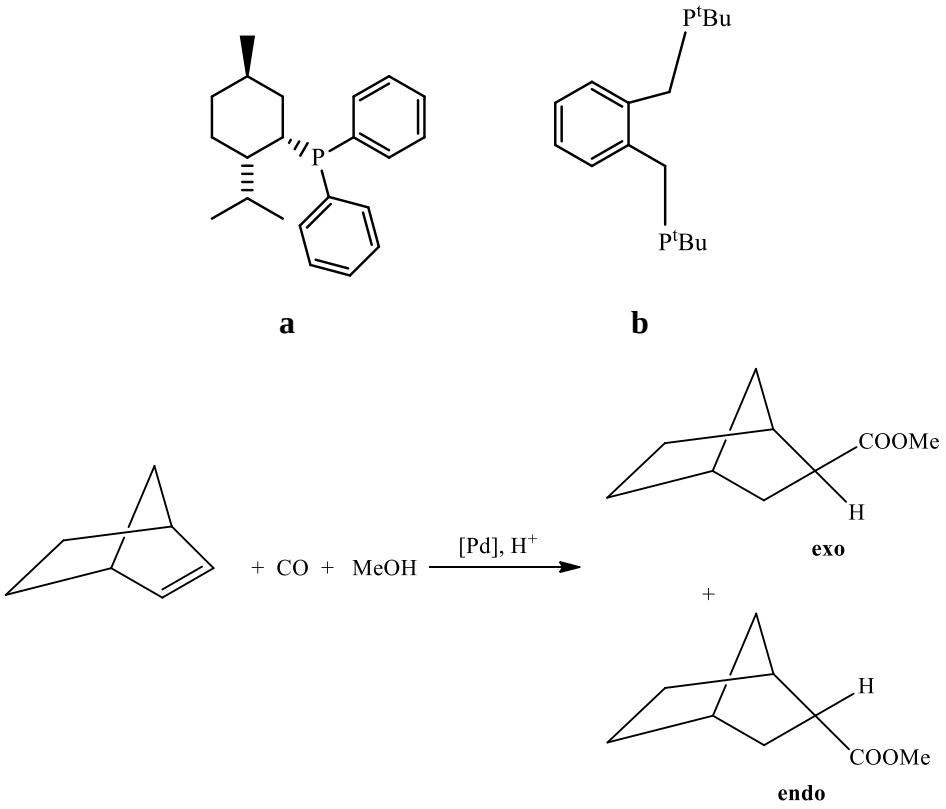
.[9]



2-methoxy-6-vinylnaphthalene branched

Scheme 2.1. Asymmetric methoxycarbonylation reaction of 2-methoxy-6-vinylnaphthalene catalysed by a monophosphine ligand coupled with palladium(II) dichloride precursor (~30 atm, 40 ^{o}C, 24 h).[9]

Vinylarenes were employed in the methoxycarbonylation reaction using a $PdCl_2$ - monodentate phosphorus ligand mixture as a catalyst. The ligands, menthyldiphenylphosphine (MDPP), neomenthyldiphenylphosphine (NMDPP), and dicyclohexyl(phenyl)phosphine (Cy_2PPh) were successful in affording branched esters with good regioselectivity under mild reaction conditions without additives such as acids. Both the electronic and steric effects of the cycloalkyl groups were found to be significant in achieving good catalytic activity.

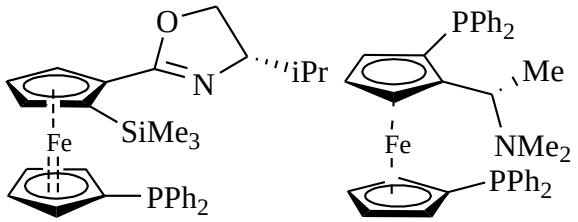


Scheme 2.2. Palladium(II) catalysed methoxycarbonylation of norbornene, **a** (chiral ligand) achieved >99% yield >99% chemo, 11% ee and **b** (achiral ligand) achieved 91% yield, >99% chemo (~30 atm, 70 ^{o}C, 24 h).[12]

Monodentate and bidentate phosphine ligands (**a** and **c**) were synthesised and palladium (II) utilized as precursor within the methoxycarbonylation of norbornene under the same reaction conditions (Scheme 2.2).[12] Excellent conversions of up to 99%, chemo- and exo-selectivities were afforded for both chiral and achiral ligands. However, the achiral ligand afforded reduced product yield (91%) and zero enantioselectivity relative to the chiral ligands.

2.2.2. Ferrocenyl-phosphine based palladium (II) catalysts

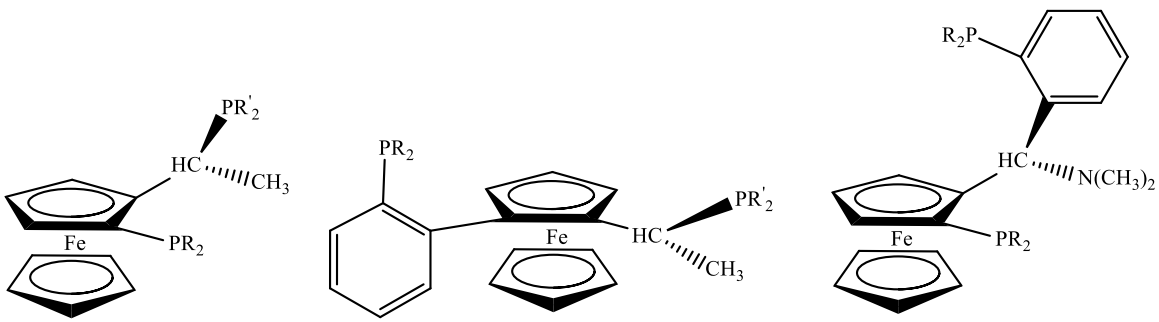
Chiral ferrocene phosphine ligands have been used in the asymmetric methoxycarbonylation reaction due to their structural abilities to be fine-tuned with substituents on the cyclopentadiene and phosphine.[13]



a **b**

Figure 2.3 Chiral ferrocene oxazoline ligands **a** (S, Sp)-1 (63% yield, 89:11 b/l ratio and 42% ee) and **b** (S, Sp)-BPPFA (91% yield, 39:61 b/l ratio and 38 % ee) respectively.[14]

Wang and co-workers reported on the asymmetric methoxycarbonylation of styrene using planar chiral ferrocene oxazoline ligands **a** and **b** (Figure 2.3), which afforded moderate to good product yield (63-91%) accompanied with regioselectivity and enantioselectivity of 89:11 b/l ratio; 42% ee and 39:61 b/ ratio, 38% ee respectively, in 20 h at 80 ^{o}C and 1800 psi CO (equivalent to 122.5 atm) pressure supply. Whereas, in the absence of co-catalysts $CuCl_2$ excellent product yield (>99%) were obtained with lower regioselectivity (16:84 b/l) and enantioselectivity (10% ee) were obtained for ligand **b** under the same reaction conditions.[14] Moreover, Inoue *et al* obtained 17% product yield, 44:66 b/l ratio and 86% ee using the same ferrocenyl oxazoline ligand **b** (20 atm CO gas, 50 ^{O}C, within 20 h).[15]



a **b** **c**

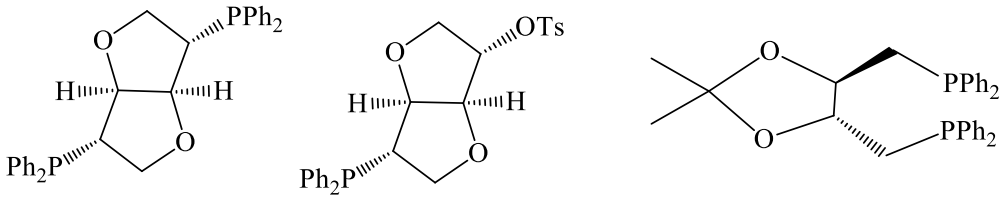
Figure 2.4. The 1,1'-bis(phosphino)ferrocenes employed Pd-catalysed asymmetric methoxycarbonylation using styrene as substrate, whereby **a**: Josiphos ligand, **b**: Walphos ligand and **c**: Taniaphos ligand.[13]

Godard and co-workers also investigated the study of the Pd-catalysed asymmetric methoxycarbonylation of styrene in the presence of chiral ferrocenyl phosphine ligands. The optimization of reaction conditions and a screening of distinctive catalyst precursors was done. Several 1,1'-bis(phosphino)ferrocenes of the Mandyphos, Josiphos, Walphos, and Taniaphos kinds (Figure 2.4) were tested in mixture with $[PdCl_2(NCPh)_2]$ since in terms of enantioselectivity it was found to be a much better precursor than the commonly used $[Pd(OAc)_2]$, $[Pd(acac)_2]$, $[Pd_2(dba)_3]$. The Josiphos ligand based catalyst produced an enantiomeric excess (ee) of 86%. These catalyst systems gave high enantioselectivities, even though the regioselectivity was found to be in favor of the (undesired) linear ester.[13]

2.2.3. Phosphine-Oxygen donor palladium(II) catalyst systems

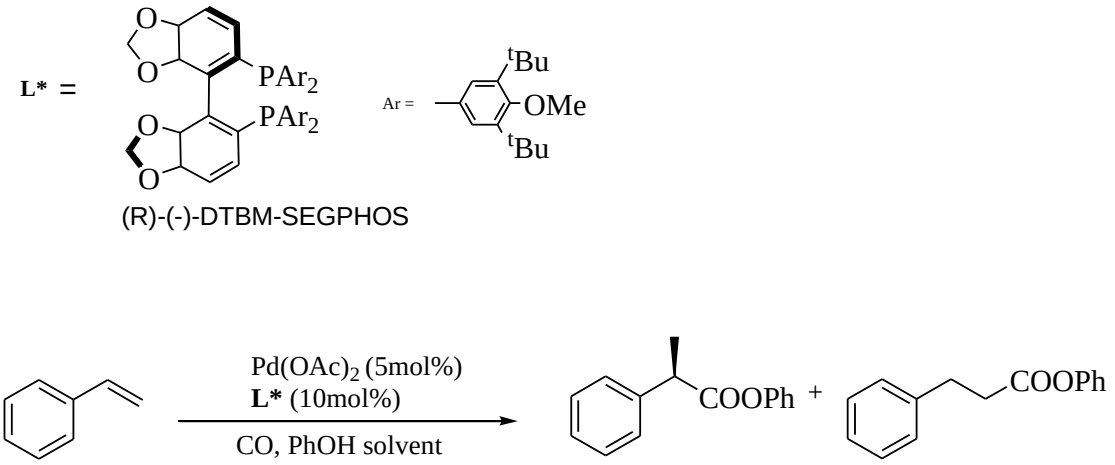
The use of $PdCl_2$-$CuCl_2$ chiral phosphine catalyst systems for asymmetric methoxycarbonylation of styrene was reported by Zhou H and his co-workers, to achieve different enantioselectivities

and regioselectivities depending on the substrate used. Under similar mild reaction conditions, complexes **a** and **b** (Figure 2.5) gave enantiomeric excess values of 99.3% and 38.5% with regioselectivities of 92.8% and ~100% towards the branched isomer products respectively (80 ^{o}C, 49 atm CO within 24 h). Complex **b** showed the highest regioselectivity but reduced enantioselectivity due to the replacement of phosphine group with OTs group.[16] When a similar chiral ((-)-DIOP) ligand **c** mixed with $Pd(OAc)_2$ precursor was used under mild reaction conditions, a much lower regioselectivity (44%) and enantioselectivity (17% ee) was observed (50 ^{o}C, 20 atm CO within 20 h).[15]



a **b** **c**

Figure 2.5. Asymmetric hydroesterification of styrene using bidentate phosphine-oxygen based ligands, gave 92.8:7.2 and 100:0 (b/l ratio); 99.3% ee and 38.5% ee for **a** and **b** complexes respectively (Pressure: 49.3 atm CO, Temp: 80 ^{o}C). (-)-(DIOP) ligand **c** gave 31:69 (b/l ratio) and 17% ee.[15]



Scheme 2.6. Pd-catalysed asymmetric hydroesterification of aryl olefins gave 92% yield, 14:1 b/l ratio and 93% ee under mild condition (absence of CO gas, 50 ^{o}C, within 24 h).[17]

Jingfu Li *et al*., performed the asymmetric hydroesterification of styrene in the absence of CO gas using the chiral $Pd(OAc)_2$ L* catalyst, gave the corresponding ester in 93% ee with a 14:1 b/l ratio (Scheme 2.3).[17] In their continuous studies 2018, using the same $Pd(OAc)_2$L* they attempted to optimize reaction conditions and broaden substrate aryl alkene scope so to improve the yield as well as enantioselectivity. Hence, the corresponding aryl ester was obtained in slightly improved 95% ee with 95% yield and 15:1 b/l ratio when the reaction was carried out in mixture of PhOH and n-Hex with ~5 atm CO gas and at 50 ^{o}C over 48 h duration. [11]

2.3 Statement of problem

In the methoxycarbonylation reactions as well as in asymmetric methoxycarbonylation reactions, controlling the catalytic activities simultaneously controlling the regio- and enantioselectivities can be challenging. Only a few complexes have been reported on the asymmetric methoxycarbonylation achieving catalytic activity and selectivity (up to 92% and 93% ee), and

especially those bearing bidentate nitrogen-donor ligands. Moreover, a limited number of complexes of this nature “isolated palladium(II) complexes” have been reported.

2.4. Justification of study

The current research focuses on designing new, isolated, selective and active transition metal catalytic systems for asymmetric methoxycarbonylation of olefins which will be investigated under various experimental conditions. We want to increase or broaden the scope of catalytic systems bearing N^N donor ligands with the attempt to improve the catalytic activity and enantioselectivities.

2.5. Aims and objectives

The overall objective of this project is to design active and stereo-selective palladium complexes for the catalytic asymmetric methoxycarbonylation of olefins.

Specific objectives:

1. To synthesize and characterize chiral (imino)pyridine and (imino)phosphine ligands and their respective palladium(II) complexes
2. To investigate the ability of these complexes to catalyse the asymmetric methoxycarbonylation of olefins.
3. To optimize these methoxycarbonylation reactions and understand the best operating conditions and gain some insights on the mechanism of the reactions.

The next chapter reports on the synthesis and characterization of ligands with their respective complexes, as well as their catalytic application in the methoxycarbonylation of olefins.

2.6.References

1. Van Leeuwen P.W.N.M. and Claver C., in Comprehensive Coord. Chem. II, 2003, Ch. 09.
2. Zolim D., de Souza R. F., Dupont J. and Monteiro A. L., Regioselective synthesis of 2-arylpropionic esters by palladium-catalyzed hydroesterification of styrene derivatives in molten salt media. Tetrahedron Lett., 1998, 39, 7071-7074.
3. Yamamoto H. and H. Tsuji, Palladium-Catalyzed Asymmetric Hydroesterification of Alkenylphenols. Synfacts, 2015, 11, 1161-1161.

4. Godard C., Perandones, B. F., Gual, A. and Claver, C., Asymmetric Carbonylations A2 Reedijk, Jan, in Comprehensive Inorganic Chemistry II (2nd Ed.), K. Poeppelmeier, Elsevier: Amsterdam, 2013, Ch. 6.13, 383-411.

5. Kégl, T. and L. Kollár, Chiral Phosphorous Ligands in Asymmetric Catalysis A2 - Reedijk, Jan, in Comprehensive Inorganic Chemistry II (2nd Ed.), K. Poeppelmeier, Elsevier: Amsterdam, 2013, Ch. 6.11, 271-308.
6. Cometti, G. and G. Chiusoli, Asymmetric induction in carbonmethoxylation of vinylaromatics. J. Organomet. Chem., 1982, 236, C31-C32.
7. Nozaki K. and Kantam M. L., Horiuchi T., Takaya H., Hydroesterification of styrene catalyzed by montmorillonite-diphenylphosphinepalladium(II) chloride in the presence of chiral phosphines. J. Mol. Catal. A: Chem., 1997, 118, 247-253.
8. Munoz B., Marinetti A., Ruiz A., Castillon S. and Claver C., Enhanced regioselectivity in palladium-catalysed asymmetric methoxycarbonylation of styrene using phosphetanes as chiral ligands. Inorg. Chem. Commun., 2005, 8, 1113-1115.

9. Kawashima Y., Okano K., Nozaki K., Hiyama T., Hydroesterification of vinylarenes catalyzed by palladium complexes of dialkylmonoaryl-and monoalkyldiarylphosphines. Bull. Chem. Soc. of Jpn, 2004, 77, 347-355.
10. Alper H. and Hamel N., J. Am. Chem. Soc, 1990, 112, 2803
11. Li J., Ren W., Dai J. and Shi Y., Palladium-catalyzed regio-and enantioselective hydroesterification of aryl olefins with CO gas. Org. Chem. Frontiers, 2018, 5, 75-79.
12. Blanco C., Godard C., Zangrando E., Ruiz A. and Claver C., Room temperature asymmetric Pd-catalyzed methoxycarbonylation of norbornene: highly selective catalysis and HP-NMR studies. Dalton Trans., 2012, 41, 6980-6991.
13. Godard C., A. Ruiz, and C. Claver, Systematic study of the asymmetric methoxycarbonylation of styrene catalyzed by palladium systems containing chiral ferrocenyl diphosphine ligands. Helv. Chim. Acta, 2006, 89, 1610-1622.
14. Wang L., Kwok W. H., Chan A. S. C., Tu T., Hou X. and Dai L., Asymmetric hydroesterification of styrene using catalysts with planar-chiral ferrocene oxazoline ligands. Tetrahedron: Asymmetry, 2003, 14, 2291-2295.
15. Oi S., Nomura M., Aiko T. and Inoue Y., Regioselective hydroesterification of styrene catalyzed by cationic palladium (II) complexes under mild conditions. J. Mol. Catal. A: Chem., 1997, 115, 289-295.
16. Zhou H., Hou J., Cheng J., Lu S., Fu H. and Wang H., Asymmetric hydroesterification of styrene by $PdCl_2$-$CuCl_2$-chiral phosphine catalyst systems. J. Organomet. Chem., 1997, 543, 227-228.

17. Li J., Chang W., Ren W., Liu W., Wang H. and Shi Y., Palladium-catalyzed highly regio- and enantioselective hydroesterification of aryl olefins with phenyl formate. Org. Lett., 2016, 18, 5456-5459.

CHAPTER 3

Synthesis and characterization of chiral iminopyridine, iminophosphine based palladium (II) complexes, and their application in methoxycarbonylation reaction

3.1. General introduction

Chiral catalysts play a significant role in the synthesis of speciality and fine chemicals such as pharmaceuticals, agrochemicals and fragrances among others.[1] It is therefore not surprising that great attention has been dedicated to the design and development of asymmetric transition metal catalysts for the production of enantiomerically enriched chemicals.[2-5] Through the methoxycarbonylation reaction, a range of important domestic and industrial products such as pharmaceuticals, food flavours, solvents, cosmetics, detergents and surfactants can be produced.[6, 7] Moreover, asymmetric methoxycarbonylation promotes the production of enantiomerically pure compounds whose demand has been on the rise, largely due to regulatory criteria and quality standards.[8]

Even though various transition metal catalysts have in the past been employed in methoxycarbonylation reactions, palladium (II) based-catalysts have over the years drawn a lot of attention in the methoxycarbonylation of olefins due to their high catalytic activities and ability to fine-tune product regio-selectivity.[9-18] Despite the significant advances in the development of palladium (II) catalysts in methoxycarbonylation reactions, there are very limited reports on the applications of chiral palladium catalysts in the asymmetric methoxycarbonylation of olefins. This would be a very versatile and important transformation as enantio-rich esters are useful feedstock for the production of fine chemicals such as perfumes and pharmaceuticals among others.[19, 20]

Few examples that report palladium catalysed asymmetric methoxycarbonylation reactions include enantioselective methoxycarbonylation of styrene by Konrad *et al* using dimetallic palladium complexes bearing phanephos ligands.[3] In another report, Wang *et al* applied chiral palladium(II) complexes anchored on dipyridylphosphine ligands in asymmetric methoxycarbonylation of styrene.[21] More recently, Olivieri *et al* applied aryl α-diimine palladium(II) pre-catalysts in asymmetric methoxycarbonylation of disubstituted olefins.[22] We have previously reported the use of palladium complexes supported on N^O and N^N donor ligands in symmetric methoxycarbonylation of higher olefins.[23-28] In this current contribution, our aim was to design chiral palladium catalysts as potential catalysts in the asymmetric methoxycarbonylation of olefins. Thus, the syntheses and structural characterization of chiral (imino)pyridine and (imino)phosphine palladium(II) metal complexes and their ability in asymmetric methoxycarbonylation of styrene and 1-hexene were investigated. The effect of complex structure/ligand design, reaction conditions, nature of substrate and catalyst deactivation pathways, have been studied and are herein discussed.

3. 2. Materials, methods and instrumentation

All solvents were purchased from Sigma Aldrich and were dried following relevant methods: Methanol was dried over 3Å molecular sieves overnight followed by distillation[29], toluene was dried over sodium wire and benzophenone while acetone and diethyl ether was dried via distillation using calcium hydride[29], dichloromethane was dried over P_2O_5 and distilled prior to use.[30] The chemicals, chloroform ($CDCl_3$) alpha (S)-α-Methylbenzylamine (≥99.5%), (R)-α-methylbenzylamine (≥99.5%), 2-pyridinecarboxaldehyde (≥99%), 2-acetylpyridine (98%) 2-(Diphenylphosphine)benzaldehyde, 2-methoxyethanamine, N^1,N^1-diethylethane-1,2-diamine 2-

hydroxybenzaldehyde and palladium acetate were purchased from Sigma Aldrich and were utilized without further purification. Starting materials [Pd(COD)Cl_2] and [PdClMe(COD)] were synthesized following literature methods.[31] Fourier transform infrared (FT-IR) spectra were recorded with a PerkinElmer spectrophotometer in the range 650-4000 cm^{-1}. All ^{1}H NMR (400 MHz) and ^{31}P NMR (162 MHz) spectra were recorded at 25ºC with deuterated $CDCl_3$ a Bruker NMR spectrometer. ^{13}C NMR spectra were obtained using a Varian Mercury 100 MHz on a Bruker spectrometer equipped with Bruker magnet (9.395 T) at 25℃. The NMR abbreviations used were s, d, dt, t, q and m denoting singlet, doublet, doublets of triplet, triplet, quartet and multiplet. The chemical shift in nuclear magnetic spectroscopies are all in ppm relative to $CDCl_3$ δ ^{1}H: 7.26 ppm and δ ^{13}C: 77.6 ppm. Elemental analyses were performed on Thermal Scientific Flash 2000 and mass spectra were recorded on a LC Premier micro-mass Spectrometer.

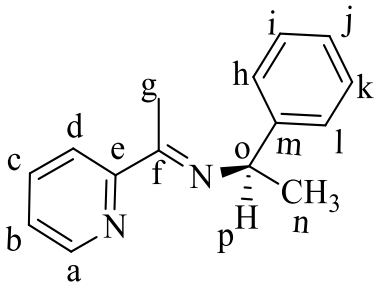
3.2.1. X-ray crystallography analyses

The recording of the X-ray data was performed on a Bruker Apex Duo coupled with an Oxford Instruments Cryojet operating at 100(2) K and an Incoatec micro-source working at 30 W power. The Mo Kα (λ = 0.71073 Å) radiation at a crystal-to-detector distance of 50 mm were used for the collection of data and by the following thes conditions: omega and phi scans with exposures taken at 30 W X-ray power and 0.50º frame widths using APEX2.[32] The data were reduced with the Programme SAINT[33] using outlier rejection, scan speed scaling, as well as standard Lorentz and polarization correction factors. A SADABS semi-empirical multi-scan absorption correction was applied to the data. To solve all structures, SHELXS-97 and WinGX[34] were used. All non-hydrogen atoms were situated in the difference density map and refined anisotropically with SHELXL-97 and all hydrogen atoms were comprised as ideal contributors in the least squares

process. Their positions were calculated employing a standard riding model with C-$H_{aromatic}$ distances of 0.93 Å and U_{iso} = 1.2 Ueq.

3.2.2. Synthesis of (imino)pyridine and (imino)phosphine ligands L1-L6

*3.2.2.1. Synthesis **L1:** (S)-1-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine*

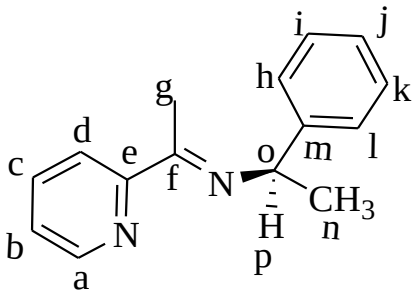


To a solution of 2-acetylpyridine (1.01 g, 8.36 mmol) in 15 mL of toluene, (*S*)-methylbenzylamine (1.01 g, 8.36 mmol) was added and the mixture was stirred at 100ºC using the Dean Stark apparatus for 4 days. After the reaction period, the solvent was evaporated and then the residue was washed with 15 mL dichloromethane and 20 mL of water using separatory funnel. To the residue, 50 g of magnesium anhydrous sulphate was added as a drying agent, thereafter, filtered through filter paper. The filtrate was evaporated to dryness, to give compound **L1** as yellow oil product. Yield = 1.70 g (91%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.61 (d, 3H, $^{3}J_{HH}$ = 6.56 Hz, H_g); 2.47 (s, 3H, H_n); 4.99 (q, 1H, $^{3}J_{HH}$ = 6.56, H_p); 7.27 (m, 1H, H_j); 7.39 (t, 2H, $^{3}J_{HH}$ = 7.5 Hz, $H_{h,l,b}$); 7.54 (d, 2H, $^{3}J_{HH}$ = 8.33 Hz, $H_{i,k}$); 7.74 (dt, 1H, $^{3}J_{HH}$ = 1.76 Hz, 6.0 Hz, H_c); 8.29 (d, 1H, $^{3}J_{HH}$ = 8.00, H_d); 8.63 (m, 1H, H_a). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 13.89 (C_g), 24.76 (C_n), 60.23 (C_p), 121.58 (C_d), 124.03 (C_j), 125.70 (C_b), 126.65 (C_h), 126.70 (C_l), 126.79 (C_i), 127.03 (C_k), 136.77 (C_c), 148.97 (C_m), 153.63 (C_a), 158.07 (C_e), 164.71 (C_f). HRMS

(ESI+) Calcd for $C_{15}H_{16}N_2$ (M+H): m/z (100%) = 224.13; Found: m/z (100%) = 225.0. FT-IR: $\upsilon_{(C=N)pyridine}$ = 1563 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1670 cm^{-1}.

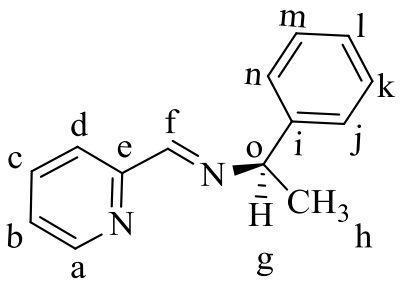
Ligand **L2** was synthesized using the similar procedure designated for the synthesis of ligand **L1**

*3.2.2.2 Synthesis **L2:** (R)-1-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine*



2-acetylpyridine (1.42 g, 11.72 mmol), (S)-methylbenzylamine (1.42 g, 11.72 mmol). **L2** Yellow oil. Yield = 2.03 g (77%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.60 (d, 3H, $^3J_{HH}$ = 6.56Hz, H_g); 2.47 (s, 3H, H_n); 4.98 (q, 1H, $^3J_{HH}$ J = 6.56Hz, H_p); 7.28 (m, 1H, H_j); 7.39 (t, 3H, $^3J_{HH}$ = 7.80Hz, $H_{h,l,b}$) 7.54 (d, 2H, $^3J_{HH}$ = 7.2Hz, $H_{i,k}$); 7.73 (dt, 1H, $^3J_{HH}$ = 1.76Hz, $^3J_{HH}$ = 6.04 Hz, H_c); 8.28 (d, 1H, $^3J_{HH}$ = 8.0Hz, H_d); 8.61 (d, 1H, $^3J_{HH}$ = 3.20Hz, H_a). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 13.89 (C_g), 24.76 (C_n), 60.23 (C_p), 121.58 (C_d), 124.03 (C_j), 125.70 (C_b), 126.65 (C_h), 126.70 (C_l), 126.79 (C_i), 127.03 (C_k), 136.77 (C_c), 148.97 (C_m), 153.63 (C_a), 158.07 (C_e), 164.71 (C_f). HRMS (ESI+) Calcd for $C_{15}H_{16}N_2$ (M+H): m/z (100%) = 224.13; Found: m/z (100%) = 224.17. FT-IR: $\upsilon_{(C=N)pyridine}$ = 1567 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1697 cm^{-1}.

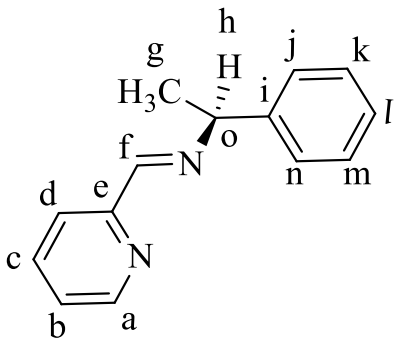
*3.2.2.3 Synthesis of **L3**: (S)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine*



To a solution of 2-pyridinecarboxaldehyde (0.44 g, 4.13 mmol) in CH_2Cl_2 (15 mL) (*S*)-methylbenzylamine (0.50 g, 4.13 mmol) was added followed by addition of approximately 25 g of magnesium anhydrous sulphate as a drying agent. The mixture was stirred at room temperature for 2 days. After the reaction periods, the solution was filtered through filter paper and the residue washed with dichloromethane (2 x 5 mL). The filtrate was evaporated to dryness to afford compound **L3** as a yellow oil. Yellow oil. Yield: 0.39 g (89%) ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.57 (d, 3H, $^3J_{HH}$ = 6.6 Hz, H_h); 4.61 (q, 1H, $^3J_{HH}$ = 6.6 Hz, H_g); 7.23 (m, 3H, $H_{n,j,l}$); 7.28 (t, 2H, $^3J_{HH}$ = 7.4 Hz, $H_{m,k}$); 7.39(d, 2H $^3J_{HH}$ = 7.4 Hz, H_b); 7.67 (dt, 1H, $^3J_{HH}$ = 6.22 Hz, 1.52 Hz, H_d); 8.03 (d, 1H, $^3J_{HH}$ J= 7.88 Hz, H_c); 8.41 (s, 1H_f); 8.57 (d, 1H, $^3J_{HH}$ =4.8 Hz, H_a). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 24.54 (C_h). 69.55 (C_o), 121.48 (C_d), 124.70 (C_i), 126.72 (C_b), 127.01 ($C_{n,j}$), 128.50 ($C_{m,k}$), 136.51 (C_c), 144.59 (C_i), 149.34 (C_a), 154.82 (C_f), 160.46 (C_e). HRMS (ESI+) Calcd for $C_{14}H_{14}N_2$ (M+H): m/z (100%) = 211.12; Found: ESI-MS (m/z, %); 211. 12 (M + H, 100). FT-IR: 1595 $\upsilon_{(C=N)pyridine}$ = 1595 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1644 cm^{-1}.

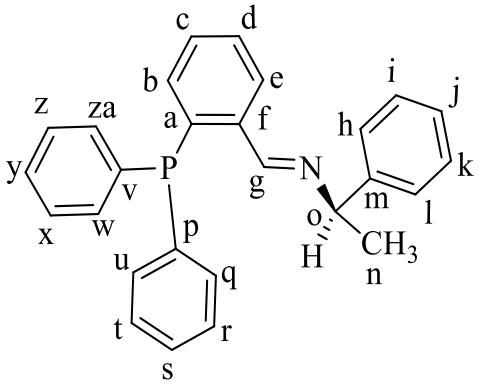
Ligand **L4** was prepared according to the procedure adopted for ligand **L3**

*3.2.2.4 Synthesis of **L4**: (R)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine*



2-pyridinecarboxaldehyde (0.92 g, 8.66 mmol), (*S*)-methylbenzylamine (1.05 g, 8.66 mmol). **L4** Yellow oil. Yield: 1.35 g (74%) ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.66 (d, 3H, $^{3}J_{HH}$ = 6.7 Hz, H_g); 4.70 (q, 1H, $^{3}J_{HH}$ = 6.6 Hz, H_h); 7.34 (3H, m, $H_{j,n,l}$); 7.40 (t, 2H, $^{3}J_{HH}$ = 7.4 Hz, $H_{k,m}$); 7.48 (d, 2H $^{3}J_{HH}$ = 7.3 Hz, H_b) 7.78 (dt, 1H, $^{3}J_{HH}$ = 6.2 Hz, 1.6 Hz, H_d); 8.14 (d, 1H, $^{3}J_{HH}$ = 7.9 Hz, H_c); 8.50 (s, 1H, H_f); 8.67 (d, 1H, $^{3}J_{HH}$ = 4.8 Hz, H_a). ^{13}C NMR (400 MHz, $CDCl_3$, δ, ppm): 24.57 (C_g), 69.56 (C_o), 121.47 (C_d), 124.69 (C_i), 126.73 (C_b), 127.02 ($C_{n,j}$), 128.51 ($C_{m,k}$), 136.49 (C_c), 144.61 (C_i), 149.35 (C_a), 154.85 (C_f), 160.47 (C_e). HRMS (ESI+) Calcd for $C_{14}H_{14}N_2$ (M+H): m/z (100%) = 211.12; Found: ESI-MS (m/z, %); 211.12 (M + H, 100). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1583 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1644 cm^{-1}.

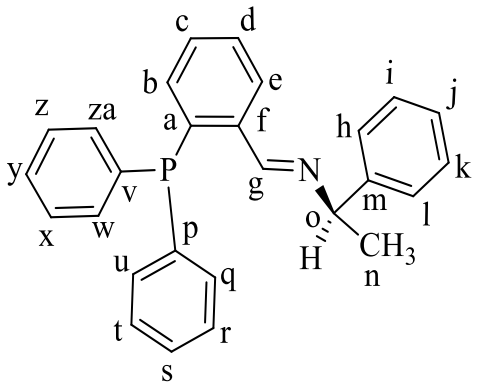
3.2.2.5 Synthesis of (S)-N-(2-(diphenylphosphino)benzylidene)-1-phenylethanamine **(L5)**



A mixture of 2-(diphenylphosphine)benzaldehyde (0.20 g, 0.69 mmol) and (*S*)-methylbenzylamine (0.84 g, 0.69 mmol) in CH_2Cl_2 (20 mL), under nitrogen atmosphere, was stirred for 3 days. After the removal of solvent by vacuum, **L5** was obtained as yellow oil. Yield = 0.26 g (95%).^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.39 (d, 3H, $^{3}J_{HH}$ = 7 Hz, H_n); 4.45 (q, 1H, $^{3}J_{HH}$ = 7 Hz, H_o); 6.91 (m, 1H, H_j); 7.37-7.21 (m, 17H, $H_{aromatic}$); 8.08 (m, 1H, H_e) 8.99 (d, 1H, $^{3}J_{HH}$ = 5 Hz, H_g). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 24.50 (C_n), 69.77 (C_o), 126.73 (C_j), 128.12 ($C_{h,l}$), 128.16 ($C_{i,k}$), 128.39 (C_r), 128.65 (C_t), 130.22 (C_y), 128.73 (C_x), 128.90 (C_z), 133.25 (C_s), 133.73 (C_d), 134.06 (C_e), 134.12 (C_c), 134.26 (C_q), 134.32 (C_{za}), 136.82 (C_w), 137.63 (C_v), 139.58 (C_b), 139.74 (C_a), 144.87 (C_m), 158.20 (C_f), 158.40 (C_g). ^{31} P NMR (400 MHz, $CDCl_3$, δ ppm): -13.0 (s). HRMS (ESI+) Calcd for $C_{27}H_{24}NP$ (M+H): m/z (100%) = 393.16. Found: ESI-MS (m/z, %); 393.50 (M + H, 100). FT-IR: $\upsilon_{(C=N)imine}$ = 1634 cm^{-1}.

Ligand **L6** will follow the same procedure employed in the synthesis of ligand **L5**

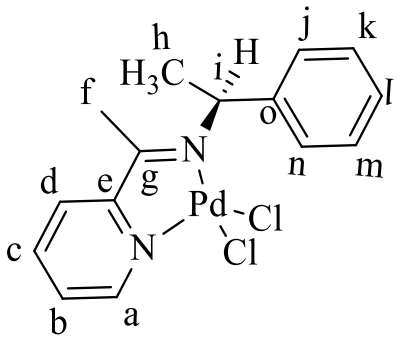
3.2.2.6 Synthesis of (R)-N-(2-(diphenylphosphino)benzylidene)-1-phenylethanamine **(L6)**



2-(diphenylphosphine)benzaldehyde (0.25 g, 0.86 mmol), (R)-methylbenzylamine (1.05 g, 0.86 mmol). **L6** Yield = 0.32 g (94%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.42 (d, 3H, $^{3}J_{HH}$ = 7 Hz, H_n); 4.49 (q, 1H, $^{3}J_{HH}$ = 7 Hz, H_o); 6.94 (m, 1H, H_j); 7.37-7.21 (m, 17H, $H_{aromatic}$); 8.08 (m, 1H, H_e); 8.99 (d, 1H,, $^{3}J_{HH}$ = 5 Hz, H_g). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 24.50 (C_n), 69.77 (C_o), 126.73 (C_j), 128.12 ($C_{h,l}$), 128.16 ($C_{i,k}$), 128.39 (C_r), 128.65 (C_t), 130.22 (C_y), 128.73 (C_x), 128.90 (C_z), 133.25 (C_s), 133.73 (C_d), 134.06 (C_e), 134.12 (C_c), 134.26 (C_q), 134.32 (C_{za}), 136.82 (C_w), 137.63 (C_v), 139.58 (C_b), 139.74 (C_a), 144.87 (C_m), 158.20 (C_f), 158.40 (C_g). ^{31}P NMR (400 MHz, $CDCl_3$, δ, ppm): -13.0 (s). HRMS (ESI+) Calcd for $C_{27}H_{24}NP$ (M+H): m/z (100%) = 393.17; Found: ESI-MS (m/z, %); 393.50 (M + H, 100). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1634 cm^{-1}.

3.2.3 Synthesis of palladium(II) complexes C1-C7

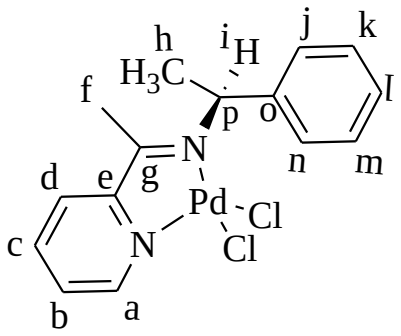
3.2.3.1 Synthesis of [{(S)-1-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine}$PdCl_2$] ***(C1)***



To a solution of [Pd(COD)Cl_2] (0.10 g, 0.39 mmol) in CH_2Cl_2 (5 mL) was added a solution of ligand **L1** (0.09 g, 0.39 mmol) in CH_2Cl_2 (5 mL) and the mixture stirred for 24 h. The solution was concentrated in *vacuo* and Et_2O (10 mL) added to precipitate an orange solid. Recrystallization of the crude product by slow diffusion of hexane in solution of dichloromethane containing the compound gave single crystals suitable for X-ray analyses. **C1** Yield = 0.14 g (82%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm) 1.86 (d, 3H, , $^3J_{HH}$ = 7.2 Hz , H_h); 2.17 (s, 3H, H_f); 6.74 (q, 1H,$^3J_{HH}$ = 7.2 Hz, H_i); 7.32 (d, 1H, $^3J_{HH}$ = 7.2 Hz, H_l); 7.38 (t, 2H, $^3J_{HH}$ = 7.6 Hz, $H_{j,l}$); 7.45 (d,2H, $^3J_{HH}$ = 7.6 Hz, $H_{k,m}$); 7.78 (t, 2H, $^3J_{HH}$ = 8.4 Hz, $H_{b,c}$); 8.15 (t, 1H, $^3J_{HH}$ = 7.6 Hz, H_d); 9.50 (d, 1H, $^3J_{HH}$ = 5.6 Hz, H). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 19.39 (C_f), 26.60 (C_h), 61.75 (C_p), 125.21 (C_d), 126.22 (C_l), 127.61 (C_b), 128.26 (C_n), 128.31 (C_j), 128.58 (C_m), 129.04 (C_k), 133.10 (C_c), 137.19 (C_o), 141.07 (C_a), 151.49 (C_e), 158.28 (C_g). LRMS (ESI+): calcd. m/z (100%) = 399.97; Found: ESI-MS (m/z, %); 424.37 (M + Na, 100). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1438 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1593 cm^{-1}. Anal. Calcd. for $C_{15}H_{16}N_2Cl_2Pd$: C, 44.97; H, 3.77; N, 6.99. Found: C, 44.89; H, 3.84; N, 6.84.

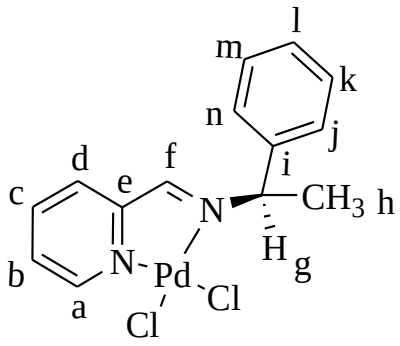
Complexes C**2**-C**4** were synthesized following the procedure described for compound **C1**.

3.2.3.2 Synthesis of [{(R)-1-phenyl-N-(1-(pyridin-2-yl)ethylidene)ethanamine}$PdCl_2$] ***(C2)***



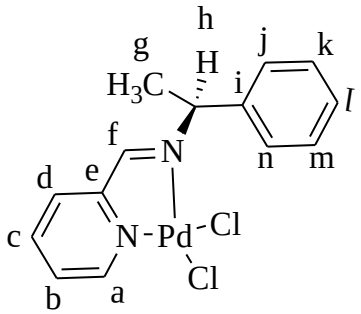
[Pd(COD)Cl_2] (0.10 g, 0.39 mmol) and **L2** (0.09 g, 0.39 mmol) were used. Yield = 0.14 g (89%). Recrystallization of complex **C2** by slow evaporation of CH_2Cl_2 solution afforded single crystals suitable for X-ray analyses ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.87 (d, 3H, $^3J_{HH}$ = 7.2 Hz, H_h); 2.16 (s, 3H, H_f); 6.73 (q, 1H,$^3J_{HH}$ = 7.2 Hz, H_i); 7.32 (d, 1H, $^3J_{HH}$ = 7.2 Hz, H_l); 7.39 (t, 2H, $^3J_{HH}$ = 7.6 Hz, $H_{j,n}$); 7.45 (d, 2H, $^3J_{HH}$ = 7.6 Hz, $H_{k,m}$); 7.72 (d, 2H, $^3J_{HH}$ = 8.4 Hz, $H_{b,c}$); 8.16 (t, 1H, $^3J_{HH}$ = 7.6 Hz, H_d); 9.52 (d, 1H, $^3J_{HH}$ = 5.6 Hz, H_a). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 19.39 (C_f), 26.60 (C_h), 61.75 (C_p), 125.21 (C_d), 126.22 (C_l), 127.61 (C_b), 128.26 (C_n), 128.31 (C_j), 128.58 (C_m), 129.04 (C_k), 133.10 (C_c), 137.19 (C_o), 141.07 (C_a), 151.49 (C_e), 158.28 (C_g). HRMS (ESI+): calcd. m/z (100%) = 399.97; Found: (m/z, %) = 404.52 (M + 4H, 100). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1445 cm^{-1}; 1601 $\upsilon_{(C=N)imine}$ = 1601 cm^{-1}. Anal. Calcd. for $C_{15}H_{16}N_2Cl_2Pd$: C, 44.67; H, 3.77; N, 6.99. Found: C, 44.77; H, 3.73; N,7.27.

3.2.3.3 Synthesis of [{(S)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine}$PdCl_2$ ***(C3)***



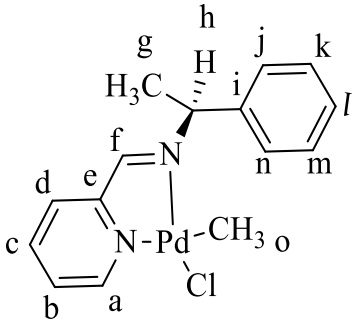
[$Pd(COD)Cl_2$] (0.10 g, 0.39 mmol) and **L3** (0.08 g, 0.39 mmol) were used. Yield = 0.12 g (80%). Recrystallization of complex **C3** by slow diffusion of hexane in a CH_2Cl_2 solution afforded single crystals suitable for X-ray analyses. ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.89 (d, 3H, $^3J_{HH}$ = 6.8 Hz, H_h); 6.09 (q, 1H,$^3J_{HH}$ = 7.2 Hz, H_g); 7.44 (t, 1H, $^3J_{HH}$ = 4.0 Hz, H_l); 7.47 (d, 4H, $^3J_{HH}$ = 4.4 Hz, $H_{j,n,m,k}$); 7.67 (t, 1H, $^3J_{HH}$ = 6.8 Hz, H_b); 7.76 (d, 1H, $^3J_{HH}$ = 7.6 Hz, H_d); 7.88 (s, 1H, H_c); 8.11 (t, 1H, $^3J_{HH}$ = 7.6 Hz, H_f); 9.35 (d, 1H, $^3J_{HH}$ = 5.2 Hz, H_a). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 21.0 (C_h), 64.74 (C_g), 128.56 ($C_{n,j;l,b}$), 129.32 ($C_{m,k}$), 138.15 (C_c), 140.45 (C_i), 151.14 (C_a), 155.54 (C_e), 167.04 (C_f). LRMS (ESI+): calcd. m/z (100%) = 385.96, Found: ESI-MS (m/z, %); 386.42 (M + H, 100) FT-IR: $\upsilon_{(C=N)pyridine}$ = 1445 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1595 cm^{-1}. Anal. calcd. for $C_{14}H_{14}N_2Cl_2Pd$.hexane: C, 44.68; H, 4.05; N, 6.99. Found: C, 44.68; H, 3.54; N, 7.77.

3.2.3.4 Synthesis of [{(R)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine}$PdCl_2$] ***(C4)***



[Pd(COD)Cl_2] (0.10 g, 0.39 mmol) and **L4** (0.08 g, 0.39 mmol) were used. Yield = 0.11 g (75%). Recrystallization of complex **C4** was done by slow evaporation of CH_2Cl_2 solution afforded single crystals suitable for X-ray analyses. ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.90 (d, 3H,, $^3J_{HH}$ = 6.8 Hz, H_g); 6.12 (q, 1H,$^3J_{HH}$ = 7.2 Hz, H_h); 7.42 (t, 1H, H_l) 7.48-7.70 (m, 4H, $H_{k,m,j,n}$); 7.78 (dt, 2H; 8.09, $H_{b,d}$) 7.80-8.06 (t, 1H, $^3J_{HH}$ = 7.6 Hz, H_c); 8.09 (s, 1H, H_f), 9.42 (d, 1H, $^3J_{HH}$ = 5.2 Hz, H_a). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 24.58 (C_g), 69.55 (C_h), 121.46 (C_d), 124.69 (C_l), 126.73 (C_b), 127.02 ($C_{j,n}$), 128.51 ($C_{k,m}$), 136.48 (C_c), 144.60 (C_i), 149.34 (C_a), 154.82 (C_e), 160.46 (C_f). LRMS (ESI+): calcd. m/z (100%) = 385.96, Found: ESI-MS (m/z, %); 384.42 (M – 2H, 78). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1445 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1594 cm^{-1}. Anal. calcd. for $C_{14}H_{14}N_2Cl_2Pd$.hexane: C, 44.68; H, 4.05; N, 6.99. Found: C, 44.86; H, 4,02; N, 6.97.

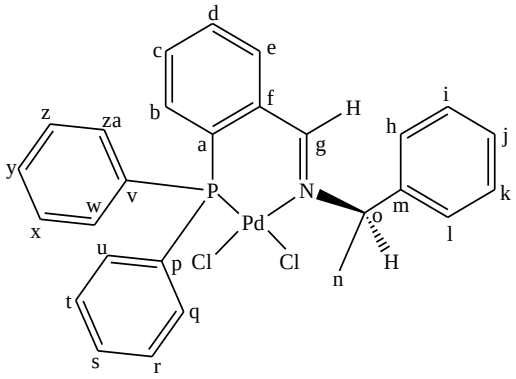
3.2.3.5 Synthesis of [{(R)-1-phenyl-N-((pyridin-2-yl)methylene)ethanamine}PdClMe] ***(C5)***



To a solution of [PdMeCl(COD)] (0.02 g, 0.09 mmol) in CH_2Cl_2 (5 mL) was added ligand **L4** (0.02 g, 0.09 mmol) in diethylether (25 mL) and the s mixture stirred for 36h. The yellow powder was recovered after filtration. Yield = 0.008 g (44%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.90 (d, 3H, $^3J_{HH}$ = 6.8 Hz, H_g); 3.52 (s, 3H, H_o); 6.10 (q, 1H,$^3J_{HH}$ = 7.2 Hz, H_h); 7.45 (t,1H, $^3J_{HH}$ = 4.0 Hz, H_l); 7.48 (d, 4H, $^3J_{HH}$ = 4.4 Hz, $H_{j,n,m,k}$); 7.66 (t, 1H, $^3J_{HH}$ = 6.8 Hz, Hc); 7.69 (d, 1H, $^3J_{HH}$ = 7.6 Hz, H_d); 7.76 (s,1H, H_b); 8.09 (t, 1H, $^3J_{HH}$ = 7.6 Hz, H_f); 9.41 (d,1H, $^3J_{HH}$ = 5.2 Hz, H_a).LRMS

(ESI+): calcd. m/z (100%) = 366.01, Found: ESI-MS (m/z, %); 370.34 (M + 4H, 56). FT-IR: $\upsilon_{(C=N)pyridine}$ = 1444 cm^{-1}; $\upsilon_{(C=N)imine}$ = 1593 cm^{-1}.

*3.2.3.6 Synthesis of [{(S)-N-(2-(diphenylphosphino)benzylidene)-1-phenylethanamine} $PdCl_2$] **(C6)***

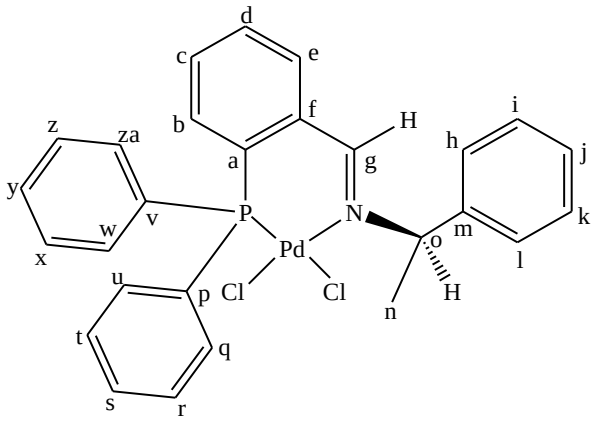


To a solution of [Pd(COD)Cl_2] (0.05 g, 0.19 mmol) in dichloromethane (5 mL) was added a solution of ligand **L5** (0.07 g, 0.19 mmol) in CH_2Cl_2 (5 mL) and the mixture stirred for 24 h. The solution was concentrated in *vacuo* and diethylether (10 mL) added to precipitate the crude product as a yellow solid. Recrystallization of the crude product by slow diffusion of hexane in solution of dichloromethane containing the compound gave single crystals of complex **C6** suitable for X-ray analyses. Yield = 0.06 g (81%). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm):1.57 (d, 3H, $^3J_{HH}$ = 7.0 Hz, H_n); 6.80 (q, 1H,$^3J_{HH}$ = 6.6 Hz, H_h); 6.95 (t,1H, $^3J_{HH}$ = 7.7 Hz, H_j); 7.12 (d, 2H, $^3J_{HH}$ = 6.8 Hz, $H_{i,k}$); 7.31 (m, 4H, $H_{z,w,t,r}$); 7.37 (d, 5H, ,$H_{c,d,y,z,x}$); 7.60 (s,1H, H_e); 7.69 (m, 1H, H_b); 7.73 (s,1H, H_g). ^{13}C NMR (400 MHz, $CDCl_3$, δ ppm): 26.60 (C_n), 69.87 (C_o), 116.61 (C_j), 121.55 (C_x), 122.04 (C_z), 124.01 (C_l), 124.62 (C_h), 126.10 (C_i), 126.67 (C_k), 128.31 (C_t), 128.91 (C_r), 129.02 (C_y), 129.14 (C_s), 132.19 (C_d), 132.61 (C_e), 133.10 (C_c), 133.85 (C_{za}), 134.38 ($C_{u,q}$), 134.49 (C_w), 135.51 (C_b), 135.59 (C_a), 137.19 (C_p), 137.66 (C_v), 139.01 (C_m), 162.03 (C_f), 162.11 (C_g). HRMS (ESI+): calcd. m/z (100%) = 569.01, Found: m/z = 573.00 (M + 4H, 100). ^{31} P NMR (400 MHz, $CDCl_3$, δ

ppm): 31.4 (s). FT-IR: $\upsilon_{(C=N)imine}$ = 1626 cm^{-1}. Anal. calcd. for $C_{27}H_{24}NCl_2PPd$.dichloromethane: C, 55.73; H, 4.19; N, 2.39. Found: C, 55.69; H, 4.07; N, 2.08.

Complexes **C7** was synthesized following the procedure described for compound **C6**

3.2.3.7 *Synthesis of [{(R)-N-(2-(diphenylphosphino)benzylidene)-1-phenylethanamine} $PdCl_2$] **(C7)***



$Pd(COD)Cl_2$] (0.15 g, 0.51 mmol) and **L6** (0.2 g, 0.51 mmol). Yield = 0.22 g (77 %). ^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 1.57 (d, 3H, $^3J_{HH}$ = 7.0 Hz, H_n); 6.80 (q, 1H,$^3J_{HH}$ = 6.8 Hz, H_o); 6.95 (t, 1H, $^3J_{HH}$ = 7.8 Hz, H_j); 7.18 (d, 2H, $^3J_{HH}$ = 6.8 Hz, $H_{h,l}$); 7.31 (m, 5H, $H_{za,u,q,i,k}$); 7.47 (d, 5H, $H_{t,r,y,s,w}$); 7.54 (m, 4H, $H_{c,d,z,x}$); 7.60 (m, 1H, H_e); 7.69 (m, 1H, H_g). 7.74 (s, 1H, H_b). ^{13}C NMR (100 MHz, $CDCl_3$, δ ppm): 26.60 (C_n), 69.87 (C_o), 116.61 (C_j), 121.55 (C_x), 122.04 (C_z), 124.01 (C_l), 124.62 (C_h), 126.10 (C_i), 126.67 (C_k), 128.31 (C_t), 128.91 (C_r), 129.02 (C_y), 129.14 (C_s), 132.19 (C_d), 132.61 (C_e), 133.10 (C_c), 133.85 (C_{za}), 134.38 ($C_{u,\ q}$), 134.49 (C_w), 135.51 (C_b), 135.59 (C_a), 137.19 (C_p), 137.66 (C_v), 139.01 (C_m), 162.03 (C_f), 162.11 (C_g). ^{31} P NMR (400 MHz, $CDCl_3$, δ ppm): 31.4 (s). HRMS (ESI+): calcd. m/z (100%) = 569.01, Found: m/z (M+H) = 574.00 (M +

5H, 80%). FT-IR: $\upsilon_{(C=N)imine}$ = 1625 cm^{-1}. Anal. calcd. for $C_{27}H_{24}NCl_2PPd$.dichloromethane: C, 54.82; H, 4.154; N, 2.34. Found: C, 53.96; H, 4.18; N, 2.12.

3.2.4. General methodology for the methoxycarbonylation reactions

The catalytic methoxycarbonylation reactions were conducted in a stainless-steel autoclave equipped with a temperature control unit and a sample valve. The Pd (II) complex, PPh_3, HCl and 1-hexene (1: 2: 10: 200) were dissolved in a mixture of methanol and toluene, in a performed experiment. The reactor was evacuated, and the catalytic mixture was introduced to the reactor using a cannula. Then the reactor was purged three times with CO, thus set at the required pressure, to desired temperature and the reaction stirred at 500 rpm. Once the reaction time was reached, the reaction was cooled down, excess CO was emitted and samples were withdrawn for GC analysis. This was done to determine the percentage conversion of the alkene substrate to esters assuming a 100% mass balance, as well as to determine the enantiomeric excess of the esters with the assistance of a chiral column. Furthermore, GC-MS analysis was done to determine and identify the branched and linear ester product, after calculating the mass percentage of branched ester to linear ester.

3.2.5. General procedure for the hydrogenation reactions

The catalytic hydrogenation reactions were done in a stainless-steel autoclave equipped with temperature control unit and a sample valve. In a typical experiment, complex and substrate were dissolved in toluene as solvent. The reactor was evacuated, flushed with nitrogen and the catalytic mixture was introduced to the reactor through a cannula. The reactor was purged three times with

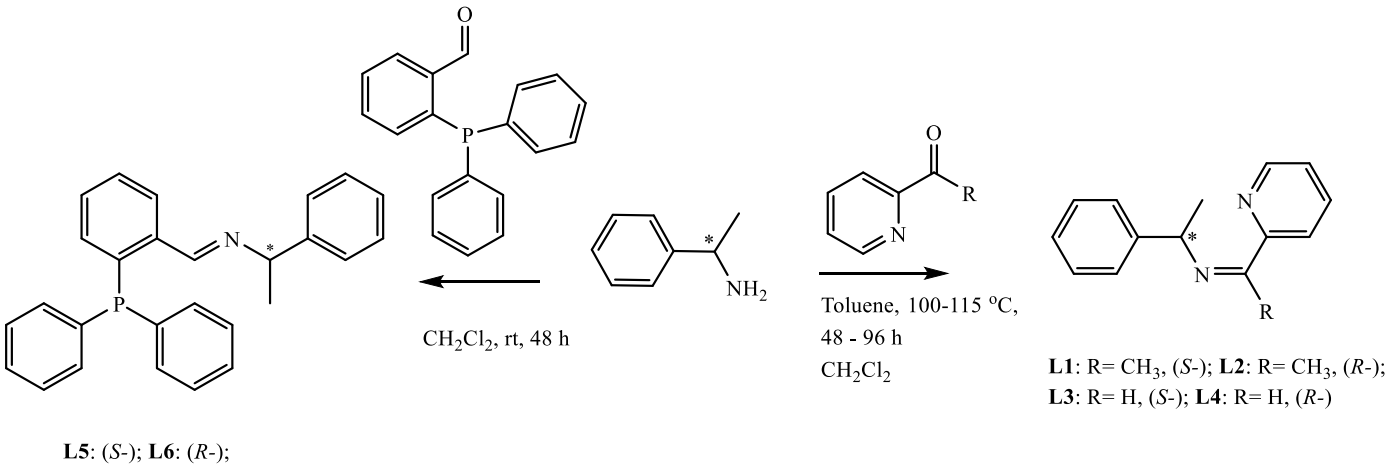
hydrogen gas, and then set at the desired pressure, temperature and the reaction stirred at 500rpm. At the end of the reaction time, the reactor was cooled down, excess hydrogen gas was emitted out of the system. Samples for GC analyses were drawn using a syringe, filtered using 0.45µm micro filters and analysed by Varian CP-3800 GC (ZB-5HT column 30m×0.25mm×0.10µm). To determine the percentage conversion of styrene to ethylbenzene a GC instrument was used. The percentage conversions were determined by comparing the peak areas of the alkene substrate and respective products, assuming 100% mass balance. Moreover, the GC-MS instrument was used to determine the molecular weights and identity of the resulting esters. For instance, comparison of peak areas of styrene and methyl-2-phenylpropanoate at regular time intervals allowed the determination of the rate of conversion of styrene (retention time = 8.93 minutes) to methyl-2-phenylpropanoate (retention time = 14.79 minutes).

3. 3. Results and discussion

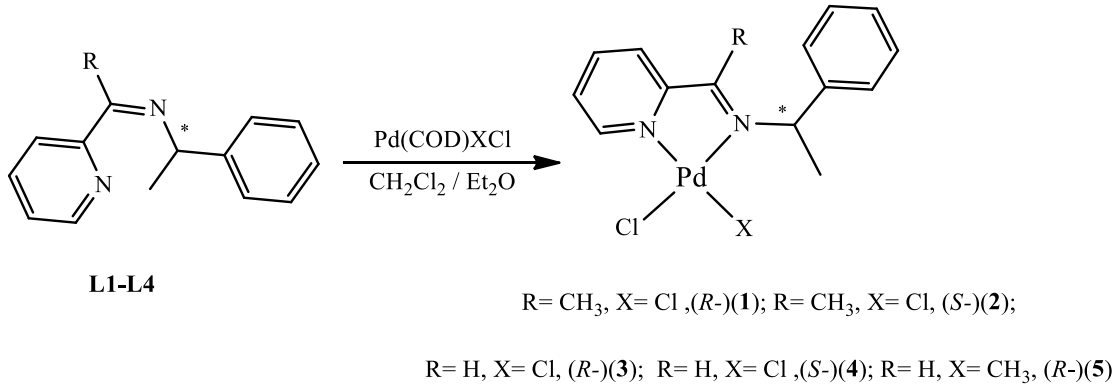
3.3.1. Synthesis of the chiral imine ligands and their palladium (II) complexes

The chiral (imino)pyridine ligands **L1**-**L4** were prepared following published procedures[35-37] by condensation reactions of (*S*)/(*R*)-methylbenzylamine with either acetylpyridine or 2-pyridinecarboxaldehyde in the presence of anhydrous magnesium sulphate as a drying agent (Scheme 3.1) and were obtained as yellow-orange oils in good yields (74% - 91%). On the other hand, the (imino)phosphine ligands **L5-L6** were obtained in excellent yield (94-95%), by reactions of (*S*)/(*R*)-methylbenzylamine with 2-(diphenylphosphino)benzaldehyde in dichloromethane solvent under nitrogen atmosphere (Scheme 3.2). Treatments of the chiral imine ligands **L1**-**L7** with [Pd(COD)Cl_2] or [Pd(COD)MeCl] produced the corresponding palladium(II) complexes **C1-**

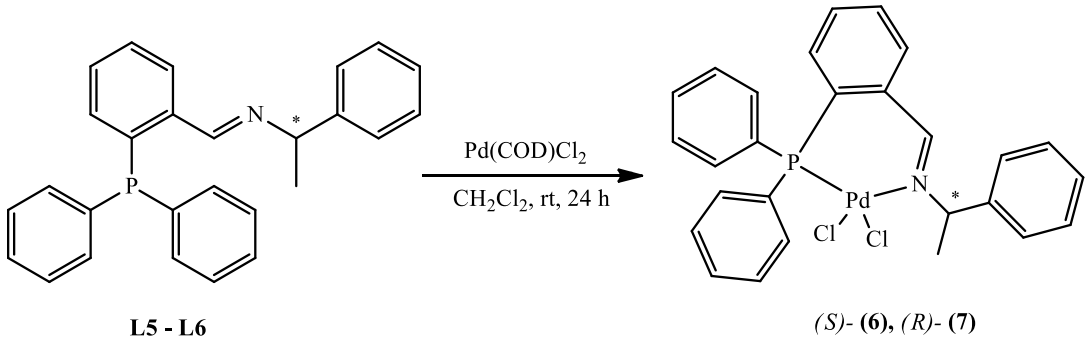
C4, C6 and **C7** in high yields up to 89% except complex **C5** which gave 44% (Scheme 3.2 and Scheme 3.3).



Scheme 3.1: Synthesis of chiral (imino)pyridine and (imino)phosphine ligands **L1-L6**.



Scheme 3.2: Synthesis of chiral (imino)pyridine palladium(II) complexes **C1-C5**.



Scheme 3.3: Synthesis of chiral (imino)phosphine palladium(II) complexes **C6** and **C7**.

The (imino)pyridine ligands were characterized by NMR, mass spectrometry and micro-analysis. In general, the ^{1}H-NMR spectra of ligands **L1**- **L4** gave signature peaks of the CH protons (adjacent to the chiral carbon) as quartets between 4.61 – 4.99 ppm. By comparison of the ^{1}H-NMR spectra of the ligands to the respective ^{1}H-NMR spectra of the complexes, we were able to infer successful coordination of the ligand to the palladium atom. For instance, ^{1}H-NMR spectrum of ligand **L4** and corresponding complex **C4** showed signals of the CH protons at 4.71 ppm to 6.11 ppm respectively (Figure 3.1). Similar trend was observed for other ligands and their respective complexes.[36]

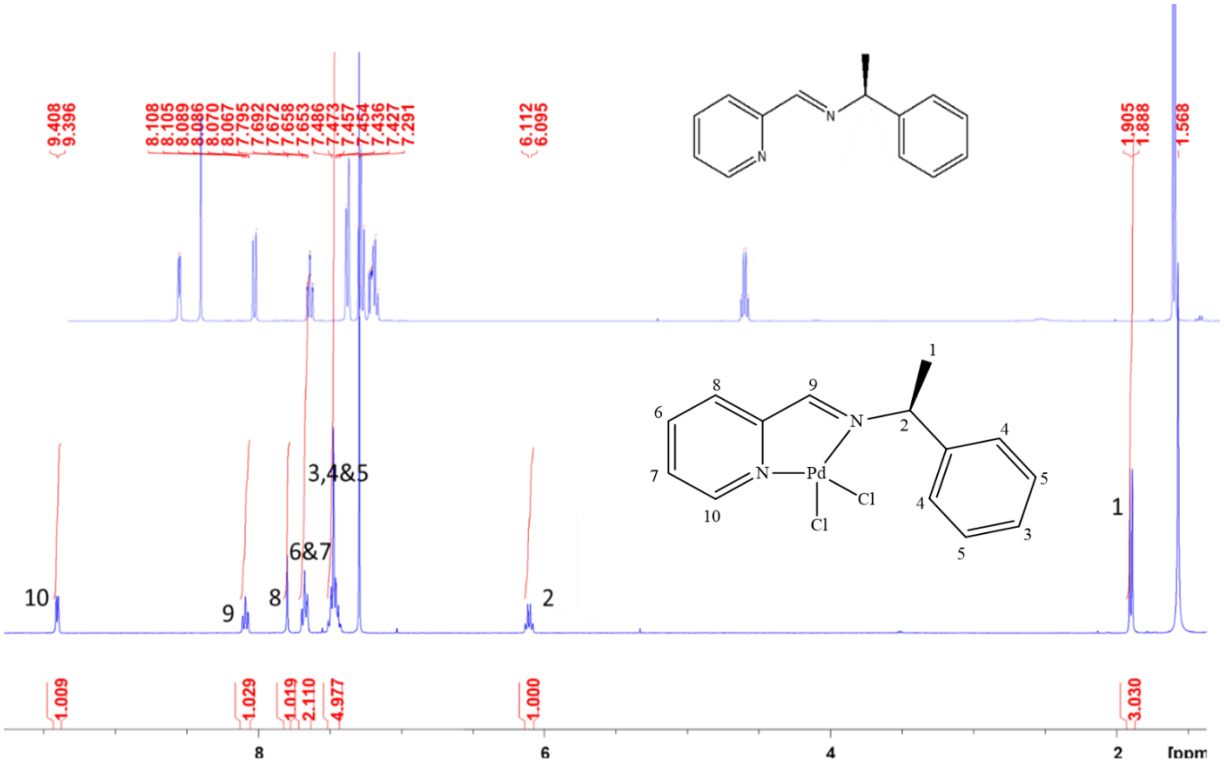


Figure 3.1. Overlaid [1]H-NMR spectra of ligand **L4** and complex **C4** showing a significant downfield shift of the proton bonded onto chiral carbon from 4.71 ppm to 6.11 ppm.

The [1]H-NMR spectra of (imino)phosphine ligands **L5**, **L6** showed a shift on the aldehyde (H-C=O) characteristic peak of the 2-(diphenylphosphine)benzylaldehyde. For example, a shift from 10.36 ppm to 8.99 ppm for **L6** indicated the conversions of the aldehyde (**H**-C=O,) group to the imine functionality (**H**-C=N). Similarly, ligands **L5** and **L6**, showed CH protons (adjacent to the chiral carbon) within the same range as ligands **L1**-**L4** at 4.45 and 4.49 ppm. Typical peaks of methyl protons were observed at 1.39 and 1.42 ppm respectively.[38] These peaks were used as diagnostic peaks in the next step to confirm that complexation of the ligands with the palladium salts had occurred. For instance, [1]H-NMR spectrum of ligand **L4** and corresponding complex **C4** showed signals of the CH protons at 4.71 ppm to 6.11 ppm respectively (Figure 3.1). A noticeable exception was given by the CH proton resonance which undergoes a downfield shift of 2.30–2.40

ppm, probably due to a conformational change of the ligand upon chelation. As an illustration, Figure 3.2 shows the ^{1}H NMR spectra of ligand **L6** and its corresponding complex **C7**.

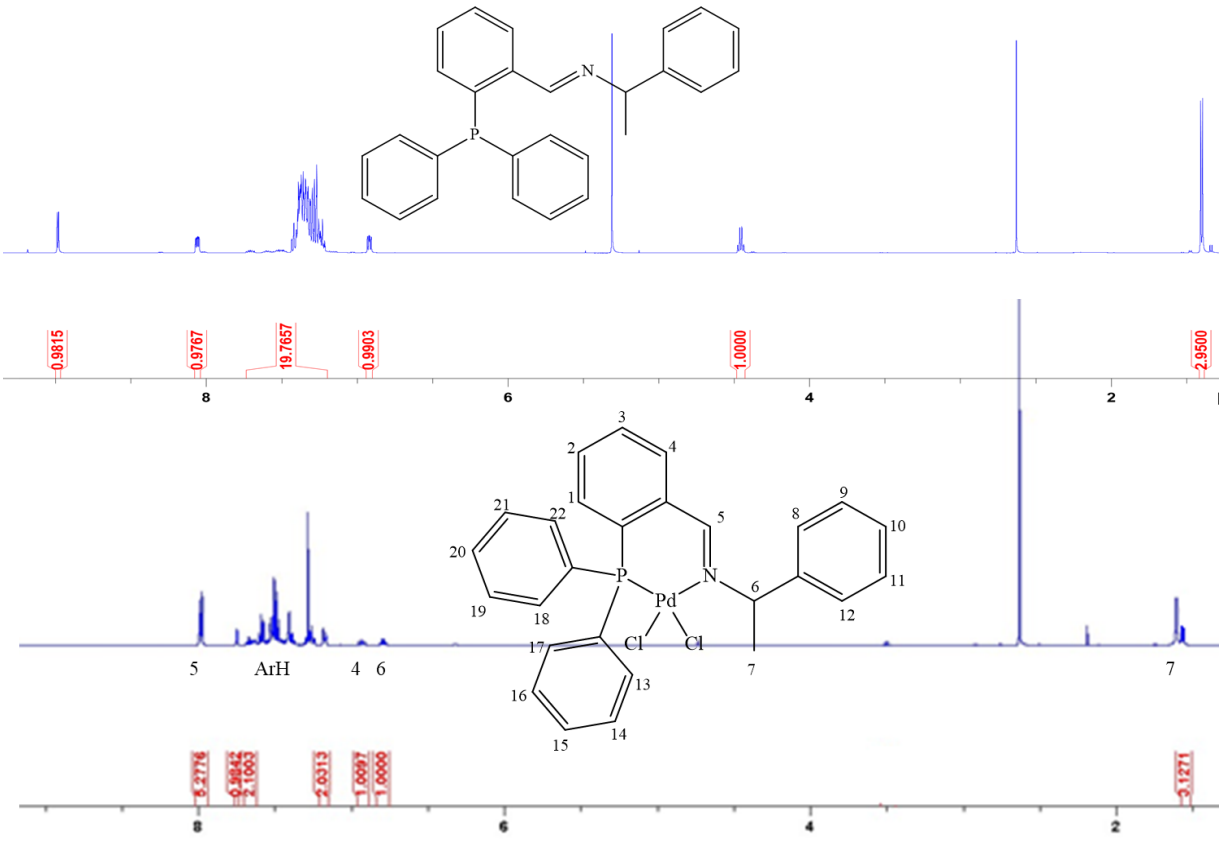


Figure 3.2. Overlaid ^{1}H-NMR spectra of ligand **L6** and complex **C7** showing a notable diagnostic proton peak downfield shift from 4.49 ppm to 6.80 ppm.

We also used two dimensional ^{1}H-^{1}H NMR to further study the structures of the complexes. For example, the COSY and NOESY NMR spectra were used to compare the solution and solid-state structure of complex **C3** (described later). The COSY spectrum of complex **C3** indicates a coupling interaction between the H at 6.06 ppm and the H at 1.92 ppm (Figure 3.3). This corresponds to the coupling of the CH group on the chiral carbon and the adjacent CH_3 group on the chiral carbon. Similarly, the peak marked (III) indicates a coupling interaction between the H at 7.69 ppm and the H at 9.35 ppm. This corresponds to the coupling of the CH on the imine carbon

and the adjacent H on the pyridine ring. There is a second set of equivalent peaks, also marked (I and III) on the other side of the diagonal. This data thus, confirmed that the complexes exhibited the same solid-state *S* configuration as in the solution state.

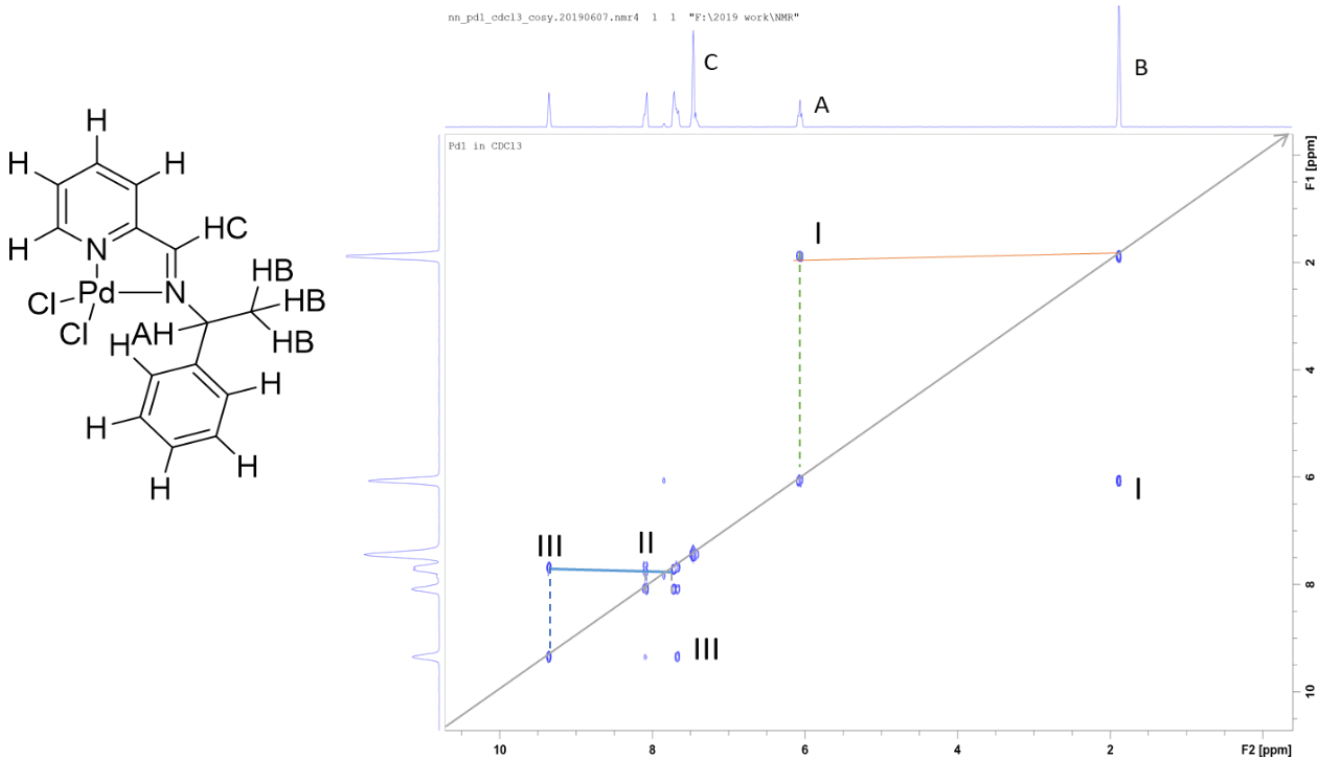


Figure 3.3. COSY NMR spectrum showing complex **C3** coupling between protons A, B and C.

The ^{13}C NMR spectroscopy was also used to structurally deduce the formation of all ligands (**L1-L6**) and their respective complexes (**C1-C7**). The number of carbons were observed to be the same as that calculated in the molecular formula for all complexes. The upfield signals between 19.39 – 26.60 ppm were assigned to the methyl carbons. From Figure 3.4, the characteristic peaks of the chiral carbon which resonated at 160.46 ppm and 167.04 ppm for ligand **L3** and its corresponding

complex **C3** respectively, indicated a change in chemical environment, hence suggesting successful complexation. In addition, the imine carbon peak for complex **C3** resonated at 64.74 ppm, an upfield shift from 69.57 ppm observed in ligand **L3**, a further proof of complexation.

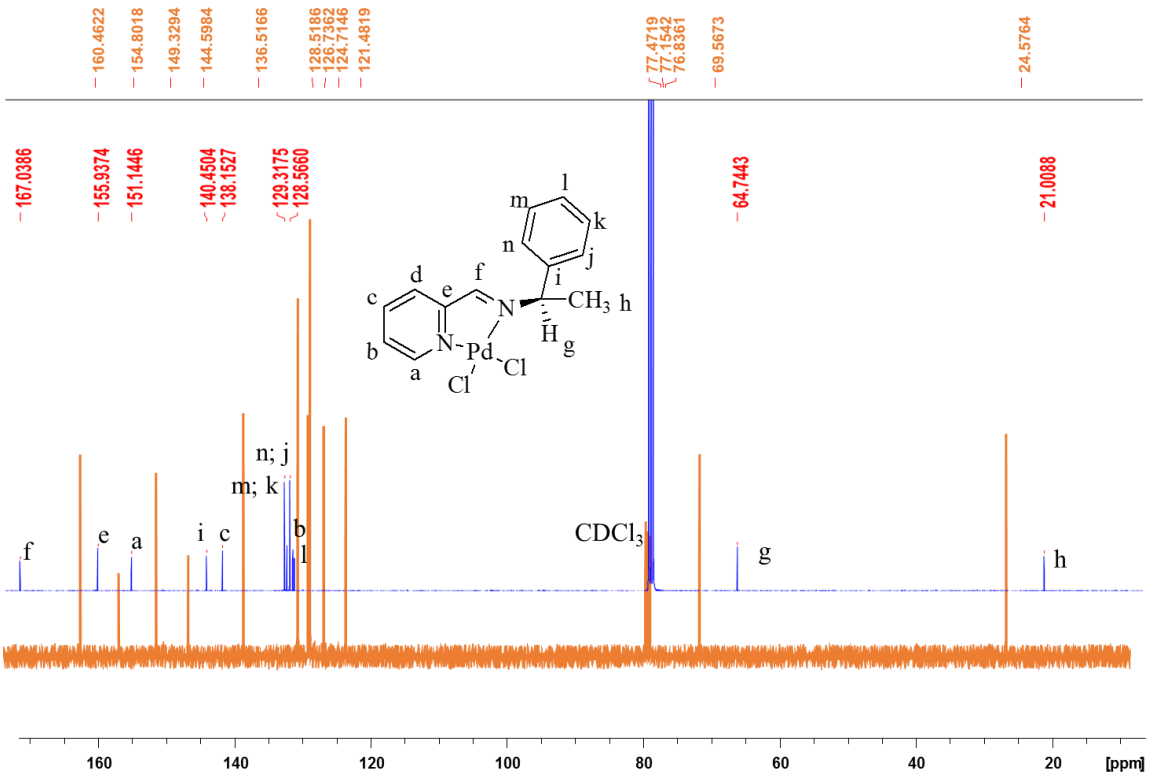


Figure 3.4. Overlaid ^{13}C NMR spectra of ligand **L3** and complex **C3** illustrating a shift of the imine carbon from 160.46 ppm in **L3** to 167.04 ppm in complex **C3**.

The ^{31}P NMR signal at -12.99 ppm and -13.00 ppm were in good agreement with literature reports for both ligands **L6-L7** respectively, confirming the presence of diphenylphosphine group. [31-33] Upon formation of complexes **C6** and **C7** (Figure 3.5), the ^{31}P NMR displayed downfield shifted signals to 31.42 and 31.43 ppm respectively (Figure 3.5).[23, 37]

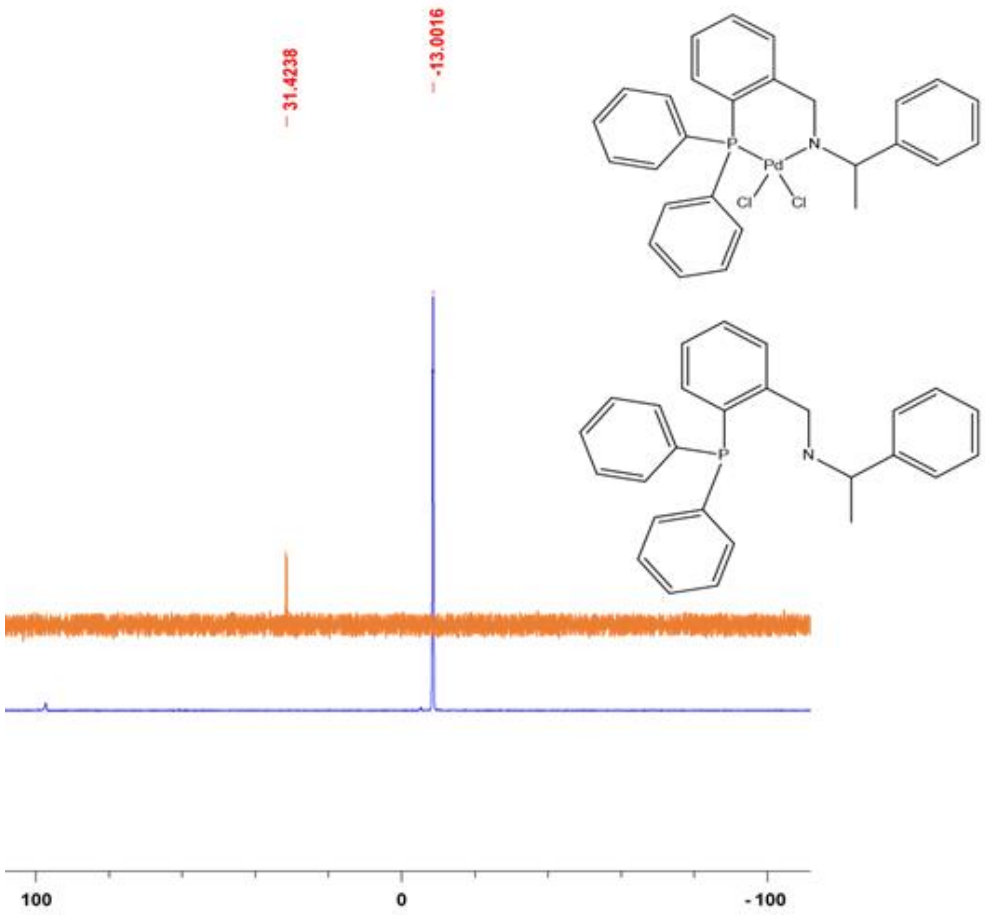


Figure 3.5 ^{31}P NMR spectrum of free ligand **L6** and the corresponding complex **C7** indicating shift of the phosphine signal from 13.00 ppm to 31.42 ppm respectively upon complex formation.

Another technique that was employed in the spectroscopic elucidation of the compounds was FT-IR spectroscopy (Table 3.1). For example, the azomethine nitrogen $\upsilon_{(C=N)imine}$ stretch of ligand **L6** and its corresponding palladium(II) complex **C7** were observed at 1634 cm^{-1} and 1626 cm^{-1} respectively (Figure 3.6) indicating a change in the imine bond chemical property, thus, the formation of the complex from its ligand. All the azomethine nitrogen wavenumber values the for the free (imino)phosphine ligand was found to be higher than that of their corresponding complexes (Table 3.1), in good agreement with literature reports.[37]

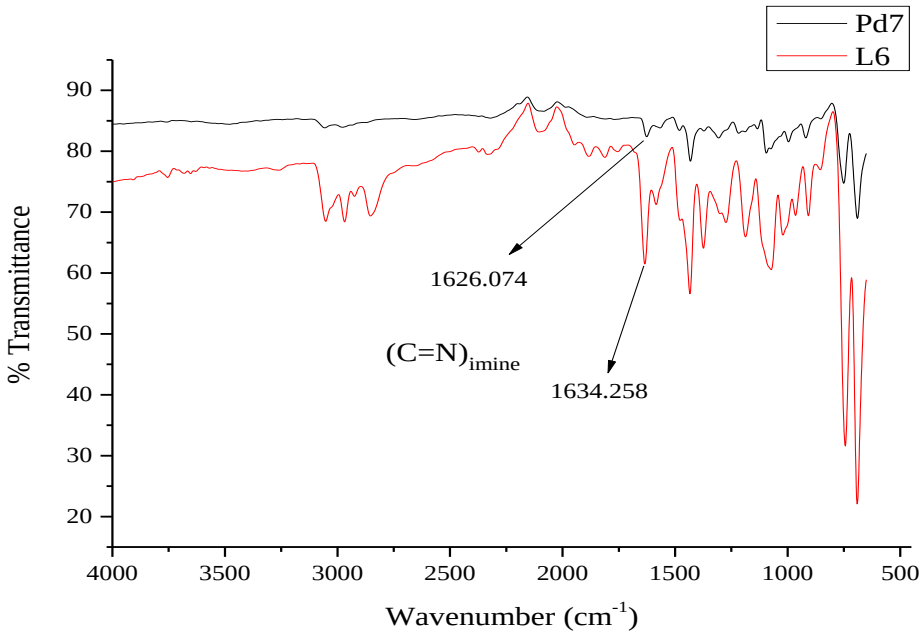


Figure 3.6. FT-IR spectra showing $\upsilon_{(C=N)imine}$ signals of the free ligand **L6** and its corresponding palladium(II) complex **C7** at 1634 cm^{-1} and 1627 cm^{-1} respectively.

Moreover, mass spectral data were also collected for ligands **L1-L6** and complexes **C1-C7** to establish their molecular weight and composition. The mass spectra of the complexes showed the molecular ion peaks along with various other isotopic peaks corresponding to molecular fragments confirming their formation. For instance, complexes **C1-C4** showed fragmentation pattern consistent with the loss of 2Cl- ion (m/z = ~314.48) as depicted in Figure 3.7 for complex **C3** mass spectrum. To mention other assignments in Figure 3.7, were observed at m/z value 316.48 [(M-2Cl) + 2H, 93%] and m/z value 388.33 [M + H, 68%]. Whilst, complexes **C6** and **C7** showed the fragment peak corresponding to (M^+ and M + H). For example, complex **C6** showed a molecular ion peak at m/z = 573.00 (M + 4H, 100%) which is in good agreement with the molar mass of 569.01 calculated. The other complexes **C1, C2, C4, C5** and **C7** were observed at m/z values 424.37 (M + Na, 71%), 404.52 (M + 4H, 100%), 384.42 (M – 2H, 78%), 370.34 (M + 4H, 56%)

and 574.00 (M + 4H, 80%) respectively. Elemental analysis of the palladium (II) complexes C**1-C4**, **C6** and **C7**, further confirmed their composition and purity.

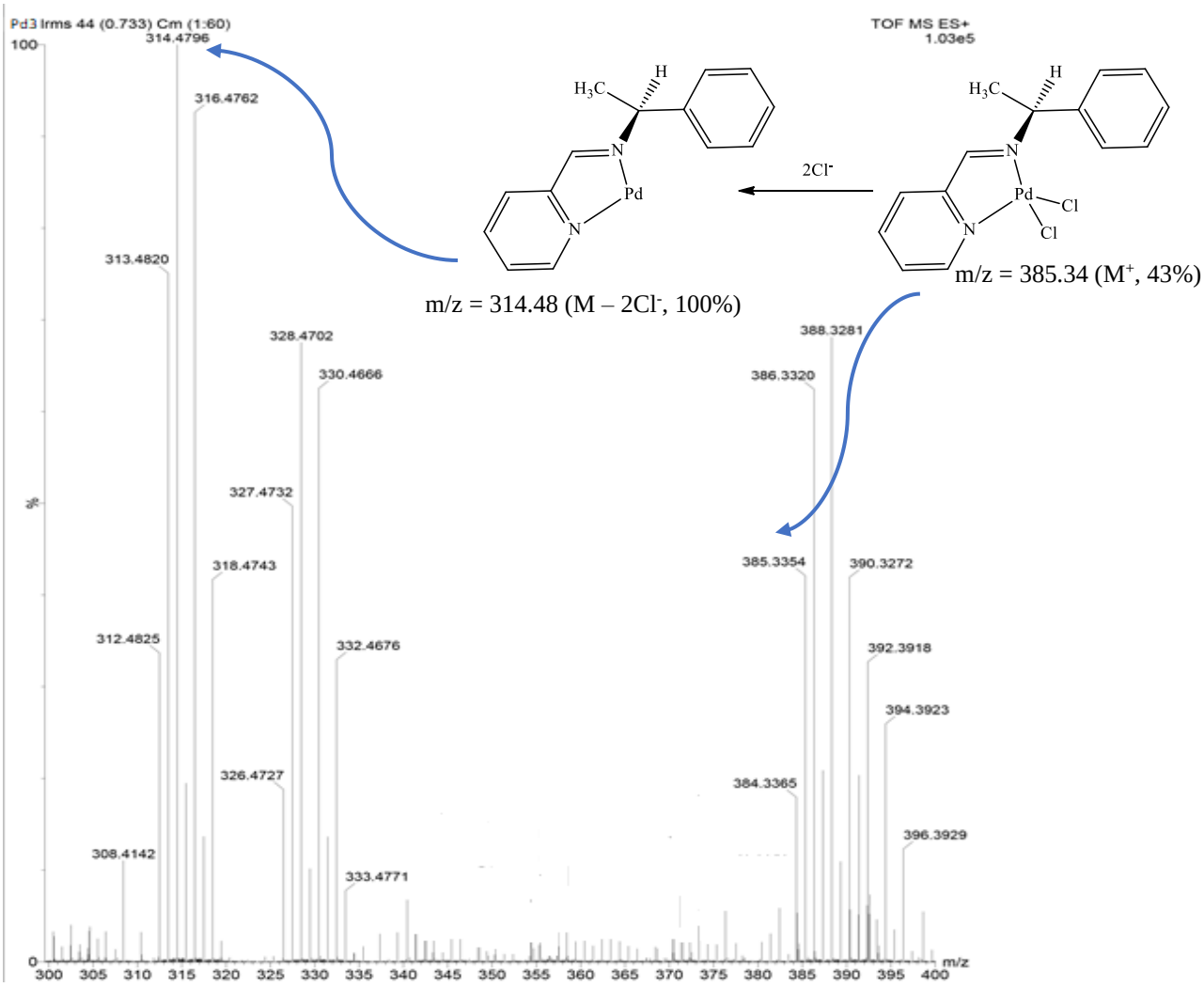


Figure 3.7. TOF Mass spectrum of complex **C3** showing fragment peaks for m/z [M^+] peak at 385.34 and [M – $2Cl^-$] peak at 314.48.

Table 3.1. Selected FT-IR spectroscopic data and mass spectral data of free ligands as well as their respective complexes

Compound	$\upsilon(cm^{-1})$ $(C=N)_{imine}$	Theoretical Mass	Experimental Mass
L2	1697	224.13	226.15 (M^+ + 2H)
C2	1601	399.97	404.52 (M^+ + 4H)
L3	1644	210.12	211.12 (M^+ + H)
C3	1595	385.96	386.42 (M^+ + H)
L4	1644	210.12	211.12 (M^+)
C5	1593	366.01	370.34 (M + 4H)
L5	1634	393.16	393.50 (M^+)
C6	1625	569.01	573.00 (M^+ + 4H)

3.3.2. Molecular structures of complexes C1-C4, C6 and C7

Single crystals suitable for X-ray analyses of complexes **C1-C4** were grown by slow diffusion of hexane solvent in their dichloromethane solutions at room temperature, while single crystals of complexes **C6** and **C7** were grown through slow evaporations of tetrahydrofuran/hexane/dichloromethane solution mixtures of the complexes. Figures 3.8-3.13 show the molecular structures of complexes **C1-C7** respectively while Table 3.2 gives the crystallographic data collection and structural refinement parameters of the complexes. It is noteworthy to mention that all the N^N-based crystals adopted monoclinic crystal systems and a $P2_1$ space groups while the N^P-based crystals afforded orthorhombic crystal system and $P2_1$ $P2_1$ $P2_1$ space group.

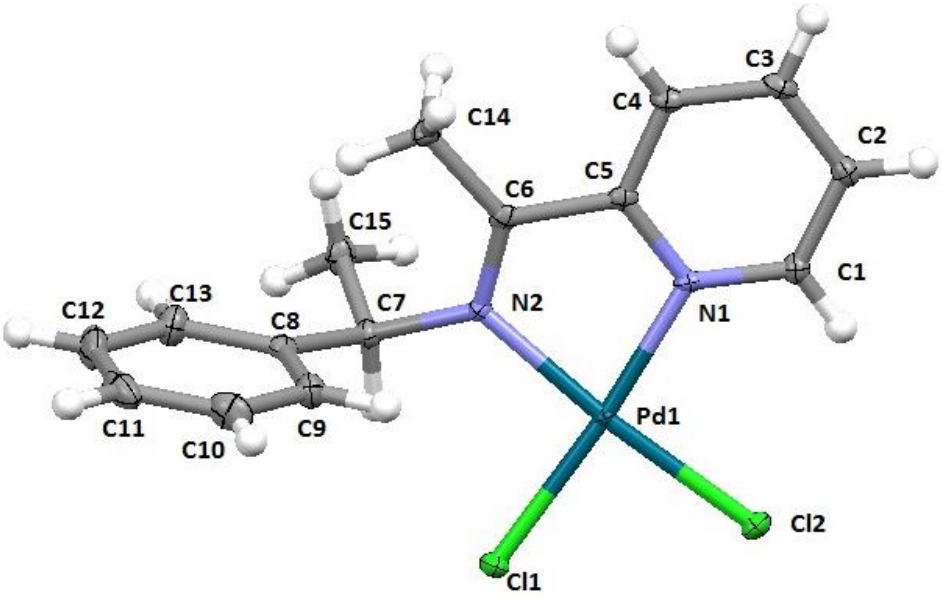


Figure 3.8. Crystal structure of complex **C1** drawn at 50 % thermal probability ellipsoids

The solid-state structures of all complexes confirmed the formation of mononuclear complexes in which ligands **L1-L6** adopt bidentate coordination modes to palladium metal atom. All these monometallic palladium (II) complexes, exhibit coordination number 4. The coordination environment around the Pd metal atom consists of one bidentate ligand motif and two chloride ligands, to give neutral four coordinate Pd(II) complexes (Figures 3.8 – 3.13). The average Cl(1)-Pd-Cl(2) bond angles for the N^N-based and N^P-based complexes were 89.762^{o} ± 0.825 and 89.730^{o} ± 0.410 respectively. The Cl(1)-Pd-Cl(2) angles of all crystals deviates from 90^{o} angle, which can attribute steric strain imposed by phenyl groups.

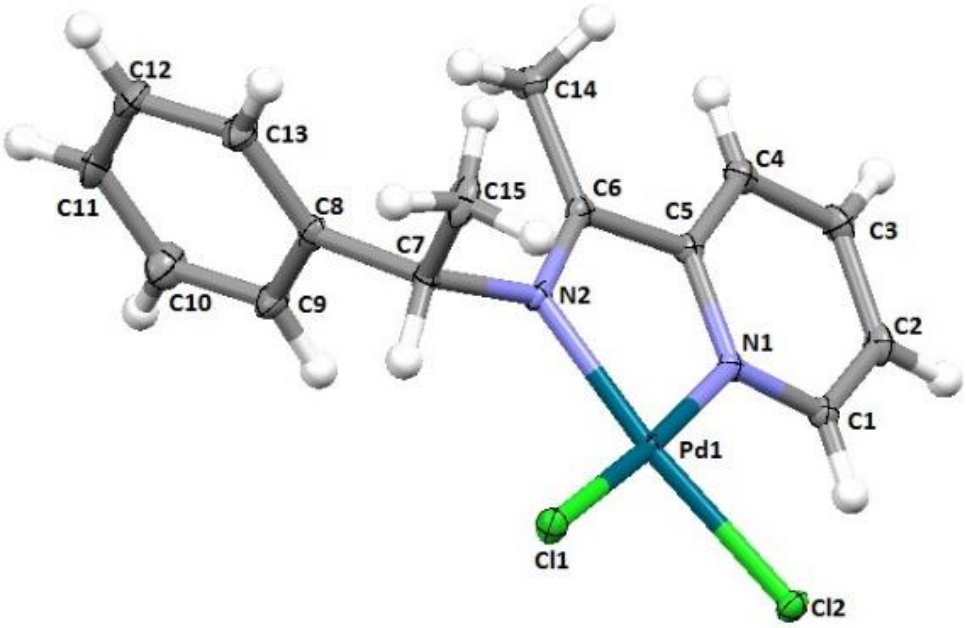


Figure 3.9. Crystal structure of complex **C2** drawn at 50% thermal probability ellipsoids.

The selected bond distances and angles of complexes **C1-C4** are summarized in Table 2. The average Pd-Cl bond distance of all N^N crystal structures **C1-C4** was determined to be 2.296 Å ± 0.0054 Å which is slightly higher than the average Pd-Cl bond length of 2.284 ± 0.022 Å obtained from 464 similar structures using MOGUL structural data search.[39] Nevertheless, it is worth mentioning that the mean Pd-Cl bond distances of the complexes lies within the range of 2.284 - 2.422 Å reported in literature for similar structures.

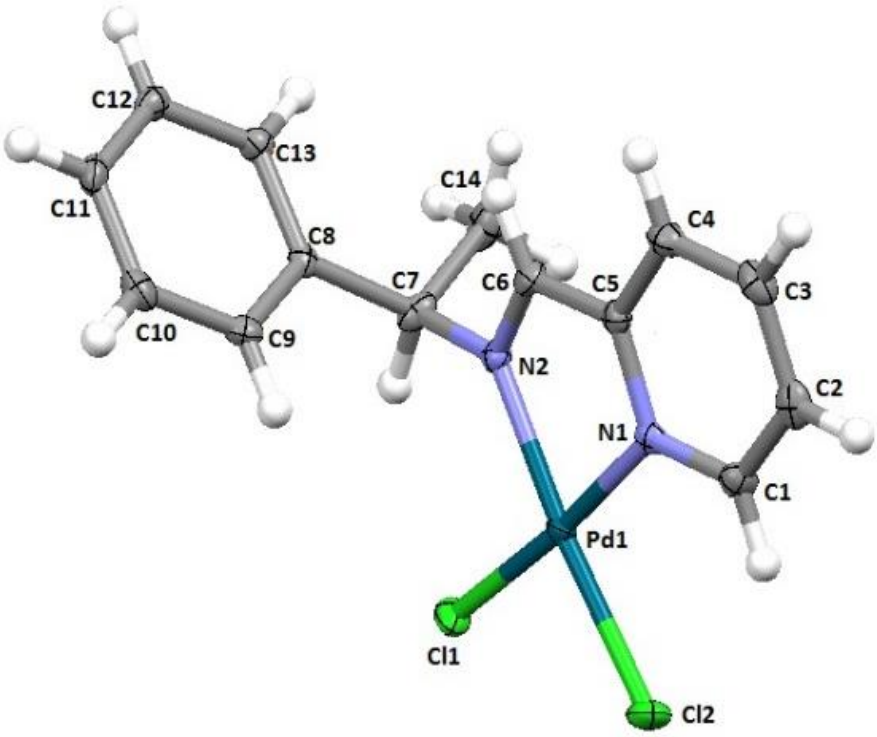


Figure 3.10. Crystal structure of complex **C3** drawn at 50% thermal probability ellipsoids.

Furthermore, the mean Pd-N_{py} (2.020 Å) and Pd-N_{imine} (2.034 Å) bond lengths obtained were statistically comparable with the Pd-N_{py} and Pd-N_{imine} average bond distances of 2.039 ± 0.029 Å (165 structures) and 2.015 ± 0.039 Å (30 structures) respectively reported in similar structures.[36] The molecular structure of complex **C3** has been reported by Mishnev and co-workers.[36] In general, the Pd-Cl bond lengths in complexes **C1-C4** are normal, averaging 2.295 Å. This value is in agreement with the Pd-Cl bond length of 2.298(15) Å averaged for 491 Pd complexes as reported in the Cambridge Structural Database (CSD).[40]

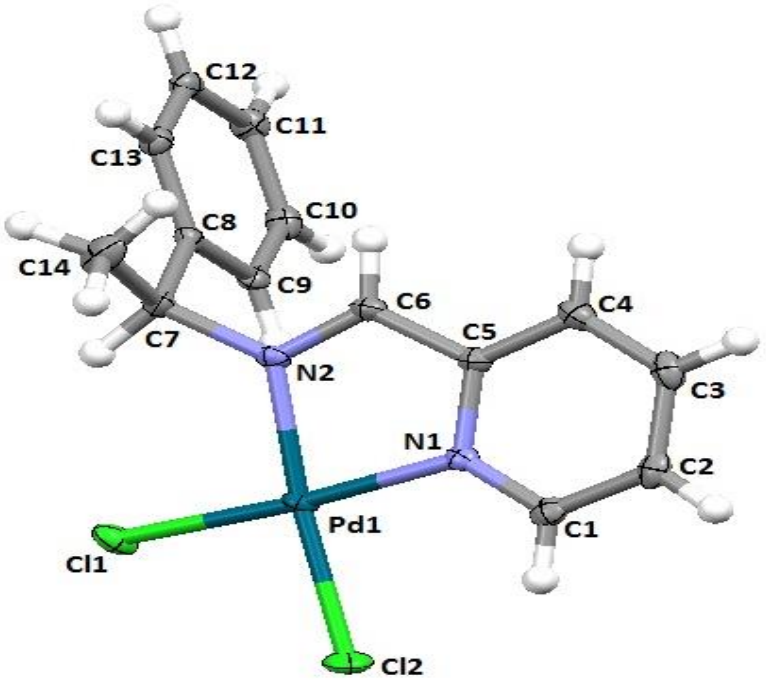


Figure 3.11. Crystal structure of complex **C4** drawn at 50% thermal probability ellipsoids.

The N_{py}-Pd-N_{imine} bite angle of complex **C3** (80.40°) is comparable to that of its analogous complex **C4** (80.27°), while complexes **C1** and **C2** had the same N_{py}-Pd-N_{imine} bite angle of 80.10°. The Cl(1)-Pd-Cl(2) bond angles of complexes **C1** (89.33º), **C2** (89.33º) and **C4** (89.39º) were of close proximity to the expected 90º of the Pd(II) square planar geometry in comparison to that of complex **C3** (91.00º) forming an obtuse angle. Consequently, crystal **3** (Figure 3.11) has a slightly higher degree of distortion of its square planar geometry. The C7 is equatorially positioned to the phenyl ring confirming the *R*-configuration of the molecule. In molecular structure of complex **C1** (Figure 3.8), the C7 is axially positioned to the phenyl ring were evident to the S-configuration.

Table 3.2. Crystal data collection and refinement parameters for complexes **C1**-C**4**, **C6** and **C7**

Parameter	**C1**	**C2**	**C4**	**C6**	**C7**
Empirical formula	$C_{15}H_{16}Cl_2N_2Pd$	$C_{15}H_{16}Cl_2N_2Pd$	$C_{14}H_{14}Cl_2N_2Pd$	$C_{27}H_{24}Cl_2NPd$	$C_{27}H_24Cl_2NO_2PPd$
Formula weight	401.60	401.60	387.57	570.74	602.74
Temperature(K)	100(2)	100(2)	100(2)	100(2)	100(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic	Monoclinic	Orthorhombic	Orthorhombic
Space group	P21	P21	P21	P 21 21 21	P 21 21 21
a (Å)	7.1677 (7)	7.1266 (5)	14.4832 (8)	9.2643(5)	9.1628(7)
*b (*Å)	24.265 (2)	24.2585 (19)	8.4803 (5)	10.3531(6)	10.3591(7)
c (Å)	9.0510 (8)	9.0656 (6)	18.3880 (10)	29.5544(16)	29.968(2)
α (º)	90.000	90.000	90.000	90.000	90.000
β (º)	105.495 (2)	105.311 (3)	103.684 (3)	90.000	90.000
γ (º)	90.000	90.000	90.000	90.000	90.000
Volume(A^3)	1517.0 (7)	1511.64 (19)	2194.3 (2)	2834.7(3)	2844.5(4)
Z	4	4	6	4	4
D_{calcd} (mg/m^3)	1.758	1.765	1.760	1.337	1.407
Absorption coefficient (mm^{-1})	1.566	1.571	1.620	0.913	0.919
F(000)	800	800	1152	1152	1216
Theta range for data collection (°)	1.678-27.469	1.677-27.501	1.447-27.703	1.378-29.010	1.359- 27.530
Reflections collected / unique	13534	25289	38574	52196	91891
Completeness to theta (%)	99.1	99.1	99.2	99.3	99.8
Goodness-of-fit on F^2	1.019	1.060	1.015	0.902	1.575
R indices (all data)	R_1 = 0.0160 wR_2 = 0.0382	R_1 = 0.0165 wR_2 = 0.0385	R_1 = 0.0141 wR_2 = 0.0323	R_1 = 0.0261 wR_2 = 0.0604	R1 = 0.0853 wR2 = 0.2396
Largest diff. peak and hole (e $Å^{-3}$)	0.401 and -0.394	0.294 and -0.461	0.361 and -0.250	0.621 and -0.834	6.970 and -0.939

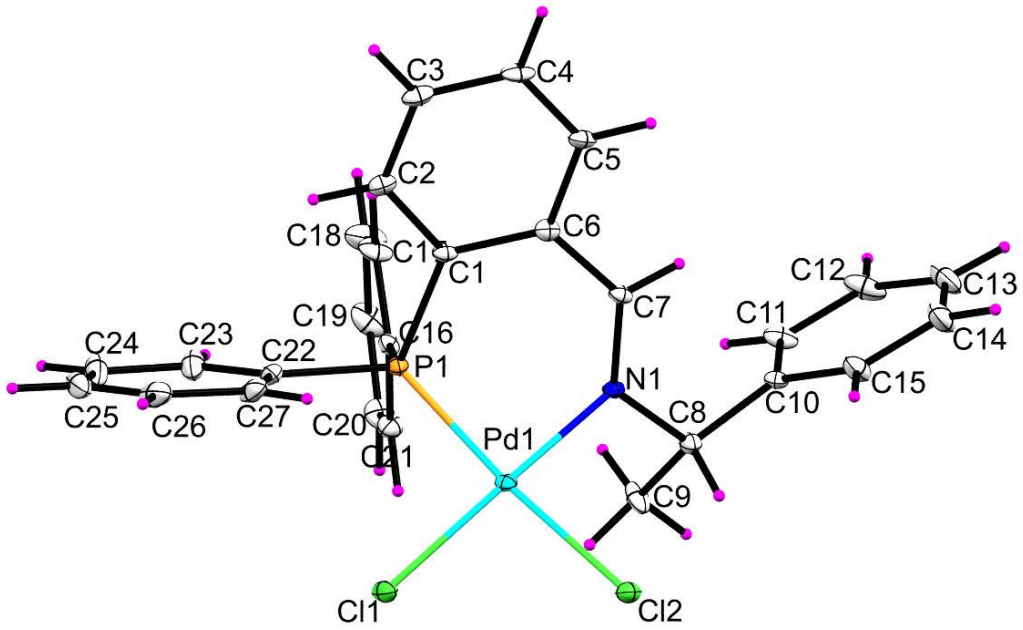


Figure 3.12. Crystal structure of complex **C6** drawn at 50% thermal probability ellipsoids.

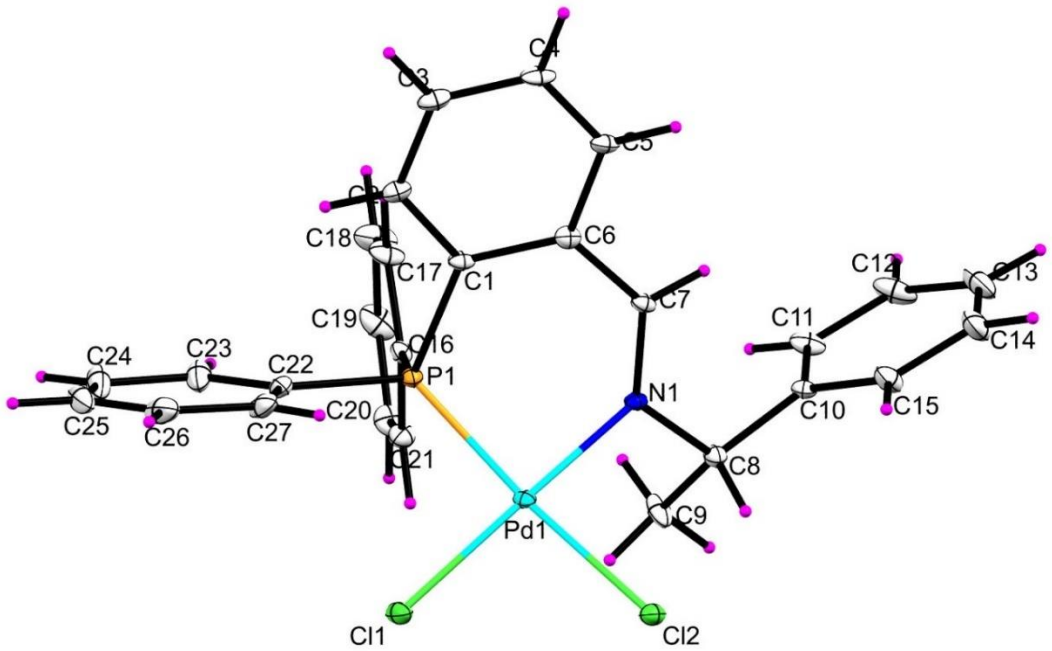


Figure 3.13. Crystal structure of complex **C7** drawn at 50% thermal probability ellipsoids.

In the molecular structures of complexes **C6** and **C7** shown in Figures 3.12 and 3.13 respectively, the chelating (imino)phosphine ligands bind to the Pd(II) metal through the phosphine donor P(1) and imine donor N(1) atoms.[41] The remaining coordination sites around the Pd(II) metal are occupied by *cis*-orientated chlorido ligands to give four coordinate compounds. The Cl(1)-Pd-Cl(2) bond angle was found to be 90.02(10)º for **C6** and 89.44(11)º for **C7.**

Table 3.3. Selected bond lengths and bond angles of the N^N complexes **C1**-C**4**.

Complex	**C1**	**C2**	**C3**	**C4**
Selected bond distances (Å)				
Pd(1)-N_{py}	2.012(3)	2.013(3)	2.027(3)	2.029(2)
Pd(1)-N_{imine}	2.031(30	2.031(3)	2.037(3)	2.037(2)
Pd(1)-Cl(1)	2.295(9)	2.295(9)	2.303(1)	2.290(7)
Pd(1)-Cl(2)	2.298(9)	2.298(9)	2.282(1)	2.300(6)
Selected bond angles (°)				
N_{py}-Pd-N_{imine}	80.10(1)	80.10(1)	80.40(1)	80.27(8)
Cl(1)-Pd-Cl(2)	89.33(3)	89.33(3)	91.00(3)	89.39(2)
N_{py}-Pd-Cl(1)	175.64(8)	175.64(8)	175.48(8)	176.48(6)
N_{py}-Pd-Cl(2)	94.20(8)	94.20(8)	93.47(8)	94.12(6)
N_{imine}-Pd-Cl(1)	96.26(8)	96.26(8)	95.08(8)	96.21(6)
N_{imine}-Pd-Cl(2)	173.56(8)	173.56(8)	173.85(8)	174.39(6)

The angles around the metal centre add up to 360.73° and 360.54° for the **C6** and **C7** complexes, respectively (Table 3.4).[42] The P(1)-Pd-N(1) bond angle of crystal **6** was 86.6(2)° and crystal **C7** was 86.2(3)°. The phosphine donor makes a longer bond to the metal than the imine (by approximately more than 0.18 Å) for both crystals **C6** and **C7**, this is consistent with the observations of Ankersmit and co-workers.[43] The Pd-N bond was shorter than the Pd-P bond due to the diphenylphosphine group which tends to reflect stronger trans-influence than the imine group.[44, 45] The bond distance of Pd-Cl(1) 2.284(3) which trans to the N-atom is shorter than the bond distance of Pd-Cl(2) 2.378(2) which is trans to the P-atom, in the solid structure of complex **C6** reflecting the stronger *trans* influence of the tertiary phosphine with regard to an imine.[46, 47] The bond distances of crystal **C7** were fairly similar, Pd-Cl(1) 2.282(3) and Pd-Cl(2) 2.380(2). The stronger trans-influence attributed by the phosphine affects the geometry of crystal to being distorted square planar.[47] The phenyl ring that is adjacent to the ethyl is axially positioned to the C8 confirming the *S*-configuration of the crystal **C6**. When comparing the degree of distortions in the molecular structures of **C1-C4**, C**6** and **C7** the N^N-donor compounds **C1-C4**, are more distorted than the N^P structures **6** and **7**. For instance, complexes **C1** and **C7** exhibited Cl(1)-Pd-Cl(2) bond angles of 89.33° and 89.44° which implies crystal **C1** deviates slightly more from the ideal 90.0° angle of a square planar geometry in comparison to crystal **C7**. The comparable distortions could be rationalized from the remote proximity of the phenyl groups from the Pd center, hence exerting little influence on the resultant geometry. This can also be due to the six-membered chelate rings in **C6** and **C7**, in comparison to the five-membered rings in **1-4**.[48]

Table 3.4. Selected bond lengths and bond angles of the N^P complexes.

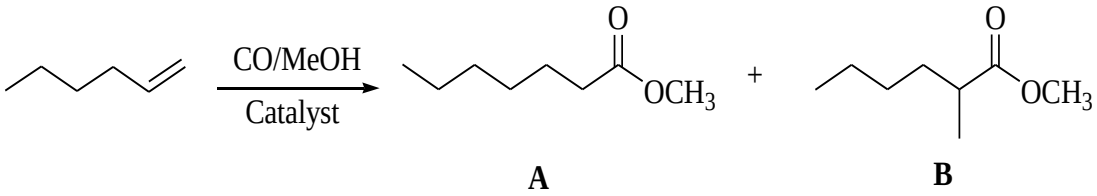
Complex	**C6**	**C7**
Selected bond distances (Å)		
Pd(1)-P(1)	2.212(3)	2.218(3)
Pd(1)-$N(1)_{imine}$	2.056(8)	2.043(10)
Pd(1)-Cl(1)	2.284(3)	2.282(3)
Pd(1)-Cl(2)	2.378(2)	2.380(3)
$N(1)_{imine}$-C(8)	1.506(12)	1.499(14)
$N(1)_{imine}$-C(7)	1.297(12)	1.301(15)
Selected bond angles (°)		
P(1)-Pd-$N(1)_{imine}$	86.6(2)	86.2(3)
Cl(1)-Pd-Cl(2)	90.02(10)	89.44(11)
P(1)-Pd-Cl(1)	92.91(10)	93.90(12)
P(1)-Pd-Cl(2)	171.85(9)	172.61(11)
$N(1)_{imine}$-Pd-Cl(1)	174.4(2)	176.0(3)
$N(1)_{imine}$-Pd-Cl(2)	91.2(2)	91.0(3)

3.4. Screening of complexes C1-C7 in the methoxycarbonylation and hydrogenation reactions

3.4.1. Methoxycarbonylation of 1-hexene substrate

In attempt to use the isolated chiral palladium complexes (**C1-C7**) in the methoxycarbonylation reactions, we first used 1-hexene as a model substrate to establish their ability to catalyze this

reaction (with temperature 90°C; time 24 h ; Pd/1-hexene ratio, 200:1, Pd/ HCl ratio; 1:10, Pd/PPh_3 ratio: 1:2; solvent: toluene (30 ml) and methanol (30 ml); CO pressure = 60 bar) (Table 3.5). The GC and GC-MS analyses (Figure 3.14), shows the m/z peak at 145.12 with the retention times of 10.51 min were found to correspond to linear product **A** and 116.63 min to branched product **B** as the two major products in the methoxycarbonylation of 1-hexene, with **A** identified as methyl heptanoate and **B** identified as methyl 2-methylhexanoate ester products (Scheme 3.4). From the data in Table 3.5, all the complexes (**C1-C5**) showed very low catalytic activities affording only conversions of about 10% within 24 h. This catalytic performance is far much lower compared to similar reported systems, which display conversions of 90 % within 24 h.[15, 16, 49] Even using a stronger acid promoter, such as hydrochloric acid (which plays a key role to stabilize the palladium (II) species, by limiting the formation of palladium (0) black species) [37, 38], did not improve the catalytic activity as only 11% conversion was achieved (Table 3.5, entry 7). When complexes **C6** and **C7** were used (entry 8 and 9), very low catalytic activity (5% and 4% conversions respectively) was observed with regioselectivity below average.



Scheme 3.4. Major products obtained from the methoxycarbonylation of 1-hexene.

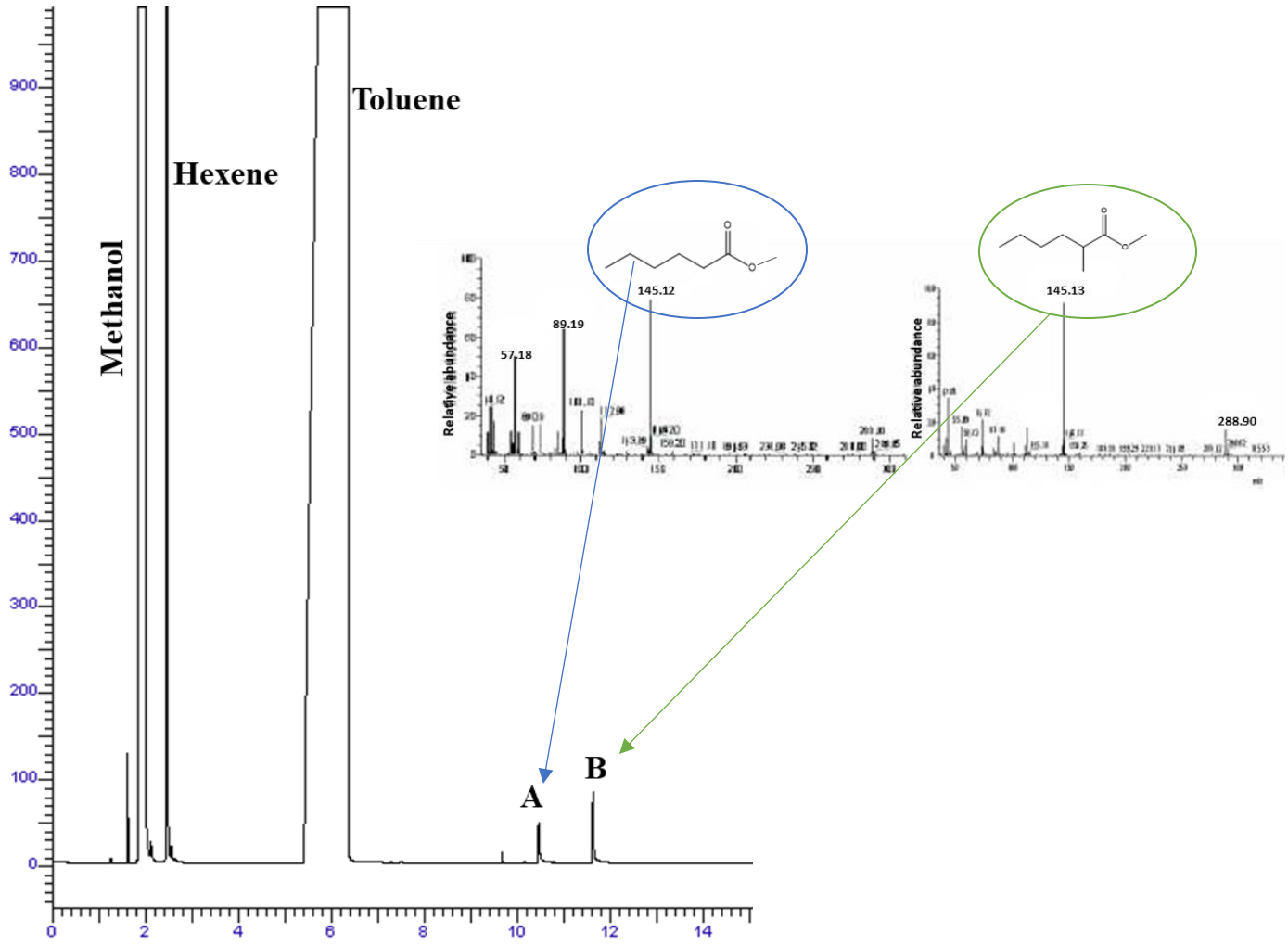


Figure 3.14. Overlaid GC and GC-MS chromatogram showing 1-hexene converted to **A** methylhexanoate and **B** methyl-2-methylhexanoate esters from methoxycarbonylation reaction using complex **C4**. Reaction conditions: Pressure: 60 bar, Temp: 90 ^{o}C, Time: 24 h, Acid; HCl, Solvent: methanol 30 ml and toluene 30 ml; [Pd]:[HCl]:[hexene] ratio; 1:10:200; GC-MS used to determine the molecular weights and identity of the resulting esters.

Table 3.5. Preliminary screening in methoxycarbonylation of 1-hexene using complexes **C1-C5**[a]

Entry	Catalyst	Time	% Conversion[b]	B/L (%)[c]
1	**1**	24	9	39/61
2	**1**	36	13	37/63
3	**2**	24	7	40/60
4	**3**	24	11	39/61
5	**4**	24	12	42/58
6	**5**	24	10	41/59
7[d]	**4**	24	11	40/60
8	**6**	24	5	42/58
9	**7**	24	4	41/58

[a]Reaction conditions: Pressure: 60 bar, temp: 90 ^{o}C, acid: PTSA, Solvent: methanol 50 mL and toluene 50 mL; time 24 h, 0.5% mol palladium; [b]% of 1-hexene converted to esters determined from GC assuming 100% mass balance; [c] Molar ratio between branched and linear ester. [d] HCl as promoter.

3.4.2. Methoxycarbonylation of styrene substrate

In order to investigate the role of substrate in controlling the catalytic activities of complexes **C1-C7** in the methoxycarbonylation reactions, we also used the more reactive styrene substrate (Scheme 3.5). Reaction conditions of 60 bar of CO pressure, temperature of 90 ^{o}C and [styrene]: HCl:[Pd] = 200:10 :1 ratio was employed (Table 3.6). As identified by GC and GC-MS the

methoxycarbonylation of styrene yielded methyl-3-phenylpropanoate (linear product **A**) and methyl-2-phenylpropanoate (branched product **B**) as the major ester products (Figure 3.15). The preliminary results obtained showed that the chiral N^N as well as the chiral N^P catalysts had low to moderate activity, high regioselectivity and the position of the chirality factor did not contribute to the enantioselectivity of the catalysts in methoxycarbonylation reaction of styrene.

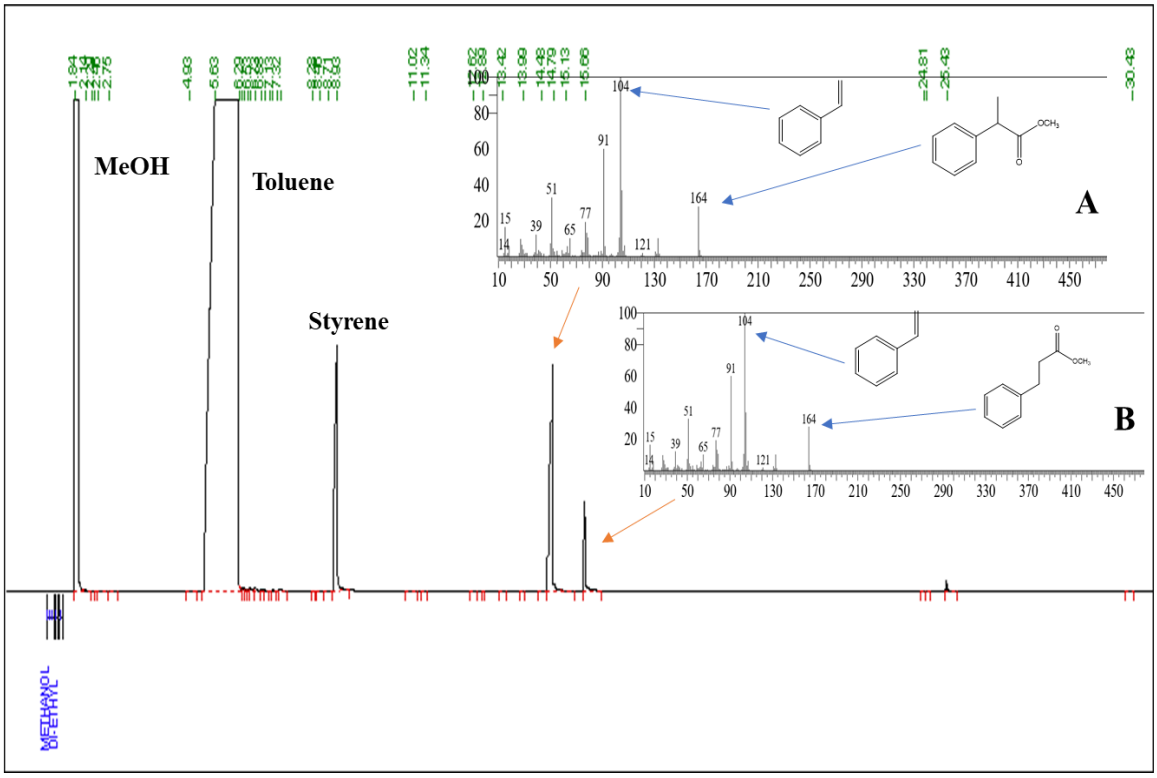
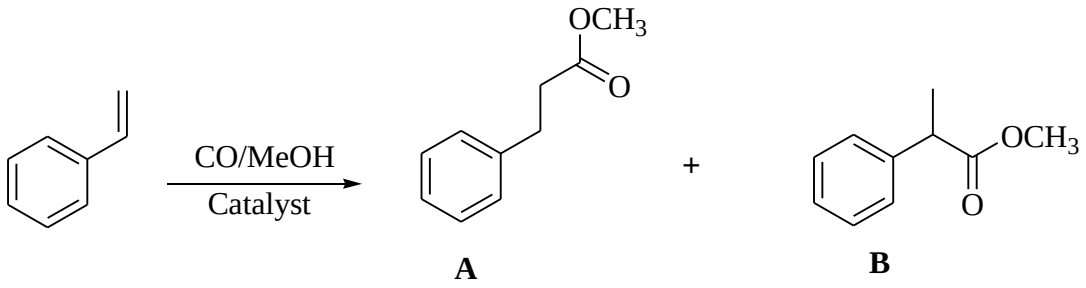


Figure 3.15. GC and GC-MS spectra of products (m/z peak at 164 corresponding to **A** 14.40 min and **B** 15.55 min, branched and linear products respectively) extracted from styrene using complex **C4** (0.09 mmol), temperature; 90°C; time 24 h ; Pd/styrene ratio, 200:1, Pd/ HCl ratio; 1:10, Pd/PPh_3 ratio: 1:2; solvent: toluene (30 ml) and methanol (30 ml); P(CO) = 60 bar.



Scheme 3.5. Methoxycarbonylation reaction of styrene as substrate

3.4.2.1. Optimization of the methoxycarbonylation reactions

3.4.2.1.1. Effect of complex structure on the methoxycarbonylation of styrene

In the attempt to establish the best operating conditions to obtain good catalytic activity, regioselectivity as well as enantioselectivity, investigating the structure of the different complexes in the methoxycarbonylation reaction must be performed. Hence, in the investigation the catalytic activities of the complexes were found to be dependent on the structure of the complexes for instance, the nature of donor atoms affected catalytic activities. Generally, complexes bearing the chelating N^N donor atoms showed superior catalytic activities as compared to the N^P donor, for instance, while complex **C4** bearing N^N donor atoms displayed a conversion of 62%, (Table 3.6, entry 13) complex **C6** bearing N^P atoms showed a far much less conversion of 23% (Table 3.6, entry 17). Another factor was the ligand substituent attached to the imine carbon. For example, under similar reaction conditions, complexes **C1** and **C2** bearing the CH_3 group displayed conversions of 29 and 38% respectively, whilst the structurally similar complexes **C3** and **C4** (Table 3.6) bearing H at the same spot gave conversions of 59 and 62% (Table 3.6 entries 12 & 13) respectively. An observation which can be explained by a slight steric encumbrance difference between the H and CH_3 groups. It is noteworthy that having an alkyl bulky groups within the

coordination sphere has a significant influence, the methoxycarbonylation reaction of styrene afforded these conversions 99% (within 6 h) Ph_2PNHpy whilst 35% (within 24 h) $Ph_2PNMepy$.[10]

Table 3.6. The methoxycarbonylation reaction using styrene as substrate

Entry	**Catalyst**	**[Pd]:PPh_3**	**% Conversion[b]**	**B/L[c]**	**ee%**
10	**1**	1:2	29	84/16	1.8
11	**2**	1:2	38	87/13	2.6
12	**3**	1:2	59	85/15	0.4
13	**4**	1:2	62	85/15	1.6
14	**4**	1:1	21	76/24	1.6
15	**4**	1:4	59	74/26	3.4
16	**4**	1:6	27	75/25	2.4
17	**6**	1:2	23	84/16	1.4
18	**7**	1:2	19	83/17	1.8

[a]Reaction conditions: Pressure: 60 bar, time temp: 90 ^oC, acid: HCl, Solvent: methanol 30 mL and toluene 30 mL; time: 24 h, 0.09% mol palladium; [b]% of 1-hexene converted to esters determined from GC assuming 100% mass balance; [c] Molar ratio between branched and linear ester.

The structure of the complexes did not have an influence on the regioselectivity of the products formed as all the complexes gave predominantly branched ester products between 83 and 87 %. The complexes also displayed poor enantioselectivities as the best ee value obtained was 3.4 %. We hypothesize that the poor obtained enantioselectivities were as a result of the position of the chiral centre which was out of the coordination spheres. Complex **C4**, was chosen for further investigation of reaction conditions on basis of better catalyst performance than the rest, shown in the preliminary methoxycarbonylation reactions using styrene (Table 3.6, entry 13).

3.4.2.1.2. Effects of palladium: phosphine ratios

Varying phosphine promoter ratios can have profound effect on the behaviour of catalysts in the methoxycarbonylation reaction.[50] The complex: phosphine ratios were then varied to obtain the best reaction condition. Using complex **C4,** a conversion of 62% was observed for [Pd]: PPh_3 ratio of 1:2, lowering the phosphine amount to a ratio of [Pd]: PPh_3 ratio of 1:1 led to a lower conversion of 21% (Table 3.6 entries 17 & 18). Unsurprisingly, the reduced catalytic activity was accompanied by observed traces of palladium black in the reactor, further pointing to the importance of phosphine additive in the stabilization of the active species.[51] Increasing ratios of PPh_3/complex **C4** from 2 to 4 and 6 concomitantly led to lower percentage conversions, an indication of hindered substrate coordination at higher phosphine quantities.[52] Similarly, varying the amount of phosphine resulted in changes in regioselectivity. While [Pd]: PPh_3 ratio of 1:2 gave 85% of the branched esters, higher or lower ratios led to significant decrease in branching, for example phosphine ratios of 1 and 6 led to 76 and 75% of branched products respectively. One the other hand, higher phosphine ratios led to slight improved enantioselectivities, as a demonstration,

whereas a phosphine ratio of 2 gave 1.6% ee, increasing the ratio to 6 more than double the ee value to 3.4% (Table 3.6 entries 15 & 18).

3.4.2.1.3. Effect of solvent system in the methoxycarbonylation reactions

In the attempt to optimize the catalytic activity as well the selectivity, the effect of solvent variation on the catalytic activity was performed. When a mixture of THF and methanol (1:1) was used as solvent (Table 3.7, entry 21), a significant decrease in catalytic activity was found when compared to the results obtained in toluene: MeOH mixture under the same conditions, 30% and 59% respectively (Table 3.7 entry 17 and 20). An observation which can be attributed to higher polarity of THF, making the catalysis solvent mixture more polar, hence lower catalytic activity. [53] Changing the solvent rations can also have a substantial effect on the methoxycarbonylation reactions. From the observations made use of either excess methanol or toluene with respect to another led to a significant drop in catalytic activities. For instance, while a ration of toluene: MeOH of 1:1 displayed a conversion of 62%, ratios of 1:15 and 15:1 led to diminished conversions of 25 and 54% respectively, an observation consistent with previous studies. Zolezzi *et al*., reported a diminished catalytic activity with the use of excess methanol.[54] Increased amount of methanol significantly led to decrease in the branched ester product, for example, while MeOH:toluene ratio of 1:15 gave a near complete branched regioselectivity of 95%, a reverse ration saw a dramatic drop of the branched ester 54% (Table 3.7 entries 20 & 21). Such an observation is consistent with previous observation and can be attributed to lower solubility of the catalyst in methanol and increased polarity of the solvent system.[55-57]

Table 3.7. Effect of solvents and solvent ratios on conversion percentages and regioselectivity

Entry[e]	Catalysts	Solvent	% Conversion	B/L	ee%
19	**4**	1:1 MeOH : Toluene	62	86/14	2.6
20	**4**	1:15 MeOH : Toluene	25	95/5	0.8
21	**4**	15:1 MeOH : Toluene	54	41/59	3.4
22	**4**	1:1 MeOH : THF	30	95/5	16.8

[a]Reaction conditions: Pressure: 60 bar, time temp: 90 ^{o}C, acid: HCl, Solvent: methanol 30 mL and toluene 30 mL; time: 24 h, 0.09% mol palladium; [b]% of 1-hexene converted to esters determined from GC assuming 100% mass balance; [c] Molar ratio between branched and linear ester. [e]Styrene as substrate.

3.4.3. Preliminary screening of complexes C1-C5 in the hydrogenation of styrene

To evaluate whether the complexes could perform better than in a different reaction, complexes **C1-C5** were investigated as catalysts in the hydrogenation reaction of styrene performed at 20 bar of H_2 pressure, 30°C and [styrene]/catalysts] = 400:1. Under these conditions, all the complexes showed low catalytic activities in converting styrene to ethylbenzene, ranging from 10% to 16% within 1h (Table 3.8). Whereas, previously reported systems in the hydrogenation of olefins had more than 80% within 1h under mild conditions.[58-62] There is no significant influence made by the structural difference of the complexes as low percentage conversions (10%, 13%, 15%, 16%, 12%) differ very slightly.

Table 3.8. Preliminary hydrogenation of styrene using complexes **C1-C5**

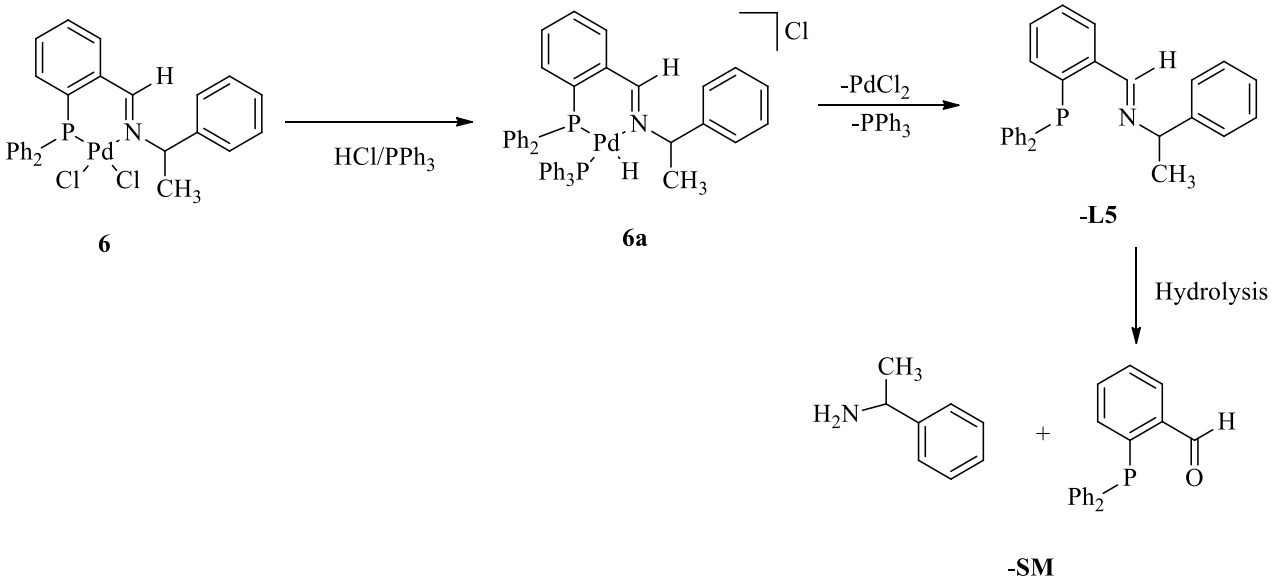
Entry	Catalyst	% conversion	TOF/h^{-1}
23	**1**	10	40
24	**2**	13	52
25	**3**	15	60
26	**4**	16	64
27	**5**	12	48

Reaction conditions: Pressure: 20 bar, temp: 30 ^{o}C, time: 1h, Solvent: toluene 20 ml; catalyst concentration: 0.25 mol % (1:400), **[b]**% of styrene converted to ethylbenzene; TOF (mol.h) determined from GC, the percentage conversion of styrene to ethylbenzene assuming 100% mass balance.

3.4.4. NMR studies of possible decomposition pathways of complexes C1-C7

The poor catalytic activities exhibited by the (imino)pyridine (N^N) catalysts contrasts that of similar palladium(II) catalysts stabilized by the chelating (imino)pyridine (N^P) ligands, under comparable experimental conditions (Pd:PPh_3 ratio as 1:2).[10, 11, 62, 63] In order to establish the low catalytic performance exhibited by the complexes, we performed in-*situ* NMR experiments that mimicked the reaction conditions. The main goal was to establish the stability of the complexes and possible formation of the active species under the existing reactions (stabilizing role of PPh_3 and HCl promotor).[28] This was done by following 1:10:2 Pd/PPh_3/HCl ratio in both the ^{31}P NMR and ^{1}H NMR spectra experiment of complex **C6** and **C3** over a 48 h period. From the ^{31}P NMR spectra, the N^N complex **C3,** had only one signal at 23 ppm (stabilized intermediate coordinated

bidentate Pd-PPh_3) [59] and no signal associated with the free PPh_3 at -5 ppm was observed (Figure 3.16). On the other hand, for N^P complex **C6**, four signals at 23 ppm, -5 ppm and -13 ppm (Figure 3.16) were observed.



Scheme 3.6. Different analogous species that were formed after the NMR experiment of complex **C6** with PPh_3 and HCl.

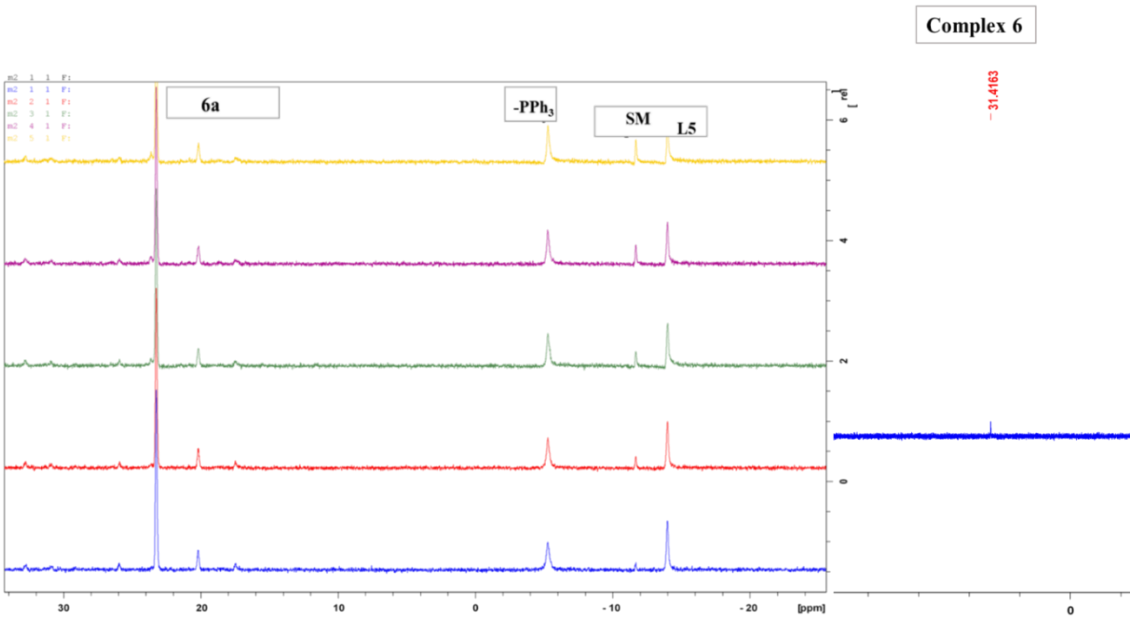


Figure 3.16. Overlaid ^{31}P NMR spectra for in situ experiment of complex **C6** mixed with Pd/HCl/PPh_3 (1:10:2 ratio) in $CDCl_3$ over 5 h period.

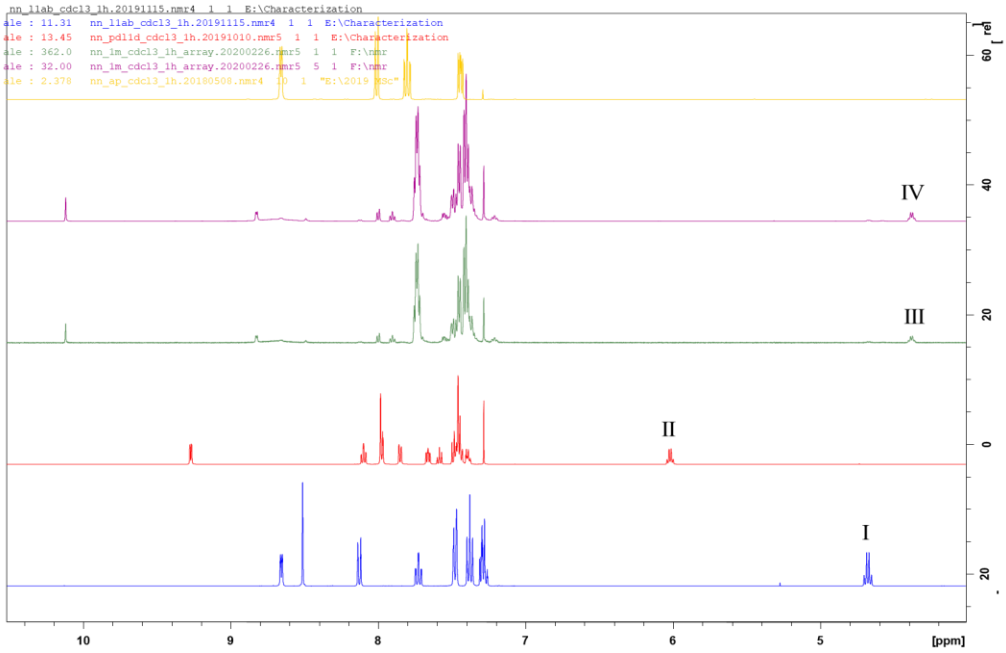


Figure 3.17. Overlaid ^{1}H-NMR spectra of an in-situ experiment of complex **C3** with Pd/HCl/PPh_3 (1:10:2 ratio) reaction mixture at 1 h (III) and 5 h (IV).

The signal at -5 ppm corresponds to the free PPh_3, the -11 ppm corresponds to the starting material (2-diphenylphosphine(benzaldehyde)) (complex **C6** signal at 31.4 ppm, Figure 3.16) and -13 pm corresponds to signal **L5** (Scheme 3.6). This might also imply that N^P catalyst was over saturated since ($Pd:PPh_3$ = 1:2). As complex **3** had the more Pd-PPh_3 species than in complex **C6**, this could explain the different levels of stabilization thus complex **C3** (and all N^N based complexes) had higher reactivity than the complex **C6** (N^P based complexes). The stability of the PPh_3-adducts was monitored over the period of 5 h.

^{1}H NMR spectroscopy was also used to assess the possibility of ligand dissociation in complex **C3**. From the ^{1}H-NMR spectra (Figure 3.17), the signature peak aldimine CH proton (adjacent to the chiral carbon) was characterized as a quartet at 6.01 ppm (II), however when complex **C3** was subjected to dichloromethane solution of HCl/PPh_3 for a duration of 5 h the same CH proton resonated at 4.37 ppm (III and IV) (Figure 3.17). This implied decomposition of complex 3 to form the free ligand (I). We can therefore attribute the low catalytic performance observed for the (imino)pyridine and (imino)phosphine complexes in both methoxycarbonylation and hydrogenation reactions to their instability and resultant decomposition, under the catalytic conditions employed.

3.5. Conclusions

In summary, four (imino)pyridine ligands (**L1–L5**) and two (imino)phosphine ligands (**L6-L7**) were prepared and fully characterized by NMR techniques, mass spectroscopy and infrared spectroscopy. Reactions of the (imino)pyridine and (imino)phosphine ligands (**L1–L5**) with either [$Pd(COD)Cl_2$] or [PdClMe(COD)] afforded the corresponding Pd(II) complexes (**C1–C7**) in good

yields. The solid-state structures of complexes **C1-C4, C6** and **C7** showed that the (imino)pyridine and (imino)phosphine ligands coordinated to the palladium(II) in a bidentate fashion *via* N^N donor and N^P donor atoms respectively with coordination number 4, and the complexes adopted a distorted square planar geometry. The complexes were investigated as catalysts in the methoxycarbonylation reactions. The N^N based complexes were better than the N^P based complexes, consequently displayed moderate to low catalytic activities for both 1-hexene and styrene as substrate. Moderate to high regioselectivities towards branched ester products as well as low enantioselectivities were exhibited. Subsequently the N^N based complexes were further employed in the hydrogenation reaction of styrene low conversions were afforded with complete regioselectivities. Poor catalytic activities attributed to possible decomposition of the active species, as deduced from in situ NMR spectral studies.

3.6. References

1. Meyer N., Lough A.J., Morris R.H., Iron (II) complexes for the efficient catalytic asymmetric transfer hydrogenation of ketones, Chem. Eur. J., 2009, 15, 5605-5610.
2. Yamamoto H., Tsuji H., Palladium-Catalyzed Asymmetric Hydroesterification of Alkenylphenols, Synfacts, 2015, 11, 1161-1161.
3. Konrad T.M., Fuentes J.A., Slawin A.M., Clarke M.L., Highly enantioselective hydroxycarbonylation and alkoxycarbonylation of alkenes using dipalladium complexes as precatalysts, Angew. Chem., 2010, 122, 9383-9386.
4. Konrad T.M., Durrani J.T., Cobley C.J., Clarke M.L., Simultaneous control of regioselectivity and enantioselectivity in the hydroxycarbonylation and methoxycarbonylation of vinyl arenes, Chem. Commun., 2013, 49, 3306-3308.
5. Harkness G.J., Clarke M.L., A highly enantioselective alkene methoxycarbonylation enables a concise synthesis of (S)-flurbiprofen, Eur. J. Org. Chem., 2017.
6. Kosswig K., Schaefer W., Hydrocarboxymethylation-an Attractive Route from Olefins to Fatty Acid Esters?, Industrial & Engineering Chemistry Product Research and Development, 1980, 19, 330-334.
7. Jang E. J., K.H. Lee K. H., Lee J. S. and Kim Y. G., Regioselective synthesis of ibuprofen via the palladium complex catalyzed hydrocarboxylation of 1-(4-isobutylphenyl) ethanol, J. Mol. Catal. A: Chem., 1999, 138, 25-36.
8. Bolm C., Beller M., Transition metals for organic synthesis, Wiley-VCH: Weinheim, 2004.
9. Abarca G., Brown K., Moya S.A., Bayón J.C., Aguirre P.A., Methoxycarbonylation of Styrene Using a New Type of Palladium Complexes Bearing P,N-donor Ligands as Catalysts, Catalysis Letters, 2015 145, 1396-1402.
10. Aguirre P.A., Lagos C.A., Moya S.A., Zúñiga C., Vera-Oyarce C., Sola E., Peris G., Bayón J.C., Methoxycarbonylation of olefins catalyzed by palladium complexes bearing P, N-donor ligands, Dalton Trans., 2007, 5419-5426.
11. Blanco C., Godard C., Zangrando E., Ruiz A., Claver C., Room temperature asymmetric Pd-catalyzed methoxycarbonylation of norbornene: highly selective catalysis and HP-NMR studies, Dalton Trans., 2012, 41, 6980-6991.

12. Godard C.A.R., and Claver C., Systematic Study of the Asymmetric Methoxycarbonylation of Styrene Catalyzed by Palladium Systems Containing Chiral Ferrocenyl Diphosphine Ligands, Helv. Chim. Acta, 2006, 89, 1610-1622.
13. Li J., Chang W., Ren W., Liu W., Wang H., Shi Y., A palladium-catalyzed enantioselective hydroesterification of alkenylphenols with phenyl formate. A facile approach to optically active dihydrocoumarins, Organic & biomolecular chemistry, 2015, 13, 10341-10347.
14. Kawashima Y., Okano K., Nozaki K., Hiyama T., Hydroesterification of vinylarenes catalyzed by palladium complexes of dialkylmonoaryl-and monoalkyldiarylphosphines, Bull. Chem. Soc. Jpn., 2004, 77, 347-355.
15. B. Munoz, Marinetti A., Ruiz A., Castillon S., Claver C., Enhanced regioselectivity in palladium-catalysed asymmetric methoxycarbonylation of styrene using phosphetanes as chiral ligands, Inorg. Chem. Commun., 2005, 8, 1113-1115.
16. Nozaki K., M.L. Kantam, T. Horiuchi, H. Takaya, Hydroesterification of styrene catalyzed by montmorillonite-diphenylphosphinepalladium(II) chloride in the presence of chiral phosphines, J. Mol. Catal. A: Chem., 1997, 118, 247-253.
17. Wang L., Kwok W.H., Chan A.S., Tu T., Hou X., Dai L., Asymmetric hydroesterification of styrene using catalysts with planar-chiral ferrocene oxazoline ligands, Tetrahedron: Asymmetry, 2003, 14, 2291-2295.
18. Zhou H., Hou J., Cheng J., Lu S., Fu H., Wang H., Asymmetric hydroesterification of styrene by $PdCl_2$-$CuCl_2$-chiral phosphine catalyst systems, J. Organomet. Chem., 1997, 543, 227-228.
19. Beller M., Catalytic carbonylation reactions, Springer, 2006.
20. Beller M., J. Seayad, A. Tillack, H. Jiao, Catalytic Markovnikov and anti-Markovnikov functionalization of alkenes and alkynes: recent developments and trends, Angew. Chem. Int. Ed., 2004, 43, 3368-3398.
21. Wang L., Kwok W., Wu J., Guo R., Terry T.-L., Zhou Z., Chan A.S., Chan K.-S., Enantioselective bis-alkoxycarbonylation of styrene catalyzed by novel chiral dipyridylphosphine cationic palladium (II) complexes, J. Mol. Catal. A: Chem., 2003 196, 171-178.
22. Olivieri D., Fini F., Mazzoni R., Zacchini S., Della Ca' N., Spadoni G., Gabriele B., Mancuso R., Zanotti V., Carfagna C., Diastereospecific Bis-alkoxycarbonylation of 1, 2-Disubstituted

Olefins Catalyzed by Aryl α-Diimine Palladium (II) Catalysts, Adv. Synth. Catal., 2018, 360, 3507-3517.

23. Tshabalala T.A., Ojwach S.O., Akerman M.A., Palladium complexes of (benzoimidazol-2-ylmethyl) amine ligands as catalysts for methoxycarbonylation of olefins, J. Mol. Catal. A: Chem., 2015, 406, 178-184.
24. Tshabalala T.A., Ojwach S.O., Tuning the regioselectivity of (benzimidazolylmethyl) amine palladium (II) complexes in the methoxycarbonylation of hexenes and octenes, Transition Met. Chem., 2018, 43, 339-346.
25. Akiri S.O., Ojwach S.O., Methoxycarbonylation of olefins catalysed by homogeneous palladium (II) complexes of (phenoxy) imine ligands bearing alkoxy silane groups, Inorg. Chim. Acta, 2019, 489, 236-243.
26. Akiri S.O., Ojwach S.O., Synthesis of MCM-41 Immobilized (Phenoxy) Imine Palladium (II) Complexes as Recyclable Catalysts in the Methoxycarbonylation of 1-Hexene, Catalysts, 2019, 9, 143.
27. Zulu S., Alam M.G., Ojwach S.O., Akerman M.P., Structural and theoretical studies of the methoxycarbonylation of higher olefins catalysed by (Pyrazolyl-ethyl) pyridine palladium (II) complexes, Appl. Organomet. Chem., 2019, 33, e5175.
28. Zulu Z., Nyamato G.S., Tshabalala T.A., Ojwach S.O., Palladium (II) complexes of (pyridyl) imine ligands as catalysts for the methoxycarbonylation of olefins, Inorg. Chim. Acta, 2020, 501, 119270.
29. Williams D.B.G. and Lawton M., Drying of Organic Solvents: Quantitative Evaluation of the Efficiency of Several Desiccants. The Journal of Organic Chemistry, 2010, 75, 8351-8354.
30. Burfield D.R., Lee K. -H. and Smithers R. H,, Desiccant efficiency in solvent drying. A reappraisal by application of a novel method for solvent water assay. J. Org. Chem., 1977, 42, 3060-3065.
31. Read R., Purification of Laboratory Chemicals, By WLF Armarego. 1997, Molecular Diversity Preservation International.
32. Bruker, APEXZ, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, 2010.
33. M.,S.G., Acta. Crysta., 2008, A64, 112.
34. J., F.L., J. Appl. Crysta., 1999, 32, 837.

35. Nayab S., Lee H., and Jeong J. H., Zinc complexes bearing N,N′-bidentate entiopure ligands: Synthesis, structure and catalytic activity toward ring opening polymerisation of rac-lactide. Polyhedron, 2012, 43, 55-62.
36. Mishnev A., I.I., Popelis J., Vosekalna I., Lukevics E.. Synthesis, characterization and X-ray structure of N-2-pyridylmethylidene-1-phenylethylamine–$PdCl_2$ complexes. J. Organomet. Chem., 2000, 608, 1-5.
37. Yilmaz M. K., Ince Simay K.H., Mustafa K., Iminophosphine palladium catalysts for Suzuki carbonylative coupling reaction. Appl. Organometal. Chem., 2018, 32, 1-8.
38. Ankersmit H. A., Kooijman L.B.H., Spek A. L., Vrieze K., van Koten G., Methyl-, acetyl- and allyl-palladium and -platinum complexes containing the novel chiral phosphorus-imine 2-(diphenylphosphino)- benzylidene-S(-)-a-methyl-benzylamine ligand. Inorg. Chim. Acta, 1996, 252, 141-155.
39. Bruno I. J., Cole J. C., Kessler M., Luo J., Motherwell W. D. S., Purkis L. H., Smith B. R., Taylor R., Cooper R. I., Harris S. E.and Orpen A. G., Retrieval of crystallographically-derived molecular geometry information. J.Chem. Inf. Comput. Sci., 2004, 44, 2133-2144.
40. Allen F. H., Crystallogr. Crystallogr., 2002, B58, 380.
41. Kermagoret A. and Braunstein P., SHOP-type nickel complexes with alkyl substituents on phosphorus, synthesis and catalytic ethylene oligomerization. Dalton Trans., 2008, 822-831.
42. Kilpin K.J. and Crowley J.D., Palladium(II) and platinum(II) complexes of bidentate 2-pyridyl-1,2,3-triazole “click” ligands: Synthesis, properties and X-ray structures. Polyhedron, 2010, 29, 3111-3117.
43. Rossetto E., Nicola B. P., de Souza R. F., Bernardo-Gusmao K. and Pergher S. B. C., Heterogeneous complexes of nickel MCM-41 with β-diimine ligands: Applications in olefin oligomerization. J. Catal., 2015, 323.
44. Doherty S., K.J.G., Scanlan T. H., Elsegood M. R. J., Clegg W., J. Organomet. Chem., 2002, 650, 231-248.
45. Motswainyana W.M., Onani M. O., Madiehe A. M., Saibu M., Thovhogi N. and Lalancette R. A., Imino-phosphine palladium(II) and platinum(II) complexes: Synthesis, molecular structures and evaluation as antitumor agents. J. Inorg. Biochem., 2013, 129, 112-118.

46. Boonseng S., R.G.W., Jones R. N., Tizzard G. J., Coles S. J., Spencer J. and Cox H., The Trans Influence in Unsymmetrical Pincer Palladacycles: An Experimental and Computational Study. Inorg., 2016, 4, 1-14.
47. Song H.-B., Zhang Z.-Z., and Mak T.C.W., Synthesis and structural characterization of palladium(II) and platinum(II) complexes containing a chiral P,N-donor iminophosphine ligand. Polyhedron, 2002. 21 1043-1050.
48. Mahamo T., Mogorosi M. M., Moss J. R., Mapolie S. F., Chris Slootweg J., Lammertsma K. and Smith G. S., Neutral palladium(II) complexes with P,N Schiff-base ligands: Synthesis, characterization and application as Suzuki–Miyaura coupling catalysts. J. Organomet. Chem., 2012, 703, 34-42.
49. Cometti G. and Chiusoli G, Asymmetric induction in carbonmethoxylation of vinylaromatics. Journal of Organometallic Chemistry, 1982, 236, C31-C32.
50. Cavinato G. and L. Toniolo, Carbonylation of ethene catalysed by Pd (II)-phosphine complexes. Molecules, 2014, 19, 15116-15161.
51. Makume B.F., Pd-catalysed methoxycarbonylation reactions of alkynes. 2013, University of Johannesburg.
52. Kiss G., Palladium-catalyzed Reppe carbonylation. Chem. Rev., 2001, 101, 3435-3456.
53. Tang C.-M., Li X.-L., and Wang G.-Y., A highly efficient catalyst for direct synthesis of methyl acrylate via methoxycarbonylation of acetylene. Korean J. Chem. Eng., 2012, 29, 1700-1707.
54. Zolezzi, S., Moya, S. A., Valdebenito, G., Abarca, G., Parada, J. and Aguirre, P.., Methoxycarbonylation of olefins catalyzed by palladium (II) complexes containing naphthyl (diphenyl) phosphine ligands. Applied Organometallic Chemistry, 2014. 28(5): p. 364-371.
55. Pugh R.I., Drent E., and Pringle P.G., Tandem isomerisation–carbonylation catalysis: highly active palladium (II) catalysts for the selective methoxycarbonylation of internal alkenes to linear esters. Chem. Commun., 2001, 1476-1477.
56. Arderne C., Holzapfel C.W., and Bredenkamp T., Branched Selectivity in the Pd-Catalysed Methoxycarbonylation of 1-Alkenes. ChemCatChem, 2016, 8, 1084-1093.
57. Rosales M., Pacheco I., Medina J., Fernandez J., Gonzalez A., Izquierdo R., Melean L. G. and Baricelli P. J., Kinetics and mechanisms of homogeneous catalytic reactions. Part 12.

Hydroalcoxycarbonylation of 1-hexene using palladium/triphenylphosphine systems as catalyst precursors. Catal. lett., 2014, 144, 1717-1727.

58. vom Stein T., P.z.M., Dobrovetsky R., Winkelhaus D., Caputo C.B. and Stephan D. W., Angew. Chem., Int. Ed., 2015, 10178-10182.
59. Pandarus V., Béland G.G.F., Ciriminna R., and Pagliaro M., Org. Process Res. Dev., 2012, 16, 1230−1234.
60. Greb L., O.a.-B.P., Schirmer B., Grimme S., Stephan D. W. and Paradies J., Angew. Chem., Int. Ed., 2012, 51, 10164-10168.
61. Woodmansee D. H. and Pfaltz A., Chem. Commun., 2011, 47, 7912-7916.
62. Van Leeuwen P.W., Decomposition pathways of homogeneous catalysts. Appl. Catal. A: General, 2001, 212, 61-81.
63. Van Leeuwen, P. W. N. M., C.C., Applications of Coordination Chemistry. Comprehensive Coord. Chem., 2003, 2.

CHAPTER 4

Overall conclusions and future work

4.1. Concluding remarks

In conclusion, this thesis reports the design of chiral nitrogen-nitrogen and nitrogen-phosphine based palladium(II) complexes as catalysts in the methoxycarbonylation of olefins. The (imino)pyridine and (imino)phosphine ligands **L1-L4** and **L5-L6** were synthesized using (S)/(R)-amine and pyridine derivatives as well as 2-(diphenylphosphino)benzaldehyde reagent. The five (imino)pyridine and two (imino)phosphine palladium(II) complexes **C1-C7** were synthesized from [Pd(COD)Cl_2/[Pd(COD)ClMe] precursors with their respective above-mentioned ligands. The (imino)pyridine and (imino)phosphine ligands chelated onto palladium(II) were prepared and structurally characterized using ^{1}H-NMR, ^{13}C NMR, ^{31}P NMR (for the phosphine bearing complexes **6**-**7**), MS, FT-IR, elemental analysis and single crystal x-ray crystallography. The solid state structures of **C1-C4**, **C1** and **C7** demonstrated that the (imino)pyridine and (imino)phosphine ligands are coordinated to Pd(II) in a bidentate manner via nitrogen – nitrogen atoms and nitrogen – phosphine atoms respectively.

In the methoxycarbonylation of olefins using the homogeneous catalysts, the nitrogen - nitrogen complexes (**C1** and **C2**) established higher catalytic activities than nitrogen - phosphine analogues (**C6 and C7**) under similar reaction conditions. The best results were obtained over a styrene substrate with 62% of conversion after 24 h of reaction, with high regioselectivity. The instability of complex architecture was responsible for the catalytic activities of these compounds. However, the regioselectivities were found to be high (up to 85%) whereas the enantioselectivities exhibited

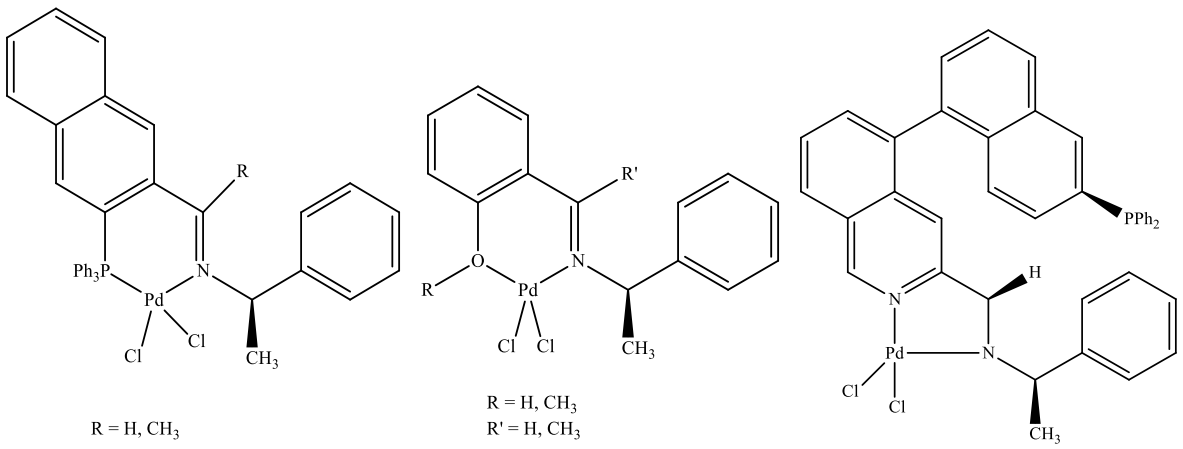
were low (up to 3.4%). The chirality possessed by these complexes demonstrated no significant influence on the enantioselectivities. These complexes were further evaluated in another different catalytic transformation, hydrogenation of 1-hexene, still were found to afford low – moderate catalytic activities. The NMR *in-situ* experiments performed, demonstrated the attributes to the low catalytic activities which were exhibited by these catalysts.

4.2. Recommendations for future work

This study revealed that the (imino)pyridine and (imino)phosphine palladium(II) complexes catalytic performance ranged between low - moderate towards the methoxycarbonylation of 1-hexene and styrene as well as low in the hydrogenation reactions of 1-hexene. Apart from the synthesis and characterization of these Pd (II) complexes, the efficiency of these complexes in catalyzing in the methoxycarbonylation and hydrogenation reactions still need to be evaluated using other substrates such as vinylarenes. This will give us clear indication of their catalytic ability as compared to already existing catalysts. It is recommended that further investigation of these complexes in terms of the influence of CO pressure, temperature variation and acid (p-toluenesulfonic acid / hydrochloric acid) variation. To enhance the enantioselectivity factor it is recommended that we change the position of chirality to be within the coordination sphere and compare their efficiency with the current (imino)pyridine and (imino)phosphine ligands reported in this study (Figure 4.1, **iii**). In addition, to use more sterically bulky ligands with more phosphine, oxygen groups with the aim to produce very stable catalysts (Figure 4.1, **i-iii**).

Once the catalytic performance of these chiral complexes has been improved to at least above 80% conversion, it is recommended that we evaluate them with an objective to produce chiral

surfactants (Figure 4.2, *i. R = CH_3 (R,E)-N-(1-(3-(diphenylphosphino)naphthalen-2-yl)ethylidene)-1-phenylethanaminePdCl_2, ii. R = H, R' = CH3 (R,E)-2-(1-((1-phenylethyl)imino)ethyl)phenolPdCl_2, iii. (R)-N-((5-(6-(diphenylphosphino)naphthalen-1-yl)isoquinolin-3-yl)methyl)-1-phenylethanaminePdCl_2*) which will be further be investigated whether their enantioselectivity has any influence on the applications of surfactants.



(i) **(ii)** **(iii)**

Figure 4.1. Palladium (II) complexes consisting groups that bring forth the steric, electronic effects around the metal center as well as the chirality.

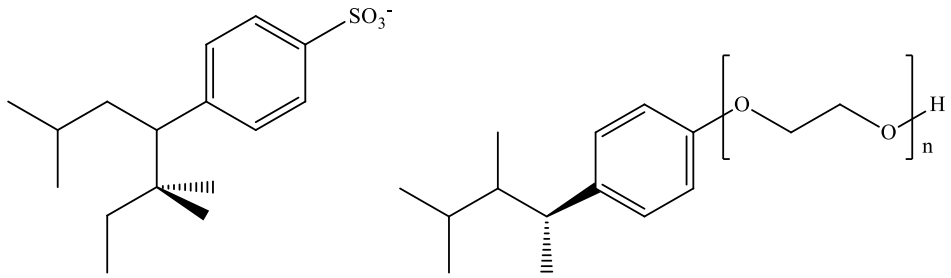


Figure 4.2. Chiral Surfactants *4-(2,5,5-trimethylheptan-4-yl)benzenesulfonate and 2-(4-(3,4-dimethylpentan-2-yl)phenoxy)alcohol.*