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Departament de Química Física I Inorgànica

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Memoria presentada por

Bianca Karelia Muñoz Moreno

Tarragona, Noviembre 2007

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Prof. Dra. CARMEN CLAVER CABRERO, Catedrática del Departamento de Química Física i Inorgànica de la Facultat de Química de la Universitat Rovira i Virgili y la Dra. AURORA RUIZ MANRIQUE, Profesora Titular del Departamento de Química Física i Inorgànica de la Facultat de Química de la Universidad Rovira i Virgili,

CERTIFICAN:

Que la memoria que lleva por título "NEW APPROACHES FOR THE DESIGN OF CHIRAL CATALYSTS. APPLICATIONS IN CARBONYLATION REACTIONS", que presenta Bianca Karelia Muñoz Moreno para obtener el grado de Doctor en Química, ha sido realizada bajo nuestra dirección en el Departament de Química Física i Inorgànica de la Universitat Rovira i Virgili.

Tarragona, Noviembre de 2007

Prof. Dra. Carmen Claver

Dra. Aurora Ruiz

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Leone per il suo aiuto nel lavoratorio e per avere fatto piú agradevole il tempo vissuto a Zurigo.

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momentos cumbres, mucha suerte! Evidentemente, no pueden faltar las personas que me han acompañado a lo largo de esta meta, Clara y Jesús. Gracias a los dos por la ayuda, comprensión, ánimos y por todo lo que me han ofrecido. Por los buenos y malos momentos que hemos atravesado. Realmente significan mucho para mí y espero que podamos celebrar juntos la meta que estamos a punto de alcanzar (Clara, moltes gràcies per las tevas classes gratuïtas de Català, Sense tu no hagués aprés lo Tortosí!!!). A Marta y Rosa, miles de gracias por todos los agradables momentos que hemos pasado juntas, por el apoyo moral y químico que me han ofrecido, por estar siempre dispuestas a una cervecita y a salir corriendo al hospital en caso de emergencia (Fugas y otras historias). Os deseo todo lo mejor porque os lo merecéis.

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Quisiera dedicar unas palabras de agradecimiento a Carmeli y Ángel por haberme animado durante estos últimos meses, ha significado mucho para mi, Gracias!

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Finalmente, quisiera agradecer a una persona que me ha apoyado siempre desde fuera del laboratorio. A Ángel, por tu apoyo y confianza incondicionales. Gracias por hacer que muchas cosas tengan sentido y recordarme que la vida es mucho mas que química.

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Structure of the thesis

This thesis is divided into eight chapters.

Chapter 1. *Introduction and Objectives*. This chapter first presents the importance of the carbonylation reactions in industrial processes. The alcoxycarbonylation and copolymerisation reactions are reviewed in detail. For each reaction general aspects, the mechanisms, antecedents and main achievements are discussed. The state-of-the-art and current requirements justify the objectives of this thesis, proposed at the end of this chapter.

Chapter 2. *Palladium complexes bearing monodentate ligands in asymmetric methoxycarbonylation of vinyl arenes.* This chapter shows the used of chiral monodentate cyclic phosphines, such as phosphetane, phospholane and binepine, in the palladium-catalysed asymmetric methoxycarbonylation of vinyl arenes. New neutral palladium complexes are synthesised and characterised by multinuclear NMR spectroscopy. The aim is to obtain an active and regioselective catalyst and to reach enantioselectivities as larger as possible.

Chapter 3. *Palladium complexes bearing bidentate ligands in asymmetric methoxycarbonylation of vinyl arenes.* This chapter describes the use of bidentate ligands with different electronic and steric properties in the methoxycarbonylation of vinyl arenes. The aim of this work is to find a catalyst capable to afford the branched product in an enantioselective way. The electronic properties of the ligands have an influence on the products distribution.

Chapter 4. *Mechanistic aspects of the methoxycarbonylation of styrene*. This chapter discusses mechanistic aspects of the methoxycarbonylation reaction. *In situ* studies are performed under similar conditions to those used in the catalytic studies. The studies are focuses in palladium systems modified with mono- and bidentate ligands, in order to establish comparison between them. The characterisation of some species by NMR spectroscopy is showed.

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Chapter 5. *Cationic palladium complexes bearing xylofuranose-derivative diphosphines in CO/ethene/propene co- and terpolymerisation reactions*. This chapter discusses the electronic effects of xylose-derivatives diphosphines ligands in the CO/ethene/propene co- and ter-polymerisation processes. The new diphosphines *o*-MeO-xylophos is synthesised. A series of new neutral and cationic palladium complexes bearing xylophos and *o*-MeO-xylophos are synthesised and fully characterised by multinuclear NMR techniques. The catalytic polymerisation reactions are performed in methanol using the cationic complexes and are compared to the reaction catalysed by analogous complexes bearing dppp and *o*-MeO-dppp to determine the effect of the backbone rigidity.

Chapter 6. *Concluding remarks*. This chapter presents the conclusions of the work presented in this thesis.

Chapter 7. *Resumen*. This chapter contains a summary of the thesis.

Appendix. The appendix contains the list of papers and meeting presentations given by the author during the period of development of this thesis.

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List of symbols and abbreviations

b = branched ester

bdpp = 2,4-pentanediylbis(diphenylphosphine)

binap = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl

biphep = 2,2'-bis(diphenylphosphino)-1,1'-biphenyl

biphemp = 2,2'-bis(diphenylphosphino)-6,6'-dimethylbiphenyl

(*S*)-bnppa = (*S*)-(+)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate

(*S*)-bppfa = (*S*)-1-[(*R*)-1',2-bis(diphenylphosphino)-ferrocenyl]ethyldimethylamine

BP = British Petroleum Company.

cod = 1,5-cyclooctadiene

Cy = cyclohexyl

Cyclo-tetraphos = *cis*, *trans*, *cis*-1,2,3,4-tetrakis (diphenylphosphin o) cyclobutane

d = doublet

dba = dibenzylideneacetone

dipydiphos = (4S,5R)-4-[6-(2-Pyridyl)pyridin-2-yl]-5-(diphenylphosphino)methyl-2,2-dimethyl-1,3-dioxolane.

ddppi =1,4:3,6-dianhydro-2,5-dideoxy-2,5-bis(diphenylphosphino)-l-iditol

diop = 4,5-[bis(diphenylphosphino)-methyl]-2,2-imethyl -1,3-dioxolane

CF_3-diop =4,5-[bis(3,5-ditrifluoro-diphenylphosphino)-methyl]-2,2-imethyl -1,3-dioxolane

MeO-diop = 4,5-[bis(2-methoxy-diphenylphosphino)-methyl]-2,2-imethyl -1,3-dioxolane

dippe = 1,2-ethanediylbis(di-*iso*-propylphosphine)

dippp = 1,3-propanediylbis(di-*iso*-propylphosphine)

DPEphos = Bis(2-diphenylphosphinophenyl)ether

dppe = 1,2-ethanediylbis(diphenylphosphine)

dppp= 1,3-propanediylbis(diphenylphosphine)

dppb= 1,4-butanediylbis(diphenylphosphine)

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dppen = bis(diphenylphosphino)ethene

d^{t}bpe = 1,2-ethanedyilbis(di-*tert*-butylphosphino)

d^{t}bpx = bis(di-*tert*-butylphosphino)-*ortho*-xilene

d^{t}bpmb = bis(di-*tert*-butylphosphino)methylbenzene

GPC = Gel permeation chromatography.

Hz = Hertz

H-H = head-to-head

H-T = head-to-tail

IR = infrared spectroscopy

J = coupling constant

l = linear ester

m = meta

MeCN = acetonitrile

MHz = Mega-Hertz

M_n = average molecular weight

n.d. = not determined.

nmdpp = *neo*-menthyldiphenylphosphino

NMR = Nuclear magnetic resonance spectrometry

o = ortho

OAc = acetate

p = para

Ph = phenyl

PhCN = benzonitrile

ppm = parts per million

pydiphos = (4S,5R)-4-(2-Pyridyl)-5-(diphenylphosphino)methyl-2,2-dimethyl-l,3-dioxolane

s = singlet

t = triplet

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p-TsOH = *p*-toluensulfonic acid

p-TsO^- = *p*-toluensulfonate anion

TfOH = trifluoromethanesulfonic acid

TfO^- = trifluoromethanesulfonate anion

THF = tetrahydrofuran

t = tert

tppts = triphenylphosphine trisulfonate

T-T = tail-to-tail

Xantphos = 9,9-dimethyl-4,6-bis(dipheny1phosphino) xanthene

WCA^- = weakly coordinating anions

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Chapter 1

Introduction and objectives

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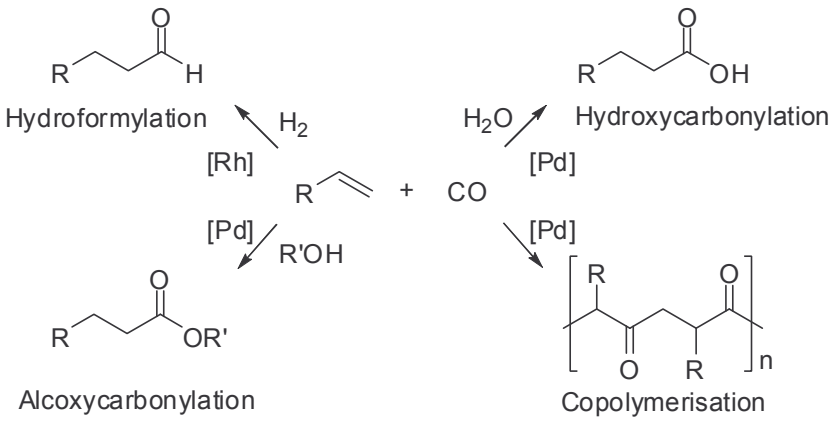
1.1 Background and history

Carbonylation reactions are one of the most important industrial processes using homogeneous transition metal catalyst (Scheme 1.1).[1] In these reactions a low cost substrate is transformed into compounds of industrial interest, such as pharmaceuticals, polymers and building blocks for synthetic applications. Since the first carbonylation process, hydroformylation (Scheme 1.1), was discovered in 1938 by Otto Roelen,[2] a series of carbonylation reactions have been developed.



Scheme 1.1 General scheme for carbonylation of olefins

Considering that the chiral aldehydes obtained by asymmetric hydroformylation of vinyl arenes are often oxidised in order to exhibit biological activities, asymmetric hydrocarboxylation and its related reactions attract much attention from both academic and industrial research groups. Moreover, the copolymerisation of carbon monoxide and olefins to afford polyketones has great industrial interest due to the application as thermoplastics with high-performance properties.[3] Palladium(II) is most commonly used for hydroxy-, alkoxycarbonylation and copolymerisation reactions. In the palladium-catalysed carbonylation processes, a stoichiometry insertion of CO, an alkene and water or an alcohol provide

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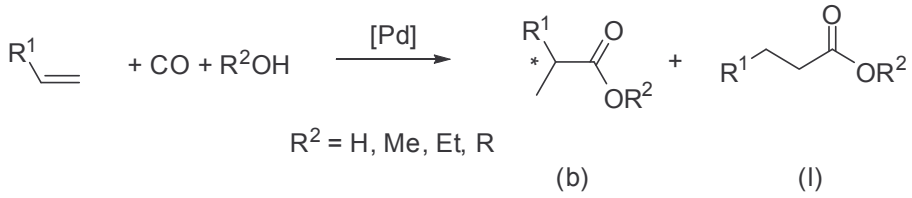
carboxylic acid or esters, whereas multiple alternating insertions provide polymers, depending on the system and conditions used. The elementary steps, initiation, migration and termination, are the same for both alkoxycarbonylation and perfectly alternating CO/alkene copolymerisation reactions. In this chapter, an overview for both processes, their mechanisms and elementary steps will be presented.

1.2 Palladium-catalysed alkoxycarbonylation of olefins

1.2.1 General aspects

The synthesis of carboxylic acids and their related esters is performed from olefins, carbon monoxide and water or alcohols (represented as R^2OH in Scheme 1.2) in the presence of a palladium catalyst.



Scheme 1.2 General scheme for alkoxy- and hydroxycarbonylation of olefins

From this reaction two possible products are obtained, the linear (l) and the branched products (b). For linear α-alkenes, the interest is to obtain the linear product due to their application as detergents and surfactants. When the substrate is a vinylarene, the relevant product is the branched one, the precursor for non-steroidal anti-inflammatory drugs, like ibuprofen and naproxen.[4] As the biologically active compound of these drugs is the (*S*)-isomer of the 2-arylpropionic acid, the studies have been oriented to perform this process using chiral catalysts. Different palladium catalysts bearing chiral mono- and bidentate

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ligands in the presence of acids have been developed. The major drawback in the asymmetric alkoxycarbonylation reaction is the difficulty for obtaining high regio- and enantioselectivity simultaneously with the same catalytic system. In the next section, the most important systems developed in the last 40 years, containing chiral bidentate, monodentate and hemilabile ligands, will be described.

1.2.2. Bidentate ligands

The first reports of asymmetric hydroxy- and alkoxycarbonylation of vinylarenes appeared in the 1970s using chiral diphosphine ligands. During these years, Consiglio and co-workers used $PdCl_2$ and (-)-diop as catalyst system and studied the effects of the reaction conditions on the enantioselectivity of the product. In 1973, they described the first alkoxycarbonylation of vinylarenes obtaining ee's up to 14% when α-methylstyrene was the substrate using *iso*-propanol as the alcohol.[5] In other studies, they observed that both alcohol and substrate had an influence on the enantioselectivity of the reaction.[6,7] They later reported that the addition of PPh_3 to the reaction mixture was found to increased the amount of the branched ester.[8] Later, Hayashi and co-workers reported the use of ligands **1**-**6** (Figure 1.1) in the asymmetric alkoxycarbonylation of α-methylstyrene with *iso*-propylalcohol under *ca.* 230 atm of CO at 100 °C.[9] With ligands **1, 3, 4** and **6**, the ee values were much higher when the ligands were bearing the dibenzophospholyl moiety (**1, 3**; in both cases, *ca.* 40%) instead of the PPh_2 unit (**4, 6**; in both cases, *ca.* 10%). When ligand **2** and **5** were used, however, the ee values were lower and the highest ee was obtained using **5** (ee=22 % with **5** and 7% with **2**).

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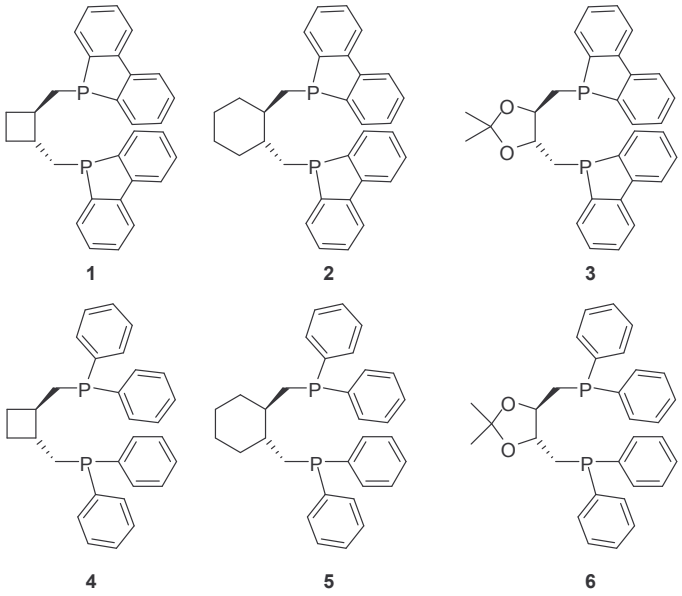

Figure 1.1 Ligands used by Hayashi and co-workers in the alkoxycarbonylation of α-methylstyrene

In 1997, a $PdCl_2$-$CuCl_2$-chiral diphosphine **7** (ddppi) (Figure 1.2) was reported to achieve 98% ee and 99% regioselectivity to the branched ester for the methoxycarbonylation of styrene at 80°C under 50 atm of CO.[10] Despite these very promising results, for some reasons, no further development was described later on this catalytic system.

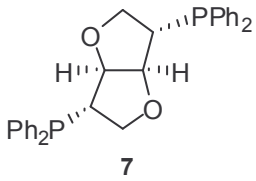

Figure 1.2 Chiral diphosphine **ddppi-7** used by Zhou *et al.* in the methoxycarbonylation of styrene

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The use of the $Pd(OAc)_2$-ddppi-*p*TsOH catalytic system was also reported by the same authors for the methoxycarbonylation of norbornene, achieving 92% ee under 50 atm of CO at 120°C.[11] The use of several chiral diphosphines was reported in the hydroxycarbonylation of styrene but only moderate regioselectivity to the branched ester (up to ca. 30%) and ee's up to 11% were achieved.[12]

The use of recoverable water-soluble diphosphine ligands in hydroxycarbonylation of vinyl arenes was reported to provide enantioselectivities up to 43%.[13] These chiral palladium-sulfonated diphosphine systems were shown to be active without addition of acid. Heterogeneous catalytic systems formed by montmorillonite-diphenylphosphinepalladium(II) dichloride in the presence of chiral mono- and bidentate phosphines were also reported in the methoxycarbonylation of styrene but afforded low enantioselectivities.[14] When the catalytic system containing the monodentate ligand **8** (Figure 1.3) was used at 125°C under 45 atm of CO and in the presence of concentrated HCl, total selectivity to the branched acid together with 12% ee were obtained.

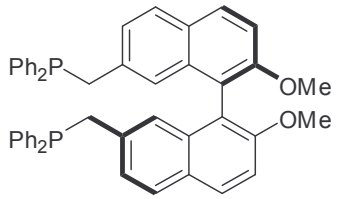

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Figure 1.3 Ligand used by Nozaki *et al.* in the heterogeneous system formed by montmorillonite-diphenylphosphinepalladium(II) systems.

In 2003, Polo and co-workers reported the asymmetric methoxycarbonylation of acenaphthylene using binap as chiral ligand at 80°C in the presence of *p*-TsOH and under 30 atm of CO.[15] Interestingly, using $[PdCl_2(NCPh)_2]$ as Pd precursor, ee's up

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to 45% with 12% conversion were achieved while the use of $Pd(OAc)_2$ only led to ee's up to 34% but in 60% conversion under identical conditions.

The use of diphosphine ligands containing a ferrocenyl unit in the methoxycarbonylation of styrene was reported to induce high enantioselectivity, although the regioselectivity to the branched product, as in general for diphosphine ligands, was usually low (Figure 1.4). In 1997, 86% ee was achieved by Inoue and co-workers together with a regioselectivity of 44% to the branched ester using $Pd(OAc)_2$ as palladium presursor in the presence of the chiral diphosphine (*S*,*R*)-bppfa **9** (Figure 1.4) and *p*-TsOH under mild conditions (20 atm of CO at room temperature).[16] However, the branched product yield was in this case 17%.

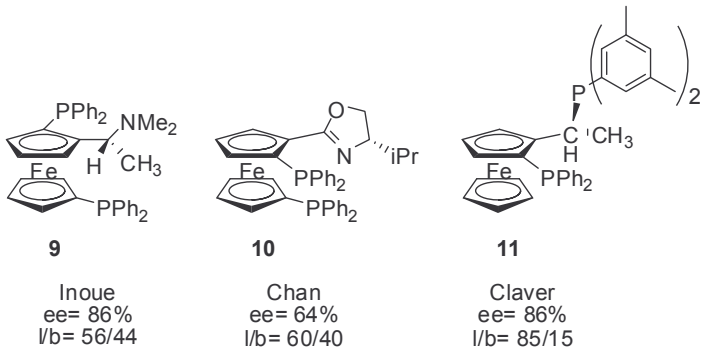

Figure 1.4 Ferrocenyl diphosphine ligands **9-11** used in methoxycarbonylation of styrene

In 2003, Chan and co-workers reported the use of ferrocenyl diphosphine containing oxazoline moieties in the methoxycarbonylation of styrene and achieved 64% ee using the bidentate phosphine **10** (Figure 1.4) with $PdCl_2$ as the Pd source in the presence of *p*-TsOH at 50°C under 170 atm of CO.[17] Although this enantiomeric excess was relatively high, it should be noted that only 40% regioselectivity was obtained and that the conversion was low (14%). More recently, our group reported the use of the families of ferrocenyl diphosphine from

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Solvias (*Josiphos*, *Mandyphos*, *Walphos* and *Taniaphos*) in the same reaction.[18] High enantioselectivities (up to 86% using ligand **11**) and conversions (*ca.* 80%) were achieved but the regioselectivities to the branched ester were in all cases very low (*ca.* 15%).

1.2.3 Monodentate ligands

In view of the results obtained with diphosphine ligands, monodentate ligands can be an interesting alternative for methoxycarbonylation reaction in order to achieve high regio- and enantioselectivities. Indeed, monodentate ligands have attracted much attention in recent years due to the excellent results obtained in different asymmetric catalytic processes.[19] In 1982, Cometti *et al.* were the first to report the use of chiral monodentate phosphine ligands, namely the neomenthyldiphenylphosphine **12** (Figure 1.5, nmdpp), in the asymmetric methoxycarbonylation of styrene with 52% ee using $Pd(dba)_2$ as precursor in the presence of trifluoroacetic acid at 50°C under atmospheric pressure of CO.[20] Ligand nmdpp **12** was also used in the asymmetric alkoxycarbonylation of styrene using a biphasic solvent system formed by a ionic liquid and an organic phase containing isopropanol.[21] Using the catalytic system $[PdCl_2(NCPh)_2]$-nmdpp-*p*-TsOH, high chemo- and regioselectivity were obtained but only enantioselectivity up to 5% could be achieved. In 1990, Alper reported high enantioselectivity (91% ee) and total regioselectivity to the branched acid (64% of isolated yield) using the $PdCl_2$-$CuCl_2$-HCl-**13** (bnppa) system (Figure 1.5) for the hydroxycarbonylation of 2-vinyl-6-methoxynaphthalene under 1 atm of a mixture of CO and O_2 at room temperature.[22] When *p*-isobutylstyrene was used as the substrate, the same catalytic system afforded 84% ee under the same conditions. Using the same ligand, the methoxycarbonylation of styrene was recently reported by Yang *et al.* but only 38% ee was achieved under identical conditions.[23]

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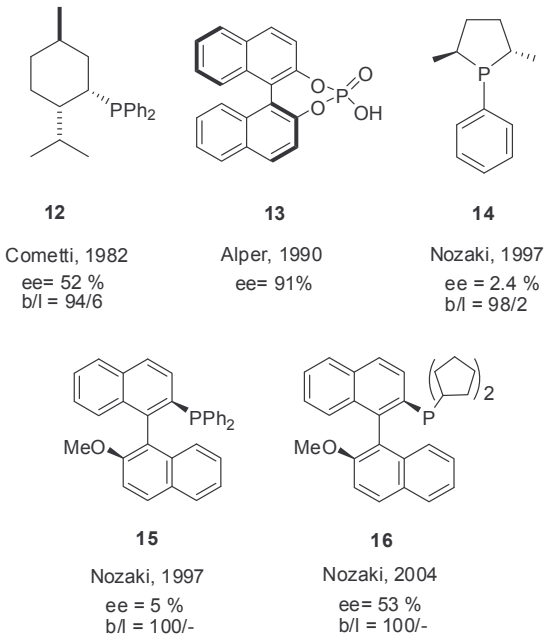

Figure 1.5 Monodentate phosphines used in asymmetric methoxycarbonylation of vinylarenes.

In 1997, Nozaki and co-workers used the (*S,S*)-2,5-dimethyl phenylphospholane **14** ligand (Figure 1.5)[14] but although this system afforded high regioselectivity, the enantioselectivity was low (2 %). In the same study, a catalytic system containing ligand (*R*)-MeO-mop **15** was tested under the same catalytic conditions, affording complete regioselectivity to the branched acid, but only 5% of ee was achieved. Later, the same authors reported on the application of palladium complexes with another binaphthol-derived phosphines (Figure 1.5) in the methoxycarbonylation of 2-vinyl-6-methoxynaphthalene under 30 atm of CO at 40°C achieving 53% of ee using **16** for the branched ester, (*S*)-naproxen methyl ester, as the only reaction product.[24]

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1.2.4 Hemilabile P-N ligands

In order to combine the properties of both mono- and bidentate phosphine ligands in terms of regio- and enantioselectivity respectively, the use of hemilabile ligands could seem to be an obvious choice. The use of mixed bidentate pyridine-phosphine ligands (Figure 1.6) was reported in 1996 by Chelucci *et al.* in the ethoxycarbonylation of styrene, yielding total selectivity to the branched ester with ee's up to 20% when the isolated precursor [$PdCl_2$(**17**)] was used at 100°C under 105 atm of CO for 10 days.[25] In view of the results, the authors concluded that under catalytic conditions, these ligands were coordinated in a monodentate manner. The use of the related ligand *dipydiphos* **18** yielded the same regioselectivity but a much lower enantioselectivity.

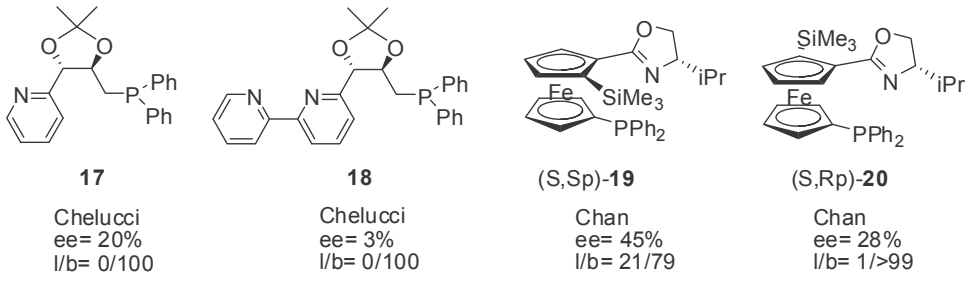

Figure 1.6 P-N ligands **17-20** used alkoxycarbonylation reactions.

Chan reported the use of the P-N ferrocenyl phosphine-oxazoline (*S*,*Sp*)-**19** ligand (Figure 1.6) and achieved 45% ee together with a regioselectivity to the branched ester of 79% using a $PdCl_2$-$CuCl_2$-*p*-TsOH system.[17] Interestingly, when the diastereoisomer (*S,Rp*)-**20** ligand was used, the regioselectivity was found to increase (>99%) but both conversion and enantiomeric excess decreased considerably (Figure 1.6).

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In the next section, the mechanistic aspects of the alkoxycarbonylation process will be discussed.

1.2.5 Mechanistic aspects about alkoxycarbonylation reaction

For the alkoxycarbonylarion reaction two mechanisms have been suggested (Scheme 1.3).[26] The catalytic cycle can either start from an alkoxycarbonyl-palladium species (Cycle A) or an hydrido-palladium complex (Cycle B). In the alkoxycarbonyl cycle, the alkene is inserted into the Pd-carbon bond of the alkoxycarbonyl-palladium complex, followed by alcoholysis to yield an alkoxy-palladium complex and the ester. Coordination and migratory insertion of CO then regenerate the initial alkoxycarbonyl-palladium complex. In the hydride cycle, the first step is the insertion of the alkene into the Pd-H bond to form an alkyl complex, followed by coordination and migratory insertion of CO to produce an acyl species. Alcoholysis of the Pd-acyl regenerates the Pd-H complex and yield the ester. The production of the Pd-H species from complexes formed in Cycle A was also demonstrated to occur through the β-elimination of an unsaturated alkylester after alkene insertion. In the following sections, the single steps of this mechanisms initiation, migration and termination will be discussed separately.

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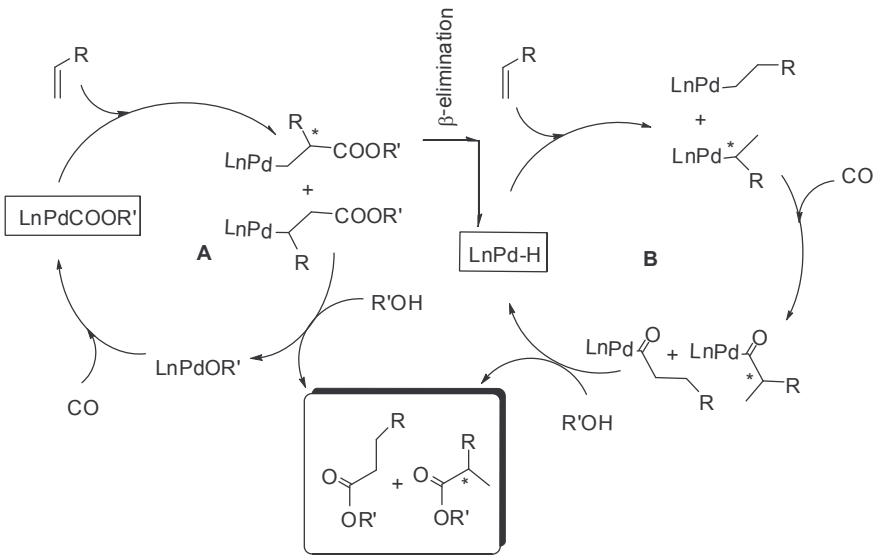

Scheme 1.3 Proposed mechanisms for the alkoxycarbonylation of olefins

Initiation

As it was shown in the catalytic cycle (Scheme 1.3), a palladium-hydrido complex is an intiatior for alkoxycarbonylation reactions[27]. The palladium hydride can be generated by different ways, starting from palladium (0) or palladium (II) species.[3,28] The equation 1 (Figure 1.7) show the formation of the hydride species by the water gas shift reaction, the nucleophilic attack of water into a palladium carbonyl. The Wacker type process (equation 2), also leads to obtain the hydride by insertion of an alkene in a palladium-alkoxy bond, followed by the β-elimination. Another synthetic route to obtain the hydride complex is the β-elimination of hydrogen starting from a palladium-methoxy complex, in which formaldehyde is generated under reaction conditions (equation 3). In some studies, hydrogen is used in order to favour the heterolytic formation of hydride in the presence of a divalent palladium-salt and a base (equation 4).[29]

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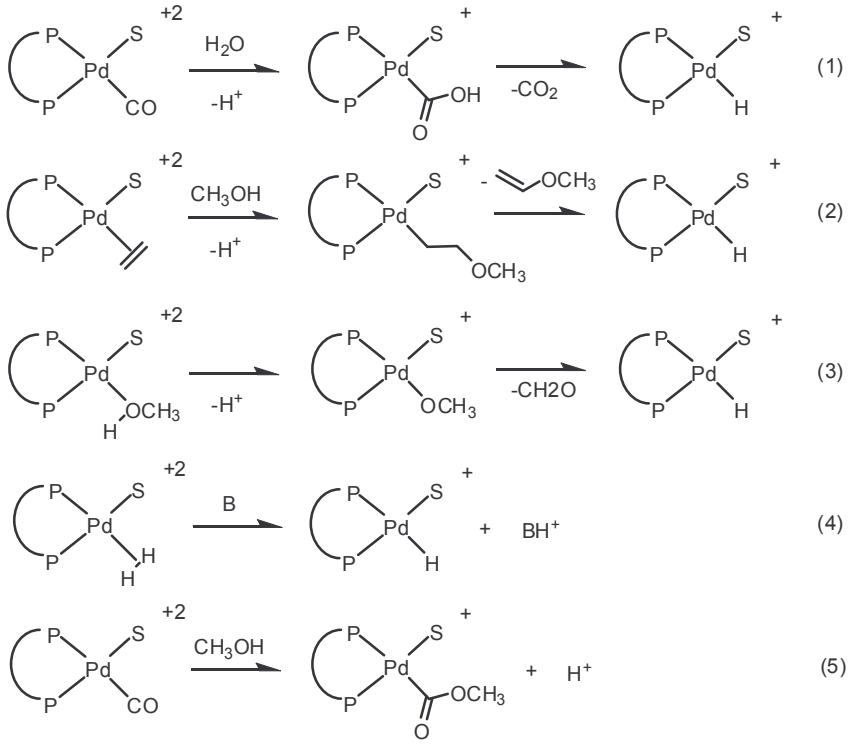

Figure 1.7 Palladium hydride and carbomethoxy formation ways

In the Scheme 1.3 the initiator of the cycle **A** is the alkoxycarbonyl species. The formation of this species can occur by CO insertion into a palladium-methoxy bond or by a direct nucleophilic attack of methanol over the CO coordinated to the Pd centre (equation 5). Experimental evidences of the hydride mechanism have been reported for systems modified with monodentate and bidentate ligands.[30,31,32] The formation of palladium-carbomethoxy species have been supported by different studies previously reported in the literature.[33,34,35,36]

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Migration reactions.

The nature of the intermediate species present during the catalytic cycle has attracted the attention of many researchers. Firstly, if the initiator is a palladium-hydrido complex, the intermediate species formed will be a Pd-alkyl; whereas, if the catalytic cycle starts with carbomethoxy-palladium complex the intermediate complex formed will be a Pd-alkylcarbomethoxy species. The first studies of the catalytic activity and reactivity of $[PdCl(COR)(PPh_3)_2]$ and $[PdCl(C(O)OMe)(PPh_3)_2]$ in alkoxycarbonylation of alkenes, showed that the former is active in methanol to form the ester, while carbomethoxy-palladium complex with 1-hexene in methanol does not reacts in absence of CO.[34] The insertion of norbornene in complexes with formula $[Pd(C(O)OMe)(P\text{-}P)(PPh_3)]$ (where P-P = dppe, dppp, dppb), have been reported.[35] Moreover, in copolymerisation reactions, the formation of diesters suggest the insertion of alkenes in palladium-carbomethoxy species.[28a] Iggo and co-workers recently demonstrate that the insertion of alkenes into Pd-carbomethoxy bond is very sensitive to the presence of coordinating anion or ligands in the fourth coordination site.[36] For long time the hydride mechanism have been proposed to be the preferred catalytic route. Thus, the insertion of CO into this Pd-alkyl complex is a very important reaction and it had been extensively studied in recent years. van Leeuwen and co-workers studied the insertion of CO into neutral $[PdCl(CH_3)(P\text{-}P)]$ or cationic $[Pd(CH_3)(S)(P\text{-}P)]OTf$ complexes bearing bidentate phosphine ligands.[37] They observed that the insertion of CO takes place faster for cationic complexes than for the neutrals and the reactivity decreased in the order bdpp ≈ dppp > dppf > dppe. Brookhart *et al.* have carried out a modelling study of the microscopic steps responsible for the insertion of CO into a cationic palladium methyl complex bearing dppp.[38] In this study they determine the free energy values for the corresponding migratory insertion in carbonyl-alkyl or ethene-acyl-Pd intermediates, finding the former kinetically favoured. Bianchini *et*

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al. have also studied this migratory insertion reaction using Pd complexes modified with dppp, *meso*- and *rac*-bdpp ligands. They found that $\Delta G^{\ddagger}$ values for migratory insertions of CO into a palladium(II)methyl complexes with chelating diphosphines were in range from 14 to 16 Kcal·mol^{-1}.[39] The rate of the CO insertion depends on the bite angles for a series of diphenylphosphino ligands.[28a] However, the steric hindrance provide by bulky ligands with small bite angles also affect the rate of insertion, improving considerably when bulky susbtituents are present in the phenyl moieties.[38a,40]

Regioselectivity of the alkoxycarbonylation

As it was shown in Scheme 1.2, two products can be formed in the alkoxycarbonylation reaction, the linear and branched esters. Different studies have been developed in order to explain what affect the regioselectivity of this reaction. The regioselectivity of these reactions is of critical importance due to the branched product contains a chiral centre. The co-existence of cycles **A** and **B** was suggested to be at the origin of the regioselectivity based on steric factors that would favour the linear insertion of styrene into a Pd-hydride bond whereas the branched insertion of styrene into a Pd- alkoxycarbonyl bond.[41] The selective formation of the branched/linear product was shown to be closely related to the ligand properties and reaction conditions, especially in the presence of acids. The use of bidentate ligands generally leads to a greater amount of linear products whereas catalytic systems bearing monodentate ligands usually favour the formation of the branched products.[42] The dissociation/association of the phosphine ligands and counter-ions have also been suggested to influence the regioselectivity.[43] In general terms when chlorides are present in the reaction media the regioselectivity to the branched ester increased, while the presence of weakly coordinating counteranions favours linear products. In 1976, Sugi and Bando reported a study of the ethoxycarbonylation of styrene using diphosphine palladium systems

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$[PdCl_2(Ph_2P(CH_2)_nPPh_2)]$ (n= 1-6, 10) and showed that the length of the alkylic chain of the ligand dramatically influenced the regioselectivity.[44] When n = 1, 6 and 10, the branched ester was preferentially produced, like in the case of monophosphines. When n= 2 (dppe), no conversion was found whereas the use of ligands with n= 3, 4 or 5 favoured the production of the linear ester. van Leeuwen and co-workers have also demonstrated that the presence of electron-withdrawing substituents on diphosphine ligands can invert the regioselectivity of the methoxycarbonylation of styrene in favour of the branched ester.[45] Despite the growing number of mechanistic studies, the origin of the regioselectivity of these reactions is still to be established.

Termination step

In the methoxycarbonylation reaction there are two different ways to release the ester out of the coordination sphere and, at the same time, regenerate the active species, the initiator (Pd-hydride or Pd-carbomethoxy). The methanol reacts in two different manners, by methanolysis over the Pd-acyl complex to produce the palladium-hydride and the ester (equation 6, Figure 1.8), or by protonolysis over a Pd-alkylcarbomethoxy complex to form the ester and the Pd-methoxy, the precursor of Pd-carbomethoxy complex (equation 7, Figure 1.8). The methanolysis have been recently studied by van Leeuwen,[32,46] Iggo,[47] Bianchini[48] and MacGregor,[49] focus on identifying some of the intermediates involved in the alcoholysis of palladium-acyl species. From these studies, the methanol is considerate to acts in different pathways in this termination step (Figure 1.9). The *intra*-molecular attack of *cis* coordinated methanol (equation 8, Figura 1.9)[32,46,47] and the *inter*-molecular attack of methanol at the acyl carbon (equation 9)[48,50] have been proposed.

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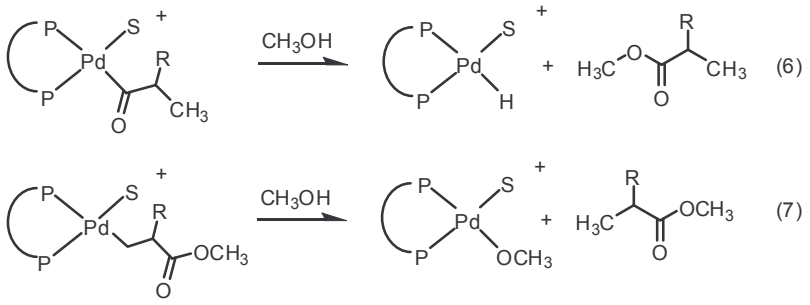

Figure 1.8 Methanol termination reactions

A third proposal for the methanolysis suggests a decoordination of an arm of the diphosphine followed by the protonation of the free phosphine moiety to generate a methoxy group on the palladium centre (equation 10).[49,51] The elimination of the ester and transfer of the proton from the protonated phosphine to palladium and recoordination of the phosphine moiety complete the methanolysis.

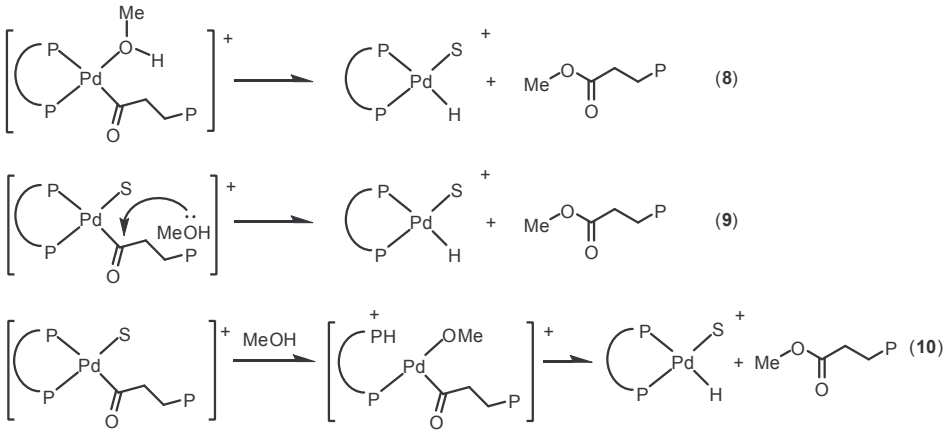

Figure 1.9 Different mechanistic ways for termination step in carbonylation reactions.

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In some cases, the methanolysis have been proposed to be the rate determining step.[50,52] However, this step depends on the effect caused by the nature of the ligand, the counterion and the solvent over the reaction rate. Recent advances have been reported on the methanolysis step using DFT calculation methods.[46,49] Bo and co-workers looked at the ethene insertion into a Pd-acyl and the methanolysis steps in order to explain the chemoselectivity of palladium catalysts containing bidentate phosphine ligands towards methoxycarbonylation of ethene or CO/ethene copolymerisation. The calculations predicted that increasing the bite angle of the diphosphine ligand increases the rate of methanolysis due to the involvement of electron-rich intermediates and/or transition states. They also pointed out that a Pd complex containing an η^2-acyl ligand is a crucial intermediates in all the methanolysis pathways that they considered and that both increasing the bite angle and the steric bulk of the diphosphine ligand stabilises this species. Macgregor and co-workers[49] investigated the *intra*- or *inter*-molecular methanolysis of Pd-acyl bonds and concluded that the *inter*-molecular attack may be important in this process and that the energetics of this process are strongly dependant on the metal coordination environment. They calculated the activation energies for intermolecular attack of MeOH with $[Pd\{C(O)Et\}(P\text{-}P)(L)]^+$ species where L= CO, MeCN or MeOH and reported that methanolysis occurs when L= CO or MeOH, but not when L= MeCN, which is in agreement with experimental data.[47] They also studied the behaviour of the monophosphine systems *cis* and *trans*-$[Pd\{C(O)Et\}(PH_3)_2(MeOH)]^+$ and reported that the transition state is somewhat higher for the *cis* species than for the *trans* complex. Furthermore, they predicted that the loss of a PH_3 ligand to form an acyl unsatured species would greatly facilitate the methanolysis step.

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1.3 Alternating copolymerisation and terpolymerisation of CO and olefins

1.3.1 General aspects

The alternating olefin/carbon monoxide copolymerisation reaction,[53] has attracted much attention of chemists for many years.[54] The polyketones or olefin/carbon monoxide copolymers (figure 1.10) are biodegradable thermoplastics with high performance properties.[3] One of the advantages of these materials is the ability to incorporate functionalised olefins, which gives a great number of new materials. Moreover, the lower production costs in comparison to other polymers as Nylon, which has physical and mechanical properties comparable to the polyketones,[28b,55] have increased the interest in this process.[56]

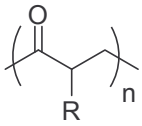

Figure 1.10 General structure of a polyketone

Palladium catalysts were found to produce alternating polyketones, under different reaction conditions.[28,57] In the early 1980s, Sen and co-workers published a report on the use of palladium complexes modified by terciary phosphines and weakly coordination tetrafluoroborate anions in dichloromethane solution under mild conditions.[58] It was only few years later, when Drent *et al.* reported that the use of catalyst modified with bidentate phosphines and non-coordinating counteranions (Figure 1.11), allowed the synthesis of high molecular weight polyketones at very high rates (up to 6 kg·(gPd·h)$^{-1}$).[28b,59]

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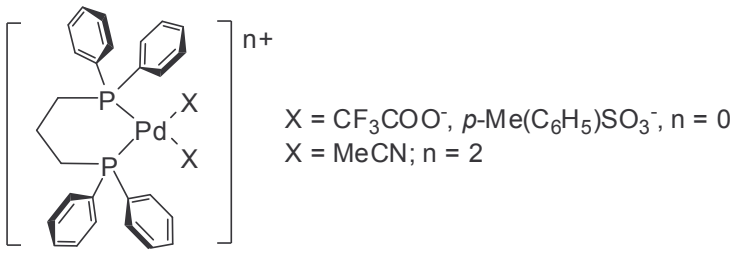

Figure 1.11 [$Pd(dppp)X_2]^{2+}$ active catalyst in alternating CO/ethene copolymerisation

The copolymerisation was carried out in methanol, which plays a role in the initiation and as a chain transfer reagent. Thus, in terms of end-groups three different combinations of diketone, keto-esters and diesters can be obtained (Figure 1.12).

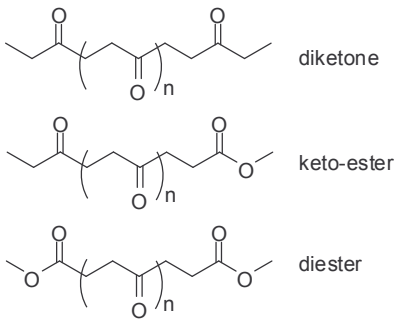

Figure 1.12 CO/ethene copolymer obtained in methanol.

Under the experimental conditions higher activities were observed in the presence of a protic acid and a strong oxidant.[60] The acid is important for decreasing catalyst deactivation as it is able to convert inactive Pd^0 complexes into catalytically active $[(P–P)PdH]^+$. Quinones are usually used as oxidants and its main role is to oxidise

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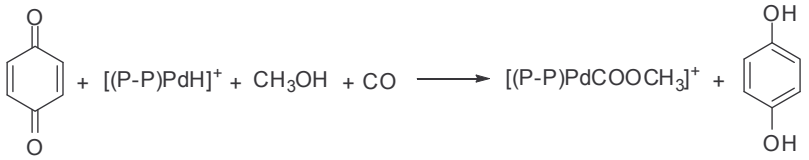
of either Pd(0) or Pd(I) to Pd(II). The oxidant also is able to convert Pd–H species into Pd–COOMe as shown in Scheme 1.4.[60]



Scheme 1.4 Formation of a palladium carbomethoxy species starting from a palladium hydride in the presence of 1,4-benzoquinone.

The industrial application of CO/ethene copolymer had been limited due to the narrow interval between the melting and decomposition temperatures, which difficult the processing of the material. The introduction of another olefin, like propene, to form terpolymers decreases the melting point, improving the properties of the material. The high molecular weight CO/ethene/propene terpolymer, was commercialised by Shell and BP under the trademark of Carilon™ and Ketonex®, respectively.[61,62] However, this material was withdrawn from the engineering plastic market in 2001. The copolymerisation of CO and propene opens the possibility of stereoregular copolymers, and other parameters, such as regiochemistry and stereochemistry should be considered. First of all, the insertion of an α-olefin like propene into a palladium-acyl or Pd-carbomethoxy bond can occur either by 1,2 or 2,1 mode (Scheme 1.5). After a primary insertion (1,2) the CH_2 group of the olefin will be bound to the palladium atom, whereas after the secondary insertion (2,1) it will be bound to the growing polymer chain. Additionally, due to the enantiotopic faces of the α-olefin, two different stereochemical outcomes per mode of insertion can arise. The possible number of regio- and stereochemical arrangements increase remarkably when multiple alternating insertions of CO and α-olefin take place.

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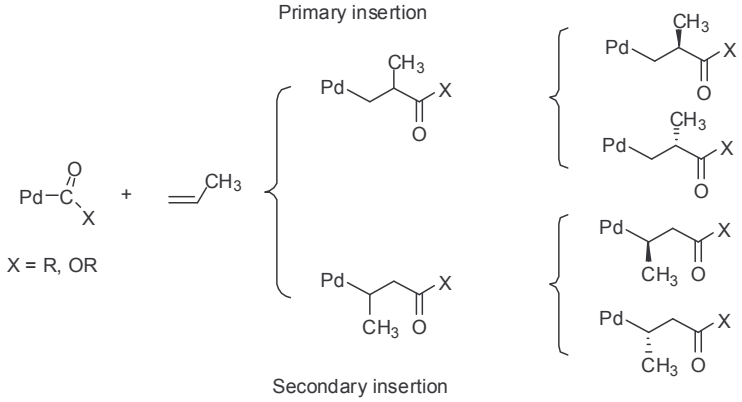

Scheme 1.5 Insertion modes of propene into a [Pd]-acyl bond

With respect to the stereochemistry and assuming a regioregular enchainment the formation of isotactic, syndiotactic and atactic copolymer structures could occur (Figure 1.13).

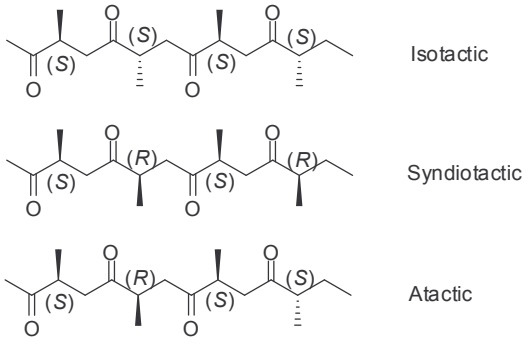

Figure 1.13 Isotactic, syndiotactic and atactic structure of a CO-propene copolymer

The structure and electronic properties of the diphosphines used have a great effect on the productivity and molecular weights of the copolymers. In the next

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section, the most important systems developed in the last 50 years, containing diphosphines, N-N, P-N and P-O ligands, will be described.

1.3.2 CO/ethene and CO/ethene/propene co- and terpolymerisation

A wide range of diphosphine ligands has been found to afford active palladium catalysts. Drent *et al.* were the first to investigate the influence of the diphosphines structure ($Ph_2P(CH_2)_nPPh_2$, n=1-6) on the activity of the Pd^{II} catalyst.[28] They observed that the chain length of the carbon backbond between the two phosphorus atoms has an important influence over the catalytic activity. In particular C_3-bridge diphosphines ligands bearing aryl substituents are most suitable (Figure 1.14) affording up to 6 Kg/(g Pd·h) for ligand **21**. Bianchini and co-workers explored palladium complexes bearing ligands **24**-**28** (Figure 1.14). They observed the highest activities for complexes bearing ligand **28** in *meso* configuration.[63]

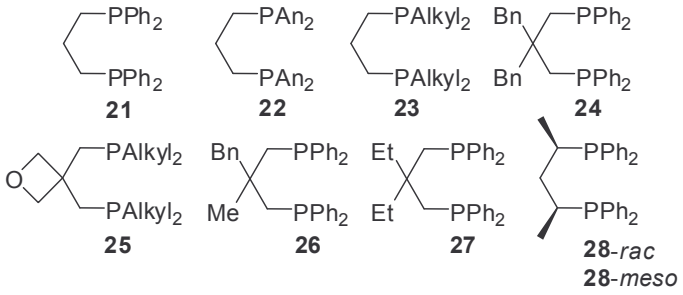

Figure 1.14 C_3-Ligands used in CO/ethene copolymerisation

Kinetic and thermodynamic studies in CH_2Cl_2 suggest that a greater rigidity of the ligand backbone as in *meso*-bdpp favors the propagation step by decreasing the stability of the β-chelates $[(P–P)Pd(CH_2CH_2COR)]^+$.[64] Various alkyl dppp-derivative ligands were also tested (**23**, Figure 1.14), affording moderately active catalyst for low molecular weights copolymers.[65] The catalytic activities using these

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systems were somewhat lower than that for the analogue system modified with dppp.[66] Introducing *ortho*-methoxy groups on the phenyl substituents in ligand **32** not only active catalysis are obtained (e.g. 12.7 kg/(gPd·h) at 90ºC, 50 bar CO/C_2H_4), but also produced co- and terpolymers with considerably higher molecular weights.[67] The effect of the backbond rigidity on the catalytic activity was studied by Bianchini and co-workers using ligands showed in Figure 1.15.[68]

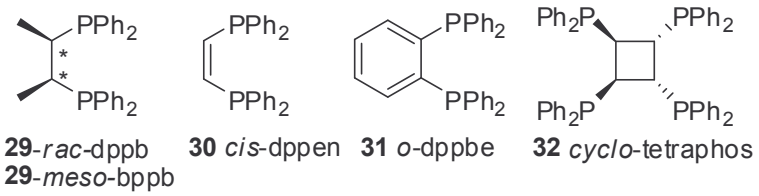

Figure 1.15 Rigid diphosphines ligands forming five-membered rings.

They observed that the backbone rigidity and the overall steric crowding at the Pd centre are more important than the chelate ring size for the catalytic activity. Doherty *et al.* carried out a similar study employing a series of bis(phospholyl) ligands (**33**-**35**, Figure 1.16) that coordinated to Pd form 5, 6 and 7 membered-ring chelate.[69]

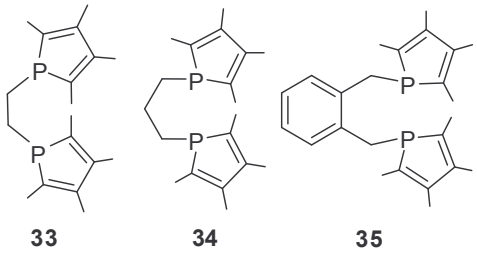

Figure 1.16 bis-phospholyl ligands used in CO/ethene copolymerisation

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They observed that the C_3-bridge ligands are not always the most effective catalytic system. Using these ligands (Figure 1.16) the activity decrease in the following order C_4-bridge > C_3-bridge >> C_2-bridge. The C_1-bridge ligands having a bulky subtituents on the phenyl groups (**36** and **37**, Figure 1.17) were found to afford very active palladium catalyst for CO/ethene copolymerisation giving high molecular weights polymers.[40]

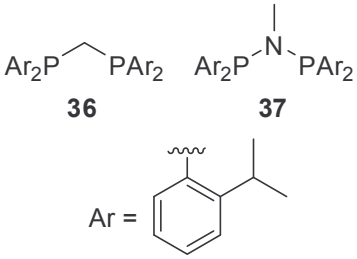

Figure 1.17 C_1-bridge diphosphine ligands active in CO/ethene copolymerisation

The catalytic activity of dppb **38** containing catalysts was reported to be about 2.6 times lower than that of the dppp **21** catalysts.[28] Again, the use of more rigid systems (Figure 1.18, **39** and **40**) was reported to be beneficial and the use of ligand **40** was found to be four times more active than the corresponding ligand **39**.[70]

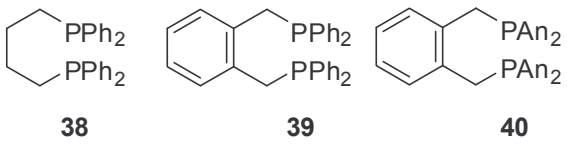

Figure 1.18 Diphosphine ligands forming seven-membered metallaring

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The C_4-bridge diphosphines shown in figure 1.19 form palladium(II) complexes of the general formula $[Pd(OAc)_2(P–P)]$ which have been used as catalyst precursors for the CO/ethene copolymerization.[71] The catalyst system based on **41**-*cis* was found to give a higher productivity in oligomeric polyketones than that based on its *trans*-isomer. In contrast, the catalyst system based on **42**-*exo*,*endo* was highly selective for the production of methyl propanoate wheareas the *endo*,*endo*-isomer gave only polyketone although in very low yield. [71a] The chemoselectivity exhibited by the **42**-*exo*,*endo*-isomer has been also observed for systems modified with ligand **43,** [71b] and was tentatively explained with the occurrence of two distinct catalysts: one containing a chelating diphosphines and the other containing a monodentate phosphine to generate methyl propanoate.

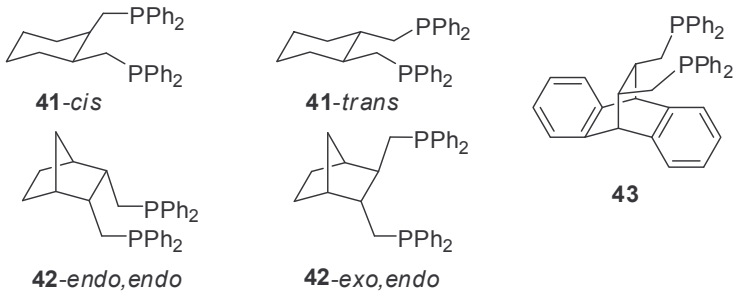

Figure 1.19 Stereoisomeric diphosphines ligands used in CO ethene copolymerisation

Recently, cationic palladium complexes bearing metallocene-diphosphines have also been tested for CO/ethene copolymerisation (Figure 1.20). The catalytic activity and the chemoselectivity of the copolymerization reaction depend on the sandwiched metal centre, on the substituents of the cyclopentadienyl ring, as well as on the substituents of the phosphorous donor atoms. In general, low molecular weights copolymers were obtained.[50,72]

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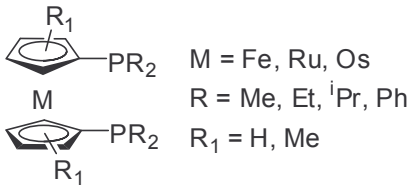

44

Figure 1.20 Bis(phosphino)metallocene ligands

In general terms, the catalytic activity on the CO/ethene copolymerisation using palladium systems modified with ligands showed in figure 1.21 are lower than those for systems bearing diphosphines ligands. However, sterically rigid dinitrogen ligands were found to afford efficient palladium catalysts for alternating CO/ethene copolymerisation in homogenous and heterogeneous conditions.[73]

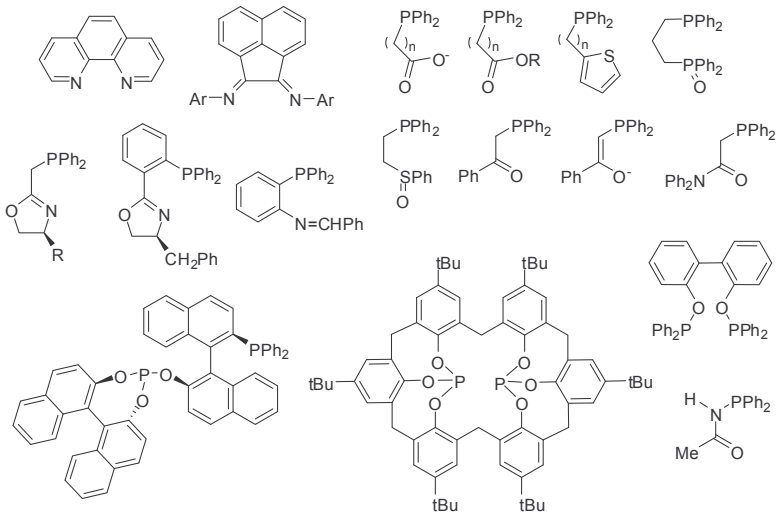

Figure 1.21 Selected ligands used in Pd-catalysed CO/ethene copolymerisation

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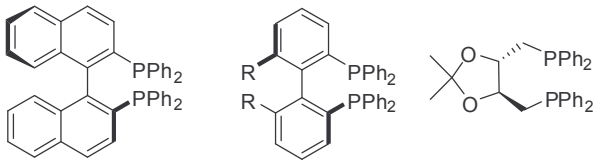
1.3.3 CO/propene copolymerisation

The first copolymer between carbon monoxide and propene, obtained using the typical C_{2v}-symmetrical catalytic systems modified by the dppp and dmppp (**21** and **22** in Figure 1.14), showed a lack of regiorregularity and stereoregularity, as was observed in the ^{13}C NMR spectroscopy.[74]



45-BINAP **46** R = CH_3, Biphemp **47** R = OCH_3, Biphep **6** DIOP

Figure 1.22 Diphosphine ligands for regioirregular CO/propene copolymers

The ligands showed in the figure 1.22 and in general, the use of bis-diarylsubstituted diphosphine ligands, even chirals, resulted in the formation of regioirregular copolymers with low stereochemistry.[75] Substituting the phosphorus phenyl groups with alkyls groups (**49**-**50** in Figure 1.23) causes a completely regioregular and highly isotactic copolymerisation.[76] Palladium complexes modified with the two diastereomeric ligands **51** and **52**, were used in CO/propene copolymerisation affording a completely regular isotactic copolymer. However a remarkable difference in reactivity was observed, catalyst **52** presented high catalytic activity while catalyst modified with ligand **51** was found to be poorly active.[76]

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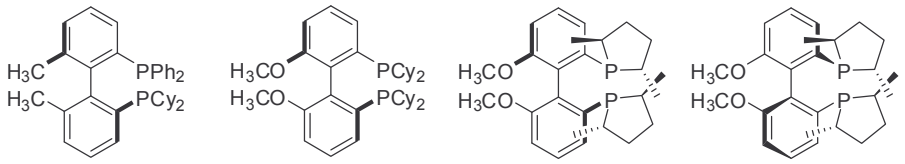
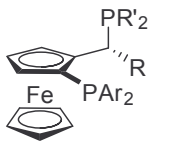


49 **50** **51** **52**

Figure 1.23 Atropisomeric diphosphine ligands for CO/propene copolymerisation

The most active class of ligands identified so far for CO/propene copolymerisation is that of C_1-symmetry ferrocenylphosphines **53**-**56** (Figure 1.24). Under the same catalytic condition the ligand containing bulky substituents in the phosphorus atom directly attached to the chiral carbon, and an electron-withdrawing substituent in the aryl phosphine (**56**) was the best combination to afford a very active and regioselective catalyst.[77]



53 Ar = Ph, R = H, R' = Et
54 Ar = Ph, R = Me, R' = Et
55 Ar = Ph, R = H, R' = *c* C_6H_{11}
56 Ar = 3,5-CF_3-C_6H_3, R = H, R' = *c* C_6H_{11}

Figure 1.24 C_1-Diphosphine ligands for regioregular isotactic CO/propene copolymerisation

An exception of the statement that the use of bis-diarylsubstituted diphosphine ligands resulted in the formation of regioirregular copolymers, are the 1,2-bis(diarylphosphinomethyl)benzene ligands showed in figure 1.25. Catalyst bearing ligands **57**-**59** give copolymers with regioregularities close to 98% of the h-t dyads.

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For these systems good regioselectivity is apparently a prerequisite for achieving good stereoregularity.[78]

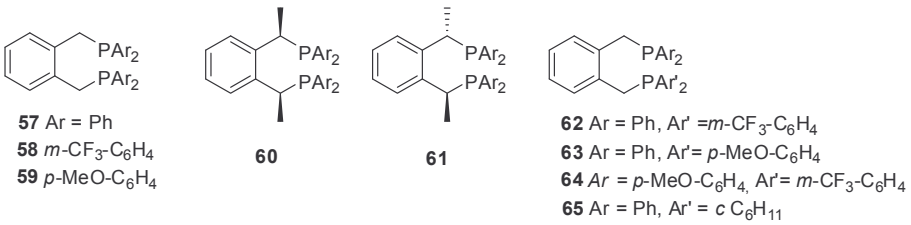

Figure 1.25 1,2-bis(diarylphosphinomethyl)benzene and related ligands for copolymerisation of CO/propene.

For complexes bearing ligand **60** and **61**, a remarkably effect on the catalytic activity was observed. The catalyst containing ligand **60** is about 84 times more active than the catalyst with the **61** ligand. Both systems afford highly isotactic materials. Recently Consiglio *et al.* reported the use of non-symmetrical diphosphines **62**-**65** in the CO/propene copolymerisation. The copolymers obtained using ligands **62**, **63** and **65** showed high regio- and stereoregularity with good activities, while the activity of catalyst bearing ligand **64** was poor affording copolymers were highly regio- and stereoregulars.[79]

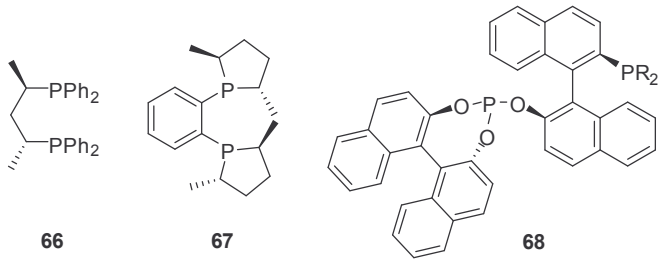

Figure 1.26 Ligands used in CO/propene copolymerisation

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Ligands **66**-**68** (Figure 1.26) have also been reported to afford highly regio-and stereoselective CO/propene copolymers.[74,80]

In following section, the mechanistic aspects of the copolymerisation process will be discussed.

1.3.4 Mechanistic aspects about CO/ethene copolymerisation reaction

The first mechanistic considerations were reported by Drent on the basis of end-group analysis of the copolymer.[28a] The mechanism proposed in Scheme 1.6 comprises two independent catalytic cycles (**A** and **B**), which can start from a palladium hydride (cycle **B**) or a palladium carbomethoxy species (cycle **A**). The cycle **A** start from the insertion of CO into a Pd-methoxy bond to give a palladium carbomethoxy complex Pd-C(O)OMe. Multiple alternating ethene and CO insertions (***P***) and the subsequence termination step by methanolysis (***M***) or protonolysis (***H***) generate copolymers containing keto-ester or diester en groups. The cycle **B** starts with the insertion of ethene into a palladium hydride bond (***I***) and affords a palladium alkyl complex. The CO insertion into the Pd-alkyl bond is reversible and generates a Pd-acyl complex. The insertion of ethene into a Pd-acyl is rapid and irreversible, thus the propagation can take place by alternating insertions of CO and ethene (***P***). The CO insertion into a Pd-acyl bond is thermodynamically disfavoured. Successive insertions of ethene are limited due to the fact that the CO insertion into a palladium alkyl is reversible and faster than the ethene insertion.

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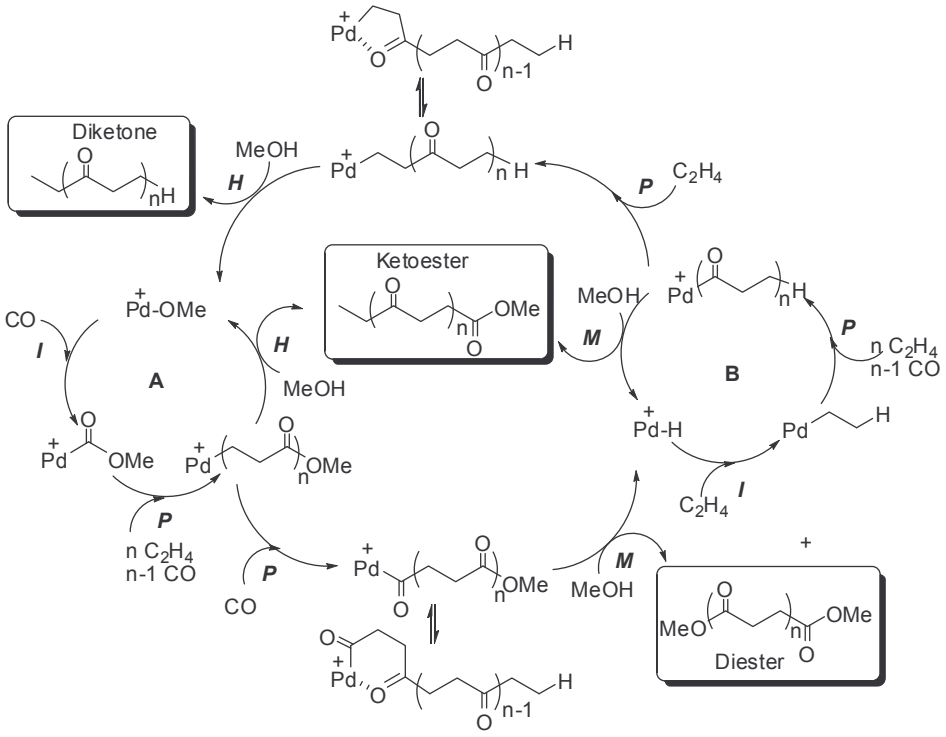

Scheme 1.6 Catalytic cycle model: The carbomethoxy cycle(A) and the hydride cycle (B)

Two possible termination processes can produce copolymers with either ketoester or diketone end groups, by methanolysis (***M***) of the Pd-acyl bond or protonolysis (***H***) of the Pd-alkyl bond, respectively. As it was shown for the mechanism of the alkoxycarbonylation reaction (section 1.2.5), the same steps of the catalytic cycle are presented in both processes being the only difference the multiple alternating insertion of olefin and carbon monoxide in case of copolymerisation reactions. Thus, the initiators Pd-H or Pd-COOMe for the copolymerisation process can be generated as was shown in section 1.2.5 (Figure 1.7). The migrations reaction and the termination steps showed above were performed using ethene as a model

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olefin. In the following sections, additional intiators, usually used in copolymerisation reaction, propagation and chain transfer mechanisms, will be described.

Initiation

The palladium complexes usually used in copolymerisation reaction are those that can generate a palladium hydride or a palladium carbomethoxy species under catalytic conditions. The formation of these species starting from Pd(II) complexes is shown in Figure 1.7. The synthesis of palladium alkyl (or aryl) species is another method for an initiating palladium complex.[81] This complex acts as initiator of the first polymer chain and is not regenerated during the polymerisation process. The typical alkyl complex used in polymerisation processes is shown in figure 1.27. These complexes are synthesised using an alkylating reagent, usually tetramethyltin $Sn(CH_3)_4$, and a palladium(II) complex or by protonation of a dimethylpalladium complex with and acid.

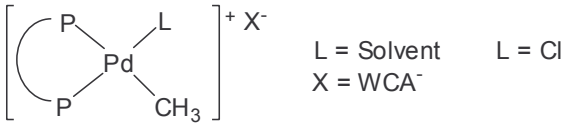

Figure 1.27 Methyl palladium complex as initiator

Chain propagation

In copolymerisation reaction two migration steps of Pd-alkyl-CO and Pd-acyl-alkene moieties are involved in the chain propagation. In contrast to alkoxycarbonylation reaction, in which the migratory insertion of a Pd-alkyl-CO or Pd-carbomethoxy-alkene occurs once, for copolymerisation reaction these migratory insertions take place alternating as is shown in Figure 1.28. The perfectly

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alternation can be explain because two CO insertions are not favoured termodinamically.[3] Moreover, two ethene insertions are not favoured as the insertion of CO into a Pd-alkyl is 10^5 times faster than ethene insertion.[38b]

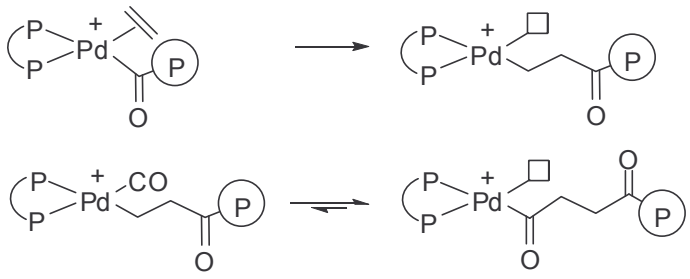

Figure 1.28 Alternating insertions responsible for the chain propagation during the copolymerisation

Mul and co-workers have used the infrared spectroscopic technique PM-RAIRS (Polarisation Modulation Reflection Absorption Infrared Spectroscopy) to monitor the CO-ethene copolymerisation catalysed by a heterogeneous Pd(II)-based catalyst, bearing dppp as ligand.[82] In this study, only the chelate forms of the Pd-alkyl **1** and Pd-acyl **2** intermediates were observed (see scheme 1.7). The five-membered palladacycle **1** is formed by ethene insertion into the Pd-acyl bond and simoultaneous coordination of the resulting ketone group to the metal centre. Subsequent insertion of CO in the formed Pd-alkyl bond and coordination of the carbonyl moiety to the palladium centre results in the six-membered palladacycle **2**. It seems that both the intermediates **1** and **2** are resting states of the catalyst. No open chain complexes were observed. Remarkably, in this heterogeneous system the insertion of ethene into the Pd-acyl bond seemed to be CO-assisted, i.e., it took place only in the presence of a substantial amount of CO.

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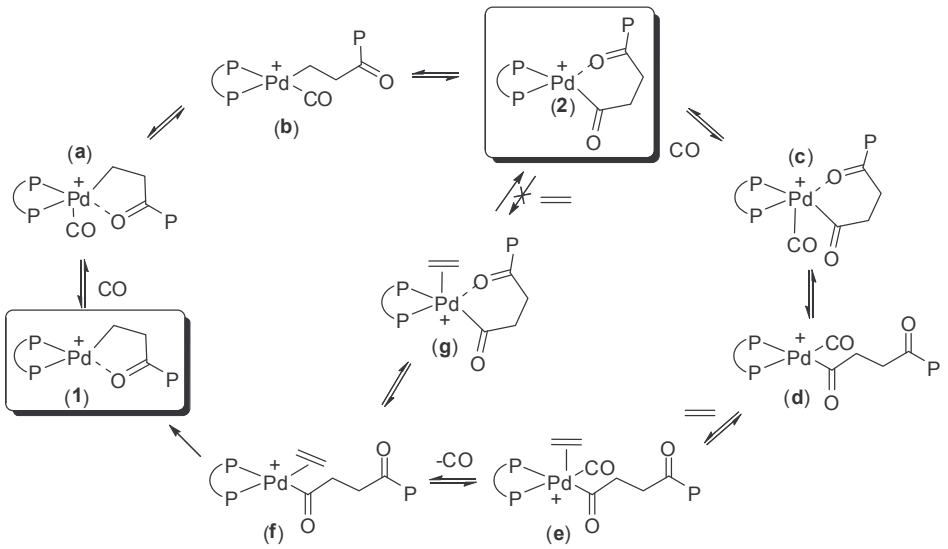

Scheme 1.7 Catalytic cycle for the propagation steps in the CO-ethene copolymerisation proposed by Mul and co-workers. P = polymer chain.

Bianchini and co-workers have studied the rates of conversion of the β-keto chelates into the corresponding Pd-acyl-carbonyl complex bearing diphosphines. They observed that the opening of the β-keto chelate is favoured when phosphines with wide bite angles were used.[39] For the reactions showed in Scheme 1.8, they proposed that the rate determining step is related to the opening of the β-keto chelate (step a and b) instead the migratory insertion (step c). The mechanism of the copolymerisation with olefin other than ethene has been less investigated due to the low stability of the intermediates. In general, Pd-acyl-alkene complexes have been synthesised, affording only stable complexes when alkenes, which are not able to suffer β-elimination of hydrogen, as norbornene, were used.[83] The x-ray structures of some alkene inserted complexes have been reported.[84] Pd-acyl complexes $[PdCl(COEt)(PPh_3)_2]$ and $[PdCl(COPr)(PPh_3)_2]$ have been characterised as intermediates in this reaction.[85]

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Blanca Karelia Muñoz Moreno
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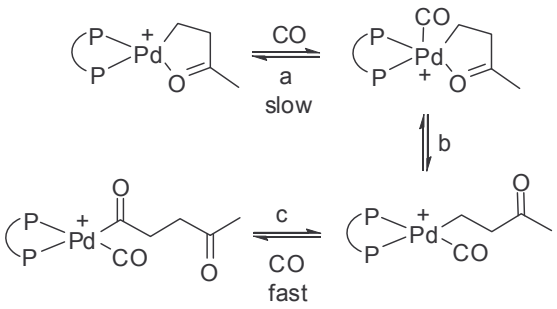

Scheme 1.8 Reactivity of Pd-β-ketochelate in the presence of CO

The study of the mechanism using unlike diphosphines ligands as N-N or P-O, have also been reported [86] In these cases, β and γ keto chelate intermediates were also characterised. In general terms, the key steps of the copolymerisation process are formation of β and γ keto chelates and the overall reaction rate is conditioned to the stability and reactivity of these species towards CO and alkenes.

Chain transfer

When copolymerisation is carried out in methanol two chain transfer reactions (or termination steps) can occur, methanolysis and protonolysis, as it was shown in Figure 1.8. However, another common chain transfer mechanisms for alkene polymerisations will be explained in this section.

When no chain transfer reagent, such as methanol, is present in the catalytic systems, the common chain transfer mechanism is the β-hydrogen elimination. The palladium complex containing an alkene group can suffer β-hydrogen elimination, releasing the polymer with a unsaturated end group and generating a Pd-H complex (Scheme 1.9). The Pd-H complex will start a new chain with an alkyl end group.

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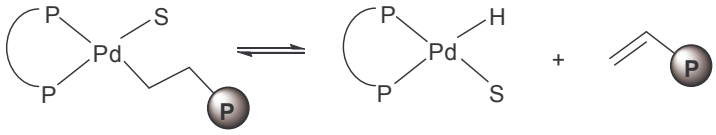

Scheme 1.9 β-Hydrogen elimination as chain transfer mechanism.
P = polymer chain.

The alkyl end group can be also obtained by addition of dihydrogen or in the presence of water and carbon monoxide (Figure 1.7; equation 1). Hydrogen is usually added to control the molecular weight and to favour the formation of oligomers. Finally, the formation of ether end group has also been observed by Sen *et al.*[73e] The mechanism proposed for ether end groups involves a Michael addition of methanol via an enolate intermediate.[87]

1.4. Copolymerisation vs. alkoxycarbonylation

In sections 1.2.5 and 1.3.4 the mechanisms of the alkoxycarbonylation and the copolymerisation have been reviewed. The mechanistic steps, initiation, insertion and termination, are the same for both reactions with the only exception of the number of multiple insertions of CO and olefin in case of copolymers (propagation step). Thus, the control in the chemoselectivity of the reactions for the formation of ester or copolymers depends on the propagation *vs.* chain termination steps. In each case, after the first olefin/CO insertion, there are two possibilities: a) termination by methanolysis to form an ester, or b) propagation of the chain by multiple alternating olefin/CO insertions to form oligomers or copolymers. The scheme 1.10 shows the two steps on the basis that the first olefin insertion occurs into a palladium hydride. The explanation of why in some cases copolymers are obtained instead esters or *viceversa* has attracted the attention of

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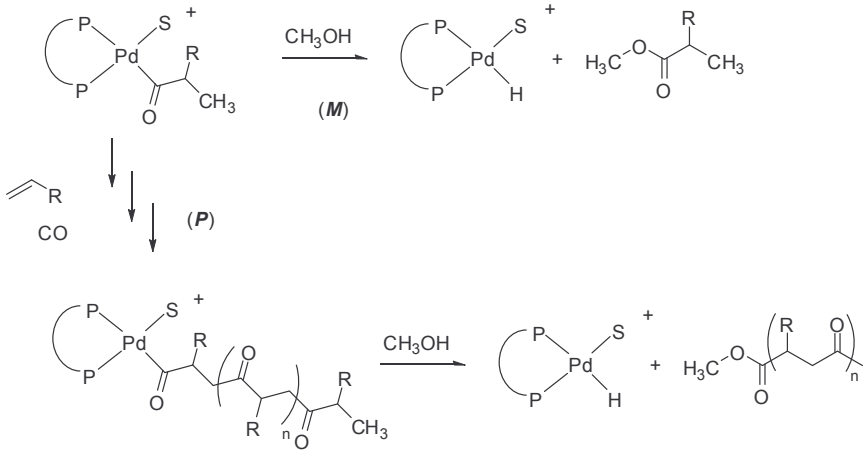
many scientists in the last years. Drent and co-workers observed that under exactly reaction conditions the palladium system modified with triphenylphosphine afforded methylpropanoate whereas the use of palladium complexes bearing bidentate diphosphines yielded copolymers.[28a] For the latter system depending on the chain length between phosphine groups, it was possible to obtain higher reaction rates and materials with different molecular weights.



Scheme 1.10 Methanolysis (***M***) *vs.* propagation (***P***) steps

Based on the experimental results, they proposed that the multiple insertions of ethene/CO can occur only if the acyl and monomer (or alkyl and CO) are in *cis*-form. Thus, the *cis*-bidentate ligands provide the conditions to favour the chain growth, while the square-planar palladium bis(triphenylphosphine) complex, existing as a mixture of *cis*/*trans* complexes, will lead to an interruption of chain propagation affording methylpropanoate preferably. Furthermore, it was suggested that the termination step for complexes with two phosphine in *trans* disposition is favoured.[32] The fact that bulky and electron-donor diphosphines as d*t*bpx and d*t*bpp (Figure 1.29) give selectively methylpropanoate in high yields, was initially

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explained on the basis that these diphosphines lead the formation of *trans*-coordinated oligomeric diphosphines complexes.[27a,30,51] The fact that the ligand becomes unidentate during some steps of the catalytic cycle, have also been proposed. [88]

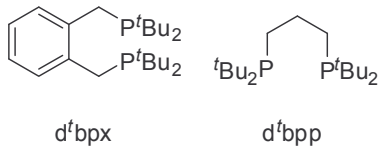

Figure 1.29 Bidentate ligands used for the methoxycarbonylation of ethene

On the basis of experimental results, van Leeuwen and co-workers proposed that a *cis*-diphosphine complex is needed for the methanolysis can take place.[32] Furthermore, in recent theoretical studies it have been demonstrated that the methanolysis of a Pd-acyl is favoured towards an additional ethene insertion, when bulky ligands with wide bite angles were used (see section 1.2.5).[46] It is clear that the selectivity to an ester or a copolymer depends on the nature of the ligand used, which favour the propagation or the termination steps.

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1.5. Objectives of the thesis

Based on the state-of-the-art presented above, the aim of the present thesis is to explore new active palladium systems for the asymmetric methoxycarbonylation of vinyl arenes, in order to obtain high regio- and enantioselectivities simoultaneously. Moreover, to find new active palladium systems for the CO/alkene co- and terpolymerisation reactions. To achieve these goals the following objectives are proposed.

1. To synthesise and characterise Pd complexes bearing chiral cyclic monophosphines as ligands, as well as, their application in the asymmetric methoxycarbonylation of vinyl arenes.
2. To synthesise and characterise neutral and cationic Pd complexes bearing chiral diphosphines as ligands and to test them in the asymmetric methoxycarbonylation of styrene.
3. To characterise the intermediate species in the methoxycarbonylation of styrene using palladium systems modified with mono- and bidentate phosphines, through multinuclear NMR experiments, including HPNMR.
4. To synthesise and characterise Pd complexes bearing xylofuranose-derivative diphosphines, as well as, to explore the effect of the electronic properties and backbone rigidity of the ligands in CO/ethene/propene co- and terpolymerisation reactions.

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Chapter 2

Monodentate phosphorus ligands in palladium catalysed asymmetric methoxycarbonylation of vinyl arenes

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2.1 Background

Phosphetane ligands have only recently been introduced in homogeneous catalysis.[1] Their restricted conformational freedom, due to the presence of a four-membered ring, is expected to enhance the chiral induction during the catalytic processes.[2] These highly hindered, chiral phosphines have been reported in asymmetric hydrogenation reactions catalysed by rhodium and ruthenium complexes.[3] Phosphetane based palladium catalysts were also used in processes such as olefin hydrosilylation and allylic nucleophilic substitutions.[4]

Concerning phospholane ligands, their use in asymmetric catalysis has been reported for several transition metal catalysed processes such as hydrogenation,[5] allylic alkylation, hydroacylation or hydrovinylation.[6] The success of these ligands has been attributed to the rigid chiral environment at the 2,5-positions of the five membered ring.[7] Their use in Rh-catalysed hydroformylation of olefins is more recent and showed to induce good enantioselectivity.[8] Phospholane ligands have also been used in the Pd-catalysed copolymerisation of α-olefins and carbon monoxide and led to the production of isotactic materials with ee's higher than 90%.[9]

The axially chiral phosphacyclic P-donor ligands, phosphepine ligands, have been introduced successfully in catalysis in the last decade.[10] High activities and enantioselectivities have been reported for the rhodium-catalysed asymmetric hydrogenation of methyl α-acetamidocinnamate,[11] *N*-acyl enamines,[12] α,β-unsaturated acids and esters[13] using monodentate phosphepine ligands. Moreover, the asymmetric hydrogenation of β-ketoesters catalysed by systems containing ruthenium and phosphepine ligands have been reported to afford up to 94% of enantioselectivity.[14]

Although phospholane ligands have been used in asymmetric methoxycarbonylation of styrene, the most of the monodentate ligands have not been completely exploited in this process. In this study, phosphetane, phospholane

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and phosphepine ligands, showed in figure 2.1, are used. The synthesis of a series of Pd complexes, their characterisation and their application in the asymmetric methoxycarbonylation of vinyl arenes are described.

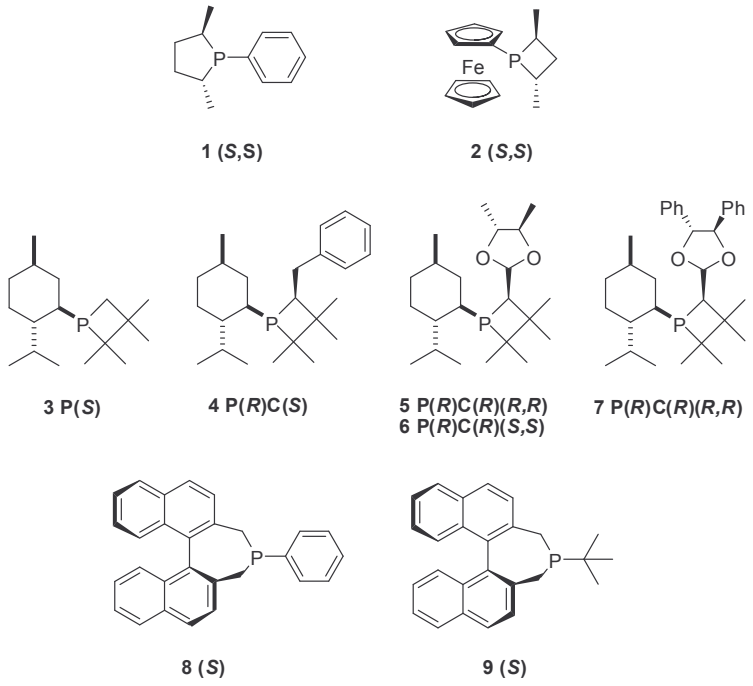

Figure 2.1 Ligands used in this study

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2.2 Experimental

2.2.1 General

All palladium complexes were synthesised using standard Schlenck techniques under nitrogen atmosphere. Diethyl ether, toluene and THF were distilled over sodium/benzophenone and dichloromethane was distilled over P_2O_5. All solvents were deoxygenated before use. The phospholane **1**,[5] the phosphetane ligands **2-4**,[4,15,16,17] and the palladium complexes $[PdCl_2(NCPh)_2]$, $[PdCl_2(\mathbf{4})_2]$ **4a**, $[PdCl_2(\mathbf{5})_2]$ **5a**, $[PdCl_2(\mathbf{6})_2]$ **6a**,[4,18] were synthesised according to previously reported methods and in a collaboration with Dr. Angela Marinetti. Ph-BINEPINE (**8**) and *t*Bu-BINEPINE (**9**) were supplied gently by Prof. Serafino Gladiali from the Università degli Studi di Sassari and Degussa, respectively. $PdCl_2$ was purchased from Johnson Matthey Inc. and used without further purification. All other reagents, except vinylnaphtalene that was purified by flash chromatography (silica gel, hexane), were used as received from commercial suppliers. Deuterated solvents used for routine NMR measurements were dried over molecular sieves. ^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ spectra were recorded on a Varian Mercury 400 spectrometer (400.14, 100.63 and 161.98 MHz, respectively). Chemical shifts were referenced to either TMS as an internal standard (^1H and $^{13}C\{^1H\}$ NMR spectra) or 85% H_3PO_4 as an external standard ($^{31}P\{^1H\}$ NMR spectra). Gas chromatography analyses were performed using a Hewlett-Packard 5890 series II chromatograph with flame ionisation detector and Ultra-2 (5% diphenylsilicone/95% dimethylsilicone) (25 m x 0.2mm Ø) capillary column. Enantiomeric excesses were determined by High Performance Liquid Chromatography analysis (Daicel CHIRACEL OJ, hexane/2-propanol = 95/5, 1.5 ml min^{-1}).

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2.2.2 Synthesis of dichloro palladium (II) complexes $[PdCl_2(1)_2]$ (1a), $[PdCl_2(3)_2]$ (3a), $[PdCl_2(8)_2]$ (8a), $[PdCl_2(9)_2]$ (9a)

A solution of corresponding ligand in dichloromethane was added to a solution of $[PdCl_2(PhCN)_2]$ in dichloromethane. The resulting yellow solution was stirred for 1 hour and concentrated under vacuum. Addition of diethyl ether yielded the precipitation of a pale-yellow solid, which was filtered and washed with diethyl ether before to be dried under vacuum.

1a:Yield: 220.6 mg (84%). ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 0.84 (m, 4H), 0.99 (br, 2H), 1.59 (br m, 2H), 1.67 (b, 1H), 1.73 (d, 3H, J_{HH}= 7 Hz), 1.78 (d, 3H, J_{HH}= 7 Hz), 1.88 (m, 1H), 2.07 (m, 1H), 2.13 (br m, 2H), 2.37 (br m, 2H), 3.02 (m, 1H), 3.09 (m, 1H), 3.59 (b, 2H), 7.15 (b, 2H), 7.27 (d, J_{HH}= 7Hz, 2H), 7.41 (t, J_{HH}= 7Hz, 2H), 7.44 (b, 1H), 7.79 (m, 2H); ^{13}C{^{1}H} ($CDCl_3$, 100.63 MHz, ppm): δ 14.8 (s), 15.4 (s), 21.1 (t, J_{PC}= 5 Hz), 22.3 (t, J_{PC}= 7 Hz), 31.8 (t, J_{PC}= 12 Hz), 32.7 (t, J_{PC}= 12 Hz), 33.05 (d, J_{PC}= 30 Hz), 34.2 (s), 34.8 (s), 35.75 (d, J_{PC} = 30 Hz), 128.05 (s), 128.1 (s), 128.15 (s), 130.4 (s), 132.4 (s), 134.05 (t, J_{PC}= 6 Hz) ^{31}P{^{1}H} ($CDCl_3$, 161.98 MHz, ppm): δ 53.1 ppm (v. br, *cis*-complex) 44.3 ppm (s, *trans*-complex). Anal.calcd. for $C_{24}H_{34}P_2PdCl_2$ (MW): 560.05 C, 51.31; H, 6.10. Found: C, 52.7 H, 6.4. MS (malditof) m/z 525 (M^+-Cl).

3a: Yield: 244 mg (75 %). ^{1}H NMR (CD_2Cl_2, 400.13 MHz, ppm): δ 0.82 (d, J_{HH} = 7 Hz, CH_3), 0.89 (d, J_{HH} = 7 Hz, CH_3), 0.97 (s, CH_3), 0.98 (d, J_{HH} = 7 Hz, CH_3), 1.30 (s, CH_3), 1.31 (t, J_{PH} = 7 Hz, CH), 1.38 (t, J_{PH} = 9 Hz, CH_3), 1.54 (s, CH_3), 1.59 (m, CH_2), 1.75 (m, 2 CH_2), 1.84 (m, CH), 2.0 (m, CH), 2.13 (m, CH), 2.66 (d, J_{HP} = 13 Hz, CH_2). ^{13}C{^{1}H} (CD_2Cl_2, 100.63 MHz, ppm): δ 17.5 (s, CH_3), 21.9 (s, CH_3), 22.5 (s, CH_3), 23.7 (s, CH_3), 23.8 (s, CH_3), 24.8 (t, J_{PC}= 6 Hz, CH_2), 25.6 (t, CH_3), 27.2 (s, CH_3), 30.9 (s, CH), 33.7 (t, J_{PC}= 6 Hz, CH), 34.8 (s, CH_2), 36.2 (s, CH_2), 40.7 (s, C), 42.9 (s, CH), 45.9 (s, CH), 49.4 (broad, CH_3); ^{31}P{^{1}H} ($CDCl_3$,

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161.98 MHz, ppm, 203 K): δ 61.1 (s, br), δ 59.9 (s). Anal.calcd. for $C_{34}H_{66}P_2PdCl_2$ (MW): 712.31 C, 57.18; H, 9.31. Found: C, 56.8 H, 9.28. MS (malditof) m/z 641 (M^+-2Cl), 677 (M^+-Cl).

8a: Yield: 98 mg (80%). ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 2.90 (dt, $^2J_{HH}$=12.6 Hz, $^2J_{HP}$=3.6 Hz, P-C_AH_2, 1H), 3.35 (dt, $^2J_{HH}$=15.2 Hz, $^2J_{HP}$=3.7 Hz, P-C_BH_2, 1H), 3.46 (dt, $^2J_{HH}$=15.2 Hz, $^2J_{HP}$=3.2 Hz, P-C_BH_2, 1H), 4.25 (d, $^2J_{HH}$=12.6 Hz, P-C_BH_2, 1H), 7.02 (d, $^2J_{HH}$=8.5 Hz, 1H), 7.20 (m, 4H), 7.39 (m, 4H), 7.54 (m, 5H), 7..77 (d, $^2J_{HH}$=8.5 Hz, 1H), 7.84 (d, $^2J_{HH}$=2.4 Hz, 1H), 7.9 (d, $^2J_{HH}$=8.5 Hz, 1H), 8.05 (d, $^2J_{HH}$=8.5 Hz, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.63 MHz, ppm): δ 26.64 (t, $J_{(CP)}$= 13.4 Hz, CH_2), 30.8 (t, $J_{(CP)}$= 13.4 Hz, CH_2), 125.84, 125.86, 126.35, 126.45, 127.14, 128.34, 128.44, 128.56, 128.77 (t, $J_{(CP)}$= 4.5 Hz), 128.9, 139.3 (t, $J_{(CP)}$= 16.6 Hz) 130.8, 131.2, 131.4, 132.0, 132.6, 132.3, 132.9, 133.3, 134.2, 134.3. ^{31}P{^{1}H} ($CDCl_3$, 161.98 MHz, ppm): δ 36.27 (s). Anal.calcd. for $C_{56}H_{42}P_2PdCl_2$ (MW): 952.12 C, 70.49; H, 4.44. Found: C, 69.62 H, 5.01. MS (malditof) m/z 881 (M^+-2Cl), 917 (M^+-Cl).

9a: Yield: 105 mg (85%). ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 1.25 (t, J_{HP}= 6.8 Hz, P-C(CH_3)$_3$, 9H), 3.06 (dt, $^2J_{HH}$=15.9 Hz, $^2J_{HP}$=4.5 Hz, P-C_BH_2, 1H), 3.53 (d, $^2J_{HH}$=15.29 Hz, P-C_BH_2, 1H), 4.04 (d, $^2J_{HH}$=12.1 Hz, P-C_BH_2, 1H), 7.04 (d, $^2J_{HH}$=8.8 Hz, 1H, H8), 7.19-7.30 (m, 3H, H7, H7', H8'), 7.41-7.44 (m, 4H, H3, H3', H6, H6'), 7.83-8.00 (m, 4H, H4, H4', H5, H5'). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.63 MHz, ppm): δ 22.56 (t, $J_{(CP)}$= 9.9 Hz, CH_2), 27.39 (t, $J_{(CP)}$= 9.9 Hz, CH_2), 29.24 (t, $J_{(CP)}$= 2.63 Hz, CH_3-^{t}Bu), 34.56 (t, $J_{(CP)}$= 6.8 Hz, -C-, ^{t}Bu), 125.4 (C6), 125.7 (C6´), 125.9, 126.4 (C7,7'), 127.1, 127.3 (C8,8'), 128.1, 128.3, 128.4, 128.5, 129.1 (C3,3',4,4',5,5'), 132.04 (t, $J_{(CP)}$= 2.8 Hz, C1'), 132.2, 132.5, 132.7, 133.0 (C9,9',10,10'), 133.36 (t, $J_{(CP)}$= 4 Hz, C1), 133.79 (t, $J_{(CP)}$= 2.3 Hz, C2'), 134.3 (t, $J_{(CP)}$= 1.2 Hz, C2). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.98 MHz, ppm): δ 58.39 (s).

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Anal.calcd. for $C_{52}H_{50}P_2PdCl_2$ (MW): 912.18 C, 68.32; H, 5.51. Found: C, 65.30 H, 6.55. MS (malditof) m/z 841 (M^+-2Cl), 877 (M^+-Cl).

2.2.3 X-ray data Collection and Structure Determination of $[PdCl_2(3)_2]$ 3a

Crystals of *trans*-$[PdCl_2(\mathbf{3})_2]$ suitable for X-ray analysis were obtained from a toluene solution at 0 ºC. Data were collected at 100(2) K. The complex crystallizes in a trigonal space group with a= 13.3102(7) Å, c= 19.1593(19) and V= 2939.5(4) Å^3. The crystal structure was solved and refined using the SHELXTL package. Structure solutions were obtained in the space groups $P3_2$ and $P3_221$. Since the heavy atom position corresponds to the higher symmetry space group, it is difficult to distinguish between twinning and disorder of the light atoms. Applying a matrix for twinning by merohedry (0 1 0 1 0 0 0 0 -1, BASF 0.5) in the space group $P3_2$ the R1 value could be lowered from 9.18 % to 6.88%. Nevertheless the atom positions were showing a strong correlation and negative atomic displacement parameters. A structure solution obtained in the higher symmetric space group $P3_221$ could be refined, applying restrains on some carbon-carbon distances, restrains on the atoms with the strongest anisotropic displacement parameters and a disorder model. In this case, the structure refined to a R1-value of 7.45% and no negative atomic displacement parameters were observed. In the disordered model, two structures can be observed with the menthyl rests on similar positions but showing slightly different conformations. For the description of the molecule the higher symmetry structure solution in $P3_221$ was selected. The hydrogen atoms were included as fixed contributions in the final stages of least-squared refinement, while anisotropic temperature factors were used for all other atoms.

2.2.4 Catalysis

High-pressure experiments were carried out in a Berghof autoclave, and the reaction mixtures were magnetically stirred and electrically heated. In a typical

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experiment, a solution of the palladium precursor (0.015 mmol), *p*-TsOH (0.15 mmol) and styrene (3 mmol) in 5 mL of THF-MeOH mixture (1:1) were introduced into the evacuated autoclave. Carbon monoxide was introduced and the system was then heated. When thermal equilibrium was reached, stirring was initiated. After reaction, the autoclave was cooled to room temperature and depressurised. The product was filtered in a short column of celite and solvent was removed under vacuum. The pure ester was isolated by column chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent. Conversions, chemo-, regio- and enantioselectivities were determined by GC and HPLC analyses.

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2.3 Results and Discussion

2.3.1 Synthesis of dichloro palladium (II) complexes [$PdCl_2(1)_2$] (1a), [$PdCl_2(3)_2$] (3a), [$PdCl_2(8)_2$] (8a), [$PdCl_2(9)_2$] (9a)

The palladium complexes were obtained by reaction of [$PdCl_2(NCPh)_2$] with 2 equivalents of the appropriate ligand in dichloromethane. The products were precipitated by addition of diethylether and obtained in high yields. In the $^{31}P\{^1H\}$ NMR spectra of a solution containing the complex **3a**, a single broad resonance at $\delta \sim 61$ was observed at 295 K. However, at 203 K, two singlet resonances were detected at δ 61.1 (major) and δ 59.9 (minor) with distinct intensities (Figure 2.2).

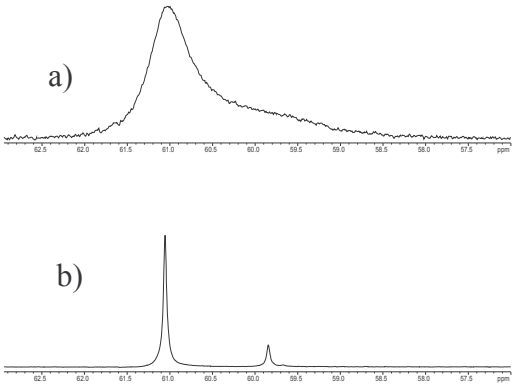

Figure 2.2 Selected region of the $^{31}P\{^1H\}$ NMR spectrum of [$PdCl_2$(**3**)$_2$] **III** in d_8-toluene at a) 295K and b) 203K

The ratio of the peak intensities was found to vary with the temperature and slightly with the nature of the solvent, as shown in Figure 2.3.

For all solvents used, an identical trend was observed with an increase of the amount of the minor species when the temperature is increased from 193 to 253 K. This ratio could not be measured at higher temperatures due to the broadness of these resonances above 253 K. Using EXSY techniques, these two resonances were found to exchange in all solvents. These results suggested the presence of

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two isomers that could correspond to the *cis* and *trans* configuration of the ligands or to two rotamers of **3a.** In the $^{13}C\{^1H\}$ spectrum of **3a**, the major isomer exhibited 3 resonances with *pseudo* triplet multiplicity that indicated a *trans* configuration of the phosphorus ligands, generating the second order pattern. However, the low intensity of the signals arising from the minor isomer did not allow to distinguish between the two possible types of isomerism. The *cis*/*trans* isomerisation of $PdCl_2(L)_2$ complexes is known to occur in an intermolecular manner[19] while in the case of two rotamers, the interchange mechanism is expected to occur in an intramolecular way.

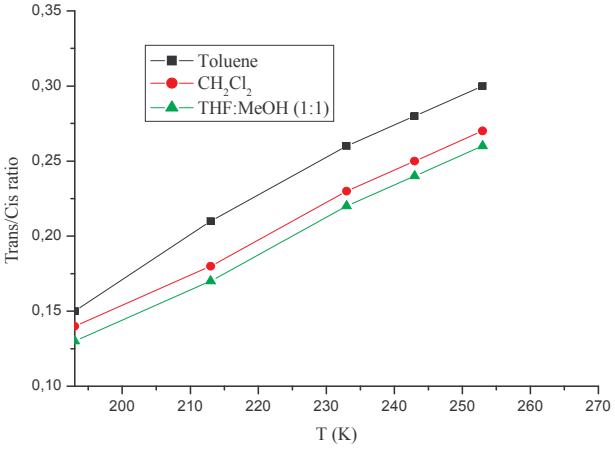

Figure 2.3 Ratio of the ^{31}P peak intensities as a function of the temperature and nature of the solvent for complex $[PdCl_2(\mathbf{3})_2]$ **3a**

In order to clearly identify the minor isomer, $^{31}P\{^1H\}$ spectra of **3a** were recorded in the presence of 1 equivalent of free ligand **3**. In these experiments, the lineshape of the resonances was found to be unaffected, indicating that no change in the rate of interchange between the two species was apparent. These results suggested that the interchange was occuring *via* an intramolecular process and that the two signals corresponded to two rotameric forms of *trans*-$[PdCl_2(\mathbf{3})_2]$ (Figure 2.4).

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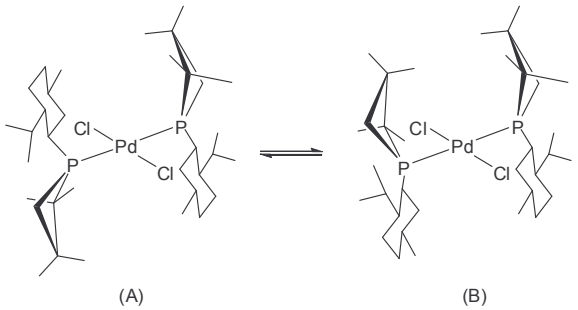

Figure 2.4 Rotamers of complex **3a**

When the X-ray diffraction of single crystals of **3a** was performed, the rotamer (B), containing both menthyl groups situated on the same side of the plane defined by the Pd, Cl and P atoms was identified. The molecular structure of complex **3a** is shown in Figure 2.5. The coordination sphere around the palladium atom was found to correspond to a slightly distorted square-planar geometry, with a value of 177.91(6)° for the Cl(1)-Pd-Cl(2) angle and 174.92(6) ° for P(1)-Pd-P(2). The Pd-Cl bond lengths were measured to be *ca.* 2.3 Å while the Pd-P bonds were *ca.* 2.33 Å. These values are very similar to those previously reported for the related complex *trans*-[$PdCl_2$(**3**)$_2$].[4a] The two groups are related *via* a C_2 symmetry axis passing through the Pd center and perpendicular to both Cl(1)-Pd-Cl(2) and P(1)-Pd-P(2) axis. This arrangement was also observed for *trans*-[$PdCl_2$(**4**)$_2$] that was previously reported.

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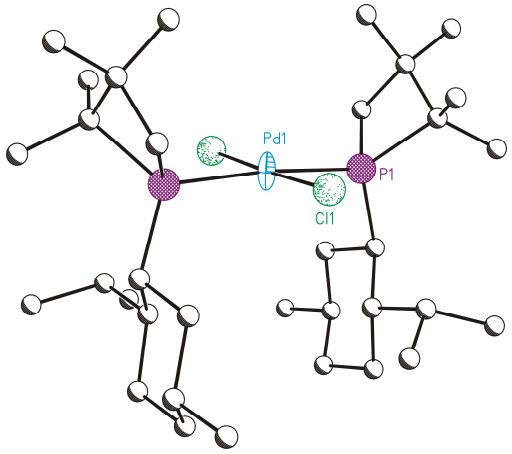

Figure 2.5 Molecular structure of the palladium complex **3a** showing one of the selected disorder models. Hydrogen atoms have been omitted for the sake of clarity

The $^{31}P\{^{1}H\}$ NMR spectra of BINEPINE complexes **8a** and **9a** shows only one sharp signal at 36.3 and 58.4 ppm, respectively, at room temperature. The large steric hindrance of both ligands maybe favours the formation of only one isomer, preferable *trans*-complex. In the carbon NMR spectrum of both complexes **8a** and **9a,** the coupling for *P-C*$(CH)_3$ showed a AXX' spin system pattern. This pattern confirms that the binepine ligands (**8** and **9**) are coordinated in a *trans* disposition.[20]

2.3.2 Catalytic Results.

The ligands **1-9** showed in Figure 2.1, were tested in the palladium-catalysed asymmetric methoxycarbonylation of vinyl arenes. All of these ligands are monodentate cyclic phosphines and the remarkable difference among them is the number of member ring, phosphetane, phospholane and phosphepine (4, 5 and 7 member ring, respectively). In the next sections the catalytic activity of all of these ligands will be discussed, starting from the larger member ring phosphepine, and followed by the phospholane and phosphetane ligands, respectively.

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Asymmetric methoxycarbonylation of styrene using the complexes [$PdCl_2$(8)$_2$] 8a and [$PdCl_2$(9)$_2$] 9a as catalyst precursors

The asymmetric methoxycarbonylation of styrene was performed using palladium complexes bearing phosphepine ligands. The results are summarised in table 2.1.

Table 2.1 Asymmetric methoxycarbonylation of styrene catalyzed by palladium-phosphepine complexes[a]

Entry	Catalyst	T (ºC)	PCO (bar)	%C	%(b+l)	b:l	% ee
1	$PdCl_2$ + **8**	70	35	8	33	90:10	4(*S*)
2	[$PdCl_2$(**8**)$_2$] **8a**	70	35	22	80	97:3	0
3	[$PdCl_2$(**9**)$_2$] **9a**	70	35	traces	-	-	-
4[b]	[$PdCl_2$(**9**)$_2$] **9a**	70	35	11	80	72:28	23 (*R*)

[a] Reaction conditions: 0.5 mol% Pd (0.015 mmol), Pd/HCl=1/100, 24 h, THF: MeOH (1:1) = 5 mL. [b] *p*-TsOH instead HCl, Pd/*p*-TsOH =1/10.

When binepine ligand **8** and palladium dichloride were used as catalytic system in the presence of hydrochloric acid, only 8% of conversion was obtained (table 2.1, entry 1). The chemo- and enantioselectivities were not so high (33 and 4%, respectively), although, the regioselectivity was found to be 90%. Using the isolated complex **8a** under the same reaction conditions (entry 2), the conversion, and regioselectivity were improved, while chemoselectivity was increased considerably (80%). Also, the palladium complex **9a** modified with the *tert*-butyl phosphepine ligand **9** (entry 3), was tested in the asymmetric methoxycarbonylation of styrene. This complex was not active under these conditions affording only traces of products. In order to improve the catalytic activity, catalyst **9a** was tested under milder acidic conditions using *p*-TsOH instead

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hydrochlorhydric acid. The conversion was enhanced up to 11% (entry 4), but the regioselectivity decreased considerably. The chemoselectivity was the same than that observed for catalyst **8a** (80%). Under acidic conditions the by-products shown in Figure 2.6 can be formed. For catalysts **8a** and **9a**, the only undesired product detected was (2-methyl)benzylmethyl-ether (M) formed by etherification of the substrate.

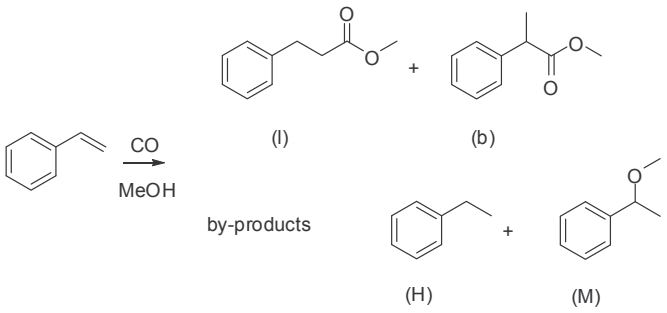

Figure 2.6 by-products observed in the methoxycarbonylation reaction under acidic conditions

Etherification products are normally formed by the acid-catalysed Michael addition of MeOH to styrene.[21] The hydrogenation products (H) could also be detected as by-product of this reaction by the presence of dihydrogen in the media *via* the water gas shift reaction.[22] The presence of water is explained by the use of *p*-toluenesulfonic acid as a monohydrate. Hydrogenation transfer could also explain the detection of the hydrogenation product.[23]

In summary the catalysts bearing the seven-membered ring phosphepine ligands afford moderate to high regioselectivities to the branched ester, even if the catalytic activity and enantioselectivity are poor.

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Asymmetric methoxycarbonylation of styrene using the phospholane complex [$PdCl_2(1)_2$] 1a as precursor

The phospholane ligand **1** was then probed due to the successful use of this type of ligands in other asymmetric carbonylation reactions.[8,9] The palladium complex [$PdCl_2$(**1**)$_2$] **1a**, containing the five-membered ring phospholane **1** was used as catalyst precursor for the asymmetric methoxycarbonylation of styrene. The catalytic reactions were carried out during a period of 24 hours at 90ºC. The presence of acid is required in order to form *in situ* the active species involved in the catalytic reaction.[24] The results obtained using this system are summarised in Table 2.2.

When the reaction was carried out under 35 bars of CO and in the presence of a 10-fold excess of *para*-toluensulfonic acid (entry 1), the conversion was measured to be 22% and moderate chemo- and regioselectivity to the branched product (70 and 75% respectively, entry 1) were obtained. When hydrochloric acid was used as the acid source (entry 2), the conversion increased to 40 %. Furthermore, both chemo- and regioselectivity to the branched ester were improved to 95% and 90%, respectively. When greater ratios of acid to Pd were used (entry 3 and 4), the conversions were found to increase up to 91%. However, a slight decrease in chemoselectivity was observed. The regioselectivity to the branched esters was measured to be up to 95% under these highly acidic conditions. When the CO pressure was decreased to 20 bars (entry 5), the conversion decreased to 55%, together with the chemo- and regioselectivities (83 and 90 %, respectively). However, when the CO pressure was increased to 50 bars (entry 6), the conversion was found to be 97% and the chemo- and regioselectivies were significantly improved to 95 and 96%, respectively. Such an effect was previously reported for this reaction.[25] When a mixture of toluene and methanol (1:1) was used as solvent (entry 7), only the chemoselectivity (79%) was found to significantly vary when

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compared to the results obtained in THF:MeOH mixture under the same conditions (entry 3).

Table 2.2 Methoxycarbonylation of styrene using complex **1a** as precursor[a]

Entry	Pd/H^+	acid	P_{CO}(bar)	%C	%(b+l)	b:l	ee (%)
1	1/10	TsOH	35	22	70	75:25	11 (S)
2	1/10	HCl	35	40	95	90:10	4 (S)
3	1/100	HCl	35	81	93	92:8	3 (S)
4	1/200	HCl	35	91	89	95:5	0
5	1/100	HCl	20	55	83	90:10	4 (S)
6	1/100	HCl	50	97	95	96:4	0
7	1/100	HCl	35	77	79	95:5	2 (S)

[a]Reaction conditions: 0.5 mol% Pd (0.015 mmol), Pd/acid =1/10, 24 h, MeOH:THF (1:1), 90ºC; C= conversion; b= branched ester; l= linear ester

The major by-product observed was (2-methyl)benzylmethyl-ether (M, Figure 2.6). Under these conditions, the ee values obtained were all found to be low (up to 11%, entry 1). It should be noted that Nozaki et al. reported an ee value of 2.4% using this ligand in the presence of Pd-clay at 125ºC and 45 atm of CO.[26]

In summary, using the palladium complex **1a** as catalyst precursor, high regioselectivity to the branched ester was obtained. However, this system was found to induce low enantioselectivity during the reaction. In the following section, the results obtained using systems bearing phosphetanes **2-7** are described.

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Asymmetric methoxycarbonylation of styrene using the phosphetanes as chiral ligands

A preliminar optimisation of the reaction conditions for the methoxycarbonylation of styrene using phosphetane-containing systems was performed using $PdCl_2$, ligands **2,4-7** and *p*-TsOH and the results are reported in Table 2.3.[27] When ferrocenylphosphetane **2** was used (entry 1) traces of products were detected and only 21% were esters. Using phosphetane **4** as ligand, 97% conversion was obtained with a chemoselectivity to the esters of 99% and a regioselectivity to the branched product of 98% (entry 2).

Table 2.3 Methoxycarbonylation of styrene using $PdCl_2$/phosphetane/*p*-TsOH system[a]

Entry	Catalyst	T(ºC)	%C	%(b+l)	b:l	%ee
1	$PdCl_2$ + **2**	70	5	21	99:1	nd
2	$PdCl_2$ + **4**	70	97	>99	98:2	12 (*R*)
3	$PdCl_2$ + **5**	70	19	62	99:1	3 (*R*)
4	$PdCl_2$ + **7**	70	35	95	96:4	12 (*S*)
5	$PdCl_2$ + **4**	50	>99	>99	99:1	10 (*R*)
6	$PdCl_2$ + **4**	25	<1	-	-	-
7[b]	$PdCl_2$ + **4**	50	48	>99	98:2	14 (*R*)
8[b, c]	$PdCl_2$ + **4**	50	37	99	97:3	4 (*R*)
9[b,d]	$PdCl_2$ + **4**	50	81	97	97:3	10 (*R*)
10[b]	$[PdCl_2(\mathbf{4})_2]$ **4a**	50	99	>99	99:1	10 (*R*)

[a]Reaction conditions: 4 mol% Pd (0.015 mmol), Pd/L = 1/2, Pd/*p*-TsOH=1/10, 24 h, THF: MeOH (1:1), P_{CO} 35 bars; [b] 1 mol% Pd [c] 60 bar CO [d] Pd/*p*-TsOH=1/100.

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Moreover, chirality was induced by the ligand **4** in this system and yielded an enantiomeric excess of 12%. However, when the bulkier ligands **5** and **7** were used for this reaction, the conversion was found to decrease considerably, although the chemo- and regioselectivity of the reactions remained high (entries 3 and 4). It should be noted that the simple replacement of the two phenyl rings of **7** by methyl groups in **5** resulted in a substantial decrease in the activity of the catalyst and in the chemoselectivity of the reaction. In view of these results, the reaction conditions were optimised using ligand **4**. In order to first determine the optimum reaction temperature for the $PdCl_2$/**4**/*p*-TsOH system, the CO pressure was kept constant at 35 bars and the reaction temperature varied from 25 to 70 ºC. Under these conditions, the highest selectivity was obtained at 50 ºC with both the conversion and the branched to linear products ratio being superior to 99% and the ee of 10% (entry 5). When the reaction was repeated with a lower concentration of $PdCl_2$ (entry 7), the conversion was found to be 48%, but illustrating an increase in catalyst activity (TOF = 2 vs. 1.03 h^{-1}). Rising the CO pressure resulted in the reduction of both conversion and enantioselectivity of the reaction (entry 8). Increasing the acidity of the media was found to be beneficial to the activity of this system (entry 9, TOF = 3.38 h^{-1}). Using an isolated catalyst instead an *in situ* system at 50ºC and with 10-fold excess of acid (entry 10), the conversion was completely improved, while chemo-, regio- and enantioselectivities were still high. Considering this results, the next experiments were performed using only isolated systems.

The results obtained for the palladium-catalysed asymmetric methoxycarbonylation of styrene using isolated complexes bearing phosphetanes **3**, **4** and **5** under the previously optimised conditions are summarised in Table 2.4. These ligands structurally differ by the nature of the substituents of the phosphetane ring: hydrogen, benzyl and dioxolane group, respectively (Figure 2.1). First, using the isolated palladium complex bearing ligand **4**, 99% conversion was obtained and

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high values for chemoselectivity (>99%) and regioselectivity to the branched ester (99%) were achieved (entry 1). However, the enantioselectivity of the reaction under these conditions was found to be 6%. When the concentration of $[PdCl_2(\mathbf{4})_2]$ **4a** was reduced to 0.25 mol% (entry 2), the conversion slightly decreased to 90% whereas high values for the chemo- and regioselectivities were measured (98% and 96%, respectively). Very low enantiomeric excess was again measured. When the reaction was repeated in the presence of an excess of ligand **4** (entry 3), the catalytic results were found to be similar. When the palladium precursor $[PdCl_2(\mathbf{3})_2]$ **3a** was used (entry 4), the conversion was 82%, although the chemoselectivity to esters was still very high (95%) and the regioselectivity to the branched product was 92% (b/l = 11.5). In these reactions, the by-product was identified by GC-MS analysis as (2-methyl)benzylmethyl-ether, corresponding to the acid-catalysed etherification products of styrene. However, no enantioselectivity was induced by this system (ee = 0%). Changing the acid used from *p*-TsOH to HCl (entry 5) did not yield an increase of the ee value. When HCl was used, the conversion was found to decrease to 58%, which is in contrast with the results observed using the Pd complex containing the phospholane **1** as ligand (Table 2.2). The effect of the polarity of the co-solvent was also probed by replacing THF by the less polar toluene. Under these conditions and using $[PdCl_2(\mathbf{3})_2]$ **3a** as the catalyst precursor (entry 6), the conversion was increased to 97%. However, no significant variations in chemo- regio- and enantioselectivity could be observed. When $[PdCl_2(\mathbf{5})_2]$ was used as catalyst precursor (entry 7), lower conversion (26%) was obtained but a significant increase of the ee value (29%) was observed. This latter result could be explained by the greater steric hindrance induced by the presence of a dioxolane group in ligand **5**.

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Table 2.4 Asymmetric methoxycarbonylation of styrene catalyzed by palladium-phosphetane complexes[a]

Entry	Catalyst	T(ºC)	%C	%(b+l)	b:l	%ee
1	$[PdCl_2(\mathbf{4})_2]$ **4a**	70	99	>99	99:1	6 (*R*)
2[b]	$[PdCl_2(\mathbf{4})_2]$ **4a**	70	90	98	96:4	2 (*R*)
3[b,c]	$[PdCl_2(\mathbf{4})_2]$ **4a**	70	92	99	99:1	6 (*R*)
4	$[PdCl_2(\mathbf{3})_2]$ **3a**	70	82	95	92:8	0
5[d]	$[PdCl_2(\mathbf{3})_2]$ **3a**	70	58	98	98:2	0
6[e]	$[PdCl_2(\mathbf{3})_2]$ **3a**	70	97	99	95:5	0
7	$[PdCl_2(\mathbf{5})_2]$ **5a**	70	26	94	97:3	29 (*R*)
8	$[PdCl_2(\mathbf{6})_2]$ **6a**	70	27	92	89:11	4 (*S*)

[a]Reaction conditions: 0.5 mol% Pd (0.015 mmol), Pd/*p*-TsOH=1/10, 24 h, THF: MeOH (1:1), P_{CO} 35 bars; [b] 0.25 mol% Pd [c] excess of ligand (1 equiv.) [d] HCl instead of *p*-TsOH [e] toluene: MeOH (1:1) as mixture of solvents

Using this system, high chemoselectivity and regioselectivity to the desired ester was again achieved (94 and 97% (b/l = 32.3), respectively). When the complex $[PdCl_2(\mathbf{6})_2]$ **6a**, containing the ligand **6** with the configuration P(R)C(R)(S,S), very similar results to those obtained with $[PdCl_2(\mathbf{5})_2]$ **5a** were obtained in terms of conversion, chemo- and regioselectivity (entry 8). However, the enantioselectivity was found to decrese from 29 to 4%, when compared to entry 7. These results indicate that the enantioselectivity induced by the phosphetane ligand **5** arises from the combination of the spatial arrangements of all the substituents of these ligands. Under these conditions, these Pd systems containing phosphetane ligands hence afford very high chemo- and regioselectivity to the branched ester for this reaction,

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independently of the nature of the substituents of the phosphetane ring. However, the catalytic activity and enantioselectivity were found to greatly depend on the nature of this substituent, with conversions measured from 26 to 99% and ee from 0, where only protons were in 4-position of the four membered ring of the ligand, to 29% when ligand **5** was used.

Asymmetric methoxycarbonylation of vinyl arenes using [$PdCl_2(3)_2$] 3a as precursor

In order to probe the effect of the nature of the substrate on the activity of these systems, the methoxycarbonylation reactions of 4-methoxystyrene, 4-methylstyrene, styrene, 4-fluorostyrene and 2-vinylnaphthalene were completed using [$PdCl_2$(**3**)$_2$] **3a** as the catalyst precursor. Catalytic reactions were performed at milder conditions, 60 ºC under 35 bar of CO, using a 10-fold excess of *p*-TsOH. The results obtained for these reactions are described in Table 2.5.

Under these conditions, the methoxycarbonylation of styrene (entry 3) was found to exhibit a conversion of 63%, a chemoselectivity *quasi*-total to the esters (98%), a regioselectivity of 94% to the branched product with 3% ee. When the reaction was carried out using 4-methoxystyrene as substrate (table 2.5, entry 1), the conversion was found to be 71%, the chemoselectivity to the esters 21% with a high regioselectivity to the branched product (94%). However, the most striking result achieved for this reaction is the ee value of 50%, which is in contrast with the value obtained when styrene was the substrate (3%). When the substrate was 4-methylstyrene (entry 2), a conversion of 33% was achieved with 58% of the products being the desired esters. The regioselectivity was again greatly in favour of the branched ester (92%), and the ee value obtained was intermediate between those of styrene and 4-methoxystyrene (25%).

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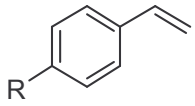
Table 2.5 Asymmetric methoxycarbonylation of olefins catalyzed by **3a**/*p*-TsOH system[a]



Entry	R	%C	%(b+l)	%M	%H	b:l	% ee
1	OMe	71	21	79	0	94:6	50 (S)
2	Me	33	58	39	3	92:8	25 (S)
3	H	63	98	2	0	94:6	3 (S)
4	F	11	75	16	9	96:4	2 (R)
5	vinylnaphthalene	36	84	11	5	93:7	8 (R)

[a] Reaction conditions: 0.5 mol% Pd (0.015 mmol), Pd/*p*-TsOH=1/10, 24 h, THF: MeOH (1:1), 60 ºC, P_{CO} 35 bars.

When the substituent in *para* position of the phenyl ring of the substrate was a fluoro group (entry 4), the conversion of the reaction decreased considerably to 11% although the regioselectivity of these reactions was still superior to 90% and the chemoselectivity was increased to 75% when compared with the result obtained with 4-methoxystyrene but still lower than in the case of styrene (98%). The ee was found to be close to 0%, like in the case of styrene. When 2-vinylnaphtalene was used as the substrate (entry 5), the conversion was measured to be 36%, the chemoselectivity was 84% to the esters with a regioselectivity of 93% to the branched product. The ee value in this case was found to be 8% to the (*R*) enantiomer. In terms of conversion, the results obtained were shown to vary considerably depending on the substituent attached to the phenyl ring of the substrate. The highest conversion was obtained when the electron donor group –

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OMe is present in 4 position of the substrate (71 %), while the lowest value was observed when the electron-withdrawing group –F is present in this position (11 %). When a hydrogen atom was in this position, an intermediate value was measured (63 %). The result obtained with 2-vinylnaphtalene was 36 %, thus lower than in the latter case. It was therefore concluded that the presence of a donor group on the phenyl ring of the substrates increases the reactivity of the substrate to different processes in competition with carbonylation reactions. The conversion observed when 4-methylstyrene is the substrate (33%) is in agreement with results previously observed by Seayad[28] and Inoue[29], who reported an important decrease of the catalytic activity for 4-alkylstyrene (alkyl= Me, ^{t}Bu, ^{i}Bu) when compared to the results obtained with styrene.

In terms of chemoselectivity, the lowest values were obtained when electron-donating groups were present in 4-position, with 4-methoxystyrene (21%) and 4-methylstyrene (58 %) while the highest value was obtained when styrene was the substrate (98%). In the case of 4-methoxystyrene, the only reaction by-product was identified as the etherification product (79%). This can be explained by the enhanced reactivity to nucleophilic attack of methanol in acidic media due to the presence of a donor group. Indeed, when the electronegativity of the substituent increases, the electronic density of the vinyl moiety of the substrate decreases and the nucleophilic attack of methanol is therefore disfavoured. In this case, the Pd-catalysed methoxycarbonylation reaction takes place much faster than the etherification process, thus improving the chemoselectivity of the reaction. However, when the substrate contains electron-withdrawing substituents (entries 4 and 5), the hydrogenation process becomes more substantial.

In terms of regioselectivity, the values obtained for these substrates were all superior to 90% to the branched product and no significant variations were observed as a function of the nature of the substrate.

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In contrast, the values of enantioselectivity for these reactions were found to vary greatly depending of the substrate used, with an increase of ee when an electron donor group is in *para* position of the vinyl unit. The ee values obtained for the methoxycarbonylation of styrene and 4-fluorostyrene under these conditions were close to 0%: However, an enantiomeric excess of 25% was obtained with 4-methylstyrene as the substrate and 50% when 4-methoxystyrene was used. The effect of the group in *para* position of the phenyl ring is therefore significant for the methoxycarbonylation reaction. However, such an effect has not been reported so far for this reaction, although Nozaki and co-workers reported that for the Pd-catalysed methoxycarbonylation of vinylarenes using systems bearing alkylarylphosphines, the highest ee value (53%) was obtained when the substrate was 2-methoxy-6-vinylnaphtalene.[30] It should also noted that an increase in ee was previously observed for other carbonylation reactions such as hydroformylation of vinyl arenes when the results obtained with 4-methoxystyrene and styrene were compared.[31] In the case of 2-vinylnaphtalene, 8% ee was measured to the other enantiomer, namely the (*R*) enantiomer.

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2.4 Conclusions

Palladium complexes $PdCl_2(L)_2$ bearing phospholane, phosphetane and phosphepine ligands were synthesised, characterised and used as catalyst precursors for the methoxycarbonylation of vinyl arenes. The bis-phosphetane complex $[PdCl_2(\mathbf{3})_2]$ **3a** was crystallised in the *trans* configuration and was characterised by X-ray crystallography. This species was found to exist as a mixture of rotamers in solution. In the methoxycarbonylation of styrene, the new dichloro palladium complexes bearing phosphepine ligands **8a** and **9a** were high regioselectives to the branched product, but poor active and enantioselective. Furthermore, both phospholane and phosphetane systems afforded excellent regioselectivities to the branched ester, although only the phosphetane systems provided moderate enantioselectivities (up to 29%). However, when other vinyl arenes were used as substrates, the enantioselectivity of the reaction was found to greatly vary depending on the nature of the substituent in 4-position of the phenyl ring. The ee values were found to vary from 3% in the case of styrene up to 50% for 4-methoxystyrene, under identical conditions.

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Chapter 3

Bidentate phosphorus ligands in palladium catalysed asymmetric methoxycarbonylation of styrene

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3.1 Background

In the methoxycarbonylation of styrene, the use of palladium precursors modified with diphosphine ligands was shown to yield high regioselectivity to the linear product. A correlation between the regioselectivity and the P-Pd-P bite angles was demonstrated using diphosphines with wide bite angles providing high conversions and almost exclusively linear product.[1] For instance, the palladium systems based on DPEphos (bite angle 103°) (**1**, figure 3.1) and Xantphos (111°) (**2**, figure 3.1) showed high regioselectivity towards the linear product.[2] In addition, other parameters such as electronic and steric effects have to be taken into consideration, since they could play an important role in the regioselectivity.[3]

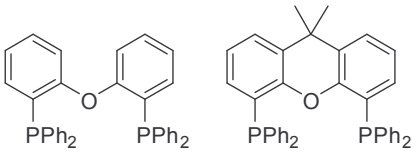

Figure 3.1 Ligands affording linear products in carbonylation reactions

To the best of our knowledge, only one example of palladium systems modified with bidentate diphosphine ligands that showed high regioselectivity to the branched ester in the methoxycarbonylation of styrene, has been reported (Figure 3.2).[4] However, no chiral version of the methoxycarbonylation of vinyl arenes has been performed using analogous chiral systems. As it was shown before, the systems modified with chiral bidentate ligands (see Chapter 1) even if they are not highly selective to the branched ester, are usually highly enantioselective.

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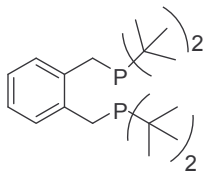

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Figure 3.2 Bidentate ligands used in methoxycarbonylation reactions

The aim of this work is to use chiral *cis*-bidentate systems to produce the branched ester selectively. This study was carried out in a framework of a collaboration with Prof. van Leeuwen, who had the idea to study the electronic effects of the ligands on the methoxycarbonylation reaction. In the following sections our investigations into the palladium-catalyzed methoxycarbonylation of styrene using neutral and cationic palladium complexes bearing chiral diphosphines (Figure 3.3) will be presented. These results have been published together to those obtained by the van Leeuwen's group in Amsterdam. [5]

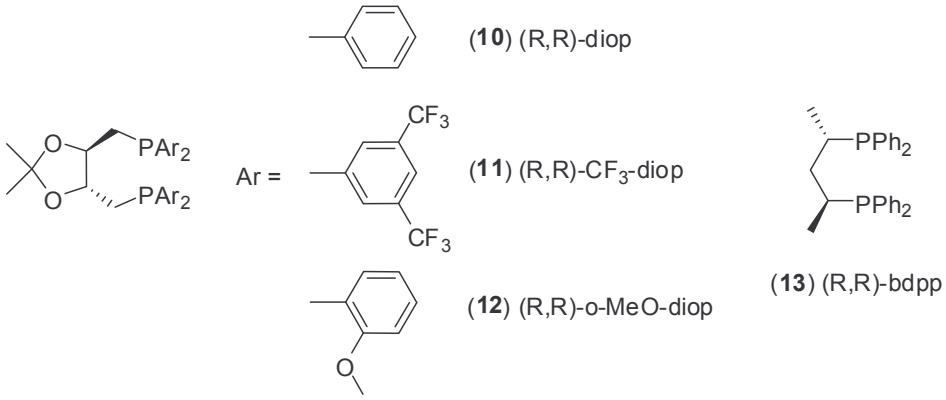

Figure 3.3 Ligands used in this study

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3.2 Experimental

3.2.1 General

All palladium complexes were synthesised using standard Schlenck techniques under nitrogen atmosphere. Diethyl ether, toluene and THF were distilled over sodium/benzophenone and dichloromethane was distilled over P_2O_5. All solvents were deoxygenated before use. $PdCl_2$ was purchased from Johnson Matthey Inc. and used without further purification. bis(*o*-methoxyphenyl)phosphine,[6] [$PdCl_2$(COD)],[7] [$PdCl_2$(*R,R*-diop)],[8] (**10a**) [$PdCl_2$(*R,R*-bdpp)],[9] (**13a**) [Pd(H_2O)(OTs)(*R,R*-bdpp)](OTs),[9] (**13b**) were prepared according to literature methods. All other reagents were used as received from commercial suppliers. Deuterated solvents used for routine NMR measurements were dried over molecular sieves. ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} spectra were recorded on a Varian Mercury 400 spectrometer (400.14, 100.63 and 161.98 MHz, respectively). Chemical shifts were referenced to either TMS as an internal standard (^{1}H and ^{13}C{^{1}H} NMR spectra) or 85% H_3PO_4 as an external standard (^{31}P{^{1}H} NMR spectra). Gas chromatography analyses were performed using a Hewlett-Packard 5890 series II chromatograph with flame ionisation detector and Ultra-2 (5% diphenylsilicone/95% dimethylsilicone) (25 m x 0.2mm Ø) capillary column. Enantiomeric excesses were determined by High Performance Liquid Chromatography analysis (Daicel CHIRACEL OJ, hexane/2-propanol = 95/5, 1.5 ml min^{-1}).

3.2.2 Synthesis of (4*R*,5*R*)-4,5-[bis(di-(3,5-ditrifluoromethylphenyl) phosphino)-methyl] -2,2-dimethyl-1,3-dioxolane (11)

This ligand was prepared following a modification of procedures reported in the literature.[10]

A solution of 1.07 g (2.33 mmol) of bis(3,5-ditrifluoromethylphenyl)phosphine in 2.5 mL of dry tetrahydrofuran was added dropwise in a mixture of KH (98 mg;

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2.39 mmol) deoiled in tetrahydrofuran (0.5 mL) previously cooled to –78ºC over a period of 15 minutes. The dark red solution was stirred at –78ºC for an additional 20 minutes, and then warmed to 25ºC. After stirring at 25ºC for 5 min, the reaction mixture was re-cooled to –78ºC and a solution of (+)-1,4-Di-O-tosyl-2,3-O-isopropylidene-D-threitol (549.8 mg; 1.16 mmol) in 3 mL of tetrahydrofuran was slowly added. The resulting mixture was stirred at –78ºC for 15 min. After warming to 25ºC the mixture was stirred for 5 hours. The solvent was evaporated under reduced pressure and the residue was dissolved in degassed Et_2O (15 mL). The solution was washed with degassed water (4 x 5 mL). The organic layer was separated, dried ($MgSO_4$) and the solvent was evaporated under reduced pressure to give a brown solid material. The product was purified by crystallization with dichloromethane/hexane. Yield: 605 mg white solid (50 %). ^1H ($CDCl_3$, 400 MHz, ppm): δ 1.26 (s, 6H, CH_3), 2.42 (m, 4H, CH_2), 4.05 (m, 2H, OCH), 7.87 (m, 12H, arom.). $^{31}P\{^1H\}$ ($CDCl_3$, 161.9 MHz, ppm): δ -16.3 (s) ppm. Anal.calcd. for $C_{39}H_{24}F_{24}O_2P_2$ (1042.53): C, 44.93; H, 2.51. Found: C, 44.89; H, 2.99. MS (electro spray): m/z 1042.9.

3.2.3 (4*R*,5*R*)-4,5-[bis(di-(2-methoxyphenyl)phosphino)-methyl]-2,2-imethyl-1,3-dioxolane (12)

This ligand was synthesised following a modification of procedures reported in the literature. [11]

BuLi (1 mL, 1.2 mmol) was added dropwise into a solution of 270 mg (1.09 mmol) of bis(*o*-methoxyphenyl)phosphine in 10 mL of dry tetrahydrofuran previously cooled to –10ºC over a period of 15 minutes. The yellow-orange solution was stirred at –10ºC for an additional 20 minutes, then warmed to 25ºC. After stirring at 25ºC for 1 hour, a solution of (+)-1,4-Di-O-tosyl-2,3-O-isopropylidene-D-threitol (250.8 mg; 0.5 mmol) in 10 mL of tetrahydrofuran was slowly added at RT. The resulting mixture was stirred overnight. The solvent was evaporated under

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reduced pressure and the residue was dissolved in degassed CH_2Cl_2 (10 mL). The solution was washed with degassed water (3 x 5 mL). The organic layer was separated, dried ($MgSO_4$) and solvent was evaporated under reduced pressure to give a white solid. The product was purified by crystallization with acetone. Yield: 215 mg white solid (65 %). ^{1}H ($CDCl_3$, 400 MHz, ppm): δ 1.32 (s, 6H, CH_3), 2.38 (dd, $^2J_{HH}$ = 14Hz, $^2J_{HP}$= 6.8 Hz, 2H, CH_2), 2.51(dd, $^2J_{HH}$ = 14Hz, $^2J_{HP}$= 4.4 Hz, 2H, CH_2), 3.69 (s, 6H, OCH_3), 3.72 (s, 6H, OCH_3), 3.99 (m, 2H, OCH), 6.79-6.91 (m, 8H, CH= arom.), 7.13-7.32 (m, 6H, CH= arom.), 7.74-7.78 (bs, *ortho*-CH, 2H). ^{13}C{^{1}H} ($CDCl_3$, 100.63 MHz, ppm): δ 27.52 (CH_3), 29.49 (CH_2), 55.7 (OCH_3), 94.77 (OCH), 110.36-133.19 (CH=, -C-). ^{31}P{^{1}H} ($CDCl_3$, 161.9 MHz, ppm): δ -40.06 (s) ppm. Anal.calcd. for $C_{35}H_{40}O_6P_2$ (618.23) C, 67.95; H, 6.52. Found: C, 68.01 H, 6.70.

3.2.4 Synthesis of [$PdCl_2$(***R,R*-CF_3-diop)] (11a)

A solution of *R,R*-CF_3-diop (250 mg, 0.24 mmol) in dichloromethane (2 mL) was added to a stirred solution of [$PdCl_2$(COD)] (65 mg, 0.23 mmol) in dichloromethane (2 mL) at room temperature, and the mixture was stirred for 1 hour. Addition of Et_2O led to the formation of a pale yellow precipitate, which was isolated by filtration, washed with Et_2O (2×5mL) and hexane (1×5mL) and dried in vacuo. Yield: 180.8 mg of pale yellow solid (64 %). ^{1}H (THF-d^8, 400 MHz, ppm): δ 1.21 (s, 6H, CH_3), 2.92 (m, 2H, CH_2), 3.44 (m, 2H, CH_2), 3.93 (m, 2H, OCH), 8.23 (m, 8H, arom.-H), 8.34 (m, 4H, arom.-H). ^{31}P{^{1}H} ($CDCl_3$, 161.9 MHz, ppm): δ 20.78 ppm (s). Anal. Calcd for $C_{39}H_{24}Cl_2F_{24}O_2P_2Pd$ (1219.85): C, 38.40; H, 1.98. Found: C, 38.29; H, 2.41. MS (malditof) m/z 1184 (M^+-Cl).

3.2.5 Synthesis of [$PdCl_2$(***R,R*-MeO-diop)] (12a)

A solution of *R,R*-MeO-diop (60 mg, 0.09 mmol) in dichloromethane (5 mL) was added to a stirred solution of [$PdCl_2$(COD)] (27.7 mg, 0.09 mmol) in

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dichloromethane (5 mL) at room temperature, and the mixture was stirred for 1 hour. Addition of Et_2O led to the formation of a pale yellow precipitate, which was isolated by filtration, washed with Et_2O (2×5mL) and hexane (1×5mL) and dried in vacuo. Yield: 63.6 mg of a pale yellow solid (74 %). ^1H ($CDCl_3$, 400 MHz, ppm): δ 1.19 (s, 6H, CH_3), 2.7 (m, 2H, CH_2), 3.2 (m, 2H, CH_2), 3.4 (m, 2H, CH), 3.70 (m, 6H,, OCH_3), 4.00 (m, 6H, OCH_3), 6.70-7.02 (m, 8H, CH=), 7.33 (m, 4H, CH=), 7.70 (m, 2H, CH=), 9.21 (m, 2H, *ortho*-H). $^{13}C\{^1H\}$ ($CDCl_3$, 100.63 MHz, ppm): δ 27.02 (CH_3), 28.52 (CH_2), 54.56 (OCH_3), 93.87 (OCH), 110.21-134.25 (CH=, -C-). $^{31}P\{^1H\}$ ($CDCl_3$, 161.9 MHz, ppm): δ 22.16 ppm (s). Anal.calcd. for $C_{35}H_{40}Cl_2O_6P_2Pd$ (795.96): C, 52.81; H, 5.07. Found: C, 53.02 H, 5.12.

3.2.6 Synthesis of [Pd(OH_2)(OTs)(*R,R*-diop)](OTs) (10b)

AgOTs (88.3 mg, 0.32 mmol) was added to a solution of [$PdCl_2$(diop)] (102 mg, 0.15 mmol) in dichloromethane (10 mL) and it was stirred at room temperature overnight. Then the solution was filtered through celite in order to remove AgCl. The solution was concentrated and diethylether was added to precipitate an orange solid, which was washed with diethylether and dried under vacuum. ^1H ($CDCl_3$, 400 MHz, ppm): δ 1.37 (s, 6H, CH_3), 2.31 (s, 6H, CH_3), 2.83 (m, 2H, CH_2), 3.22 (m, 2H, CH_2), 4.34 (m, 2H, CH), 5.97 (s, 2H, H_2O), 6.89 (d, $^3J_{HH}$ = 8 Hz, 4H, Ph-OTs), 7.21 (d, $^3J_{HH}$ = 8 Hz, 4H, Ph-OTs), 7.46 (m, 12H, Ph), 7.74 (m, 8H, Ph). $^{13}C\{^1H\}$ ($CDCl_3$, 100.63 MHz, ppm): δ 21.03 (CH_3-OTs), 26.79 (CH_3), 31.2 (CH_2), 76.33 (OCH), 126.05 (Ar-OTs), 128.51 (Ar-OTs) 128.7-134.4 (CH=, -C-). $^{31}P\{^1H\}$ ($CDCl_3$, 161.9 MHz, ppm): δ 22.07 ppm (s). Anal.calcd. for $C_{45}H_{48}O_9P_2Pd_2S_2$ (965.35): C, 55.99; H, 5.01. Found: C, 56.05 H, 5.20. MS (malditof) m/z 604 ([Pd(DIOP)]$^{+2}$, -2OTs, -H_2O), 793 (M^+-OTs)

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3.2.7 Synthesis of [Pd(OH_2)(OTs)(*R,R*-CF_3-diop)](OTs) (11b)

AgOTs (79 mg, 0.28 mmol) was added to a solution of [$PdCl_2$(CF_3-diop)] (155.3 mg, 0.13 mmol) in dichloromethane (10 mL) and it was stirred at room temperature overnight. Then the solution was filtered through celite in order to remove AgCl. The solution was concentrated and diethylether was added to precipitate a light orange solid, which was washed with diethylether and dried under vacuum. ^{1}H ($CDCl_3$, 400 MHz, ppm): δ 1.26 (s, 6H, CH_3), 2.32 (m, 4H, CH_2), 2.44 (s, 6H, CH_3-OTs), 4.13 (m, 2H, CH), 5.4 (s, 2H, H_2O), 7.3 (d, $^3J_{HH}$ = 8 Hz, 4H, Ph-OTs), 7.7 (d, $^3J_{HH}$ = 8 Hz, 4H, Ph-OTs), 7.81-7.82 (m, 12H, arom-Ph). ^{31}P{^{1}H} ($CDCl_3$, 161.9 MHz, ppm): δ 30.53 ppm (s). Anal.calcd. for $C_{53}H_{40}F_{24}O_9P_2Pd_2S_2$ (1509.34): C, 42.18; H, 2.67. Found: C, 42.32 H, 2.77.

3.2.8 Synthesis of [Pd(OH_2)(OTs)(*R,R*-MeO-diop)](OTs) (12b)

AgOTs (36.1 mg, 0.13 mmol) was added to a solution of [$PdCl_2$(MeO-diop)] (49 mg, 0.06 mmol) in dichloromethane (10 mL) and it was stirred at room temperature overnight. Then the solution was filtered through celite in order to remove AgCl. The solution was concentrated and diethylether was added to precipitate a light orange solid, which was washed with diethylether and dried under vacuum. ^{1}H ($CDCl_3$, 400 MHz, ppm): δ 1.25 (s, 6H, CH_3), 2.23 (s, 6H, CH_3-OTs), 2.83 (m, 2H, CH_2), 3.24 (m, 2H, CH_2), 3.56 (m, 2H, OCH), 3.81 (s, OCH_3, 6H), 4.21 (s, OCH_3, 6H), 5.7 (broad, 2H, OH_2), 6.63-6.73 (m, 4H, arom.-H), 6.94 (d, $^3J_{HH}$ = 8 Hz, 4H, OTs), 7.05 (m, 4H, arom.-H), 7.43-7.60 (m, 8H, arom.-H + TsOH), 7.78 (m, 2H, *ortho*-CH=). ^{13}C{^{1}H} ($CDCl_3$, 100.63 MHz, ppm): δ 21.02 (CH_3-OTs), 26.34 (CH_3), 28.97 (CH_2), 54.36 (OCH_3) 94.32 (OCH), 112.36-141.19 (CH=, -C-). ^{31}P{^{1}H} ($CDCl_3$, 161.9 MHz, ppm): δ 27.5 ppm (s). Anal.calcd. for $C_{49}H_{56}O_{13}P_2Pd_2S_2$ (1085.46): C, 54.22; H, 5.20. Found: C, 52.48 H, 5.59 S, 4.90. MS (malditof) m/z 724 ([Pd(MeO-DIOP)]$^{+2}$, -2OTs, -H_2O).

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3.2.9 Catalysis

High-pressure experiments were carried out in a Berghof autoclave, and the reaction mixtures were magnetically stirred and electrically heated. In a typical experiment, a solution of the palladium precursor (0.015 mmol), *p*-TsOH (0.15 mmol) and styrene (3 mmol) in 5 mL of THF-MeOH mixture (1:1) were introduced into the evacuated autoclave. Carbon monoxide was introduced and the system was then heated. When thermal equilibrium was reached, stirring was initiated. After reaction, the autoclave was cooled to room temperature and depressurised. The product was filtered in a short column of celite and solvent was removed under vacuum. The pure ester was isolated by column chromatography on silica gel using hexane/ethyl acetate (9/1) as the eluent. Conversions, chemo-, regio- and enantioselectivities were determined by GC and HPLC analyses.

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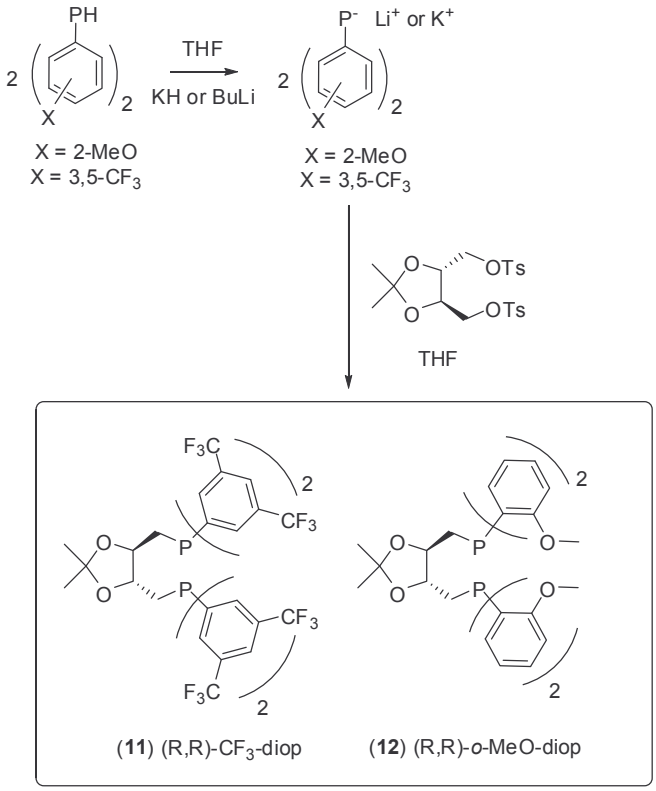
3.3. Results and discussion

3.3.1 Synthesis of diop derivatives ligands

The ligands **11** and **12** were synthesised by reaction between the bis-(3,5-di-trifluoromethylphenyl)phosphine as potassium salt or bis(-2-methoxyphenyl)phosphine as lithium salt and (+)-1,4-Di-O-tosyl-2,3-O-isopropylidene-D-threitol (Scheme 3.1). The ligands were isolated by recrystallisation with dichloromethane/hexane for ligand **11** and acetone for ligand **12** and characterised in solution by multinuclear NMR spectroscopy and in solid state by elemental analysis.



Scheme 3.1 Synthesis of diphosphine ligands **11** and **12**.

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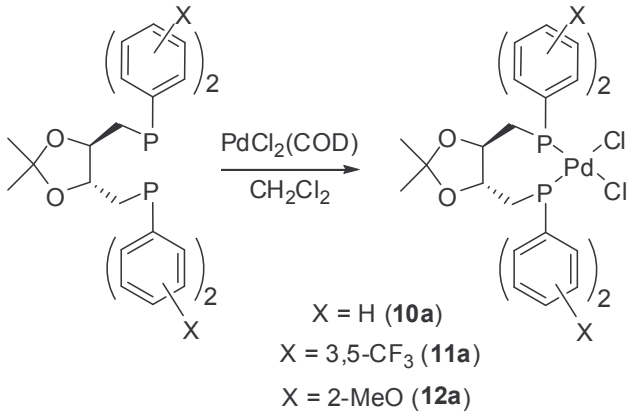
The $^{31}P\{^{1}H\}$ NMR spectra of ligands **11** and **12** showed a singlet at -16.3 and -40.0 ppm, respectively, in accordance with two equivalent phosphorus donor atoms. The aliphatic region of the ^{1}H NMR spectra of ligand **11** showed signals at 1.25 (s), 2.41 (m) and 4.05 (s) ppm, corresponding to a CH_3, CH_2 and CH of the diop-skeleton. In the aliphatic region of the ^{1}H NMR spectra for ligand **12,** the signals at 1.32 (s, C*H*$_3$), 2.38 (dd, $^{2}J_{HH}$ = 14Hz, $^{2}J_{HP}$= 6.8 Hz, C*H*$_2$), 2.51 (dd, $^{2}J_{HH}$ = 14 Hz, $^{2}J_{HP}$ = 4.4 Hz, C*H*$_2$), 3.69 (s, OCH_3), 3,72 (s, OCH_3) and 3.99 (s, C*H*), corresponding to the diop skeleton and methoxy groups of the anisyl moiety, were detected.

3.3.2 Synthesis of neutral palladium(II) dichloro complexes 11a and 12a

The neutral palladium complexes containing CF_3-diop (**11**) and *o*-MeO-diop (**12**) were obtained by reaction of the [$PdCl_2$(COD)] with the ligands in dichloromethane at room temperature (Scheme 3.2).



Scheme 3.2 Synthesis of neutral palladium complexes **10-12a**

The solids were isolated in a pure form as yellow solids, air stables and characterised by multinuclear NMR and elemental analysis. The $^{31}P\{^{1}H\}$ NMR

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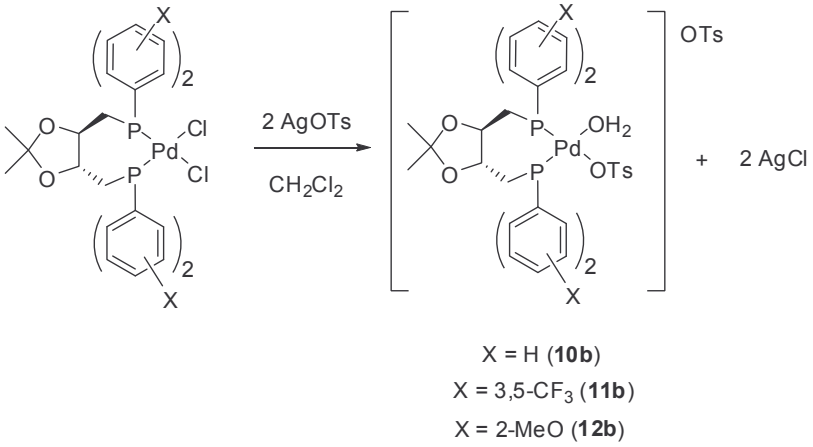
spectrum of the complexes **11a** and **12a** showed a singlet signal at 20.78 and 22.16 ppm, respectively. The complex **12a** shows a high-field shifted ^{1}H multiplet centred at 9.21 ppm, due to the interactions between the *ortho*-aromatic protons in the two apical phenyl rings and the palladium centre.[12]

3.3.3 Synthesis of cationic palladium complexes 10b, 11b and 12b

The cationic palladium (II) complexes were obtained by reaction of dichloro-di-phosphine palladium (II) complexes with silver *p*-tosylate in dichloromethane at room temperature (scheme 3.3).



Scheme 3.3 Synthesis of cationic palladium complexes **10-12b**

The complexes were isolated by precipitation with diethyl ether, as yellow-orange, air-stable solids. The complexes were characterised by multinuclear NMR spectroscopy and elemental analysis. The $^{31}P\{^{1}H\}$ NMR spectra of all complexes showed one singlet centred at 22.01, 30.53 and 27.5 ppm, respectively. The singlet signal for all complexes can be explained considering that the complex can contain two water molecules coordinated to the palladium centre or due to a fast exchange

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of a water molecule with the coordinating tosylate anion. The ^{1}H NMR spectrum of complex **12a** showed a high-field shifted of the *ortho*-aromatic protons in the two apical phenyl rings, as expected.

3.3.4 Catalytic reactions

Asymmetric methoxycarbonylation of styrene using neutral dichloro palladium complexes (10-13)a as catalyst precursors.

In order to test the catalytic behaviour of the neutral complexes towards the methoxycarbonylation of styrene, a series of catalytic reactions were performed using as catalytic system the neutral complexes **10a-12a** in the presence of hydrochlorhydric acid. The results are summarised in table 3.1. All reactions were carried out at 90ºC and for 24 hours using similar reaction conditions of that used for DPEphos-derivative ligands.[5] When of complex **10a** was tested using 100 equiv. of HCl at 30 bar of CO (entry 1) 25% of conversion, 77% of chemoselectivity and 51% of regioselectivity were obtained. The enantiomeric excess was measured to be 30%. When the complex **11a** was used under the same reaction conditions (entry 3) higher activity and chemoselectivity were obtained (65 and 92%).

As it was observed for DPEphos derivatives ligands (Figure 3.1), high regiocontrol was obtained when the reaction was performed using the complex **11a** (92% to the branched product). Unfortunately, the complex **11a** was hardly enantioselective and only 3% of enantiomeric excess was obtained. In contrast to complexes **10a** and **11a**, the complex **12a** (entry 7) was poorly active and chemoselective (17 and 7%, respectively) and the regioselectivity was not determined due to the low yield of esters.

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Table 3.1 Asymmetric methoxycarbonylation of styrene using neutral palladium complexes (**10a-12a**) modified by diop-derivative ligands[a]

Entry	Precursor	Pd/H+/St	P_{CO} (bar)	t_r (h)	%C	%Q	b:l	% ee
1	**10a**	1/100/100	30	24	25	77	51:49	30 (*S*)
2	**10a**	1/100/100	40	24	26	75	32:68	42 (*S*)
3	**11a**	1/100/100	30	24	65	92	92:8	3 (*S*)
4	**11a**	1/100/100	40	24	82	94	65:35	12 (*S*)
5	**11a**	1/10/100	30	24	73	95	67:33	14 (*S*)
6[b]	**11a**	1/10/100	30	24	76	94	48:52	23 (*S*)
7	**12a**	1/100/100	30	24	17	7	-	nd

[a]Reaction conditions: 0.015 mmol Pd, $V_{(THF/MeOH)}$ = 5 mL, THF/MeOH 1:1, H^+ = HCl, 90ºC. [b] *p*-TsOH.

Increasing the CO pressure up to 40 bar (entries 2 and 4), the activity and chemoselectivity remain constant when **10a** was used. For the reaction using **11a**, the conversion and the chemoselectivity were increased (82% and 94%, respectively). However in both cases, similar trends were observed for the regioselectivity and enantioselectivity. The regioselectivity was observed to decrease when the CO pressure was increased. Presumably, higher CO pressures favour linear carboxylic esters, due to a faster insertion of CO into de Pd-$C_{linear\text{-}alkyl}$ bond[13] (Scheme 3.4). Such effect was previously reported by Consiglio *et al.*[14]
Nevertheless, when the CO pressure was increased the complexes **10a** and **11a** showed higher enantiocontrol; 12% with (*R,R*)-CF_3-diop and 42% with (*R,R*)-diop. Concerning the acid, when **11a** was used as catalyst precursor, lower concentration of the Brønsted acid promoted a decrease of the branched/linear ratio (b/l) but enhanced the enantioselectivity (entries 4 and 5).

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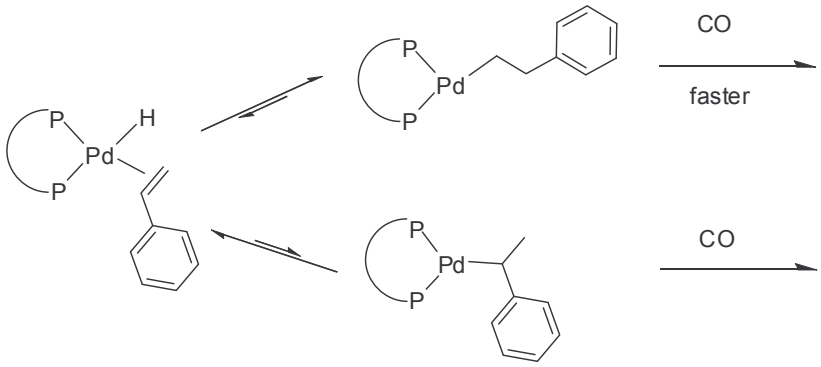
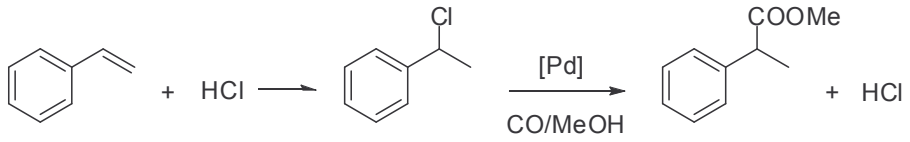


Scheme 3.4 Insertion of CO in the σ-alkyl species

The use of weakly-coordinating anions (such us TsO^-) was preferred over that of coordinating anions (such as Cl^-) in order to achieve higher enantioselectivities (entry 5 and 6). Although, when *p*-TsOH was used the regioselectivity to the branched product decreased. Lee *et al.* have reported that the hydrochlorhydric acid can be inserted into the double bond of the substrate to form the branched 2-methyl benzylchloride.[15] This new branched benzyl halide can also be carbonylated to form 2-aryl propionic carboxylic esters (Scheme 3.5).[16]



Scheme 3.5 Pathway proposed for carbonylation of benzyl chloride under methoxycarbonylation catalytic conditions

In order to clarify if our results are in agreement with the hypothesis of an electronic control of the regioselectivity by means of electron-poor bidentate ligand or if the enhancement in the regioselectivity is due to the aforementioned

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insertion of hydrochlorhydric acid, new cationic palladium precursors were synthesised to be test in methoxycarbonylation of styrene.

Asymmetric methoxycarbonylation of styrene using cationic palladium complexes 10b, 11b and 12b as catalyst precursors.

The reactions catalysed by cationic complexes [Pd(OH_2)(OTs)(P-P)](OTs) bearing ligands **10-12** were performed at 30 bar of CO and 90ºC. The results are summarised in Figure 3.4.

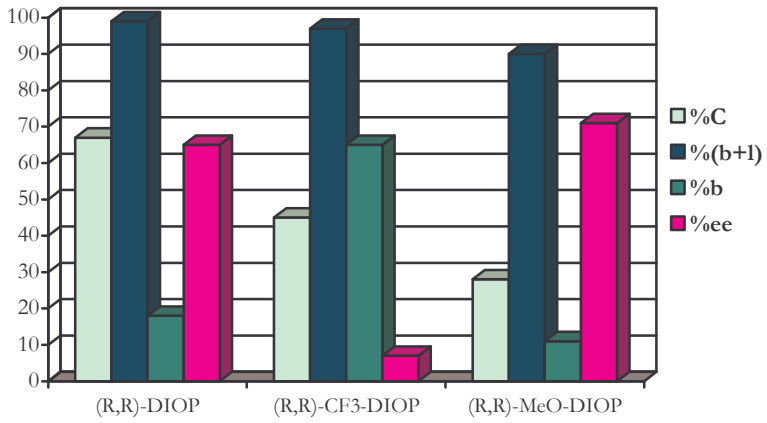

Figure 3.4. Asymmetric methoxycarbonylation of styrene using [Pd(OTs)(OH_2)(L)](OTs) (**10b-12b**) (reaction conditions: 0.015 mmol Pd, $V_{(THF/MeOH)}$ = 5 mL, THF/MeOH 1:1, 30 bar CO, 90ºC)

In terms of activity and chemoselectivity the best system found was using diop as ligand, affording 67% of conversion and 99% of esters. When ligand **11b** was used the activity dropped down to 45%, whereas using ligand **12b** the conversion was only 28%. The chemoselectivities obtained using ligands **11b** and **12b** were 97 and 90%, respectively. In terms of regioselectivity, the ligand **11b** affords the highest

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value to the branched ester (64%). In contrast to this result, when ligands **10b** and **12b** were used in the catalytic systems the regioselectivities to the branched ester were found to be lower (<18%) than when **11b** was used. This value is similar to those obtained when the neutral palladium complex **11a** was used (Table 3.1, entries 3, 4 and 5). From these results, it can be concluded, that the chlorides present in the reaction media are not the responsible for the selectivity observed. Furthermore, the fact that the electron-withdrawing substituents in the ligand **11** have an influence in controlling the regioselectivity was confirmed. A correlation between the electronic properties of the diop and diop-derivatives ligands with the regioselectivity was established. In terms of enantioselectivity, cationic systems provide better enantioselectivities (up to 71% when ligand **12b** was used) than the neutral palladium complexes.

In summary, the electron withdrawing groups on the phenyl moieties favoured the formation of branched product; while the use of the ligand containing electron donor groups on the phenyl moiety afforded high regioselectivity to the linear product. This finding is remarkable in terms of catalysts design, in order to control the regioselectivity of the reaction. However, explanation of these results remains somewhat speculative. Three possibilities are suggested: In the presence of ligand **11b**, the corresponding electron-poor catalyst might lead to the formation of (alkoxycarbonyl)palladium species which direct the insertion of the olefin to branched compounds. An alternative explanation for the branched regiocontrol observed, might be found in the capability of the electron-poor ligand **11b** to enhance isomerization to a *trans*-coordinated species during the catalytic cycle or even to act as a monodentate ligand (Figure 3.5).[17] In general, these results show that the regioselectivity could be controlled by the electronic properties of the ligands. However, the role played by the acid media and conditions can also controlled the selectivity and activity of the process and cannot be discarded as important factors for developing new catalyst systems.

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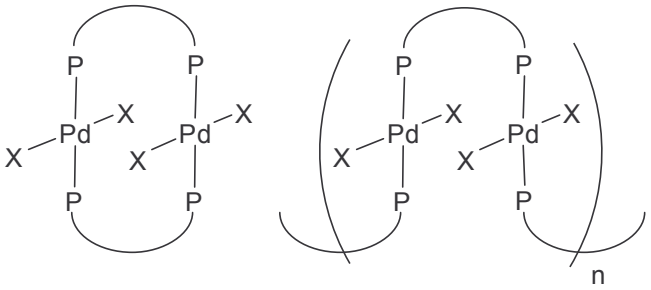

Figure 3.5 Possibility of *trans*-coordination of diphosphines

Asymmetric methoxycarbonylation of styrene using palladium complexes 13a and 13b as catalyst precursors

The asymmetric methoxycarbonylation of styrene was also tested using (*R,R*)-bdpp (**13**) as ligand in different neutral (**13a**) and cationic (**13b**) palladium precursors. The results obtained are shown in table 3.2. First of all, the effect of Brønsted acids in combination with the neutral palladium (II) complex was studied (entries 1-4). When hydrochlorhydric acid was used (HCl/Pd =100, entry 1), low conversion and chemoselectivity were obtained. Surprisingly, the regioselectivity to the branched ester was high 91%. Reducing the amount of acid from 100 to 10 equivalents (entry 2), the conversion was even lower but the chemoselectivity was improved. For this system, the regioselectivity was low affording 57% of the branched ester. No chiral induction was observed when hydrochlorhydric acid was used. When *p*-toluensulfonic acid was used introducing weakly-coordinating counteranions in the system (entry 3) the conversion was 91%, whereas the chemoselectivity was only 62%. Although the regioselectivity went down to 18%, the enantiomeric excess improved considerably up to 45%. When the amount of *p*-toluensulfonic acid decreases (entry 4) an increased in the chemoselectivity up to 92% was observed. It is well-known that in the presence of large amount of acid,

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the formation of (2-methyl)benzylmethyl-ether is favored.[18] Moreover, formation of oligomers was detected. It has been observed that the systems containing bidentate diphosphines afford preferably oligomers and copolymers, for CO/ethene copolymerisation reaction.[19]

Table 3.2 Asymmetric methoxycarbonylation of styrene using the cationic palladium complex modified with bdpp (**13**)[a]

Entry	Precursor	Pd/H$^+$/St	t_r (h)	%C	%Q	b:l	% ee
1	**13a + HCl**	1/100/100	24	19	59	91:9	nd
2	**13a + HCl**	1/10/100	24	5	71	57:43	nd
3	**13a + TsOH**	1/100/100	24	91	62	18:82	45 (*S*)
4	**13a + TsOH**	1/10/100	24	93	92	19:81	48 (*S*)
5	**13b**	1/-/100	24	97	98	18:82	51 (*S*)
6	**13b**	1/-/100	6	66	>99	16:84	56 (*S*)
7[b]	**13b**	1/-/100	6	53	98	16:84	58 (*S*)

[a]Reaction conditions: 0.015 mmol Pd, $V_{(THF/MeOH)}$ = 5 mL, THF/MeOH 1:1, 30 bar CO, 90ºC. [b]15 bar CO.

Performing the reaction with the cationic palladium(II) precursor **13b** without acid (entry 5), high conversion and chemoselectivity was obtained (97 and 98%, respectively). The regioselectivity was constant and the enantiomeric excess slightly increased (51%). When the reaction was carried out during 6 hours (entry 6), the conversion was found to be 66%. The chemo-, regio and enantioselectivity were unchanged. Diminishing the CO pressure down to 15 bar shows a decreased in the conversion of styrene (53%). However, the highest enantioselectivity was observed under these conditions. The results obtained with this system showed that the conversions and selectivities are influenced by the nature of counteranions.

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Moreover, the results obtained using neutral complex **13a** in the presence of *p*-TsOH are similar to that obtained using complex **13b** in absence of acid. This observation suggests that similar starting species can be formed in both systems. The fact that the complex **13b** presents the same catalytic activity of **13a** but in absence of acid is an important approach.

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3.4. Conclusions

In conclusion, the substituents of the phenyl ring moiety contained in DIOP derivative diphosphines influences the regioselectivity of the methoxycarbonylation of styrene. We have demonstrated that electron-poor diphosphines containing CF_3-groups in the 3,5-positions of the phenyl rings afford high regioselectivities to the branched ester. It should be noted that the same effect was observed with diphosphines exhibiting important differences in terms of rigidity (DPEphos). However, the explanation of the role of the electronic properties of the phosphine on the regioselectivity of the reaction is not completely understood. Under the same reaction conditions the cationic system containing bdpp was more active than the system modified by diop, although the enantioselectivity was lower. The highest enantioselectivity was observed for the system containing electron-donor susbtituents **12**, but affording low regioselectivity to the branched ester.

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Chapter 4

Mechanistic studies for palladium systems modified with monodentate and bidentate phosphines

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4.1. Background

One of the key step in the design of new catalytic systems is the understanding of the mechanisms operating in the catalytic reactions. For mechanistic studies, NMR and IR spectroscopy are the most common tools to identify the resting states of the reactions.[1] Theoretical calculations have also been used to determine transition states of low energy.[2] The important advances of these techniques in the study of the resting intermediates for processes such as Rh-catalysed hydroformylation are well-known.[3] However, the detection of intermediates in Pd-carbonylation reactions have proven to be more difficult. As previously mentioned, palladium hydrides and/or palladium-alkoxycarbonyl species are proposed to start the catalytic cycle involved in the palladium-catalysed alkoxycarbonylation reaction, of alkenes (Chapter 1, Scheme 1.3). Both types of complexes have been previously identified by HPNMR and HPIR techniques, as well as some intermediates of the methoxycarbonylation of ethylene.[4,5,6,7] Theoretical calculations have also been used to investigate the methanolysis step.[8,9] In this section, an overview of the mechanistic studies previously reported for the alkoxycarbonylation of styrene using mono- and bidentate ligands will be described.

All mechanistic studies using monodentate ligands were reported using systems containing triphenylphosphine as ligand. Chaudhari *et al.* reported an *in situ* HPNMR study using $[Pd(OTs)_2(PPh_3)_2]$ as precursor, and identified the palladium hydride complex $[PdH(L)(PPh_3)_2](OTs)$ (**A**, Scheme 4.1) L = CO, PPh_3) and several palladium(0) species $[Pd(CO)_{(4-n)}(PPh_3)_n]$ (n=2-4) (**B**-**D**, Scheme 4.1). [10] In this report, the dimers **E** and **F,** containing bridging hydride and carbonyl ligands and bridging hydroxyl groups respectively, were also detected (Scheme 4.1). Acyl and alkyl complexes were also proposed for comparison of the ^{31}P resonances reported in the literature for similar complexes. They concluded that the catalytic cycle proceeds through an hydride mechanism rather than a carbomethoxy mechanism.

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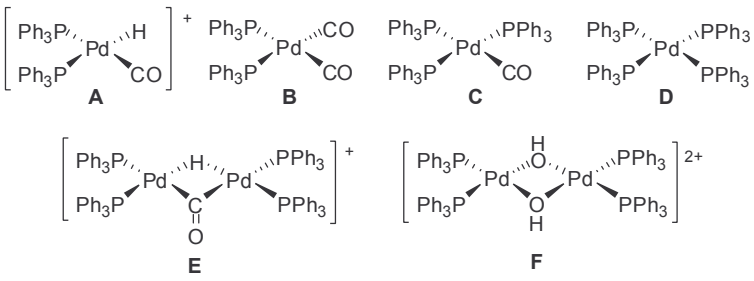

Scheme 4.1 Species detected by Chaudhari *et al* in the methoxycarbonylation of styrene using $[Pd(OTs)_2(PPh_3)_2]$ as precursor.

Claver and co-workers studied the hydroxycarbonylation of styrene using an *in situ* system including palladium(II) precursor, triphenylphosphine and oxalic acid.[11] Using $[Pd(OAc)_2]$ as precursor, several Pd(0) species of formula $[Pd(CO)(PPh_3)_n]$ (n= 2, 3) were observed, as well as free phosphine and phosphine oxide. When $[PdCl_2(PhCN)_2]$ was used as precursor, the palladium hydride $[Pd(H)Cl(PPh_3)_2]$ and both linear and branched acyl chlorides complexes were detected at high and low CO pressures. From this study, they concluded that the regioselectivity of the system was dependent on the temperature and pressure; with high temperatures and low pressures favouring the formation of the linear acid. Elsevier and co-workers recently reported the formation of similar hydride species, starting from Pd(0)alkene complexes bearing triphenylphosphine in the presence of *p*-TsOH.[12] Heil *et al.* reported a deuterium-labelling study of the alkoxycarbonylation of styrene using the system $[PdCl_2(PPh_3)_2]/SnCl_2$.[13] They concluded that the alkyl-metal intermediates easily undergo β-hydride elimination and that their results supported that the hydrido route was operating under these conditions.

Recently, Wendt *et al.* reported a mechanistic study of the hydroxycarbonylation of styrene using TPPTS as ligand.[14] They observed different palladium (II) complexes of the type $[Pd(TPPTS)_n]^{2+}$ (3 or 4), as well as, the hydride complex $[PdH(TPPTS)_3]$ and the hydrido-carbonyl dimer **E**. In the presence of ^{13}C-labelled

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styrene, the η^3-benzylic complex was detected (a, Figure 4.1). Acyl complexes were also detected in this study.

Mechanistic studies into the palladium-catalysed alkoxycarbonylation of styrene using bidentate ligands have also been performed. van Leeuwen *et al.* studied the insertion of styrene into palladium acyl and carbomethoxy complexes [PdR(L)(P-P)] (R=COOMe or COMe, L=MeCN or PPh_3, P-P= dppe, dppp and dppb).[15] They observed that palladium η^3-benzyllic complexes are obtained by the insertion of styrene into the Pd-$C(O)CH_3$ (b, Figure 4.1), while the insertion into the palladium carbomethoxy bond was not observed under the conditions of this study.

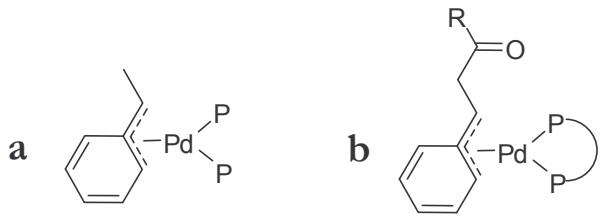

Figure 4.1 η^3-benzylic species observed under carbonylation conditions

Claver and co-workers study the precursors $Pd(OAc)_2$ and $PdCl_2(PhCN)_2$ in the presence of dppb and oxalic acid.[11] They observed the presence of hydride species at high temperatures in the presence of carbon monoxide.

Bianchini *et al.* studied the methoxycarbonylation of styrene using cationic palladium complexes modified with the 1,1'-bis(diphenylphosphino)metallocene ligands showed in Figure 4.2.[16] All reactions were studied using HPNMR spectroscopy in methanol and in the presence of *p*-TsOH and styrene. They also observed the formation of the bridge hydrido-carbonyl dinuclear complex [$Pd_2(\mu$-H)(μ-CO)(P-P)$_2$] (analogue of **E** in Scheme 4.1).

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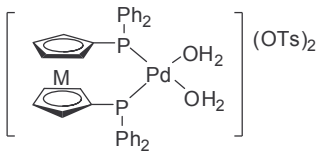

Figure 4.2 Diphosphine-metallocene ligands

Analogous dinuclear species of complex **E** have also been reported for dippp,[17,18] and (*S,S*)-bdpp,[19] in carbonylation studies and have been proposed as a resting state in the palladium-catalysed carbonylation processes.[20,21,22]

Although these mechanistic studies have elucidated important steps of the mechanism, the factors that govern the regioselectivity of the alkoxycarbonylation are still to be established.

Considering the importance of the mechanism operating in this reaction for the design of new catalytic systems and in order to identify some of the palladium intermediates involved in the systems developped in this work, a mechanistic study based on NMR experiments was completed. The spectroscopic study of two palladium systems modified with monodentate and bidentate ligands will be described in this chapter.

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4.2. Experimental

4.2.1 General

All palladium complexes were synthesised using standard Schlenck techniques under nitrogen atmosphere. Diethyl ether, toluene and THF were distilled over sodium/benzophenone and dichloromethane was distilled over P_2O_5. All solvents were deoxygenated before use. The phosphetane **3**[23] and the palladium complexes $[PdCl_2(NCPh)_2]$,[24] $[PdCl_2(COD)]$,[25] $[PdCl_2(\mathbf{3})_2]$ **3a**,[26] $[PdCl_2(R,R\text{-bdpp})]$ **13a**,[22b] $[Pd(H_2O)(OTs)(R,R\text{-bdpp})](OTs)$ **13b**,[27] were prepared according to literature methods. All other reagents were used as received from commercial suppliers. Deuterated solvents used for routine NMR measurements were dried over molecular sieves. ^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ spectra were recorded on a Varian Mercury 400 spectrometer (400.14, 100.63 and 161.98 MHz, respectively). Chemical shifts were referenced to either TMS as an internal standard (^1H and $^{13}C\{^1H\}$ NMR spectra) or 85% H_3PO_4 as an external standard ($^{31}P\{^1H\}$ NMR spectra). High-pressure NMR experiments (HPNMR) were carried out in a 10 mm diameter sapphire tube with a titanium cap and the spectra recorded using a Varian 300 MHz spectrometer.[28]

4.2.2 HPNMR measurements

In a typical experiment, the NMR tube was charged under N_2 with a solution containing the palladium precursor (0.04 mmol), *p*-TsOH (when needed, 0.4 mmol) and styrene (0.8 mmol) in a mixture of deuterated solvents CD_3OD/tetrahydrofuran-d^8 (1:1) (2 mL). The tube was then pressurised with CO to the desired pressure.

4.2.3 Synthesis of $[PdCl_2(3)]_2$ 3c

To a solution of **3a** (89.5 mg, 0.12 mmol) in dichloromethane (5 mL) was added a solution of $[PdCl_2(COD)]$ (35.8 mg, 0.12 mmol) in dichloromethane (5 mL). The

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reaction was left to stir at room temperature overnight. The solution was concentrated under vacuum and diethylether (3 mL) was added to precipitate the complex. The orange solid was recrystallised in hexane to obtain complex **3c** as red crystals. Yield: 65 mg (58%). ^{1}H NMR (CD_2Cl_2, 400.13 MHz, ppm): δ 0.82 (d, $^{3}J_{(H-H)}$ = 7 Hz, CH_3), 0.97 (d, $^{3}J_{(H-H)}$ = 7 Hz, CH_3), 1.01 (s, CH_3), 1.02 (d, $^{3}J_{(H-H)}$ = 7 Hz, CH_3), 1.11 (m, CH_2), 1.26 (d, $^{2}J_{(H-H)}$ = 18 Hz, CH), 1.51 (d, $^{2}J_{(H-H)}$ = 21 Hz, CH), 1.56 (s, CH_3), 1.65 (m, CH_2), 1.71 (s, 2 CH_3), 1.90 (m, 2 CH_2), 2.64 (m, CH). ^{13}C{^{1}H} NMR (CD_2Cl_2, 100.63 MHz, ppm): δ 17.8 (s, CH_3), 20.1 (s, CH_3), 22.6 (s, CH_3), 23.8 (s, CH_3), 25.0 (s, CH_3), 25.2 (CH_2), 25.9 (d, $J_{(P-C)}$ = 16 Hz, CH_3), 28.3 (s, CH_3), 31.6 (s, CH), 34.0 (d, $J_{(P-C)}$= 13 Hz, CH_2), 34.5 (s, CH_2), 36.4 (d, $J_{(P-C)}$= 11 Hz, CH), 36.7 (s, C), 42.3 (s, CH), 45.7 (broad, CH); ^{31}P{^{1}H} NMR (CD_2Cl_2, 161.98 MHz, ppm): δ 94.5 (s).

4.2.4 X-ray data collection and structure determination of $[PdCl_2(3)]_2$ 3c

Data collection for crystal structure analysis was carried out at 293(2) K on an Enraf Nonius CAD4 single crystal diffractometer (Mo-Kα radiation, λ = 0.71073 Å). Cell refinement, indexing and scaling of all the data set were performed using programs Denzo and Scalepack.[29] The structure was solved by direct methods and subsequent Fourier analyses[30] and refined by the full-matrix least-squares method based on F^2 with all observed reflections.[30] A difference Fourier map revealed in the asymmetric unit a molecule of chloroform. All the calculations were performed using the WinGX System, Ver 1.70.01.[31]

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4.3. Results and discussion

In order to identify metallorganic species which might be formed during catalytic methoxycarbonylation of vinyl arenes, systems containing monodentate and bidentate ligands were studied under conditions close to those used during catalytic experiments. The catalyst precursor [$PdCl_2$(**3**)$_2$] **3a** containing the phosphetane **3** (Figure 2.1, chapter 2) was first chosen as a model system. The cationic complex [Pd(OH_2)(OTs)(*R,R*-bdpp)](OTs) **13b** (Figure 3.3, chapter 3) was used later. The attempts to synthesise a cationic complex bearing the phosphetane **3**, in order to compare the same precursor, were unsuccessful. Thus, the palladium dichloro-complex modified with monodentate ligand **3** in the presence of *p*-toluensulfonic acid was used. This system was previously tested in this reaction and the corresponding results were described in Chapter 2. In the next sections the monitoring of the reactions by NMR experiments using these two systems will be described.

4.3.1 Study of the $PdCl_2$(3)$_2$ (3a)/*p*-TsOH system modified with monodentate phosphine ligand, under methoxycarbonylation conditions.

As was shown in chapter 2, the system involving [$PdCl_2$(**3**)$_2$] and *p*-TsOH presents catalytic activity in the asymmetric methoxycarbonylation of vinyl arenes, affording high regioselectivity to the branched ester. In order to know more about the nature of the catalytic species formed during the catalysis, a series of NMR and HPNMR experiments were carried out. In the following sections the reaction of the complex [$PdCl_2$(**3**)$_2$] in the presence of *p*-TsOH, CO and styrene will be described.

Complex 3a in CD_3OD/THF-d^8

A solution of complex **3a** (0.02 mmol) in CD_3OD/THF-d^8 was prepared in a 5 mm NMR tube. In the corresponding $^{31}P\{^1H\}$ NMR spectrum acquired at room temperature the signal at 61 ppm, corresponding to the starting material, was

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detected. A new $^{31}P\{^{1}H\}$ NMR spectrum was acquired at 323 K and no new signals were observed. The tube was kept at this temperature and new $^{31}P\{^{1}H\}$ NMR spectra were recorded every 30 min for 6 hours. At the end of the experiment, only the signal corresponding to the starting complex was observed, suggesting that the complex **3a** is stable in methanol at 323 K.

Reaction of complex 3a in CD_3OD/THF-d^8 in the presence of p-TsOH.

In a 5 mm NMR tube, *p*-TsOH (5 equiv) was added to a solution of complex **3a** (0.02 mmol) in CD_3OD/THF-d^8. The signal at 61 ppm, corresponding to the starting material, was readily detected in the corresponding $^{31}P\{^{1}H\}$ NMR spectrum acquired at room temperature (a, Figure 4.3). No other signals were detected at this temperature.

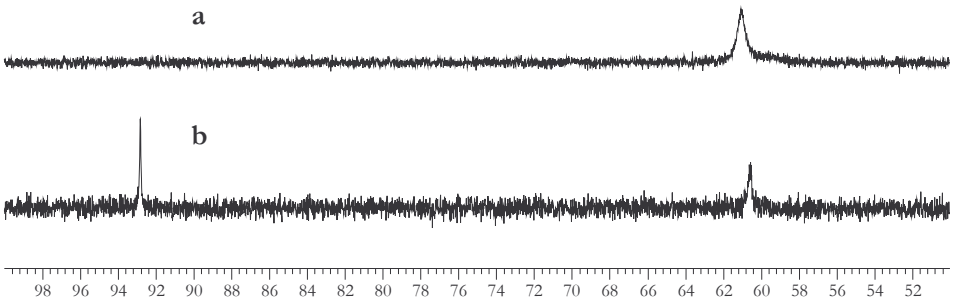

Figure 4.3 Spectra of complex **3a** in CD_3OD/THF-d^8 in the presence of 5 equiv. of *p*-TsOH a) at room temperature, b) at 323 K.

However, when a $^{31}P\{^{1}H\}$ NMR spectrum was acquired at 323 K, two signals were observed: the signal at 61 ppm and a new singlet resonance at 93 ppm (b, Figure 4.3). This new signal indicated that a reaction between the complex **3a** and *p*-toluensulfonic acid in CD_3OD/THF-d^8 had ocurred. In the ^{1}H NMR spectrum in the aliphatic region, signals corresponding to those of the complex **3a** and new signals (selected signals: 0.97 (d, J_{HH} = 7 Hz), 1.02 (d, J_{HH} = 7 Hz), 1.26 (d, J_{HH} =

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18 Hz), 1.51 (d, J_{HH} = 18 Hz)) were detected. This new signals were similar to those of **3a**, suggesting that the new species contained one or several phosphetane ligands coordinated. In the corresponding $^{13}C\{^1H\}$ spectrum, signals of the new species revealed an AX pattern for the *ipso*-carbons, suggesting that this species did not contain phosphetane ligands in *trans* configuration (chapter 2), in contrast to complex **3a** for which the *trans* disposition of two phosphetane ligands gave rise to a AXX' pattern for the *ipso* carbons. After a few days at room temperature, red and yellow crystals appeared from the solution. X-ray diffraction of both sets of crystals revealed that the yellow crystals corresponded to the starting material **3a** (x-ray structure shown in chapter 2) and that the red crystals corresponded to a new complex which was identified as [Pd(μ-Cl)Cl(**3**)]$_2$ **3c**. The molecular structure of **3c** is shown in Figure 4.4. Selected bond lengths and angles are listed in Table 4.2. When some of these crystals were dissolved in CD_2Cl_2, the signal at 93 ppm was again detected in the corresponding $^{31}P\{^1H\}$ NMR spectrum, demonstrating that **3c** was the species formed at 323 K. In the X-ray structure of **3c**, both palladium centres exhibit a distorted square planar geometry and the menthyl groups are situated on the same side of the plane defined by the Pd(1)Cl(4)Cl(3)Pd(2). The angle between the mean coordination planes Cl(1)/P(1)/Cl(3)/Cl(4) and Cl(2)/P(2)/Cl(3)/Cl(4) was 16.98(6)º. The angles for Cl(1)-Pd(1)-Cl(3) and Cl(2)-Pd(2)-Cl(4) were found to be 174.19(6)º and 173.96(7). The Pd(1)-Cl(1) and Pd(2)Cl(2) bond lengths were measured to be *ca.* 2.27 Å while the Pd-P bonds were *ca.* 2.23 Å and 2.22 Å for Pd(1)P(1) and Pd(2)P(2), respectively. As expected, the Pd-$Cl_{bridging}$ bond lengths were found to be larger than the Pd-$Cl_{terminal}$. The Pd(1)Cl(3) and Pd(2)Cl(4) bond lengths were smaller than Pd(1)Cl(4) and Pd(2)Cl(3), suggesting that each choro ligands are bonded to the palladium centers 1 and 2 in a covalent and dative manner. The X-ray structure of the analogue compound bearing triphenylphosphine ligands was reported by Chatt and Mann.[32]

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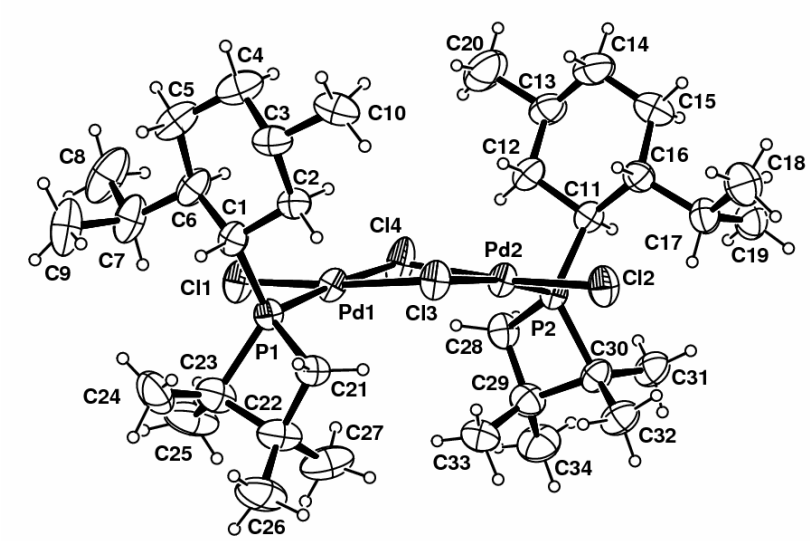

Figure 4.4 ORTEP drawing (35% probability ellipsoids) with atom labelling scheme of the dinuclear complex **3c**. The lattice $CHCl_3$ molecule not shown

They suggested that although this dimeric complex crystallise in a *trans* disposition, the symmetric *cis* complex $[(PPh_3)ClPd(\mu\text{-}Cl)PdCl(PPh_3)]$ and the complex $[Cl_2Pd(\mu\text{-}Cl)Pd(PPh_3)_2]$ exist in solution. However, in the $^{31}P\{^1H\}$ spectra of **3c** in CD_2Cl_2, only one signal was detected, suggesting the presence of only one isomer in solution. Under our experimental conditions, the formation of **3c** can be explained by the dissociation of one phosphetane ligand followed by the reaction of two 14 e^- fragments.

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Table 4.1 Experimental X-ray diffraction parameters and crystal data for **3c**

Empirical formula	$C_{34}H_{64}Cl_4P_2Pd_2 \cdot CHCl_3$
M	1008.76
Crystal system	Monoclinic
Space group	P 2_1
a/Å	11.279(3)
b/Å	14.873(3)
c/Å	14.891(3)
β/°	109.58
Unit cell volume/Å^3	2353.5(9)
D_{calcd}/g cm^{-3}	1.423
Z	2
μ(Mo Kα)/mm^{-1}	1.252
F(000)	1032
T/K	293(2)
λ/ Å	0.71073
Absorption correction	DIFABS
Refinement method	Full-matrix least-squares on F^2
Data/parameter	8093/430
Final *R* indices	[$I > 2\sigma(I)$] $R_1 = 0.0413$, $wR_2 = 0.0998$
R indices (all data)	$R_1 = 0.0550$, $wR_2 = 0.1054$
Goodness-of- fit on F^2	0.901
Absolute structure parameter	0.00(3)
Largest diff peak and hole (e/Å^3)	0.602/-0.450

Table 4.2 Selected bond length (Å) and angles (°) for **3c**

Pd(1)-P(1)	2.230(1)
Pd(1)-Cl(1)	2.267(1)
Pd(1)-Cl(3)	2.335(1)
Pd(1)-Cl(4)	2.416(1)
Pd(2)-P(2)	2.224(1)
Pd(2)-Cl(2)	2.273(1)
Pd(2)-Cl(4)	2.305(1)
Pd(2)-Cl(3)	2.479(1)
P(1)-Pd(1)-Cl(1)	90.36(5)
P(1)-Pd(1)-Cl(3)	94.59(4)
Cl(1)-Pd(1)-Cl(3)	174.19(6)
P(1)-Pd(1)-Cl(4)	175.98(6)
Cl(1)-Pd(1)-Cl(4)	89.50(5)
Cl(3)-Pd(1)-Cl(4)	85.78(5)
P(2)-Pd(2)-Cl(2)	91.09(5)
P(2)-Pd(2)-Cl(4)	91.94(5)
Cl(2)-Pd(2)-Cl(4)	173.96(7)
P(2)-Pd(2)-Cl(3)	171.68(5)
Cl(2)-Pd(2)-Cl(3)	92.73(5)
Cl(4)-Pd(2)-Cl(3)	84.97(5)
Pd(1)-Cl(3)-Pd(2)	92.38(4)
Pd(2)-Cl(4)-Pd(1)	94.79(5)

In order to check the role of this new complex in catalysis, attempts to synthesise the dimer **3c** were performed following reported procedure.[32] However, this method was found to be unsuccessful. Nevertheless, when a solution of

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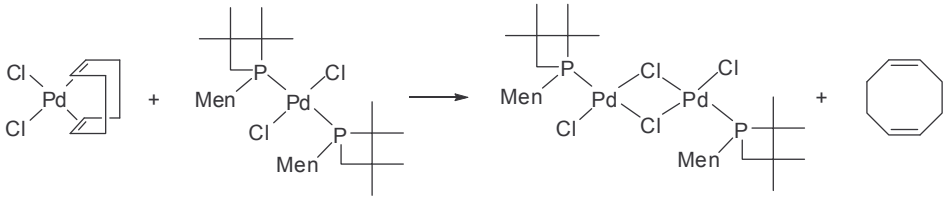
[$PdCl_2$(COD)] and [$PdCl_2$(**3**)$_2$] was stirred for 2 hours in dichloromethane, the formation of **3c** was observed (Scheme 4.2).



Scheme 4.2 Synthesis of the dimer **3c**

The dimer was obtained in a pure form by recrystallisation in hexane. When the dimer **3c** was tested in catalysis, under the same catalytic conditions than those used for complex **3a**, the new dimer was found to be scarcely active in the methoxycarbonylation of styrene. The complex only afforded 12% of conversion in contrast to that obtained with complex **3a** (97%). The chemo- and regioselectivity were 70 and 85%, respectively, and the enantiomeric excess was 8%. This result was interesting since no enantioselectivity was observed using the complex **3a**. From this result it was concluded that the complex **3c** is active in this reaction, but is not responsible for the overall selectivity of our system. As free phosphetane should be produced during the formation of **3c**, the reactivity of phosphetane **3** in the presence of acid was investigated.

Reaction of free phosphetane in CD_3OD in the presence of p-TsOH

When a sample of phosphetane **3** was dissolved in CD_3OD a $^{31}P\{^1H\}$ NMR spectrum was acquired, a signal at 18 ppm was detected and readily assigned to the free ligand.[23] When *p*-TsOH (0.5 equiv.) was added to the solution, the $^{31}P\{^1H\}$ NMR spectra acquired at room temperature showed a very broad signal at *ca.* 30 ppm. In the ^1H NMR spectrum, new signals corresponding to the *p*-TsOH at 2.3

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(s, CH_3), 7.1 (d, $^3J_{HH}$ = 8.4 Hz) and 7.7 (d, $^3J_{HH}$ = 8.4 Hz) ppm were detected. When the spectrum was acquired at 223 K (a, Figure 4.5) the signal corresponding to the free phosphetane and a new signal at 39.0 ppm as a pseudo triplet with 1:1:1 intensity pattern were observed. The multiplicity of the signal at 39.0 ppm suggested the formation of a new species containing deuterium with a P-D coupling of 140 Hz.

The experiment was then repeated in proteo methanol instead of CD_3OD and 1 equiv. of *p*-TsOH was added. After evaporation of the methanol, the residue was redissolved in deuterated dichloromethane. In the $^{31}P\{^1H\}$ NMR spectrum at room temperature the signal at 39.0 ppm was again detected as a broad singlet (b, Figure 4.5).

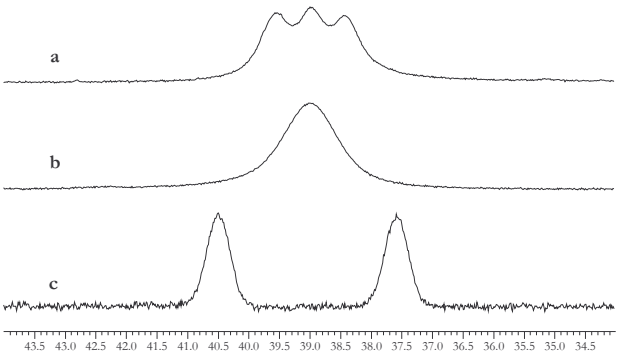

Figure 4.5 $^{31}P\{^1H\}$ NMR spectra of free phosphetane **3**. a) **3** + 0.5 equiv. *p*-TsOH in CD_3OD at 223 K, b) **3** + 1 equiv. *p*-TsOH in CD_2Cl_2 at RT, c) ^{31}P spectrum of **3** + 1 equiv. *p*-TsOH in CD_2Cl_2 at at 223 K.

In the ^1H NMR spectrum recorded at room temperature a new broad signal at 7.4 ppm was observed together with the signals of *p*-TsOH and those of free phosphetane. When a ^{31}P spectrum was recorded at 223 K, the signal previously observed at 39.0 ppm exhibited a doublet multiplicity $J_{P\text{-}H}$ = 470 Hz (c, Figure 4.5).

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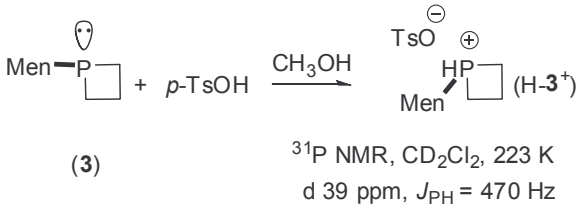
The same multiplicity and coupling constant were observed in the ^{1}H NMR spectrum for the signal previously observed at 7.4 ppm. The value of the $J_{P\text{-}H}$ is characteristic of a compound containing a P-H bond. The species corresponding to this signal at 39.0 ppm was therefore identified as H-**3**$^{+}$ in Scheme 4.3.



Scheme 4.3. Protonation of the free phosphetane **3.** The methyl groups in 2,2',3,3' positions of the phosphetane ring are not shown for clarity

McFarlane et al, reported the $^{1}J(^{31}P\text{-}H)$ spin coupling values for a series of protonated tervalent organophosphorus compounds.[33] The coupling constants varied from 457 and 506 Hz for alkyl and phenyl phosphines. These values are in agreement with that measured for **3**-H^{+}. Leoni *et al.* observed the formation of Cy_3PH^{+} by addition of CF_3SO_3H to a solution of $[Pd(H)(OH_2)(PCy_3)_2]BF_4$ in $CDCl_3$ and THF-d^8. with a $J_{P\text{-}H}$ =475 Hz, which is very similar to that observed for phosphetane H-**3**$^{+}$.[34] The formation of the dimer **3c** from complex **3a** and *p*-toluensulfonic acid is proposed as shown the Scheme 4.4.

Reaction of complex 3a in CD_3OD/d^8-THF in the presence of p-TsOH and carbon monoxide (35 atm)

A solution of the precursor **3a** (0.04 mmol) and *p*-TsOH (5 equiv.) in CD_3OD/THF-d^8 as solvents was prepared and placed in the HPNMR tube. After pressurising with CO (35 bar) a $^{31}P\{^{1}H\}$ NMR spectrum was acquired at room temperature. The signal at 61 ppm corresponding to the starting material **3a** was

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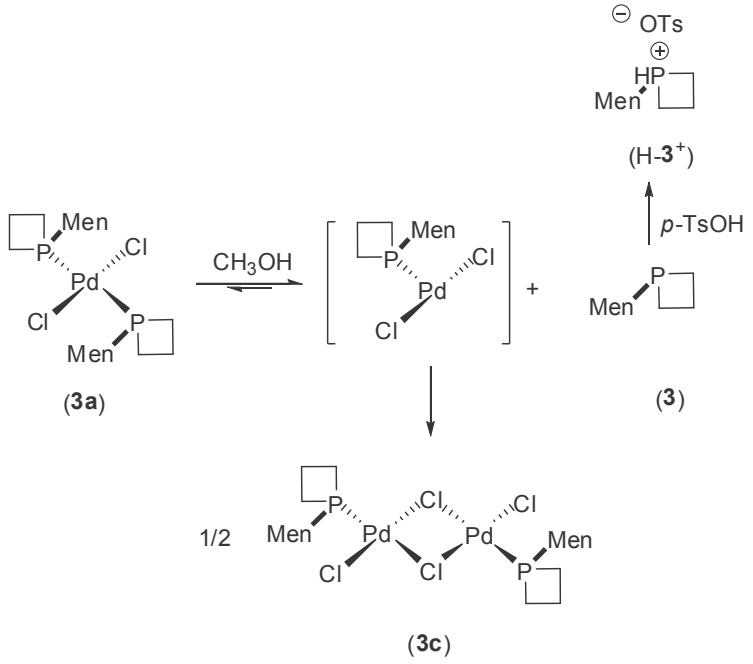
detected. At this temperature no other signals were detected. The temperature was then increased up to 323 K and a new $^{31}P\{^{1}H\}$ NMR spectrum was recorded, but no changes were observed.



Scheme 4.4 Proposed mechanism for the formation of complex **3c**.

This observation suggested that no reaction had occurred under these conditions. As the lack of stirring could explain this observation, the complex **3a** and *p*-TsOH (5 equiv.) in CD_3OD/THF-d^8 was stirred in a schlenck overnight at 323 K and the solution was later transferred to the 10 mm HPNMR tube. A first $^{31}P\{^{1}H\}$ NMR spectrum was acquired at room temperature before pressurising with CO and two signals were detected: the signal at 61 ppm (major species), corresponding to the starting complex $PdCl_2(\mathbf{3})_2$ **3a** and a singlet signal at 93 ppm, previously identified as the dimer **3c** (a, Figure 4.6). In the ^{1}H NMR spectrum no hydride signals were observed, as could be expected in CD_3OD. The tube was then charged with CO

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(35 bar) and the reaction was monitored by ^{31}P NMR spectroscopy. The decrease in intensity of the signal at 93 ppm was apparent, while the signal at 61 ppm remained unchanged (b, Figure 4.6). When the temperature was increased to 323 K, the signal at 93 ppm corresponding to the dimer **3c** was not observed and only the signal at 61 ppm was detected (c, Figure 4.6).

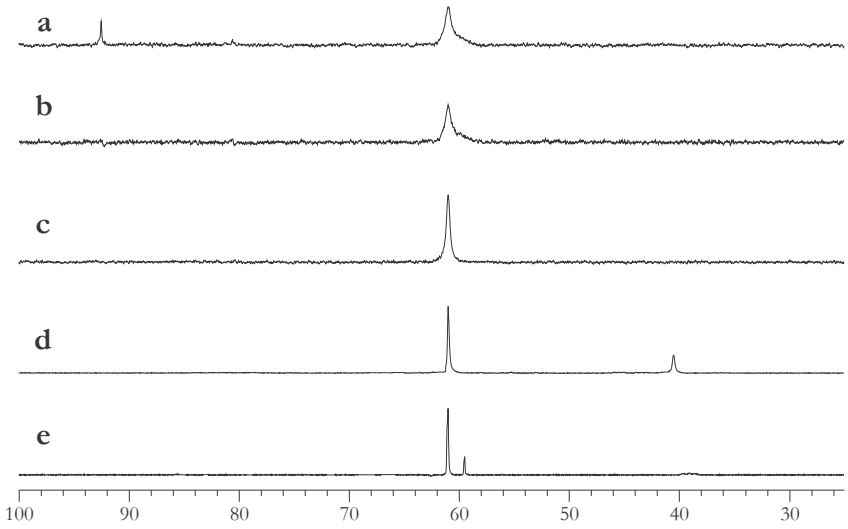

Figure 4.6 Sequence of ^{31}P NMR spectra of complex **3a** in CD_3OD/THF-d^8. a) **3a**+ *p*-TsOH at RT before pressurising CO, b) **3a**+ *p*-TsOH at RT after pressurising CO 35 bar, c) **3a**+ *p*-TsOH at 323 K after pressurising CO bar, d) **3a**+ *p*-TsOH at RT, e) **3a**+ *p*-TsOH at 223 K.

After few minutes at this temperature a new signal was detected at 39.0 ppm, while the signal at 61.0 ppm, corresponding to the starting material, remained unchanged (d, Figure 4.6). The signal at 39.0 ppm was readily assigned to the protonated phosphetane H-**3**$^+$. At this point, in order to stabilise palladium species involved in the reaction, the temperature was rapidly decreased to room temperature. The $^{31}P\{^1H\}$ NMR spectrum at this temperature revealed the presence of the starting complex **3a** and the protonated phosphetane H-**3**$^+$, that had been previously

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observed at 323 K. No new signals were detected. When the experiment was repeated using ^{13}CO, the same signals were detected in the $^{31}P\{^{1}H\}$ spectrum. In the corresponding $^{13}C\{^{1}H\}$ NMR spectrum at 323 K, two singlet resonances were detected at 185.0 and 186 ppm. The former signal was readily assigned to free CO. Although the chemical shift of the resonance at 186 ppm is characteristic of a carbonyl ligand coordinated to palladium, its singlet multiplicity indicated that no phosphetane ligand was contained in this species. When the temperature was decreased down to 223 K, the signal at 61 ppm in the $^{31}P\{^{1}H\}$ NMR spectrum (e, Figure 4.6) corresponding to the starting material, was resolved into two singlets at 61.2 and 59.7 ppm. These signals were readily assigned to the two rotameric forms of complex **3a** in solution (chapter 2). The signal at 39 ppm appeared as a pseudo triplet with 1:1:1 intensity pattern, ($J_{P\text{-}D}$ = 140 Hz), as expected for the P-D bond of D-**3**$^{+}$. In the $^{13}C\{^{1}H\}$ NMR spectra at 223 K, the signal at 186 ppm was again detected as a singlet. The chemical shift of this signal indicates the formation of a Pd-CO species, in which the CO is a terminal ligand. Pd-carbonyl complexes that would fit with this signal are proposed in Figure 4.7. Calderazzo *et al.* reported that the complex **a** (Figure 4.7) can be synthesised from $PdCl_2$ in the presence of CO pressure (50 bar) and 120ºC.[35] Complex di-μ-chloro-bis[carbonylpalladium(I)] (**b**, Figure 4.7) has been synthesised, characterised by x-ray diffraction and study by theoretical calculations.[36,37,38] The complex **c** (Figure 4.7) has been recently reported.[39] The species corresponding to this ^{13}C resonance could not be identified in the context of this study.

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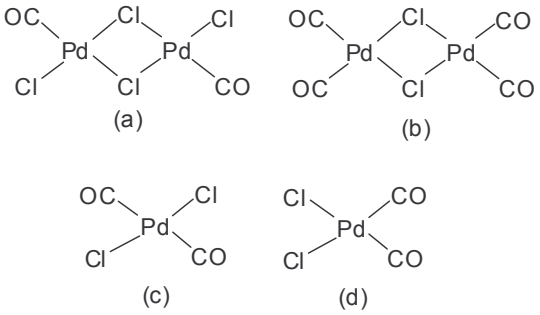

Figure 4.7 Proposed carbonyl palladium complexes for the $^{13}C\{^1H\}$ signal observed at 186 ppm.

Reaction of complex 3a in CD_3OD/d^8-THF in the presence of p-TsOH, styrene and carbon monoxide (35 atm)

A solution of the precursor **3a** (0.04 mmol) and *p*-TsOH (5 equiv.) in CD_3OD/THF-d^8 as mixture of solvents was stirred in a schlenck overnight at 323 K. Styrene (20 equiv.) was added and the solution was transferred to the 10 mm HPNMR tube. A first $^{31}P\{^1H\}$ NMR spectrum was acquired at room temperature before pressurising with CO. In the spectrum the signal at 61 ppm (starting complex $PdCl_2$(**3**)$_2$ **3a**, major species) and a singlet signal at 93 ppm (dimer **3c**) were detected. The tube was then charged with CO (35 bar) and the reaction was monitored by ^{31}P NMR spectroscopy. The signal at 61 ppm remained unchanged while the signal corresponding to **3c** decreased in intensity. When the temperature was increased to 323 K, the signal at 61 ppm (**3a**) and a signal at 39.0 ppm (H-**3**$^+$) were detected. The experiment was repeated using ^{13}CO and no changes were observed in the $^{31}P\{^1H\}$ spectrum. In the corresponding $^{13}C\{^1H\}$ NMR spectrum at 323 K, four singlet resonances were detected at 186.0, 185.0, 173.8 and 175.4 ppm. The former signal at 186.0 ppm was previously detected in absence of styrene. The signals at 185.0, 173.8 and 175.4 ppm were readily assigned to free CO, the linear and the branched ester, respectively. The detection of the latter

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signals indicated that the methoxycarbonylation reaction was taking place. When the HPNMR tube was cooled at 223 K, no changes were detected in the $^{31}P\{^{1}H\}$ and $^{13}C\{^{1}H\}$ NMR spectra. It was concluded that the intermediates of reaction were not stable enough to be detected by NMR spectroscopy under these conditions. However, since compounds **3a**, **3c** and H-**3**$^{+}$ can be detected throughout the HPNMR study, it was concluded that only a small quantity of these species take part in the catalytic cycle.

Reaction of protonated phosphetane H-3^{+} and palladium complexes

In order to investigate the reactivity of the protonated phosphetane H-**3**$^{+}$, observed as a major product in the HPNMR experiment, towards palladium complexes, an experiment involving **3**-H^{+} in the presence of $Pd(OAc)_2$ was performed. The experiment was carried out by addition of $Pd(OAc)_2$ (0.25 equiv.) into a solution of protonated phosphetane in dichloromethane-d^2. The reaction was first monitored by ^{1}H NMR spectroscopy. When a ^{1}H NMR spectrum was acquired at room temperature, no new signals were observed. In order to favour the formation of new species the tube was heated to 333 K overnight. When a new ^{1}H NMR spectrum was then recorded at room temperature an hydride signal at -18.3 ppm was apparent as a broad singlet (a, Figure 4.8). When the spectrum was acquired at 193 K, three singlet signals were detected in the hydride region at -17.5, -17.9 and -18.3 ppm (b, Figure 4.8). It was therefore concluded that reaction of protonated phosphetane H-**3**$^{+}$ with $Pd(OAc)_2$ yielded palladium hydride species at 323 K. The fact that the protonated phosphetane is able to form palladium-hydrides in the presence of palladium sources is key in this process, as these species are initiators in the alkoxycarbonylation reaction (see Chapter 1, section 1.2.5).

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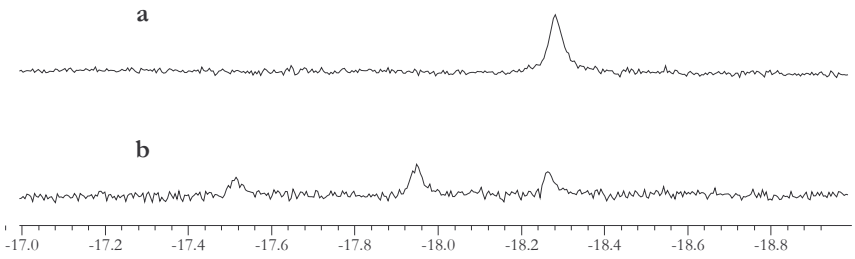

Figure 4.8 Selected region of the ^{1}H NMR spectra of phosphetane **3** + *p*-TsOH + 0.25 equiv. $Pd(OAc)_2$ in CD_2Cl_2. a) at room temperature, b) at 193 K.

This experiment indicated that the presence of **3**-H^+ during the catalytic reaction can lead to the formation of Pd-H species by reaction with Pd complexes present in solution, thus offering the possibility of initiating a new catalytic cycle.

In the $^{31}P\{^{1}H\}$ spectrum acquired at 323 K, 5 signals were detected: that corresponded to the protonated phosphetane at 39 ppm, that at 84 ppm previously assigned to the phosphetane oxide and three new signals at 50.9, 66.1 and 150 ppm (a, Figure 4.9). The singlet signal at 66.1 ppm was suggested to a palladium complex of the type $PdX_2(P)_2$, where (X = OAc, OTs), by comparison to the chemical shift corresponding to complex $PdCl_2(\mathbf{3})_2$ **3a**.. The two signals at 50.9 and 150 ppm exhibited a doublet multiplicity ($^{2}J_{PP}$ = 357 Hz), corresponding to two both mutually coupled phosphorus, and thus indicating the formation of a palladium complex with two non-equivalent phosphorus based ligands. When the spectrum was acquired at 193 K (b, Figure 4.9) the signals at 50.9 and 150 ppm were found to greatly sharpen. When a ^{31}P spectrum coupled to ^{1}H was acquired at 193 K (c, Figure 4.9), the signals at 50.9 and 150 ppm did not exhibit extra couplings, indicating that the corresponding ligands did not contain a P-H moiety.

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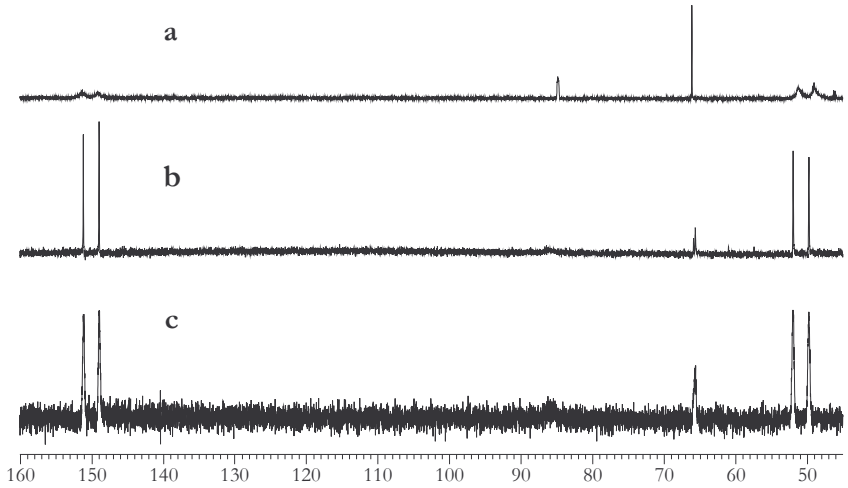

Figure 4.9 Selected sequence of $^{31}P\{^{1}H\}$ NMR spectra. a) **3** + *p*-TsOH + 0.25 equiv. $Pd(OAc)_2$ in CD_2Cl_2 at 60ºC overnight, spectrum acquired at RT. b) **3** + *p*-TsOH + 0.25 equiv. $Pd(OAc)_2$ in CD_2Cl_2 at 60ºC overnight, spectrum acquired at 193 K. c) ^{31}P NMR spectrum **3** + *p*-TsOH + 0.25 equiv. $Pd(OAc)_2$ in CD_2Cl_2 at 60ºC overnight, spectrum acquired at 193 K.

In the ^{1}H-^{31}P HMBC spectrum, no correlation between the hydride signals and phosphorus resonances was detected, indicating that the species containing hydrides were not containing phosphetane ligands. Furthermore, comparison of the intensities of the hydride signals in ^{1}H spectrum and the signals observed in the $^{31}P\{^{1}H\}$ spectrum suggested that the hydrides and phosphorus are not present in the same complex. The weak intensities of the hydride signals revealed that these species are present in low concentrations. Concerning the signals in the $^{31}P\{^{1}H\}$ spectrum, the high field signal (150 ppm) and the coupling constant ($^{2}J_{PP}$ = 357 Hz) suggested the presence of a bridging phosphido group, as was previously reported for similar compounds.[40] It was therefore concluded that the new species formed contained two types of phosphorus based ligands: a bridging phosphido

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group (δ 150.0 ppm) and a terminal phosphetane group (δ 50.9 ppm). Two structures that would fit to these features are described in Figure 4.10. The formation of a phosphido group would involve a carbon phosphorus bond cleavage.

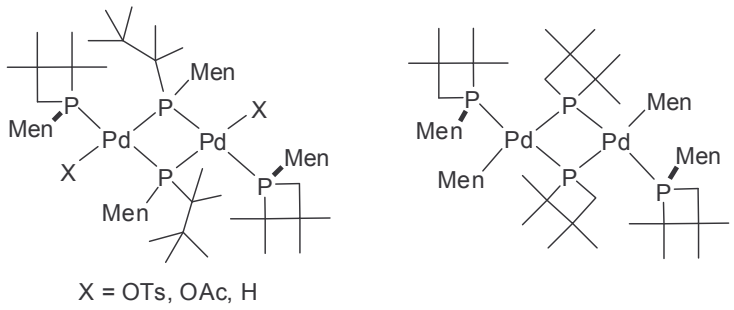

Figure 4.10 Phophido-phosphetane palladium complexes proposed.

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Conclusions of this study

In view of the results obtained in section 4.3.1, the following conclusions relative to our catalytic system could be extracted.

- The complex **3c** was shown to be formed from **3a** in the presence of acid.
- The complex **3c** was shown to be active in the methoxycarbonylation of styrene, affording 12% of conversion, 70% chemoselectivity, 85% of regioselectivity to the branched product and 8% of ee.
- The phosphetane ligand **3** used in this study was shown to react with *p*-TsOH to form a protonated species containing a P-H moiety. It was demonstrated that this latter species could be involved in the formation of palladium hydride complexes.
- When HPNMR experiments were completed in the presence of styrene, the detection of new palladium species was not achieved as the reaction was to fast on the NMR time scale.
- During the HPNMR experiment, palladium carbonyls species were detected.

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4.3.2 Study of Palladium Systems Modified with Bidentate Phosphine Ligand [Pd(OH_2)(OTs)(*R,R*)-bdpp](OTs) 13b under methoxycarbonylation conditions.

In chapter 3, the cationic complex **13b** was used as catalyst precursor for the methoxycarbonylation of styrene. This complex was active in the absence of acid, affording enantioselectivity up to 58%. However, the drawback of this system was the low regioselectivity to the branched esters. In order to obtain more information about the behaviour of this catalytic system, the reactivity of the complex **13b** with methanol, *p*-TsOH, CO and styrene was studied stepwise as follow.

Reaction of complex 13b in methanol

In an NMR tube a solution of complex **13b** in dichloromethane-d^2 was prepared. When a ^{1}H NMR spectrum was acquired at room temperature, 5 signals were observed in the aliphatic region at δ 1.34 (dd, J_{PH}=6.8 Hz and J_{HH}= 16 Hz, 6H, Me), δ 2.29 (s, 6H, Me_{TsO}), δ 2.30 (m, 2H, CH_2), δ 2.96 (m, 2H, CH) and 4.38 (br s, 2H, H_2O). The latter signal was assigned to the hydrogen atoms of the coordinated water molecule. In the corresponding $^{31}P\{^1H\}$ spectrum, a single peak at 27.9 ppm was detected. However, when the ^{1}H NMR spectrum of **13b** was acquired in CD_3OD, only 4 signals were detected in the aliphatic region at δ 1.21 (dd, J_{PH}=7 and J_{HH}= 16 Hz, 6H, Me), δ 2.25 (tt, J_{PH}=6.8 and J_{HH}= 21 Hz, 2H, CH_2), δ 2.30 (s, 6H, Me_{TsO}), and δ 2.98 (m, 2H, CH). The absence of a ^{1}H signal for the coordinated water molecule could be explained by a substitution of H_2O by CD_3OD as described in Scheme 4.5. In the corresponding $^{31}P\{^1H\}$ spectrum, recorded at room temperature, a single peak at 31.5 ppm was detected. At this temperature, no other signals could be observed.

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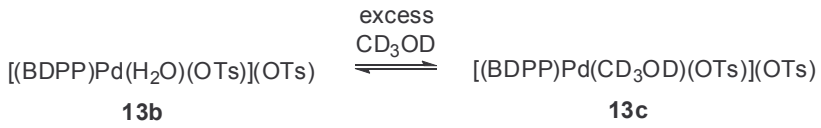

Scheme 4.5 Reactivity of **13b** in CD_3OD

When the sample was heated to 323 K and the reaction monitored by ^{31}P NMR spectroscopy, two new signals were detected at δ 29.5 and δ 6.8 ppm as two mutually coupled doublets ($^2J_{PP}$= 52 Hz) after a few minutes (Figure 4.11).

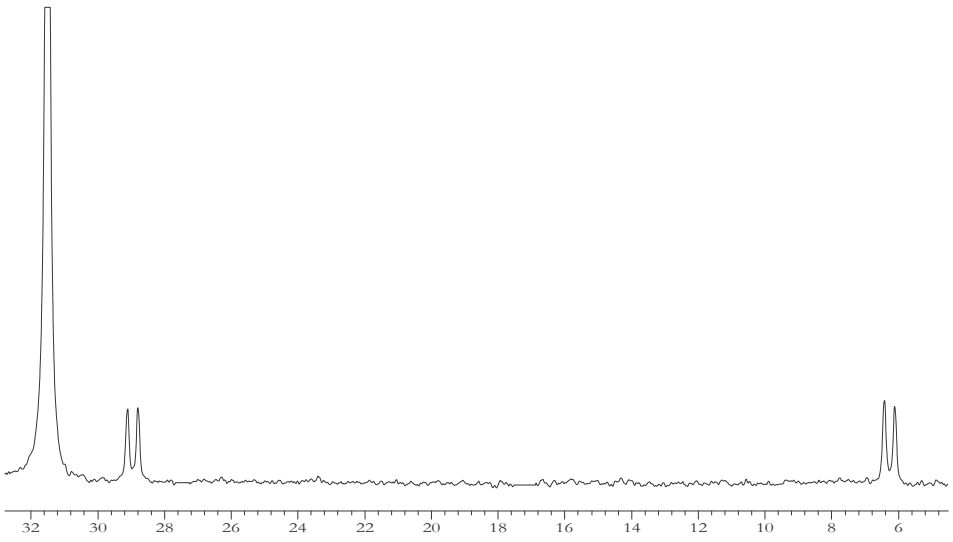

Figure 4.11 $^{31}P\{^1H\}$ NMR spectra. a) Complex **13b** in CD_3OD at RT, b) complex **13b** in CD_3OD at 323 K

This indicated the formation of a new species containing two inequivalent phosphorus centres. One of the chemical shifts is very close to that of the starting material and suggests the presence of a TsO group *trans* to this atom. The other

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chemical shift at 6.8 ppm suggests the presence of a different type of ligand in *trans* position to this atom. After a few minutes at 323 K, 20% conversion to this new species was measured. When the sample was left at this temperature for longer time, the conversion was found to remain unchanged, suggesting that this new species **13d** was in equilibrium with the starting complex [Pd(CD_3OD)(OTs)(*R,R*-bdpp)]OTs **13c**. Taking into account the reagents present in solution, two possibilities can be proposed. First, as the coordination of methanol is a plausible step, the formation of a palladium-methoxy complex can occur. However, in the presence methanol, the formation of palladium-hydrides by β-hydrogen elimination from methoxy complexes usually occurs (see Chapter 1, section 1.2.5). The new complex **13d** can therefore be identified as [Pd(X)(OTs)(bdpp)](OTs) where X is a hydride or a methoxy ligand, as shown the Figure 4.12.

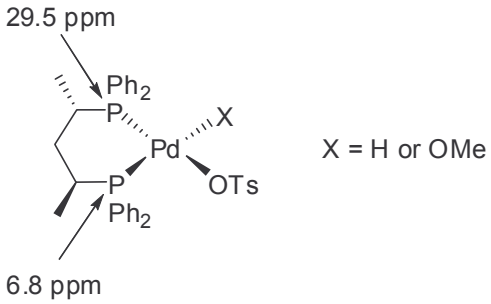

Figure 4.12 New complex **13d**.

Elsevier et al reported the synthesis of the complex [Pd(CH_3)(OCH_3)(*S,S*-bdpp)] at low temperatures.[19] Iggo and co-workers synthesised and characterised the complex [Pd(CH_3CN)(OCH_3)(dippp)]OTf at 193 K.[6] However, they have not studied the reactivity of this species at higher temperatures.

The formation of hydride species via the oxidation of MeOH into formaldehyde has previously been proposed (Scheme 4.6).[17,19] Moreover, Heaton *et al.* recently

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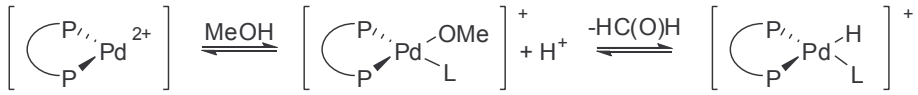
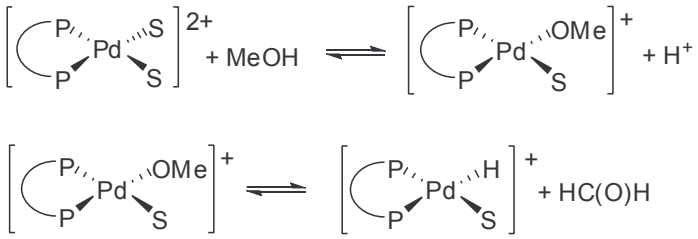
reported the synthesis of a series of palladium(II) hydrido-solvento complexes starting from palladium complexes of the type [Pd(dba)(P-P)] in the presence of BQ and TfOH.[4a,b]



Scheme 4.6 Proposed route to obtain palladium hydrides in methanol

Reaction of 13c in methanol and in the presence of p-TsOH

The presence of acid has been proposed to inhibit the formation of palladium-methoxy and palladium-hydride (Scheme 4.7).[16]



Scheme 4.7

Moreover, Heaton *et al.* also observed that the formation of the complex $[Pd(solv)_2(d^tbpx)]^+$, direct precursor of the Pd-methoxy and Pd-hydride, is inhibited by the formation to $[Pd(d^tbpx)(\eta^2\text{-}RSO_3)]^+$ when R = Me or *p*-MeC_6H_4 as shown Scheme 4.8.[4a]

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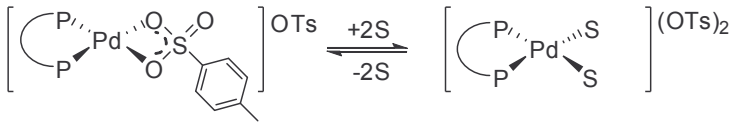
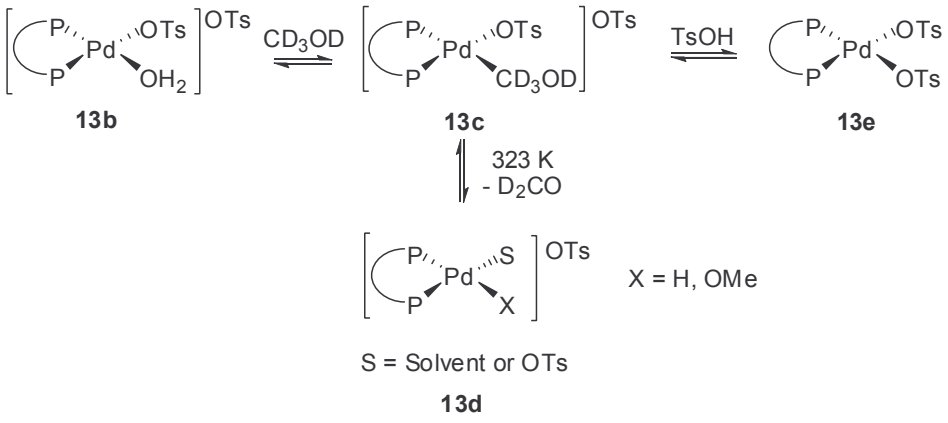


Scheme 4.8

In order to investigate the reactivity of **13b** in the presence of acid, a sample of **13b** was dissolved in CD_3OD and 5 eq of TsOH were added. When a $^{31}P\{^1H\}$ spectrum was recorded, the signal at 31.5 ppm was readily detected. Under these conditions no other signals could be observed, even when the temperature was increased up to 323K. The absence of the previously detected signals at δ 29.5 and δ 6.8 at 323 K indicated that the formation of the species **13d** was inhibited by the presence of acid. This result confirmed the identity of **13d** as a Pd-H or Pd-OMe species. The formation of the complex **13d** could be explained by the proposed mechanism described in Scheme 4.9, where the equilibrium is displaced towards the complex **13e** in the presence of an excess of *p*-TsOH..



Scheme 4.9 Formation of active species starting from $[Pd(OH_2)(OTs)(R,R\text{-bdpp})](OTs)_2$

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Reaction of complex 13b in CD_3OD in the presence of carbon monoxide (1 bar)

Once explored the reactivity of complex **13b** in the presence of MeOH and *p*-TsOH, the behaviour of complex **13b** towards CO at 1 and 15 bar was studied. When an NMR tube was charged with a CD_3OD solution of **13b** and CO was bubbled through the solution for 5 min, the corresponding ^{1}H and $^{31}P\{^{1}H\}$ spectra were found to be identical to those of **13b** without CO, indicating that no reaction had occurred.

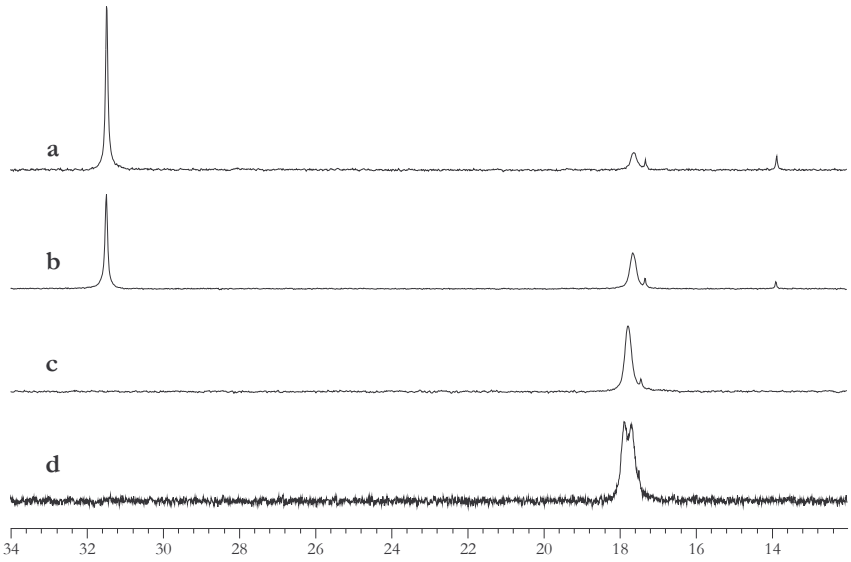

Figure 4.13 $^{31}P\{^{1}H\}$ NMR spectra of complex **13b** in CD_3OD in the presence of CO (1 bar) a) at 323 K, b) at 323 K after 4 hours, c) complex **13b** in CD_3OD in the presence of ^{13}CO (1 atm) at 323 K after 4 hours.

When the temperature of the sample was heated to 323 K for a few minutes, in the $^{31}P\{^{1}H\}$ NMR spectrum, the signals of the starting material and three new singlet signals at 14.1, 17.5 and 17.8 ppm were detected (a, Figure 4.13). After a few

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minutes the same signals were detected. However, the signal at 17.8 was found to increase in intensity (b, Figure 4.13). After 2 hours at 323K, only two resonances were visible in the $^{31}P\{^{1}H\}$ spectrum: the ^{31}P resonance at δ 17.8 was found to correspond to the main reaction product (ca. 95 %) whereas the signal at δ 17.5 was detected as a minor product (ca. <5%) (c, Figure 4.13). At this point, the signal corresponding to **13b** was not detected, indicating that full conversion had been reached. When the reaction was repeated with ^{13}CO (c, Figure 4.13), the ^{31}P resonance at δ 17.8 was detected as a broad doublet (J_{PC}= 32 Hz) (d, Figure 4.13). In the ^{1}H spectrum (a, Figure 4.14), a new signal was detected at δ -4.92 as a quintet (J_{PH}= 44 Hz), that correspond to a hydride coupled with four equivalent phosphorus atoms. In the corresponding $^{13}C\{^{1}H\}$ spectrum (b, Figure 4.14), a quintet was detected at δ 241.0 (J_{PC}= 32 Hz).

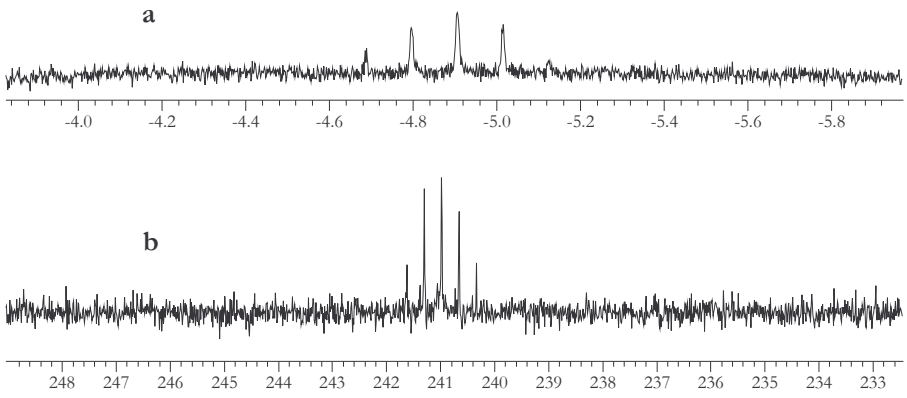

Figure 1.14 Selected regions of the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra. a) Hydride region in the ^{1}H spectrum, b) Carbonyl region in the $^{13}C\{^{1}H\}$ spectrum.

The chemical shift of the latter signal suggests the presence of a bridging carbonyl between two palladium centres. Elsevier and co-workers previously reported the formation of a dinuclear palladium hydrido-carbonyl complex using (*S,S*)-bdpp as

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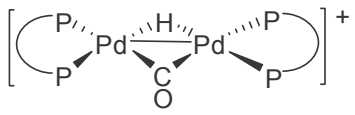
ligand.[19] Comparing the spectroscopic features reported by Elsevier *et al.*, the major product of the reaction under these conditions was identified as the dimer $[Pd_2(\mu\text{-}H)(\mu\text{-}CO)(R,R\text{-bdpp})_2](OTs)$ **13g** (Figure 4.15).



13g

Figure 4.15 Palladium hydrido-carbonyl dimer

As it was previously reported, the dinuclear species **13g** is not rigid.[17,19] While in the solid state, the two phosphorus atoms coordinated to the same palladium atom are not equivalent, the $^{31}P\{^1H\}$ NMR in solution at room temperature exhibits a singlet signal. From this observation, it was concluded that the species [Pd(X)(OTs)(*R,R*-bdpp)]OTs **13d**, previously observed in the last section, was the hydride [Pd(H)(OTs)(*R,R*-bdpp)]OTs.

In order to investigate the reactivity of the species **13g** in the presence of the substrate, styrene was added to the previously formed dimer and $^{31}P\{^1H\}$ and $^{13}C\{^1H\}$ NMR spectra were recorded at room temperature at 323, 333 and 343 K. However, no changes were observed and it was concluded that no reaction between **13g** and styrene was occurring under these conditions.

Reaction of complex 13b in CD_3OD in the presence of carbon monoxide (15 atm)

In order to study the reactivity of **13b** at higher CO pressures, the experiment was repeated using 15 atm of CO at room temperature. In the $^{31}P\{^1H\}$ NMR spectrum recorded a few minutes after the introduction of the CO pressure, two signals were detected at 31.5 ppm, corresponding to the starting material (**13b**) and at 14.1 ppm.

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After 30 minutes the spectrum showed the signals at 31.5 (**13b**), 14.1 and a new broad signal at 17.8 ppm. The latter signal was readily assigned to the hydrido-carbonyl dimer [Pd(μ-H)(μ-CO)(*R*,*R*-bdpp)]$_2$ (**13g**), previously observed (see last section). After 2 hours, the intensity of the signal corresponding to the starting material had decreased considerably, while signals at 17.8 and 14.1 appear as the major products together with a new signal at 17.5 ppm which appeared as a well-defined singlet. In the carbonyls region of the $^{13}C\{^1H\}$ NMR spectrum the signal at 241 ppm corresponding to **13g** and two new signals at 191.3 ppm (t, J_{PC}= 55 Hz) and 191.7 (br) were detected. The chemical shifts of latter signals can correspond to palladium species containing terminal carbonyls. When the $^{31}P\{^1H\}$ NMR spectrum was recorded after 14 hours at room temperature three signals were observed. The major signal at 17.8 ppm (the dimer **13g**), the signal at 17.5 ppm and a new signal at 41.5 ppm were detected. The latter signal was readily assigned to the phosphine oxide. The signal at 14.1 ppm was not detected at this stage, indicating that the corresponding species is an intermediate complex in the formation of the dimer **13g**. Both signals at 14.1 and 17.5 ppm could correspond to palladium (0) species such as [Pd(CO)$_n$(bdpp)] (n = 1 or 2). Milstein *et al.* reported the synthesis of the analogue of **13g** with dippp and suggested that a palladium (II)-hydride and Pd(0)-carbonyl fragment species are involved in the formation of this complex.[17] Elsevier and Tóth previously reported the complex Pd(CO)$_2$(*S,S*-bdpp) and characterised this compound by ^{31}P spectroscopy as a singlet at 18.7 ppm.[41,19] Moreover, Pörschke *et al.* reported the characterisation of the same complex bearing dᵗbpe.[20] Palladium(0) carbonyl complexes Pd(CO)(P-P) and Pd(CO)$_2$(P-P) using dippp have been recently reported by Perez *et al.*[18] They did not observe P-C coupling in the $^{31}P\{^1H\}$NMR spectrum for these compounds, even at 193 K, and suggested that the CO bonded to palladium exchange with free CO in solution. Considering the similarities of the signals detected during the experiment with those previously described, the signals at 14.1 and 17.5 ppm

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observed in the corresponding $^{31}P\{^{1}H\}$NMR spectrum were assigned to the Pd^{0} species **13h** and **13i** (Figure 4.16), respectively.

13h **13i**

Figure 4.16 Pd^{0} carbonyl species proposed to be formed in solution.

At the end of the HPNMR experiment, in the $^{31}P\{^{1}H\}$ NMR spectrum, the signal at 17.8 corresponding to the dimer was detected as the major product. In the corresponding ^{1}H NMR spectrum recorded at room temperature, no hydride signals were detected. However, when the temperature was increased to 323 K, the hydride signal at -4.93 ppm was readily detected.

Reaction of complex 13b in CD_3OD in the presence of styrene

An NMR tube was charged with **13b** and 5 equivalents of styrene in CD_3OD and the reaction was monitored by ^{31}P NMR spectroscopy. At room temperature, only the signal corresponding to **13b** was detected. When the temperature of the sample was raised to 323 K, 4 new signals were detected as two sets of mutually coupled doublets at δ 14.71 ($^{2}J_{PP}$= 73.9 Hz), δ 17.9 ($^{2}J_{PP}$= 73.2 Hz), δ 28.9 ($^{2}J_{PP}$= 73.2 Hz) and δ 29.2 ($^{2}J_{PP}$= 73.9 Hz), indicating the presence of two species containing two inequivalent phosphorus atoms (a, Figure 4.17). The difference in intensities (1.4/1) indicated that the signals at 29.2 and 14.7 ppm corresponded to the same species and is the major product, while the resonances at 28.9 and 17.9 correspond to a second product of reaction. After 30 min at this temperature, the conversion had reached a maximum of ca. 30 %. The ^{1}H NMR spectrum showed new aliphatic signals, but due to the overlap of the signals in the aliphatic region, it was not possible to extract useful information from this spectrum.

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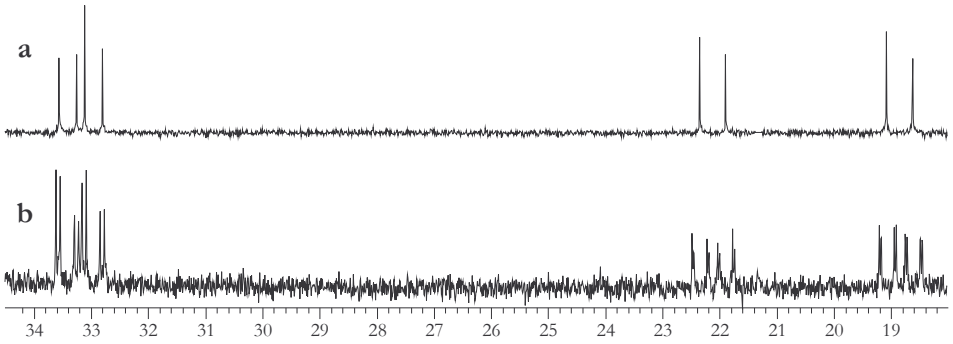

Figure 4.17 $^{31}P\{^{1}H\}$ NMR spectra. a) complex **13b** in CD_3OD at RT, b) complex **13b** and ^{13}C-styrene in CD_3OD at 323 K

When ^{13}C-labelled styrene (^{13}C enriched in α, β carbons of the double bonds) was used, the signal at 31.5 ppm corresponding to the starting material remained unchanged. However, the two sets of doublets exhibited extra couplings (b, Figure 4.17). The two doublets at 28.9 and 29.2 ppm appeared as doublet of doublets ($^2J_{PP}$= 73.2 Hz, J_{PC}= 12.3 Hz and $^2J_{PP}$= 73.9 Hz, J_{PC}= 11.6 Hz, respectively) (b, Figure 4.17). Whereas the signals at 14.71 and 17.9 ppm exhibited two extra coupling to ^{13}C and appeared as a set of two doublet of doublet of doublets ($^2J_{PP}$= 73.9 Hz, J_{PC}= 42.9 Hz, J_{PC}= 5.8 Hz and $^2J_{PP}$= 73.2 Hz, J_{PC}= 42.2 Hz, J_{PC}= 5.0 Hz). In the $^{13}C\{^{1}H\}$ NMR spectrum (Figure 4.18), two doublets of doublets at 16.4 and 17.3 ppm (J_{CC}= 40 Hz, J_{PC}= 5.8 Hz and J_{CC}= 40 Hz, J_{PC}= 5 Hz, a, Figure 4.17) and two sets of doublet of doublet of doublets at 72.0 and 73.0 (J_{CC}= 40 Hz, J_{PC}= 42.9 Hz J_{PC}= 11.6 Hz and J_{CC}= 40 Hz, J_{PC}= 42.2 Hz J_{PC}= 12.3 Hz, b, Figure 4.17) were observed. The chemical shifts of the signals at 16.4 and 17.3 ppm are characteristic of aliphatic carbons, while the chemical shift of signals at 72.0 and 73.0 ppm, suggested the presence of allylic carbons. These observations in the $^{31}P\{^{1}H\}$ and $^{13}C\{^{1}H\}$ spectrums suggested the formation of a η^3-π-benzylic species. The ^{31}P

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signals at 14.71 and 17.9 exhibited the corresponding two extra couplings to ^{13}C (α and β carbons, J_{PC} =*ca.* 5 Hz, J_{PC}= *ca.* 42 Hz), indicating that P is situated in *trans* position to the ^{13}CH-$^{13}CH_3$ fragment of the allyl moiety (Scheme 4.10 and 4.11).

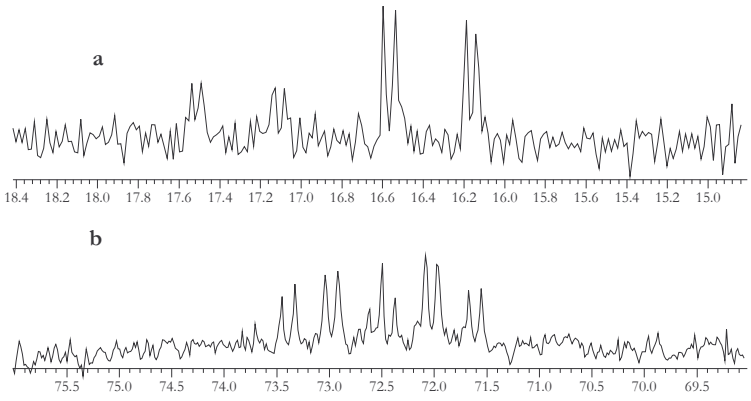
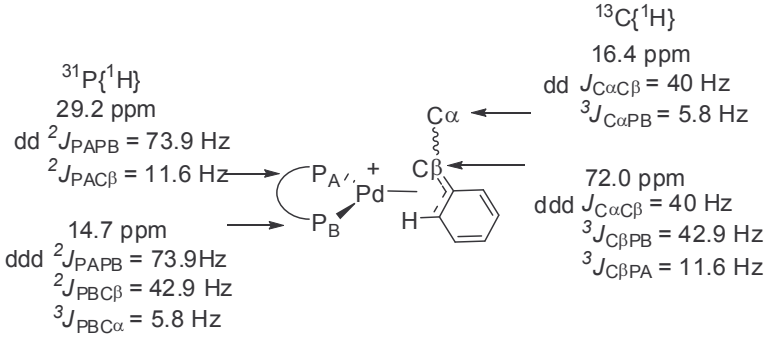


Figure 4.18 Selected regions of the $^{13}C\{^1H\}$ NMR spectrum of **13b** and ^{13}C-styrene in CD_3OD at 323 K.

These signals were therefore assigned to P_B's. The signals at lowfield (28.9 and 29.2 ppm) were assigned to P_A's (Scheme 4.10 and 4.11).



Scheme 4.10 Proposed structure for **13f** and $^{31}P\{^1H\}$ and $^{13}C\{^1H\}$ signals.

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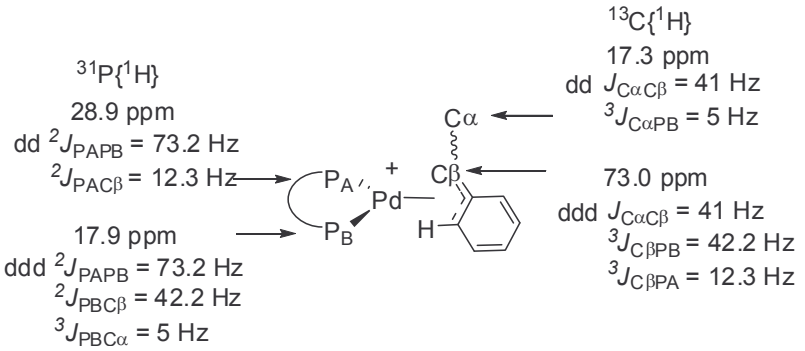

Scheme 4.11 Proposed structure for **13f'** and $^{31}P\{^{1}H\}$ and $^{13}C\{^{1}H\}$ signals.

The insertion of styrene into a Pd-H or Pd-CH_3 bonds to form η^3–π-benzyl species was previously reported.[11,42] Becker and Stille observed an AX coupling pattern with a P-P coupling constant of 82 Hz for η^3-allylic palladium complexes bearing triethylphosphine.[43] Similar palladium complexes bearing dppe and PPh_3 generally give very low anti/syn ratios (*ca.* < 10% anti).[44] Musco and co-workers reported the characterisation of a similar η^3–π-benzylic species using dppp as ligands and observed only the formation of the *syn* complex [Pd(η^3-α-methylbenzyl)(dppp)].[45] The ^2J(P-P) for complex this was 74 Hz. These results present a striking similarity to those observed in this study. Therefore, due to the small structural differences between the ligand used by Musco (dppp) and that used in our investigations, the species detected here were assigned to two disateresoisomers of the complex *syn*-**13f** (Figure 4.19). Indeed, although the *syn*/*anti* ratio was reported to be dependant on the ligand used,[46] the presence of 2 methyl groups on the C_3-bridge of the bdpp, was not thought to be sufficient to explain the change of syn/anti ratio from 100:1 to 1.4:1.[45] To the best of our knowledge, this is the first time that a η^3-benzyllic palladium complex bearing a chiral diphosphine is observed.

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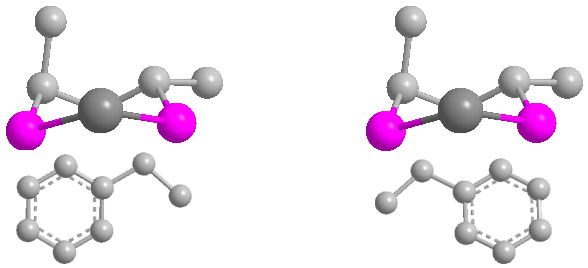
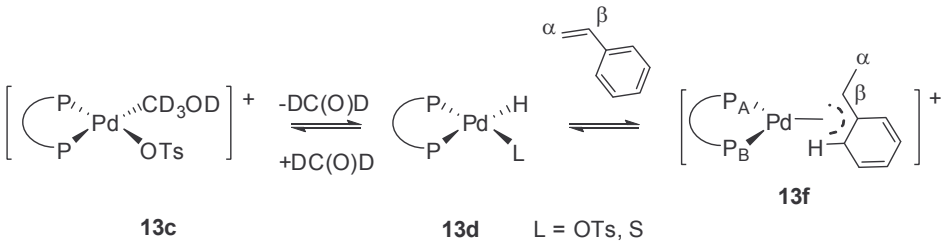


Figure 4.19 *Syn*-diastereoisomers of [Pd(η^3-α-methylbenzyl)(dppp)](OTs)

Based on these NMR results, the following scheme for the reactivity of **13b** with styrene in methanol is proposed. The hydride formation is proposed as first step. In the presence of styrene the insertion of the styrene occurs rapidly to form the allylic species **13f**.



Scheme 4.12 Styrene insertion into palladium hydride bond

Reaction of complex 13b in CD_3OD in the presence of styrene and carbon monoxide (1 atm)

An NMR tube was first charged with a CD_3OD solution of **13b** and 20 equivalents of styrene. CO was bubbled through the solution for *ca.* 5min and the reaction was monitored by ^{31}P NMR spectroscopy. When a $^{31}P\{^1H\}$ was recorded at room temperature, the signals corresponding to starting material and the allylic species

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13f and **13f '** (see Scheme 4.10 and 4.11) were immediately detected, as well as another set of mutually coupled doublets at δ 28.7 (J_{PP}= 73 Hz) and δ 15.0 (J_{PP}= 73 Hz). At 323 K, the signals corresponding to the starting material (as minor product) and the species **13f** and **13f** ' were detected in the $^{31}P\{^{1}H\}$ spectrum, while the set of doublets at 28.7 and 15.0 ppm were not observed. When the reaction was repeated using ^{13}CO, in the $^{31}P\{^{1}H\}$ NMR spectrum recorded at room temperature, the signals of starting material and allyl species were detected. The set of doublets at 28.7 and 15.0 ppm appear as doublet of doublets exhibiting an extra P-C couplings of 12 Hz. When a $^{13}C\{^{1}H\}$ spectrum was acquired, three peaks were detected in the carbonyl region of the spectrum: a large singlet at δ 185 that was assigned to free CO, a triplet resonance at δ 173.4 (J_{PC}= 12 Hz) and a singlet at δ 169.3 ppm. The chemical shift of the latter signal suggests a carbonyl group of an organic compound and the multiplicity confirmed that no P-C couplings are present. The chemical shift of the signal at 173 ppm also suggests a carbonyl group of an organic species, such as an ester. The same P-C coupling (12 Hz) confirmed that this species corresponded to the same species previously observed in the $^{31}P\{^{1}H\}$ spectrum at 28.7 and 15.0 ppm. The formation of terminal carbonyls or acyls can be discarded considering that its resonances usually have higher chemical shifts. Iggo *et al.* recently studied the carbomethoxy mechanism in the hydroxycarbonylation of ethene and they reported the synthesis of a series of intermediates starting from the Pd-carbomethoxy cycle.[6] In this study, the chemical shift observed for Pd-alkyl-carbomethoxy complex using dibpp in ^{13}C spectroscopy was 179 ppm, and the signal presented a long-range coupling to both phosphorus atoms. van Leeuwen and co-workers proposed the formation of similar allylic species when styrene was used as olefin (see backgroung).[15] Due to the similarities, the new set of doublets in the $^{31}P\{^{1}H\}$ spectrum were assigned to an allyl-carbomethoxy species, as shown in Figure 4.20. The multiplicity of the signal at 173 ppm in the $^{13}C\{^{1}H\}$ spectrum is proposed to be a doublet of doublet

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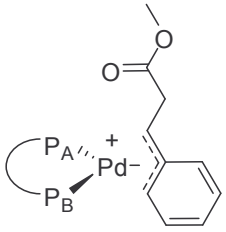
with the similar coupling constant $^4J_{(P\text{-}C)}$ = 12 Hz. The fact of this species was found to rapidly disappear is consistent with the high rate of CO insertion into a palladium alkyl complex as it was previously proposed for ethene copolymerisation.[22]



13j

Figure 4.20

At 323K, the signals detected were readily assigned to **13b**, **13f** and **13f '**. The intensities of the signals corresponding to **13f** and **13f'** was found to rapidly increase at 323K in the presence of CO and after a few hours, the signal corresponding to **13b** could not be detected. No new ^{31}P signals were detected during the experiments. After 24 h at this temperature, the sample was cooled to RT the signals for **13f**, **13f'**, **13g** and smalls signals at 29.9, 29.4 and 27.7 ppm, were detected. When the reaction was repeated at 323 K in the presence of ^{13}CO, 3 new peaks were detected in the carbonyl region of the $^{13}C\{^1H\}$ NMR spectrum, at δ 202.2 (s), δ 185.5 (s) and δ 169.3 (s) ppm. The signal at δ 185.5 was assigned to free CO and the resonance at δ 169.3 ppm (already detected at room temperature) remained unchanged at this temperature. The signal at δ 173.4 ppm could not be detected. The new singlet signal at 202.2 ppm was assigned to CO/styrene co-oligomers. After 6 h at this temperature, the carbonyl signal corresponding to the linear ester appeared at δ 175.25 ppm together with the peaks previously observed at δ 202.2 (s), δ 185.5 (s) and δ 169.3 (s) ppm. After 12 h, the branched ester was

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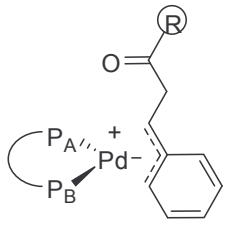
also detected at δ 176.9 ppm (s) (ratio b : l = 0.25) and a new signal at δ 213.1 ppm (t, J_{PC}= 9 Hz, dd at RT with $^{2}J_{PC}$=7 and 9 Hz) was observed. The chemical shift of this new signal suggested the presence of a carbonyl and the multiplicity suggests a coupling with two phosphorus atoms. The coupling constants values were similar to those observed for the species **13j** (Figure 4.20) suggesting a long-range coupling to both phosphorus atoms or two phosphorus atoms *cis* to the carbonyl. After 24 h, new singlets at δ 212.05 (s), δ 210.4 (s) and δ 200.5 (s) ppm appeared, corresponding to a CO/styrene co-oligomers.[47] Although no correlation between the ^{13}C signal at 213.1 ppm and a ^{31}P resonances could be found, the observation of a J_{PC} coupling for the ^{13}C signal led us to the conclusion that this signal correspond to a species containing the bdpp ligand. The allyl-ketone complex shown in Figure 4.21 matches the observation of such resonance.[48]



13k

Figure 4.21 Proposed acyl species formed in the presence of styrene and CO

Reaction of complex 13b in CD_3OD in the presence of styrene and carbon monoxide (15 atm)

Finally, to complete these series of experiments, the last experiment using higher CO pressures (15 bar), as in the catalytic reactions (Chapter 3), was performed. Into a solution of the complex **13b** in deuterated methanol, styrene (50 equiv.) was

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added. The solution was transferred to a 10 mm sapphire tube and then was charged with 15 atm of CO (mixture of ^{12}CO and ^{13}CO). The $^{31}P\{^{1}H\}$, $^{13}C\{^{1}H\}$ and ^{1}H NMR spectra were acquired at room temperature just after pressurising the tube. The $^{31}P\{^{1}H\}$NMR spectra reveales that the signal corresponding to the starting material **13b** and the Pd(0)-carbonyl **13i,** were the major products. In the same spectrum small signals corresponding to the allyl-palladium complexes **13f** and **13f'** and two new doublets at 28.1 and 25.6 ($^{2}J_{PP}$= 42 Hz) were also detected. The corresponding $^{13}C\{^{1}H\}$ NMR spectrum showed only the signal of the free CO. At 323 K, in the $^{31}P\{^{1}H\}$ NMR spectrum the signals corresponding to the starting material **13b**, the allyl-palladium complexes **13f** and **13f'**, the palladium dimer **13g**, the Pd(0)-carbonyl **13i** and phosphine oxide at 41 ppm. In the $^{13}C\{^{1}H\}$NMR spectrum, the signals corresponding to the linear and branched esters, free CO and oligomers at 202 ppm, were readily detected. After 3 hours the signals corresponding to the starting material was detected in the $^{31}P\{^{1}H\}$ NMR spectrum as a minor peak, whereas the signal corresponding to the hydrido-carbonyl palladium dimer **13g** and allyl species **13f** and **13f'** increased in intensity. The signal corresponding to the phosphine oxide was again detected. The $^{13}C\{^{1}H\}$NMR spectrum showed a very small peak at 210 ppm corresponding to the co-oligomers, while the other signals previously observed remained unchanged. At the end of the experiment, the tube was cooled to room temperature and new spectra were acquired. In the $^{31}P\{^{1}H\}$ NMR spectrum, the signals corresponding to the allyl palladium complexes **13f**, **13f'**, the dimer **13g** and phosphine oxide were observed. Three sets of new signals were also detected at 25.9 and 17.2 ppm ($^{2}J_{PP}$ = 78 Hz), 24.4 and 19.8 ppm ($^{2}J_{PP}$ = 75 Hz) and 24.1 and 18.9 ppm ($^{2}J_{PP}$ = 69 Hz). These signals suggest the presence of three new complexes with non equivalent phosphorus atoms. In the ^{1}H NMR spectrum, the signal corresponding to the dimer **13g** at -4.9 ppm was observed. In the $^{13}C\{^{1}H\}$NMR spectrum, the signals corresponding to the branched ester, linear ester and free CO were present. The

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signals at 202, 210 and 212 ppm previously assigned to co-oligomers were also detected. The doublet of doublets at 213.1 ppm previously assigned to the allyl-ketone complex **13k**, and the quintet at 240 ppm corresponding to the hydrido-carbonyl palladium dimer **13g** were still present and new broad signal at 236 ppm appeared. This latter signal suggests the presence of a dinuclear carbonyl bridged species. The identity of this dinuclear species was not determined.

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Mechanistic considerations for this study

From the study of the reactivity of the complex [Pd(OH_2)(OTs)(*R,R*-BDPP)](OTs) **13b** describe above, the following conclusions can be drawn:

- In methanol, substitution of the water molecule from **13b** yields complex [Pd(CH_3OH)(OTs)(R,R-BDPP)](OTs) **13c**.
- At 323 K, complex **13c** reacts to form the hydride species [Pd(H)(OTs)(R,R-BDPP)](OTs) **13d**.
- In the presence of styrene, reaction of **13d** yields the diastereoisomeric allyl complexes **13f** and **13f'**.
- In the presence of CO (1 bar) at room temperature, complex **13b** reacts in methanol to form the dinuclear hydrido-carbonyl species [Pd_2(μ-H)(μ-CO)(R,R-BDPP)$_2$](OTs) **13g**. At higher CO pressures (15 bar) the carbonyl species [Pd$(CO)_n$(*R,R*-BDPP)] **13h** (n = 1) and **13i** (n = 2) are detected.
- In the presence of styrene (20 equivalents) and CO (1 atm) at room temperature, complex **13b** form the allylic complexes **13f**, **13f'** and the η^3-benzyl-ester complex [Pd(η^3-C_6H_5-CH-CH_2COOCH_3)](OTs) **13j**. At higher CO pressures (15 bar) the η^3-benzyl-keto complex [Pd(η^3-C_6H_5-CH-CH_2COR)](OTs) **13k**, was observed.
- The allylic species **13f**, **13f'**, **13k** and the dimer **13g** are considered resting states under our experimental conditions.
- The detection of the species **13j** is an evidence that the carbomethoxy cycle is operative under the same conditions.

The information extracted from all experiments can be integrated in the following scheme proposed (Scheme 4.13). The NMR spectroscopy data for complexes

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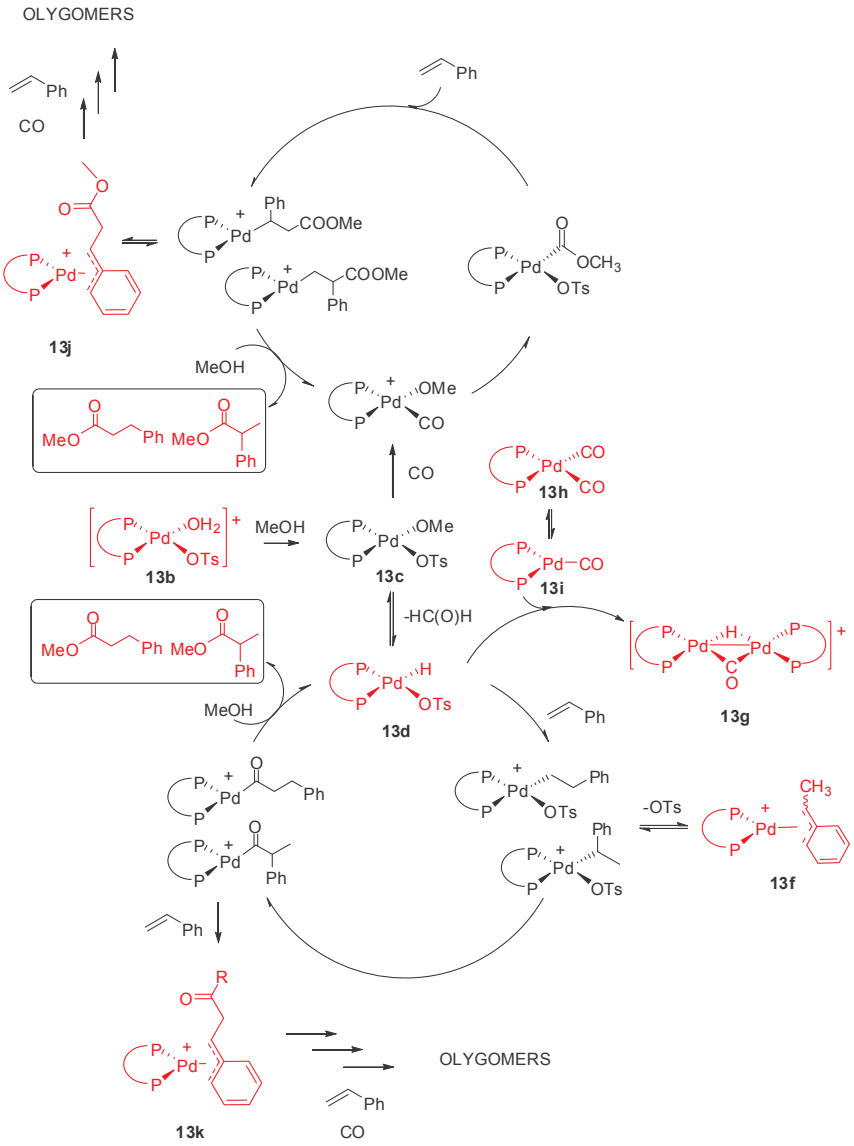
identified in the experiments (red complexes, Scheme 4.13) are reported in Table 4.3.



Scheme 4.13 Mechanistic proposal based on the experimental results

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Table 4.3 NMR spectroscopic data for the complexes involved in Scheme 4.14.

Complex	δ $^{31}P\{^1H\}$[ppm]	$J_{(P,P)}$ [Hz]	$J_{(P,C)}$ [Hz]	δ $^{13}C\{^1H\}$ ppm]
13b	31.5 s			
13d	29.5 d	52		
	6.8 d	52		
13f	29.2 d	73.9		
	14.7 d	73.9		
13f'	28.9 d	73.2		
	17.9 d	73.2		
^{13}C-sty-13f	29.2 dd	73.9	11.6	16.4 dd (J_{CC}=40)
	14.7 ddd	73.9	42.9; 5.8	72.0 ddd (J_{CC}=40)
^{13}C-sty-13f'	28.9 dd	73.2	12.3	17.3 dd (J_{CC}=41)
	17.9 ddd	73.2	42.2; 5	73.0 ddd (J_{CC}=41)
13g	17.8 (br)		32	241 q
13h	17.5 (br)			191.7 (br)
13i	14.1 (br)		55	191.3 t
13j	28.7 d	73		
	15.0 d	73		
^{13}CO-13j	28.7 dd	73	12	173.4 t
	15.0 dd	73		
13k	nd	nd	9	213.1 dd
			7	

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4.4. General conclusions

Comparisons between the systems modified with monodentate and bidentate phosphine ligands led to the following conclusions:

- In contrast to the system modified with bidentate ligands, the reaction using monodentate systems was found to be too fast on the NMR timescale to permit the detection of intermediates.
- The detection of the protonated monodentate ligand, suggests that dissociation of this phosphine occurs during the catalysis. As far as we know, the bidentate ligand remains coordinated during all the experiment.
- In the presence of *p*-TsOH in methanol the complex modified with monodentate ligand reacts to partially form the dinuclear species $[PdCl_2(\mathbf{3})]_2$ **3c**. The complex bearing the bidentate ligand was found to be very stable in the presence of acid at 323K and the formation of hydride species was inhibited by the presence of acid.
- For the system bearing (*R,R*)-bdpp **13** ligand, there are evidence for both hydride and carbomethoxy mechanisms. For the system modified with the phosphetane, no conclusions could be drawn on this subject.
- Analogue allylic species to those observed in the study using the complex $[Pd(OH_2)(OTs)(bdpp)](OTs)$ **13b**, were not detected during the HPNMR experiments performed using $[PdCl_2(\mathbf{3})_2]$ and *p*-TsOH. These allylic species might be involved in the regioselectivity to the branched due to their high stability under catalytic conditions.
- The species $[Pd_2(\mu\text{-}CO)(\mu\text{-}H)(bdpp)_2](OTs)$ was present only when the diphosphines was used as ligand. This complex was inactive towards the methoxycarbonylation of styrene under the experimental conditions used in this work.

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Chapter 5

Cationic palladium complexes bearing xylofuranose-dervative diphosphines in the co- and terpolymerisation of CO/ethene/propene

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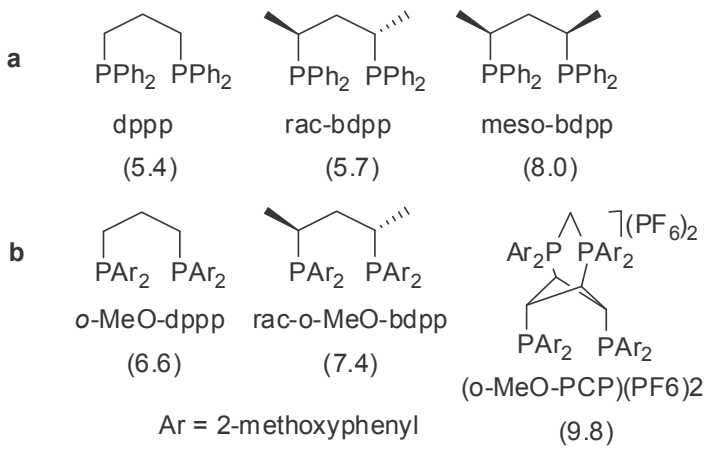
5.1. Background

The design of conformationally rigid diphosphine ligands for the coordination to late transition metals is a subject of much current interest in organometallic chemistry and homogeneous catalysis.[1] In reactions catalysed by metal complexes the selectivity and activity are influenced by the conformational properties of the metal-diphosphine complex. In the CO-ethene copolymerisation a strict relation between ligand rigidity and catalytic productivity has been observed especially for palladium complexes bearing C_2 and C_3-carbon bridged diphosphines. [2,3]



Scheme 5.1 C_3-carbon bridged diphosphines reported for CO/ethene copolymerisation. Productivities expressed in KgCP/(gPd·h) are between brackets.

Scheme 5.1a shows the molecular structure of phenyl-substituted 1,3-diphosphines with increasing ligand rigidity, compared to the reference ligand 1,3-bis(diphenylphosphino)propane (dppp): *rac*- and *meso*-bdpp; bdpp = 2,4-bis(diphenylphosphino)pentane, while Scheme 5.1b shows the molecular structure of two rigid 2-methoxyphenyl modified diphosphine ligands, namely *rac*-2,4-bis(di(2-methoxyphenyl)phosphino)pentane, (*rac*-*o*-MeO-bdpp) and 6,7-di-(di-2-

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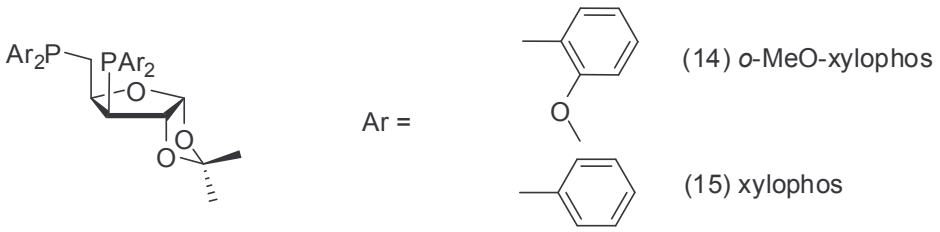
methoxy-phenyl)- phosphino -2,2,4,4-tetra-(di-2-methoxyphenyl)-2λ^4,4λ^4-diphosphonium-bicyclo-[3.1.1] heptane as its PF_6 salt, (*o*-MeO-PCP)$(PF_6)_2$,[4] compared to the reference ligand 1,3-bis(di(2-methoxyphenyl)phosphino)propane, (*o*-MeO-dppp). Below each sketch is reported the productivity as kg(polyketone)(g(Pd) × h)$^{-1}$ exhibited by the corresponding Pd^{II} catalysts under comparable reaction conditions. Previous results have shown that the introduction of *o*-MeO groups in the phenyl moiety improve the catalytic activity towards CO/ethene copolymerisation.[5]

In this chapter, the synthesis of the rigid 2-methoxy-modified, C_3 carbon bridged diphosphine, 3,5-Dideoxy-1,2-O-isopropylidene-3,5-bis (di(2-methoxyphenyl)phosphanyl)-α-D-xylofuranose, (*o*-MeO-xylophos, **14**) and 3,5-Dideoxy-1,2-O-isopropylidene-3,5-bis (diphenylphosphanyl)-α-D-xylofuranose, (xylophos, **15**)[6] (Scheme 5.2) will be described.



Scheme 5.2 Xylofuranose-derivate diphosphines used in this study.

Both corresponding cationic complexes of the type [Pd(OTs)(H_2O)(P-P)](OTs) (OTs = *p*-toluenesulfonate) (P-P = *o*-MeO-xylophos, **14c**; xylophos, **15c**) have been synthesized and employed to catalyze the CO-ethene and CO-propene copolymerisation as well as the CO-ethene-propene terpolymerisation in MeOH. For comparison purpose the analogous flexible palladium [Pd$(H_2O)_2$(*o*-MeO-dppp)](OTs)$_2$ (*o*-MeO-dppp= 1,3-bis(di(2-methoxyphenyl)phosphanyl)propane)

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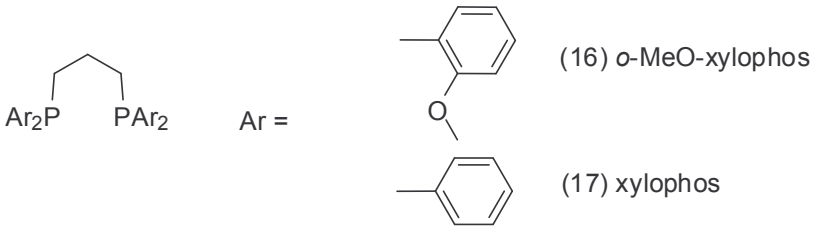
(**16c**) and [Pd(OTs)(H_2O)(dppp)](OTs) (**17c**) (Scheme 5.3) were tested under identical catalytic conditions as applied for precatalysts **14c** and **15c**.



Scheme 5.3 Dppp and *o*-MeO-dppp diphosphines.

This study was performed in the framework of a collaboration with Dr. Claudio Bianchini and his group at the CNR-ICCOM, Florence, Italy.

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5.2. Experimental

5.2.1 General

All reactions and manipulations were carried out under nitrogen atmosphere by using Schlenck-type techniques. The reagents were used as purchased from Aldrich or Fluka. 1,2-*O*-isopropylidene-3,5-di-*O*-trifluoromethansulfonyl-α-D-ribofuranose,[7] di-(2-methoxyphenyl) phosphine,[8] $[PdCl_2(COD)]$,[9a] $[PdClMe(COD)]$,[9b] $[PdCl_2(xylophos)]$ (**15a**),[10] $[PdCl_2(o\text{-MeO-dppp})]$ (**16a**), $[PdCl_2(dppp)]$ (**17a**), $[Pd(H_2O)_2(o\text{-MeO-dppp})](OTs)_2$ (**16c**)[11] $[Pd(H_2O)(OTs)(dppp)](OTs)$ (**17c**),[11] were prepared according to literature methods. Catalytic reactions were performed using a 320 mL stainless steel autoclave equipped with a mechanic stirrer and a Parr 4842 temperature and pressure controller. When needed, the autoclave was connected to a gas reservoir to maintain a constant pressure during the catalytic reactions. GC/MS analysis of the solutions were performed on a Shimadzu QP2100S apparatus equipped with a SPB-1 Supelco fused silica capillary column (30 m, 0.25 nm i.d., 0.25 μm film thickness). Deuterated solvents for routine NMR measurements were dried over molecular sieves. ^{1}H, ^{13}C, and ^{31}P NMR spectra were obtained on either a Bruker ACP 200 (200.13, 50.32, 81.01 MHz, respectively), Bruker Avance II DRX 300 spectrometer (300, 75.4, 121.4 MHz, respectively) or a Bruker Avance DRX-400 spectrometer (400.13, 100.62, 161.98 Mhz). Chemical Shift are reported in ppm (δ) relative to TMS, referenced to the chemical shifts of residual solvent resonances (^{1}H and ^{13}C NMR) or 85% H_3PO_4 ($^{31}P\{^{1}H\}$ NMR). The assignment of ^{1}H, ^{13}C and ^{31}P NMR signals was based on 1D and 2D NMR experiments, such as ^{1}H COSY, ^{1}H-^{13}C and ^{1}H-^{31}P correlations using deareated nonspinning samples. All the 2D NMR spectra were recorded with a Bruker Avance DRX-400 instrument. All NMR spectra were recorded at room temperature since stated otherwise. High pressure NMR experiments (HPNMR) were carried out on a Bruker ACP 200 spectrometer, using a 10 mm HPNMR tube (Saphikon sapphire tube equipped

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with a titanium high pressure charging head constructed at ICCOM-CNR).[12] The conductivity of ionic compounds was measured with an Orion model 990101 conductance cell connected to a model 101 conductivity meter. The conductivity data were obtained at a sample concentration of 10^{-3} M in nitroethane solutions.[13] GPC-analyses were performed in THF (HPLC grade) on a SEC-MALLS system made up of a WATERS 510 GPC pump, three-serial linear columns (Shodex K80M, Plgel 5 μ Mixed-D Plgel 3 Mixed-E), a precolumn (Shodex K800P), and two serial detectors, a laser light scattering detector (miniDAWN from Wyatt Technology Corp.) and a refractive index detector (RID-6A from Shimadzu). The data were analysed with ASTRette 1.2 software for Macintosh from Wyatt Technology.

5.2.2 1,2-O-isopropylidene-3,5-bis-(di-o-anysilphosphine)-α-D-xylofuranosa, anysil-xylophos (14)

Butyllithium (6.9 mmol) was slowly added to a solution of di-*o*-anysilphosphine (1.14 g, 4.6 mmol) in THF (30 mL) at –10°C (ice/acetone). The suspension was stirred at room temperature for 1 hour, then a solution of 1,2-*O*-isopropylidene-3,5-di-*O*-trifluoromethansulfonyl-α-D-ribofuranose (1.00 g, 2.2 mmol) in THF (20 mL) was added dropwise and the mixture was allowed to react for 3 hours. After the solvent was evaporated and the residue was redisolved in dichloromethano, washed with water and dried with magnesium sulfate. The solution was evaporated to obtain brownish foam. The residue was purified by recrystallization from toluene and ethanol to give the diphosphine as a white solid. Yield: 0.91 g (65 %). $C_{36}H_{39}O_7P_2$ (646.27): calc. C 67.90, H 6.19; found C 67.80, H 6.12. ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 1.17 (s, 3H, C*H*$_3$), 1.34 (s, 3H, C*H*$_3$), 2.67 (dd, $^2J_{(H5,H5')}$ = 13.4 Hz, $^3J_{(H5,H4)}$ = 6.7 Hz, 1H, H5), 2.94 (m, 1H, H5'), 3.10 (m, 1H, H3), 3.62 (s, 3H, OC*H*$_3$), 3.70 (s, 3H, OC*H*$_3$), 3.78 (s, 3H, OC*H*$_3$), 3.83 (s, 3H, OC*H*$_3$), 4.55 (m, 1H, H2), 4.59 (m, 1H, H4), 4.75 (d, $^3J_{(H1,H2)}$ = 3.6 Hz, 1H, H1), 6.77-7.57

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(m, 16H, Ar-*H*). $^{13}C\{^1H\}$NMR ($CDCl_3$, 100.62 MHz, ppm): δ 26.39 (s, *C*H_3), 26.57 (s, *C*H_3), 26.91 (br s, C5), 44.65 (d, $^1J_{(C3,P)}$ = 19.1 Hz, C3), 55.43 (s, O*C*H_3), 55.52 (s, O*C*H_3), 77.00 (d, $^2J_{(C4,P)}$ = 30.4 Hz, C4), 84.47 (s, C2), 104.21 (s, C1), 109.87 (s, C6), 110.23, 110.57, 120.19, 120.72, 121.01, 124.45, 129.95, 130.09, 130.32, 132.85, 132.92, 133.01, 133.33, 161.44, 161.75, 161.93 (Ar-*C*). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 161.98 MHz, ppm): δ = -50.83 (d, $^4J_{(P,P)}$ = 15.9 Hz, C3-*P*), -41.86 (d, $^4J_{(P,P)}$ = 15.9 Hz, C5-*P*).

5.2.3 1,2-O-isopropylidene-3,5-bis-(diphenylphosphine)-α-D-xylofuranosa, xylophos (15)

This phosphine was synthetised doing a modification of the procedure previously reported in the literature. Butyllithium (5.48 mmol) was slowly added to a solution of diphenylphosphine (0.63 mL, 3.65 mmol) in THF (10 mL) at –10°C (ice/acetone). The suspension was stirred at room temperature for 1 hour, then a solution of 1,2-*O*-isopropylidene-3,5-di-*O*-trifluoromethansulfonyl-α-D-ribofuranose (0.79 g, 1.74 mmol) in THF (15 mL) was added dropwise and the mixture was allowed to react for 1 hour. After the solvent was evaporated and the residue was redisolved in dichloromethano, washed with water and dried with magnesium sulfate. The solution was evaporated to obtain brownish foam. The residue was purified by recrystallization from ethanol to give the diphosphine as a white solid. Yield: 0.45 g (54 %).^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) = 1.16 (s, 3H, CH_3), 1.32 (s, 3H, CH_3), 2.43 (dd, $^2J_{(H5\text{-}H5')}$ = 13.2 Hz, $^3J_{(H5\text{-}H4)}$ = 6.6 Hz, 1H, H-5), 2.64 (dd, $^2J_{(H5'\text{-}H5)}$ = 13.2 Hz, $^3J_{(H5'\text{-}H4)}$ = 8.2 Hz, 1H, H-5'), 3.08 (d, $^3J_{(H3\text{-}H4)}$ = 4.3 Hz, 1H, H-3), 4.41 (m, 1H, H-4), 4.49 (d, $^3J_{(H2\text{-}H1)}$ = 4.3 Hz, 1H, H-2), 5.06 (d, $^3J_{(H2\text{-}H1)}$ = 4.0 Hz, 1H, H-1), 7.40 – 8.20 (m, 20H, C=H, Ph); ^{13}C NMR (100.613 MHz, $CDCl_3$), δ (ppm) = 26.1 (s, CH_3), 26.3 (s, CH_3), 31.1 (dd, $J_{(C5\text{-}P)}$ = 17.5 Hz, $J_{(C5\text{-}P)}$ = 14.8 Hz, CH, C-5), 46.2 (dd, $J_{(C3\text{-}P)}$ = 20.9 Hz, $J_{(C3\text{-}P)}$ = 5.5 Hz, CH, C-3), 76.6 (dd, $J_{(C4\text{-}P)}$ = 16.9 Hz, $J_{(C4\text{-}P)}$ = 13.0 Hz, CH, C-4), 83.9 (d, $^2J_{(C2\text{-}P3)}$ = 5.9 Hz,

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CH, C-2), 104.2 (s, CH, C-1), 110.7 (s, C, C-6), 128.4-134.2 (CH=, Ph); ^{31}P NMR (161.976 MHz, $CDCl_3$, H_3PO_4). δ (ppm) = -27.4 (d, $^4J_{(P,P)}$ = 8 Hz, 1P), -21.1 (d, $^4J_{(P,P)}$ = 8 Hz, 1P).

5.2.4 [$PdCl_2$(*o*-MeO-xylophos)] (14a)

A solution of OMe-xylophos (219 mg, 0.34 mmol) in dichloromethane (10 mL) was added to a solution of $PdCl_2$(COD) (91.8 mg, 0.32 mmol) in dichloromethane (10 mL) and it was stirred at room temperature for one hour. Then the solution was concentrated and diethylether was added to precipitated a pale yellow solid, which was washed with diethyl ether and dried under nitrogen flux. Yield: 74% (207.2 mg, 0.25 mmol). $C_{36}H_{40}Cl_2O_7P_2Pd$ (823.58): calc. C 52.50, H 4.85; found C 52.10, H 4.72%. ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 1.14 (s, 6H, C*H*$_3$), 2.77 (ddd, $^2J_{(H5,H5')}$ = 13.4 Hz, $^3J_{(H4,H5)}$ = 12.2 Hz, $^2J_{(H5,P)}$ = 7.2 Hz, 1H, H5), 3.15 (ddd, $^2J_{(H5,H5')}$ = 13.4 Hz, $^3J_{(H4,H5)}$ = 6.4 Hz, $^2J_{(H5,P)}$ = 10.4 Hz, 1H, H5'), 3.55 (dd, $^3J_{(H3,H4)}$ = 6.2 Hz, $^3J_{(H3,P)}$ = 6.9 Hz 1H, H3), 3.73 (s, OC*H*$_3$), 3.75 (s, OC*H*$_3$), 3.91 (s, OC*H*$_3$), 4.04 (s, OC*H*$_3$), 4.2 (m, 1H, H4), 4.72 (dd, $^3J_{(H1,H2)}$ = 3.9 Hz, $^3J_{(H2,P)}$ = 7.6 Hz, 1H, H2), 5.56 (d, $^3J_{(H1,H2)}$ = 3.9 Hz, 1H, H1), 6.7-7.8 (m, 14H, Ar-*H*), 9.16 (m, 1H, *o*-Ar-*H*(P-C5)), 9.38 (m, 1H, *o*-Ar-*H*(P-C3)). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.62 MHz, ppm): δ 24.81 (dd, $^1J_{(C5,P5)}$ = 33.6 Hz, $^3J_{(C5,P3)}$ = 19.9 Hz, C5), 26.34 (s, *C*H$_3$), 26.54 (s, *C*H$_3$), 44.39 (dd, $^1J_{(C3,P3)}$ = 25.05 Hz, $^3J_{(C3,P5)}$ = 11.87 Hz, C3), 54.87 (s, OCH$_3$), 55.88 (s, OCH$_3$), 56.60 (s, OCH$_3$), 73.61 (s, C4), 83.47 (s, C2), 104.21 (s, C1), 110.68 (s, C6), 110.90-135.40 (s + m, Ar-*C*), 142.83 (d, $^2J_{(C,P)}$ = 22.9 Hz, *o*-Ar$_{(C5\text{-}P)}$-*C*), 143.95 (m, *o*-Ar$_{(C3\text{-}P)}$-*C*), 159.74, 160.27, 160,77, 161.66 (s, *o*-Ar-*C*). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.98 MHz, $CDCl_3$, ppm): δ 22.27 (br s, C3-*P*), 19.47 (br s, C5-*P*).

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5.2.5 [PdClMe(*o*-MeO-xylophos)] (14b)

A deareated solution of ligand **14** (119.0 mg, 0.18 mmol) in dichloromethane (5 mL) was added to a deareated solution of PdClMe(COD) (48.3 mg, 0.18 mmol) in dichloromethane (5 mL). The clear solution was stirred for half an hour at room temperature, followed by its concentration to half of the original volume (5 mL) and the addition of diethyl ether (20 mL) to yield a off white solid, which was filtered off, washed with diethyl ether (8 mL) and dried in a stream of nitrogen. Yield: 76% (112.4 mg, 0.14 mmol). $C_{37}H_{43}ClP_2O_7Pd$ (803.1): calc. C 54.33, H 5.35; found C 54.22, H 5.15%. The product was obtained as mixture of stereo-isomers A and B in 3:1 ratio. Integrals are not reported, due to overlapping of signals, stemming from both isomers. ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 0.28 (dd $^3J_{(H,P)}$ = 7.1 Hz, $^3J_{(H,P)}$ = 3.8 Hz, Pd-CH_3(A + B)), 1.14 + 1.15 (s, CH_3), 2.51 (m, H5(B)), 2.80 (m, H5(A)), 3.08 (m, H5'(B)), 3.18 (m, H5'(A)), 3.31 (d, $^3J_{(H3,H4)}$ = 6.0 Hz, H3(A)), 3.50 (d, $^3J_{(H3,H4)}$ = 5.5 Hz, H3(B)), 3.72 + 3.75 + 3. 98 (s, OCH_3(A + B)), 4.14 (m, H4(A)), 4.21 (m, H4(B)), 4.71 (br s, H2(B)), 4.80 (br s, H2(A)), 5.50 (s, H1(A)), 5.53 (s, H1(B)), 6.68 - 7.82 (m, Ar-*H*), 8.72 (*o*-Ar-*H*), 9.10 (o-Ar-*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.62 MHz, ppm): δ 9.25 (d, $^2J_{(C,P)}$ = 105.7 Hz, Pd-*C*H_3(A)), 10.68 (d, $^2J_{(C,P)}$ = 81.2 Hz, Pd-*C*H_3(B)), 26.09 + 26.19 + 26.25 (s, *C*H_3), 26.84 (dd, $^1J_{(C5,P)}$ = 33.2 Hz, $^3J_{(C5,P)}$ = 20.2 Hz, C5(A + B), 43.73 (br s, C3(A)), 46.03 (dd, $^1J_{(C3,P)}$ = 21.5 Hz, $^3J_{(C3,P)}$ = 11.2 Hz, C3(B)), 54.52 + 55.67 + 55.73 + 56.21 (s, O*C*H_3(A)), 54.62 + 55.56 + 55.74 + 55.98 (s, O*C*H_3(B)), 74.36 (s, C4(A + B)), 84.07 (s, C2(B)), 84.15 (s, C2(A)), 104.19 (s, C1(A)), 104.26 (s, C1(B)), 110.06-161.62 (s + d, Ar-*C*(A + B)). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.98 MHz, ppm): δ 1.38 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 48.7 Hz, C5-*P*(B)), 5.22 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 46.9Hz, C3-*P*(A)), 26.19 (d, C5-*P*(A)), 31.10 (d, C3-*P*(B)).

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5.2.6 [Pd(OH$_2$)(OTs)(*o*-MeO-xylophos)](OTs) (14c)

AgOTs (74 mg, 0.27 mmol) was added to a solution of PdCl$_2$(OMe-xylophos) (104 mg, 0.13 mmol) in dichloromethane (20 mL) and it was stirred at room temperature for two hour. Then the solution was concentrated and diethylether was added to precipitate a yellow solid, which was washed with diethyl ether and dried under nitrogen flux. Yield: 61% (88.8 mg, 0.08 mmol). $C_{50}H_{58}O_{14}P_2S_2Pd$ (1114.9): calc. C 53.86, H 5.20; found C 53.71, H 5.06%. ^{1}H NMR (CDCl$_3$, 400.13 MHz, ppm): δ 1.15(s, 3H, C*H*$_3$), 1.18 (s, 3H, C*H*$_3$), 2.36 (s, 6H, Ar-C*H*$_3$), 2.76 (m, 1H, H5), 3.18 (m, 1H, H5') 3.59 (m, 1H, H3), 3.78 (s, 6H, OC*H*$_3$), 3.96 (s, 3H, OC*H*$_3$), 4.13 (s, 3H, OC*H*$_3$), 4.33 (m, 1H, H4), 4.76 (br s, 1H, H2), 5.61 (s, 1H, H1), 6.50-7.90 (m, 22H, Ar-*H*), 8.90-9.20 (br m, 2H, *o*-Ar-*H*). ^{1}H NMR (CDCl$_3$, 400.13 MHz, 213K, ppm): δ 1.11 (s, 3H, C*H*$_3$), 1.16 (s, 3H, C*H*$_3$), 2.12 (s, 6H, Ar-C*H*$_3$), 2.80 (m, 1H, H5), 3.28 (m, 1H, H5'), 3.41 (m, 1H, H3), 3.77 (s, 6H, OC*H*$_3$), 4.04 (s, 3H, OC*H*$_3$), 4.14 (s, 3H, OC*H*$_3$), 4.28 (br m, 1H, H4), 4.80 (s, 1H, H2), 5.58 (s, 1H, H1), 6.55-7.90 (m, 22H, Ar-*H*), 9.09 (m, 1H, *o*-Ar$_{(C5\text{-}P)}$-*H*), 9.42 (m, 1H, *o*-Ar$_{(C3\text{-}P)}$-*H*). ^{13}C{^{1}H} NMR (CDCl$_3$, 100.62 MHz, ppm): δ 21.04 (s, Ar-*C*H$_3$), 24.08 (dd, $^1J_{(C5,P5)}$ = 38.9 Hz, $^3J_{(C5,P3)}$ = 18.4 Hz, C5), 26.09 (s, *C*H$_3$), 26.23 (s, *C*H$_3$), 43.80 (d, $^1J_{(C3,P3)}$ = 32.5 Hz, C3), 55.52 (s, O*C*H$_3$), 56.08 (s, O*C*H$_3$), 56.25 (s, O*C*H$_3$), 56.64 (s, O*C*H$_3$), 73.31 (s, C4), 82.51 (s, C2), 104.35 (s, C1), 110.81 (s, C6), 111.20-161.25 (s + m, Ar-C). ^{31}P{^{1}H} NMR (CDCl$_3$, 161.98 MHz, ppm): δ 25.76 (br s). ^{31}P{^{1}H} NMR (CDCl$_3$, 161.98 MHz, 213K, ppm): δ 25.94 (br s, C5-*P*), 26.92 (br s, C3-*P*). Λ_M (nitroethane, 28 °C): 79 Ω^{-1} cm^2 mol^{-1}.

5.2.7 [PdClMe(xylophos)] (15b)

A deareated solution of ligand **15** (165.0 mg, 0.31 mmol) in dichloromethane (5 mL) was added to a deareated solution of PdClMe(COD) (83.0 mg, 0.31 mmol) in dichloromethane (5 mL). The clear solution was stirred for half an hour at room temperature, followed by its concentration to half of the original volume (5 mL)

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and the addition of diethyl ether (20 mL) to yield a off white solid, which was filtered off, washed with diethyl ether (8 mL) and dried in a stream of nitrogen. Yield: 83% (175.8 mg, 0.26 mmol). $C_{33}H_{35}ClP_2O_3Pd$ (683.14): calc. C 58.02, H 5.12; found C 58.17, H 5.22%. The product was obtained as a mixture of stereo-isomers A and B in 5: 2 ratio. Integrals are not reported, due to overlapping of signals, stemming from both isomers.^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 0.45 dd, $^2J_{(H,P)}$ = 8.4 Hz, $^2J_{(H,P)}$ = 4.4 Hz Pd-CH_3(B)), 0.58 (dd, $^2J_{(H,P)}$ = 8.0 Hz, $^2J_{(H,P)}$ = 4.0 Hz Pd-CH_3(A)), 1.16 (s, CH_3(A)), 1.18 (s, CH_3(B)), 1.27 (s, CH_3(A)), 1.29 (s, CH_3(B)), 2.17 (ddd, $^2J_{(H5,H5')}$ = 13.9 Hz, $^3J_{(H4,H5')}$ = 10.6 Hz, $^2J_{(H5',P)}$ = 1.8 Hz, H5'(B)), 2.65 (ddd, $^2J_{(H5,H5')}$ = 14.6 Hz, $^3J_{(H4,H5')}$ = 10.1 Hz, $^2J_{(H5',P)}$ = 2.9 Hz, H5'(A)), 2.71 (dd, $^3J_{(H3,H4)}$ = 6.7 Hz, $^3J_{(H2,H3)}$ = 2.6 Hz, H3(A)), 2.84 (ddd, $^2J_{(H5,H5')}$ = 13.8 Hz, $^3J_{(H4,H5)}$ = 6.5 Hz, $^2J_{(H5,P)}$ = 3.3 Hz, H5(B)), 2.98 (ddd, $^2J_{(H5,H5')}$ = 14.5 Hz, $^3J_{(H4,H5)}$ = 5.8 Hz, $^2J_{(H5,P)}$ = 5.6 Hz, H5(A)), 3.11 (dd, $^2J_{(H3,P)}$ = 6.4 Hz, $^3J_{(H3,H4)}$ = 6.5 Hz, H3(B)), 4.56 (m, H4(A + B)), 4.79 (dd, $^3J_{(H1,H2)}$ = 3.9 Hz, $^3J_{(H2,P)}$ = 4.9 Hz, H2(A)), 4.82 (dd, $^3J_{(H1,H2)}$ = 4.1 Hz, $^3J_{(H2,P)}$ = 7.1 Hz, H2(B)), 5.47 (d, $^3J_{(H1,H2)}$ = 4.0 Hz, H1(A)), 5.67 (d, $^3J_{(H1,H2)}$ = 4.0 Hz, H1(B)), 7.40-8.10 (m, Ar-*H*(A + B). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100.62 MHz, ppm): δ 11.86 (d, $^2J_{(C,P)}$ = 102.4 Hz, Pd-*C*H_3(A)), 14.09 (d, $^2J_{(C,P)}$ = 104.0 Hz, Pd-*C*H_3(B)), 26.03 (s, CH_3(A)) 26.08 (s, CH_3(B)), 26.17 (s, CH_3(B)), 26.20 (s, CH_3(A)), (C5(B) overlapped by the CH_3-groups), 29.60 (dd, $^1J_{(C5,P)}$ = 30.3 Hz, $^3J_{(C5,P)}$ = 20.2 Hz, C5(A)), 43.97 (dd, $^1J_{(C3,P)}$ = 10.6 Hz, $^3J_{(C3,P)}$ = 5.4 Hz, C3(A)), 47.30 (dd, $^1J_{(C3,P)}$ = 22.3 Hz, $^3J_{(C3,P)}$ = 11.7 Hz, C3(B)), 74.41 (s, C4(A)), 74.54 (s, C4(B)), 82.96 (d, ^2J(C2,P) = 2.9 Hz, C2(A)), 83.22 (s, C2(B)), 103.63 (s, C1(A)), 103.74 (s, C1(B)), 111.28 (s, C6(A + B)), 127.02-135.07 (Ar-*C*). $^{31}P\{^1H\}$ NMR ($CDCl_3$, 161.98 MHz, ppm): δ -4.43 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 48.6 Hz, C5-*P*(B)), 1.18 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 46.8 Hz, C3-*P*(A)), 25.70 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 46.8 Hz, C5-*P*(A)), 31.20 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 48.6 Hz, C3-*P*(B)).

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5.2.8 [Pd(OH$_2$)(OTs)(xylophos)](OTs) (15c)

AgOTs (67 mg, 0.24 mmol) was added to a solution of $PdCl_2$(xylophos) (80.6 mg, 0.11 mmol) in dichloromethane (8 mL) and it was stirred at room temperature for two hour. Then the solution was concentrated and diethylether was added to precipitated a yellow solid, which was washed with diethyl ether and dried under nitrogen flux. Yield: 64% (69.9 mg, 0.07 mmol). $C_{46}H_{48}P_2O_{10}S_2Pd$ (992.9): calc. C 56.64, H 4.83; found C 56.74, H 4.95%. ^{1}H NMR ($CDCl_3$, 400.13 MHz, ppm): δ 1.25 (s, 3H, C*H*$_3$), 1.40 (s, 3H, C*H*$_3$), 2.33 (s, 6H, Ar-C*H*$_3$), 2.73 (m, 2H, H5 + H5'), 3.24 (dd, $^3J_{(H3,H4)}$ = 7.2 Hz, $^3J_{(H3,P3)}$ = 8.0 Hz, 1H, H3), 4.88 (m, 1H, H4), 5.08 (d, $^3J_{(H2,H1)}$ = 2.8 Hz, 1H, H2), 5.90 (br s + d, $^3J_{(H1,H2)}$ = 2.8 Hz, 3H, *H*$_2$O + H1), 6.97-8.02 (m, 28H, Ar-*H*). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.62 MHz, ppm): δ 21.02 (s, Ar-*C*H$_3$), 25.44 (dd, $^1J_{(C5,P)}$ = 36.6 Hz, $^3J_{(C5,P)}$ = 17.9 Hz, C5), 26.1 (s, *C*H$_3$), 26.3 (s, *C*H$_3$), 42.30 (dd, $^1J_{(C3,P)}$ = 29.8 Hz, $^3J_{(C3,P)}$ = 11.0 Hz, C3), 73.91 (s, C4), 82.19 (s, C2), 104.40 (s, C1), 112.19 (s, C6), 123.48-141.50 (m, Ar-*C*). ^{31}P{^{1}H} NMR ($CDCl_3$, 161.98 MHz, ppm): δ 21.70 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 17.2 Hz, C5-*P*), 21.93 (d, $^2J_{(P,P)}$ + $^4J_{(P,P)}$ = 17.2 Hz, C3-*P*). Λ_M (nitroethane, 28 °C): 65 Ω^{-1} cm^2 mol^{-1}.

5.2.9 High temperature NMR spectroscopy of compound 14c in CD$_3$OD

In a Schlenk tube compoung **14c** (11.1 mg, 0.01 mmol) was dissolved in deareated CD_3OD (1.5 mL). This solution was transferred into a 5 mm NMR tube under nitrogen. The NMR tube was placed in a NMR probe and ^{31}P{^{1}H} as well as ^{1}H NMR spectra were recorded in the temperature range from 20-85 °C. In the following are reported ^{31}P{^{1}H} and ^{1}H NMR spectra at 20 °C and 85 °C.

^{1}H NMR (CD_3OD, 400.13 MHz, ppm): δ 1.15 (s, 3H, C*H*$_3$), 1.16 (s, 3H, C*H*$_3$), 2.39 (s, 6H, Ar-C*H*$_3$), 2.79 (m, 1H, H5), 3.28 (m, 1H, H5'), 3.55 (dd, $^3J_{(H3,H4)}$ = 6.6 Hz, $^2J_{(H3,P1)}$ = 9.6 Hz, 1H, H3), 3.82 (s, 6H, OC*H*$_3$), 4.12 (s, 6H, OC*H*$_3$), 4.32 (m, 1H, H4), 4.80 (dd, $^3J_{(H1,H2)}$ = 4.0 Hz, $^3J_{(H2,P1)}$ = 7.2 Hz, 1H, H2), 5.72 (s, 1H, H1), 6.64-8.00 (m, 23H, Ar-*H*), 8.85 (m, 1H, *o*-Ar-H). ^{1}H NMR (CD_3OD, 400.13 MHz,

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358K, ppm): δ 1.16 (s, 6H, CH_3), 2.36 (s, 6H, Ar-CH_3), 2.82 (m, 1H, H5), 3.25 (m, 1H, H5'), 3.61 (m, 1H, H3), 3.88 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.13 (s, 3H, OCH_3), 4.35 (m, 1H, H4), 4.80 (m, 1H, H2), 5.70 (br. s, 1H, H1), 6.70-7.98 (m, 22H, Ar-*H*), 8.81 (m, 2H, *o*-Ar-*H*). $^{31}P\{^1H\}$ NMR (CD_3OD, 161.98 MHz, ppm): δ 26.52 (br s). $^{31}P\{^1H\}$ NMR (CD_3OD, 161.98 MHz, 358K, ppm): δ 24.99 (br s, P1), 26.20 (d, $^2J_{(P,P)} + {}^4J_{(P,P)} = 9.0$ Hz, P2).

5.2.10 X-Ray crystallographic data collection and refinement of the structure of 14a

Crystals, suitable for a single crystal X-ray structure analysis were obtained by slow evaporation of a 1:1 (v:v) $CHCl_3$-1,4-dioxane solution of compound **14a** at room temperature. Diffraction intensity data were collected at 170K with an Oxford Diffraction CCD diffractometer with graphite –monochromated Cu-K_α radiation (λ = 1.54184) using ω-scans. Cell refinement, data reduction, and empirical absorption correction were carried out with the Oxford diffraction software and SADABS.[14a] All structure determination calculations were performed with the WINGX package[14b] with SIR-97[14c] SHELXL-97[14d] and ORTEP-3 programs.[14e] The structure was solved by direct methods and refined by full-matrix F^2 refinement. Final refinements based on F^2 were carried out with anisotropic thermal parameters for all non-hydrogen atoms, which were included using a riding model with isotropic U values 20% larger than those of the adjacent carbon atoms. CCDC reference number for **14a**: 660552.

5.2.11 Catalytic co- and terpolymerisation reactions

HPNMR experiment in CD_3OD with 14c as catalyst precursor. A 10 mm sapphire HPNMR tube was charged with **14c** (22.3 mg, 0.02 mmol) in deareated CD_3OD (2 mL) under nitrogen and then placed into a NMR probe at 20 °C. After a $^{31}P\{^1H\}$ and ^1H NMR spectra had been acquired, the sapphire tube was removed

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from the probe, charged with a 1:1 gas-mixture of CO and propene to a total pressure of 13.8 bar at room temperature. Then the tube was placed again in the NMR probe and $^{31}P\{^{1}H\}$ and ^{1}H NMR spectra were acquired at room temperature, followed by heating the NMR probe to 50 °C and then to 85 °C, acquiring $^{31}P\{^{1}H\}$ and ^{1}H NMR spectra at each temperature. After heating the sapphire tube at 85 °C for half an hour, the probe was cooled to room temperature, $^{31}P\{^{1}H\}$ and ^{1}H NMR spectra were acquired at that temperature, followed by removing the tube from probe, releasing the excess of gases and analysing the solution by means of GC/MS.

Autoclave experiments: CO-ethene copolymerisation in MeOH with (14-17)c as catalyst precursors. In a typical experiment, a MeOH (100 mL) solution containing the catalyst precursor (0.0048 mmol), was introduced by suction into the autoclave (320 mL), previously evacuated using a vacuum pump. When the catalytic reactions were performed in the presence of 1,4-benzoquinone (BQ), this reagent was dissolved in MeOH. The autoclave was charged with a 1:1 CO-C_2H_4 mixture to 20.7 bar at room temperature and then heated to 85 °C, where the pressure was adjusted to 41.4 bar and the reaction conducted under stirring (1200 rpm) at constant pressure, feeding the autoclave with an 1:1 CO/ethene gas mixture. After the desired time, the autoclave was cooled by means of an ice-water bath and the unreacted gases were released. The insoluble copolymer was filtered off, washed with methanol, and dried under vacuum at 50 °C to constant weight.

Autoclave experiments: CO-propene copolymerisation in MeOH with (14-17)c as catalyst precursors. In a typical experiment, a MeOH (100 mL) solution containing the catalyst precursor (0.0048 mmol) and BQ (0.0384 mmol) was introduced by suction into the autoclave (320 mL), previously evacuated using a vacuum pump. The autoclave was cooled to 0 °C, followed by charging it with

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propene (30 g). Then the autoclave was warmed to 20 °C and charged with CO (6.9 bar), followed by heating the autoclave to 85 °C. At this temperature stirring (1200 rpm) was started and the total pressure was adjusted with CO to 41.4 bar. The reaction was performed at constant pressure by a constant feeding of the autoclave with CO. After a reaction time of 3 hours, the autoclave was cooled by means of an ice-water bath and the unreacted gases were released. The MeOH solution of the oligomeric material was evaporated at room temperature by means of a vacuum pump to reach constant weight of the cooligomers.

Autoclave experiments: CO-ethene-propene terpolymerisation in MeOH with (14-17)c as catalyst precursors. In a typical experiment, a MeOH (100 mL) solution containing the catalyst precursor (0.0048 mmol) and BQ (0.0384 mmol) was introduced by suction into the autoclave (320 mL), previously evacuated using a vacuum pump. The autoclave was cooled to 0 °C, followed by charging it with propene (30 g). Then the autoclave was warmed to 20 °C and charged with ethene (6.9 bar) and CO (6.9 bar), followed by heating the autoclave to 85 °C. At this temperature the total pressure was adjusted with CO to 41.4 bar and the reaction was conducted under stirring (1200 rpm) and constant CO pressure, feeding the autoclave with CO. After three hours, the autoclave was cooled to room temperature by means of an ice-water bath and the unreacted gases were released. The viscous MeOH solutionss of the terpolymer were evaporated by means of a vacuum pump to reach constant weight.

5.2.12 Characterization of the CO-ethene, CO-propene copolymers and the CO-ethene-propene terpolymers.

The alternating CO-ethene copolymers were analysed by ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy, carried out in a 1:1 (v:v) solvent mixture of 1,1,1,3,3,3-hexafluoroisopropanol-d_2 and C_6D_6. ^{1}H and $^{13}C\{^{1}H\}$ NMR signals were assigned

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based on literature reports,[11,15] and the molecular weight determination was based on integration of the corresponding ^{1}H signals.

The alternating CO-propene cooligomers and CO-ethene-propene terpolymers were analysed by ^{1}H and $^{13}C\{^{1}H\}$ spectroscopy, carried out in $CDCl_3$. The ratio of the regioisomeric propene incorporation was determined upon integration of the corresponding carbonyl signals in the $^{13}C\{^{1}H\}$ NMR spectra,[16] while the propene incorporation in the terpolymers was determined by integration of the corresponding ^{1}H NMR signals. The molecular weight of the terpolymers was determined by GPC, dissolving the terpolymer (25 mg) in THF (5 mL, HPLC grade). To this solution was added toluene (10 μL, HPLC grade) as standard.

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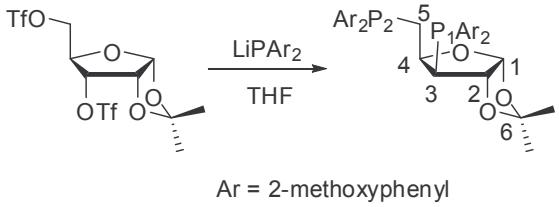
5.3 Results and discussion

5.3.1 Synthesis of ligands

The new chiral diphosphane ligand 3,5-Dideoxy-1,2-O-isopropylidene-3,5-bis(2-methoxyphenylphosphanyl)-α-D-xylofuranose, *o*-MeO-xylophos (**14**) was synthesised by the reaction of the lithium-salt of bis-(2-methoxyphenyl)phosphine[8] with 1,2-*O*-isopropylidene-3,5-di-*O*-trifluoromethanesulfonyl- α-D-ribofuranose[7] in THF (Scheme 5.4). The ligand was obtained with 65% yield as white semi-crystalline compound.



Scheme 5.4 Synthesis of ligand the **14**.

Ligand **14** was characterized in solution by multinuclear NMR spectroscopy and in the solid state by elemental analysis. In accordance with two non equivalent phosphorus donor atoms, the $^{31}P\{^{1}H\}$ NMR spectrum of **14** shows two doublets centred at -50.83 (P1) and -41.86 (P2) ppm (Scheme 5.4) with a ^{4}J (P,P) of 15.9 Hz, which is double the value compared to the known phenyl-counterpart 3,5-Dideoxy-1,2-O-isopropylidene-3,5-bis(diphenylphosphanyl)-α-D-xylofuranose (**15**) xylophos.[6]

5.3.2 Synthesis and characterisation of palladium complexes

The reaction of $PdCl_2$(COD) with ligands **14** and **15** in dichloromethane yielded the neutral complexes $PdCl_2$(*o*-MeO-xylophos) (**14a**) and $PdCl_2$(xylophos) (**15a**)[10] as pale yellow air stable compounds in 74% and 80% yield, respectively (Scheme 5.5).

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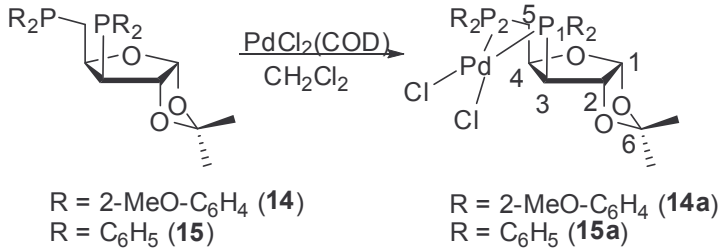

Scheme 5.5 Synthesis of the neutral palladium complexes **14a** and **15a**.

Both complexes were characterized in solution by multinuclear NMR spectroscopy and in the solid state by elemental analysis. Crystals of compound **14a,** suitable for a single crystal X-ray diffraction analysis were obtained. As far as we know, this is the first crystal structure of a transition metal complex bearing a modified α-D-xylofuranose moiety. The $^{31}P\{^{1}H\}$ NMR spectrum of the palladium complexes **14a** and **15a** showed two signals centred at 19.47 and 22.27 ppm (**14a**) and 18.20 and 22.8 ppm (**15a**).[10] While the latter compound shows a *J*(P,P) of 7.4 Hz, the former one exhibits two broad singlets. The high field $^{31}P\{^{1}H\}$ NMR signal of both complexes at 19.47 (**14a**) and 18.20 (**15a**) ppm are assigned to the phosphorus atom P2 (Scheme 5.5) by means of ^{1}H-^{31}P correlation spectroscopy. The former complex shows two high-field shifted ^{1}H multiplets centred at 9.16 and 9.38 ppm, due to palladium-*ortho*-hydrogen atom interactions,[11,17] which has also been observed in a single crystal X-ray structure of compound **14a**. Experimental diffraction parameters and crystal data as well as selected bond distances and angles for **14a** are reported in Tables 5.1 and 5.2, respectively, while a selected ORTEP drawing is shown in Figure 5.1.

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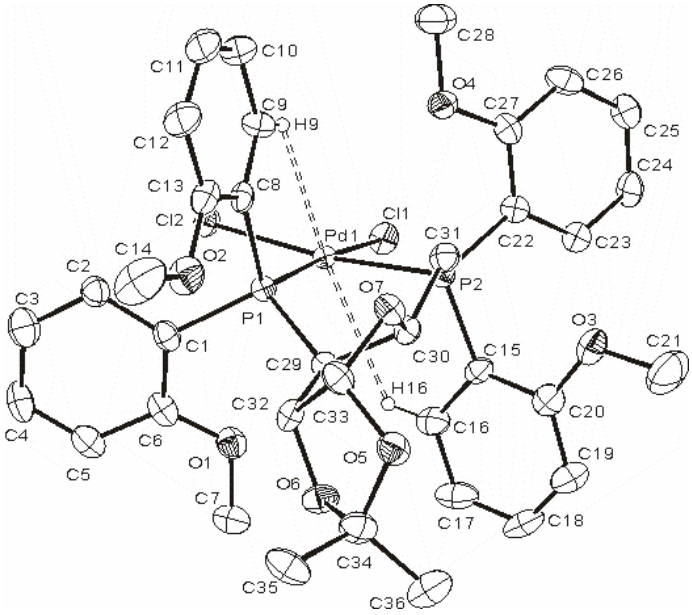

Figure 5.1 ORTEP diagram of **14a**. The thermal ellipsoids are presented at a 30% probability level and hydrogen atoms are omitted for clarity.

The crystal structure of compound **14a** exhibits a square planarly coordinated palladium atom, which deviates from the least-square coordination plane defined by the atoms Cl(1), Cl(2), P(1) and P(2) of 0.0257(8) Å in direction of C(29). The Pd-P bond lengths of 2.269(1) and 2.246(1) Å (Table 5.2) are significantly different from each other, due to the different σ-donor property of both phosphine donor atoms, which is stronger for P(2) than for P(1). As a consequence the *trans* influence of P(2) is higher compared to that of P(1) and thus the Pd(1)-Cl(2) bond length of 2.362(1) Å is significantly longer compared to the Pd(1)-Cl(1) bond length of 2.349(1) Å.

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Table 5.1 Experimental X-ray diffraction parameters and crystal data for **14a**

Empirical formula	$C_{36}H_{40}Cl_2O_7P_2Pd$
M	823.92
Crystal system	Orthorhombic
Space group	P 2_1 2_1 2_1
a/Å	11.395(5)
b/Å	17.986(5)
c/Å	20.001(5)
α/°	90.0
β/°	90.0
γ/°	90.0
Unit cell volume/Å^3	4099(2)
D_{calcd}/g cm^{-3}	1.335
Z	4
μ(Mo Kα)/mm^{-1}	5.936
F(000)	1688
T/K	170(2)
λ/ Å	1.54184
Absorption correction	SADABS
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameter	5206/0/439
Final *R* indices	[$I > 2\sigma(I)$] R_1 = 0.0415, wR_2 = 0.0900
R indices (all data)	R_1 = 0.0574, wR_2 = 0.0954
Goodness-of- fit on F^2	0.967
Absolute structure parameter	-0.016(8)
Largest diff peak and hole (e/Å^3)	1.045/-0.684

Table 2 Selected bond length (Å) and angles (°) for **14a**

Pd(1)-Cl(1)	2.349(1)
Pd(1)-Cl(2)	2.362(1)
Pd(1)-P(1)	2.269(1)
Pd(1)-P(2)	2.246(1)
Cl(1)-Pd(1)-Cl(2)	92.81(5)
P(1)-Pd(1)-P(2)	91.27(5)
Cl(1)-Pd(1)-P(1)	174.71(6)
Cl(2)-Pd(1)-P(2)	172.38(5)
Intramolecular distances (Å)	
Pd(1)…O(1)	3.673(4)
Pd(1)…O(2)	5.207(4)
Pd(1)…O(3)	5.171(4)
Pd(1)…O(4)	3.477(4)
Pd(1)…H(9)	2.756
Pd(1)…H(16)	2.894

The two bridging carbon atoms C(29) and C(31), which are directly attached to the phosphorus atoms P(1) and P(2), respectively, show a non symmetrical deviation from the least-square coordination plane of -0.968(5) (C29) and 0.874(6) Å (C31), respectively, in accordance with a twist conformation of the six membered ring, which includes the palladium atom. A similar conformation of the latter heterocyclic ring was predicted for a related Rh-COD complex (COD: cycloocta-1,5-diene) of the type [Rh(COD)(xylophos)]BF_4 by means of molecular mechanics calculations.[6] The carbon atoms C(29) and C(30), which show S and R configuration, respectively, share a six and a five membered heterocyclic ring. The latter ring is further connected to a 1,3-dioxolane ring, through the carbon atoms

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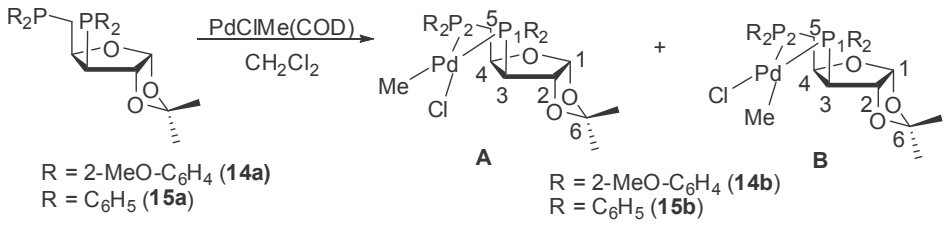
C(32) and C(33), which exhibit R configuration. Both five membered heterocyclic rings show an envelope conformation. Like related *ortho*-methoxy modified palladium-diphosphine complexes,[11,17a] the relative spatial orientation of the four anisyl groups leads to pair-wise short and long palladium-*ortho*-methoxy-oxygen distances (Table 5.2).

In order to compare the different σ-donor character of both phosphorus donor atoms of xylophos and *o*-MeO-xylophos, neutral palladium complexes of the type PdClMe(P-P) (P-P = *o*-MeO-xylophos, (**14b**); xylophos, (**15b**)) were synthesized and characterized (Scheme 5.6).



Scheme 5.6 Synthesis of the neutral complexes **14b** and **15b**.

The NMR characterization of both compounds in solution showed clearly the presence of geometrical isomers in both cases. The ratio between the two isomers A and B (Scheme 5.6) was found to be 3:1 and 5:2 for **14b** and **15b**, respectively. The major isomer A exhibited the methyl group coordinating to palladium in *trans* position to the phosphorus atom P1 as shown in Scheme 5.6. Since the methyl group exerts a higher *trans* influence compared to that of the chloride atom, the phosphorus atom with the lower σ-donor property (P1) is preferentially located *trans* to methyl group (Scheme 5.6).

The neutral complexes **14a** and **15a** were transformed into the corresponding mono-cationic complexes of the type [Pd(OTs)(H_2O)(P-P)](OTs) (P-P = *o*-MeO-xylophos, (**14c**) and xylophos (**15c**) upon reaction of both former complexes with AgOTs in dichloromethane as shown in Scheme 5.7.

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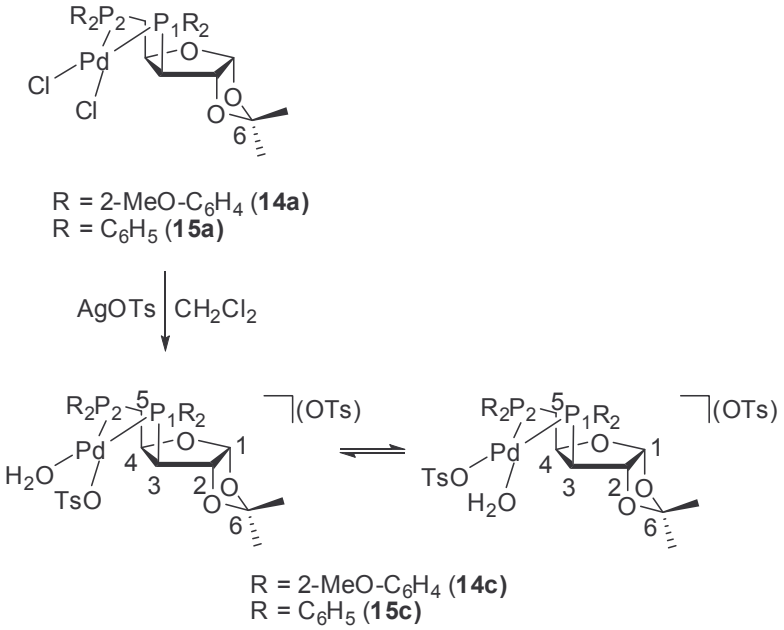

Scheme 5.7 Synthesis of the cationic palladium complexes **14c** and **15c**.

Both palladium-aqua complexes **14c** and **15c** were isolated as yellow compounds with 61% and 64% yield, respectively. Conductivity measurements of either complex in nitroethane solutions showed that both compounds behave as 1:1 electrolytes, with one tosylate anion coordinated to palladium.[11,18] The fourth coordination site at palladium is occupied by a water molecule, which is in fast exchange with the coordinating tosylate anion as shown in Scheme 5.7. The $^{31}P\{^{1}H\}$ NMR spectra for the methoxy derivative **14c** showed one singlet centred at 25.75 ppm, at room temperature. A variable temperature $^{31}P\{^{1}H\}$ NMR study of compound **14c** in $CDCl_3$ showed at the coalescent temperature and at 233K the slow-exchange limit for the fast aqua-tosylate exchange process at palladium, showing at this temperature two rather broad singlets centred at 25.94 and 26.92

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ppm, which were assigned to the phosphorus atoms P1 and P2, respectively. The ^{1}H NMR spectrum acquired at 233K showed two unresolved multiplets centred at 9.09 and 9.42 ppm for the two *ortho*-hydrogen atoms belonging to the axially orientated anisyl-moieties, while the corresponding ^{1}H NMR spectrum acquired at room temperature, exhibited for this latter hydrogen atoms only a broad unresolved hump centred at 9.05 ppm. Similar high-field shifts of *ortho*-hydrogen atoms, due to palladium-hydrogen interactions, have been observed for related neutral and cationic 2-methoxyphenyl-modified Pd(P-P) complexes.[11,17a] The phenyl counterpart, complex **15c**, exhibited an AB pattern at room temperature for the two non-equivalent phosphorus atoms, with two doublets centred at 21.70 and 21.90 ppm, which were assigned to the phosphorus atoms P2 and P1, respectively, showing a *J*(P,P) of 17.2 Hz.

5.3.3 Catalytic reactions

Both cationic palladium complexes **14c** and **15c** were employed to catalyze the CO-ethene and CO-propene copolymerisation reactions as well as the CO-ethene-propene terpolymerisation reaction in methanol, which is the solvent of choice for Pd-aqua precursors.[15] It is important to emphasise at this point that under the catalytic conditions applied, no hydrolysis reaction of the ligand was observed. For comparison reasons identical catalytic reactions employing the analogous flexible palladium complexes [Pd(H_2O)$_2$(*o*-MeO-dppp)](OTs)$_2$ (**16c**)[11] (*o*-MeO-dppp= 1,3-bis(di-(2-methoxyphenyl)phosphino)propane) and [Pd(H_2O)(OTs)(dppp)](OTs) (**17c**)[11] (dppp= 1,3-bis(diphenylphosphino)propane) were carried out. All the results are reported in Tables 5.3, 5.4 and 5.5.

CO/ethene copolymerisation

The results obtained for the CO-ethene copolymerisation reaction are summarised in table 5.3. Irrespective of the presence or absence of BQ, the trend of

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productivity of the *ortho*-methoxy modified palladium-precatalysts with increasing the ligand rigidity, is opposite to that of the analogous phenyl-derivatives (Table 5.3, entries 7, 8 vs 1, 2 and 10, 11 vs 4, 5).

Table 5.3 Copolymerisation reaction in methanol employing the cationic palladium-aqua-complexes (**14-17**)**c**[a]

Entry	Precatalyst	t(h)	BQ(equiv)	Productivity[b]	M_n[c]
1[d]	**14c**	1	-	8.4	10.5
2[d]	**14c**	1	80	14.8	
3[d]	**14c**	3	-	5.6	
4	**15c**	1	-	9.0	3.8
5	**15c**	1	80	10.0	
6	**15c**	3	-	8.4	
7[d]	**16c**	1	-	13.6	>35
8[d]	**16c**	1	80	18.1	
9[d]	**16c**	3	-	13.2	
10	**17c**	1	-	3.5	15
11	**17c**	1	80	4.1	
12	**17c**	3	-	2.5	

[a]Catalytic conditions: catalytic precursor, 0.0048 mmol; MeOH, 100 mL; p(CO) and p(C_2H_4), 20.7 and 20.7 bar; Temperature, 85ºC; stirring rate, 1200. [b]Productivity expressed as kg(CP)(g(Pd) x h)-1. [c]Mn expressed as kg x mol-1. [d]Catalytic precursor, 0.0024 mmol.

The presence of an *ortho*-methoxy substituent on the phenyl ring (**14**) and an increased rigidity of the C_3-carbon backbone may reduce the accessibility for either monomer to palladium. On the other hand ligand rigidity influences notably the molecular weight the copolymers obtained, which are keto-esters, featured by a 1:1 distribution between keto and ester-end groups.[15] Indeed, both rigid precatalysts **14c** and **15c** produce copolymers of much lower average molecular weight,

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compared to the more flexible palladium-counterparts **16c** and **17c** (Table 5.3, entries 1 and 4 vs 7 and 10), obtaining the lowest-average-weight copolymers with precatalyst **15c** (Table 5.3, entry 4). Indeed, protonolysis and methanolysis, which are the most important chain-transfer reactions in the CO-ethene copolymerisation carried out in methanol, are strongly influenced by steric and electronic effects of the coordinating ligand exerted on the palladium atom.[15,4] The influence of the ligand rigidity on the Lewis-acidity of the metal centre has been determined by comparing the IR carbonyl stretching frequencies of Rh-dicarbonyl complexes of the type $[Rh(CO)_2(P\text{-}P)](PF_6)$ (P-P= *o*-MeO-xylophos and *o*-MeO-dppp). The IR spectra of a CH_2Cl_2 solution of both Rh-dicarbonyl complexes show two carbonyl stretching bands at 2094 and 2047 cm^{-1} (*o*-MeO-xylophos) and at 2088 and 2038 cm^{-1} (*o*-MeO-dppp), evidencing the lower σ-donor ability of *o*-MeO-xylophos compared to *o*-MeO-dppp. Indeed, an increase of the Lewis acidity of the palladium atom accelerates both the protonolysis and the methanolysis reaction, bringing about the formation of low molecular weight copolymers.[11] A similar observation concerning the effect of the backbone strain on the Lewis-acidity of Pd(P-P) complexes has been observed recently.[4] On the other hand the substitution of the phenyl- by the 2-methoxyphenyl-groups at the phosphorus donor atom leads to an increase of the σ-donor ability of the latter atom, decreasing thus the Lewis-acidity of the palladium centre.[11] As a consequence the chain-transfer reactions in MeOH (methanolysis and protonolysis) are hampered compared to the propagation step of the catalytic process, bringing about the formation of copolymers, featured by an increased molecular weight.[11]

CO/propene copolymerisation

Analogously to the CO/ethene copolymerisation reactions, CO-propene copolymerisations in MeOH, employing the same precatalysts were carried out at

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85 °C with a fixed amount of propene (30 g) and a total gas pressure of 41.4 bar, due to a constant feeding of the autoclave with CO (Table 5.4, entries 1-4).

Table 5.4 CO/propene copolymerisation reaction in methanol employing the cationic palladium-aqua-complexes (**14-17**)**c**[a]

Entry	Precatalyst	BQ(equiv)	Productivity[b]	M_n[c]	Regioregularity[d] h-t %
1	**14c**	80	1.8	1.0	48
2	**15c**	80	0.7	0.5	57
3	**16c**	80	1.1	0.8	57
4	**17c**	80	1.2	0.5	66

[a]Catalytic conditions: catalytic precursor, 0.0048 mmol; MeOH, 100 mL; p(CO) and p(C_2H_4), 20.7 and 20.7 bar constant pressure (41.4 bar); Propene, 30g Temperature, 85ºC; stirring rate, 1200; time 3 hours. [b]Productivity expressed as kg(CP)(g(Pd) x h)-1. [c]Mn expressed as kg x mol-1. [d]Relative intensity of the corresponding $^{13}C\{^1H\}$ NMR signals

Under these catalytic conditions viscous CO-propene cooligomers were obtained, featured by a low regioregularity of the propene enchainment (Table 5.4, entries 1-4), which was determined by $^{13}C\{^1H\}$ NMR spectroscopy, based on the integration of the corresponding ^{13}C (carbonyl) signals, which stem from tail to tail (t-t), head to tail (h-t) and head to head (h-h) regioisomers (Scheme 5.8).[19] It is known, that Pd(P-P) precatalysts, based on the chelating diphosphine ligand dppp, show high performance in the CO-ethene copolymerisation, while in the CO-propene copolymerisation only regioirregular copolymers were obtained, evidencing thus, that both 1,2 and 2,1 propene insertion in the growing polymeric chain is operative.[19] In the case at hand, neither the substitution of the phenyl groups by the more electron-donating 2-methoxyphenyl group, nor the introduction of the chiral α-D-xylofuranose back-bone increased the regioregularity of the propene enchainment (Table 5.4).

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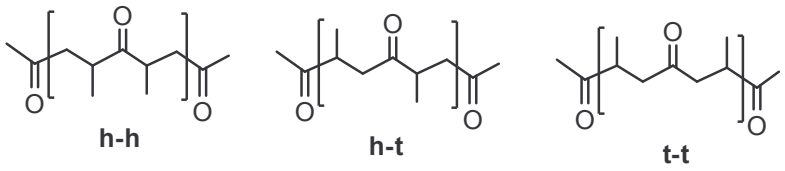
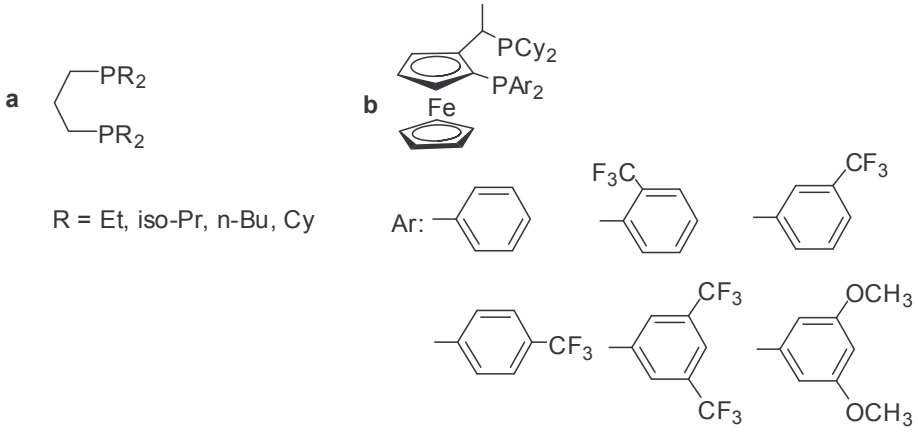


Scheme 5.8 Possible regiochemical structures within a propene *dyad*.

Indeed, much higher regioregularity was obtained with symmetrically substituted C_3-carbon bridged diphosphines bearing alkyl substituents at the phosphorus donor atoms (Scheme 5.9a)[20] or bearing two electronically different phosphorus atoms in conjunction with a chiral carbon skeleton of the Josiphos-type (> 99% head-to-tail enchainment) (Scheme 5.9b).[21]



Scheme 5.9 Ligands reported for the palladium-catalysed CO/propene copolymerisation

^1H and $^{13}C\{^1H\}$ NMR spectra of the CO-propene cooligomers acquired in $CDCl_3$ clearly showed that the latter were present as poly(1-oxo-2-methyltrimethylene)

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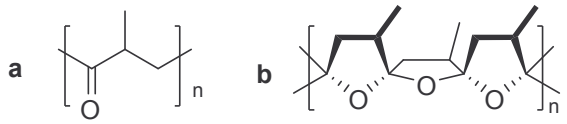
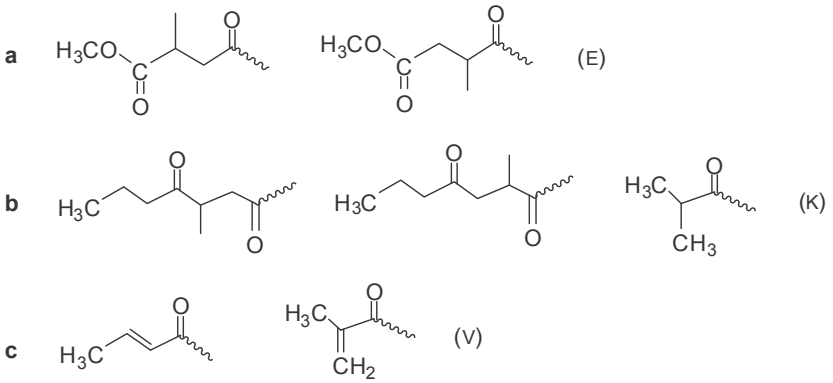
(Scheme 5.10a) and not as poly[spiro-2,5-(3-methyltetrahydrofuran)] (Scheme 5.10b),[20b,22] showing, irrespective of the precatalyst employed, ester (E) (Scheme 5.11a), ketone (K) (Scheme 5.11b) and vinyl (V) end groups (Scheme 5.11c), which stem from methanolysis, protonolysis and Pd-β-hydride elimination reactions.[15,19]



Scheme 5.10 Poly(1-oxo-2-methyltrimethylene) and poly[spiro-2,5-(3-methyltetrahydrofuran)] structures observed for CO/propene copolymers.

Due to the partial overlapping of the ^{1}H NMR signals assigned to the ketone-end groups with that of the methyl group belonging to the repeating propyl unit, only a ^{1}H NMR based integral ratio between vinyl and ester end groups can be given, showing the following V:K ratios: 1.2:3.0 (**14c**), 1.3:3.0 (**15c**), 1.0:3.0 (**16c**), 1.6:3.0 (**17c**).



Scheme 5.11 Possible end groups for CO/propene copolymers

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In an attempted of gaining more information on the CO-propene copolymerisation reaction in methanol, a high pressure NMR experiment (HPNMR) in the absence of BQ was carried out, employing the most active precatalyst **1c** (Table 5.4, entry 1). A selected sequence of the variable temperature $^{31}P\{^{1}H\}$ HPNMR study carried out in CD_3OD is presented in Figure 5.2.

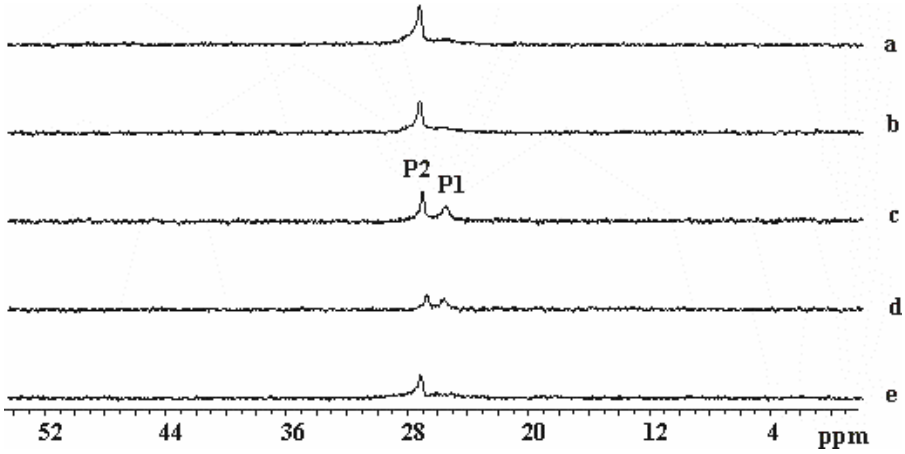

Figure 5.2 Selected variable temperature $^{31}P\{^{1}H\}$ HPNMR spectra (sapphire tube, CD_3OD, 20-85 °C, 81.01 MHz) recorded during a CO-propene copolymerisation reaction catalysed by **14c**: (a) **14c** dissolved in CD_3OD at 20 °C; (b) after pressurization of the tube with a 1:1 mixture of CO and propene (13.8 bar total pressure) at 20 °C; (c) after heating to 50 °C; (d) after heating to 85 °C; (e) after cooling the tube to 20 °C.

A 10 mm sapphire tube was charged with **14c** (0.02 mmol) in CD_3OD (2 mL). A $^{31}P\{^{1}H\}$ NMR spectrum acquired at 20 °C showed a singlet centred at 27.7 ppm along with a broad hump centred at ca. 26.0 ppm (trace a), which were assigned to the phosphorus atom P2 and P1, respectively. The HPNMR tube was then charged with a 1:1 mixture of CO and propene to a total pressure of 13.8 bar at

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room temperature and then again a $^{31}P\{^{1}H\}$ NMR (trace b) and a ^{1}H NMR spectrum were acquired at 20 °C, showing no significant changes in the $^{31}P\{^{1}H\}$ NMR spectrum, while the ^{1}H NMR spectrum showed the beginning of the copolymerisation process. Then the probe was heated to 50 °C and a $^{31}P\{^{1}H\}$ NMR spectrum acquired at the this temperature revealed a narrowing of the $^{31}P\{^{1}H\}$ signal assigned to P1, while the shape of the $^{31}P\{^{1}H\}$ NMR signal assigned to P2 remained unchanged. On heating the sapphire tube further to 85 °C, which corresponded to the reaction temperature employed in the catalytic batch reactions, both $^{31}P\{^{1}H\}$ NMR singlets reached almost the same intensity (trace d).

Table 5.5. CO/ethene/propene terpolymerisation reaction in methanol employing the cationic palladium-aqua-complexes (**1-4**)**c**[a]

Entry	Precatalyst	Productivity[b]	M_n[c]	Propene(%)[d]
1	**14c**	3.7	3.7 (2.7)	58
2[e]	**14c**	4.0	4.7 (2.2)	56
3[f]	**14c**	1.9	2.2 (2.0)	62
4	**15c**	1.0	0.8 (2.3)	49
5	**16c**	2.5	3.1 (1.8)	53
6	**17c**	2.4	1.0 (2.1)	43

[a]Catalytic conditions: catalytic precursor, 0.0048 mmol; MeOH, 100 mL; propene, 30g and $p(C_2H_4)$, 6.9 bar at 20ºC, p(CO) constant pressure, 41.4 bar; Temperature, 85ºC; stirring rate, 1200; time 3 hours. [b]Productivity expressed as kg(CP)(g(Pd) x h)-1. [c]Mn expressed as kg x mol-1. [d] Propene content in the chain calculated by ^{13}C NMR. [e] 30 g C_3H_6, $P(CO/C_2H_4)$ = 5:1, constant and total pressure 41.4 bar. [f] 30 g C_3H_6, $P(H_2)$= 6.9 bar, $P(CO/C_2H_4)$ = 5:1, constant and total pressure 41.4 bar.

This $^{31}P\{^{1}H\}$ pattern didn't change at this temperature with time, which was proved by the acquisition of $^{31}P\{^{1}H\}$ NMR spectra at 10 min time-intervals for half an hour. Afterwards the NMR tube was cooled to room temperature and a

$^{31}P\{^{1}H\}$ NMR spectrum was acquired at this temperature (trace e), showing the same $^{31}P\{^{1}H\}$ NMR pattern as observed before heating the sapphire tube (Figure 2, trace b). An independent variable temperature $^{31}P\{^{1}H\}$ and ^{1}H NMR spectroscopic study of compound **14c** carried out in CD_3OD in the temperature range from 20-85 °C showed a comparable sequence of $^{31}P\{^{1}H\}$ NMR spectra as observed during the HPNMR study, evidencing that in the course of the HPNMR study only the temperature dependent conformational dynamic of the phosphorus atom P1 can be observed and at high temperature (85 °C) the phosphorus atom P1 showed a *J*(P,P) of 9 Hz. Since compound **14c** can be detected throughout the HPNMR study, only a small quantity of the latter compound enters the catalytic cycle, which has also been observed in other similar experimental circumstances.[23]

CO/ethene/propene terpolymerisation

All four precatalysts (**14-17**)**c** were used to catalyse the terpolymerisation reaction of CO, ethene and propene in MeOH, employing a fixed amount of propene (30 g) and ethene (6.9 bar at 20 °C) (Table 5.5, entries 1-6).

Under this catalytic condition highly viscous terpolymers, which are known as Carilite,[15,24] were obtained, showing a low average molecular weight ranging from 0.8 to 3.7 kg × mol^{-1} along with a propene incorporation ranging from 43 to 58% and a high polydispersity (Table 5.5, entries 1,4-6). Both ^{1}H and $^{13}C\{^{1}H\}$NMR spectra of $CDCl_3$ solutions of the terpolymer showed the same type of chain-ends as were observed for the CO-propene cooligomers.[24] The highest catalytic productivity was obtained with precatalyst **14c** (Table 5.5, entry 1), which is rationalized by the fact, that this latter precatalyst showed in the CO-propene copolymerisation the highest propene incorporation rate.

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5.4. Conclusions

The new methoxy modified diphosphine (*o*-Meo-xylophos) as well as neutral and cationic Pd^{II} complexes bearing this ligand **14** and its phenyl counterpart **15** were synthesised and characterised. Analogous cationic palladium complexes of the type [Pd(OTs)(H_2O)(P-P)](OTs), bearing *o*-MeO-xylophos (**14c**) and its phenyl-counterpart, **15c** were employed to catalyse the CO-ethene, CO-propene copolymerisation and the CO-ethene-propene terpolymerisation reaction, comparing their catalytic performance with that of the analogous Pd-aqua complexes, bearing the corresponding more flexible ligands dppp and *o*-MeO-dppp.

From this comparative catalytic screening arose that: (i) Both rigid palladium complexes **14c** and **15c** brought about the formation of significantly lower-weight CO-ethene copolymers compared to their flexible counterparts. (ii) Neither the substitution of phenyl- by 2-methoxyphenyl units at the phosphorus donor atoms, nor the introduction of an α-D-xylofuranose based carbon backbone, increased the low regioselectivity of propene insertion observed for dppp-based Pd^{II} precatalysts.[16] (iii) The palladium complex **14c** exhibited under comparable conditions the highest propene insertion rate, leading to the highest productivity of low-molecular-weight terpolymers (Carilite oligomers), which is comparable to that obtained with a [$Pd(OAc)_2$(*o*-MeO-dppp)] precatalyst, performing the catalytic reaction in a complex mixture of protic solvents at a much higher gas total pressure (71 bar).[24]

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Chapter 6

CONCLUDING REMARKS

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On the basis of the present work the following conclusions, for the asymmetric methoxycarbonylation of vinyl arenes, can be drawn:

1. The palladium complexes $[PdCl_2(L)_2]$ bearing phospholane, phosphetane and phosphepine ligands were active, as catalyst precursors, for the methoxycarbonylation of vinyl arenes. The activity was found to decrease when increased the phosphorus-membered ring number (phosphetane > phospholane > phosphepine).
2. The complexes bearing phosphetane and binepine ligands were found to exist in a *trans* configuration. The complex bearing phospholane as ligand exits as a mixture of *cis* and *trans*-isomers in solution.
3. The complexes studied in this work bearing monodentate ligands provide high regioselectivity to the branched product (up to >99%). These ligands did not provide good enantioselectivities when styrene is the substrate (ee up to 29%). However, it has been found that the enantioselectivity depend on the nature of the substituent in *para*-position of the substrate. The highest enantioselectivity was obtained for *para*-methoxystyrene (ee 50%).
4. About the palladium complexes bearing bidentate ligands, the neutral palladium complexes modified with (*R,R*)-bdpp, (*R,R*)-diop, (*R,R*)-diop derivative ligands were found to be active for the methoxycarbonylation of styrene in the presence of a Brønsted acid.
5. All cationic palladium complexes of the type $[Pd(OH_2)(OTs)(P\text{-}P)](OTs)$ bearing (*R,R*)-bdpp, (*R,R*)-diop, (*R,R*)-diop derivative ligands were active for the methoxycarbonylation of styrene in absence of acid.
6. The regioselectivity of the reaction was found to be greatly affected by the susbtituents in the phenyl moiety of (*R,R*)-diop, (*R,R*)-CF_3-diop and (*R,R*)-*o*-MeO-diop. The diphosphine containing the electron-withdrawing groups

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afforded regioselectivities up to 92%, comparable to those obtained for monodentate ligands.

From the study of the intermediate species using the palladium system modified with mono- and bidentate diphosphine ligands, the following conclusions were drawn:

1. From the HPNMR experiments using the palladium system modified with the monodentate phosphetane **3** (**3** = 2,2,3,3-(tetramethyl)menthylphosphetane) under similar conditions to those used in catalysis, evidences of the protonation of the phosphetane ligand were observed. However the reaction was found to be too fast on the NMR timescale to permit the detection of intermediates, under our experimental conditions.
2. The formation of the dinuclear species $[PdCl_2(\mathbf{3})]_2$ **3c** was observed by reaction of $[PdCl_2(\mathbf{3})_2]$ **3a** in the presence of *p*-TsOH. This complex **3c** was found to be active in the asymmetric methoxycarbonylation of styrene. However, this species cannot be hold responsible for the overall selectivity previously observed when complex **3a** was used as precursor.
3. In the HPNMR experiment using the palladium system modified with the bidentate diphosphine **13**, evidence of both hydride and carbomethoxy mechanisms were obtained under our experimental conditions.
4. Using the system $[Pd(OH_2)(OTs)(R,R\text{-BDPP})](OTs)$ **13b** as catalyst precursor, oligomerisation process occurs competitively to the methoxycarbonylation reaction.
5. The palladium hydrido-carbonyl dimer **13g** and the allylic species **13f** are the resting states of our system. The stability of these species could be crucial in controlling the chemo- and regioselectivity.

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On the basis of the study of the CO/ethene/propene co- and terpolymerisation, the following conclusions can be drawn:

1. Systems containing (D)-(+)-xylofuranose derivative diphosphine were found to be active in the CO/ethene /propene co- and terpolymerisation reactions.
2. The introduction of an *ortho*-methoxy group in the phenyl moieties of the diphosphine had a possitive effect on the productivity in the CO/ethene copolymerisation.
3. The rigidity of the backbone increased the rate of the methanolysis process, since low molecular weight products are obtained in the CO/ethene copolymerisation process using xylofuranose-derivative ligands.
4. Neither the use of a highly electron-donor groups in the diphosphine nor the used of a chiral rigid backbone enhance the regio- and stereoregularity of the CO/propene copolymers.
5. The complex containing *ortho*-MeO groups in the xylofuranose backbone afforded the highest productivity towards the formation of CO/ethene/propene terpolymer (carilite oligomer).

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Resumen

Actualmente, el interés industrial de los productos carbonilados ha atraído la atención de los científicos hacia el desarrollo de nuevos sistemas catalíticos eficientes. La reacción de alcoxicarbonilación de vinil arenos ha sido considerada una ruta alternativa para la obtención de ácidos 2-aril propiónicos, la clase más importante de antiinflamatorios no esteroides.[1] Por otro lado, los copolímeros de monóxido de carbono y olefinas son materiales de gran interés industrial debido a su aplicación potencial como termoplásticos.[2] El concepto de economía atómica ha influenciado el desarrollo de los procesos catalíticos industriales. El máximo aprovechamiento de los reactivos y la disminución de residuos han hecho de la catálisis un proceso altamente atractivo en el marco de tecnologías de desarrollo sostenible. El conocimiento de los mecanismos operantes en las reacciones de carbonización es de gran importancia para el diseño de nuevos sistemas catalíticos altamente efectivos.

Basándose en las consideraciones anteriores, el primer objetivo de esta tesis se ha centrado en el desarrollo de nuevos sistemas catalíticos de paladio y su aplicación en la metoxicarbonilación asimétrica de vinil arenos, con el fin de obtener altas regio- y enantioselectividades, simultáneamente. Un segundo objetivo, ha sido el desarrollo de nuevos catalizadores catiónicos de paladio y el estudio de su actividad catalítica en las reacciones de co- y terpolimerización de CO/etileno/propileno. Para alcanzar el primer objetivo, se ha planteado la exploración de complejos de paladio modificados con fosfinas monodentadas (Capítulo 2) y fosfinas bidentadas (Capítulo 3). Con el fin de conocer mejor ambos sistemas e identificar algunos intermedios de reacción, se llevó a cabo un estudio de la metoxicarbonilación de estireno bajo condiciones similares a las catalíticas (Capítulo3).

Para lograr el segundo objetivo, se han sintetizado nuevos catalizadores de paladio catiónicos modificados con difosfinas derivadas de D-(+)-xilofuranosa. Los nuevos complejos se aplicaron en las reacciones de copolimerización de

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CO/etileno y CO/propileno, así como, en la terpolimerización CO/etileno/propileno.

Después de revisar los antecedentes bibliográficos en la introducción y planteados los objetivos (Capítulo 1), en el Capítulo 2 "*Palladium complexes bearing monodentate ligands in asymmetric methoxycarbonylation of vinyl arenes*" se presenta la síntesis y caracterización de complejos de paladio modificados con fosfinas cíclicas quirales, tales como, fosfetanos, fosfolanos y fosfepinos (Figura 1). Estos nuevos complejos se aplican en la metoxicarbonilación asimétrica de vinil arenos, mostrando que la actividad decrece a medida que aumenta el número de miembros del ciclo fosforado. Estos complejos modificados con fosfinas cíclicas monodentadas mostraron altas regioselectividades hacia el éster ramificado. No obstante, las enantioselectividades obtenidas con estos sistemas fueron menores del 30%.

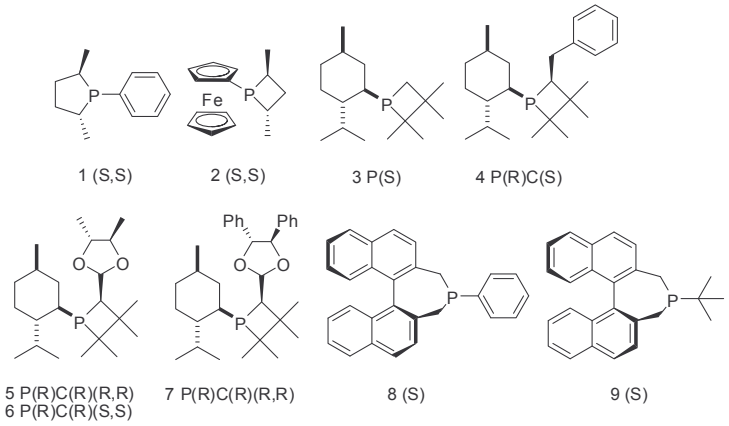

Figura 1. Ligandos ultilizados en el Capítulo 2.

En el Capítulo 3 "*Palladium complexes bearing bidentate ligands in asymmetric methoxycarbonylation of styrene*" se describe la aplicación de complejos de paladio neutros y catiónicos modificados con ligandos bidentados, en la metoxicarbonilación asimétrica de estireno. Los ligandos ultilizados en este

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capítulo (Figura 2) presentan propiedades estéricas y electrónicas diferentes. Los sistemas catalíticos formados por complejos neutros en presencia de ácido clorhídrico o ácido p-toluensulfónico, resultaron activos en esta reacción. Además los complejos catiónicos resultaron activos incluso sin adición de ácidos. En términos generales, para los sistemas neutros y catiónicos, la presencia de sustituyentes electroatractores en los grupos fenilos del ligando, tiene una gran influencia sobre la regioselectividad de la reacción hacia el producto ramificado. Por otro lado, los sistemas que contienen sustituyentes electrodadores en los fenilos del ligando incrementa la enantioselectividad de la reacción.

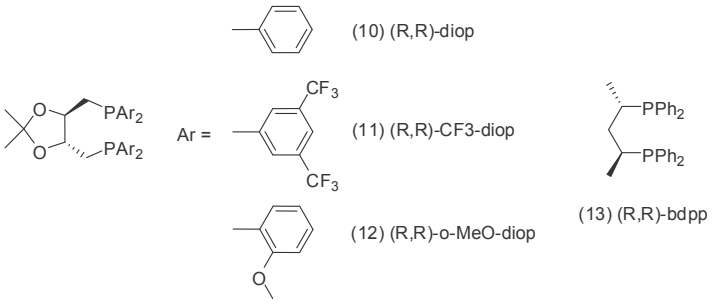

Figura 2. Ligandos bidentados utilizados en el Capítulo 3.

En el Capítulo 4 "*Mechanistic aspects of the methoxycarbonylation of styrene*" se discuten algunos aspectos mecanísticos de la metoxicarbonilación de estireno, utilizando complejos de paladio modificados con los ligandos **3** y **13** (Figuras 1 y 2). La reactividad de los complejos con los diferentes componentes del sistema catalítico, se llevó a cabo paso a paso y mediante experimentos in situ en condiciones similares a las empleadas en la catálisis. Durante el estudio realizado utilizando el complejo de paladio modificado con el ligando **3**, se detectaron un dímero de paladio de formula [(**3**)ClPd(μ-Cl)$_2$PdCl(**3**)] y fosfina protonada. El estudio realizado con el complejo catiónico de paladio modificado con el ligando **13**, arrojó

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interesantes resultados. La regioselectividad de la reacción puede estar determinada por los intermedios del tipo alilo identificados, dependiendo de su estabilidad.

Finalmente en el Capítulo 5 "*Cationic palladium complexes bearing xylofuranose-derivative diphosphines in CO/ethene/propene co- and terpolymerisation reactions*" se describe la síntesis de una difosfina derivada (14) D-(+)-xilofuranosa (Figura 3), así como la síntesis y caracterización de nuevos complejos neutros y catiónicos modificados con los ligandos mostrados en la figura 3. Las reacciones catalíticas se llevaron a cabo utilizando los complejos catiónicos en metanol. Los resultados obtenidos han sido comparados con los complejos análogos modificados con dppp y o-MeO-dppp, con el fin de discutir cómo afectan los efectos electrónicos y la rigidez del ligando en la copolimerización perfectamente alternada.

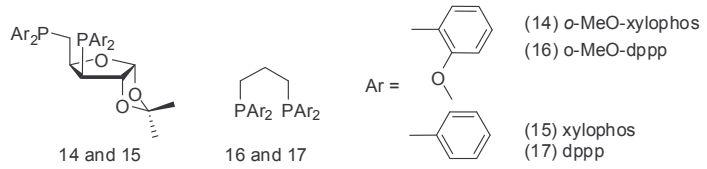

Figura 3. Ligandos utilizados en el capítulo 5.

[1] W. Gerharzt, in *Ullmanns Enciclopedia of Industrial Chemistry*, vol.3, VCH, Weiheim, (**1985**) p.41.

[2] A. Sommazzi, F. Garbassi, *Prog. Polym. Sci. 22* (**1977**) 1547.

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CONGRESSES AND SCIENTIFIC MEETINGS

2006

15th International Symposium on Homogeneous Catalysis (XVI ISHC). **S**un City, South Africa. August 2006.
Poster Presentation: "**Electronic Effect of Diphosphines on the Regioselectivity of the Palladium Catalysed Methoxycarbonylation of Styrene**".

XXII International Conference on Organometallic Chemistry (ICOMC), Zaragoza, Spain. July 2006.
Poster contribution: **"Copolymerisation of CO/Propene and Terpolymerisation of CO/ethene/propene Catalysed by Palladium Precursors Bearing Sugar Derivative Ligands"**.

2005

Palladium Network Meeting, Florence, Italy. October 21st 2005.
Oral contribution: **"Ligands Tuning for Palladium-Catalyzed Asymmetric Methoxycarbonylation of Styrene"**.

COST D17 Meeting, Budapest, Hungary. September 2005.
Oral contribution: **"Terpolymerization of CO-propene-ethene catalysed by palladium systems containing sugar derivatives ligands"**.

XVI FECHEM Conference on Organometallic Chemistry. Budapest, Hungary. September 2005.
Poster Contribution: **"Enhanced Regioselectivity in Palladium Catalysed Asymmetric Methoxycarbonylation of Styrene using Chiral Phosphetanes as Ligands"**.

2004

Mid-Term Palladium Network Meeting, Amsterdam, The Netherlands. September 21st 2004
Oral Contribution: **"Monodentate Phosphorus Ligands in Palladium-Catalyzed Asymmetric Hydroesterification of Styrene"**.

14th International Symposium on Homogeneous Catalysis (XIV ISHC). Munich, Germany. July 2004.
Poster Contribution: **"Monodentate Phosphorus Ligands in Palladium-Catalyzed Asymmetric Hydroesterification of Styrene"**.

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PUBLICATIONS BASED ON THE CONTENT OF THIS THESIS

2007

B. K. Muñoz, C. Godard, A. Ruiz and C.Claver. **"Intermediates in palladium-catalysed methoxycarbonylation of styrene. The influence of the ligand"** *Manuscript in preparation* **2007**.

B. K. Muñoz, C. Claver, A. Ruiz, Bianchini and W. Oberhauser. **"Synthesis and application of palladium-diphosphine complexes bearing an a-D-xylofuranose backbone in the co and terpolymerisation of CO-ethene and propene"**. *Manuscript in preparation* **2007**.

C. Godard, B. K. Muñoz, A. Ruiz and C.Claver. **"Pd-catalysed asymmetric mono- and bis-alkoxycarbonylation of vinylarenes"** *Dalton Trans.* **2007** submitted.

B. K. Muñoz, C. Godard, A. Marinetti, A. Ruiz, J. Benet-Buchholz and C.Claver. **"Pd-catalysed methoxycarbonylation of vynilarenes using chiral monodentate phosphetanes and phospholane as ligands. Effect of substrate substituents on enantioselectivity"**. *Dalton Trans.* **2007** in press.

2006

E. Guiu, M. Caporali, C. Müller, B. Muñoz, C. Claver and P.W.N.M. van Leeuwen. **"Electronic Effect of Diphosphines on the Regioselectivity of the Pd-Catalyzed Hydroesterification of Styrene"** *Organometallics 25*, **2006**, 3102-3104.

2005

B. Muñoz, A. Marinetti, A. Ruiz, S. Castillon and C. Claver. **"Enhanced Regioselectivity in Palladium Catalysed Asymmetric Methoxycarbonylation of Styrene using Chiral Phosphetanes as Ligands"**. *Inorg. Chem. Commun*, *8*, **2005**, 1113-1115.