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Grau de Química

Treball Final de Grau

Synthesis and coordination to Rh and Co of methylene-bridged diphosphines designed for asymmetric hydrogenation

Síntesi i coordinació a Rh i Co de difosfines amb pont metilè dissenyades per a hidrogenació asimètrica

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"Answer. That you are here. That life exists, and identity; that the powerful play goes on, and you may contribute a verse."

Walt Whitman

This is my verse.

A l'Arnald, per ser el fòsfor que va il·luminar-me el camí a través de la foscor quan no creia en la química, per finalment fer que m'enamorés d'ella i per donar sentit a l'elecció que vaig fer fa quatre anys en escollir aquest camí. Gràcies de nou per creuar-te al meu camí i creure en mi des del principi, per ser com ets i per ensenyar amb tanta passió com ho fas. I si us plau, no canviïs mai.

A la Gemma, per ser-hi tots aquests anys al meu costat incondicionalment i per canviar-me la vida.

Als meus pares i la meva família, per fer-me costat i encoratjar-me encara que no entenguin ni la meitat del que els explico.

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REPORT

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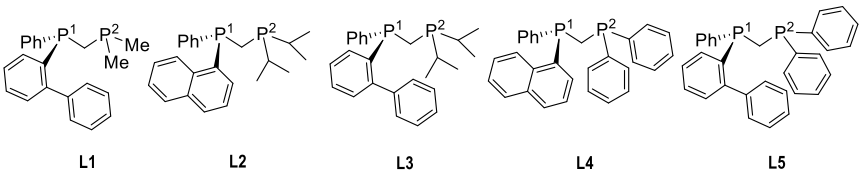
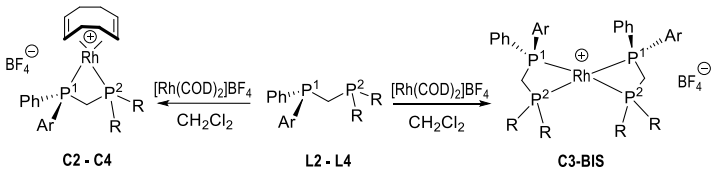
1. SUMMARY

In this *TREBALL DE FI DE GRAU* (TFG), a new *one-pot* synthetic method to obtain methylene-bridged diphosphines bearing only one *P*-stereogenic moieity is described. Using this method, the ligand **L1** was synthesised as *proof of concept* from a *P*-stereogenic methylmonophosphine-borane, obtained previously in the group. Four other diphosphines (**L2-L5**) were synthesised by a published method and three of them complexed to Rh(I) giving four complexes, **C2, C4, C2-CO, C3-BIS**, which were fully characterised. Preliminary, *in situ* complexation studies of the four diphosphines with Co were also performed.



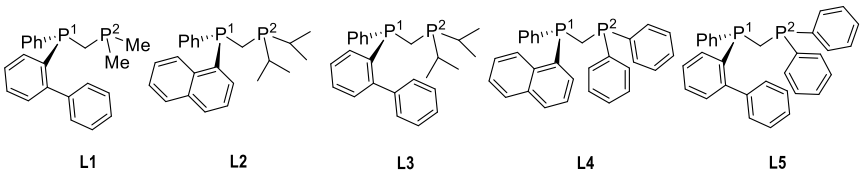
The Rh(I) complexes as well as diphosphine ligands were found to be unstable in air, so they were synthesised under inert atmosphere. Two types of Rh(I) complexes, monochelated and bisquelated were isolated. Cobalt(I) complexes are known to be very air-sensitive, hence their syntheses were performed in a dry box also under inert atmosphere. The complexes have been used as catalytic precursors in the hydrogenation of benchmark substrates **S1-S3**.



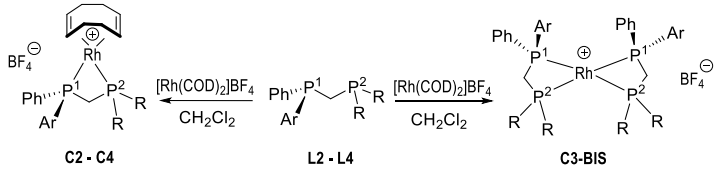
Keywords: *P*-stereogenic, short bridge diphosphines, rhodium, cobalt, asymmetric hydrogenation

2. RESUM

En aquest *TREBALL DE FI DE GRAU* (TFG), un nou *one-pot* mètode sintètic per obtenir lligands difosfines amb pont de metilè amb només un subsituent P-estereogènic ha estat descrit. Utilitzant aquest mètode, el lligand L1 ha sigut sintetitzat com a demostració conceptual a partir d'una metilmonofosfinaborà P-estereogènica prèviament obtinguda pel grup. Quatre altres difosfines (**L2-L5**) han estat sintetitzades seguint un mètode publicat i tres d'elles s'han complexat amb Rh(I) per donar quatre complexos, **C2, C4, C2-CO, C3-BIS,** que han sigut completament caracteritzats. Preliminarment, s'han realitzat estudis de complexació *in situ* de les quatre difosfines amb Co.



Els complexos de rodi, així com els lligands difosfina, han estat considerats inestables en contacte amb l'aire, per tant han sigut sintetitzats sota atmosfera inert. Dos tipus de complexos de Rh(I), monoquelats i bisquelats, s'han aïllat. Els complexos de cobalt (I) són també sensibles a l'aire i les síntesis s'han realitzat a una caixa seca, també sota atmosfera inert.. Els complexos han estat utilitzats com a precursors catalítics en substrats estàndard d'hidrogenació **(S1-S3)**.



Paraules clau: P-estereogènic, difosfines de pont curt, rodi, cobalt, hidrogenació asimètrica

3. INTRODUCTION

3.1. CATALYSIS

When the term "catalyst" is employed, it refers to a substance that increases the rate of a reaction without being consumed. As such, catalysts do not have any effect on the chemical equilibrium of reactions, but do provide a mechanism with a lower activation energy and often a affect to the product distribution of a reaction. Its productivity is often measured by the Turnover Number (TON), the ratio between the amount of product obtained and the amount of catalyst used, and the catalytic activity by the Turnover Frequency (TOF), the ratio between the turnover number and time.

The chemical industry has grown exponentially throughout the years thanks to the development of catalysts that facilitate the industries' economic and environmental demands. Nowadays more than 80% of manufactured chemical products are obtained through processes that involve catalysts at some point of the reaction.[1]

For a long time, the term "catalysis" was inevitably linked to industrial processes, associated to heterogeneous reactions. It was Sabatier who gave an accurate classification of the two different types of catalysis: homogeneous, if catalysts and reactants are in the same phase, normally as solutes in a liquid mixture; and heterogeneous if they are in different phases, in which the catalyst is often found in solid phase and the reactants in either liquid or gas phase.[2] In the latter, the reaction takes place at the interphase, which happens to be the surface of the catalyst.

Homogeneous Catalysis (HC) is very useful as their mechanisms can be determined in reasonable depth and facility and the properties of catalysts can be altered in order to obtain high selectivities and activities. Hence, HC is widely used in synthetic laboratories and also in the fine chemistry industry rather than in bulk chemistry, dominated by heterogeneous catalysis. Our research group works on homogenous catalysis, so it will be the main focus of this TFG.

3.1.1. HYDROGENATION

A reaction in which one or more hydrogen atoms are added to an unsaturated substrate is known as a hydrogenation reaction. This hydrogen can come either from molecular hydrogen or be supplied by a molecule that contains it, like an alcohol.[1]

Paul Sabatier, mentioned earlier, discovered that finely divided metallic nickel catalysed the addition of hydrogen to gaseous hydrocarbons, which he named as the Sabatier process, granting him the Nobel Prize in Chemistry in 1912. The Haber-Bosch process is also worth mentioning, as it also uses metal-based catalysts to produce ammonia from nitrogen and hydrogen, from which Haber also won the award in 1919 and Bosch in 1931.[3] The Fischer-Tropsch process is also an important process, catalysed by metal catalysts to produce liquid hydrocarbons from carbon monoxide and hydrogen.

These processes defined heterogeneous hydrogenation and are still very much used in the industrial chemistry. Nevertheless, the field of homogeneous catalysis underwent its biggest breakthrough in the 1960s, when Halpern *et al.* began studying the catalytic hydrogenation of unsaturated acids with ruthenium(II) chloride, which also inspired Wilkinson's studies in 1966 into discovering the Wilkinson catalyst, $[RhCl(PPh_3)_3]$, still used industrially for the hydrogenation of olefins.[4] These discoveries paved the way for an explosive growth of homogeneous catalysis.

3.2. ASYMMETRIC CATALYSIS

Enantioselective catalysis, traditionally known as asymmetric catalysis, is a type of catalysis in which a chiral catalyst favours the formation of one particular stereoisomer over the other of a prochiral compound.

Barely two years after the discoveries of the preceding paragraph, Knowles[5] revolutionised yet again the field by using chiral phosphines with rhodium precursors in the first catalytic enantioselective hydrogenation, which would from then on be called "asymmetric hydrogenation". For their contributions, Knowles and Noyori, who used a ruthenium(II) catalyst for hydrogenation of ketones, were awarded the Nobel Prize *"for their work on chirally catalysed hydrogenation reactions"* in 2001[6]. The first asymmetric hydrogenation process to be industrially employed was

that of the synthesis of L-DOPA, a drug employed to treat Parkinson's disease, thanks to the Rh-chiral phosphine catalyst DIPAMP, also discovered by Knowles.[4]

3.2.1. ASYMMETRIC CATALYSIS WITH TRANSITION METALS

The complexes used for asymmetric synthesis are usually transition metal complexes and organometallics, particularly of late transition metals with tertiary phosphine ligands. This is because transition metals have a wide range of oxidation states. Late noble transition metals such as Rh(I), Ru(II) or Pd(II) are considered "soft" in Pearson's HSAB theory, and prefer soft ligands such as P-donors like phosphines, phosphites and phosphinites. For this reason, phosphines and derivatives are the most important type of ligands for asymmetric catalysis.

In the last decade or so, due to economic and ecological restraints, first-row transition metals such as Fe, Ni and Co are starting to take over late-transition ones. Unfortunately, these metals have their limitations, since they form weaker bonds with the ligands, requiring synthetically challenging polydentate ligands to form effective catalysts. In addition, they often form species with oxidation states differing only in one unit (i.e. Fe(II)/Fe(III)), a feature not generally welcome for homogeneous catalysis and finally many of the oxidation states yield paramagnetic complexes, complicating their characterisation.

In this TFG, complexes from a noble metal (Rh) and an earth-abundant metal (Co) will be synthesised to study their catalytic applications. Rhodium complexes have been used as catalytic precursors since the discovery of Wilkinson's catalyst, mostly for the hydrogenation of functionalised olefins, those having coordinating substituents. They are the most successful substrates in these reactions due to their ability to chelate to the rhodium atom through the alkene and another donor atom.[7] Similarly, cobalt(I) complexes have been recently studied by Chirik's group [8], showing a more difficult synthesis process but giving with good enantioselectivities in hydrogenation of the same substrates.

3.3. CHIRAL LIGANDS

As mentioned earlier, chirality is conferred to the catalyst by the ligands, in our case enantiopure *P*-stereogenic diphosphines.

Phosphorus and its derivatives are of interest since trivalent atoms normally adopt a pyramidal geometry, much as nitrogen trivalent derivatives like NH_3 and amines. The latter are known for suffering pyramidal inversion, a process that interconverts the two enantiomers of the pyramidal compound, called invertomers. The difference between the equilibrium geometry (pyramidal) and the transition state (planar) is the energy barrier that determines such inversion.[9]

The interesting trait of phosphorus derivatives is that their energy barrier is much higher than that of nitrogen, therefore suffering the pyramidal inversion so slowly that it allows them to be configurationally stable, having chirality.[10]

Chiral phosphine ligands can be categorised into two classes: the first one constituted by ligands with chiral centres on the linking carbon chain, while the second one includes *P*-stereogenic phosphine ligands with the phosphorus atoms bearing the chirality centres (Figure 1). This project will be focused on the latter type, given that they play a very important role in asymmetric hydrogenation[11].

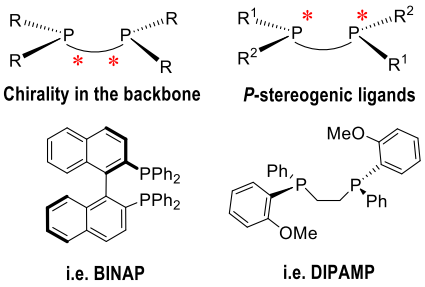


Figure 1. Diphosphines with a chiral backbone (left) and with stereogenic phosphorus atoms (right).

As mentioned earlier, Knowles discovered that these phosphines with rhodium precursors were useful in that field and thus searched for more efficient ligands of the kind. That is how PAMP, CAMP and DIPAMP ligands were synthesised. It is interesting to note that with the C_2-symmetric ligand DIPAMP an extremely high (for the time) enantioselectivity of 96% was obtained[12] (Figure 2).

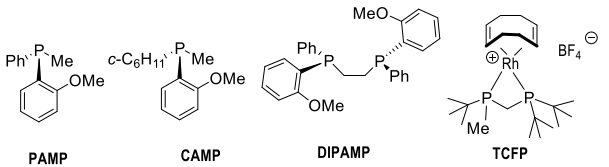


Figure 2. Structure of several important *P*-stereogenic ligands.

However, this class of chiral phosphine ligands were not thoroughly studied because of their difficult synthesis and lack of availability of the chiral precursors, until it was found that they could be prepared with phosphine–boranes as intermediates in the 1990 decade.[13]

A longstanding *dogma* was that C_2-symmetric phosphine ligands were able to achieve a higher enantiomeric excess, the measurement of purity for chiral substances, in asymmetric catalysis than C_1-symmetric (those lacking in symmetry)[14] ones, but this has proven wrong in the last years, opening up the underdeveloped field of C_1-symmetric phosphine ligands(Helmchen, Pfaltz 2000).

In 2004, Hoge obtained one of the best enantioselectivities in asymmetric hydrogenation to date, when he designed a C_1-symmetric diphosphine ligand bearing three bulky substituents: the TriChickenFootPHOS (TCFP).[15] (Figure 3). It is a ligand widely used nowadays, where two phosphines are linked by a methylene bridge, one of them bearing two *tert*-butil groups and the other one a *tert*-butil and a methyl group.

In this TFG, we aimed to explore synthesis and catalytic properties of other methylene-bridged C_1-symmetric diphosphines.

3.3.1. METHYLENE-BRIDGED DIPHOSPHINES

The bite angle, the P–M–P angle in bidentate ligands, in diphosphines, is a very important factor to consider when designing a complex due to the fact that its alteration can have profound effects in catalysis. In general, wider-angle diphosphines push the substituents of phosphorus towards the metal centre, generating more steric shielding (Figure 3)[16].

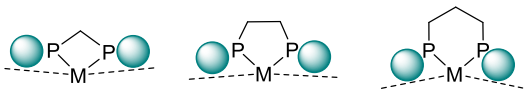


Figure 3. Steric effects of the bite angle.

It is also important to take into account that the phosphorus atoms with alkyl substituents are good σ-donors and form strong bonds with transition metals, especially with the late ones, since alkyl groups make more electron rich P-donors. By decreasing the bite angle, the HOMO increases its energy and thus, reactivity is enhanced.

This TFG focuses on methylene-bridged diphosphines with aryl substituents at the stereogenic phosphorus atom. The ligands should form 4-membered chelated rings and have not been used

in asymmetric catalysis because the other (some very successful) chiral methylene-bridged ligands for asymmetric catalysis bear alkyl substituents, such as TCFP. Some of the ligands used in this TFG have been previously described[17]. They were coordinated to Pd(II), and the obtained complexes showed unexpected structures. For this reason, it was deemed that exploring the coordination of the same ligands to Rh(I) could be very interesting.

4. OBJECTIVES

The objectives set at the beginning of this TFG were:

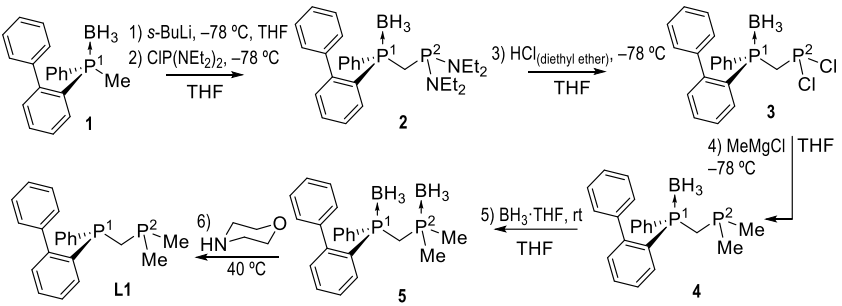
- Development of a new *one-pot* synthetic method for methylene-bridged diphosphines
- Synthesis and coordination of methylene-bridged diphosphines to rhodium and cobalt
- Asymmetric hydrogenation of olefines catalysed by the obtained complexes

5. NEW "ONE-POT" SYNTHETIC METHOD

In the first part of this TFG, a *one-pot* methodology for the synthesis of methylene-bridged diphosphines with one *P*-stereogenic centre (P^1) and a second phosphorus (P^2) atom with two equal substituents is described. The method should allow to vary the substituents of P^2 at will, including standard aliphatic or aromatic groups but also other moieties that are difficult to introduce in the usual way, such as alkoxydes or amino groups.

The method is based on optically pure *P*-stereogenic methylphosphine-boranes, known precursors prepared through the Jugé-Stephan method[18] and used in previous research of the group[17, 19, 20]. The borane group makes the methyl group somewhat acidic, making it susceptible to deprotonation by strong bases, particularly organolithiums. Therefore, the usual published method to prepare the ligands is based on the deprotonation of the methyl by *s*- or *n*-BuLi, followed by a quenching of the carbanion by with a clorophosphine ($PClR_2$) bearing the desired substituents. However, some diphosphines cannot be obtained by this method because the

chlorophosphine is not available or very difficult to prepare, and therefore we envisaged a new flexible "one-pot" method to expand the range of ligands. A particular example of this method (Ar = 2-biphenylyl; R = Me) is given in Scheme 1.



Scheme 1. The planned *one pot* method to methylene-bridged diphosphines.

Phosphine-borane **1** (**BiphMe**) was chosen as the starting monophosphine because it had been previously synthesised in multigram quantities and some of the derived complexes showed good stereoselectivities in catalysis[20]. Furthermore, methylmagnesium chloride was chosen in order to obtain diphosphine **L1**, because the *standard* preparation of this ligand would imply the use of $PClMe_2$ which is quite expensive and highly pyrophoric.

The devised method involves the formation of the boronated phosphine-diaminosphosphine **2** with the second phosphorus atom having a protonable diethylamino group, which with anhydrous HCl should be easily displaced to give the versatile intermediate **3**. This is a dichlorophosphine which should react smoothly with Grignard reagents (but also with alcohols, amines, thiols etc.) to give the monoboronated diphosphine **4**. Finally, since these ligands are quite unstable, a protection with BH_3·THF should yield the desired storable diphosphineboranes **5**. Each step of the method is known in phosphorus chemistry[21] and indeed have been already used by our research group to prepare monophosphines[22], but to our knowledge have never been employed to synthesise diphosphines.

Since the syntheses of the starting monophosphine-boranes are long and tedious, it was mandatory to work in small quantities (0.5-1.0 mmol). To monitor our synthetic route, an aliquot of the reaction mixture was taken after each step and analysed directly by $^{31}P\{^1H\}$ NMR

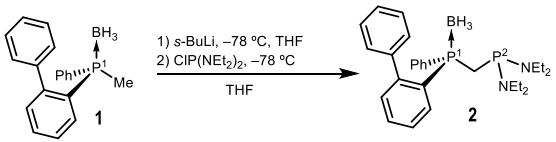
spectroscopy using a home-made capillary "insert" of $P(OMe)_3$ (TMP) in C_6D_6 (δ_P = +140.100 ppm).

5.1. FIRST SYNTHESIS

For the first synthesis following Scheme 2, 1.0 mmol of monophosphine **1** and *s*-BuLi were used.

5.1.1. First step: deprotonation and reaction with $ClP(NEt_2)_2$

The first step consists on the deprotonation of the methyl group of the initial phosphine (1 mmol, 290 mg) with *s*-BuLi (1.3 mmol) and its reaction with $ClP(NEt_2)_2$ (1.2 mmol) (Scheme 2).



Scheme 2. First step of the first synthesis.

The $^{31}P\{^1H\}$ NMR spectrum obtained with the insert method (Figure 4) showed that the deprotonation was not quantitative, since the spectrum showed that there was still some initial monophosphine-borane **1** (δ_P = +14.0 ppm) in the solution. Therefore, either the base (*s*-BuLi) was not adequate or the problem laid in the reaction of the generated carbanion with $ClP(NEt_2)_2$.

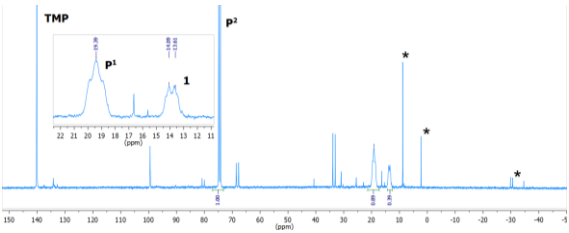


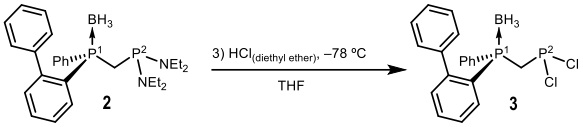
Figure 4. $^{31}P\{^1H\}$ NMR spectrum (162 MHz, C_6D_6) of **2**. *Impurities present in the insert, therefore not present in the reaction mixture.

The expected intermediate **2**, however, was clearly present, and appeared as a wide resonance at δ_P = +19.4 ppm, assignable to P^1 and a sharp doublet at δ_P = +75.0 ppm ($^2J_{P1P2}$ =

98.8 Hz), corresponding to the unprotected, P^2 atom. The latter chemical shift is typical of diaminophosphines[22].

5.1.2. Second step: chlorination with HCl

Treatment of the solution containing **2** with excess of a 2 M ethereal solution of hydrogen chloride at –78 ºC (Scheme 3) provided a cloudy suspension due to the expected formation fo the ammonium salts. After filtration, the yellow, clear solution was analysed again by $^{31}P\{^1H\}$ NMR spectroscopy (Figure 5).



Scheme 3. Second step of first the synthesis.

The spectrum proved the absence of **2** and the presence of the desired chlorophosphine **3** (δ_{P1} = 15.0 ppm, δ_{P2} = 180.4 ppm; $^2J_{P1P2}$ = 51.8 Hz) but also shows that the chlorination reaction did not proceed cleanly, since even more initial **1** was present. Indeed, the ratio **3**:**1** was close to 2:1, which lead to believe that the HCl partially cleaved the methylene bridge. In addition, several newly formed minor peaks were observed.

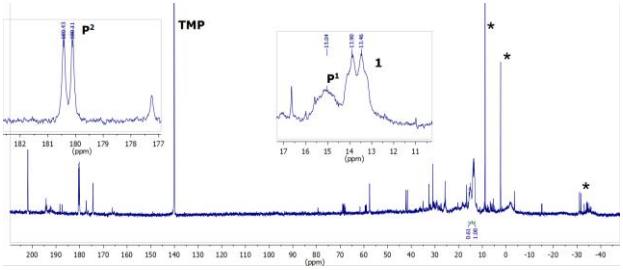
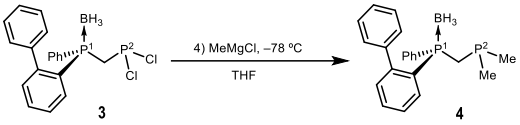


Figure 5. $^{31}P\{^1H\}$ NMR spectrum (162 MHz, C_6D_6) of **3**.

Despite that **3** was obtained in impure form, it was decided to continue with the synthesis to ascertain whether the desired ligand could be synthesised through the one-pot method after optimisation of the chlorination step.

5.1.3. Third step: methylation with MeMgCl

The solution containing chlorophosphine **3** was treated with an excess of methylmagnesium chloride (Scheme 4) in order to obtain **4**.



Scheme 4. Third step of the first synthesis.

Pleasingly, the accomplishment of this reaction was confirmed by $^{31}P\{^{1}H\}$ NMR spectroscopy (Figure 6).

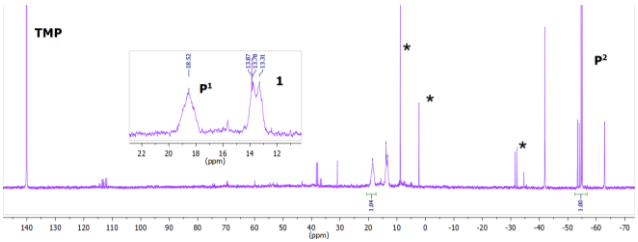
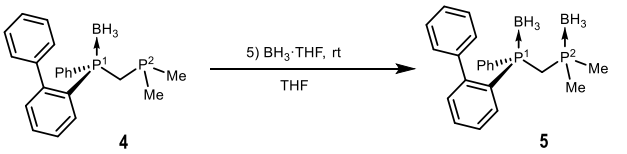


Figure 6. $^{31}P\{^{1}H\}$ NMR spectrum (162 MHz, C_6D_6) of **4**.

The diagnostic doublet ($^{2}J_{P1P2}$ = 63,93 Hz) at δ_P = –55 ppm, assignable to P^2, proves the success of the methylation. The electron-donating and sterically unhindred nature of the methyl groups effectively shield the phosphorus atom, an effect that is clearly seen in ^{31}P NMR spectroscopy.

5.1.4. Fourth step: boronation with BH_3·THF

A boronation with BH_3·THF, followed by an extractive work-up with water/dichloromethane was performed to obtain diphosphine-borane **5** (Scheme 5). A very small quantity of white solid was obtained from the organic phase after a recrystallisation and the mother liquor was also evaporated to dryness, giving an oily liquid.



Scheme 5. Fourth step of the first synthesis.

The white solid, according to both $^{31}P\{^{1}H\}$ (δ_{P1} = 16.5 ppm, δ_{P2} = 8.4 ppm) and ^{1}H NMR sepectroscopy (Figure 7), was indeed relatively pure **5** (with some **1** still present) whereas the oil from the mother liquor also contained this compound, but in a very impure form.

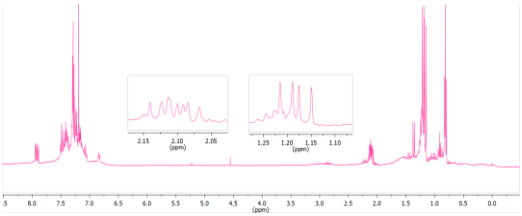
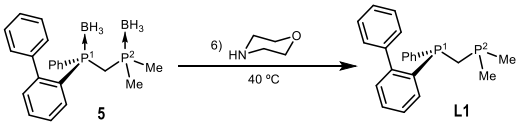


Figure 7. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of the white solid, mainly **5**.

The ^{1}H NMR spectrum presents two doublets at 1.16 and 1.20 ppm corresponding to the diastereotopic methyl groups of P^2. The protons of the methylene bridge appear as complicated multiplet centered at 2.10 ppm, due to the coupling between them and to P^1 and P^2.

5.1.5. Fifth step: deprotection with morpholine

The impure oily residue containing **5** was subjected to deboronation with morpholine for 72 h at 40 ºC merely to check whether the reaction was successful (Scheme 6).



Scheme 6. Fifth step of the first synthesis.

The $^{31}P\{^{1}H\}$ NMR spectrum of the morpholine solution showed the presence of **L1**, appearing as a pair of high-field doublets at δ_P = 31.7 and –53.4 ppm ($^{2}J_{P1P2}$ = 107.9 Hz), corresponding to P^1 and P^2, respectively. As expected, many other peaks appeared in this highly impure sample and therefore no attempts to isolate **L1** were carried out.

The analysis of the first synthesis clearly shows that the one-pot procedure is feasible but in order to be practical, both the formation of **2** and its chlorination to **3** had to be optimised.

5.2. SECOND SYNTHESIS

The quantity of the initial phosphine-borane **1** was changed to 0.5 mmol and the base was also changed to *n*-BuLi, since some phosphines are better deprotonated with this base rather than with *s*-BuLi[17]. In addition, two equivalents of $ClPNEt_2$ were employed to maximise the conversion.

Satisfyingly, the $^{31}P\{^1H\}$ NMR spectrum showed that this base worked better as there was no trace of **1** as in the first step of the synthesis, and that **2** was formed as a pure compound (Figure 8).

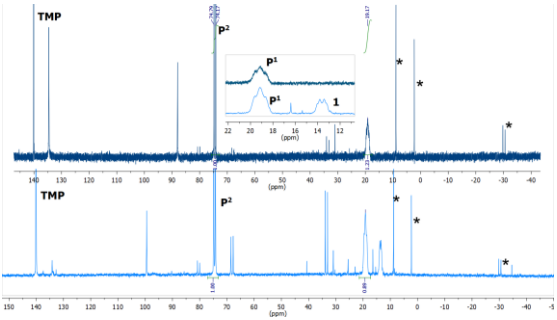


Figure 8. $^{31}P\{^1H\}$ NMR spectra (162 MHz, C_6D_6) of **2**. First synthesis (bottom) and second synthesis (top).

Unfortunately, the $^{31}P\{^1H\}$ NMR spectrum after the chlorination step showed the presence of **1**, confirming that hydrogen chloride partially breaks the methylene bridge of the ligand. In this case, after pursuing the synthesis only an impure oil was obtained, which was not used further.

In a second attempt, the same amount of initial phosphine was used and only one equivalent of the $ClP(NEt_2)_2$ was added and **2** was obtained again as an essentially pure compound according to $^{31}P\{^1H\}$ NMR spectroscopy. Still, the addition of HCl caused the formation of starting methylphosphine-borane **1** along with **3**. It is clear, hence, that the problem is with the addition of this reagent.

In a third attempt, everything was the same except the addition of HCl, which was performed slowly during ten minutes with a dropping funnel. Once again, however, the $^{31}P\{^1H\}$ NMR spectrum showed the same amount of initial phosphine **1** and an impure oil was also obtained. At this point it was clear that the chlorination step had to be changed.

5.3. THIRD SYNTHESIS

The third synthesis aimed to solve the problem of HCl by proposing four different methods that would either avoid such step, change the reactant, or make the diphosphine more resilient to the breaking of its bridge:

1. Boronating the diphosphine once the first step was performed (since it was known that it had 100% conversion) and adding the HCl on the boronated compound.
2. Reacting directly **2** with methylmagnesium chloride.
3. Chlorinating the aminophosphine **2** with PCl_3 instead of HCl, since the former is a milder reagent and should not break the bridge.
4. Reacting the carbanion from **1** with one equivalent of PCl_3 to arrive directly to **3**, completely avoiding the use of HCl and shortening the synthetic route.

1. The first synthesis did not work as expected since the $^{31}P\{^1H\}$ NMR spectrum showed no signs of **3** or its borane (**3·BH$_3$**) after adding HCl. This means that the diaminophosphine-borane unit is not sufficiently reactive towards HCl.

2. Since the first step worked perfectly and the problem came with the HCl, it was thought possible that by skipping the chlorating step and directly adding the Grignard reagent to the aminophosphine **2**. Unfortunately, the reaction did not take place and only **2** was present according to $^{31}P\{^1H\}$ NMR spectroscopy.

3. For the third attempt, PCl_3 acted just as HCl did, forming the chlorophosphine **3** in the same amount as the initial phosphine **1**. This is unexpected due to the much less acidic character of PCl_3 compared to HCl.

4. The fourth synthesis consisted on adding 1 equivalent of PCl_3 to the initial carbanion from **1** to obtain directly **3.** Unfortunately, $^{31}P\{^1H\}$ NMR spectrosopy showed very little amount of such diphosphine-monoborane but important amounts of the triphosphine-diborane **3'** and tetraphosphine-triborane **3''** (Figure 9).

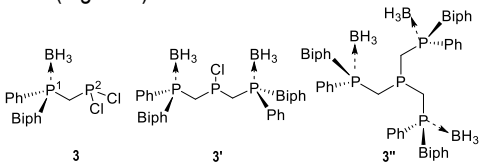


Figure 9. Structures of **3, 3'** and **3''**.

The $^{31}P\{^{1}H\}$ NMR spectrum is given in Figure 10. It can be clearly seen that there is nearly no diphosphine **3** (a doublet at δ_P = +180.0 ppm,), but a sharp triplet at δ_P = +88.7 ppm, corresponding to **3'** and a sharp quadruplet at δ_P = –38.0 ppm, corresponding to **3''** are obvious.

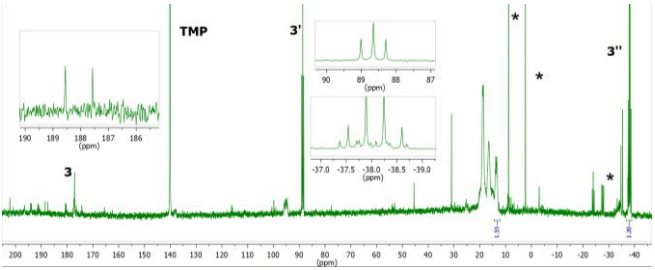


Figure 10. $^{31}P\{^{1}H\}$ NMR spectrum (162 MHz, C_6D_6) of the reaction of **1** with *n*-BuLi and PCl_3.

It can be concluded, hence, that the dichlorophosphine **3** is very reactive and reacts with further carbanions to give **3'** and **3''**.

Although this method is not suitable to prepare pure **3**, it is very interesting since it means that *P*-stereogenic tri- and or tetraphosphines could be prepared. This compounds are extremely rare in the literature[23, 24] and will be the object of future studies.

Finally, as the first step worked perfectly, we tried to isolate deboronated **2** as a pure compound for coordination. While the $^{31}P\{^{1}H\}$ NMR spectrum of the morpholine showed that the deprotection had worked perfectly (δ_P = –27.6 and 82.7 ppm for P^1 and P^2 respectively; $^{2}J_{P1P2}$ = 135.1 Hz; see Figure 11), the particular electronic properties of the nitrogenated substituents on P^2 resulted in the diphosphine getting stuck in the column and could not be isolated.

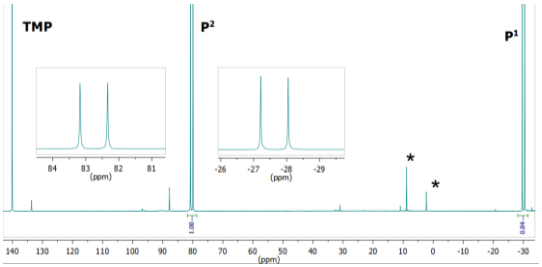


Figure 11. $^{31}P\{^{1}H\}$ NMR spectrum (162 MHz, C_6D_6) of deboronated **2**.

It can be concluded that a one-pot procedure to synthesise unsymmetric diphosphines has been successfully developed. Unfortunately, it did not allow to isolate **L1** in enough quantity for full characterisation or perform complexation studies. In the near future, other modifications such as starting from larger quantities of **1**, deprotecting both phosphorus before beginning the synthesis or adding MeLi to the aminophosphine to avoid the chlorination step, will be studied.

6. LIGAND SYNTHESIS

The second part of this TFG describes the synthesis of four different C_1-symmetric diphosphine-boranes (Figure 12) starting from methylphosphine-boranes previously obtained in the group.[17] These phosphine-boranes were obtained by series of stereoselective reactions, starting from an oxazaphospholidine-borane[18] and obtained as pure stable white solids.

The ligands differ in the aryl group at the *P*-stereogenic atom P^1 (Ar = BiPh, Np) and in the substituents of non stereogenic P^2 (R = Ph, iPr). While the aryl groups of the *P*-stereogenic phosphorus make it slightly π-acidic, the substituents of the second phosphorus can also be a little bit π-acidic (Ph) or bulky and very σ-donor (iPr).

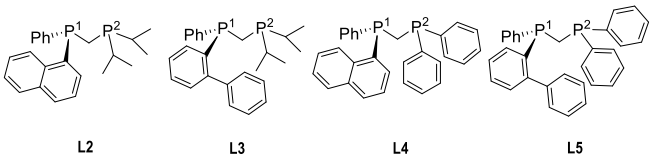
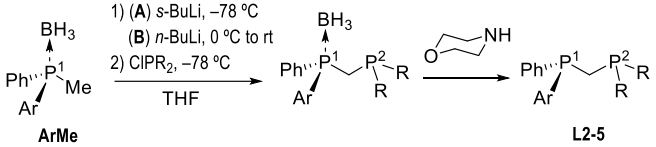


Figure 12. Diphosphine ligands **L2-L5**.

These ligands had already been reported by our group, albeit they were coordinated to allylpalladium moieities, and a hemilabile behaviour was observed, forming a bischelated structure binding two ligands and an “A-frame” structure binding the metal atoms.

The procedures for the synthesis of the ligands have been previously reported[17], and are both based on the deprotonation of its methyl substituent with *n*- or *s*-BuLi and coordination to the corresponding clorophosphines (Scheme 7).



Scheme 7. Synthetic route to obtain ligands **L1-L4**.

While in method A *s*-BuLi is used for two hours at –78 ºC, in method B *n*-BuLi is used for half an hour at 0 ºC. The group also reported method A to be more effective with the phosphinating agent chlorodiisopropylphosphine, while method B was reportedly better for chlorodiphenylphosphine. Thus, the most suitable method will depend on the ligand synthesised: method A for **L2** and **L3**, and method B for **L4** and **L5**. A final deprotection step with morpholine gives the free ligands as air-sensitive semisolids ready for complexation. A quick chromatographic column in alumina with toluene is very effective to remove the morpholine-borane, which stays stuck to the column.

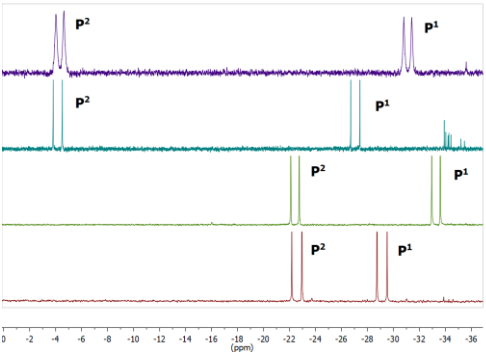


Figure 13. $^{31}P\{^{1}H\}$ NMR spectra (162 MHz, $CDCl_3$) of the four ligands synthesised. From top to bottom: **L2** (Np – iPr), **L3** (BiPh – iPr), **L4** (Np – Ph) and **L5** (BiPh – Ph).

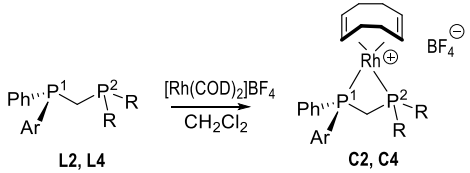
As expected the $^{31}P\{^{1}H\}$ NMR spectra show two doublets corresponding to the coupled phoshporus atoms. As mentioned before, the ligands bearing iPr substiuents in P^2 (**L2** and **L3**) resonate at lower fields than those with Ph (**L4** and **L5**).

7.COMPLEXATION STUDIES

7.1. RHODIUM

Rhodium complexes with diphosphines of the type [Rh(COD)(diphosphine)]BF_4 (COD = 1,5-cyclooctadiene) are archetypical hydrogenation catalysts that have the reputation to be very stable but very active in hydrogenation. With our short-bridged diphosphines, however, exploratory studies of the group demonstrated that was not case and that oxidation and decoordination of the ligands took place when the complexes were exposed to air. Thus, the syntheses were performed under N_2 atmosphere, and the isolated complexes were stored in a dry box.

To prepare the complexes, **L2** and **L4** were reacted with an equimolar amount of [Rh(COD)$_2$]BF_4 in CH_2Cl_2 to render the corresponding **C2** and **C4** complexes (Scheme 8).



L2, L4 **C2, C4**

Scheme 8. Synthesis of complexes **C2** and **C4**.

While these complexes were later used in asymmetric hydrogenations (described in section 7.1.1), we attempted to obtain crystals to fully characterise the complexes, unfortunately without success. Therefore, two further syntheses were performed, both to obtain a monocrystal and from it the X-ray crystal structure. The syntheses are described in the following paragraphs.

7.1.1 PREPARATION OF C2

The complexation of diphosphine **L2** (Np-iPr) produced the expected monochelated complex **C2** as an orange pure solid that was fully characterised (Figure 14).

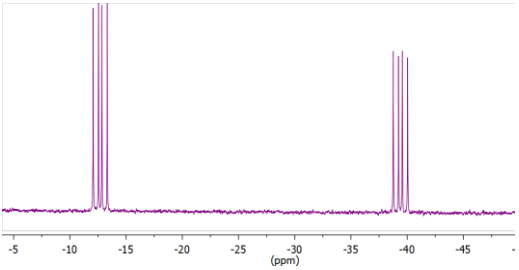
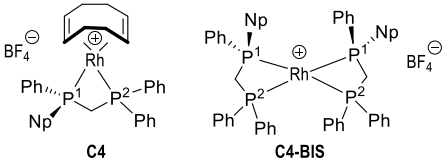


Figure 14. $^{31}P\{^{1}H\}$ NMR spectrum (162 MHz, CD_2Cl_2) of **C2**.

The $^{31}P\{^{1}H\}$ NMR spectrum shows two doublets of doublets (δ_P = –12 and –39 ppm for P^1 and P^2, respectively; $^{1}J_{P1Rh}$ = 130.97 Hz; $^{2}J_{P1P2}$ = 53.83 Hz) each of coupled to the other phosphorus atom and the rhodium centre, which also is a ½ nuclear spin nucleus. In the ^{1}H NMR the four doublets of doublets from the methyl groups of the isopropyl substituents can be seen (2.2–0.8ppm). Four peaks at 5.6, 5.5, 5.1 and 4.9 ppm correspond to the diastereotopic protons in olefins of the COD.

7.1.2 PREPARATION OF C4

The analogous complexation of **L4** (Np-Ph) also gave the expected monochelated complex **C4** as an orange solid, but some impurities were present, especially free COD, possibly due to the formation of the bisquelated complex **C4-BIS** (Figure 15).



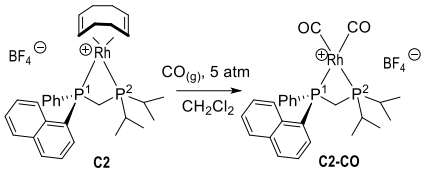
C4 C4-BIS

Figure 15. Structures of **C4** and **C4-BIS**.

It seems that either the complex did not form quantitatively or the bischelated structure was also formed, explaining the presence of free COD in the ^{1}H NMR spectrum. the ^{31}P{^{1}H} NMR spectrum shows the coordination of the ligand to the metal as two doublets of doublets at –28.9 and –33.1 ppm ($^{1}J_{P1Rh}$ = 130.09 Hz; $^{2}J_{P1P2}$ = 77.53 Hz).

7.1.3 REACTION OF C2 WITH CO

In order to obtain a more stable complex, we aimed to replace the COD ligand with two carbon monoxide molecules by passing a CO flow through a Schlenk containing a dichloromethane solution of **C2**. The formation of the expected complex **C2-CO** was observed when the solution turned canary yellow from its initial orange (Scheme 9).



Scheme 9. Synthesis of **C2-CO** from **C2**.

The solution was left stirring under a CO atmosphere for 1 h, brought to dryness and recrystallised with diethylether. Unfortunately, the solid obtained contained much more COD-complex **C2** than **C2-CO**. It seems that the CO molecules are labile and decoordinated when the solution of the complex was placed under vacuum.

Therefore, a gentle flux of carbon monoxide was bubbled into an NMR tube containing **C2** dissolved in CD_2Cl_2 for a few minutes. This time, the ^{31}P{^{1}H} NMR spectrum (Figure 16) showed no trace of the initial **C2**. Thus, **C2-CO** was fully characterised by NMR, including COSY, HSQC and NOESY experiments.

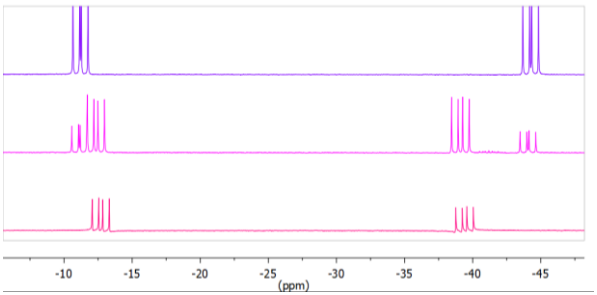


Figure 16. $^{31}P\{^{1}H\}$ NMR spectra (162 MHz, CD_2Cl_2) of the evolution of **C2** (bottom) towards **C2-CO** (top).

The $^{31}P\{^{1}H\}$ NMR spectrum shows the evolution of the set of two doublets of doublets from **C2** (bottom) to the other set belonging to **C2-CO** (top). The spectrum in the middle is from the first experiment in which the carbonyl ligands had been partially removed by vacuum.

The slow recrystallisation of **C2-CO** in DCM/Et_2O yielded beautiful crystals, which were submitted to X-ray diffraction. Unfortunately, the crystal structure could not be obtained, due to the formation of carbon monoxide bubbles inside the crystal as can be seen in Figure 17.

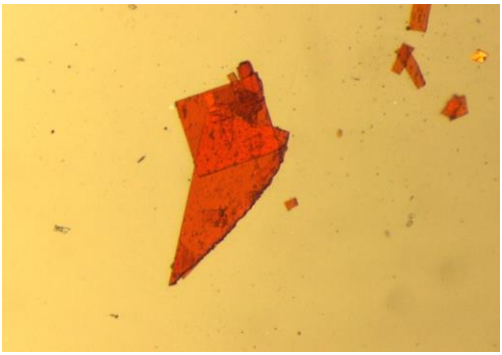
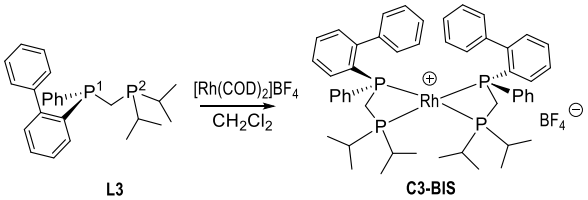


Figure 17. Crystal of **C2-CO** showing small CO bubbles.

7.1.4 PREPARATION OF C3-BIS

A modified synthesis was devised to obtain, with ligand **L3**, a bischelated rhodium(I) complex similar to the reported palladium counterpart[17]. Hence, two equivalents of **L3** were reacted with one equivalent of $[Rh(COD)_2]BF_4$ (Scheme 10). Bis(chelated) complexes are very interesting because they have given good results in asymmetric hydrogenation[25].



L3 C3-BIS

Scheme 10. Synthesis of **C3-BIS**.

The synthesis was successful and rendered the desired bischelate complex, albeit slightly impurified with **C3** (Figure 18). An equilibrium between **C3** and **C3-BIS** although unlikely, cannot be completely excluded.

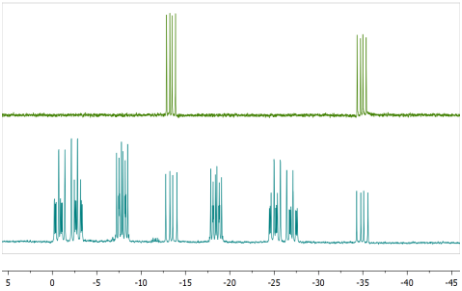


Figure 18. $^{31}P\{^{1}H\}$ NMR spectra (162 MHz, CD_2Cl_2) of **C3-BIS** (bottom) and pure **C3** (top).

The NMR spectra of the bischelated complex **C3-BIS** can be compared to the monochelated one (**C3**) previously obtained by the group. The $^{31}P\{^{1}H\}$ spectrum of the former is a complex, strongly cloupled AA'MM', second order spin system, which will be simulated with the appropriate software in future studies to extract the chemical shifts and coupling constants.

After many attempts, a suitable crystal for X-ray diffraction studies of the complex could be finally obtained (Figure 19).

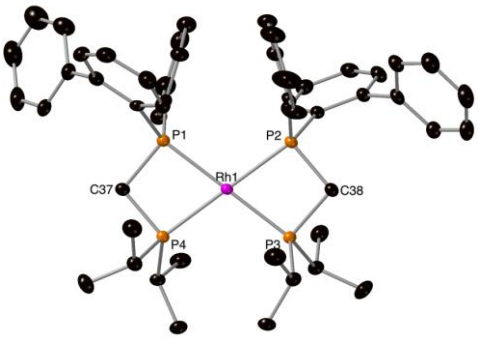


Figure 19. Representation of the structure of **C3-BIS**. The ellipsoids have been drawn at 50% of probability level and the hydrogen atoms and the tetrafluoroborate anions have been removed for clarity. Selected distances (Å) and angles (deg): Rh1-P1 2.3283(12), Rh1-P2 2.2949(11), Rh1-P3 2.2910(11), Rh1-P4

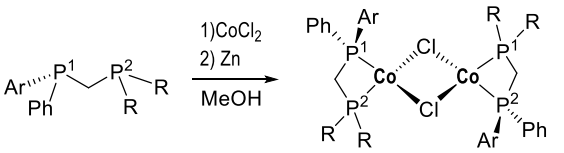
2.2966(11), P1-C37 1.847(4), P2-C38 1.847(4), P3-C38 1.855(4), P4-C37 1.840(4), P1-Rh1-P4 72.72(4), P4-Rh1-P3 106.98(4), P3-Rh1-P2 72.60(4), P2-Rh1-P1 107.72(4), P1-C37-P4 96.1(2), P2-C38-P3 94.35(17).

As it happened with Pd(II)[17], it shows a *cis* configuration. The Rh atom sits in perfectly planar environment (the sum of the angles around Rh is 360.02º) and the bite angle of the phosphines are 72.60º and 72.72º, typical values for methylene-bridged diphosphines [16]. It can be pointed out that a search on the Cambridge Structural Data Base reveals that there are only 5 structures[25-29] of complexes containing the $[Rh(diphos)_2]^+$ cation with methylene-bridged diphoshpines reported so far none of them with a chiral, non-symmetric ligand.

7.2. COBALT

Cobalt, as opposed to its heavier congener rhodium, is a first-row and Earth-abundant transition metal. While these metals would be perfect for catalytic applications because of their availability and price, they have been severely understudied. It often form Co(II) paramagnetic species, which enormously difficult the monitoring of reactions by NMR spectroscopy, because the spectra are extremely broad. In hydrogenation, the most interesting species would be, in principle, Co(I) precatalysts.

This type of complexes was presumably synthesised in this TFG in a form of Co(I) dimer generated *in situ* by treating $CoCl_2$ with Zn in presence of the ligand (Scheme 11). This synthetic route has been reported by Chirik's group[8] to provide almost perfect conversions and high enantioselectivities with some ligands. In this TFG, we tested diphosphines **L2-L5**.



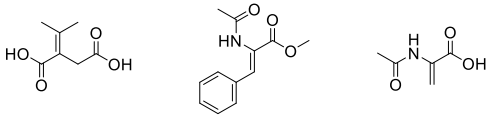
Scheme 11. Presumed *in situ* preparation of Co(I) dimers from **L2-L5.**

The synthesis of was performed in the dry box to prevent the oxidation of both the ligand and the cobalt(I) centre. As the complexes were generated *in situ*, they were not characterised, so the

structure is supposed to be analogous to those reported by Chirik. The solutions of the complexes were directly used as catalytic precursors, as explained later. Future studies will be focused on confirming the nature of the complexes after isolating and fully characterising them.

8. ASYMMETRIC HYDROGENATION

Functionalised olefins are interesting substrates in asymmetric hydrogenation for their potential uses in pharmaceutical applications and because they are the benchmark substrates for Rh. Therefore, for this TFG, three model substrates (Figure 20) were chosen: **S1** (DMI (dimethylitaconate)), **S2** (MAC (methyl (Z)-α-acetamidocinnamate)) and **S3** (MAA (α-acetamidoacrylate)).



S1
DMI

S2
MAC

S3
MAA

Figure 20. Structures of substrates **S1-S3**.

These common benchmark substrates were chosen because they allow us the comparison of our hydrogenation results with plenty of data with the same substrates found in the literature.

8.1. RHODIUM CATALYSTS

Both monochelated rhodium complexes **C2** and **C4** were used in the catalytic hydrogenation of **S1-S3** with a catalyst loading of 1% and substrate concentration of 0.2 M, using THF as a solvent. The hydrogenations were performed at 20 bar for 24 h at room temperature (Table 2). The results are given in Table 1.

	Substrate	Conversion [%]	Enantiomeric excess [%]
C2 (Np – iPr)	**S1**	100	20 (*R*)
	S2	100	29 (*R*)
	S3	100	7 (*R*)
C4 (Np – Ph)	**S1**	100	*rac*
	S2	100	16 (*R*)

Table 1. Hydrogenation results with precursors **C2** and **C4**.

Both of the complexes rendered a 100% conversion and thus, are very active in hydrogenation. Precursor **C2**, bearing aliphatic substituents, gives some enantioselectivity in asymmetric hydrogenation although unfortunately the enantioselectivities remain very poor.

8.2. COBALT CATALYSTS

The four cobalt complexes generated *in situ* were also used in the catalytic hydrogenation of **S1** and **S2** but not under the same conditions. The complex formed with **L2** was employed under the same conditions as the rhodium complexes: methanol, 1% of catalyst, substrate concentration of 0.2 M 20 bar, rt, 24 h. For the systems with **L3**, **L4** and **L5** the conditions were hasher: 10% of catalyst, 35 bar, 50 ºC (Table 3).

	Substrate	Conversion [%]	Enantiomeric excess [%]
L2 (Np – iPr)	**S1**	0	–
	S2	0	–
L3 (BiPh – iPr)	**S1**	96	–
	S2	73	25 (*S*)
L4 (Np – Ph)	**S1**	62	*rac*
	S2	21	8 (*S*)
L5 (BiPh – Ph)	**S1**	25	–
	S2	0	–

Table 3. Hydrogenation results of the cobalt precursors of **L2-L5.**

The catalytic hydrogenation with **L2** did not work probably because of the reaction conditions. Therefore, the next three hydrogenations with **L3**, **L4** and **L5** took place at higher pressures and temperatures. A higher conversion can be observed in the hydrogenations of **S1**

for all complexes. **L3** gives a better conversion for **S1** but no enantioselectivity, while lower conversion but higher enantioselectivity is found for **S2**. **L4** produces moderate conversion for **S1** but low for **S2**, but with some enantioselectivity. Finally, **L5** showed very low conversion for **S1** and no enantioselectivity.

9. EXPERIMENTAL PART

9.1. MATERIALS AND METHODS

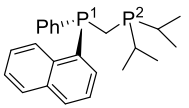
All compounds were prepared under a purified nitrogen atmosphere using standard Schlenk and vacuum-line techniques or in a glove box Mbraun filled with purified nitrogen. The solvents were obtained from a solvent purification system and, if needed, were degassed by three freeze-pump-thaw cycles. They were always kept under nitrogen. ^{1}H and $^{31}P\{^{1}H\}$ NMR spectra were recorded with a 400 Hz spectrometrer with degassed deuterated solvents. Some of the $^{31}P\{^{1}H\}$ NMR spectra were recorded with the sample dissolved in non-deuterated solvent but using a capillary "insert" of 1% $P(OMe)_3$ in C_6D_6 (δ_P = +140.100 ppm).

9.2. SYNTHESES OF THE LIGANDS

9.2.1. Synthesis of L2

NpMe (264 mg, 1 mmol) was dissolved in 5 mL of THF, and the solution was cooled to −78 °C. *s*-BuLi (1 mL of a 1.6 M solution, 1.3 mmol) was added, and the solution was stirred for 2 h at −78 °C. Chlorodiisopropylphosphine (200 μL, 1.2 mmol) was added, and the mixture was warmed to room temperature overnight. 20 mL of water were carefully added. The solvents were removed under vacuum, and the suspension extracted with DCM (3×10 mL). The combined organic fractions were washed with 100 mL of water, dried over anhydrous Na_2SO_4, and filtered. The solution was concentrated to dryness, giving an oily resin. Then, such oily resin (198 mg, 0.5 mmol) was dissolved in 5 mL of morpholine and stirred for 72 h at 40 °C. The mixture was brought to dryness, and the residue was subjected to column chromatography purification (alumina,

toluene) under nitrogen to yield, after elimination of the solvent, the desired product as a white pasty solid, **L2**.

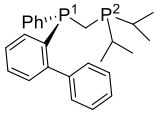


L2

The characterisation data of this compound matched the published data [17]

9.2.2 Synthesis of L3

L3 was synthesised and deprotected analogously to **L2** using **BiphMe** (**1**) (290 mg, 1 mmol), yielding **L3** (210 mg, 0.5 mmol).

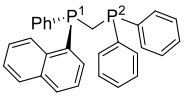


L3

The characterisation data of this compound matched the published data [17].

9.2.3 Synthesis of L4

NpMe (145 mg, 0.5 mmol) was dissolved in 5 mL of THF, and the solution was cooled to 0 °C. *n*-BuLi (0.5 mL of a 1.6 M solution, 0.8 mmol) was added, and the solution was stirred for 30 min at 0 °C and then warmed to room temperature. The solution was cooled to –78 °C, chlorodiphenylphosphine (110 μL, 0.6 mmol) was added, and the mixture was slowly warmed to room temperature overnight. 20 mL of water was carefully added. The organic solvents were removed under vacuum, the suspension was extracted with DCM (3×10 mL), and the combined organic fractions were washed with 100 mL of water, dried over anhydrous sodium sulphate, and filtered. The solution was concentrated to dryness, giving an oily resin. Such oily resin (115 mg, 0.25 mmol) was dissolved in 5 mL of morpholine and stirred overnight at room temperature. The mixture was brought to dryness, and the residue was subjected to column chromatography purification (alumina, toluene) under nitrogen to yield, after elimination of the solvent, the title product as a white pasty solid, **L4**.

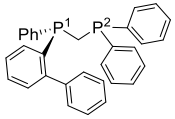


L4

The characterisation data of this compound matched the published data [17].

9.2.4 Synthesis of L5

L5 was synthesised and deprotected analogously to **L4** using BiphMe (132 mg, 0.5 mmol), to yield **L5** (122 mg, 0.25 mmol).



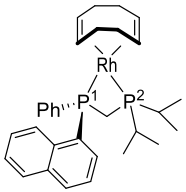
L5

The characterisation data of this compound matched the published data [17].

9.3. SYNTHESES OF THE COMPLEXES

9.3.1. Synthesis of C2

L2 (0.21 mmol) was dissolved in 10 mL of DCM and stirred with 0.95 equivalents of $[Rh(COD)_2]BF_4$ (82 mg, 0.20 mmol) for 1 h. Then it was brought to dryness to give **C2**.

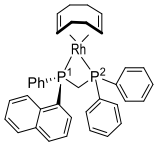


C2

Orange solid. ^{1}H NMR (400 MHz, CD_2Cl_2): 8.41–7.35 (m, 13H, Np), 5.68 (s, 1H, CHCOD), 5.46 (s, 1H, CHCOD), 5.08 (s, 1H, CHCOD), 4.85 (s, 1H, CHCOD), 4.10–3.96 (m, 1H, CHbridge), 3.62–3.48 (m, 1H, CHbridge), 2.45–2.23 (m, 8H, CH_2(COD)), 2.24–2.11 (m, 2H, CHiPr), 1.19 (dd, J= 15.0, 6.9, 3H, CH_3(iPr)), 1.12–0.97 (m, 6H, CH_3(iPr)), 0.76 (dd, J= 17.3, 6.9, 3H, CH_3(iPr)). ^{13}C{^{1}H} NMR (CD_2Cl_2): 138–124 (m, 16C, CHAr), 102.85–102.70 (m, 1C, CHCOD), 99.60–99.44 (m, 1C, CHCOD), 99.13–98.97 (m, 1C, CHCOD), 96.22–96.06 (m, 1C, CHCOD), 33.77–33.33 (m, 1C, CH_2(bridge)), 30.82–29.42 (m, 4C, CH_2(COD)), 25.52–25.21 (m, 2C, CHiPr), 19.39–17.37 (m, 6C, CH_2(iPr)). ^{31}P NMR (CD_2Cl_2): –12.33 (dd, $^2J_{PP}$ = 126.7, $^1J_{PRh}$ = 77.4, PiPr), –39.07 (dd, $^2J_{PP}$ = 131.7, $^1J_{PRh}$ = 77.4, PNp)

9.3.2. Synthesis of C4

C4 was synthesised analogously to **C2** but using **L4**.

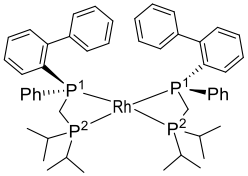


C4

Orange solid. ^{1}H NMR (400 MHz, CD_2Cl_2): 8.25–7.22 (m, 22H, Ar), 5.47 (s, 1H, CHCOD), 5.32 (s, 1H, CHCOD), 2.42–2.21 (m, 8H, CH2(COD)). ^{31}P NMR (CD_2Cl_2): –28.86 (dd, $^{2}J_{PP}$ = 130.2, $^{1}J_{PRh}$ = 78.0), –33.08 (dd, $^{2}J_{PP}$ = 130.1, $^{1}J_{PRh}$ = 78.0). LRMS: calcd. for $[(NpPh)_2Rh–BF_4]+$ 971.80, found 971.18. Calcd. for $[(NpP(O)–PPh_2)_2Rh–BF_4]+$ 1003.80, found 1003.17.

9.3.3. Synthesis of C3-BIS

L3 (0.2 mmol) was dissolved in 10 mL of DCM and stirred with 1/2 equivalent of $[Rh(COD)_2]BF_4$ (164 mg, 0.4 mmol) for 1 h, then brought to dryness to give **C3-BIS** slightly impurified with **C3**.



C3-BIS

Orange solid. ^{31}P NMR (CD_2Cl_2): –0.22 - –3.36 (m), -7.23 – -8.48 (m), –13.40 (dd), –17.83 - –19.07 (m), – 24.44 - –27.70 (m), –34.9 (dd) ($^{1}J_{PRh}$=129,42 Hz, $^{2}J_{PP}$=53,28 Hz)

10. CONCLUSIONS

A *one pot* synthetic method to synthesise unsymmetric diphosphines has been developed to give a novel diphosphine ligand with dimethylphosphino moiety, **L1**. In further r studies, more quantity will be synthesised in order to properly purify it and perform a full characterisation. Although the methodology clearly works, it will have to be optimised to be useful.

The synthesis of the known ligands **L2-L5** was successfully reproduced, and the ligands have been used in complexation studies with Rh(I) moieties. New monochelated Rh(I) complexes **C2** and **C4** were successfully synthesised, as well as the bischelated complex **C3-BIS**. All these complexes are unstable in air and have been fully characterised, including the determination of the crystal structure for **C3-BIS**. Finally, the carbonyl complex **C2-CO**, was also obtained and characterised by multinuclear NMR. This complex suffers spontaneous decarbonylation, even in solid state.

Preliminary complexation studies have also been carried out with Co(I) but the obtained species have not been characterised but only obtained *in situ*.

Both Rh and Co precursors have been used in asymmetric hydrogenation of benchmark substrates **S1-S3**. The Rh systems are very active, promoting full conversions but only complexes **C2** and **C4** have exhibited some low enantioselectivity. The Co systems, however, exhibited some conversion albeit almost no enantioselectivity.

The methylene-bridged diphosphines studied in this TFG present an interesting coordination chemistry that merits to be more fully explored. They seem, however, not to be adequate ligands for asymmetric hydrogenation, unless with the substrates and conditions explored. Their use in other asymmetric reactions will be pursued in the future.

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12. ACRONYMS

HC: Homogeneous Catalysis

L-DOPA: Levodopa or L-3,4-dihydroxyphenylalanine

DIPAMP: (Ethane-1,2-diyl)bis[(2-methoxyphenyl)phenylphosphane]

HSAB: Hard and Soft (Lewis) Acids and Bases

TCFP: TriChickenFootPHOS

HOMO: Highest Occupied Molecular Orbital

BiphMe: (*S*)-(2-biphenyl)phenylmethylphosphine-P-borane

NpMe: (*S*)-phenylmethyl(1-naphthyl)phosphine-P-borane

s-BuLi: sec-Buthyllithyum

n-BuLi: n-Buthyllithium (linear)

THF: Tetrahydrofuran or oxolane

MeLi: Methyllithium

COD: 1,5-Cyclooctadiene

DCM: Dichloromethane

Et_2O: Diethyl ether

DMI: Dimethyl itaconate

MAC: Methyl (Z)-α-acetamidocinnamate

MAA: α-Acetamidoacrylate