Anna M Segarra González

Catalytic Asymmetric Hydroboration Reaction of Alkenes

Recycling of a Catalyst

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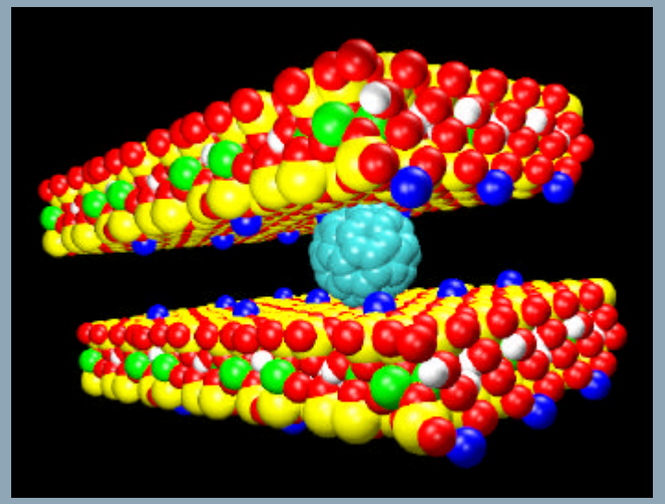

UNIVERSITAT ROVIRA I VIRGILI

JUNE 2004

Table of contents

Chapter 3. Recovery of the catalyst

Chapter 4. Catalytic asymmetric hydroboration of perfluoroalkenes and dihydroboration of internal alkynes. Recovery of the catalyst

Universitat Rovira i Virgili

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CATALYTIC ASYMMETRIC HYDROBORATION REACTION OF ALKENES. RECYCLING OF A CATALYST.

Memòria presentada per

Anna M. Segarra González

Per a optar al grau de Doctor per la URV.

Tarragona, Abril 2004

El model molecular de la portada és una representació de la montmorillonita i ha estat realitzat per la Dr.Marianna Fanti de la Universitat de Bologna.

‘No hi ha camí per a la pau, la pau és el camí’

There is no way to peace. Peace is the way.

Mahatma Gandhi

Chapter 1

Introduction and scope

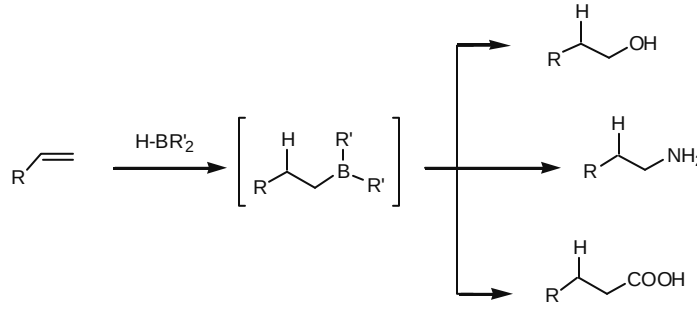
The catalytic asymmetric hydroboration reaction has proved to be one of the most useful reactions in organic synthesis. It provides a way of transforming alkenes into many different types of C-X and C*-R bonds through the optically enriched organoboron adduct C*-B. In addition, there are a wide range of unsaturated substrates, which can react with a borane reagent through transition metal complexes.*

There are several challenges involved in applying chiral catalysts in the hydroboration reaction: the catalytic performance must be excellent, the development of the activity and selectivity during the process must be understood and chiral catalytic systems must be designed so that they can be recovered and reused, and, in this way, ensure the environmental and economic viability of the process. Taking these factors into account, we considered various hypotheses for our work. At that time, the academic challenges for this thesis were being defined and outlined in a paper but, as in any study of a chemical transformation, there is a hierarchy of goals to be met, the first of which was to know the state of the art.

Therefore, this section attempts to provide the reader with a general overview of the principal concepts and applications of the homogeneous catalytic hydroboration reaction, as well as the leading approaches involved in the recycling of soluble catalysts through immobilisation pathways.

1. Hydroboration reaction

The hydroboration reaction is a classical method for synthesising organoboron compounds and one of the most studied reactions in organic synthesis. Introduced by H. C. Brown [1] in 1959, it is based on the *syn* addition of borane reagent H-BR'$_2$ to alkenes or alkynes. In fact, it is considered to be the initial step in the introduction of a very wide variety of functional groups and it can also be used to construct carbon frameworks (Scheme 1). The uncatalysed hydroboration reaction is one of the most common and useful methodologies for large-scale preparations, but metal-catalysed reactions are more efficient and selective. However, catalysed hydroboration did not start to show significant results until Männing and Nörth's developments in 1985 [2]. They reported that the addition of the borane reagent, catecholborane (**1**), to alkenes is generally very slow at room temperature but that it can be considerably accelerated by small amounts of transition-metal complexes, such as Wilkinson's complex [RhCl(PPh$_3$)$_3$]. In addition, catalysed hydroboration is an interesting strategy for highlighting the chemo-, regio-, diastereo-, and enantioselectivity of the process. This opened up a completely new field of chemistry, which prompted intensive investigation [3].



Scheme 1

The different products of the catalysed and uncatalysed [4] reactions reflect different mechanisms for the hydroboration transformation. Moreover, the asymmetric

version of the hydroboration reaction can be performed by using catalysts containing chiral ligands and/or chiral borane reagents [5].

Organoboron compounds have been shown to be of practical help in synthetic organic reactions, such as asymmetric, combinatorial and polymer synthesis [3], [6-8], molecular recognition such as host-guest compounds [9], and neutron capture therapy in the treatment of malignant melanomas and brain tumours [10].

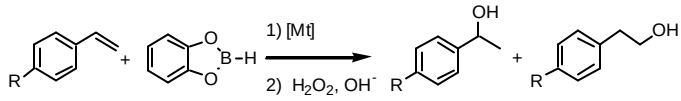
2. Metal-catalysed hydroboration

The first significant difference between the uncatalysed and catalysed hydroboration reaction is the reaction conditions. The B-H addition to unsaturated functional groups in the absence of catalyst requires elevated temperatures and long reaction times. In contrast, the hydroboration reaction catalysed by transition metal complexes can not only be carried out at room temperature [3a] but can also provide different chemo- [11], regio- and stereoselectivities in the process. The hydroboration reaction of unsaturated substrates catalysed by transition metal complexes has been intensively studied, particularly from the point of view of its mechanism. In this introduction we only consider the most general mechanistic features because any specific mechanism will depend on the nature of the substrate, the catalyst, the reagent and the conditions.

2.1. Hydroboration of alkenes and alkynes

Unsaturated vinylarenes, aliphatic terminal alkenes, perfluoroalkenes, alkynes, conjugate dienes, allenes and enynes have been shown by the literature to be suitable substrates for the catalytic hydroboration reaction. The hydroboration of vinylarenes has been extensively studied, and perhaps these are the best substrates that a discussion of the efficiency and selectivity of the catalyst should consider. The following review aims to provide an overall picture of the catalysed hydroboration of unsaturated substrates, particularly vinylarenes (Table 1).

Table 1. Catalytic systems for hydroboration/oxidation of vinylarenes with catecholborane[a]



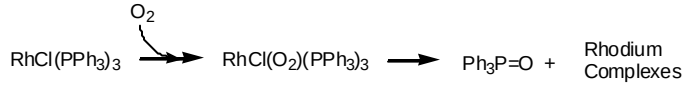
1 **2** **3**

Entry	Catalytic system	Yield (%)	**2** (%)	**3** (%)
1	$RhCl(PPh_3)_3$	80	>99	<1
2[b]	$RhCl(PPh_3)_3$		24	76
3	$[Rh(\mu\text{-}Cl)I(cod)]_2$	45	20	80
4	$[Rh(\mu\text{-}Cl)(cod)]_2/4PPh_3$	90	98	2
5	$[Rh(\mu\text{-}Cl)(cod)]_2$/2dppe	50	34	66
6	$[Rh(\mu\text{-}Cl)(cod)]_2$/2dppb	83	45	55
7	$[Rh(\mu\text{-}Cl)(cod)]_2$/2dppf	83	10	90
8	$[Rh(\eta^3\text{-}2\text{-Me-allyl})(dppb)]$		>99	<1
9	$[Rh(BABAR\text{-}Phos)_4]CF_3SO_3$	99	99	1
10	$[Rh(cod)_2]BF_4/2PPh_3$	93	99	1
11	$[Rh(cod)_2]BF_4$/dppb	94	99	1
12	$[Ir(cod)(Py)(PCy_3)]OTf$		22	78
13	$RuCl_2(PPh_3)_4$		-	100
14	$RuCl_2(PPh_3)_4(MeOH)$		1	99
15[c]	Cp_2TiMe_2	89	-	100
16[c]	$Cp^*_2Sm(THF)$	89	-	100

[a] Standard conditions. Solvent: THF. T: 25^{0}C, under argon; [b] under air;
[c] Standard conditions. Solvent: benzene. T: 25^{0}C, under argon

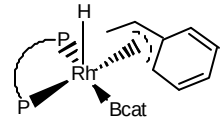
Neutral rhodium-phosphine complexes, such as Wilkinson's catalyst, $[RhCl(PPh_3)_3]$, are the catalysts that have been most studied for the hydroboration of alkenes. However, the sensitivity of the metal complex to air and, therefore, its undesired influence on the regioselectivity of the hydroboration reaction have been described in the literature (Table 1, entries 1 and 2) [12-13]. The oxidation of the

phosphine to their corresponding oxide decreases the phosphine/rhodium ratio and, consequently, there are changes in regioselectivity [14], (Scheme 2). Thus, the *in situ* preparation of the catalyst from $[Rh(\mu\text{-}Cl)(cod)]_2$ and the phosphine (Table 1, entries 3-7) [12-15] or the use of an air-stable complex such as π-allylrhodium, $[Rh(\eta^3\text{-}2\text{-}Me\text{-}allyl)(dppb)]$ (Table 1, entry 8) [16] or the cationic complex $[Rh(BABAR\text{-}Phos)_4]CF_3SO_3$ (Table 1, entry 9) [17] are convenient alternatives. Also the *in situ* addition of monophosphines, (PPh_3), or diphosphines, (dppb), to the cationic rhodium complex $[Rh(cod)_2]BF_4$, generates highly active species that can catalyse the hydroboration reaction, even at low temperatures (Table 1, entries 10-11) [15].



Scheme 2

In the hydroboration of vinylarenes, the preference for branched (**2**) or linear (**3**) alkylboronate ester products (Table 1) depends on the catalytic system, the ligand and the borane reagent. Unfortunately, however, until now this has not been well understood. Hayashi et al. suggested that the high internal selectivity of the catalytic hydroboration of vinylarenes on the branched products could be favoured by a contribution from the η^3-benzylrhodium complex (**4**) (Figure 1) as a key intermediate [15a]. But in general, substrates such as perfluoroalkenes [18] and α,β-unsaturated esters or amides [19], which contain an electron-withdrawing group, commonly have high internal selectivities in the hydroboration reaction catalysed with cationic rhodium complexes and catecholborane (**1**).



4

Figure 1

Most studies of the catalysed hydroboration reaction have used the five-member ring heterocycle diorganyloxyborane catecholborane (**1**), (Figure 2), because of its high degree of Lewis acidity and the favourable steric profile of the borane coordinated to the metal [20]. However, during the hydroboration reaction the intrinsic instability of **1** favours side reactions, which lead to undesirable products such as alkanes or vinylboronate esters [21]. The pinacolborane (**5**), (Figure 2), has recently been found to be an excellent alternative as a borane reagent because it is more stable, easily stored and easily prepared [22]. Other borane reagents including 4,4,6-trimethyl-1,3,2-dioxaborilane (**6**) [23], oxazaborolidines (**7**) [24], benzo-1,3,2-diazaborolane (**8**) [25] and borazine (**9**) [26] might also be used, but the total scope of these reagents remains to be explored.

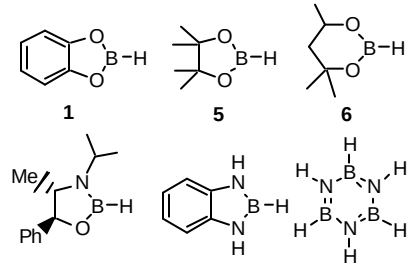
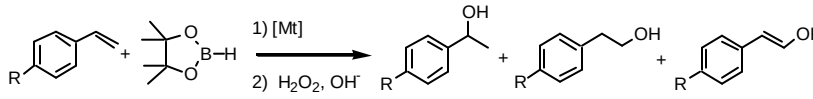


Figure 2

Several transition metals are used in the catalytic hydroboration/oxidation reaction with catecholborane as the borane reagent. Iridium (I) [27] and ruthenium (II) or (III) [28] are some of the transition metals that have been studied. Modified with phosphines, their selectivity towards terminal alcohols is high (Table 1, entries 12-14). However, the scope of these catalysts has not yet been studied in detail. The Ti and Sm metals modified with cyclopentadienyl ligands, Cp_2TiMe_2 [29] and $Cp^*_2SmMe_2$ [30] have proved to be excellent catalysts for the addition of boron to the terminal carbon of the substrate (Table 1, entries 15-16). Recently Lin et al., made a theoretical study of the mechanism in the hydroboration reaction of $Cp_2Ti(\eta^2\text{-HBcat})$ [31]. They suggested that there was a strong tendency to form a five-member ring

structural intermediate through the C-B interaction, which leads to the exclusive linear product. The steric effect of borane reagents also plays an important role in this selectivity. Throughout the literature, it can be observed that changes in the nature of the catalytic complex or in the hydroboration reagent have effects on the regioselectivity of the hydroboration reaction. When the catecholborane (**1**) is replaced by the pinacolborane (**5**) (Figure 2), the selectivity in the hydroboration reaction of vinylarene rhodium catalysts decreases. Thus, pinacolborane is added selectively to the terminal carbon of vinylarenes because of its bulkiness (Table 2, entries 1 and 2), which is in sharp contrast to the addition of catecholborane according to the electronic effect of the vinylarene. However, $RhCl(PPh_3)_3$ provides an undesired product, PhCH=CHOH (**10**), due to the 'dehydrogenative borylation' reaction (Table 2, entry 1). In addition, Ni(II), and Ir(I) catalysts reveal high terminal selectivity (Table 2, entries 3-4), [32-33].

Table 2. Catalytic systems for hydroboration/oxidation of vinylarenes with pinacolborane.



5 **2** **3** **10**

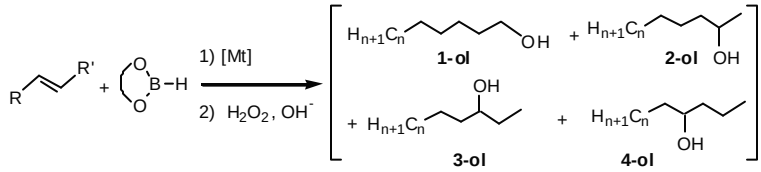
Entry	Catalytic system	Yield (%)	**2** (%)	**3** (%)	**10** (%)
1	$RhCl(PPh_3)_3$	99	35	50	15
2	$RhCO(PPh_3)_2Cl$	99	1	99	-
3	$CpNiCl(PPh_3)$	99	1	99	-
4	$[Ir(\mu\text{-}Cl)(cod)]_2$/2dppp	97	<1	>99	-

[a] Standard conditions. Solvent: CH_2Cl_2. T: 25^0C, under argon

It is worth mentioning that various metal complexes also catalyse the addition of catecholborane and pinacolborane to aliphatic terminal alkenes [2]. Neither the borane reagents nor the modified catalysts were able to change the high terminal regioselectivity (Table 3) also provided by the uncatalysed hydroboration

reaction with catecholborane (Table 3, entry 1) [13]. Similarly, the catalytic systems based on Rh, Zr, and Ir with pinacolborane show terminal regioselectivity (Table 3, entries 4-6) [32-35]. The terminal aliphatic alkene, 1-octene, and the internal alkene, 4-octene, can isomerise from internal or terminal alkenes to terminal or internal ones, respectively, in the presence of rhodium complexes and BH_3 as the borane reagent (Table 3, entries 3, 7) [13], [36]. In the case of internal alkenes, for example, the hydroboration/oxidation of 4-octene yields terminal or internal alcohols depending on the borane and catalyst used. The neutral rhodium and the cationic iridium complexes

Table 3. Catalytic hydroboration/oxidation of aliphatic alkenes. Isomerisation pathways[a]

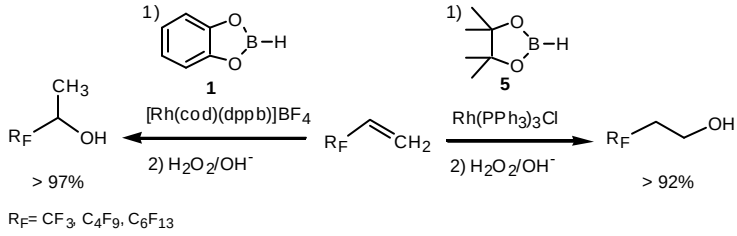


Entry	Catalytic system		Olefin	1-ol	2-ol	3-ol	4-ol
1	None	**1**	1-decene	98	2	-	-
2[b]	$RhCl(PPh_3)_3$	"	"	99	1	-	-
3[b]	$RhCl_3$	BH_3	1-octene	2	17	37	43
4	$RhCl(PPh_3)_3$	**5**	"	100	-	-	-
5	Cp_2ZrHCl	"	"	100	-	-	-
6	$[Ir(\mu\text{-}Cl)(cod)]_2$/2dppm	"	"	>99	<1	-	-
7[b]	$RhCl_3$	BH_3	4-octene	2	16	35	46
8	$RhCl(PPh_3)_3$	**5**	"	100	-	-	-
9	$[Ir(\mu\text{-}Cl)(cod)]_2$/2dppm	**5**	"	100	-	-	-
10[b]	$RhCl(PPh_3)_3$	**1**	"	-	-	-	100
11[b]	$[Rh(nbd)(dppb)]BF_4$	"	"	4	2	7	87
12	$[Rh(CO)(PPh_3)_2Cl]$	**5**	"	3	-	-	97
13	$Cp_2NiCl(PPh_3)_3$	"	"	1	-	-	99

[a] Standard conditions. Solvent: CH_2Cl_2. T: 25 ^{0}C, under argon; [b] Solvent: THF. T: 25 ^{0}C, under argon

are more prone to isomerise the boron atom to the terminal carbon in the presence of a bulky pinacolborane [32], [34]. This illustrates the superiority of pinacolborane for synthesising terminal boron compounds (Table 3, entries 8 and 9) [32-34]. However, catalytic systems based on rhodium and nickel provide mainly the 4-ol product regardless of whether the borane used is pinacolborane or catecholborane (Table 3, entries 10-13) [13], [32]. The alkene isomerization is caused by olefin insertion into the Rh-H bond, followed by β-hydride elimination, which seems to take place much more quickly than reductive elimination to give the C-B bond.

The regioselectivity of the hydroboration/oxidation of perfluoroalkenes ($R_FCH=CH_2$) is clearly reversed with regard to the borane reagent or the catalytic system used in the hydroboration reaction. P.V.Ramanchandran et al. [18] observed that branched perfluoroalkylboranate esters could be achieved by cationic rhodium complexes with unhindered boranes such as catecholborane. However, the same authors reported that linear perfluoroalkylboranate esters can also be easily prepared from neutral rhodium complexes with hindered boranes such as pinacolborane (Scheme 3).



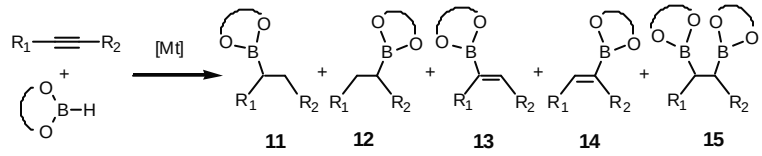
Scheme 3

On the other hand, whereas uncatalysed hydroboration of alkynes with dioxaborinanes requires either elevated temperatures or an excess of borane reagent [22-23], the catalysed hydroboration of alkynes with catecholborane or pinacolborane afforded (E)-1-alkenylboron compounds at room temperature. In fact, the transition metal-catalysed hydroboration of alkynes had not received much attention until Burgess and coworkers reported that the hydroboration of phenylacetylene with catecholborane catalysed by rhodium complexes gave a complex mixture of two

regioisomers of alkenylboronates (**13** and **14**), two hydrogenation products of **13** and **14** (**11** and **12**) and a diboration product **15** (Table 4, entry 1) [12].

The regioselectivity towards the terminal alkenylboronate isomer **14** is improved in the hydroboration/oxidation of phenylacetylene with $Cp_2Ti(CO)_2$ (Table 4, entry 3) [29] and nickel or palladium complexes modified with phosphine [37]. The regioselectivities obtained with rhodium [32], nickel [32] and zirconium [38] complexes with the borane reagent pinacolborane are similar (Table 4, entries 5-7). The results in Table 4 for hydroboration of phenylacethylene seem to show that the catalysed borane addition to terminal alkynes has no significant advantages over the uncatalysed reaction, as far as the regioselectivity is concerned. However, regiodifferentiation is greater between the catalysed and uncatalysed hydroboration of internal alkynes. For example, depending on the catalytic system, the regioselectivity can be reversed in the hydroboration of 1-phenyl-1-propyne (Table 4, entries 8 and 9).

Table 4. Catalytic hydroboration reaction of alkynes[a]



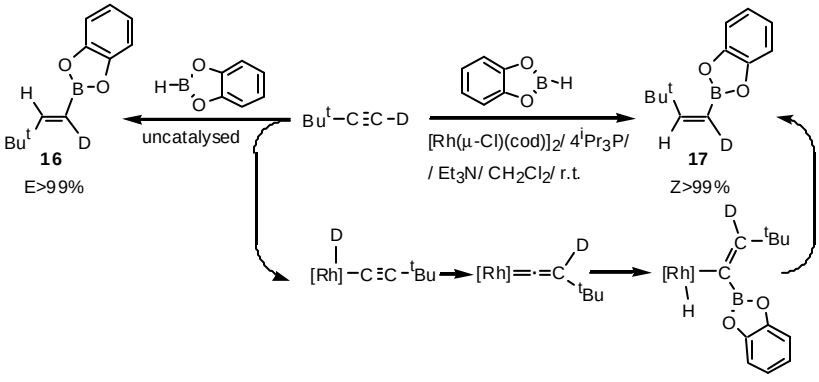
Entry	Catalytic system		R_1	R_2	Product distribution (%) **11**	**12**	**13**	**14**	**15**
1	$RhCl(PPh_3)_3/PPh_3$	**1**	Ph	H	29	9	16	17	29
2	$[Rh(\mu\text{-}Cl)(cod)]_2/8PPh_3$	"	"	"	54	19	-	-	27
3	$Cp_2Ti(CO)_2$	"	"	"	-	-	-	100	-
4	$RhCl(PPh_3)_3$	**5**	Ph	H	-	-	52	48	-
5	$[Rh(CO)(PPh_3)Cl]$	"	"	"	-	-	2	98	-
6	Cp_2ZrHCl	"	"	"	-	-	1	99	-
7	$CpNiCl(PPh_3)$	"	"	"	-	-	2	98	-
8	$Cp_2Ti(CO)_2$	**1**	Ph	Me	-	-	67	33	-

9	$NiCl_2$(dppe)	"	"	"	-	-	33	67	-

[a] Standard conditions. Solvent: THF, T: 25°C, under argon

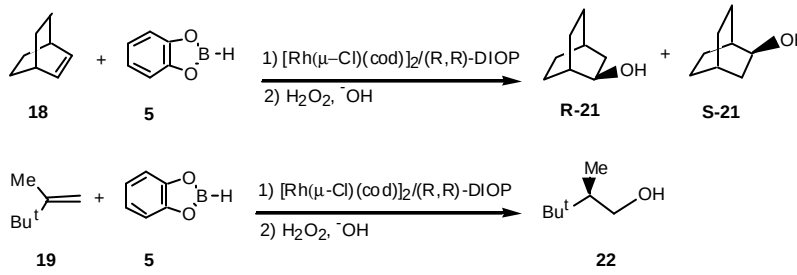
Whereas the $Cp_2Ti(CO)_2$ [32] favours the addition of boron to the carbon adjacent to the phenyl group because of electronic considerations, the steric hindrance of the phosphine ligand of $NiCl_2$(dppe) [39] forces the addition to the β-carbon.

Recently, Miyaura et al., [40], reported an interesting catalysed *trans*-hydroboration reaction for terminal alkynes, which directly provides the (Z)-1-alkenylboronate product. The uncatalysed route for obtaining the *cis*-1-alkenylboron compounds involves steps based on the intramolecular S_N2 substitution of 1-halo-1-alkenylboronates with metal hydrides [41-43] and the *cis*-hydrogenation of 1-alkynylboronates [44]. The hydroboration of 2-*tert*-butylethyne in the presence of the Rh(I)/P^iPr_3 and Ir(I)/P^iPr_3 catalytic systems with an excess of catecholborane or pinacolborane and one equivalent of triethylamine mainly provided the *cis*-1-alkenylboron compound **17** shown in scheme 4. The deuterated studies that they made showed that the presence of the amine should favour the oxidative addition of the C-D bond to the metal, rather than the oxidative addition of the borane reagent [45] (Scheme 4). Another example of contrasting ethynyl hydroboration pathways has recently been reported [46]. This study describes the synthesis of a novel tris-hydroboration product from the reaction of dimesitylborane with 2,5-diethynylpyridine.



Scheme 4

In 1988, the first catalytic asymmetric hydroboration of olefins was reported by Burgess et al. [47] for substrates such as norbornene (**18**) and 2-*tert*-butylpropene (**19**) in the presence of $[Rh(\mu\text{-}Cl)(cod)]_2$ with the chiral diphosphine (R,R)-Diop, (**20**) (Figure 3), as the catalyst (Scheme 5). Both substrates were transformed into the enantiomerically enriched mixture of the alcohols norbornol (**21**) (57% e.e in R) and 2,3,3-trimethylbutanol (**22**) (69% e.e in R) [47a] (Table 5, entries 1 and 2).



Scheme 5

Burgess and coworkers improved the enantiomeric excess in the hydroboration of norbornene using analogous reaction conditions but varying the bidentate chiral diphosphine ligand to (S,S)-BDPP (**23**) and 2-MeODiop (**24**) (Figure 3) (Table 5, entries 3 and 4) [47b].

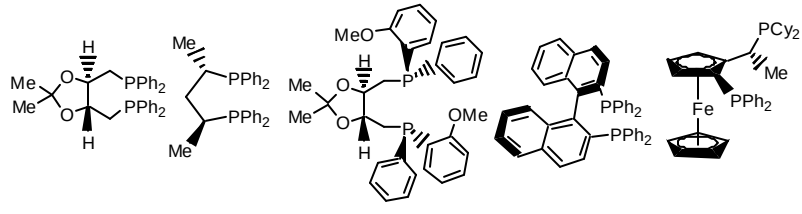
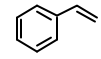


Figure 3

Table 5. Catalytic asymmetric hydroboration reaction of alkenes with Rh/(P,P) complexes[a]

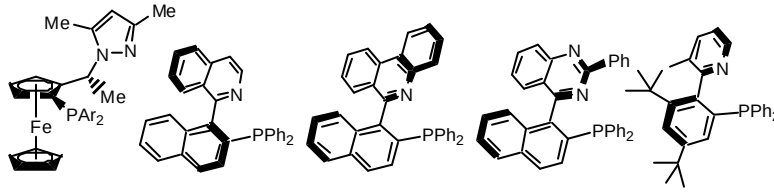
Entry	Ligand (P,P)	Substrate	T(^{0}C)	Yield (%)	e.e (%)[b]
1[e]	(R,R)-(-)-Diop (**20**)		-25	>99	57
2[e]	"		-25	>99	69
3[e]	(S,S)-BDPP(**23**)		-25	>95	80
4[c], [e]	2-(R,R)-MeODiop (**24**)	"	-25	>95	82
5[d]	(R)-(+)-Binap (**25**)		-30	90	70
6[d], [f]	"	"	-78	91	96
7[d], [g]	(S,R)-Josiphos (**26**)	"	-70	65	91.5

[a] Standard conditions. Solvent: THF, under argon; [b] Absolute Configuration R; [c] Solvent: Toluene; [d] Solvent: DME; [e] Rh cat.: $[Rh(\mu\text{-}Cl)(cod)]_2$; [f] Rh cat.: $[Rh(cod)_2]BF_4$; [g] Rh cat.: $[Rh(nbd)_2]BF_4$

The hydroboration of styrene catalysed by rhodium complexes modified with the atropoisomeric type chiral P,P ligand Binap (**25**) was found to proceed regioselectively in DME at low temperatures (-30ºC), followed by oxidation to give 1-phenylethanol with 70% enantiomeric excess (Table 5, entry 5) [15]. In addition, the enantioselectivity increased to 96% when the reaction was carried out at -78% (Table 5, entry 6).

Togni et al [48] obtained a similar enantiocontrol in the hydroboration oxidation of styrenes when they used rhodium complexes modified with ferrocenyldiphosphine, Josiphos (**26**), (Figure 3) (Table 5, entry 7) and the related pyrazole containing phosphinamine **27** ligand (Figure 4) (Table 6, entry 1). However, so far the best results have been obtained by Brown et al. in the catalytic hydroboration/oxidation reaction of vinylarenes using the effective chiral P,N-type ligand Quinap (**28**) (Figure 4) coordinated to rhodium complexes (Table 6, entries 2-

4). Substrates such as *p*-MeO-styrene were transformed into their corresponding α-alcohol with 94% e.e [49] at room temperature. The Quinap is less bulky than Binap in the region of the isoquinoline, which replaces one of the diphenylphosphino-naphthalene moieties and thus facilitates the oxidative addition of a sterically demanding secondary borane reagent. The structural modifications permitted by the synthetic route to phosphinoisoquinolines [50] makes it possible to synthesise analogous P,N ligands such as Phenap (**29**) [51] and 2-phenylquinazolin-4-yl-2-(diphenylphosphino)naphthalene (**30**) [52]. These P,N-type ligands were also coordinated to rhodium so that they could be applied in the hydroboration/oxidation reaction of vinylarenes (Table 6, entry 5-8). Nevertheless, the hydroboration reaction developed with these rhodium-analogous P,N ligand complexes achieved minor enantiomeric excesses. In addition, the efficiency of asymmetric hydroboration varies with the electronic properties of the substituents at phosphorus in Quinap derivates, [49c].



(S,R)-**27** (S)-**28** (R)-**29** (R)-**30** (R)-**31**

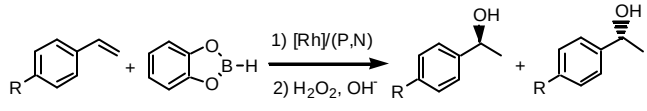
27a Ar= Ph

27b Ar=4-$CF_3C_4H_6$

Figure 4

Recently, Chan et al. developed a new atropoisomeric P,N ligand for rhodium-catalysed asymmetric hydroboration, called Pyphos (**31**) (Figure 4), [53]. When it was applied in rhodium-catalysed asymmetric hydroboration of vinylarenes, the enantiomeric excesses were similar to those of Rh-Quinap when the reaction was carried out at 0ºC (Table 6, entry 9-11).

Table 6. Catalytic asymmetric hydroboration of vinylarenes with Rh/(P,N ligand) complexes[a]



1 **(S)-2** **(R)-2**

Entry	Ligand (P,N)		R	T(^{0}C)	**2**(%)	e.e(%)	Conf.
1	**27**		H	20	76	94	R
2[b]	(S)-Quinap	**28**	MeO	20	95	94	S
3[b]	"		H	"	97	88	S
4[b]	"		Cl	"	98	78	S
5[b]	(R)-Phenap	**29**	H	0	94	67	R
6[b]	(R)-**30**		MeO		77	81	R
7	"		H	"	80	79	R
8	"		Cl	"	83	49	R
9	(R)-Pyphos	**31**	MeO	0	98	94	R
10	"		H	"	99	90	R
11	"		Cl	"	99	79	R

[a] Standard conditions. Solvent: THF, under argon, [Rh]: [Rh(cod)]$_2$]BF_4/(P,N); [b] [Rh]: [Rh(cod)(P,N)]BF_4

The regioselectivity in favour of branched alcohol product **2** does not depend on the electron-releasing or electron-withdrawing nature of the substituents in the phenyl ring of the substrates. However, the enantioselectivity shows slight differences, and is higher for electron-rich substrates than for electron-poor vinylarenes (Table 6). The Hammett plot of the e.e value of the hydroboration of several vinylarenes substrates obeys a linear free energy relationship [49c], [53-54], which suggests a simple trend related to the inductive effect of the substituents.

2.2. Catalytic cycles

The catalytic hydroboration reaction consists of several different steps. This introduction has shown that the hydroboration reaction can be catalysed with a wide variety of complexes for a significant number of substrates. The catalytic cycle then needs to be generalized although it is somewhat tricky. In addition, the nature of the catalytic complex, the steric and electronic properties of the substrate, the nature of the ligand, the solvent, the temperature, and the hydroborating reagent may have a significant effect on the mechanism of the hydroboration reaction catalysed with transition metals [55-58].

It seems clear that the mechanism of rhodium-catalysed hydroboration reactions is fundamentally different from that of the corresponding uncatalysed processes [59]. The role of the transition-metal complex in the process suggests that alkenes do not coordinate to the metal and that a free boron hydride does not attack the opposite π-face (Figure 5.a) because $^{2}\eta$-coordination deactivates alkenes toward electrophilic attack. On the other hand, the oxidative addition of the borane reagent to the metal makes the boron atom less electron deficient due to the electronic donation from metal *d* orbitals to boron. For this reason, it is assumed that hydride-η^{1}-borylrhodium complexes, likely intermediates in the catalytic cycle, are not added to free alkenes, as indicated in Figure 5.b. It might be concluded, then, that both the boron-hydride and the alkene are probably coordinated to the metal in the first steps of the rhodium-catalysed hydroboration.

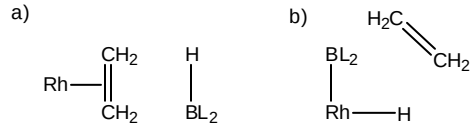
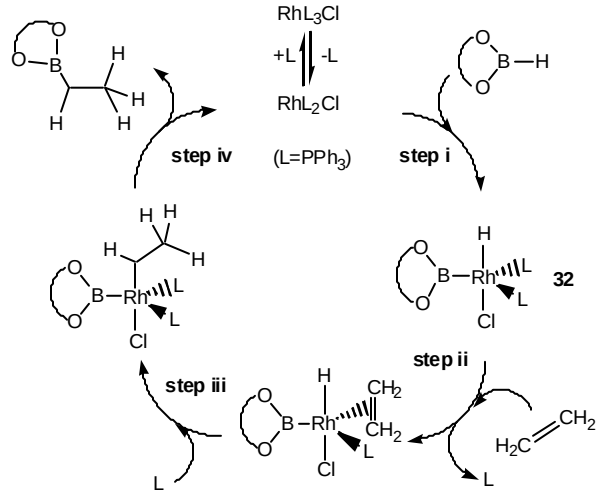


Figure 5

The transition-metal catalysed olefin hydroboration reaction using Wilkinson's catalyst $RhCl(PPh_3)_3$ with catecholborane has become an important and

well-established synthetic method [2]. Although the reaction was first reported by Männing and Nörth in 1985, an earlier key experiment by Kono and Ito led to the development of the catalytic transformation [60]. They demonstrated that B-H activation by Wilkinson's catalyst provides the hydride-η -borylrhodium complex **32**. As far as the catalytic mechanism is concerned, they proposed a dissociative pathway which involved oxidative addition of catecholborane to the rhodium complex (step i), followed by ethylene coordination with simultaneous dissociation of one PPh_3 group (step ii). Furthermore, migratory insertion of the olefin into the Rh-H bond (step iii), and reductive C-B bond coupling (step iv) (Scheme 6) could eventually provide the alkylboronate ester. Their suggested mechanism for $RhCl(PPh_3)_3$ catalysed hydroboration with catecholborane is analogous to that proposed for other, more thoroughly investigated rhodium-catalysed olefin addition reactions such as hydrogenation, hydrosilylation, and hydroformylation [61]. In the case of asymmetric



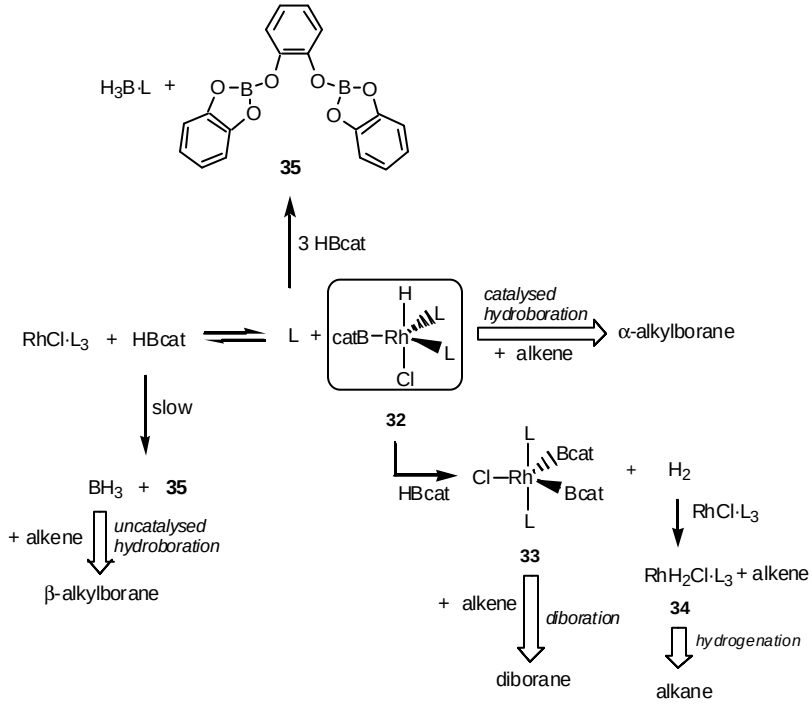
Scheme 6

hydrogenation, the relative stability of such key metal intermediates as hydridealkylrhodium, has given a detailed picture of the reaction mechanism [62]. Unfortunately, the intermediates in the hydroboration process are quite transient, at

least when catecholborane is used. Even though hydroboration is a relatively recent reaction, several in-depth studies of the catalytic hydroboration cycle have been published in the literature. Evans, Fu and Anderson [13] suggested a related and more detailed mechanism. According to this mechanism, results for deuterium labelling experiments of selected catalytic hydroboration reactions have been rationalised by reversible olefin complexation in Rh-H(D) bond and reversible hydride migration. Furthermore, the label distributions were different when these reactions were repeated by Burgess and van der Donk [12] with a commercial, partially oxidised, catalyst.

On the basis of their experiments, Burgess et al. [12] proposed an alternative associative mechanism which involves boron migration followed by β-H elimination, (also called 'dehydrogenative borylation'), as a competitive process in the catalytic hydroboration of hindered styrenes that yield vinylborane compounds CH_2=CH(BR_2). The vinylborane compounds were part of a complex mixture of products derived not only from catalysed hydroboration but also from uncatalysed hydroboration and the hydrogenation of alkenes, because the reaction of $RhCl(PPh_3)_3$ with catecholborane gives an unexpected mixture of borane and rhodium species (Scheme 7). The oxidative addition of catecholborane to $RhCl(PPh_3)_3$ affords a hydride-η^1-borylrhodium complex **32** [60], [63]. However, a second oxidative addition of the borane can carry out and generate H_2 and a diborylrhodium complex **33** [64]. The diboryl complex **33** can then undergo diboration or reductive monoborylation of alkenes, and the H_2 generated can hydrogenate alkenes. Thus, the hydroboration of RHC=CH_2 is often accompanied by the formation of small amounts of RCH(Bcat)CH_2(Bcat), RC(Bcat)=CH_2, RCH=CH(Bcat), and RCH_2CH_3, along with the desired hydroboration product. Therefore, the *in situ* degradation of catecholborane makes the reaction more complex when the catalysed reaction is very slow. In addition, the uncoordinated phosphine can react with catecholborane to yield $H_3B{\cdot}L$ and B_2cat_3 (cat=$O_2C_6H_4$) (**35**) [64]. Although the borane/phosphine adduct thus generated fortunately does not hydroborate alkenes, **35** may contribute to the production of other rhodium species, which have high catalytic activities similar to those of **32**. The reaction can also undergo competitive uncatalysed hydroboration with BH_3, and the formation of such hydroborated products does not reflect the true selectivity of the

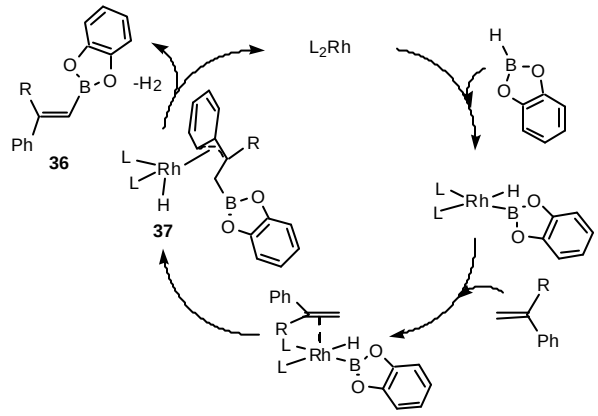
catalysed reactions [12], [28], [65]. The degradation of catecholborane to BH_3 and B_2cat_3 (**35**) is, in general, very slow at room temperature. However, the hydroboration with BH_3 can compete with the catalysed hydroboration even when the reaction is very slow, because the catalyst also decomposes and its activity is also low. Although many processes may generate side reactions, catecholborane undergoes clean hydroboration when the appropriate catalyst is selected.



Scheme 7

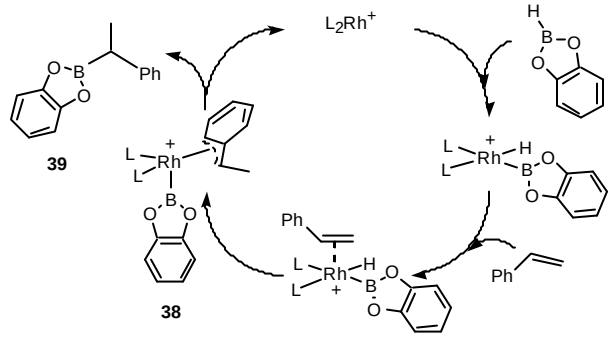
Westcott and Marder [56] have also contributed to this discussion with Burgess et al. [12]. They agreed with the 'dehydrogenative borylation' pathway which provides the vinylborane (**36**) (Scheme 8) subproduct. As far as the catalytic steps are concerned, the insertion of the alkene into the M-B bond can be followed by β-hydride elimination, which leads to the production of hydrogen. Formation of the hindered

tertiary alkylrhodium complex may be facilitated by formation of a $^{3}\eta$-benzylrhodium intermediate **37** (Scheme 8). Previously, Hayashi et al. have suggested that in the hydroboration of 2-phenylpropene with catecholborane, a $^{3}\eta$-benzylrhodium **38** complex may form and participate as an intermediate species in the catalytic cycle [15] (Scheme 9).



Scheme 8

Many authors have suggested that the rhodium-catalysed hydroboration reaction proceeds through a rhodium(III)/alkyl/boryl intermediate, which is formed by the oxidative addition of catecholborane to rhodium (I) followed by the insertion of alkene into the resulting H-Rh bond [2], [12-13] [60] (Scheme 6). Hayashi et al. [15] suggested that $^{3}\eta$-benzylrhodium complex **38** was a key intermediate in the catalytic cycle, after they observed the high regioselectivity obtained in the hydroboration of styrene (Scheme 9). In addition, they proposed that the vacant coordination site in the cationic rhodium intermediate, instead of neutral complexes, favours the formation of the $^{3}\eta$-benzylrhodium **38**. Finally, the reductive elimination step provided the branched borane (**39**) regioselectively.

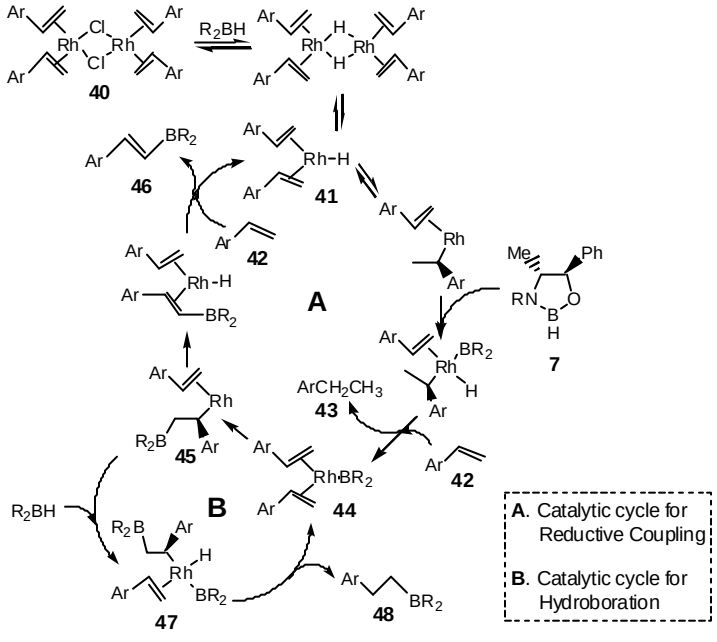


Scheme 9

In fact, it is difficult to present a general catalytic cycle for the catalytic hydroboration reaction, because of the important role of the nature of the catalyst, the borane and the substrate. Brown and Lloyd [24] studied the catalytic hydroboration of p-MeO-styrene by chiral borane **7** and the catalytic rhodium precursor **40** (Scheme 10). Under those catalytic conditions, the hydroboration of **42** yielded 50% of alkane **43** and 50% of vinylborane **46**. They proposed the mechanism shown in scheme 10, where the rate-limiting addition of B-H to rhodium led to the elimination of alkane and the formation of rhodium-boryl **44**. The vinylborane was then formed by β-migration of boron to coordinated alkene and β-elimination, which also regenerates hydriderhodium **41**. However, when the analogous reaction was carried out with catecholborane as the borane reagent, the hydroborated product was entirely the primary borane **48**. In order to explain their findings with catecholborane, they proposed a modified version of cycle A. Cycle B, then, involves catecholborane being added to intermediate **45** to give **47**, which eventually yields primary borane **48** with regeneration of **44** (Scheme 10).

Hydroboration has also been studied by theoretical methods. Morokuma et al. [66] focused on the associative mechanism of model reaction a), shown in equation 1. They found that the most favourable pathway involved oxidative H-B bond

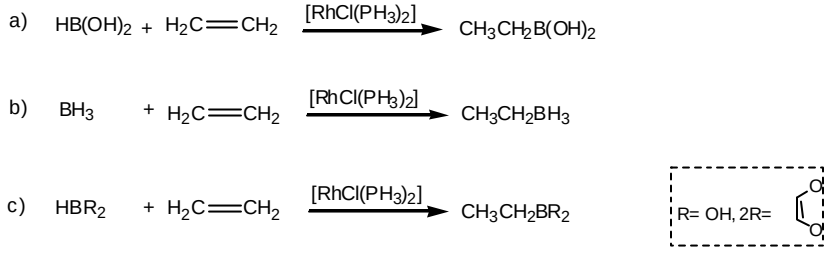
addition to $RhCl(PH_3)_2$ followed by the coordination of ethylene *trans* to chlorine, migratory ethylene insertion into the Rh-B bond, and finally reductive C-H bond coupling as the



Scheme 10

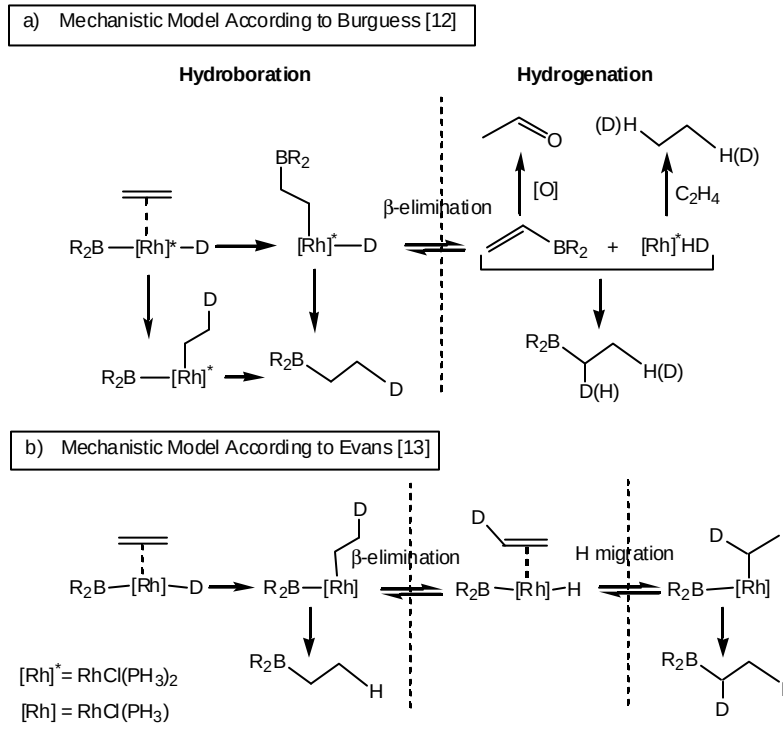
rate-determining step of the catalytic cycle. This last observation was in agreement with previous NMR studies by Burgess and Ohlmeyer [3a], who revealed that reductive elimination could be the slow step in overall formation. Subsequently, Dorigo and Schleyer made an *ab initio* study of the dissociative mechanism for model reaction b) illustrated in equation 1, where the model hydroborating reagent is simplified [67]. Their results supported the catalytic cycle originally presented by Mäning and Nörth [2]. They also excluded the possibility of an associative mechanism. Recently, Ziegler et al., [68] made a comparative study based on DFT type calculations of associative and dissociative mechanism of the model reactions c) shown in equation 1. They concluded that they agreed with Burgess et al. [12] on the

associative mechanism, and favoured the β-elimination for obtaining side products such as vinylboranes and alkanes. On the other hand, the dissociative mechanism in



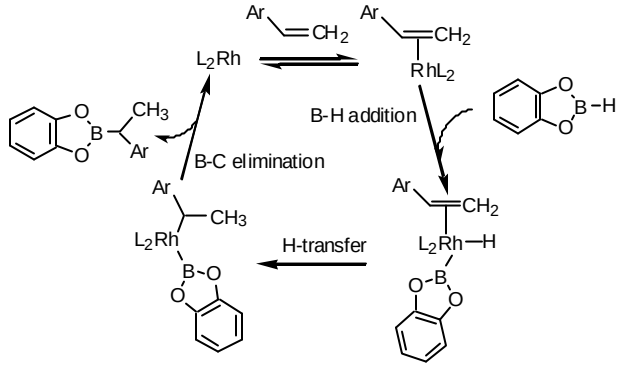
Equation 1

which hydride migration might be involved is in agreement with the mechanistic model of Evans [13]. According to calculations of Ziegler et al. [68], this mechanism might prefer the boron migration to the hydride migration (Scheme 11).



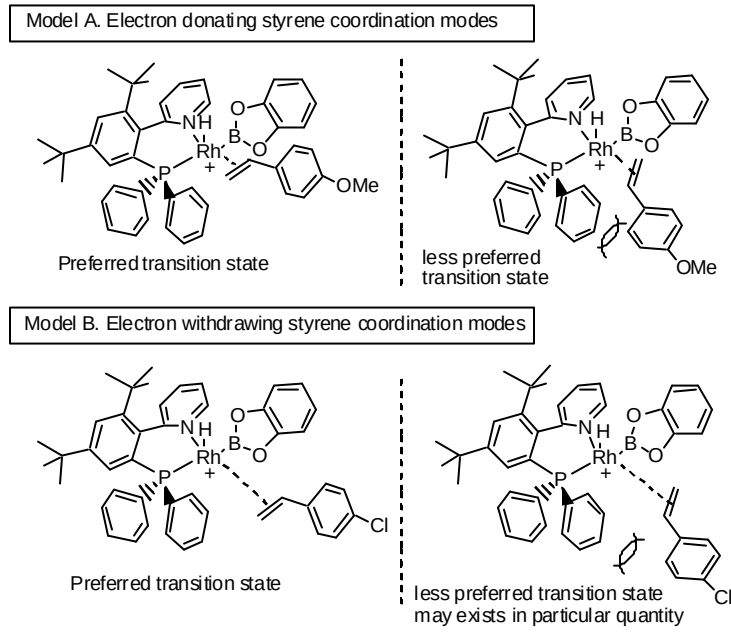
Scheme 11

In this context, Brown et al. suggested that the catalytic cycle for the hydroboration of vinylarenes follows the pathway in which the hydride could transfer regiospecifically to give the hydride $^{3}\eta$-benzylrhodium complex, which undergoes reductive elimination to the formation of the hydroboration product [49b]. A plausible complete sequence for the consecutive steps in the catalytic hydroboration cycle of vinylarenes is outlined in scheme 12. These steps are: 1) the reversible coordination of the alkene, 2) the oxidative addition of the catecholborane; 3) the hydride migratory insertion; and 4) the reductive elimination, which yields the final product and regenerates the catalytic active species. The same authors pointed out that the stereochemistry of hydroboration is rather general and predictable for various vinylarenes. They also suggested that the configuration of the new stereogenic centre could be determined in the hydride transfer step.



Scheme 12

Recently, Chan et al. [53] used the coordination of vinylarenes to the penta-coordinated Rh/H/(P,N)/catecholborane/vinylarene complexes to suggest that transition state models might explain the enantioselectivity observed in the hydroboration of electronically different vinylarenes (Scheme 13).



Scheme 13

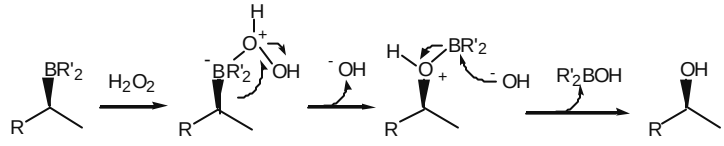
Vinylarenes with electron-releasing substituents might therefore coordinate more strongly *trans* to the pyridine moiety of the ligand than the vinylarenes with electron-withdrawing substituents. Therefore, the electron-rich substrates may be closer to the rhodium centre than their electron-poor analogues, thus providing better stereochemical communication and a higher enantioselectivity.

However, despite all these mechanistic approaches, the origin of the regio- and enantioselectivity of the catalytic hydroboration reaction has yet to be explained.

2.3. Synthetic applications

The high chemio-, regio- and enantioselectivity which might be imparted in one of the initial steps of the catalytic cycle, is coupled with the stereochemical integrity of the subsequent C*-X or C*-C bond forming stage. An interesting

application which has been used in numerous examples is the formation of C*-O bonds from C*-B bonds [3c], [15], [49c], [79-70], through the oxidation reaction. This transformation can be carried out because the alkylboronate esters react easily with a variety of neutral or negatively charge bases to form thermally stable adducts. Therefore, the oxidation of the borane involves the ambiphilic nucleophile hydroperoxide ion. This provides a 1,2-migration of an alkyl group from boron to oxygen with concurrent loss of the hydroxide ion. The step occurs with essentially complete retention of configuration (Scheme 14).



Scheme 14

The catalysed hydroboration reaction has been used in various synthetic applications because of its exceptional selectivities. The order of reactivity permits selective hydroboration at the terminal double bond in preference to other double bonds (Figure 6.a) [13], [71] or the ketone carbonyl group [3b] (Figure 6.b).

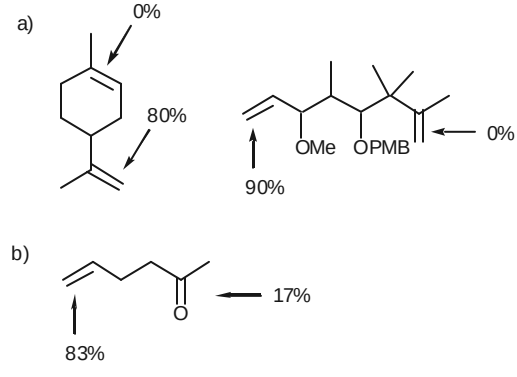
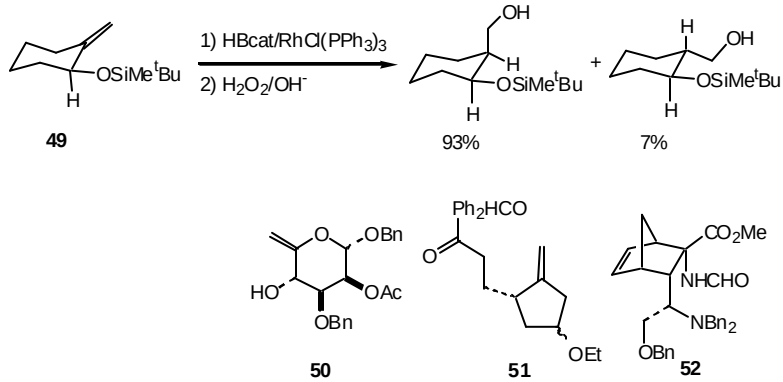


Figure 6

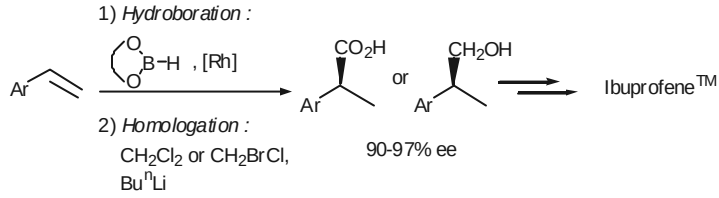
The hydroboration of *exo*-cyclic alkenes affords stereochemically complementary products between the catalysed and uncatalysed reaction (Scheme 15). Thus, the hydroboration/oxidation of **49** with 9-BBN yields two alcohols in a ratio of 39:61 in favour of the *trans* isomer. These results are in stark contrast to the catalysed hydroboration where the *cis*-alcohol is mainly produced (93%). This is because the catalysed reaction seems to be more sensitive to the steric effects than the electronic effects, whereas in the uncatalysed reaction the stereoelectronic effect prevails [72-74]. The high *cis*-stereo-selectivity observed in *exo*-cyclic alkenes can also be observed in various syntheses of natural products. Consequently, the alcohols obtained through the catalytic hydroboration/oxidation are used as precursors for the synthesis of several more complex compounds. For example, the catalysed hydroboration/oxidation reaction of **50** forms the antineoplastic Bleomycin A2 [75]. The catalysed hydroboration/oxidation of **51** leads to the sesterpene (+)-Luffariolide E [76], and the catalysed hydroboration/oxidation of **52** leads to the (-)-Altemicidin, which is an acaricidal and antitumor substance [77] (Scheme 15).



Scheme 15

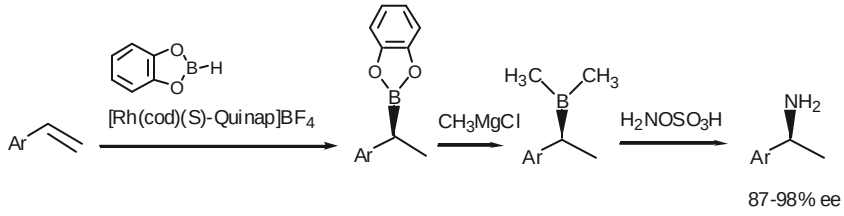
The one-carbon homologation of chiral alkylboronate esters has recently been demonstrated to occur also with complete retention of configuration, [78]. The catalytic asymmetric hydroboration-homologation sequence yields the

enantioselective synthesis of 2-aryl substituted carboxylic acids, which are of particular importance because they are non-steroidal anti-inflammatory agents such as Naproxen™ or Ibuprofen™. The latter can be synthesised as the enantiomerically enriched 2-arylpropionic acids shown in equation 2. The positive medicinal effects of these pharmaceuticals are ascribed to only one of the enantiomeric forms [79].



Equation 2

Another interesting asymmetric, two-step, “one-pot” reaction, in which catalytic asymmetric hydroboration is followed by an amination step, has made it possible to transform alkenes into chiral amines, through alkylboronate esters [80] (Equation 3).



Equation 3

Recently, Maeda and Brown have shown that the hydroboration/amination sequence can be used for the preparation of the antidepressant Sertraline using the Rh-Quinap catalyst complex [80d].

3. Recovery of the catalyst

Homogeneous catalysts generally provide higher activities, regio- and stereoselectivities than heterogeneous catalysts; in fact, most chiral catalysts are homogeneous. On the other hand, they are more difficult to separate, recover and reuse than the technically well established heterogeneous catalysts. The properties of these two catalytic systems are different but complementary so it could be very useful to combine their best properties. The heterogenisation or immobilisation of the homogeneous metal complex in an insoluble support makes it possible for the reacting organometallic complex to keep its high activities and selectivities and also to be recovered and recycled. Consequently, the catalytic complex can be separated from the products and unreacted reagents by an easy filtration, precipitation or phase separation [81-83]. Significant examples of different types of catalyst immobilisation, as well as their application in a variety of asymmetric reactions, have recently been reported [84-94]. However, chiral catalysts have also been immobilised in special liquid phases (aqueous, florous, ionic), occluded into membranes, or tethered to dendrimers. In this overview, we have focused on the immobilisation of catalytic complexes on solid supports.

The organometallic complex can be immobilised on an organic or inorganic solid support through different anchored or immobilised methods.

A wide variety of organic supports, (principally insoluble polymers) [95], take part in the common procedures for immobilising chiral ligands/catalysts. Although organic supports favour reaction rates that are higher than those of inorganic supports, the random distribution of the ligand units along the polymeric chain and swelling effects may be serious limitations. We have focused on the immobilisation of catalysts on inorganic supports, which are generally inert materials based on insoluble porous structures with a highly specific surface area. Amorphous oxides (in particular silica and, to a lesser extent, alumina) [96-97], zeolites [98-104], pillared clays, LDHs [105] and clay minerals (in particular, smectite laminar minerals) are most routinely used.

In general, immobilised single-site catalysts may be classified according to the nature of either the support material or the linkage between the support and the chiral ligand. Thus, the catalytic system can be immobilised by covalent binding, grafting by adsorption, grafting by ion-pairing, grafting by supported hydrogen-bond (SHB) and as a 'ship in a bottle' grafted catalyst. Figure 7 illustrates some of the immobilisation or heterogenisation strategies that have been described in the literature.

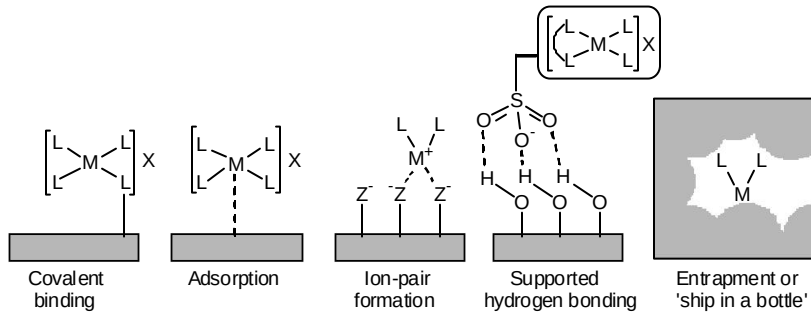


Figure 7

The *heterogenisation via covalently bound ligands* onto a solid support is one of the most frequent and versatile ways to heterogenise a chiral transition-metal complex. Both organic polymers and inorganic solids are useful supports here, although the latter have the advantage of being more robust and stable. The high stability of the covalent bond formed between the metal ligation and the support make the leaching of the catalytic complex more difficult. However, the most important disadvantage is that the ligand has to be functionalised, which means a long and delicate synthetic process and purification. Heterogenised catalysts are much more complex than their homogeneous counterparts and, therefore, generally, they often provide slight changes in activity and selectivity. In order to disturb the chiral induction as little as possible, the point of attachment of the tether to the ligand should be as far as possible from the stereogenic centre. The catalyst or ligands can be attached covalently onto the support via one-step or multistep functionalisation. The second methodology is the most efficient because it prevents the metal complexes from

dimerising and functionalises the ligand through a tether that is usually a linear chain that contains triethoxy- or methoxysilyl groups. The complex modified with the functionalised ligand is then anchored through the alkoxysilyl groups with the external silanols of the support (Figure 8).

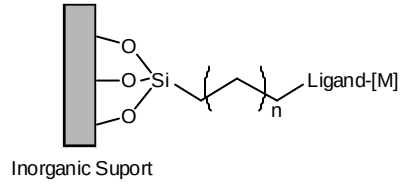


Figure 8

In 1994, Matlin et al. [106] presented an early example of a heterogeneous enantioselective catalyst that was even more active than its homogeneous counterpart. The β-diketone camphor was converted into their $SiCl_3$-derivative and the next step was the reaction between the functionalised ligand and the silanol groups of silica. The Cu-form of this complex was applied in the cyclopropanation of alkenes. The recuperation of catalyst was possible especially on those substrates, such as indene, where the side reaction of polymerization was absent.

Eisen et al. [107] and Kinting et al. [108] developed trimethoxysilyl-functionalised di-Rh-complexes, which reacted with silica to be immobilised. The heterogenised catalysts gave greater stability than their homogeneous forms and were applied to catalyse the asymmetric hydrogenation reaction of prochiral unsaturated acids and esters. Although the heterogenised catalytic system proved to be enantioselective in the first run, leaching of the metal was observed. Corma and coworkers anchored Rh-complexes through the triethoxysilyl groups contained in modified bidentate amino acid ligands, both on silica and on USY-zeolite [109-110]. The complex anchored via the covalent bond to the zeolite showed a higher activity for alkene hydrogenation and a considerable increase in enantioselectivity (>95%) in the hydrogenation of ethyl (Z)-α-benzoylaminocinnamate. This introduced a new concept: the important role of the steric limitation of the support. The zeolite

supported catalyst was reused several times with no loss in activity or metal content. In addition, no induction period was required, probably as a consequence of the concentration effect of the zeolite and the interaction of the catalyst with the electrostatic fields present in the zeolite, which assist the formation of the catalytic active species. Also, Johnson et al. [111] observed a positive confinement effect of the support because the results obtained with MCM-41 were significantly better than when a silica support was used. The heterogenised Pd-ferrocene catalyst showed high conversions and e.e in the allylic amination of cinnamyl acetate. Surprisingly, the regioselectivity changed drastically.

Ferrocenyldiphosphine complexes were first functionalised with suitable silylating agents before they were attached to a variety of supports. They have been used with relative success in the heterogenised hydrogenation of imines for Ciba-Geigy [112].

Mayoral et al. [113] studied the Diels-Alder reaction catalysed by chiral Lewis acids immobilised on alumina and silica. The best strategy was to use the metal and not the chiral auxiliary to graft the Lewis acid onto the solid. This decreased the influence of the conformation of the chiral auxiliary and hence affected the stereochemistry of the reaction.

Recently, several reactions have been developed with heterogenised catalytic systems prepared via covalent anchoring principally to silica, or other inorganic supports (such as USY-zeolites, or mesoporous MCM-41). Some of these reactions are the following: cyclopropanation [114], hydrogenation [114], [115], hydroformylation [115], olefin polymerization [116], asymmetric addition of diethylzinc to benzaldehyde [117], sulphide oxidation [118], Suzuki cross-coupling [119], cyanosilylation of aldehydes [120a], epoxide ring opening [120b], olefin metathesis [121a, b] and epoxidation of cyclohexane [121c]. All these heterogenised systems carried out an active and, in the case of the asymmetric reactions, selective performance which, in addition, was recycled and re-used in numerous catalytic cycles without loss of conversion or enantiomeric excess.

Augustine and coworkers proposed a new technique for anchoring homogeneous catalysts to a support material without having to modify the ligand [122]. In this way, the reactivity and selectivity of the corresponding homogeneous

catalyst is retained even on re-use. The original immobilisation procedure, called *three-component inorganic systems*, consists of a preformed metal complex grafted to a solid support through an anchoring agent (Figure 9).

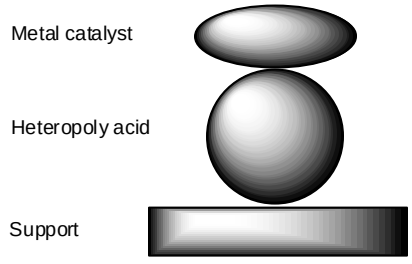
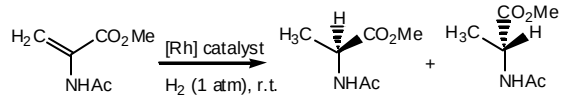


Figure 9

The anchoring agents are heteropoly acids [123] (phosphotungstic acid (PTA), phosphomolybdic acid, silicontungstic acid, silicomolybdic acid), which can be attached to several supports (alumina, carbon, lanthana, montmorillonite K) by interaction of the acidic protons of the acid with basic sites on the support. Although the nature of the bonds is not clear, it has been suggested that the metal (Rh, Ir) is attached to the heteropoly acid by the oxygen atoms on its surface [124].

Augustine and coworkers applied the supported-heteropoly acid-metal catalyst technique to the hydrogenation reaction of methyl-2-acetamidoacrylate (**53**) with rhodium catalyst complex. The results were best with the Rh(DiPAMP)/ /PTA/Montmorillonite K catalyst, (Table 7). In the first run, the immobilised catalyst was less active and selective than the homogeneous one. However, when this catalyst was reused for this reaction, it became more active and selective, and retained the same activity and selectivity for 15 consecutive runs.

Table 7. Enantioselectivity data from multiple consecutive hydrogenation reactions[a]



53 **(S)** **(R)**

Cat. system	Run	ee (%)
Homog. Rh/L-L	-	76
Rh/L-L/PTA/MK[b]	1	67
	2	92
	3	94
	6	96
	9	97
	15	97

[a] Standard conditions: at 25 ^{0}C under 1 atm H_2, 20 μmol of supported catalyst, 0.8 mmol of **53** for each run; [b] L-L: (DiPAMP), PTA: phosphotungstic acid, MK: montmorillonite K.

The *heterogenisations via entrapment or encapsulation*, also often related with the 'ship in a bottle' concept, involves two different preparative strategies to immobilise transition-metal catalysts in the cavities of a solid support. The encapsulation is based on building up catalysts in well-defined cages of porous supports [125-126], and entrapment consists of building up an inorganic sol gel [127] or organic polymeric network around a pre-formed catalyst. Encapsulating a transition metal complex in cages of a support fully depends on the respective size of the metal complex and the cage, to prevent leaching during reaction, [128]. The zeolites are excellent candidates for this immobilisation because of their dimensional and regular pores or cages. The encapsulation of chiral Mn(salen) complexes in zeolites, which are then applied in the epoxidation reaction of alkenes, was described simultaneously by two groups, who used Y and EMT zeolites as solid supports. Corma and coworkers developed a smaller salen complex without *tert*-butyl groups, which were immobilised in a zeolite Y [126]. This immobilised catalyst system restricted the diffusion of the substrate and products through the micropores of the solid, and

decreased the reaction rate. In addition, the heterogenised catalytic system showed a slightly reduced performance in asymmetric induction. This was interpreted as a combination of a non-catalysed, epoxidation reaction in the liquid phases and/or the existence of residual amounts of non-complexed Mn^{2+} acting as the catalytic system. However, the study by Bein et al., which used larger cages of the EMT-structure allowed positions 5 and 5' to accommodate larger complexes bearing methyl groups and 3 and 3' to accommodate *tert*-butyl groups [125]. The activities of the heterogenised catalysts were lower than those of the homogeneous catalysts, too, but the enantioselectivity was unchanged. Table 8 compares the catalytic behaviour of the homogeneous and heterogeneised catalytic systems for the asymmetric epoxidation reaction.

In 1996 Capka and coworkers immobilised Rh-complexes onto silica and alumina via entrapment in a hydrophobic surface layer [129]. On comparing the activity and enantioselectivity of the immobilised catalyst with the analogous homogeneous counterpart, they found that the heterogenised catalytic system performed better. Recycling experiments kept the enantioselectivity constant, but the activity decreased gradually during the subsequent cycles, probably due to leaching of the rhodium complex.

Table 8. Asymmetric epoxidation of *cis*-β-methylstyrene catalysed by Mn–salen complexes.

Catalytic system	C(%)	Epoxide selectivity (%)	e.e (%)[c]
(salen)$Mn^{III}Cl$ [a]	28	100	74
(salen*)$Mn^{III}Cl$ [b]	85	97	80
(salen)Mn^{III}-Y [a]	5	76	58
(salen*)Mn^{III}-EMT [b]	15	67	80
(salen*)Mn^{III}-EMT [b]	47	58	88

[a] salen= *trans*-(R,R)-1,2-bis(salicylideneamino)-cyclohexane. Epoxidation run at 5^0C, 2h, CH_2Cl_2, 5%(salen)$Mn^{III}Cl$ or 15h with 90g (salen)Mn^{III}-Y (3.8% complex content); [b] salen*= (S,S)-N,N'-bis(3-*tert*-butyl-5-methylsalicylidene)-cyclohexanediamine. Epoxidation run at 0^0C, 1h, CH_2Cl_2, 5% catalyst complex; [c] (S, R) Configuration.

The polydimethylsiloxane (PDMS) is an organic-inorganic support. PDMS is formed by an inorganic backbone which contains short organic side chains. It was used as a support in the immobilisation processes of catalytic systems, via entrapment, carried out by Jacobs. A promising example was reported by Jacobs' group, who entrapped Jacobsen's Mn-salen epoxidation catalyst in PDMS. The epoxidation of 1,3-cyclooctadiene with this catalytic system provided an enantiomeric excess of 50% [130], and Noyori's Ru-Binap hydrogenation catalyst immobilised in PDMS provided 92% of enantiomeric excess for the hydrogenation of methyl acetoacetate in the presence of toluene-*p*-sulfonic acid [131]. Leaching depended heavily on the size and the solubility of the metal complex and the swelling of the polymer [132].

Recently, a new heterogenisation strategy has been reported: *heterogenisation via supported hydrogen bonding (SHB)*. It is a non-covalent method for preparing silica-immobilised metal catalysts for use in solid-liquid reactions with apolar solvents [133-135]. The terminal silanols of different types of silica interact with the oxygen atoms of sulfonate groups from both phosphine ligands contained in the metal complex or triflate counter-anion. The transition metal catalyst is linked to the support only through a hydrogen bonding interaction. Different types of chiral catalysts have been immobilised with this technique: i) zwitterionic cationic complexes of ruthenium with triflate as counter-anion, [(sulphos)Ru(NCMe)$_3$]OTf (Figure 10.a), [133], [134], ii) zwitterionic neutral complexes of rhodium (I) such as [Rh(cod)(R,R)-BDPBzPSO$_3$)] (Figure 10.b), [135], iii) cationic complexes of rhodium(III) containing a triflate counter-anion, [Rh(nbd)(P,P)]OTf where (P,P)= (S)-Binap, (R,R)-Me-DuPHOS, (R,R)-Diop (Figure 10.c) [136]. Types i) and ii) are examples of the immobilisation of the optically active rhodium diphosphine complex. This immobilisation involves that the sulfonate group must be introduced into the chiral ligand previously. In contrast, cationic complexes stay close to the silica surface by hydrogen-bonding interactions and by electrostatic interactions with the triflate ions which, in turn, are immobilised on the support via hydrogen bonds. On the other hand, no immobilisation at all was observed when the triflate anion (Figure 10.c) was replaced by counter-anions that cannot interact through hydrogen bonds such as BPh_4^-, BAr_F^- [136]. The chiral SHB rhodium catalysts have been applied in the enantioselective hydrogenation of

prochiral olefins, particularly itaconates and 2-acetamido acrylates [135], [136], in *n*-heptane and *n*-hexane. The conversions were generally similar to those of the homogeneous reaction. Moreover, unlike the analogous homogeneous reactions, the immobilisation of the chiral precursors on silica did not reduce asymmetric induction and in some cases it even increased it. No metal leaching was observed in several consecutive runs. In addition, effective catalyst recycling meant that the catalytic system remained active and enantioselective.

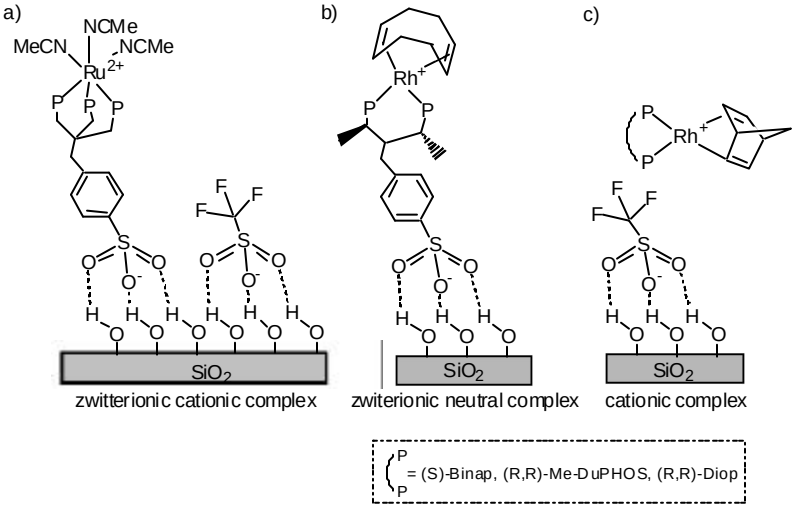


Figure 10

Redge and coworkers [136] made an interesting study of the non-covalent immobilisation of [Rh(cod)(R,R)-Me-(DuPHOS)]OTf onto mesoporous silica, such as MCM-41. The NMR spectroscopy of ^{31}P and ^{19}F nucleus indicated that there is an interaction between the support and the triflate ($^{-}SO_3CF_3$), probably through hydrogen bonding similar to that demonstrated by Bianchini's group.

Pérez and coworkers have suggested a different immobilisation via the hydrogen bond method [137]. They proposed a complex interaction through classical hydrogen bonds and nonclassical dihydrogen bonds between a preformed

polypyrazolylborane copper(I) complex and silica, for the olefin cyclopropanation reaction (Figure 11). The external silanol groups of the silica can interact via a hydrogen bond with the NH of the ligand. In addition, the B-H bonds of the ligand are available to interact with the silica surface via a DHB (dihydrogen bond) O-H···H-B similar to the one found by Crabtree et al. in the molecules of BH_3NH_3 [138]. Initially, leaching was present during the catalytic process, but it was minimised by using an appropriate solvent. The catalyst was reused with no significant loss in the catalytic activity for 10 consecutive cycles.

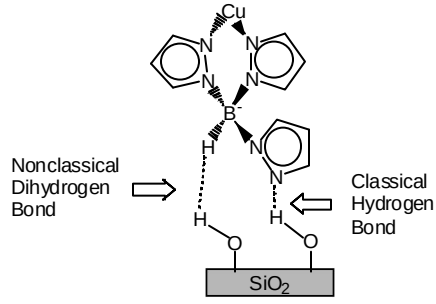


Figure 11

In most cases, the immobilisation requires the functionalisation of the ligands, such as in the covalent bonding or in some cases of the supported hydrogen bonding (SHB) immobilization. From a practical point of view, the *heterogenisation via adsorption or ion-pair formation* is simpler, because very often the chiral ligand does not need to be altered [139-140]. Consequently, the integrity of the chiral ligand can minimise the different activities and selectivities expected between the performance of the homogeneous and hetereogenised catalytic systems.

The adsorption and ion-pair formation immobilisation protocols usually take advantage of the properties of the support. However, occasionally ion-pair formation needs the support to be modified, for example by creating charges on silica via the functionalisation of the silylating groups (Figure 12.a) [141], or by modifying the ligand as the sulfonated Binap complex (bearing 4 negative charges) to be retained in LDHs via coulombic interactions (Figure 12.b) [142].

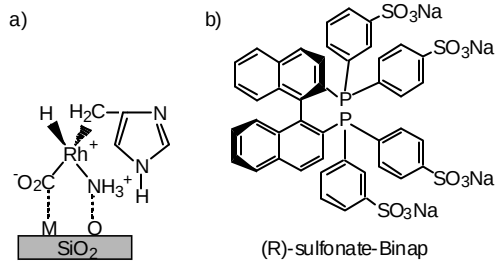


Figure 12

Taking into account the importance of the support we have focused on the smectites clay's group.

Smectite clays, such as montmorillonite K and bentonite, have recently attracted interest as supports for the heterogenisation homogeneous catalysts, because they have a combination of cation exchange, intercalation and swelling properties which makes them unique [95b], [143]. Smectites are a family of clays mainly consisting of hydrated sodium calcium aluminium silicate, the chemical formula of which is $(M^{n+}{}_{x/n})\cdot yH_2O[Al_{4.0-x}Mg_x]_O[Si_{8.0}]_T\ O_{20}(OH)_4$. Their basic structural unit is the tetrahedron SiO^{-4}. This mineral clay is constructed of a single octahedral sheet sandwiched between two tetrahedral sheets, with the octahedral sheet sharing the apical oxygens of the tetrahedral sheet. In the case of bentonite and montmorillonite, the octahedral sheet may be dioctahedral (only 2/3 of the octahedral positions are empty) (Figure 13). A layer charge is created by substitutions in either the octahedral sheet (typically by the substitution of low-charge species such as Mg^{2+}, Fe^{2+}, or Mn^{2+} for Al^{3+}) or the tetrahedral sheet (where Al^{3+} or occasionally Fe^{3+} substitutes for Si^{4+}), which produce one negative charge per substitution. They have a charge deficiency in either the octahedral or tetrahedral layer. The neutrality of the smectite crystalline structure or structural unit is obtained by the adsorption of exchangeable cations (either anhydrous or hydrated) in the interlayered space, generating its cation-exchange capacity (capacity of reversible exchange of cations). The usually reversible exchangeable cations are: Na^+, K^+, Ca^{2+}, Mg^{2+}, rarely Al^{+3}, Fe^{3+} or Fe^{2+}, and H_3O^+. The differences in the smectite compositions cause the

diversity in the family. In addition, their principal properties (intercalation, laminar swelling, ionic exchange, and adsorption capacity) are related to their composition and structural characteristics. Consequently, the immobilisation process is different for each smectite.

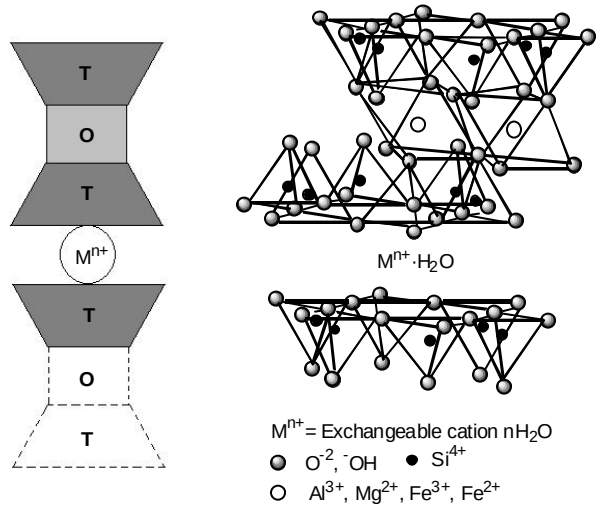


Figure 13

In previous projects [144], our group has studied the immobilisation process of the organometallic complex [M(cod)(P,P)]X on montmorillonite K-10 (MK-10) through the adsorption of the catalyst on the external surface. The crystalline structure of bentonite (BDH), which has the same chemical composition, means that it has a considerable cationic exchange capacity (Figure 14). Crocker and Herold [145] suggested that montmorillonite and bentonite clay minerals behave differently because of structural differences. The MK-10 is obtained via an aggressive acid treatment of the natural BDH smectites. As a result, the octahedral layers of the clay are partially destroyed and the lattice negative charge is partially suppressed and the crystallinity of the solid is reduced. Thus, MK-10 increases the surface area and favours the adsorption capacity over the ionic exchange properties.

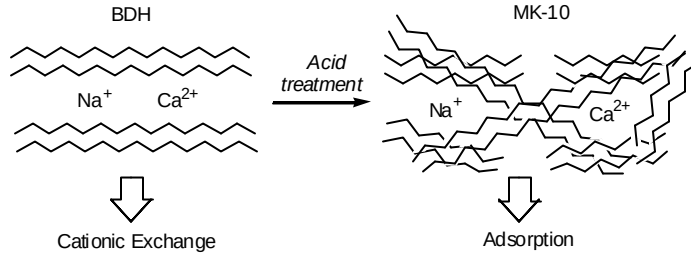


Figure 14

Most of the applications of the catalytic systems immobilised via ion exchange or adsorption have been carried out in reduction (mainly hydrogenation) [91], [146], reductive alkylation of amines [144c] cyclopropanation reactions [139], [147], and cyclocarbonylation reactions [148]. More recently, studies of other reactions involving C-C bond formation, such as Heck [149], have been added to the list of applications.

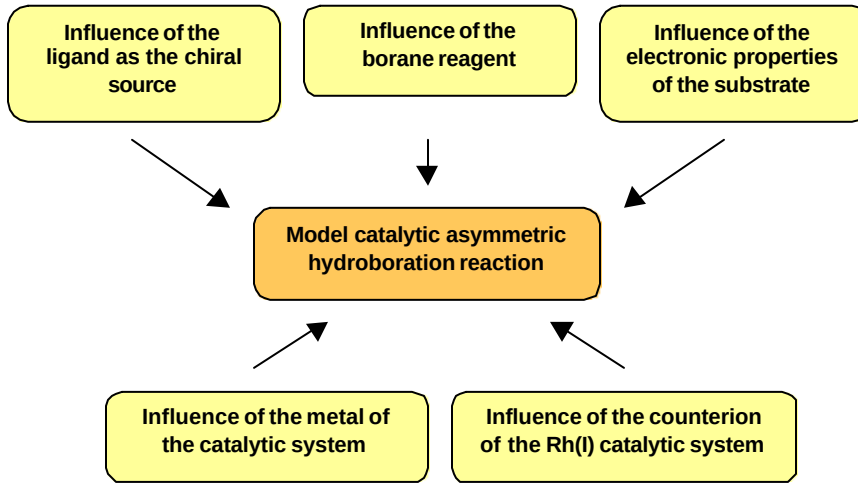
4. Scope of this thesis

This introduction clearly shows the interest in the catalytic asymmetric hydroboration reaction. The effort that various authors have made to develop chiral catalytic systems for this transformation has been rewarded by obtaining excellent catalytic performances. It is also noteworthy the intense dedication to develop an environmental and economic viability of chemical transformations through the design of catalytic systems that can be removed and reused.

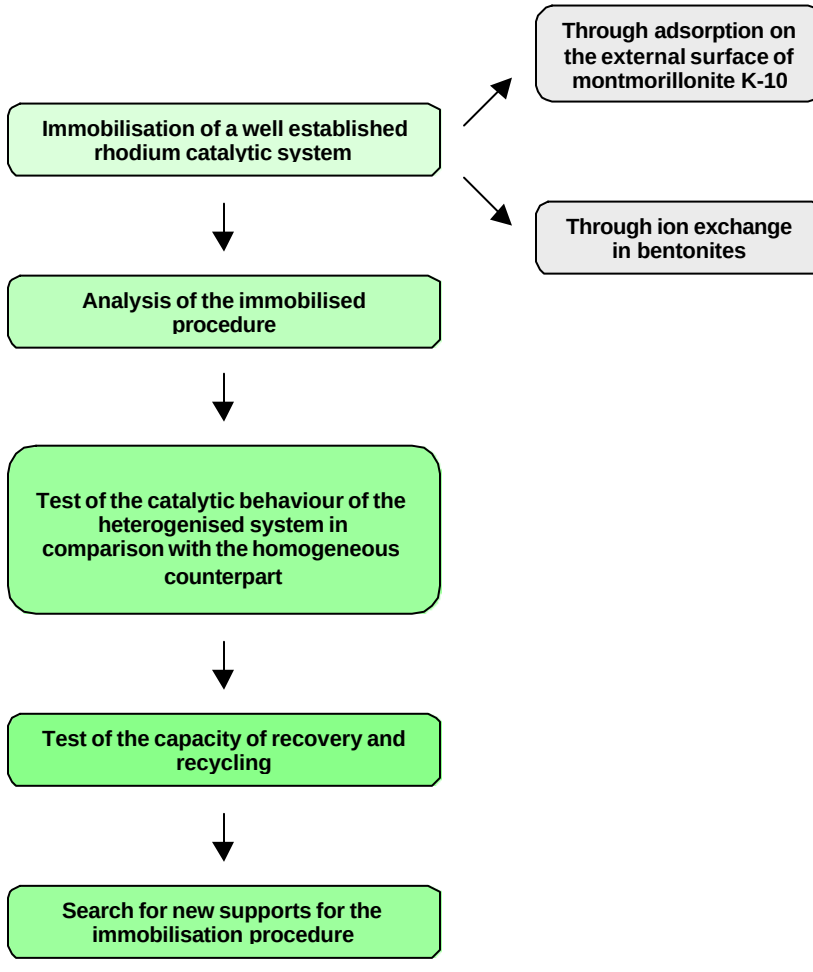
At this point, we planned to develop in this thesis the following aspects:

1) Understand how high activity and selectivity can be generated throughout the hydroboration process.

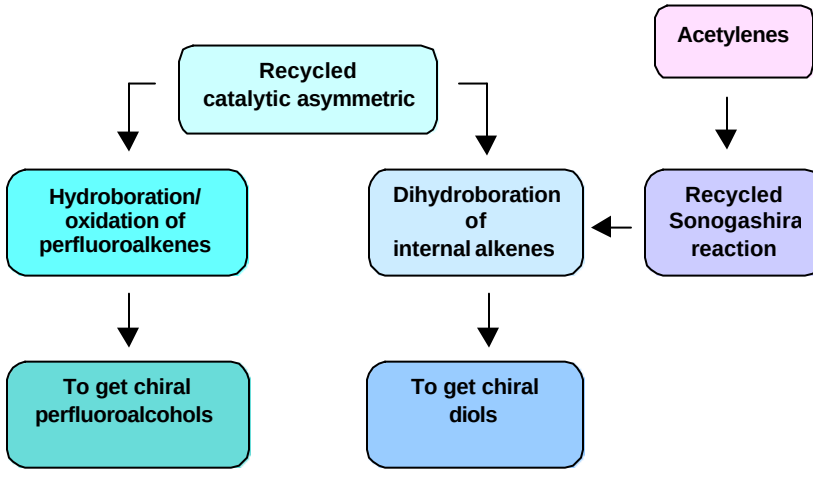
To create an overall picture of the various influences on the catalytic asymmetric hydroboration reaction, we take into account a model reaction where the substrate is styrene, the catalytic system is a cationic rhodium complex, the source of chirality is the atropoisomeric P,N ligand Quinap, and the borane reagent is catecholborane. To facilitate the analysis, we fixed the reaction conditions and oxidised the hydroborated products to alcohols, before initiating the following systematic study:



2) Design of a chiral catalytic system that can be easily recovered from the products and reused in the catalytic asymmetric hydroboration reaction, and which responds to the challenge of improving the environmental and economic viability of the asymmetric process



3) Extension of the accumulated know how on chiral organoboron compounds to other substrates. In particular we focused on:



References

[1] H.C.Brown, B.S.Subba Rao, *J. Am. Chem. Soc*. **1959**, *81*, 6423.

[2] a) Männing, H.Nörth, *Angew. Chem* . **1985**, *97*, 979; b) Männing, H.Nörth, *Angew. Chem* . *Int. Ed. Engl*. **1985**, *24*, 878.

[3] *Reviews for catalysed hydroboration, see*: (a) K.Burgess, M.J.Ohmeyer, *Chem. Rev.* **1991**, *91*, 1179; (b) L.Delox, M.Srebnik, *Chem. Rev*. **1993**, *93*, 763; (c) I.Beletskaya, A.Pelter, *Tetrahedron* **1997**, *53*, 4957; (d) C.Fu, M.Beller, C.Bolm, *In the Transition Metals for Organic Synthesis;* Wiley-VCH: Weinheim **1998**, *Vol.2*, 141; (e) T.Hayashi, E.N.Jacobsen, A.Pfaltz, H.Yamamoto, *In the Comprehensive Asymmetric Synthesis*; Springer: Berlin **1999**, *Vol.1*, 351; (f) C.M.Crudden, D.Edwards, *Eur. J. Org. Chem.* **2003**, 4695.

[4] (a) H.C.Brown, P.V.Ramachandran, *Curr. Top. In the Chemistry of Boron*; ed. G.W.Kabalka, R.S.C.: London **1994**, 101; (b) A.Pelter, K.Smith, H.C.Brown, *In the Borane Reagents*; Academic: New-York **1988**.

[5] D.S.Matteson, *Stereodirected In the Synthesis with Organoboranes*; Springer: Berlin **1995**;

[6] N.Miyaura, A.Suzuki, *Chem. Rev.* **1995**, *95*, 2457.

[7] A.Suzuki, *In the Metal Cross-coupling Reactions*; eds. F.Diederich, P.J.Stang, Wiley-VCH: Weinheim **1998**, 49.

[8] N.Miyaura, L.S.Liebeskind, *In the Advances in Metal-Organic Chemistry*, JAI: Stamford **1998**, *Vol.6*, 187.

[9] (a) R.E.London, S.A.Gabel, *J. Am. Chem. Soc.* **1994**, *116*, 2562; (b) K.R.A.S.Sandanayake, K.Nakashima, S.Shinkai, *J. Chem. Soc. Chem. Commun.* **1994**, 1621.

[10] (a) M.F.Howthorne, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 950; (b) A.H.Soloway, *Chem. Rev.* **1998**, *98*, 1515.

[11] C.F.Lane, G.W.Kabalka, *Tetrahedron* **1975**, *32*, 981.

[12] K.Burgess, W.A.van der Donk, S.A.Westcott, T.B.Marder, B.T.Baker, J.C.Calabrese, *J. Am. Chem. Soc.* **1992**, *114*, 9350.

[13] D.A.Evans, G.C.Fu, B.A.Anderson, *J. Am. Chem. Soc*. **1992**, *114*, 6679.

[14] a) M.J.Benett, P.B.Konaldson, *Inorg. Chem.* **1997**, *16*, 1581-1594; b) M.T.A.Lay, L.R.Grahan, K.Kite, K.Moss, G.Read, *J. Mol. Catal.* **1990**, *7*, 31.

[15] (a) T.Hayashi, Y.Matsumoto, Y.Ito, *J. Am. Chem. Soc.* **1989**, *111*, 3426; (b) T.Hayashi, Y.Matsumoto, Y.Ito, *Tetrahedron: Asymmetry* **1991**, *2*, 601.

[16] S.A.Westcott, H.P.Blom, T.B.Marder, R.T.Baker, *J. Am. Chem. Soc*. **1992**, *114*, 8863.

[17] J.Liedtke, H.Rüeffer, S.Loss, H.Grützmaher, *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 2478.

[18] P.V.Ramachandram, M.P.Jennings, H.C.Brown, *Org.Lett.* **1999**, *1*, 1399.

[19] D.A.Evans, G.C.Fu, *J. Org. Chem*. **1990**, *55*, 5678.

[20] A.Lang, H.Nörth, M.Thomann-Albach, *Chem. Ber.* **1997**, *130*, 363.

[21] D.A.Evans, A.R.Murci, R.Stürmer, *J. Org. Chem.* **1993**, *58*, 5307.

[22] C.E.Tucker, J.Davidson, P.Knochel, *J. Org. Chem.* **1992**, 57, 3482.

[23] W.G.Wood, P.L.Strong, *J. Am. Chem. Soc*. **1966**, *88*, 4667.

[24] a) J.M.Brown, G.C.Lloyd-Jones, *J. Chem. Soc., Chem. Commun.* **1992**, 710; b) J.M.Brown, G.C.Lloyd-Jones, *J. Am. Chem. Soc*. **1994**, *116*, 866.

[25] a) H.R.Molales, H.Talhuext, F.Santi-Esteban, R.Contreras, *Spectrochim. Acta.*

[26] a) A.T.Kynch, L.G.Sneddon, *J. Am. Chem. Soc.* **1987**, *109*, 5867; b) P.J.Fazen, L.G.Sneddon, *Organometallics* **1994**, *13*, 2867; c) A.T.Lynch, L.G.Sneddon, *J. Am. Chem. Soc*. **1989**, *111*, 6201.

[27] S.A.Westcott, T.B.Marder, R.T.Baker, J.C.Calebrese, *Can. J. Chem.* **1993**, *71*, 930.

[28] K.Burgess, M.Jaspars, *Organometallics* **1993**, *12*, 4197.

[29] a) X.He, J.F.Hartwing, *J. Am. Chem. Soc*. **1996**, *118*, 1696; b) J.F.Hartwig, C.N.Muhori, *Organometallics* **2000**, *19*, 30.

[30] a) K.N.Harrison, T.J.Marks, *J. Am. Chem. Soc*. **1992**, *114*, 9220; b) E.A.Bijpost, R.Duchateau, J.H.Teuben, *J. Mol. Cat.* **1995**, *95*, 121.

[31] D.Liu, Z.Lin, *Organometallics* **2002**, *21*, 4750.

[32] S.Pereira, M.Srebnik, *Tetrahedron Lett.* **1996**, *37*, 3283.

[33] T.Umemoto, Y.Yamamoto, N.Miyaura,*(in press)*

[34] S.Pereira, M.Srebnik, *J. Am. Chem. Soc*. **1996**, *118*, 909.

[35] I.Aoyama, Y.Tamaka, T.Fujisawa, T.Watanabe, H.Toi, H.Ogoshi, *J. Am. Chem. Soc*. **1986**, *108*, 943.

[36] T.C.Morrill, C.A.D'Souza, L.Yang, A.J.Sampagnaro, *J. Org. Chem.* **2002**, *67*, 2481.

[37] D.Y.Yang, X.Huang, *J. Chem. Research (S)* **1997**, 62.

[38] S.Pereira, M.Srebnik, *Organometallics* **1995**, *14*, 3127.

[39] I.D.Gridnev, N.Miyaura, A.Suzuki, *Organometallics* **1993**, *12*, 589.

[40] T.Ohmura, Y.Yamamoto, N.Miyaura, *J. Am. Chem. Soc*. **2000**, *122*, 4990.

[41] E.Negishi, R.M.Williams, G.Lew, T.I.Yoshida, *J. Organomet. Chem.* **1975**, *92*, Capther: 4.

[42] J.B.Jr.Campbell, G.A.Molander, *J. Organomet. Chem.* **1978**, *156*, 71.

[43] H.C.Brown, T.Imai, Organometallics, **1984**, *3*, 1392.

[44] a) M.Srebnik, N.G.Bhat, H.C.Brown, *Tetrahedron Lett.* **1988**, *29*, 2635; b) L.Deloux, M.Srebnik, *J. Org.Chem.* **1994**, *59*, 6871; c) K. Takahashi, J. Takagi, T. Ishiyama, N. Miyaura, *Chem. Lett*., **2000**, 126.

[45] a) D.S.Sethi, G.C.Joshi, D.Devaprabhakara, *Can. J. Chem.* **1969**, *47*, 1083; R.H.Fish, *J. Am. Chem. Soc*. **1968**, *90*, 4435; b) H.C.Brown, R.Liotta, G.W.Kramer, *J. Am. Chem. Soc*. **1979**, *101*, 2966.

[46] Ch.D.Entwistle, A.S.Batsanov, J.A.K. Howard, M.A.Fox. T.B.Marder, *J. Chem*. *Commun*. **2004**, 702.

[47] a) K.Burgess, M.J.Ohlmeyer, *J. Org. Chem.* **1988**, *53*, 5178; b) K.Burgess, W.A.Donk, M.J.Ohlmeyer, *Tetrahedron: Asymmetry* **1991**, *2*, 613.

[48] a) A.Togni, C.Breutel, A.Schnyder, F.Spindler, H.Landert, A.Tijani, *J. Am. Chem. Soc*. **1994**, *116*, 4062; b) A.Schnyder, L.Hintermann, A.Togni, *Angew. Chem. Int. Ed. Engl.* **1995***, 34,* 931*;* c) H.C.L.Abbenhuis, Y.Burcklharalt, V.Gramlich, A.Martelletti, J.Spencer, J.Steiner, A.Togni, *Organometallics* **1996***, 15,* 1614*.*

[49] a) J.M.Brown, D.I.Hulmes, T.P.Layzell, *J. Chem. Soc., Chem Commun.* **1993**, 1673; b) N.W.Alcock, J.M.Brown, D.I.Hulmes, *Tetrahedron: Asymmetry* **1993**, *4*, 743; c) H.Doucet, E.Fernandez, T.P.Layzell, J.M.Brown, *Chem. Eur. J*. **1999**, *5*, 1320.

[50] a) J.M.Valk, T.Clavidge, J.M.Brown, D.Hibbs, M.B.Hursthouse, *Tetrahedron* **1997**, *53*, 4035; b) J.M.Brown, H.Doucet, *Tetrahedron: Asymmetry* **1997**, *8*, 3775.

[51] J.M.Valk, G.A.Whitlock, T.P.Layzell, J.M.Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2593.

[52] a) M.McCarthy, M.Hooper, P.J.Guiry, *Chem. Commun*. **2000**, 1333; b) M.McCarthy, P.J.Guiry, *Tetrahedron* **2001**, *57*, 3809.

[53] F.Y.Kwong, Q.Yang, T.C.W.Mak, A.S.C.Chan, K.S.Chan, *J. Org. Chem.* **2002**, *67*, 2769.

[54] *For the values of Hammet constant, see:* A.J.Gordon, R.A.Ford, *In The Chemist's Companion*; J.Wiley: New York, **1972**.

[55] J.Zhang, B.Lou, G.Guo, L.Dai, *J. Org. Chem.* **1991**, *56*, 1670.

[56] A.Westcott, T.B.Marder, R.T.Baker, *Organometallics* **1993**, *12*, 975.

[57] T.Davan, E.W.Corcoran, L.G.Sneddon, *Organometallics* **1983**, *2*, 1693.

[58] W.C.Still, J.C.Berrish, *J. Am. Chem. Soc*. **1983**, *105*, 2487.

[59] a) H.C.Brown, *In Hydroboration*; Wiley-Interscience: New York **1962**; b) H.C.Brown, G.W.Kramer, A.B.Levy, M.M.Midland, *Organic Synthesis via Boranes*, Wiley-Interscience: New York **1975**.

[60] K.Kono, K.Ito, Y.Nagari, *Chem. Lett.* **1975**, 1095.

[61] a) J.P.Collam, L.S.Hegedus, J.R.Norton, R.G.Finke, *In Principles and Application of Organotransition Metal Chemistry*; University Science Books: C.A.MillValley **1987**; b) A.Togni, H.Grützmacher, *In Catalytic Heterofunctionalization*; eds. A.Togni, H.Grützmacher, Wiley-VCH Publichers: Weinheim **2001**.

[62] R.Noyori, *In the Asymmetric Catalysis in Organic Chemistry*; Wiley: New York **1994**.

[63] S.A.Westcott, N.J.Taylor, J.C.Calabrese, *J. Chem. Soc., Chem. Commun.* **1991**, 304.

[64] S.A.Westcott, H.P.Blom, T.B.Marder, R.T.Baker, J.C.Calabrese, *Inorg. Chem.* **1993**, *32*, 2175.

[65] K.Burgess, W.A.von der Donk, .*Organometallics* **1993**, *13*, 3616.

[66] D.G.Musaev, A.M.Mebel, K.Morokuma, *J. Am. Chem. Soc*. **1994**, *116*, 10693.

[67] A.E. Dorigo, P.V.R.Schleyer, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 115.

[68] C.Widauer, H.Grützmacher, T.Ziegler, *Organometallics* **2000**, *19*, 2097.

[69] A.Schnyder, A.Togni, U.Wiesly, *Organometallics* **1997**, *16*, 255.

[70] S.Demay, F.Volant, P.Knochel, *Angew. Chem. Int. Ed*. **2001**, *40*, 1235.

[71] D.A.Evans, J.R.Gage, *J. Org. Chem.* **1992**, *17*, 1958.

[72] Y.Nomoto, N.Miyaura, A.Suzuki, *Synlett* **1992**, 727.

[73] X.L.Hou, Q.C.Xie, L.X.Dai, *J. Chem. Research (S)* **1997**, 436.

[74] K.Burgess, W.A. van der Donk, M.B.Jarstfer, M.J.Ohlmeyer, *J. Am. Chem. Soc*. **1991**, *113*, 6139.

[75] D.L.Boger, T.Honda, *J. Am. Chem. Soc*. **1994**, *116*, 5647.

[76] G.Hareau-Viltini, P.J.Kocienski, *Synlett* **1995**, 893.

[77] A.S.Dende, K.Liu, K.M.J.Brands, *J. Am. Chem. Soc*. **1995**, *117*, 10597.

[78] A) A.C.Chen, L.Ren, C.M.Crudden, *Chem. Commun*. **1999**, 611; b) L.Ren, C.M.Crudden, *Chem. Commun*. **2000**, 721.

[79] J.P.Rieu, A.Boucherle, H.Cousse, G.Mouzin, *Tetrahedron* **1986**, *42*, 4095**.**

[80] a) E.Fernandez, M.W.Hooper, F.I.Knight, J.M.Brown, *Chem. Commun*. **1997**, 173; b) E.Fernandez, K.Maeda, M.W.Hooper, J. M. Brown, *Chem. Eur. J.* **2000**, *6*, 1840; c) E.Fernandez, J.M.Brown, *In the Modern Amination Methods*; ed. A.Ricci, VCH Publishers: Weinheim **2000**; d) K.Maeda, J.M.Brown, *Chem. Commun*. **2002**, 310.

[81] F.R.Harley, *In the Chemistry of Metal Carbon Bond*; Ed. F.R.Harley, John Wiley & Sons Ltd **1986** *Vol. 4*, 1163.

[82] R.Selke, K.Häupke, H.W. Krause, *J. Mol. Catal.* **1989**, *56*, 315.

[83] S.J.Shuttleworth, S.M.Allin, P.K.Sharma, *Synthesis* **1997**, 1217.

[84] H.U.Blaser, *Tetrahedron: Asymmetry* ***1991***, *2*, 843.

[85] F.Fache, E.Schulz, M.L.Tommasino, M.Lemaire, *Chem. Rev*. ***2000***, *100*, 2159.

[86] O.Piccolo, *Chim. Ind* ***1998***, *80*, 1177.

[87] a) D.Pini, A.Mandoli, A.Petri, P.Salvadori, *Chim. Ind* ***1999***, *81*, 189; b) P.Salvadori, D.Pini, A.Petri, *Synlett* ***1999***, *8*, 1181.

[88] B.Pugin, H.Y.Blaser, *In Comprehensive Asymmetric Catalysis*; Eds. E.N.Jacobsen, A.Pfaltz, H.Yamamoto, Springer: Berlin **1999**, *Vol.3*.

[89] C.Bolm, A.Gerlach, *Eur. J. Org. Chem.* **1998**, 21.

[90] C.U.Pittman, *In Comprehensive Organometallic Chemistry*; Eds. G.Wilkinson, F.G.A.Stone, E.W.Abel, Pergamon: Oxford **1983**, *ch.55*.

[91] a) H.U.Blaser, B.Pugin, *In Chiral Reactions in Heterogeneous Catalysis*; Eds. G.J.James, V.Dubois, Plenum Press: New York **1995**; b) D.E.De Vos, I.F.J.Vankelecom, P.A.Jacobs, *In Chiral Catalyst Immobilization and Recycling*; Wiley-VCH: Weinheim, **2000**.

[92] B.Clapham, T.S.Reger, K.D.Janda, *Tetrahedron* **2001**, *57*, 4637.

[93] C.Saluzzo, R.ter Halle, F.Touxhard, F.Fache, E.Schulz, M.Lemaire, *J. Organomet. Chem.* **2000**, *30*, 603.

[94] K.Soai, S.Niwa, *Chem. Rev.* **1992**, *92*, 833.

[95] a) Y.Yermakow, I.Yu, B.N.Kuznetsow, V.A.Zakharow, *In Studies in surface science and catalysis*; Elveir scientific publishing company: Amsterdam **1981**, *vol.8*; b) T.J.Pinnavaia, *Science* **1983**, *220*, 365; c) J.M.Andersen, *Platinium Metals Rev.* **1997**, *41*, 132; d) P.Gamez, B.Donjic, F.Fache, M.J.Lemaire, *J. Chem. Soc., Chem. Commun.* **1994**, 1417.

[96] T.Wasaki, Y.Aoiuma, *J. Am. Chem. Soc.***1999**, *121*, 4793.

[97] C.J.Brinker, G.W.Scherer, *In Sol-gel Science, the Physics and Chemistry of Sol-gel Processing;* Academic Press **1999**.

[98] J.M.Thomas, S.Ramdas, G.R.Millward, J.Klinowsky, M.Audier, J.Conzalex-Calbet, C.A.Fyfe, *J. Solid*. *State Chem*., **1982**, *45*, 368.

[99] A.Corma, *Chem. Rev.* **1997**, *97*, 2373.

[100] S.Scurrell, *In La Chimica e l'industria* **1979**, *69*, 219.

[101] M.Berry, R.K.Champaneria, J.A.S.Howell, *J. Mol. Catal.* **1986**, *37*, 243.

[102] M.E.Davis, J.Schnitzer, J.A.Rosin, *J. Mol. Catal.* **1987**, *39*, 243.

[103] J.M.Fraile, J.I.García, J.A.Mayoral, *Chem. Commun.* **1996**, 1319.

[104] A.Guerte, M.Iglesias, F.Sánchez, *J. Organomet. Chem.* **1999**, *58*, 186.

[105] F.Cavani, F.Trifiro, A.Vaccari, *Catal. Today* **1991**, *11*, 173.

[106] S.A.Matlin, W.J.Lough, L.Chan, D.M.H.Abram Z.Zhou, *J. Chem. Soc., Chem. Commun.* **1994**, 1038.

[107] M.Eisen, J.Blum, H.Schumann, B.Gorella, *J. Mol. Cat.* **1989**, *56*, 329.

[108] A.Kiting, H.Krause, M.Capka, *J. Mol. Cat.* **1985**, *33*, 215.

[109] A.Corma, M.Iglesias, C.del Pino, F.Sanchez, *J. Chem. Soc., Chem. Commun.* **1991**, 1253.

[110] A.Corma, M.Iglesias, C.del Pino, F.Sanchez, *J. Organomet. Chem.* **1992**, *431*, 233.

[111] B.F.G.Johnson, S.A.Raynor, D.S.Sherphard, T.Maschmeyer, J.M.Thomas, G.Sankar, S.Bromley, R.Oldroyd, L.Gladden, M.D.Mantle, *Chem. Commun.* **1999**, 1167.

[112] a) B.Pugin, *WO 9632400 A1* **1996**; b) B.Pugin, *WO 9702232 A1* **1997**; c) B.Pugin, *EP 72996 A1* **1996**.

[113] J.M.Fraile, J.I.Garcia, J.M.Mayoral, A.J.Royo, *Tetrahedron: Asymmetry* **1996**, *7(8)*, 2263.

[114] a) M.J.Alcon, A.Corma, M.Iglesias, F.Sánchez, *J. Organomet. Chem.* **2002**, *655(1-2)*, 134; b) C.Perez, S.Perez, G.A.Fuentes, A.Corma, *J. Mol. Cat. A: Chemical* **2003**, *197(1-2)*, 275.

[115] A.J.Sandee, J.N.H.Reek, P.C.J.Kamer, P.W.N.M. van Leeuwen, *J. Am. Chem. Soc.* **2001**, *123*, 8468.

[116] J.R.Serveren, R.Duchateau, R.A.van Santen, D.D.Ellis, A.L.Spek, *Organometallics* **2002**, *21*, 4.

[117] J.M.Fraile, J.M.Mayoral, J.Serrano, M.A.Pericas, L.Solà, D.Castellnou, *Organic Lett.* **2003**, *5(23)*, 4333.

[118] A.Fuerte, M.Iglesias, F.Sanchez, A.Corma, *J. Mol. Catal. A: Chemical* **2004**, *211*, 227.

[119] C.Beleizao, A.Corma, H.Garcia, A.Leyva, *J. Org. Chem.* **2004**, *69*, 439.

[120] a) C.Beleizao, B. Gigante, H.Garcia, A.Corma, *J. Org. Chem.* **2004**, *221(1)*, 77; b) C.Beleizao, B. Gigante, M.J.Sabater, H.Garcia, A.Corma, *App. Catal. A: General* **2002**, *228(1-2)*, 279.

[121] a) M.Chabanas, A.Baudouin, C.Coperet, J.M.Basset, W.Lunkens, A.Lesage, S.Hediger, L.Emsley, *J. Am. Chem. Soc.* **2003**, *125(2)*, 492; b) M.Chabanas,

C.Coperet, J.M.Basset, *Chem. A Eur. J.* **2003**, *9(4)*, 971; c) Q.H.Yang, C.Coperet, C.Li, J.M.Basset, *New J. Chem.* **2003**, *27*, 319.

[122] a) R.L.Augustine, S.K.Tanielyan, S.Anderson, H.Li, *Presentation ChiraTech'98* **1998**; b) R.Augustine, S.Tanielyan, S.Anderson, H.Yang, *Chem. Commun.* **1999**, 1257.

[123] Y.Izumi, Y.Urabe, M.Onaka, *In Zeolite Clay and Heteropoly Acid in Organic Reactions*; VCH: New York **1992**, *Chapter 3.*

[124] M.Pohl, D.K.Lyon, N.Mizuno, K.Nomiya, R.G.Finke, *Inorg. Chem.* **1995**, *34*, 1413.

[125] S.B.Ogunwumi, T.Bein, *Chem. Commun.* **1997**, 901.

[126] M.J.Sabater, A.Corma, A.Domenech, V.Fornes, H.Garcia, *Chem. Commun.* **1997**, 1285.

[127] I.F.J.Vankelecom, D.Tas, R.F.Parton, V. van der Wyner, P.A.Jacobs, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1346.

[128] T.Bein, *In Curr. Opin. Solid. State Mater Sci*. **1999**, *4*, 85.

[129] H.N.Flach, I.Grassert, G.Oehme, M.Capka, *J. Colloid. Polym. Sci.* **1996**, *274*, 261.

[130] I.F.J.Vankelecom, K.Vercruysse, P.Neys, D.Tas, K.B.M.Janssen, P.P.Knops-Gerrits, P.A.Jacobs, *Topics in Catal.* **1998**, *5*, 125.

[131] D.Ras, I.Thoelen, I.Vankelecom, P.A.Jacobs, *Chem. Commun.* **1997**, 2323.

[132] R.B.M.Janssen, I.Laquiere, E.Dehaen, R.F.Parton, I.F.J.Vankelecom, P.A.Jacobs, *Tetrahedron: Asymmetry* **1997**, *8*, 3481.

[133] C.Bianchini, D.G.Burnaby, J.Evans, P.Frediani, A.Meli, W.Oberhauser, R.Psaro, L.Sordelli, F.Vizza, *J. Am. Chem. Soc.* **1999**, *121*, 5961.

[134] C.Bianchini, V.Dal Santo, A.Meli, W.Oberhauser, R.Psaro, F.Vizza, *Organometallics* **2000**, *19*, 2433.

[135] C.Bianchini, P.Barbaro, V.Dal Santo, R.Gobetto, A.Meli, W.Oberhauser, R.Psaro, F.Vizza *Adv. Synth. Catal.* **2001**, *343*, 41.

[136] F.M.de Rege, D.K.Morita, K.C.Ott, W.Tumas, R.D.Broene, *Chem. Commun.* **2000**, 1797.

[137] M.M.Diaz Requejo, T.R.Belderrain, M.C.Nicasio, P.J.Perez, *Organometallics* **2000**, *19*, 285.

[138] W.T.Klooster, T.F.Koetzle, P.E.M.Siegbahn, T.B.Richardson, R.H.Crabtree, *J. Am. Chem. Commun.* **1999**, *121*, 6337.

[139] J.M.Fraile, J.I.García, J.A.Mayoral, T.Tarnai, *Tetrahedron: Asymmetry,* **1997**, *8(13)*, 2089.

[140] J.M.Fraile, J.I.García, J.A.Mayoral, T.Tarnai, *Tetrahedron: Asymmetry,* **1997**, *9*, 3997.

[141] R.Selke, M.Capka, *J. Mol. Catal.* **1990**, *63*, 319.

[142] D.Tas, D.Jeanmart, R.F.Parton, P.A.Jacobs, *In Stud. Surf. Sci. Cat. Part 108. Heterogeneous catalysis and Fine chemicals IV*; Eds. H.U.Blaser, A.Baiker, R.Prins, Elveiser **1997**, 493.

[143] a) B.M.Choudary, G.Vasantha, M.Sharma, P.Bharathi, *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 465; b) B.M.Choudary, K.R.Kumar, M.L.Kantam, *J. Catal.* **1991**, *130*, 41.

[144] a) R.Margalef-Català, P.Salagre, E.Fernández, C.Claver, *Catalysis Letters* **1999**, *60*, 121; b) C.Claver, E.Fernández, R.Margalef-Català, F.Medina, P.Salagre, J.E.Sueiras, *J. Catal.* **2001**, *201*, 70; c) R.Margalef-Català, P.Salagre, E.Fernández, C.Claver, *Tetrahedron Lett.* **2000***, 41*, 6583; d) R.Margalef-Català, P.Salagre, E.Fernández, C.Claver, *Tetrahedron: Asymmetry.* **2000***, 11*, 1469.

[145] M.Crocker, R.H.M.Herold, *Catalysis Letters* **1993**, *18*, 243.

[146] T.Sento, S.Schimazu, N.Ichikuni, T.Vematsu, *J. Mol. Catal. A: Chemical* **1999**, *137*, 263.

[147] a) J.M.Fraile, J.I.García, J.Massam, J.A.Mayoral, *J. Mol. Catal. A: Chemical* **1998**, *136*, 47; b) A.Cornejo, J.M.Fraile, J.I.Garcia, M.J.Gil, C.I.Herrerias, G.Lagarreta, V.Martinez-Merino, J.A.Mayoral, *J. Mol. Catal. A: Chemical* **2003**, *196*, 102.

[148] A.Orejon, H.Alper, *J. Mol. Catal. A: Chemical* **1999**, *143*, 137.

[149] a) M.Poyatos, E.Peris, C.Claver, E.Fernandez, *New J. Chem.* **2003**, *27*, 425; b) A.Corma, H.Garcia, A.Leyva, A.Primo, *App. Catal. A: General* **2003**, *247(1)*, 41.

Chapter 3

Recovery of the catalyst

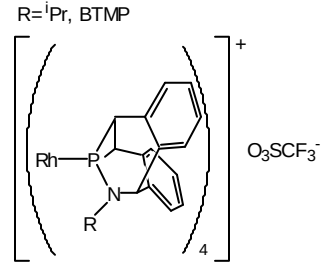
Recently there has been considerable interest in the heterogenisation of chiral homogeneous catalytic systems. Many reports have shown that it is possible to design and produce new chiral catalytic system that has obvious advantages over their soluble counterparts: they can induce asymmetry, they can be removed from the reaction mixture by simple filtration and, in many cases, they can be recycled and used again.

This chapter describes, for the first time, the rhodium and iridium chiral complexes immobilised on either natural or synthetic solid supports, to be applied in the catalytic asymmetric hydroboration reaction of vinylarenes.

1. Introduction

The catalytic asymmetric hydroboration reaction provides a way of transforming alkenes into optically enriched organoboron adducts, C*-B. The oxidation of the chiral organoboron, (via H_2O_2/OH^-), achieves the respective alcohol C*-OH with complete retention of the configuration.

When turnover is complete in the catalytic hydroboration of vinylarenes, with most rhodium complexes modified with bidentate chiral ligands, the resting state of the catalyst decomposes as a result of its instability. In recent times, in an attempt to be able to reuse the catalytic system several times, Grützmacher and coworkers have synthesised an air-stable polycyclic phosphirane ligand called BABAR-Phos which after modifying a cationic rhodium complex **68**, (Figure 1), provides a more stable resting state which continues hydroborating after the re-addition of alkenes [1]. There was no decrease in catalytic activity even after five catalytic cycles. However, the BABAR-Phos rhodium complex **68** has the drawback that the catalyst is destroyed during the workup that provides the corresponding alcohols, because this is done in a H_2O_2/OH^- medium.



[Rh(BABAR-Phos)$_4$]OTf

68

Figure 1

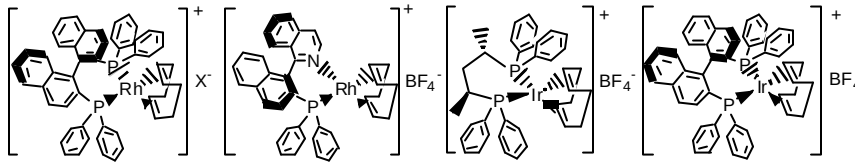
Therefore, the destruction of the catalyst during the workup should be prevented by separation before the oxidation. This would guarantee the stability of the catalytic system and make it possible for it to be reused in new consecutive hydroboration reactions.

It has been mentioned above that the catalytic system Rh(I) modified with phosphinamine Quinap provides high regio- and enantioselectivity towards the hydroboration/oxidation of vinylarenes and β-substituted vinylarenes working at room temperature [2]. The catalytic systems based on Rh(I) with the analogous diphosphine ligand Binap gave high regioselectivity but only moderate enantioselectivity under the same reaction conditions for the catalytic hydroboration reaction [3]. However, the instability of the resting state of both homogeneous catalyst and the difficulty of separating and recycling the expensive chiral rhodium complexes are still serious disadvantages. A recent report has described that an atropoisomeric P,N ligand which is configurationally stable in an acidic medium, Pyphos (**31**), can be recovered from the solution through the acid/aqueous extraction of the pyridine moiety of the P,N ligand [4]. This meant that the recovery of the expensive chiral ligand was also a possibility. However it should be pointed out that the totality of the P,N ligand cannot be recovered and that the transition metal complex cannot be recovered at all. In view of these limitations, the problem of developing a method for separating, recovering and reusing metal complexes modified with chiral ligands from a catalytic process remains unresolved.

The advantages of immobilising the homogeneous catalyst on a heterogeneous support are that separation is straightforward and the catalyst can be reused. The activities and selectivities are similar to those of homogeneous systems. Indeed, all these properties are particularly significant for the economic viability of the process, especially when sophisticated chiral ligands are involved, [5, 6]. Of the different immobilisation procedures, the non-covalent grafting of homogeneous chiral cationic catalysts on solid supports could be an interesting alternative, because it is efficient and easy to prepare.

From our experience [7], we became interested in immobilising catalytic systems in clay structures through absorption or cationic exchange, which is an easy and clean alternative to heterogenisation. We attempted to immobilise optically pure

rhodium (I) complexes, [M(cod)(L,L)]X where (L,L)= (R)-Binap, (S)-Quinap, (S,S)-bdpp; M= Ir or Rh; X= BF_4, PF_6, BPh_4, OTf , (Figure 2), through adsorptive forces onto natural clay structures (montmorillonite K-10) and through electrostatic forces into natural smectites (bentonites) [8,9] or on synthetic organo(bis-silantriolates) [10].



[Rh(cod)(R)-Binap]X [Rh(cod)(S)-Quinap]BF_4 [Rh(cod)(S,S)-bdpp]BF_4 [Ir(cod)(R)-Binap]BF_4

69 X=BF_4
70 X=PF_6
71 X=SO_3CF_3
72 X=BPh_4

Figure 2

2. Results and discussion

2.1. Heterogenised catalytic hydroboration using natural supports

2.1.a. Study of the immobilisation process

We immobilised the organometallic complexes [M(cod)(L,L))]X (M= Rh and Ir; (L,L)= (R)-Binap, (S,S)-bdpp, (S)-Quinap; X= BF_4, PF_6, SO_3CF_3, BPh_4), (Figure 2), onto the clays montmorillonite K-10 (MK-10) and bentonite (BDH), by the previously described solvent-impregnation method [11]. Coloured solutions of the ionic complexes in anhydrous dichloromethane were stirred with the solid support for 24 h under nitrogen. The amount of metal complex [Rh(cod)(R)-Binap]BF_4 (**69**) adsorbed by the clay was determined by gravimetric analysis in which the difference between the weights of the complex before and after the immobilisation was measured, (Table 1). These data suggest that when the montmorillonite K-10 was predried for 24 h at 100^0C

($MK\text{-}10_T$), the amount of rhodium complex **69** adsorbed onto the clay was higher because any adsorbed water could be eliminated. However, when the montmorillonite K-10 was calcined to 400^0C, the resulting calcined solid ($MK\text{-}10_{400}$) did not adsorb more rhodium complex than $MK\text{-}10_T$, probably because of the loss of interlamellar water which resulted in layer collapse. The dehydroxylation process during the calcinations modifies the residual microporosity and the values of the BET surface area from 221 m^2g^{-1} for $MK\text{-}10_T$ to 211 m^2g^{-1} for $MK\text{-}10_{400}$. Similar behaviour was observed in the immobilisation process of $[M(cod)(PPh_3)_2]BF_4$ (M= Ir and Rh) onto clays in previous study [7b].

The percentages of rhodium complexes with other counterions ($X=PF_6$, SO_3CF_3, BPh_4) adsorbed onto $MK\text{-}10_T$ were very similar (Table 1). Conductimetric and ^{19}F and ^{11}B NMR analyses of the liquid filtrate after the impregnation process indicated that the counterions (BF_4, PF_6, SO_3CF_3, BPh_4) were not present in the filtrates, presumably because they were adsorbed on the support.

Table 1. Amounts of immobilised metal complexes [M(cod)(L,L)]X on the clays.

Solid[a]	Heterogenised catalytic system	mmol complex per g solid[b]
MK-10	**69**-MK-10	0.055
$MK\text{-}10_T$	**69**-$MK\text{-}10_T$	0.084
$MK\text{-}10_{400}$	**69**-$MK\text{-}10_{400}$	0.058
BDH_T	**69**-BDH_T	0.046
$MK\text{-}10_T$	**70**-$MK\text{-}10_T$	0.074
$MK\text{-}10_T$	**71**-$MK\text{-}10_T$	0.085
$MK\text{-}10_T$	**72**-$MK\text{-}10_T$	0.062
$MK\text{-}10_T$	**73**-$MK\text{-}10_T$	0.092
$MK\text{-}10_T$	**74**-$MK\text{-}10_T$	0.093

[a] MK-10: commercial montmorillonite K-10; $MK\text{-}10_T$: preheated at 100^0C for 24 h; $MK\text{-}10_{400}$: previously calcined at 400^0C for 3 h; BDH_T: commercial bentonite preheated at 100^0C for 24 h; [b] Calculated from the equation [(mg initial complex-mg final complex)/molecular weight complex]/(g solid + g adsorbed complex).

Powder X-ray diffraction (XRD) is very useful technique for characterising of heterogenised organometallic systems [7c], [12-13]. This method shows how the basal distance between the layers varies in relation to the position of the (001) reflection peak.

It is known that although both montmorillonite K-10 (MK-10) and bentonite (BDH) are the same montmorillonite clay material, their crystallinity is significantly different [9]. The powder X-ray diffractograms of BDH and MK-10 do not show significant differences in the characteristics peaks associated with the (001) reflection, although the peaks are better defined when BDH is the support. This suggests that the bentonite has a major laminar ordination, or crystallinity, (Figure 3). In fact MK-10 is prepared from BDH by acid treatment, which partially destroys the bentonite layer structure. This disorders the BET surface area and increases it from 53 m^2g^{-1} to 221 m^2g^{-1}, favouring the adsorption properties in MK-10 in contrast to cation exchange in BDH.

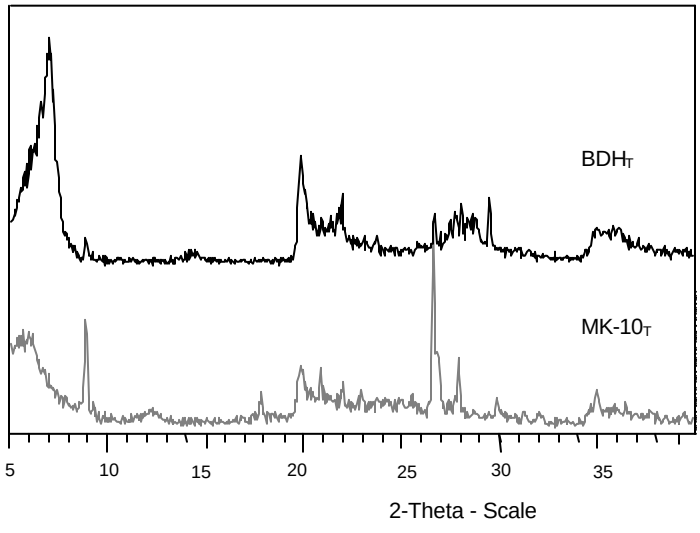


Figure 3

The powder-X-ray diffractogram of BDH$_T$, MK-10$_T$ Fluka; montmorillonite (nº 15-0135 in JCPDS-ICDD), flogopite (nº 16-0344 in JCPDS-ICDD), quartz (nº 33-1161 in JCPDS-ICDD).

In fact, there was a noticeable difference when preheated bentonite (BDH_T) was used as support. Following the same impregnation procedure, the amount of metal complex **69** adsorbed was only 0.046mmol per gram of clay, (Table 1). This data is in agreement with the fact that the surface area of BDH (53 m^2g^{-1}) is smaller than that of MK-10. Also, conductimetric analyses made after washing the immobilised catalytic system in bentonite revealed the presence of ionic species, which indicate that immobilisation took place mainly through a cation exchange process rather than adsorption. The powder X-ray diffraction data showed an insignificant shift in the (001) diffraction line on the diffractogram between $MK\text{-}10_T$ and **69**-$MK\text{-}10_T$, but a basal distance that increased from 12.3 Å in BDH_T to 16 Å in **69**-BDH_T, (Figure 4).

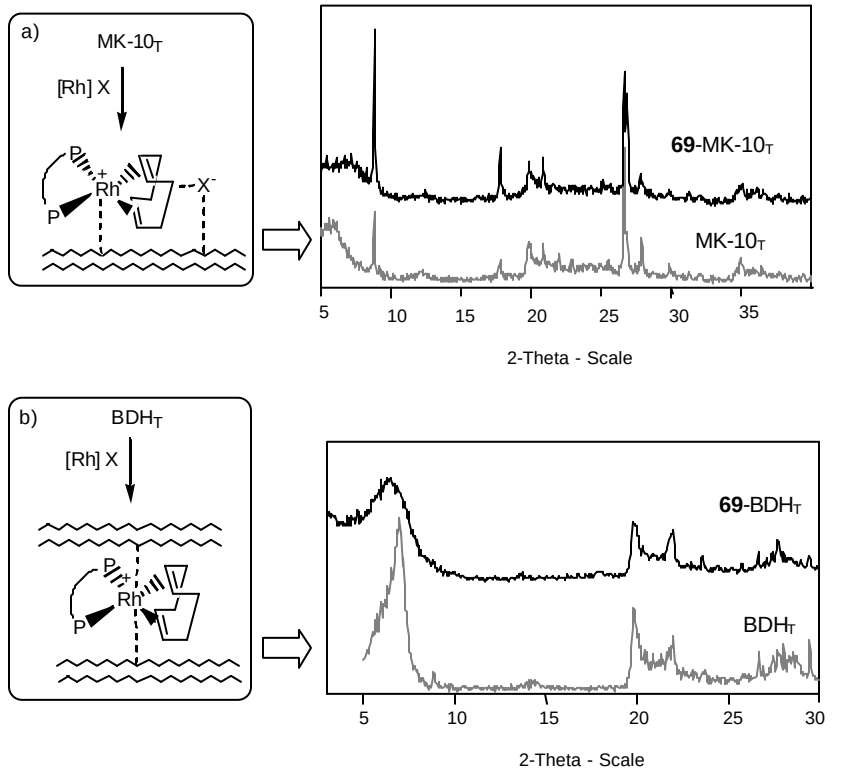


Figure 4

We recorded ^{19}F, ^{31}P and ^{11}B NMR spectra in $CDCl_3$ during the impregnation process. These experiments provided evidence that MK-10_T could adsorb ionic metal complexes through the cationic and anionic counterparts. In contrast, the immobilisation of the same complexes into bentonite occurred through only the cation counterpart by ionic exchange.

The ^{19}F NMR spectrum of **69** had two singlets at δ=-154.20 and -154.30ppm with an intensity ratio of 1:4, which is consistent with the isotopic distribution between ^{19}F and ^{10}B and ^{11}B, respectively (Figure 5b), while the ^{31}P spectrum has a doublet at δ=26.21ppm ($J_{P\text{-}Rh}$= 145.4 Hz) (Figure 5a). The intensity of these signals decreases significantly in the ^{31}P and ^{19}F NMR locked spectra of a slurry in $CDCl_3$ when MK-10_T is added little by little to complex **69** (Figure 6). This is because the concentration of **69** decreases in solution during the immobilisation process. To ensure that the disappearance of the signals was not caused by a shimming problem in the presence of the solid, we carried out the above experiments with the addition of an inert reactant, such as the free ligand Binap (10mg). Figure 5a and Figure 6a show that after the consecutive addition of MK-10_T, the intensity of the doublet ($\delta(^{31}P)$= 26.40ppm) due to P nuclei from the coordinated Binap ligand decreases significantly in comparison with that of the singlet due to the free Binap ligand ($\delta(^{31}P)$= -14.60ppm). This is in agreement with the fact that complex **69** is being immobilised onto MK-10_T.

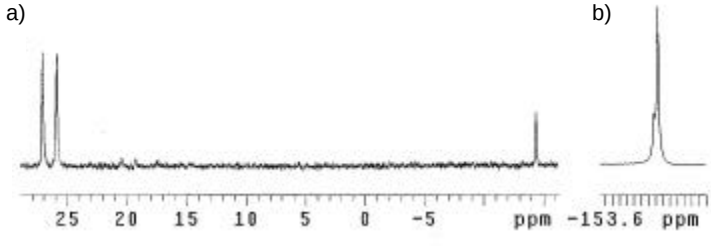


Figure 5

a) ^{31}P NMR spectra of 20 mg of **69** in $CDCl_3$ + 10 mg of free Binap; b) ^{19}F NMR spectra of 20 mg of **69** in $CDCl_3$.

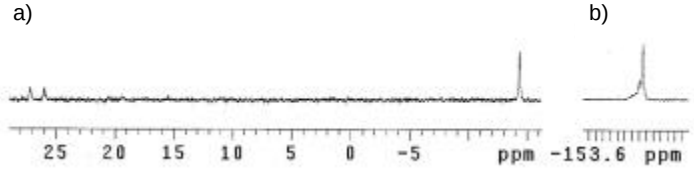
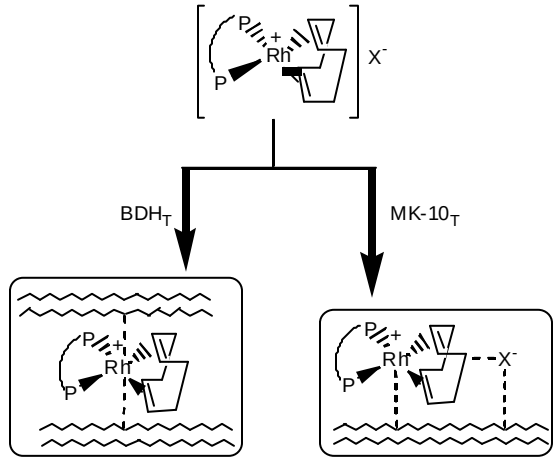


Figure 6

a) ^{31}P NMR spectra of 20 mg of **69** in $CDCl_3$ + 10 mg of free Binap + 100 mg of MK-10_T; b) ^{19}F NMR spectra of 20 mg of **69** in $CDCl_3$ + 100 mg of MK-10_T.

Because both nuclei (F and P) were affected in the immobilisation process, we suggest that the two ionic parts of the metal complex may interact with MK-10_T through weak forces such as electrostatic and/or hydrogen bonding interactions (Scheme 1). The fact that both, the cation and anion counterparts, from the complex seem to be adsorbed onto the solid implies a new concept which differs from the other supported hydrogen-bonded catalysts previously reported in the literature in which immobilisation mainly takes place in a monodentate way between the terminal silanols



Scheme 1

of different types of silica and the oxygen atom of sulfonate groups from phosphine ligands contained in the zwitterionic rhodium(I) complexes [14] and [15] or from triflate

counteranions of cationic ruthenium(II) [16] and rhodium(I) [12], [15] complexes. Unfortunately, as the loading level of the immobilised complexes was low, we could not confirm the presence of hydrogen bonding by IR spectroscopy.

Therefore, taking into account the lack of supporting experimental data, we can only suggest that the nature of the interactions between the solid and complex **69** could be due to weak forces such as electrostatic and/or hydrogen bonding.

The MAS ^{31}P NMR spectrum of the grafted complex **69**-MK-10_T is shown in Figure 7.b. It consists of a broad signal centred at δ= 30.00ppm. The CP MAS ^{31}P NMR spectrum of the unsupported complex **69** has a double doublet centred at δ= 28.00ppm (Figure 7.a). Comparison of the two solid-state NMR spectra suggests that they are highly similar and thus consistent with the immobilisation of the complex onto montmorillonite K-10.

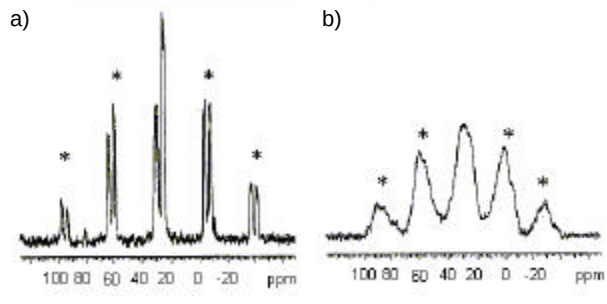


Figure 7

a) CP MAS ^{31}P NMR spectrum of [Rh(cod)(R)-Binap]BF_4 (**69**); b) MAS ^{31}P NMR spectrum of [Rh(cod)(R)-Binap]BF_4/MK-10_T. Spinning side bands are denoted by asterisks.

Similar spectroscopic features have been observed during the immobilisation of [Rh(cod)(R)-Binap]PF_6 **70**, [Rh(cod)(R)-Binap]SO_3CF_3 **71**, and [Rh(cod)(R)-Binap]BPh_4 **72** onto MK-10_T. With **70**-**72**, the intensity of the signals decreased significantly on the ^{19}F, ^{31}P, ^{11}B NMR locked spectra of the slurry obtained by consecutively addition of MK-10_T to a $CDCl_3$ solution of the complexes. It is noteworthy that the counteranion BPh_4 is also adsorbed onto MK-10_T according to the

disappearance of the singlet attributed to B nuclei in the ^{11}B NMR locked spectra of the slurry obtained by the consecutive addition of MK-10_T to a solution of complex **72** (Figure 8.b and d). The adsorption of lipophilic counteranions has not been previously observed in analogue immobilisation processes onto MCM-41 of ionic rhodium complexes containing BAr_F as counteranion [12].

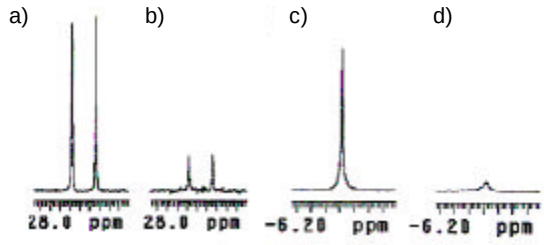


Figure 8

^{31}P NMR spectrum of a) 20 mg of [Rh(cod)(R)-Binap]BPh_4 (**72**) in $CDCl_3$; b) slurry of a) + 125 mg of MK-10_T. ^{11}B NMR spectrum of c) 20 mg of **72** in $CDCl_3$; d) slurry of c) + 125 mg of MK-10_T.

A significant difference was observed between the ^{19}F and ^{31}P NMR experiments carried out during the immobilisation process of **69** into BDH_T. While the intensities of the signals of ^{31}P NMR spectra decrease significantly when BDH is added, (Figure 9.a and b), the intensities of the signals in the ^{19}F NMR spectra did not change throughout the addition (Figure 9.c and d). The reduction of the signals in the ^{31}P spectra during the impregnation process suggests that the cationic counterpart of complex **69** is no longer in solution. Therefore, the countercation could be immobilised into the solid through cation exchange. This agrees with the ^{19}F NMR spectra, in which the intensity of the signals for F nuclei from BF_4^- did not decrease during the impregnation process. This shows that it might remain mainly in the solution, probably as MBF_4 (where M is the interlamellar metal cation from BDH_T), after the cation exchange with [Rh(cod)(R)-Binap]$^+$ (Scheme 1).

In summary, the mechanism for grafting the ionic complexes to MK-10_T and BDH_T seems to be different. In the first case, we suggest that the kind of interaction between the countercation and counteranion to MK-10_T could be due to weak forces,

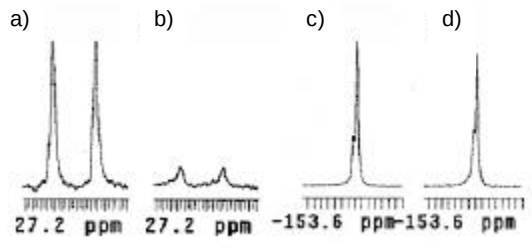


Figure 9

^{31}P NMR spectrum of: a) 20 mg of **69** in $CDCl_3$; b) slurry of a) + 125 mg of BDH_T. ^{19}F NMR spectrum of : c) 20 mg of **69** in $CDCl_3$; d) slurry of c) + 125 mg of BDH_T.

such as electrostatic and/or hydrogen bonding, but in the second case the electrostatic attraction between the countercation and the bentonite layers could be the significant feature of this immobilisation. The different ways in which these catalysts are grafted on the clays could also lead to further differences in the activities and selectivities when they are used as catalytic systems in the asymmetric hydroboration of vinylarenes.

2.1.b. Study of the heterogenised catalytic hydroboration

At this point we focused on the potential catalytic activity of the immobilised system towards the asymmetric hydroboration of vinylarenes. We first concentrated our efforts on a model reaction with styrene as substrate. In order to consider the most important parameters that affect this asymmetric transformation, (Chapter 2), we also studied the influence of the couteranion, the chiral ligand, the metal and the support. Once the heterogenised process had been optimised, we extended the study to other substrates with significant electron differences.

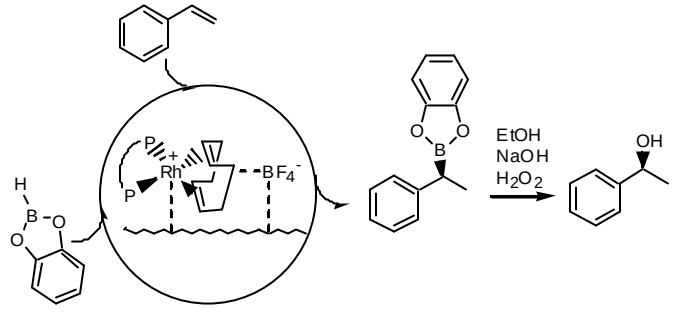
We started by examining the catalytic properties of the model rhodium complex [Rh(cod)(R)-Binap]BF_4, (**69**), adsorbed on commercial montmorillonite MK-10. In the homogeneous hydroboration/oxidation of styrene, the catalyst precursor **69** provides high yields and regioselectivities for 1-phenylethanol, but only moderate enantiomeric excesses [3], (Table 2, entry 1). This behaviour justifies our choice of this catalytic system, since it can reveal any increase [7b], [17] or decrease in the stereoselectivity induced by the supported catalyst.

Table 2. Asymmetric hydroboration/oxidation of styrene towards (R)-(+)-1-phenylethanol catalysed by the immobilised [Rh(cod)(R)-Binap]BF_4, (**69**).[a]

Entry	Heterogenised catalytic system	Run (%)	Yield (%)	Branched (%)	e.e[b] (%)
1	**69**	1	92	99	57
2	**69**-MK-10	1	41	92	47
3	**69**-MK-10_T	1	96	97	55
		2	99	97	60
4	**69**-BDH_T	1	26	35	5
		2	94	63	35

[a] Standard conditions: styrene/catecholborane/Rh complex=1:1.1:0.02. Solvent: THF. T: 25^0C. Time: 2 h; [b] *R* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm.

Once the solid-supported catalyst had been prepared, it was tested for activity, regioselectivity, enantioselectivity, resistance to degradation and reusability in the hydroboration/oxidation of the model substrate styrene (Scheme 2). To compare the



Scheme 2

activity and stability of the supported catalyst with its homogeneous counterpart, we performed the hydroboration of styrene under standard conditions: styrene/ /catecholborane/Rh=1:1.1:0.02, THF as solvent, 25^0C, 2 h. As can be seen in Table 2, the activity and selectivity of catalyst **69**-MK-10 was lower than those of the homogeneous catalytic system under the same reaction conditions (Table 2, entries 1 and 2). The significant amount of interlamellar water in montmorillonite could have favoured the degradation of catecholborane and/or the transition metal complex. ^{11}B NMR experiments carried out on MK-10 and catecholborane over the time scale of the catalytic experiment showed that the doublet at $\delta(^{11}B)$= 26.50ppm from catecholborane decreases in intensity as a new broad signal emerges at $\delta(^{11}B)$= 20.00ppm, which can be attributed to the catecholboronate acid formed. However, when the montmorillonite was heated to at least 100^0C before the immobilisation of **69**, the activity and selectivity of the resulting supported catalytic system **69**-MK-10_T were similar to those of the homogeneous system. The supported catalyst was removed by filtration under inert atmosphere and repeated catalytic hydroborations were carried out without loss of activity or selectivity (Table 2, entry 3). Leaching of the rhodium complex was not considered because no product was formed when styrene and catecholborane were added to the filtrate of the first run. We found significant differences in the hydroboration/oxidation of styrene when we prepared the supported catalytic system from the preheated clay bentonite BDH_T and complex **69**, (Table 2, entry 4). The closed environment of complex **69** immobilised mainly in the internal surface of the bentonite may be different to that of complex **69** grafted onto the external surface of

montmorillonite K-10. The low conversion and selectivity of the branched product may be related to the restricted diffusion of the substrate, reactant and product, although the activity improves slightly in the second consecutive run.

The MAS ^{31}P NMR spectrum of the solid **69**-MK-10_T that was recovered after two consecutive runs had a broad signal centred at 30.00ppm (Figure 10). If compared with Figure 7.a and b, this is consistent with the permanence of complex **69** or a closed Rh-Binap complex involved in the reaction, which is immobilised onto the MK-10_T.

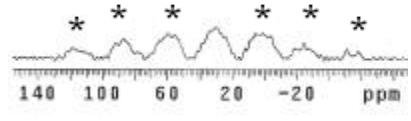


Figure 10

MAS ^{31}P NMR spectrum of **69**-MK-10_T after two consecutive runs. Spinning side bands are denoted by asterisks.

Influence of the counteranion. In an attempt to rationalise the catalytic activity exhibited by the supported rhodium complex **69**-MK-10_T, (Figure 11), we decided to extend our

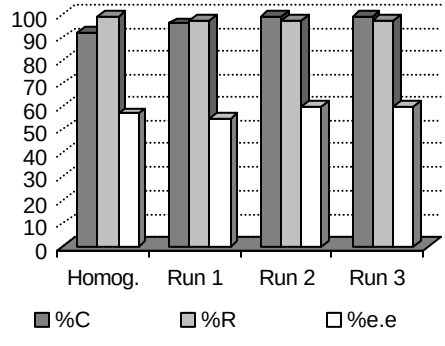


Figure 11

Catalytic activity provided by [Rh(cod)(R)-Binap]BF_4 (**69**) in the

homogeneous and heterogenised hydroboration of styrene.

study to a wider variety of cationic rhodium complexes with different counteranions, such as [Rh(cod)(R)-Binap]X (X= PF_6, SO_3CF_3, and BPh_4). We therefore immobilised complexes **70-72** onto MK-10_T following the same impregnation procedure described above. The immobilised complex **71** was found to provide the same activity and selectivity as the unsupported complex **71**. It also provided recoverability of at least three consecutive runs in the hydroboration/oxidation of styrene, which was used as the test substrate (Figure 12). Additional insight into a slight enhancement of the enantioselectivity by using the triflate anion is also noteworthy. It has already been reported in the literature that the presence of anions such as sulfonate enhances asymmetric catalysis [13].

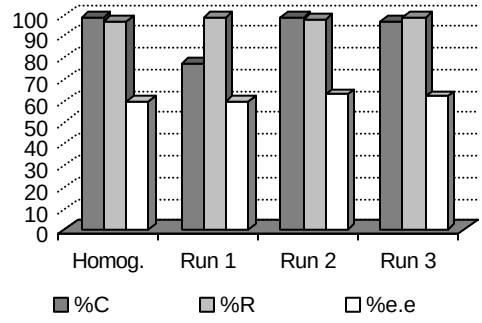


Figure 12

Catalytic activity provided by [Rh(cod)(R)-Binap]SO_3CF_3 (**71**) in the homogeneous and heterogenised hydroboration of styrene.

The recyclability of the immobilised catalytic system **70**-MK-10_T is also demonstrated (Figure 13), although the selectivity decreased slightly after the third

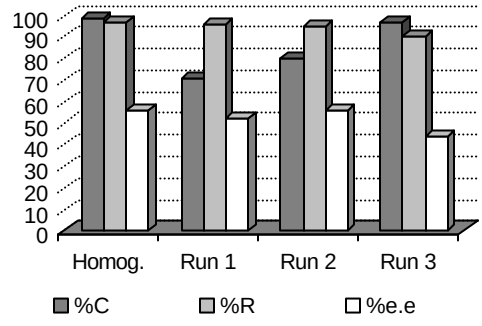


Figure 13

Catalytic activity provided by [Rh(cod)(R)-Binap]PF_6 (**70**) in the homogeneous and heterogenised hydroboration of styrene.

consecutive run. The reduction of the regio- and enantioselectivities with this system may be because the immobilised catalytic system is less stable when the counteranion PF_6 is involved.

We observed similar features when the ionic iridium catalytic system $[Ir(cod)(PPh_3)_2]X$ (X= PF_6 or BF_4) was tested in the hydrogenation of imines [7a]. Even more striking was that the regio-and enantioselectivities provided by the immobilised catalytic system **72**-MK-10_T were greater than those of its homogeneous counterpart (Figure 14). The proven tendency of BPh_4 to form π-complexes and tight ion pairs [18]

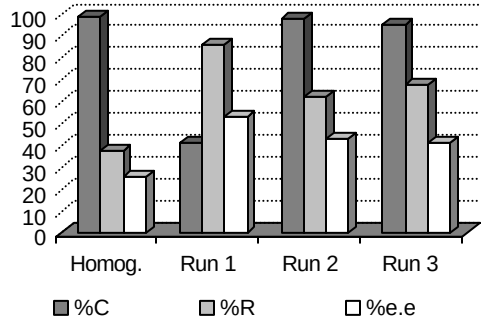


Figure 14

Catalytic activity provided by [Rh(cod)(R)-Binap]BPh_4 (**72**) in the homogeneous and heterogenised hydroboration of styrene.

might be the cause of the low regio- and enantioselectivities provided by the homogeneous catalytic system **72**. Immobilisation of both the cationic and anionic counterparts of **72** onto montmorillonite K-10 seems to be beneficial for the hydroboration reactions, probably because the counteranion is prevented from coordinating to the metal [18g]. However, although the regio- and enantioselectivities are higher than with the homogeneous version, they do not reach the selectivity of the supported catalytic systems where X= PF_6, SO_3CF_3 and BF_4.

Influence of the ligand. We made a comprehensive study of several ligands including (S,S)-bdpp and (S)-Quinap, to determine how they affect the hydroboration/oxidation of styrene. The use of (S,S)-bdpp as chiral ligand can provide four possible conformers of a six-membered chelate ring when it is coordinated to a metal [19]. Two of these conformers are achiral chair conformations with the phenyl rings in an achiral array, and the other two conformers are chiral δ-skew conformations. We wondered whether immobilising a rhodium complex modified with (S,S)-bdpp would favour the formation of any one of these conformers and modify the low asymmetric induction provided by the homogeneous catalytic system. Thus, we carried out the hydroboration/oxidation of styrene with [Rh(cod)(S,S)-bdpp]BF_4, (**74**), and the grafted complex **74**-MK-10_T. There was no significant difference between the catalytic behaviour of the homogeneous version and that of the hetereogenised version. The activity and regioselectivity of 1-phenylethanol from complex **74** were high, but the enantioselectivity was low and was reproduced with **74**-MK-10_T after the second consecutive run (Table 3, entries 1 and 2).

Table 3. Asymmetric hydroboration/oxidation of styrene towards (S)-(-)-1-phenylethanol catalysed by the immobilised [Rh(cod)(L,L)]BF_4.[a]

Entry	Heterogenised catalytic system	Run (%)	Yield (%)	Branched (%)	e.e[b] (%)

1	**74**	1	98	98	20
2	**74**-MK-10$_T$	1	82	87	14
		2	97	94	19
3	**73**	1	99	95	88
4	**73**-MK-10$_T$	1	51	68	50
		2	98	97	89
		3	92	97	86
		4	98	98	88

[a] Standard conditions: styrene/catecholborane/Rh complex=1:1.1:0.02. Solvent: THF. T: 25^{0}C. Time: 2 h; [b] *S* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm.

The other interesting ligand which chelates with the metal to form a six-membered ring is Quinap. This P,N ligand is less bulky than its parent ligand Binap in the region of the isoquinoline because one of the diphenylphosphinonaphthalene moieties has been replaced. This structural difference, in addition to the electronic features of the P,N ligand, explains why the asymmetric induction is higher with chiral Quinap than with Binap [2]. Other axially chiral P-N ligands, such as Phenap (**29**) [20], 2-Ph-quinazolinap (**30**) [21] and Pyphos (**31**) [4], have been developed over the last few years for use in the hydroboration of vinylarenes. However, optimised values for the regioselectivities of the branched product and enantioselectivities were only obtained by using lower reaction temperatures. Thus, since the recovered catalytic systems **69**-MK-10$_T$ and **74**-MK-10$_T$ could be reused with no loss of activity or selectivity, we extended the study to the cationic rhodium complex [Rh(cod)(S)-Quinap]BF_4, (**73**), which provides the highest asymmetric induction in the hydroboration of vinylarenes carried out at room temperature [2]. We examined just four consecutive runs in the hydroboration/oxidation of styrene with **73**-MK-10$_T$ (Table 3, entry 4), and from the second consecutive run the activity, regio- and stereoselectivities were constant and comparable to those of the homogeneous version (Table 3, entry 3). However, the catalytic system **73**-MK-10$_T$ seems to need an induction period to reach the maximum values already achieved by its homogeneous counterpart. To clarify this point, we stirred the immobilised catalytic system **73**-MK-

10_T in THF for 2 h. The solid was then filtered and dried under vacuum before we started the first run. Figure 15 shows how the activity, and the regio- and enantioselec

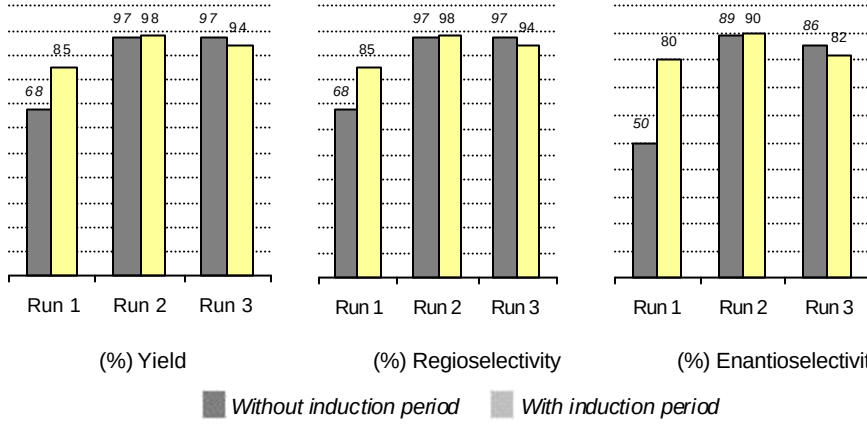


Figure 15

tivity, significantly increased during the first run. It is noteworthy that the filtrates from the induction period of **73**-MK-10_T in THF did not provide any catalysis.

Another interesting catalytic feature of this system is the high degree of stability achieved by the resting state of the catalyst when it is exposed to air.

To illustrate the last point, the solid **73-**MK-10_T was filtered from the reaction products in air between the four consecutive runs. The values for activity, regio- and stereoselectivity were similar after the third consecutive run and these remained constant after recycling (Figures 16 and 17).

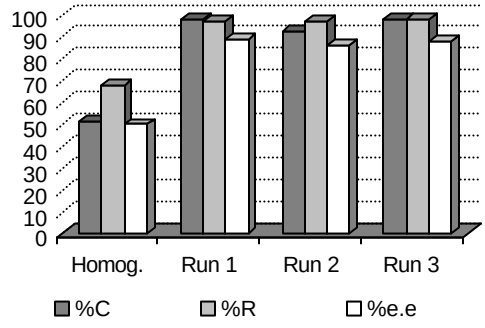


Figure 16

Catalytic activity provided by **73**-MK-10_T filtered under N_2 between the consecutive runs.

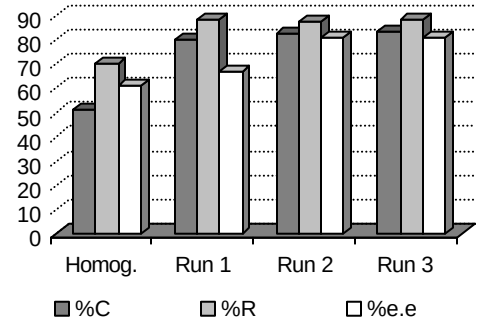


Figure 17

Catalytic activity provided by **73**-MK-10_T filtered under air between the consecutive runs.

It seems that clay is not only an appropriate support for recycling the catalyst, but that it also prevents oxidation or degradation of the catalytic metal species involved in the hydroboration transformations.

Influence of the metal. As has been mentioned in chapter 2, catalytic systems based on rhodium complexes perform better than their iridium analogues in the catalytic hydroboration reaction. In order to observe any effect in the activity and selectivity of the heterogenised iridium complex with respect to its homogeneous analogues, we carried out the hydroboration reaction of styrene with the immobilised complex

[Ir(cod)(R)-Binap]BF_4/MK-10_T, (Table 4). Thus, when [Ir(cod)(R)-Binap]BF_4 (**75**) was used under the same hydroboration conditions as the rhodium system (Table 4, entry 1), conversion was complete but enantioselectivity was almost nil and regioselectivity was only about 30% on 1-phenylethanol. In our ongoing research, we have found that the low enantioselectivity provided by ionic iridium complexes can be improved by immobilising the catalyst precursor onto clays.

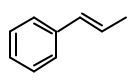
Table 4. Asymmetric hydroboration/oxidation of styrene towards (R)-(+)-1-phenylethanol catalysed by the immobilised [Ir(cod)(R)-Binap]BF_4 (**75**).[a]

Entry	Heterogenised catalytic system	Run (%)	Yield (%)	Branched (%)	e.e[b] (%)
1	**75**	1	99	30	2
2	**75**-MK-10_T	1	70	17	5
		2	93	31	2

[a] Standard conditions: styrene/catecholborane/Ir complex=1:1.1:0.02. Solvent: THF. T: 25^0C. Time: 2 h.; [b] *R* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm.

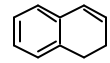
This is the case of [Ir(cod)(S,S)-bdpp]PF_6 which efficiently catalyses the hydrogenation of imines such as N-(α-methyl-*p*-methoxybenzylidene)benzylamine with complete conversion but no enantiomeric excess. However, when [Ir(cod)(S,S)-bdpp]PF_6 was immobilised onto MK-10_T, the catalytic system became more enantioselective on re-use, giving values up to 60% of e.e, in a third consecutive run, [7b]. To find a similar effect we immobilised [Ir(cod)(R)-Binap]BF_4 on MK-10_T, and found that after two consecutive runs the activities and selectivities were similar to those provided by the analogous homogeneous systems, (Table 4).

Scope of the recyclable catalytic asymmetric hydroboration reaction. Subsequently, we studied several other vinylarenes, (Figure 18), as substrates for the recyclable catalytic asymmetric reaction, with **73**-MK-10_T as the immobilised catalytic system, following a procedure that was similar to the one described for the hydroboration of styrene.



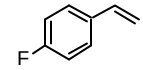
trans-β-methylstyrene

76



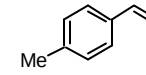
1,2-dihydronaphthalene

77



p-fluorostyrene

78



p-methylstyrene

79

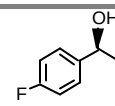
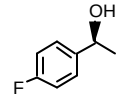
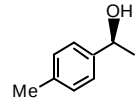
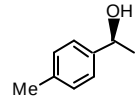
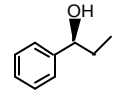
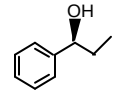
Figure 18

We focused on vinylarene substrates, paying particular attention to those that would highlight how different aryl substituents and β-substitution would affect reactivity and enantioselectivity. In each hydroboration reaction, the immobilised catalytic system was recovered for recycling by filtration. The filtrates were then directly oxidised with H_2O_2 to afford the corresponding alcohol. The results are given in Table 5. When **73**-MK-10_T was used, the electron-deficient substrate *p*-fluorostyrene produced similar activities, regio- and enantioselectivities, after the second consecutive run, to those of the homogeneous system **73** (Table 5, entries 1 and 2).

The asymmetric induction is lower than that of the hydroboration/oxidation of styrene, which agrees with the trends observed with Quinap and other P,N ligands for the hydroboration of styrene reactants with electron-withdrawing substituents [2], [4], [21]. The regio- and stereoselectivities were more satisfactory when electron-releasing aryl substituents were used on the styrene substrate. It is known [2] that electron-rich alkenes are better for achieving maximum stereoselectivity. Therefore, hydroboration/oxidation of the electron-rich *p*-methylstyrene provided an enantiomeric excess of over 90%, both in the homogeneous version and in the hetereogenised version from the third consecutive run, remaining constant on recycling (Table 5, entries 3 and 4).

Table 5 Asymmetric hydroboration/oxidation of vinylarenes towards (S)-(-)-sec-alcohol catalysed by the immobilised [Rh(cod)(S)-Quinap]BF_4 (**73**).[a]

Entry	Catalytic System	Substrate	(S)-(-)-*sec*-alcohol	Run	Yield (%)	Branched (%)	e.e[b] (%)

1	**73**	**78**		1	97	95	78
2	**73**-MK-10$_T$	**78**		1 2 3 4	38 83 92 82	59 89 90 87	40 75 73 67
3	**73**	**79**		1	96	99	91
4	**73**-MK-10$_T$	**79**		1 2 3 4	31 98 92 98	74 97 97 98	70 89 86 88
5	**73**	**77**		1	95	99	98
6	**73**-MK-10$_T$	**77**		1 2 3	26 71 95	98 95 98	54 70 97
7	**73**	**76**		1	92	99	93
8	**73**-MK-10$_T$	**76**		1 2 3 4	5 66 66 64	99 99 99 99	13 87 86 85

[a] Standard conditions: styrene/catecholborane/Rh complex=1:1.1:0.02. Solvent: THF. T: 25 ^{0}C. Time: 2 h; [b] *S* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm.

For the electron-withdrawing and electron-releasing substrates studied, the supported catalytic system needed an induction period to reproduce the homogeneous values, which may be a little longer for *p*-methylstyrene. The hydroboration/oxidation of 1,2-dihydronaphthalene illustrates the effect of an increase in steric demand around the reaction site. However, enantiomeric excess was highest with the homogeneous catalytic system **73** (e.e= 98%) and the heterogenised system **73**-MK-10$_T$ (e.e= 97%) from the third consecutive run (Table 5, entries 5 and 6). In addition to these results,

we can also see that the induction period required by **73**-MK-10_T in the hydroboration of 1,2-dihydronaphthalene is similar to that of *p*-methylstyrene. A likely explanation is that the more hindered the substrate is, the longer the induction periods need to be. A similar argument can be found in the literature to explain why in the homogeneous hydroboration of vinylarenes with [Rh(cod)(L,L)]X, the higher steric demand of the olefin is more easily accommodated by these less sterically demanding ligands, [21]. Consistently, the hydroboration/oxidation of the β-substituted substrate (E)-propenylbenzene with **73**-MK-10_T gave percentages of the branched product as high as those of its homogeneous counterpart and remained constant on recycling (Table 5, entries 7 and 8). Again, we noted from the catalytic data that increasing the steric demand of the olefin led to a retardation of the reaction.

In all the substrates studied, the catalytic system can be easily separated from the reaction products and recycled for at least the four consecutive runs explored; this demonstrates the scope of this method for recovering and reusing an efficient catalytic system.

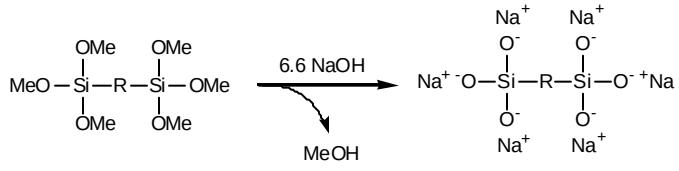
2.2. Comparative study of heterogenised hydroboration between natural bentonites and synthetic organo(bis-silantriolates) supports

During our search for solids that can be used as supports for immobilising transition metal complexes through ion exchange abilities, we became interested in finding alternative silicate materials. We were particularly attracted by the possibility of using hybrid organic-inorganic materials such as organosilanolates. The literature shows that the simultaneous presence of hydrophilic and hydrophobic interactions can favour the formation of ordered structures, such as organo(bis-silanetriols), which appear as layered structures [10a, b]. This is mainly attributed to the fact that the formation of a strongly hydrogen-bonded network can induce the organisation of hydrophobic organic groups. Similar structural organisation has been found for sodium salts of organo(bis-silantriolates) [10c]. Therefore, we studied the immobilisation process of complex [Rh(cod)(S)-Quinap]BF_4 (**73**), with sodium phenyl-1,4-bis(silantriolate) (**82**) and sodium ethyl-1,2-bis(silantriolate) (**83**), (Scheme 3). As far as

we knew, no previous study had been made on the use of organo(bis-silantriolates) as supports for catalysts. To obtain an overall picture of the influence of supports with ion exchange ability, we also studied two natural bentonites, which differ in surface area and structural features.

2.2.a. Synthesis of hybrid supports: organo(bis-silantriolates)

The sodium phenyl-1,4-bis(silantriolate) (**82**) and sodium ethyl-1,2-bis(silantriolate) (**83**) were prepared by adding a slight excess of NaOH to 1,4-bis(trimethoxysilyl)benzene **80** and to 1,2-bis(trimethoxysilyl)ethane **81**, respectively, (Scheme 3). The compounds **81** and **83** were synthesised for the first time during this thesis, using a methodology that was identical to that for **80** and **82**, as previously reported in the literature [10c].



80, R= 1,4-C_6H_4
81, R= 1,2-C_2H_4
82, R= 1,4-C_6H_4
83, R= 1,2-C_2H_4

Scheme 3

The organosilicate compound **83** was identified and characterised by IR, ^{1}H, ^{13}C and ^{29}Si NMR spectroscopy and X-ray powder diffraction studies. The FTIR spectra (KCl pellets) exhibited adsorption bands centred at 1446, 1139 and 974cm^{-1} attributed to Si-O bond vibration modes, and a broad band centred at 756cm^{-1} probably due to Si-C vibration. Moreover, adsorption bands corresponding to C-H vibrations were detected around 2929 and 2888cm^{-1}. The NMR data was collected in deuterated water, D_2O. ^{1}H and ^{13}C NMR spectra had the expected resonances for the organic moiety, (δ= 0.29ppm, (s, 4H) and δ= 7.27ppm, (s, 2C), respectively). The ^{29}Si NMR spectra showed a sharp resonance at –51.72ppm, in agreement with the chemical shifts already reported for silanetriols [10a, b]. From its X-ray powder diffraction pattern, (Figure 19), the solid was indexed. Si 640b NBS was mixed with the

sample as internal standard. The sample showed the presence of small quantities of Na_2CO_3 whose peaks were well identified. The peak positions were extracted for indexing, with the WinPLOTR package [22]. The first 20 lines of the X-ray powder diffraction pattern were indexed with the program TREOR [23] on the basis of a triclinic cell: a= 6.4108(4) Å, b= 11.0738(8)Å, c= 6.3107(4)Å, α= 103.508(4)^0, β= 91.525(4)^0, γ= 94.033(4)^0, V= 433.7(5)Å^3. The reliability of the unit cell and the indexing is indicated by the figures of merit M_{20}= 59 and F_{20}= 101(0.05523, 36), [24], [25]. The cell parameters were then refined from the complete powder data with the option Pattern Matching of the program FULLPROF [26].

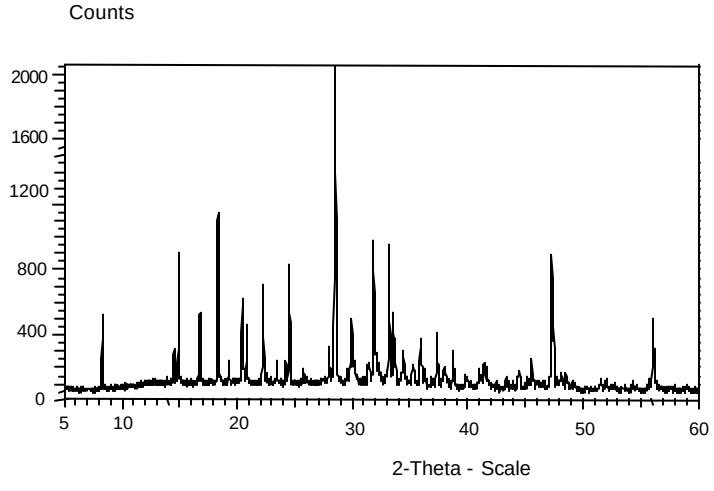


Figure 19

Experimental pattern for the powder-X-ray diffractogram of sodium ethyl-1,2-bis(silantriolate)

2.2.b. Study of the immobilisation process

Section 2.1 of this chapter, showed that natural clays, montmorillonite MK-10 (MK-10) and bentonite (BDH), are viable as solid supports for immobilising transition metal complexes. We have also shown how the differences in crystallinity between both smectite clays van influence the immobilisation pathways observed, because ionic rhodium complexes are mainly immobilised onto MK-10 through adsorptive

forces such as hydrogen bonds [7], but into bentonite through electrostatic forces [5], [6], via previous ion exchange.

In this context, the present section studies the ion exchange immobilisation of ionic complexes with two natural bentonites and two synthetic organo(bis-silantriolates). The solvent-impregnation method [11] was used to immobilise organometallic complex **73** in both clays: bentonite A and bentonite B. Both bentonites differ from each other in terms of surface area (bentonite A: BET surface area =53 m^2 g^{-1}, bentonite B: BET surface area =150 m^2 g^{-1}), and structural features. The X-ray patterns of the bentonite A and bentonite B supports, (Figure 20), were compared with

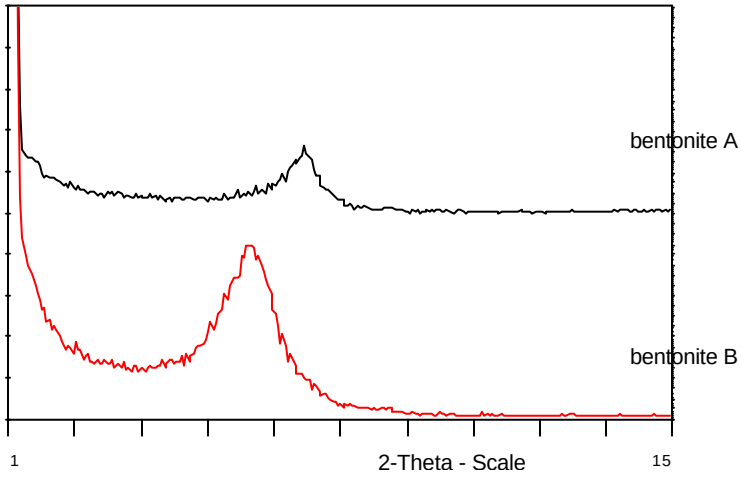


Figure 20

those in the JCPDS-ICDD database. The supports were identified as montmorillonite clay, but the characteristic peaks associated with the (001) reflection were different. In bentonite B the width of this reflection is wider than in bentonite A, and the position is shifted to lower 2-theta values. It is according to an increased basal distance from 12.3Å in bentonite A to 14.5Å in bentonite B.

The chemical analyses of bentonite A and B using scanning electron microscopy are compatible with a structure of dioctahedral smectites of theoretical

formula (H, M^{+}, $M^{2+}_{1/2})_x$ $(Mg_x\ Al_{2-x})Si_4O_{10}$ $(OH)_2$. However the percentage of Al^{3+} in bentonite B is significantly lower than in bentonite A, (Table 6). This, together with the fact that the percentage of Mg^{2+} is far higher in bentonite B than in A, could indicate a major replacement of Al^{3+} by Mg^{2+} in the octahedral positions of the layer. This substantial substitution may cause an overall increased negative charge on the layer of bentonite B, which requires more hydrated interlayer cations to compensate for the charge, than in the case of bentonite A. This data could be consistent with the increased basal distance observed in bentonite B.

Table 6. Chemical analyses of bentonites and immobilised catalytic systems [Rh(cod)(S)-Quinap]BF_4/bentonites.

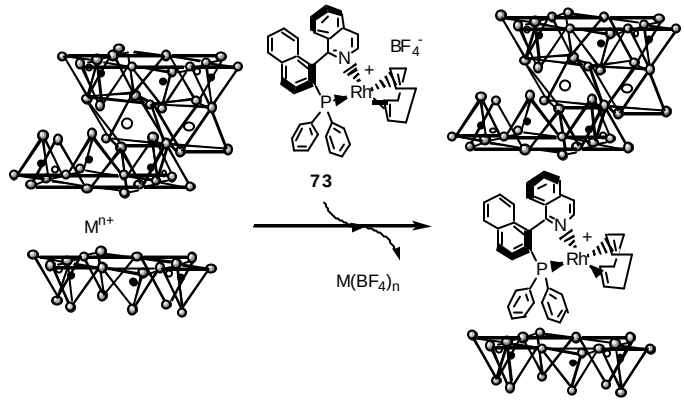
M^{n+}	Bentonite A	**73**-Bentonite A	Bentonite B	**73**-Bentonite B
Si	28.7	27.5	25.2	23.0
Al	9.4	9.4	3.2	3.0
O	51.8	48.2	48.2	43.2
Mg	1.7	1.7	14.3	12.4
Na	2.0	2.0	---	---
K	0.8	0.6	0.7	0.8
Ca	1.3	1.1	0.3	0.3
Fe	1.9	2.0	1.5	1.3
Rh	---	0.5	---	0.9

[a] Percentages calculated as (%) from the scanning electron microanalyser analysis.

The bentonites used in the immobilisation procedure were previously dried at 100^0C for 24 h to eliminate any adsorbed water. Coloured solutions of the ionic complex in anhydrous dichloromethane were stirred with the solid support for 24h under nitrogen, (scheme 4). The amount of metal complex adsorbed by the clay was determined by gravimetric analysis which measured the difference between the weights of the complex before and after the immobilisation, (Table 7). It should be pointed out that the amount of metal immobilised in bentonite B was approximately twice the amount immobilised in bentonite A, (44.2mg of **73** in 0.5g of bentonite B,

20mg of **73** in 0.5g of bentonite A). This agrees with the fact that the surface area of bentonite B is greater than that of bentonite A. The scanning electron microscopy analyses of **73**-bentonite A and **73**-bentonite B provide the percentages of Rh(I) which agree with the expected amount of Rh(I) in the immobilised metal complex **73** on the solid supports, (Table 6).

The conductimetric analyses made after washing the immobilised catalytic system in both bentonites revealed the presence of ionic species, which indicate that the process that took place was mainly cation-exchange rather than adsorption. As has been seen in section 2.1, we also recorded ^{19}F and ^{31}P NMR spectra in $CDCl_3$ during the impregnation process. These provided evidence that both bentonites could adsorb the ionic metal complex throughout only the cationic counterpart by ion exchange. We concluded that intensities of the signals of ^{31}P NMR spectra decreased significantly when bentonite A was added, although the intensities of the signals in the ^{19}F NMR spectra did not change throughout the addition of the solid. The reduction of the signals in the ^{31}P spectra during the impregnation process suggests that the cationic counterpart of complex **73** is no longer in solution. In contrast, the F nuclei signals from BF_4^- did not decrease during the impregnation process. This shows that the counteranion might remain mainly in solution, probably as MBF_4 (in which M is the interlamellar metal cation from the bentonites), after exchange with $[Rh(cod)(S)\text{-Quinap}]^+$. The spectroscopic features for immobilisation with bentonite B were similar. The chemical analyses before and after immobilisation in bentonites show a decrease in the percentages of interlayer cations: K^+ and Ca^{2+} in the case of bentonite A, and Mg^{2+} in the case of bentonite B.



Scheme 4

Table 7. Amounts of immobilised metal complex **73** on the solid supports.

Solid[a]	Mmol complex per g solid	Mg complex per 0.5g solid
Bentonite A	0.066	20
Bentonite B	0.110	44.2
Sodium phenyl-1,4-bis(silantriolate)	0.058	22.6
Sodium ethyl-1,2-bis(silantriolate)	0.015	5.6

[a] All solids were preheated at 100 ^{0}C for 24h; [b] Calculated from the equation [(mg initial complex – mg final complex)/molecular weight complex]/(g solid + g adsorbed complex).

Following the same impregnation procedure mentioned above, we focused our attention at this point on the synthetic organo(bis-silantriolates) supports. The packing structure of the sodium phenyl-1,4-bis(silantriolate) is due to the organisation of the phenylene groups, which are all parallel to each other and oriented in the same direction [10c], (Figure 21). Therefore, taking all these structural features into account, we considered about the possibility of using these hybrid salts as supports for ionic metal complexes, through ion exchange. We also explored the influence of the organic pillar, (from phenyl to ethyl), of the organo(bis-silantriolates) in the immobilisation

ability of the solid and their application in recyclable catalytic asymmetric hydroboration reactions.

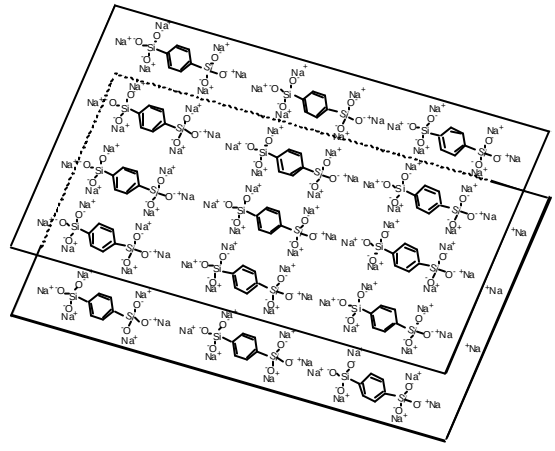
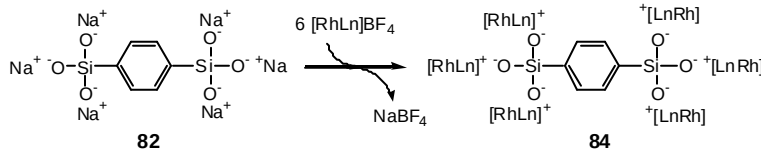


Figure 21

We first looked at the immobilisation process of complex **73** with sodium phenyl-1,4-bis(silantriolate), (scheme 5).



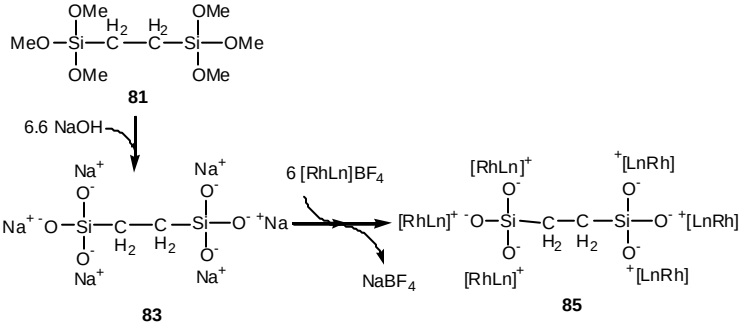
82 **84**

Scheme 5

The amount of metal complex **73** immobilised in sodium phenyl-1,4-bis(silantriolate) (**82**), was 22.6 mg in 0.5 g of the solid. These data are similar to those of the immobilisation of **73** into bentonite A, (Table 7). After the immobilisation process, the new solid turned yellow, which confirmed the presence of the complex in the support. To determine whether the ion-exchange process had taken place, the immobilised solid was filtered off and washed thoroughly with dichloromethane and

water. Conductimetric analysis and the ^{19}F NMR spectra of the liquid indicated that the counter anion BF_4^- remained in solution, probably as $NaBF_4$, after the Na^+ from the solid had been replaced by the cationic complex, as is illustrated in Scheme 5.

In our study of synthetic organo-bis(silantriolates) as supports for immobilising metal complexes, we included a new solid: sodium ethyl-1,2-bis(silantriolate), **83**, (scheme 6). Only 5.63 mg of complex **73** was immobilised in 0.5 g of the sodium ethyl-1,2-bis(silantriolate), (Table 7), during the impregnation procedure. The lack of rigidity in the organic moiety could influence the final organised structure of the solid and, as a result, affect the ion-exchange ability. The different ways of grafting complex **73** to the bentonites and the organo-bis(silantriolates) may lead to differences in their catalytic behaviour when they were used as catalytic systems in the asymmetric hydroboration of vinylarenes.



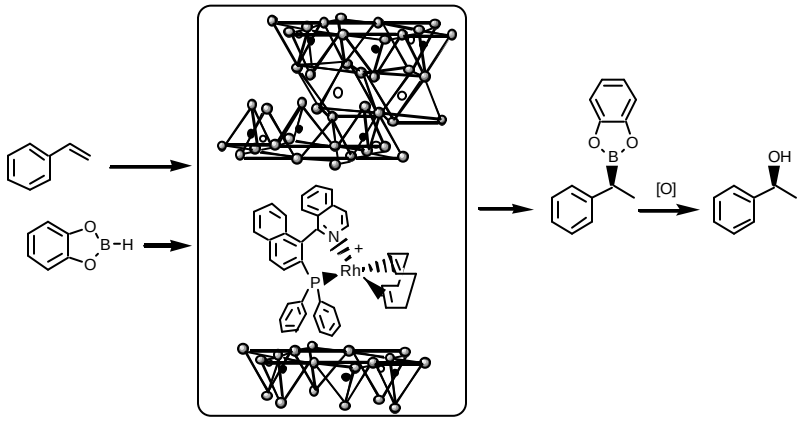
Scheme 6

2.2.c. Study of the heterogenised catalytic hydroboration

The next step was to study the potential of these immobilised systems for the asymmetric hydroboration of vinylarenes. We started by examining the catalytic properties of complex **73** immobilised on both bentonites (bentonite A and B) and the two organo(bis-silantriolates) (**82** and **83**), towards hydroboration/oxidation of styrene as a model substrate. The borane reagent of choice for this study was catecholborane,

because of its efficiency, (Scheme 7). Heterogenised homogenous catalysis makes it possible to separate the chiral alquilborane from the solid catalytic system by simple filtration and then transformed it into its corresponding alcohol via alkaline oxidation, (H_2O_2, NaOH). We performed the hydroboration of styrene under standard conditions, so that the activity and stability of the supported catalysts could be compared with their homogenous counterparts.

As shown in table 8, the activity and selectivity of complex **73** immobilised in bentonites is much higher than that observed for **73** when it is immobilised in organo(bis-silantriolates). We examined just four consecutive runs in the hydroboration/oxidation of styrene in all the cases. Only when **73**-bentonite A was used as the catalytic system, was it possible to get values of conversion, regio- and stereoselectivity from the third consecutive run, that were similar to those of the homogeneous system, remaining constant on recycling, (Table 8, entries 1 and 2).



Scheme 7

Leaching of the rhodium complex is not considered because no product was formed when styrene and catecholborane were added to the filtrate of the first run. However, the catalytic system **73**-bentonite A seems to need an induction period to reach the maximum values achieved by its homogeneous counterpart. This induction period seems to be longer than the one required for the heterogenised catalytic system

based on **73** immobilised onto MK-10, (section 2.1.b). This significant difference between the two catalytic systems may be due to the fact that **73** is mainly immobilised in the internal surface of bentonite but mainly grafted on the external surface of montmorillonite K-10.

The closed environment of the metal complex in bentonite A may mean that initially there is a restricted diffusion of the substrate, reactant and product. On the other hand the recyclability of **73**-bentonite B is more irregular than that of **73**-bentonite A, (Table 8, entry 3) and does not achieve the values of conversion, regio- and

Table 8. Asymmetric hydroboration/oxidation of vinylarenes towards (S)-(-)-sec-alcohol catalysed by the immobilised catalytic system [Rh(cod)(S)-Quinap]BF_4 (**73**).[a]

Entry	Catalytic system	Run	Yield (%)	Branched (%)	e.e[b] (%)
1	**73**	1	99	95	88
2	**73**-Bentonite A	1	33	26	5
		2	93	77	73
		3	93	89	85
		4	90	87	82
3	**73**-Bentonite B	1	51	57	18
		2	30	62	37
		3	78	90	71
		4	56	87	60
4	**73**- Sodium phenyl-1,4-bis(silantriolate)	1	33	35	3
		2	44	16	1
		3	26	20	27
		4	50	18	20
5	**73**- Sodium ethyl-1,2-bis(silantriolate)	1	21	21	1
		2	26	19	1
		3	22	8	3

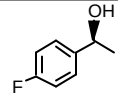
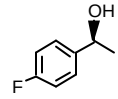
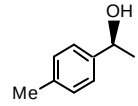
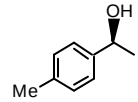
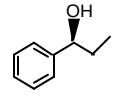
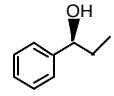
[a] Standard conditions: styrene/catecholborane/Rh complex=1:1.1:0.02. Solvent: THF. T: 25^{0}C. Time: 2 h.; [b] *S* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm.

enantioselectivity observed in the homogeneous version. Finally, when **73** is immobilised in the organo(bis-silantriolates), the activity and selectivity observed is very low and is not recovered on recycling, (Table 8, entries 4 and 5). This seems to indicate that the catalytic metal species immobilised in the organo(bis-silantriolates) became less active than when it was immobilised into bentonites.

The scope of the recyclable catalytic asymmetric hydroboration reaction with system **73**-bentonite A, involved an extensive study with several other vinylarenes as substrates. We paid particular attention to those substrates that showed how different aryl substituents and β-substitution can affect reactivity and enantioselectivity. In each hydroboration reaction, the immobilised catalytic system was recovered for recycling by filtration. The filtrates were then directly oxidised with H_2O_2 to afford the corresponding alcohol. The results are given in table 9.

The catalytic system **73**-bentonite A enabled the substrate p-fluorostyrene to be converted into its corresponding (S)-(-)-*sec*-alcohol, and the values of activity, regio- and stereoselectivity, after the second consecutive run, were similar to those observed in the homogenous systems, (Table 9, entries 1 and 2). Although table 9 only shows the four consecutive runs, the catalytic activity remains constant on recycling. When electron-releasing aryl substituents such as *p*-methylstyrene, were used as substrates, the results in terms of stereoselectivity were more satisfactory. In both, the homogenous and the heterogenised version after the second consecutive run, the enantiomeric excess was about 87-91%, (Table 9, entries 3 and 4). On the other hand, the hydroboration/oxidation of the β-substituted substrate (E)-propenylbenzene with **73**-bentonite A, gave percentages of the branched product as high as those of its homogeneous counterpart (99%), but the maximum yield was not higher than 61%. It was probably the increased steric demand of the olefin that delayed the reaction. In all the examples studied, the supported catalytic system seems to need an induction period to reproduce the homogenous values.

Table 9. Asymmetric hydroboration/oxidation of vinylarenes towards (S)-(-)-sec-alcohol catalysed by [Rh(cod)(S)-Quinap]BF_4 (**73**) and **73**-Bentonite A.[a]

Entry	Substrate	(S)-(-)-*sec*-alcohol	Run	Yield (%)	Branched (%)	e.e[b] (%)
1[c]	**78**		1	97	95	78
2[d]	**78**		1	54	72	61
			2	77	85	74
			3	86	88	83
			4	82	87	83
3[c]	**79**		1	96	99	91
4[d]	**79**		1	57	85	87
			2	86	90	87
			3	70	90	85
			4	75	89	86
5[c]	**76**		1	92	99	93
6[d]	**76**		1	15	99	7
			2	33	99	61
			3	61	99	83

[a] Standard conditions: styrene/catecholborane/Rh complex=1:1.1:0.02. Solvent: THF. T: 25ºC. Time: 2 h; [b] *S* configuration determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25 mm; [c] catalytic system **73**; [d] catalytic system **73**-bentonite A.

3. Conclusions

A well-defined recyclable catalytic process has been developed in the hydroboration/oxidation reaction of vinylarenes. Immobilised ionic rhodium complexes, [Rh(cod)(L,L)]X, were prepared by adsorption onto MK-10_T and by ionic exchange into BDH_T. In addition, the method for preparing the immobilised catalytic system is efficient, uncomplicated and can generally be applied to other ionic complexes.

NMR spectroscopic studies of the resulting solids during the impregnation process suggest that the cationic and anionic counterparts of the complex interact with the MK-10_T clay probably through weak hydrogen bonding and/or electrostatic forces in a plausible concerted way. The same study also suggested that only the cationic counterpart of the complex is grafted to the bentonite support, probably through electrostatic interactions, and that counteranion remains in solution.

The immobilised rhodium complexes [Rh(cod)(L,L))]X/MK-10_T exhibits in the catalytic asymmetric hydroboration/oxidation reaction, a comparable activity and selectivity to those of the homogeneous catalyst, irrespective of the nature of the counteranion (when X= BF_4, PF_6, SO_3CF_3) or ligand (when (L,L)= (R)-Binap, (S,S)-bdpp, (S)-Quinap). The tendency of the BPh_4^- to coordinate to the metal in ionic rhodium complexes can be prevented by immobilising the complex on MK-10_T, which produces a more active and selective catalytic system than its homogeneous counterpart. In addition, the heterogenised chiral catalyst can be separated from the reaction mixture by simple filtration and reused for several consecutive runs with no loss in activity or selectivity. No leaching of the metal was detected.

The highest activity and selectivity of the hetereogenised hydroboration/oxidation reaction of vinylarenes was achieved using the [Rh(cod)(S)-Quinap]BF_4 immobilised on predried MK-10 (MK-10_T), although some induction period is required to reproduce the optimum values of the analogous homogeneous catalytic system.

The catalytic asymmetric hydroboration reaction with supported ionic complexes was efficiently applied to several vinylarenes: *p*-substituted, *b*-substituted and bulky styrenes.

The recovered catalytic system seems to become stable in the absence of excess alkenes and it can be recycled even if the solid is exposed to air when it is manipulated between the consecutive runs.

The reuse and reproducibility of the heterogenised catalytic asymmetric hydroboration/oxidation reaction for a wide number of vinylarenes, makes it viable and practical from both economic and technical perspectives.

The recycling ability of [Rh(cod)(S)-Quinap]BF_4/bentonite A towards hydroboration/oxidation of vinylarenes is similar to that of the catalytic system immobilised onto MK-10 although the grafting of the metal complex seems to be essentially different.

The synthetic organo(bis-silantriolates) were prepared and characterised as new supports for immobilising metal rhodium complexes. However their grafting capacity was lower than that of natural clays for anchoring complex **73**. The [Rh(cod)(S)-Quinap]BF_4, immobilised in both synthetic supports (sodium phenyl-1,4-bis(silantriolate), and sodium ethyl-1,2-bis(silantriolate), were applied to the catalytic asymmetric hydroboration reaction. The activity and selectivity observed were very low and were not recovered on recycling.

4. Experimental Section

General Comments. All reactions and manipulations were carried out with standard vacuum line techniques under an atmosphere of dry nitrogen. All rhodium and iridium organometallic complexes were synthesised using standard Schlenk techniques. All organic solvents were distilled, stored on a molecular sieve (0.4 nm Aldrich), and degassed with a nitrogen flow prior to use. The complexes $[M(\mu\text{-Cl})(cod)]_2$ [27], $[M(cod)_2]BF_4$ [28], [29], [M(cod)(R)-Binap]BF_4 [30], [M(cod)(R)-Quinap]BF_4 [2], (where M=Rh, Ir) were prepared as previously reported. They were characterized by elemental analysis, ^1H and ^{31}P NMR, and FTIR spectroscopies. MK-10 was purchased from Fluka and bentonite BDH was purchased as Majorbenton B from AEB Iberica S.A. Predried clays were obtained as follows: clay (5g) was kept in a melting pot in the oven at 100^0C for 24 h. Calcined MK-10 ($MK\text{-}10_{400}$) was obtained as described below: MK-10 (5 g) was kept in a melting pot in the oven at 400^0C for 3h. NMR spectra were recorded on a Varian Gemini 300 and Mercury 400 spectrometer. Chemical shifts were reported relative to tetramethylsilane for ^1H as internal reference, 85% H_3PO_4 for ^{31}P and BF_3OEt_2 for ^{11}B as the external reference. Solid-state ^{31}P NMR spectra were recorded at room temperature on a Varian Mercury spectrometer equipped with a 7 mm BB-CP MAS probe at a working frequency of 161.97MHz. The spectra were recorded by using the cross-polarisation pulse sequence at room temperature under magic angle spinning at a spinning rate of 5.5kHz. For the unsupported rhodium complex, the CP MAS ^{31}P NMR spectrum was collected after 200 scans with a recycle delay of 5s. The MAS ^{31}P NMR spectrum of the supported complex was acquired with 1600 scans and a relaxation delay of 5s. The line broadening was set to be at 90Hz for the free complex and 1300 Hz for the supported complex. 85% H_3PO_4 was used as the external reference. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 II with a flame ionisation detector equipped with a chiral column FSCyclodex β-IP, 50m x 0.25mm. The elemental analysis of organometallic complexes was carried out on an Carlo-Erba Microanalyser EA 1108. IR spectra (range 4000-400cm^{-1}) were recorded on a FTIR MIDAC PROSPECT-IR spectrometer with KBr pellets. Powder X-ray diffraction (XRD) measurements were made using a Siemens D5000 diffractometer (Bagg-Brentano parafocusing geometry and vertical θ-θ

goniometer) fitted with a curved graphite diffracted-beam monochromator, incident and diffracted-beam Soller slits, a 0.06^0 receiving slit and scintillation counter as a detector. The patterns were recorded for 2θ angles between 3^0 and 70^0. The data were collected with an angular step of 0.02^0 at 10s per step and sample rotation. CuKα radiation was obtained from a copper X-ray tube operated at 40kV and 30mA. XRD analyses of all the samples were performed in thin films. X-ray diffraction was used to determine the basal spacing of the free supports and the supports with the adsorbed complexes. The basal spacing of each sample was calculated from the (001) reflection in its X-ray pattern. This basal spacing was associated with the distance between (001) layers (d_{001}) and was located at angles (2θ) between 5^0 and 7^0. BET surface areas were calculated from nitrogen adsorption isotherms at 77K by using a Micromeritics ASAP 2000 surface analyser and a value of $0.164nm^2$ for the cross section of the nitrogen molecule. The conductivity of the filtrates obtained in the immobilisation process was measured with a Crison microCM 2201 conductimeter. The filtrates were first concentrated under vacuum and diluted with 50 ml of dichloromethane. The scanning electron microscopy analyses were made in a JEOL, JSM-640 with an accelerating voltage=15KV and a prove current = $(3\text{-}6)x10^{-9}$ A for a representative area (575 x 466 μm) for each sample.

Preparation of the heterogenised complexes. The ionic rhodium complex was immobilised in the following manner. The solid supports (smectite clays or organo(bis-silantriolates)) were added to an organometallic solution prepared with 10ml of deoxygenated dichloromethane and 0.2mmol of the complex under nitrogen. Then, it was stirred for 24h under nitrogen at room temperature. The suspension was filtered off and the solid was washed with dichloromethane and dried under vacuum. The amount of metal complex immobilised on the clay was determined by gravimetric analysis and SEM analysis.

Homogeneous catalytic hydroboration/oxidation of styrene with catecholborane. Vinylarene (2mmol) was added to a solution of catalyst (1 mol%) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2mmol) was then added. The mixture was stirred at ambient temperature for 1h and

then quenched with EtOH (2mL). Work up must be carried out carefully because of the risk of explosion when using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with Et_2O (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by NMR and quantification was carried out by gas chromatography.

Heterogenised catalytic hydroboration/oxidation of styrene with catecholborane. Styrene (2mmol) was added to a suspension of supported catalyst (1 mol% immobilised in 0.5g of solid) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2mmol) was then added. The mixture was stirred at ambient temperature for 2h, using the chemical assembly shown in Figure 22. The solution was filtered off under vacuum and the filtrates were then

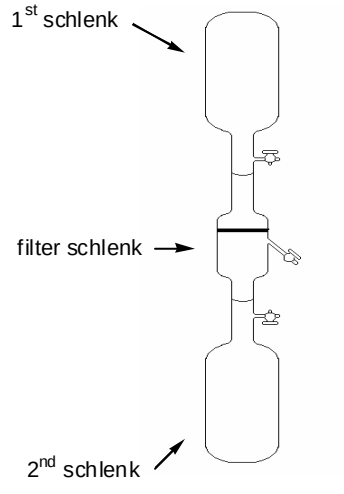
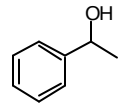


Figure 22

quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. The quenched filtrates were treated with NaOH (2M, 2mL) and H_2O_2 (2mL) and the mixture was stirred for

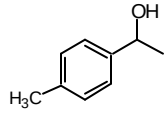
several hours. The mixture was finally extracted into Et_2O, washed (NaOH 2M, H_2O, saturated brine) and dried over $MgSO_4$. The products were then characterised by NMR and quantification was carried out by gas chromatography. The solid that contained the complex was dried under vacuum for 10 minutes and put into the *schlenk* for another run.

Phenylethanol [3]



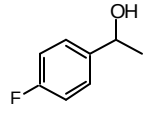
^{1}H RMN ($CDCl_3$): δ(ppm)= 7.50-7.20 (m ,5H), 4.55 (q ,$^3J_{H-H}$=6.7Hz, 1H), 1.80(br s, 1H), 1.50 (d ,$^3J_{H-H}$=6.6Hz, 3H).

1-(4-Methylphenyl)etanol [2]



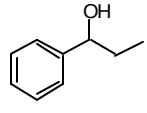
^{1}H RMN ($CDCl_3$): δ(ppm)= 7.29 (d ,$^3J_{H-H}$=8.2Hz, 2H), 7.19 (d, $^3J_{H-H}$= =8.2Hz, 2H), 4.86 (q ,$^3J_{H-H}$=6.6Hz, 1H), 2.36 (s, 3H), 1.80(br s, 1H), 1.48 (d ,$^3J_{H-H}$=6.6Hz, 3H).

1-(4-Fluorophenyl)etanol [2]



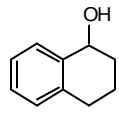
^{1}H RMN ($CDCl_3$): δ(ppm)= 7.40-7.10 (m, 4H), 4.86 (q ,$^3J_{H-H}$=6.4Hz, 1H), 1.90 (br s, 1H), 1.48 (d ,$^3J_{H-H}$=6.4Hz, 3H).

1-phenylpropanol [2]



^{1}H RMN ($CDCl_3$): δ(ppm)= 7.50-7.20 (m, 5H), 4.55 (q ,$^3J_{H-H}$=6.7Hz, 1H), 2.23 (br s, 1H), 1.90-1.50 (m, 2H), 0.88 (d ,$^3J_{H-H}$=6.7Hz, 3H).

1,2,3,4-Tetrahydro-1-naphthol [2]



^{1}H RMN ($CDCl_3$): δ(ppm)= 7.50-7.10 (m, 4H), 4.80 (t ,$^{3}J_{H-H}$=4.3Hz, 1H), 3.10-2.70(m, 2H) 2.10-1.70 (m, 4H).

References

[1] J.Liedtke, H.Rüegger, S.Loss, H.Grützmacher, *Angew. Chem.* **2000**, *112*, 2596; *Angew. Chem. Int. Ed.* **2000**, *39*, 2478.

[2] H.Doucet, E.Fernandez, P.T.Layzell, J.M.Brown, *Chem. Eur. J*. **1999**, *5*, 1320.

[3] T.Hayashi, Y.Matsumoto, Y.Ito, *Tetrahedron: Asymmetry* **1991**, *2*, 601.

[4] F.Y.Kwong, Q.Yang, T.C.W.Mak, A.S.C.Chan, K.S.Chan, *J. Org. Chem.* **2002**, *67*, 2769.

[5] R.Selke, M.Capka, *J. Mol. Catal. A: Chem.* **1990**, *63*, 319.

[6] D.Tas, D.Jeanmart, R.F.Parton, P.A.Jacobs, *Stud. Surf. Sci. Catal.* **1997**, *108*, 493.

[7] *For hydrogenation of imines, see*: (a) R.Margalef-Catala, P.Salagre, E.Fernandez, C. Claver, *Catal. Lett.* **1999**, *60*, 121; (b) R.Margalef-Catala, C.Claver, P.Salagre, E.Fernandez, *Tetrahedron: Asymmetry* **2000**, *11*, 1469; (c) C.Claver, E.Fernandez, R.Margalef-Catala, F.Medina, P.Salagre, J.E.Sueiras, *J. Catal.* **2001**, *201*, 70; *for reductive alkylation of amines, see*: (d) R.Margalef-Catala, C.Claver, P.Salagre, E.Fernandez, *Tetrahedron Lett.* **2000**, *41*, 658; *for Heck reaction, see*: (e) M.Poyatos, E.Peris, C.Claver, E.Fernandez, *New. J. Chem.* **2003**, *27*, 425.

[8] A.Küchritz, S.Bischoff, V.Morawsky, U.Pröβe, K.D.Vorlop, *J. Mol. Catal. A: Chem.* **2002**, *180*, 231.

[9] M.Crocker, R.H.M.Herold, *J. Mol. Catal.* **1991**, *70*, 209.

[10] (a) G.Cervau, R.J.P.Corriu, B.Dabiens, J.Le Bideau, *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 4533; (b) G.Cervau, S.Chappellet, R.J.P.Corriu, B.Dabiens, J.Le Bideau, *Organometallics* **2002**, *21*, 1560; (c) B.Boury, F.Carre, R.J.P.Corriu, R. Nuñez, *Chem. Commun.* **1998**, 2309.

[11] (a) C.S.Chin, B .Lee, I.Yoo, T.Know, *J. Chem. Soc. Dalton Trans.* **1993**, 581-593: (b) M.Crocker, R.H.M.Herold, *J .Mol. Catal.* **1993**, *141*, 70; (c) V.L.K.Valli, H.Alper, *Chem. Mater.* **1995**, *7*, 359; (d) B.M.Choudhary, K.Ravidumar, M.Lakshmi Kantam, *J. Catal.* **1991**, *130*, 41; (e) D.Kotkar, N.V.Takkar, *Proc.*

Indian Acad. Sci. **1997**, *109*, 99; (f) M.Bartók, G.Szollosi, A.Mostalir, I.Dékánmy, *J. Mol. Catal.* **1999**, *139*, 227.

[12] F.M.Rege, D.K,Morita, K.C.Ott, W.Tumas, R.D.Broene, *Chem. Comun.* **2000**, *6*, 139.

[13] J.M.Buriak, J.C.Klein, D.G.Herrington, H.A.Osborn, *Chem. Eur. J.* **2000**, 1797.

[14] C.Bianchini, D.G.Burnaby, J.Evans, P.Frediani, A.Meli, W.Oberhauser, R.Psaro, L.Sordelli, F.Vizza, *J. Am. Chem. Soc.* **1999**, *121*, 5961.

[15] C.Bianchini, P.Barbaro, V.Dal Santo, R.Gobetto, A.Meli, E.Oberhauser, R.Psaro, F.Vizza, *Adv. Synth. Catal.* **2001**, *343*, 41.

[16] C.Bianchini, V.Dal Santo, A.Meli, E.Oberhauser, R.Psaro, F.Vizza, *Organometallics* **1999**, *19*, 2433.

[17] R.Augustine, S.Tanielyan, *Chem. Commun.* **1999**, 1257.

[18] (a) R.R.Schrock, J.A.Osborn, *Inorg. Chem.* **1970**, *9*, 2339; (b) M.Bochmann, G.Kargerm A.J.Jaggar, *J. Chem. Soc. Chem. Commun.* **1990**, 1038; (c) A.D.Horton, J.H.Frijns, *Angew. Chem.* **1991**, *103*, 1181; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1152; (d) C.J.Schaverien, *Organometallics* **1992**, *11*, 3476; (e) F.Calderazzo, U.Englert, G.Pampaloni, L.Rocchi, *Angew. Chem.* **1992**, *104*, 1230; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1235; (f) E.Solari, F.Musso, E.Gallo, C.Floriani, N.Re A.Chiesi-Villa, C.Rizzoli, *Organometallics* **1995**, *14*, 2265; (g) M.Crocker, R.H.M.Herold, *Catal. Lett.* **1993**, *18*, 243.

[19] (a) P.A.MacNeil, N.K.Roberts, B.Bosnich, *J. Am. Chem. Soc.* **1981**, *103*, 2273; (b) J.Bakos, I.Töth, B.Heil, G.Szalontai, L.Párkányi, V.Fülöp, *J. Organomet. Chem.* **1989**, *370*, 263.

[20] J.M.Valk, G.A.Whitlock, T.P.Layzell, J.M.Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2593.

[21] (a) M.McCarthy, M.W.Hooper, P.J.Guiry, *Chem. Commun.* **2000**, 1333; (b) M.McCarthy, P.J.Guiry, *Tetrahedron* **2001**, *57*, 3809.

[22] T. Roisnel, J. Rodriguez-Carvajal, March **2000**, LLB-LCSIM

[23] P. E.Werner, L.Erikson, M.J.Westdahl, *J. Appl. Crystallog*. **1985**, *18*, 367.

[24] P.M. De Wolff, *J. Appl. Crystallog*. **1968**, *1*, 108.

[25] G.S.Smith, R.L.Snyder, *J. Appl. Crystallog*. **1979**, *12*, 60.

[26] J.Rodriguez-Carvajal, Collected Abstracts of the Powder Diffraction Meeting, Toulouse, France **1990**, 127.

[27] J.Chatt, L.M.Venanzi, *J. Chem. Soc. Part VI* **1957**, 4735.

[28] M.D.Fryzyk, B.Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262.

[29] M.Green, S.H.Kuc, S.H.Taylor, *J. Chem. Soc.* **1971**, 2334.

[30] T.Tani, T.Akutagawa, H.Kumobayashi, T.Taketomi, H.Takaya, A.Miyashita, R.Noyori, S.Otsuka, *J. Am. Chem. Soc.* **1984**, *106*, 5208.

Chapter 4

Catalytic asymmetric hydroboration of perfluoroalkenes and dihydroboration of internal alkynes. Recovery of the catalyst.

In this chapter we focus on the applicability of enantioselective B-H addition to interesting unsaturated substrates, such as perfluoroalkenes and internal alkynes.

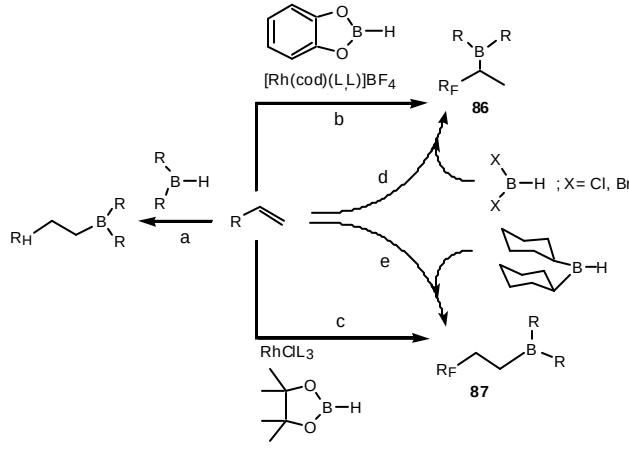
Because of the synthetic utility of chiral perfluoroalcohol and diol compounds, we decided to make for the fist time, a systematic study of the asymmetric rhodium-catalysed hydroboration/oxidation of perfluoroalkenes and dihydroboration/oxidation of internal alkynes, respectively.

We also felt that it would be interesting to find out how to convert these transformations into recyclable processes and even make possible a new concept of consecutive recyclability of substrate preparation and substrate transformation, as two consecutive recyclable catalytic cycles.

1. Introduction

The synthesis of fluoroorganic compounds involves synthesising molecules with fluorine instead of hydrogen. This often improves the biological activity properties of organic molecules. Also, fluorinated compounds are increasingly being used in analytical, materials, and polymer chemistry because of their unique properties [1]. The hydroboration of perfluoroalkenes is an interesting pathway to get perfluoro-organoboronates intermediates which can be furthermore functionalised.

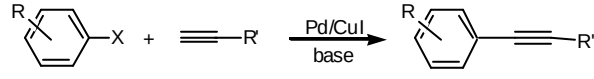
The directing effects of electronegative substituents on 2-substituted-1-alkenes can substantially modify the regioselectivity expected both in the transition-metal catalysed (Scheme 1, pathways b and c) [2] and uncatalysed (Scheme 2, pathways d and e) [3], hydroboration reaction. Thus, the reversed regioselectivity from the Markovnikov "B-H" addition in unfunctionalised terminal olefins to the *anti*-Markovnikov manner in perfluoroalkylethylenes, [4], makes it possible to obtain the branched product. However, other factors that must be taken into account to control the regioselectivity in the hydroboration of perfluoroalkenes are the hydroborating reagents, the reaction temperature and the electronic nature of the rhodium complex when it is used as a catalyst precursor, (Scheme 1).



Scheme 1

The regioselectivity for a series of fluorinated terminal olefins can be controlled by choosing the appropriate reaction conditions. This makes it possible to synthesise the suitable *anti*-Markovnikov perfluoroalkylborane isomer. Recently, P.V.Ramanchandran and H.C.Brown [2] studied the control of the regioselectivity of the hydroboration/oxidation of perfluoroalkenes where the neutral Rh(I) complexes with pinacolborane provided the terminal perfluoroalkylborane **87**, (Scheme 1, pathway c), whereas the cationic Rh(I) complexes with catecholborane provided the branched perfluoroalkylborane isomer **86** (Scheme 1, pathway b). However, the latter process has not been subjected to an asymmetric catalytic version in order to get the chiral product.

In another context, coupling reactions are important methods for carrying out carbon-carbon bond formation. These processes, developed from early work by Tsuji now have a central place in organic chemistry [5]. All coupling reactions are catalysed by a number of palladium complexes, or simply by a mixture of $Pd(OAc)_2$ and PR_3 ligands. Mild conditions are usually used for this reaction, often room temperature, which means that numerous functional groups can be tolerated. The reaction, known as the Sonogashira cross coupling (Scheme 2), converts terminal alkynes into internal alkynes and generally involves the use of a palladium catalyst in conjunction with copper iodide. The copper (I) seems to react with the alkyne to form an alkynylcuprate.

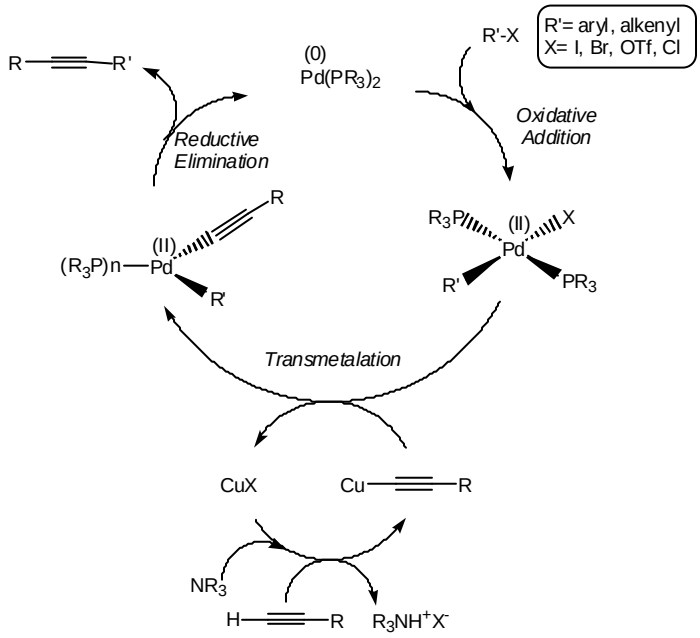


Scheme 2

Recently, Sonogashira proposed the catalytic cycle illustrated in Scheme 3, [6]. This cross-coupling reaction takes place through the oxidative addition of R-X to generate an R-Pd(II)-X intermediate, followed by a transmetalation step, and finally reductive elimination to give the C-C product and the regenerated Pd(0) catalytic system.

G.C.Fu et al. have recently reported examples of Suzuki, Sonogashira, and Stille couplings of the appropriate RX, where X=Cl, using a convenient catalytic

system [7]. The best ligands seem to be bulky and electron rich-phosphines, such as PCy_3 and P^tBu_3 [8]. The reactions are very sensitive to the bulk of the ligand. Also, Eberhard et al. [9] and Plenio et al. [10],obtained significant results in the coupling of aryl chlorides. They described high-yielding palladium catalytic system modified with phosphonito pincer ligands and bis-adamanthyl benzylphosphine ligands, respectively. In this context, the nucleophilic N-heterocyclic carbenes have attracted considerable attention as possible alternatives for the widely used phosphine ligands.



Scheme 3

The main advantages of these ligands are that they do not readily dissociate from the metal center, they have a strong σ-donor character and they are considered to be of low toxicity [11]. All these beneficial effects, together with the fact that they are synthesised more readily than many conventional phosphine ligands mean that they have become versatile ligands in catalysed organic transformations [12], such as cross

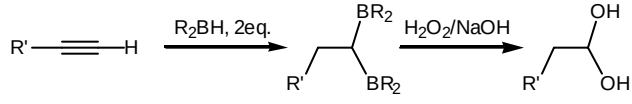
coupling reactions [13]. They have shown that they are efficient at coupling aryl halides with amines [14], amides [15], and alkenes (Heck reaction) [16]. The homogeneous coupling of aryl halides with terminal acetylenes to produce aryl alkynes in the Sonogashira reaction [17] has been extensively studied because it is frequently used as a key step in the synthesis of antimycotics [18], antibiotics [19], liquid crystals, polymers and optical or electronic materials [20]. However, the use of nucleophilic carbenes in the Sonogashira coupling has been studied much less [16b and 16d], [21], although recent results with palladium complexes modified with carbamoyl imidazolium salts under mild conditions [22] and imidazolium chloride assisted coupling of aryl bromides with alkynilsilanes, have been promising [23].

The Sonogashira reaction permits us to obtain internal alkynes such as diphenylacetylene and related compounds *via* a catalysed reaction. Functionalised alkynes are important building blocks for the synthesis of biologically active molecules and, surprisingly, have common structural features no natural products which have been isolated from plants and marine organisms, or synthetic drugs [6], [24-25]. Therefore, the Sonogashira reaction is frequently used as a key step in the synthesis of pharmaceuticals, such as the enediyne antibiotics or the contraceptive pill [26]. In addition, unsaturated internal alkynes are the unsaturated substrates of several hydrometalation reactions.

From the industrial point of view, the recyclability of palladium catalyst is interesting because it can compensate for the cost of the transition-metal catalyst in the process. The catalytic system in the Sonogashira cross-coupling reaction can be immobilised so that it can be recovered and reused in consecutive runs. However, there are few examples for this in the literature that in the case of Sonogashira reaction. As far as we know, in the last couple of years there have only been five attempts to immobilise the catalytic palladium system in: in an aqueous film supported on mesoporous silica [27], in a fluorous reversed-phase silica gel (FRPSG) [28], soluble polymers [29], in ionic liquids in microflow systems [30], in layered double hydroxide supported nanopalladium catalysts [31], and more recently, immobilisation in zeolite by ion exchange [32]. All these attempts succeeded in separating the palladium catalytic system from the products, but the recyclability was heavily dependent on the nature of the immobilisation.

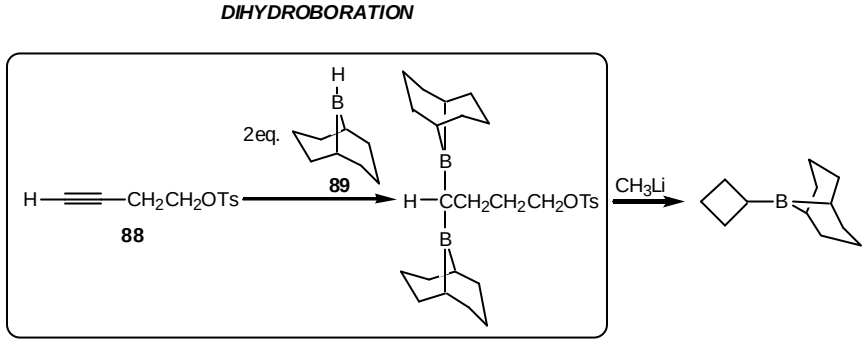
The enantiomerically pure hydrobenzoins have proved to be very useful chiral auxiliaries [33] and ligands [34-35], for stereoselective organic synthesis. These diols, which were previously accessible only through kinetic resolution [36], can now be obtained by dihydroxylation of olefins [37], reduction of benzyls [38] or *via* carbon-carbon bond formation [39], [40]. However, to the best of our knowledge, nobody has yet studied the enantioselective synthesis of hydrobenzoin through the catalytic asymmetric dihydroboration/oxidation of the diphenylacetylene with boranes such as hydroborating reagents.

Terminal alkynes can undergo the dihydroboration with an excess of hydroborating reagents (H-BR_2), giving rise to diborane adducts. In addition, the diorganoborane compounds can be transformed into several functionalised compounds such as diols through oxidation with alkaline hydrogen peroxide (Scheme 4).



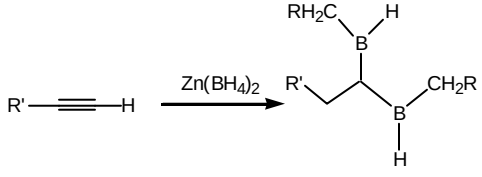
Scheme 4

The dihydroboration of terminal alkynes with dialkylboranes provides the synthesis of diborane, B-C-B, compounds. This reaction is used principally as an intermediate step in the synthesis of cycloalkylboranes. The first example was reported by Binger and Köster who reacted propargyl chloride with diethylborane *via* dihydroboration [41]. H.C.Brown and Rhodes [42], introduced 9-BBN (**89**) as reagent in the dihydroboration of the tosylate of 3-butyl-1-ol (**88**) followed by treatment with methyllithium (Scheme 5). Recently, there has been a slight increase in the number of reports about this reaction in the literature [43-45], although they all show the formation of gem-diboron compounds.



Scheme 5

From the point of view of catalytic synthesis, and to the best of our knowledge, only Narashimhan and Balakumar [46] have carried out the catalytic dihydroboration of terminal and internal alkynes with $Zn(BH_4)_2$, which also give the gem-diborone (Scheme 6).



Scheme 6

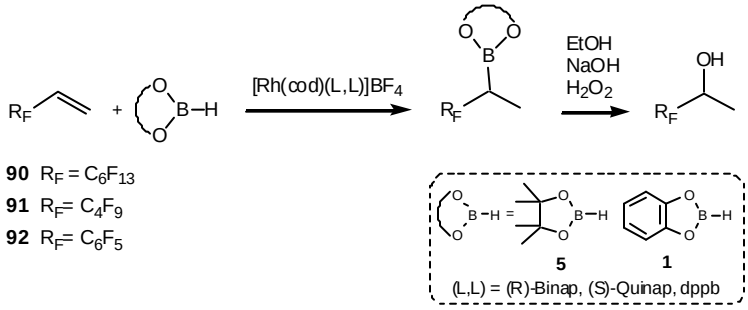
In this context, it seemed interesting to develop a catalytic asymmetric dihydroboration reaction of internal alkynes such as diphenylacetylene in order to get the vic-diborone chiral product. In addition, the immobilised catalytic dihydroboration would provide a clean economic methodology for synthesising chiral compounds, such as the hydrobenzoin, in few steps.

2. Results and discussion

2.1. Catalytic asymmetric hydroboration of perfluoroalkenes

2.1.a. Homogeneous version

As a consequence of the observations by P.V.Ramanchandran and H.C.Brown [2], that cationic Rh(I) complexes are effective for the Markovnikov hydroboration/oxidation of perfluoroalkenes with catecholborane, we decided to examine how a cationic catalytic system modified with chiral diphosphine ligands affected the process, (Scheme 7).



Scheme 7

For purposes of comparison with previous studies in which diphosphine dppb was used as the bidentate ligand, we chose (R)-Binap because both ligands make seven membered chelate with rhodium in the complex.

We started by examining the hydroboration/oxidation of a model substrate 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene (**90**) with 1 mol% of [Rh(cod)(R)-Binap]BF_4 (**69**) and catecholborane, (Scheme 7). The reaction was almost complete within 1h at room temperature, (Table 1, entry 1). Regioselection on the secondary alcohol was favoured and increased at low reaction temperatures, (Table 1, entries 2 and 3). Similar behaviour was attributed to the catalytic system [Rh(cod)(dppb)]BF_4, (Table 1, entries 4-6) [2], although in this case the regioselectivity was almost

quantitative. When (R)-Binap was used instead of dppb as the chiral ligand; enantiomeric excesses were between 60 and 65.5%, under these reaction conditions.

Table 1. Rh-diphosphine-catalysed enantioselective hydroboration/oxidation of perfluoroalkenes with catecholborane.[a]

Entry	Catalytic system [Rh(cod)(*L*,*L*)]BF_4	R_F	T(^{0}C)	Yield (%)	Branched (%)	e.e[b] (%)
1	(R)-Binap	C_6F_{13}	20	99	70	62(+)
2	"	"	0	99	84	65.5(+)
3	"	"	-78	23	81	60(+)
4[c]	dppb	"	20	82	72	-
5[c]	"	"	0	84	90	-
6[c]	"	"	-25	89	98	-
7[d]	(R)-Binap	"	20	99	46	60.5(+)
8[e]	"	"	20	99	35	50(+)
9[f]	"	"	20	99	-	-
10	"	C_4F_9	0	99	80	64(+)
11	"	C_6F_5	20	86	97	19.5[g]

[a] Standard conditions: alkene/catecholborane/Rh complex=1:1.1:0.01. Solvent: THF. T: 20^{0}C. Time: 1h; [b] Determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25mm; [c] Ref. [2] with 2 mol% of catalyst; [d] Precursor of catalyst: $[Rh(\mu\text{-}Cl)(cod)]_2$/(R)-Binap; [e] Addition of 0.03mmol of $BnMe_3NCl$; [f] Pinacolborane; [g] (R) Enantiomer.

Unlike the cationic catalysts, a preferentially primary insertion of the perfluoroalkenes into neutral-Rh complex formed from $[Rh(\mu\text{-}Cl)(cod)]_2$/2eq (R)-Binap has been detected. However, this had very little effect on enantioselectivity, as the e.e values remained at about 60.5%, (Table 1, entry 7). The neutralising influence of chlorine as a coordinated counterion was confirmed in a new experiment where the salt $BnMe_3NCl$ was added to the catalytic system [Rh(cod)(R)-Binap]BF_4. The results confirmed that the products were distributed similarly to those observed with the neutral system, (Table 1, entry 8). A complete undesired regioselection towards the primary alcohol was obtained when a sterically hindered borane pinacolborane, was

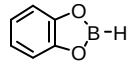
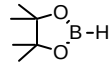
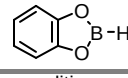
used instead of catecholborane as the hydroborating reagent in presence of [Rh(cod)(R)-Binap]BF_4 (Table 1, entry 9).

The generality of this reaction was demonstrated by carrying out the hydroboration/oxidation of 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene (**91**). The results were similar to those when catecholborane was used as the hydroborating reagent (Table 1, entry 10). Alkene isomerisation was not observed during the reaction, in contrast to the observed trend with hydroboration of unfunctionalised alkenes [47].

Because the steric factors of the catalyst alter as much as the electronics in the substrate to the access towards the sterically hindered 2-perfluoroalkyl-rhodium intermediate, we studied the influence of the [Rh(cod)(S)-Quinap]BF_4 [48]. The Quinap is less bulky than its parent ligand Binap and, in addition, the P,N ligand forms a six-member chelate ring with rhodium in the complex.

Using catecholborane as the hydroborating reagent, **90** and **91** were transformed into their corresponding alcohols with complete regioselectivity (Table 2, entries 1 and 3). However, the induced chirality was lower than the chirality provided

Table 2. Rh-Quinap-catalysed enantioselective hydroboration/oxidation of perfluoro-alkenes.[a]

Entry	Borane	R_F	T(^{0}C)	Yield (%)	Branched[b] (%)	e.e[b] (%)
1		C_6F_{13}	20	99	99	20(+)
2	"	"	0	99	99	19(+)
3	"	C_4F_9	20	99	99	25(+)
4		C_6F_{13}	20	99	99	55(+)
5	"	C_4F_9	20	99	99	53.5(+)
6		C_6F_5	20	97	97	18[c]

[a] Standard conditions: alkene/catecholborane or pinacolborane/Rh complex=1:1.1:0.01. Solvent: THF. T: 20^{0}C. Time: 1h.; [b] Determined by GC with chiral column FS-Cyclodex β-IP, 50 m x 0.25mm; [c] (S) Enantiomer.

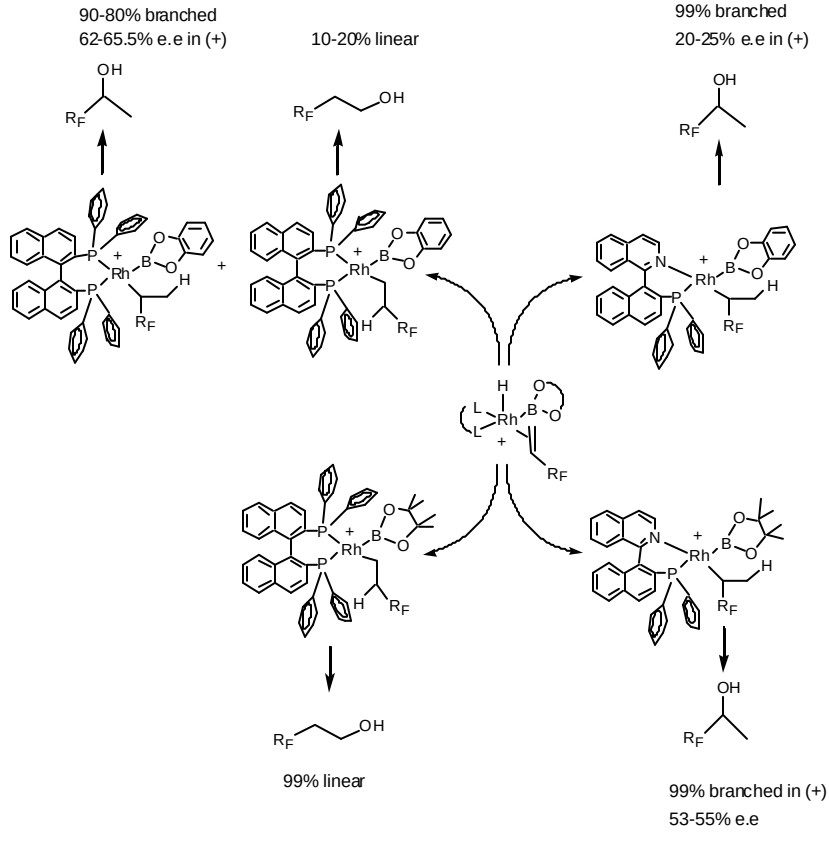
by the analogue (R)-Binap derived Rh-catalyst, even at low temperatures (Table 2, entry 2). We then conducted the hydroboration of **90** and **91** with the more sterically demanding hydroborating reagent pinacolborane, and surprisingly, we also obtained the secondary perfluoroalkylborane quantitatively, with e.e values as high as 55% (Table 2, entries 4 and 5). In the literature, there are examples of symmetrically internal alkyl pinacolboronate products formed in the presence of [$RhCl(CO)(PPh_3)_2$] and [$NiCpCl(cod)(PPh_3)Cl$] but not with $RhCl(PPh_3)_3$, [49].

It should be pointed out that both cationic Rh-catalytic systems behave differently towards the formation of the secondary-alkyl rhodium complexes, principally because of the steric properties of the hydroborating reagent involved in the intermediates. As can be seen in scheme 8, pinacolborane almost exclusively provides the secondary insertion of the perfluoroalkenes on the (S)-Quinap-Rh catalyst, but the primary insertion of the same substrates on the (R)-Binap-Rh catalyst. Presumably the more congested (R)-Binap-Rh-pinacolboryl intermediate could be the reason for the terminal olefin insertion. However, it cannot be excluded that this product may also be the result of the isomerisation of a plausible secondary alkyl-rhodium intermediate into the primary alkyl-rhodium, because of a β-H elimination process, which could also be favoured by the steric demand around the metal.

A high and complete degree of the secondary alkyl-rhodium complex is obtained by using both (R)-Binap-Rh and (S)-Quinap-Rh complexes, respectively, when catecholborane is involved in the reaction. In these cases, the lower steric demand around the reaction site means that the metal is affixation in the most hindered carbon, as is expected because of the electronic effect exerted by the fluorinated alkene.

To obtain a total picture of the process, it should be mentioned that the oxidation of the secondary alkyl-rhodium intermediate, obtained from both chiral complexes, (S)-Quinap-Rh and (R)-Binap-Rh, provided principally the same (+)-enantiomer. This contrasts substantially with the trend observed in the hydroboration/oxidation of styrene, where the (S)-Quinap-Rh catalyst provided the (S)-1-Phenylethanol and the (R)-Binap-Rh catalyst provided the (R)-enantiomer [50]. The enantiodifferentiation in the case of the vinylarenes has previously been explained by some intermolecular π-π stacking interactions between the ligand and the substrate

[51]. The lack of phenyl groups in the perfluoroalkenes **90** and **91** suggests that the coincidence in the main enantiomer formed could be due to the configuration of the Rh-H fragment when it is transferred to the coordinated alkenes. This extreme is confirmed by an additional experiment, where 2',3',4',5',6'-pentafluorostyrene was subjected to the hydroboration/oxidation reaction with catecholborane and both chiral catalytic systems. In accordance with the regioselective trend observed with the hydroboration/oxidation reaction with catecholborane and both chiral catalytic systems. In accordance with the regioselective trend observed with the hydroboration of vinylarenes, the aromatic perfluoroalkenes gave the (S) enantiomer product in the presence of the (S)-Quinap-Rh and the (R) enantiomer with (R)-Binap (Table 1, entry 11 and Table 2, entry 6, respectively).

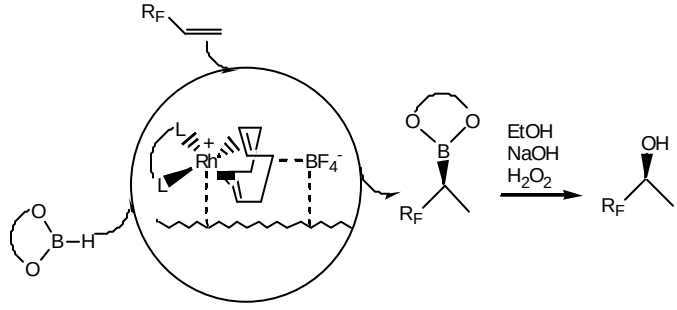


Scheme 8

The consistently moderate e.e values, (55-65%), that we obtained in the hydroboration/oxidation of aliphatic perfluoroalkenes were even higher than those observed in the asymmetric B-H addition on aromatic perfluoroalkenes, such as 2',3',4',5',6'-pentafluorostyrene (**92**), (18-19.5%), and in electron-deficient vinylarenes such as 3,5-bis-trifluoromethylstyrene (5%), and 2,6-difluorostyrene (<15%).

2.1.b. Heterogenised version

In a subsequent investigation, we focused on perfluoroalkenes as the substrates for the recyclable catalytic asymmetric hydroboration reaction with $[Rh(cod)(L_2)]BF_4$/ /MK-10_T (where MK-10_T= preheated montmorillonite K10, L_2= (R)-Binap and (S)-Quinap). We used a similar heterogenised procedure to that described for the hydroboration of vinylarenes in chapter 2, (Scheme 9).



Scheme 9

We started by examining the catalytic properties of the model rhodium complex $[Rh(cod)(R)\text{-Binap}]BF_4$ adsorbed onto preheated commercial montmorillonite K10, MK-10_T, using catecholborane as hydroborating reagent. In the homogeneous hydroboration/oxidation of 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octene (**90**), the catalyst precursor provided high yields (99%), moderate regioselectivities for the branched alcohol and moderate enantioselectivities. As far as catalytic activity is concerned, the results were similar to those of the homogeneous counterpart.

However, in subsequent runs the regio- and enantioselectivity decreased slightly. After the third run, the selectivity remained constant (Figure 1).

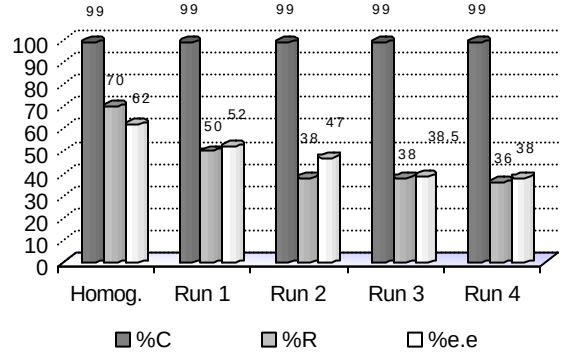


Figure 1

Catalytic activity provided by [Rh(cod)(R)-Binap]BF_4 in the homogeneous and heterogenised hydroboration of **90**.

Similar results were observed when the reaction was performed with the hydroboration/oxidation of 3,3,4,4,5,5,6,6,6-nonafluoro-1-hexene (**91**), under similar reaction conditions, (Figure 2).

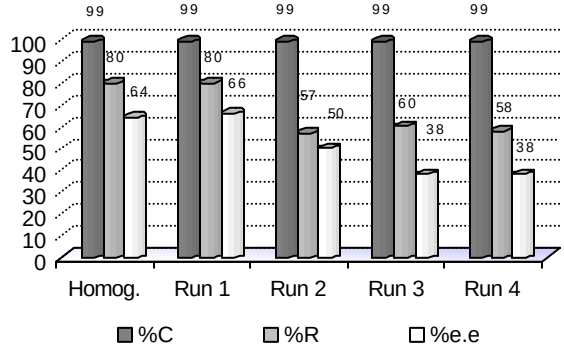


Figure 2

Catalytic activity provided by [Rh(cod)(R)-Binap]BF_4 in the homogeneous (0^0C) and heterogenised hydroboration of **91**.

When the rhodium catalytic system was based on [Rh(cod)(R)-Quinap]BF_4 anchored onto preheated commercial montmorillonite MK-10, (MK-10_T), the catalytic hydroboration/oxidation reaction of **90** with pinacolborane provided a slight decrease in regio- and enantioselectivity. In addition, unlike the homogeneous version, the selectivity continued decreasing in further consecutive runs until it remained constant after the third, (Figure 3).

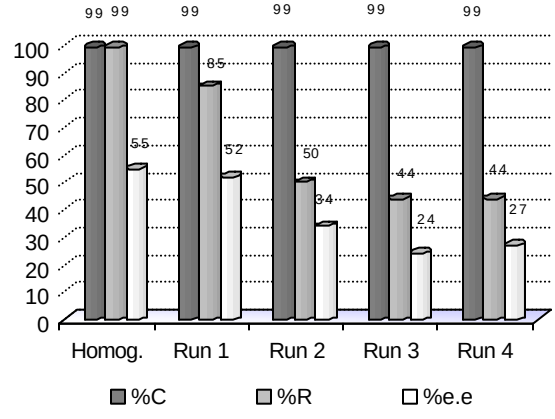


Figure 3

Catalytic activity provided by [Rh(cod)(S)-Quinap]BF_4 in the homogeneous and heterogenised hydroboration of **90**.

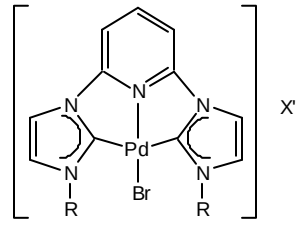
These results showed that, independently of the immobilised catalytic system and/or the perfluoroalkene, the heterogenised catalytic asymmetric hydroboration/oxidation reaction behaves in a similar way to the homogeneous version. However, we observed a slight loss of catalytic system during the filtration. This observation together with the decrease in the selectivity from the hydroboration/oxidation of perfluoroalkenes could be related to fluorides competing to interact with the external surface of montmorillonite K-10, probably through hydrogen bond interactions.

2.2. Catalytic dihydroboration of internal alkynes

2.2.a. Synthesis of internal alkynes *via* heterogenised Sonogashira C-C coupling

Generally the homogeneous Sonogashira reaction is carried out in an organic solvent such as toluene, THF or DMF, with at least a stoichiometric amount of base, and a Pd(0)/Cu(I) catalytic system [52]. Homogeneous Pd-catalysts make the separation and recovery of the catalysts tedious if not impossible and might result in unacceptable palladium contamination of the product. The intensive application of the Sonogashira reaction in the chemical industry depends on the development of new, stable heterogenised palladium catalysts. With this aim, we made a systematic study of immobilising organopalladium complexes onto clays through adsorptive and electrostatic interactions, following the same methodology described in previous sections.

Our work involved selecting an optimised palladium catalyst modified with the C,N,C-pincer bis-carbene ligand (**93**) [53], (Figure 4), in both homogeneous and heterogenised versions. Once we had established the methodology with model substrates, we extended it to include more attractive starting materials.



X'= Br^-, BF_4^-; R= Bu, Me, Bn

93

Figure 4

The pincer-heterocyclic-carbene ligands are very efficient at C-X activation and extremely stable at high temperatures, [16a,16b] which made it possible for them

to be used in the C-C coupling of the test substrates phenylacetylene and phenyliodide at the refluxing temperature (87^0C) of pyrrolidine, (which acts both as a solvent and as a base to intercept the HI formed). Of all the solutions described to date for suppressing the side reaction of the oxidative homocoupling (Glaser coupling) of the alkyne to the corresponding symmetrical diyne, [23], [54] we decided to perform the reaction under nitrogen by slow addition of the alkyne, keeping its concentration in the reaction mixture low. Under these homogeneous reaction conditions, the catalyst [PdBr(CNC-Bu_2)]Br proved to be highly efficient, and it afforded the desired product in a 99% yield in 45 min (Figure 5).

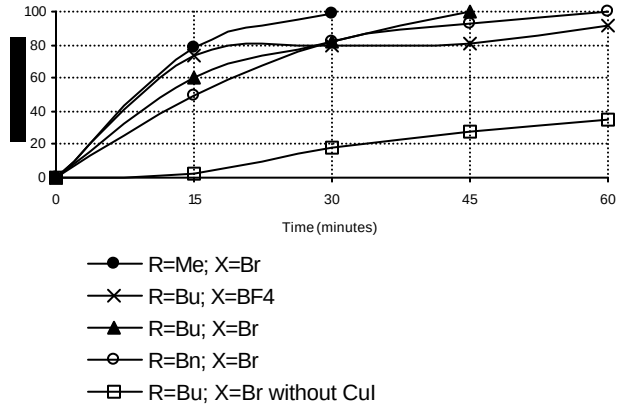


Figure 5

Reaction profiles for Sonogashira coupling of (C_6H_5)CCH and (C_6H_5)I with [PdBr(CNC-R_2)]X.

As has been shown above in scheme 3 for the Sonogashira reaction, the co-catalyst CuI, (probably involved in the transmetalation step), seems to be necessary because, otherwise, conversions are only moderate (38% yield in 1h, Figure 5). However, the addition of CuI to other palladium catalytic systems modified with carbene ligand [16d], surprisingly resulted in almost complete deactivation of the catalyst, probably because carbene ligands may be transferred to Cu [55].

A search for the best tridentate pincer bis-carbene ligand showed the influence of the wingtip groups (R= methyl, butyl and benzyl) on the catalytic activity. Whereas the solubility in non-polar solvents increases from C,N,C pincer bis-carbene with R=Me to R=Bu or Bn, the C-C coupling reaction was substantially affected by the difference in the nature of the substituents. The activity was highest activity (99% yield in 30 min) when the catalytic system was [PdBr(CNC-Me_2)]Br, (Figure 5). Similar increases in activity have been observed in the literature when non-hindered substituents on imidazolium chlorides modify the palladium catalytic system $Pd(OAc)_2$ [23]. The reaction rates were also significantly influenced by the identity of the counterion in the catalytic system [PdBr(CNC-Bu_2)]X. The C-C coupling proceeded more rapidly when the counterion was X=Br than when it was X=BF_4, (Figure 5). We did not observe the formation of Pd-black during the reaction, but the black deposit started to form some time after all the substrate had been consumed if the solution was maintained at the refluxing temperature of the solvent.

To test the long-term stability of the catalyst and its recovery and reuse in consecutive runs, we initiated the immobilisation of [PdBr(CNC-Me_2)]Br in smectite clays. We used the solvent-impregnation method [56] to immobilise the ionic palladium complex in three types of solids: montmorillonite K-10 (MK-10), bentonite A: (bA), bentonite B: (bB). Chapter 2 showed the structural differences between the montmorillonite K-10 and both bentonites and how these differences affect the immobilisation process. The higher crystallinity of bentonites A and B favours the immobilisation process to take place *via* cation exchange while the higher surface area of the MK-10 as a result of their partially destroyed lamellar structure means that the immobilisation will mainly take place *via* adsorption [57]. The different ways for grafting complex [PdBr(CNC-Me_2)]Br onto the clays affect the quantity of the palladium complex immobilised, attending to the chemical analyses of the solids (Table 3). This can also lead to differences in their catalytic behaviour when used as catalysts in the Sonogashira reaction.

The scanning electron microscopy analyses of MK-10_T/[Pd]Br, bA_T/[Pd]Br, and bB_T/[Pd]Br, (Table 3), provide the percentages of palladium complex which agree with the expected amount of metal in the solid catalytic system, (0.6-0.7%).

Table 3. Chemical analyses of solids and immobilised catalytic systems [PdBr(CNC-Me_2)]Br/clay.[a]

M^{n+}	MK-10_T[b]	MK-10_T/[Pd]Br	bA_T[b]	bA_T/[Pd]Br	bB_T[b]	bB_T/[Pd]Br
Si	32.3	31.9	28.7	26.3	25.2	23.9
Al	7.3	7.7	9.4	9.9	3.2	3.6
O	53.6	48.6	51.8	44.9	48.2	41.1
Mg	0.6	0.9	1.7	1.8	14.3	13.4
Na	0.2	0.2	2.0	1.9	---	---
K	1.3	0.8	0.8	0.9	0.7	0.4
Ca	0.2	0.3	1.3	0.7	0.3	0.1
Fe	1.5	2.1	1.9	2.5	1.5	1.1
Pd	---	0.6	---	0.7	---	0.7

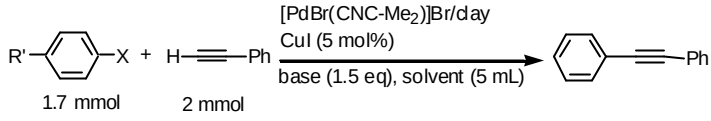
[a] Percentages calculated as (% by weight) from the scanning electro microanalyser analysis; [b] MK-10: montmorillonite K-10, bA: bentonite A, bB: bentonite B. All the clays were predried at 100^0C for 24h.

Initial experiments with the heterogenised catalytic system [PdBr(CNC-Me_2)]Br/clay, (catalyst loading of 1,7 mol% in MK-10_T/[Pd]Br and 1.8 mol% in bA_T/[Pd]Br and bB_T/[Pd]Br) were carried out using the previously optimised conditions for the homogeneous Sonogashira coupling between phenylacetylene and phenyliodide. The three supported catalysts proved to be highly efficient and afforded 92-94% yield of the product between 0.5 and 1h (Table 4, entries 1-3). Therefore, the different structural nature of the clay and the different grafting of the palladium complex did not make a significant difference to the catalytic activity of the solid system.

The coupling reaction of more challenging substrates, such as activated arylbromides with MK-10_T/[Pd]Br, bA_T/[Pd]Br, and bB_T/[Pd]Br, was almost complete within 0.5 h for *p*-nitrobromobenzene, and quantitative within 2.5 h for *p*-bromobenzaldehyde and *p*-bromoacetophenone (Table 4, entries 4-6).

These results indicate that the activity of the catalytic system is higher than of previously reported Pd-carbene catalysts [16d], [22] or Pd-immobilised catalytic systems [28-29], for the coupling of the same substrates. We also studied the role of pyrrolidine, piperidine and Cs_2CO_3 as the base, and we concluded that activity was highest with piperidine [23] (Table 4, entries 1, 7 and 9).

Table 4. Chemical analyses of solids and immobilised catalytic systems [PdBr(CNC-Me$_2$)]Br/MK-10$_T$.[a]



Entry	X	R'	Clay[b]	Base[c]	Solv.	T(^{0}C)	t(h)	Yield (%)[d]
1	I	H	MK-10$_T$	Pyrr	Pyrr	87	0.5	92
2	I	H	bA$_T$	Pyrr	Pyrr	87	1	94
3	I	H	bB$_T$	Pyrr	Pyrr	87	1	92
4	Br	NO_2	MK-10$_T$	Pyrr	Pyrr	87	0.5	99
5	Br	CHO	MK-10$_T$	Pyrr	Pyrr	87	2.5	77
6	Br	MeCO	MK-10$_T$	Pyrr	Pyrr	87	2.5	73
7	I	H	MK-10$_T$	Pip	Pip	106	0.5	99
8	I	H	MK-10$_T$	Pip	DMA	100	1	86
9	I	H	MK-10$_T$	Cs_2CO_3	DMA	100	1	64
10	I	H	bA$_T$	Pip	DMA	100	1	97
11	I	H	bB$_T$	Pip	DMA	100	1	93.5
12	Br	NO_2	MK-10$_T$	Pip	DMA	100	0.5	99
13	Br	CHO	MK-10$_T$	Pip	DMA	100	2	98
14	Br	MeCO	MK-10$_T$	Pip	DMA	100	2	72

[a] 0.029mmol [Pd]Br in 0.5 of MK-10$_T$; 0.032mmol [Pd]Br in 0.5 of bA and bB; [b] MK-10$_T$: montmorillonite K-10 predried, bA$_T$: bentonite A predried, bB$_T$: bentonite B predried; [c] Pyrr: pyrrolidine, Pip:piperidine; [d] Conversion of the arylalkynes determined by GC.

Before validating the concept of effective catalyst recycling, we selected an appropriate solvent to simplify the protocol of washing the solid catalyst system after it has been separated from the products via filtration. Therefore, we demonstrated that the use of DMA, (N,N-dimethylacetamide), as solvent, could be a suitable solvent for efficient catalysis and for removing all the products and ammonium salts involved in the reaction, from [PdBr(CNC-Me$_2$)]Br/clay (Table 4, entries 8-14). Catalyst recycling studies were carried out after [PdBr(CNC-

Me_2)]Br/clay had been recovered, and washed with DMA and CH_2Cl_2. Pd-black deposit was not observed in the washed solid, which confirmed the great stability of the catalyst when it is immobilised. The resulting recovered solids were successfully reused and the activity was the same as for the first run in the coupling of phenylacetylene and phenyliodide (Figure 6 i, ii and iii).

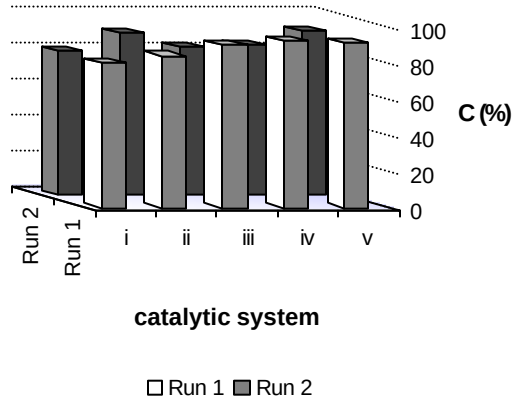


Figure 6

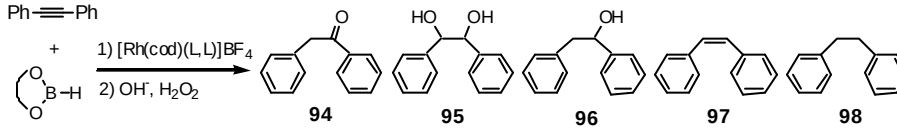
Reusability of [PdBr(CNC-Me_2)]Br/clay in the coupling of phenylacetylene and R'-C_6H_4-X. i) R'= H, X = I, clay = MK-10_T; ii) R'= H, X = I, clay = bA_T; iii) R'= H, X = I, clay = bB_T; iv) R'= NO_2, X = Br, clay = MK-10_T; v) R'= CHO, X = Br, clay = MK-10_T.

Encouraged by the satisfactory recycling capacity of these systems, we extended our study of the reusability of [PdBr(CNC-Me_2)]Br/MK-10_T to the consecutive coupling of phenylacetylene with *p*-nitrobromobenzene and *p*-bromobenzaldehyde, (Figure 6 iv and v, respectively). Reaction rates were similar for the first and second consecutive runs in both cases.

2.2.b. Study of the homogeneous and heterogenised catalytic dihydroboration of internal alkynes.

The internal alkyne diphenylacetylene, obtained from the Sonogashira cross-coupling, was used as a model substrate in the tandem dihydroboration/oxidation reaction. First we selected the optimised standard reaction conditions: solvent, catalytic system and hydroborating reagent in the homogeneous version. Once we had established the most suitable methodology, we extended it to the heterogenised version.

We started by examining the catalytic properties of the rhodium complex $[Rh(cod)(dppp)]BF_4$ in THF, with an equimolecular amount of catecholborane.



Scheme 10

Table 5. Hydroboration/oxidation and dihydroboration/oxidation of diphenylacetylene with $[Rh(cod)(dppp)]BF_4$.[a]

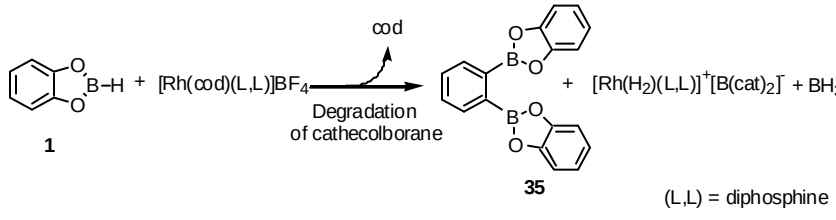
Entry	Eq. Borane	C (%)	Selectivity (%)				
			94	**95**	**96**	**97**	**98**
1	1.1eq	37	17	50	25	8	-
2	2.2eq	98	3	60	33	3	-

[a] Standard conditions: phenylacetylene/catecholborane/Rh complex=1:1.1 or 2.2:0.01. Solvent: THF. T: 25 ^{0}C. Time: 2h.

Although the ketone **94** was expected to be the major product obtained, in fact it was the diol diphenyl-1,2-ethanediol (**95,** hydroxybenzoin) that was the most favoured, (Scheme 10, Table 5, entry 1). The low conversion is consistent with the total consumption of catecholborane. Therefore, the double amount of borane reagent (2.2 equivalents) could guaranteed a higher conversion. However, not only was

conversion significantly improved, but selectivity towards the diol **95** also increased to 60%, (Table 5, entry 2).

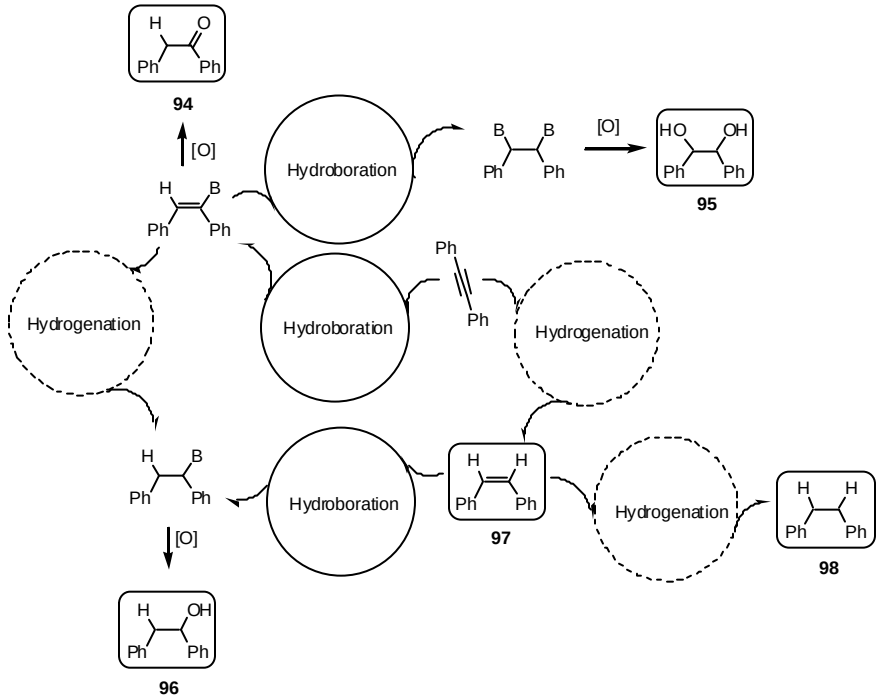
Some other by products, (scheme 10), were observed as a consequence of competitive catalytic reactions, such as hydrogenation. The reason for these secondary reactions could be related to the degradation of catecholborane in the reaction media which depends on the nature of the phosphine ligands, the rhodium complex and the solvent. It seems that, catecholborane breaks down to give a variety of boron products such as **35** plus metaldihydro species such as $[Rh(H_2)(dppb)]^+[B(cat)_2]^-$ (Scheme 11), [58]. The production of rhodium dihydrido species might be responsible for the formation of hydrogenation products.



Scheme 11

The ^{11}B NMR spectra determined during the dihydroboration reaction, showed two broad signals at $\delta(^{11}B)$= 33.00ppm and $\delta(^{11}B)$= 21.50ppm in agreement with the alkylboronate products and compound **35**, respectively.

On the basis of these observations, we suggest that diphenylacetylene was involved in competitive hydroboration and/or hydrogenation reactions as is illustrated in scheme 12. While the dihydroboration of diphenylacetylene provided the desired hydroxybenzoin **95**, hydroboration followed by the hydrogenation of the substrate gave the 1,2-diphenylethanol **96**. Alkene **97** and alkane **98**, were also formed from the catalytic hydrogenation of the alkyne and alkene, respectively.



Scheme 12

As far as the catalytic asymmetric dihydroboration of diphenylacetylene was concerned, the chiral complex [Rh(cod)(S,S)-bdpp]BF_4 with catecholborane provided conversion and selectivity, (Table 6, entry 1) similar to those of [Rh(cod)(dppb)]BF_4. However, the diphenyl-1,2-ethanediol (**95**) was characterised mainly as the ery*thro* compound, not the expected *threo*. Unfortunately, even modifying the rhodium complex with other chiral ligands, such as Quinap and Binap, did not change this trend towards the formation of the ery*thro* compound, (Table 6, entries 2 and 3). In addition, the formation of the diol **95** is not favoured in the latter bidentate ligands.

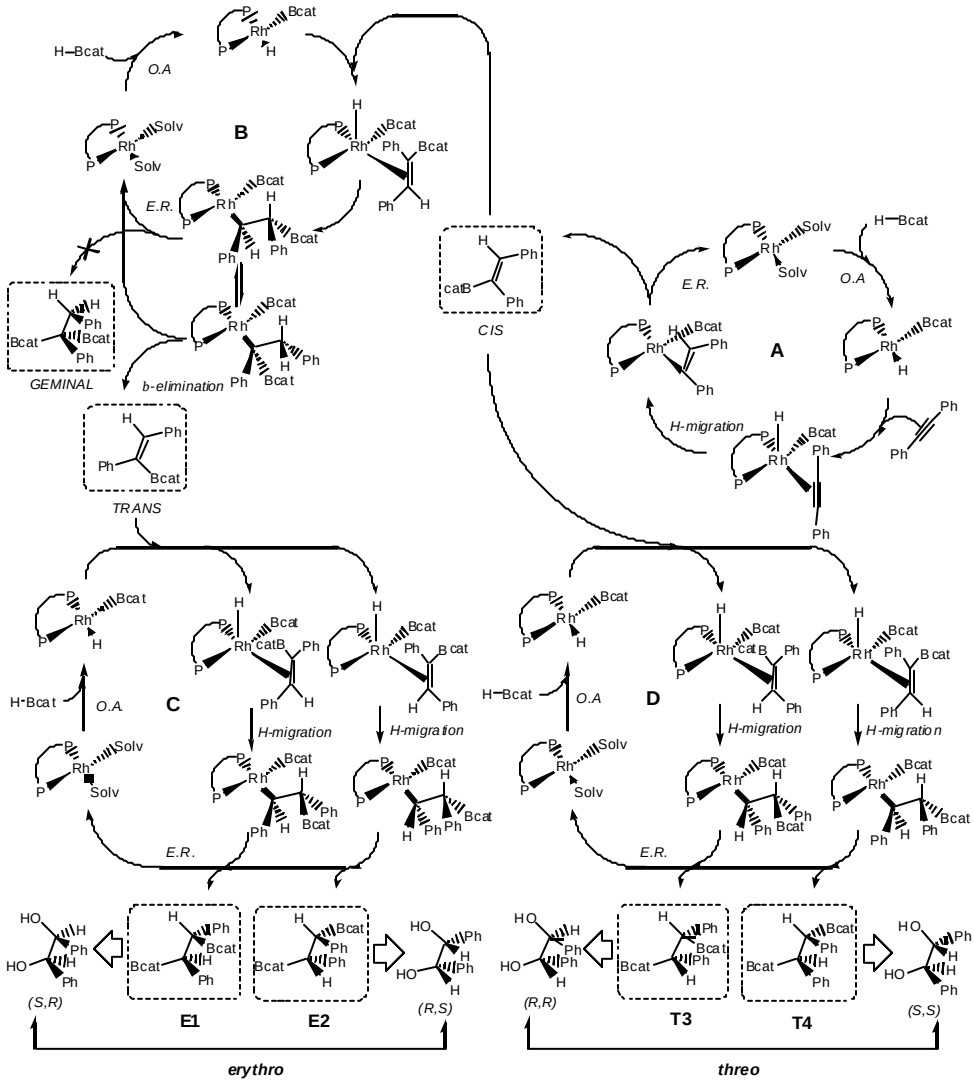
Table 6. Catalytic asymmetric dihydroboration of diphenylacetylene with $[Rh(cod)(L,L)]BF_4$ and catecholborane (**1**).[a]

Entry	L_2	run	C (%)[b]	Selectivity (%)[b]				
				94	**95** (erythro:threo)[c]	**96**	**97**	**98**
1	(S,S)-bdpp	-	98	4	68 (96:4)	26	2	-
2	(S)-Quinap	-	78	68	17	15	-	-
3	(R)-Binap	-	63	15	31 (88:12)	31	23	-
4[d]	(S,S)-bdpp	1	99	9	17 (58:42)	74	-	-
		2	56	23.5	47 (66:34)	29.5	-	-

[a] Standard conditions: phenylacetylene/catecholborane/Rh complex=1:2.2:0.01. Solvent: THF. T: 25^0C. Time: 2h.;[b] Determined by ^{1}H RMN; [c] Determined by HPLC; [d] 0.02mmol Rh system into 250mg MK-10_T

One explanation of the formation of the syn-diol, could be that the alkenylboronate ester isomerises from the *cis* to the *trans* isomer, because of the favoured β-elimination, (Scheme 13). The *trans* isomer could then be transformed into the *syn* diboronate, during the second catalytic hydroboration.

The heterogenisation of $[Rh(cod)(S,S)\text{-bdpp}]BF_4$ in montmorillonite K-10 (MK-10), yielded almost complete conversion in the first run, although the percentage of the diol **95** diminished substantially in comparison with the homogeneous version. Also, the erythro:threo ratio was 58:42 in this case, (Table 6, entry 4). In a second consecutive run, the conversion was only 56% but the percentage of diol **95** increased to 47% with a mixture of erythro:threo= 66:34. The more restricted environment in the heterogenised system could be the reason for these changes in selectivity. However, the decomposition of the catecholborane provided the compound B_2cat_3 (**35**), which is insoluble in THF and could justify the low conversion on recycling.


H–Bcat
O.A
B
E.R.
GEMINAL
b-elimination
TRANS
CIS
A
H-migration
C
D
H-migration
H-migration
(S,R)
E1
E2
(R,S)
erythro
(R,R)
T3
T4
(S,S)
threo

Scheme 13

3. Conclusions

It has been developed the catalytic asymmetric hydroboration of perfluoroalkenes in which the regioselectivity towards the branched perfluoroalkylboronate compound is controlled with the rhodium complex, the ligand and the borane reagent. The moderate e.e values (55-65%) obtained in the hydroboration of aliphatic perfluoroalkenes, are even higher than those observed in the aromatic perfluoroalkenes (18-19.5%), and in electron deficient vinylarenes such as 3,5-bis-trifluoromethylstyrene (5%), and 2,6-difluorostyrene (<15%).

It was possible to reuse the catalytic system in the heterogenised hydroboration/oxidation reaction of perfluoroalkenes but the selectivities diminished slightly.

Diphenylacetylene was synthesised through a suitable palladium phosphine-free catalytic system which has significant advantages in the Sonogashira coupling of alkynes with aryliodides and bromides. Not only does it catalyse the reaction successfully, it is also easily recovered and reused when it is immobilised on clays, because it is very stable.

Dihydroboration/oxidation of diphenylacetylene can provide 1,2-diphenyl-1,2-ethanediol (hydrobenzoin (**95**)) with a selectivity of 68% but the resulting diol is the ery*thro* isomer.

4. Experimental section

General comments. All reactions and manipulations were carried out with standard vacuum line techniques under an atmosphere of dry nitrogen. All rhodium organometallic complexes were synthesised using standard Schlenk techniques. All organic solvents were distilled, stored on a molecular sieve (0.4nm Aldrich), and degassed with a nitrogen flow prior to use. The complexes $[Rh(\mu\text{-}Cl)(cod)]_2$ [59], $[Rh(cod)_2BF_4$ [60], [61], $[Rh(cod)(R)\text{-}Binap]BF_4$ [62], $[Rh(cod)(S)\text{-}Quinap]BF_4$ [50b] were prepared as previously reported. They were characterised by elemental analysis, ^1H and ^{31}P NMR, and FTIR spectroscopies. MK-10 was purchased from Fluka and bentonite A and B was purchased as Majorbenton B from AEB Iberica S.A. Predried clays were obtained as follows: clay (5g) was kept in a melting pot in the oven at 100^0C for 24h. NMR spectra were recorded on a Varian Gemini 300 and Mercury 400 spectrometer. Chemical shifts were reported relative to tetramethylsilane for ^1H as internal reference, 85% H_3PO_4 for ^{31}P and BF_3OEt_2 for ^{11}B as the external reference. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 II with a flame ionisation detector equipped with a chiral column FSCycoldex β-IP, 50m x 0.25mm. The HPLC analyses were performed in a chiral column Chiralcel OJH. BET surface areas were calculated from nitrogen adsorption isotherms at 77K by using a Micromeritics ASAP 2000 surface analyser and a value of $0.164nm^2$ for the cross section of the nitrogen molecule. The scanning electron microscopy analyses were made in a JEOL, JSM-640 with an accelerating voltage=15KV and a prove current = $(3\text{-}6)x10^{-9}$ A for a representative area (575 x 466 μm) for each sample.

Preparation of the supported complexes. The ionic rhodium complex and the palladium complex were immobilised in the following manner. The solid support (montmorillonite K-10 or bentonite A and B was added to an organometallic solution prepared with 10ml of deoxygenated dichloromethane and 0.2mmol of the complex under nitrogen. Then it was stirred for 24h under nitrogen at room temperature. The suspension was filtered off and the solid was washed with dichloromethane and dried

under vacuum. The amount of metal complex immobilised on the clay was determined by gravimetric analysis and SEM analysis.

Homogeneous catalytic hydroboration/oxidation of perfluoroalkenes 90, 91, 92 with catecholborane or pinacolborane. Perfluoroalkenes (2mmol) were added to a solution of catalyst (1 mol%) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane or pinacolborane (2mmol) was then added. The mixture was stirred at ambient temperature for 1h because there is a risk of explosion when using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with Et_2O (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by chromatography.

Heterogenised catalytic hydroboration/oxidation of perfluoroalkenes 90, 91 and 92 with catecholborane or pinacolborane. Perfluoroalkenes (2mmol) were added to a suspension of supported catalyst (1 mol% immobilised in 0.5g of solid) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2mmol) was then added. The mixture was stirred at ambient temperature for 2h. The solution was filtered off under vacuum and the filtrates were then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. The quenched filtrates were treated with NaOH (2M, 2mL) and H_2O_2 (2mL) and the mixture was stirred for several hours. The mixture was finally extracted into Et_2O, washed (NaOH 2M, H_2O, saturated brine) and dried over $MgSO_4$. The products were then characterised by chromatography. The solid that contained the complex was dried under vacuum for 10 minutes and put into the *schlenk* for another run.

Homogeneous catalytic Sonogashira reaction. To a solution of arylhalide (1,7mmol), Pd catalyst complex (17μmol, 1 mol%), and CuI (85μmol, 5 mol%) in dry base (pyridine, pyrrolidine or Cs_2CO_3) PhC≡CH (2mmol, 1.2eq) was added under

nitrogen, and the mixture were reacted at reflux temperature for 0.5-2.5h. The products were characterised by chromatography.

Heterogenised catalytic Sonogashira. CuI (85μmol, 5 mol%) in dry base (pyridine, pyrrolidine or Cs_2CO_3) was added to a suspension of supported Pd catalyst (1 mol% metal complex in 250mg of clay) under nitrogen and arylhalide (1.7mmol). The solution was stirred for several minutes and PhC≡CH (2mmol, 1.2 eq) was then added under nitrogen. The mixture was reacted at reflux temperature for 0.5-2.5h. The products were characterised by chromatography.

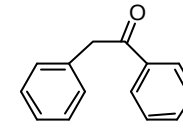
Homogeneous catalytic dihydroboration/oxidation of diphenylacetylene. Diphenylacetylene (1mmol) was added to a solution of catalyst (1 mol%) in solvent (THF or toluene) (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane or pinacolborane (2.2mmol) was then added drop by drop for 15 min. The mixture was stirred at ambient temperature for 2h and then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with ethyl acetate (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by ^{1}H NMR and chiral HPLC.

Heterogenised catalytic dihydroboration/oxidation of diphenylacetylene with catecholborane (1). Diphenylacetylene (1mmol) was added to a suspension of supported catalyst (2 mol% immobilised in 0.250g of solid) in THF (2mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2.2mmol) was then added drop by drop for 15 min. The mixture was stirred at ambient temperature for 2h, using the chemical assembly exemplified in Figure 7. The solution was filtered off under vacuum and the filtrates were then quenched with EtOH (2mL). Work up must be carried out carefully because there is a risk of explosion when using peroxides with ether and THF. The quenched filtrates were treated with NaOH (2M, 2mL) and H_2O_2 (2mL) and the mixture was stirred for several hours. The mixture was

finally extracted into Et_2O, washed (NaOH 2M, H_2O, saturated brine) and dried over $MgSO_4$. The products were then characterised by ^1H NMR and HPLC. The solid that contained the complex was dried under vacuum for 10 minutes and put into the *schlenk* for another run.

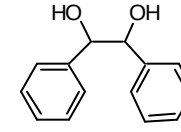
Deoxybenzoin (94) [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.99(d, 2H), 7.50(m, 2H); 7.46(m, 2H), 7.27(s, 4H), 4.25(s, 2H)



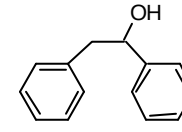
Hydroxybenzoin (95) [63b]

^1H RMN($CDCl_3$): δ(ppm)=7.09-7.22(m, 10H), 4.80(s, 2H), 2.17(br s, 2H); HPLC (diol): Chiralcel OJ-H, 10% ^{i}PrOH in Hexane, flow rate 1.0mL/min, t_R= 15.29 (R,R); t_R= 17.70 (S,S); t_R= 21.50 (R,S) and (S,R)



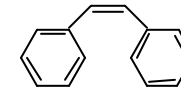
1,2-diphenylethanol (96) [50b]

^1H RMN($CDCl_3$): δ(ppm)= 7.40-7.10 (m, 10H), 4.90 (dd ,$^3J_{H-H}$=8.0 and 5.4Hz, 1H),3.20-2.90 (m, 2H), 1.80(br s, 1H)



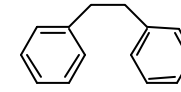
***cis*-stilbene (97)** [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.38-6.98 (m, 10H); 6.57 (s, 2H)



Bibenzyl (98) [63a]

^1H RMN($CDCl_3$): δ(ppm)= 7.42-6.99 (m, 10H); 2.91 (s, 4H)



References

[1] P.V.Ramachandran, H.C.Brown, *in Enantiocontrolled Síntesis of Fluoro-Organic Compounds: Stereochemical Challenges and Biomedical Targets,* V.A.Soloshonok (Ed.);John Wiley and Sons Ltd, **1999**.

[2] P.V.Ramanchandran, M.P.Jennings, H.C.Brown, *Org. Lett.* **1999**, *1*, 1399.

[3] a) H.C.Brown, G.M.Chen, M.V.Jennings, P.V.Ramachandran, *Angew. Chem. Int. Ed.* **1999**, *38*, 2058; b) P.V.Ramachandran, M.V.Jennings, *Chem. Commun.* **2002**, 386.

[4] a) B.Barotcha, W.A.G.Graham, F.G.A.Stone, *J. Inorg. Nucl. Chem.*, **1958**, *6*, 119; b) J.R.Phillips, F.G.A.Stone, *J. Chem. Soc.* **1962**, 94.

[5] J.Tsuji, In *Palladium Reagents*, B.Barotcha, W.A.G.Graham, F.G.A.Stone (Eds.): *J. Inorg. Nucl. Chem.* **1999**, *576*, 1 (special issue).

[6] K.Sonogashira, *J. Organometallic Chem.* **2002**, *653*, 46.

[7] a) K.Menzel, G.C.Fu, *J. Am. Chem. Soc.* **2003**, *125*, 3718; b) G.C.Fu, *Angew. Chem. Int. Ed.* **2002**, *41*, 1945; c) M.R.Netherton, C.D.K.Neuschütz, G.C.Fu, *J. Am. Chem. Soc.* **2001**, *123*, 10099.

[8] a) V.P.W.Böhm, W.A.Herrmann, *Chem. Eur. J.* **2000**, *22*, 3679; b) T.Hundertmark, A.F.Littke, S.L.Buchwald, C.G.Fu *Org. Lett.* **2000**, *2*, 1729.

[9] M.R.Eberhard, Z.Wang, C.M.Jensen *Chem. Commun.* **2002**, 818.

[10] A.Köllhofer, Th.Pullmann, H.Plennio, *Angew. Chem.* **2003**, *42*, 1056.

[11] a) A.J.III Arduengo, R.L.Harlow, M.J.Kline, *J. Am. Chem. Soc.* **1991**, *113*, 161; b) A.J.III Arduengo, *Acc. Chem. Res.* **1999**, *32*, 913.

[12] D.Bourisson, O.Guerret, F.P.Gabbaï, G.Bertrand, *Chem. Rev.* **2000**, *100*, 39.

[13] W.A.Herrmann, M.Elison, J.Fischer, C.Köcher, J.G.R.Artus, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2371.

[14] a) J.Huang, G.Grasa, S.P.Nolan, *Org. Lett.* **1999**, *1*, 1307: b) S.R.Stauffer, S.Lee, J.P.Stambuli, S.I.Hauck, J.F.Hartwig, *Org. Lett.* **2002**, *2*, 1423.

[15] S.Lee, J.F.Hartwig, *Org. Lett.* **2001**, *66*, 3402.

[16] a) E.Peris, J.A.Loch, J.Mata, R.H.Crabtree, *Chem. Commun.* **2001**, 201; b) J.A.Loch, M.Albrecht, E.Peris, J.Mata, J.W.Faller, R.H.Cabtree,

Organometallics **2002**, *21*, 700; c) J.Schwarz, V.P.W.Böhm, M.G.Gardiner, M.Grosche, W.A.Herrmann, W.Hieringer, G.Raudaschl-Siever, *Chem. Eur. J.* **2000**, *6*, 1773; d) D.S.McGuinnes, K.J.Cavell, *Organometallics* **2000**, *19*, 741; e) C.Yang, H.M.Lee, S.P.Nolan, *Org. Lett.* **2001**, *3*, 1511.

[17] K.Sonogashira, Y.Tohda, N.Hagihara, *Tetrahedron Lett.* **1975**, *16*, 4467.

[18] U.Beutler, J.Mazacek, G.Penn, B.Schenkel, D.Wasmuth, *Chimia,* **1996**, *50*, 154.

[19] J.W.Grissom, G.U.Gunawardena, D.Klingenberg, D.Huang, *Tetrahedron*, **1996**, *52*, 6453.

[20] a) K.T.Wong, C.C.Hsu, *J. Org. Lett.* **2001**, *3*, 173; b) K.T.Wong, C.C.Hsu, *J. Org. Lett.* **2000**, *2*, 3959.

[21] a) W.A.Herrmann, C.P.Reisinger, M.Spiegler, *J. Organomet. Chem.* **1998**, *557*, 93; b) W.A.Herrmann, V.P.W.Böhn, C.W.K.Gstöttmayr, M.Groscher C.P.Reisinger, M.Spiegler, *J. Organomet. Chem.* **2001**, *616*, 617.

[22] R.A.Batey, M.Shen, A.Lough, *J. Org. Lett.* **2002**, *4*, 1411.

[23] Ch.Yang, S.P.Nolan, *Organometallics* **2002**, *21*, 1020.

[24] a) J.S.Moore, *Acc. Chem. Res.* **1997**, *30*, 402 and references cited therein; b) T.Hiyama, In *Metal-Catalyzed Cross-Coupling Reactions*; F.Diederich, P.J.Stang (Eds.); Wiley-VCH: Weinheim **1998**, *Chapter 10* and references cited therein; c) K. Sonogashira, In *Handbook of Organopalladium Chemistry for Organic Synthesis*; E.Neguishi (Ed.); Wiley-VCH: New York **2002**; d) R.R.Tykwinski, *Angew. Chem., Int. Ed.* **2003**, *42*, 1566; e) E.-J.Neguishi, L.Anastasia, *Chem. Rev.* **2003**, *103*, 1979.

[25] a) *Modern Acetylene Chemistry;* P.J.Stang, F.Diederich (Eds.); Wiley-VCH: Weinheim **1995**; b) *Modern Arene Chemistry*; D.Astruc (Ed.); Wiley-VCH: Weinheim **2002**.

[26] a) L.Bradsma, S.F.Vasilevsky, H.D.Verkruijsee, *Applications of Transition Metal Catalysts in Organic Synthesis*; Springer: Berlin, **1998**, *Chapter 10*, 179; b) K.C.Nicolou, E.J.Sorensen, In *Classics in Total Synthesis*; Wiley-VCH: Weinheim **1996**, 582; c) A.E.Graham, D.McKerrecher, D.H.Davies, R.J.K.Taylor, *Tetrahedron Lett.* **1996**, *37*, 7445; d) M.W.Miller, C.R.Johnson, *J. Org. Chem.* **1997**, *62*, 1582; e) A.Sakai, T.Aoyama, T.Shiori, *Tetrahedron*

Lett. **1999**, *40*, 4211; f) F.Yoshimura; S.Kawata, M.Hirama, *Tetrahedron Lett.* **1999**, *40*, 8281; g) M.Toyota, C.Komori, M.Ihara, *J. Org. Chem.* **2000**, *65*, 7110; h) I.Paterson, M.R.D.Davies, R.Marquez, *Angew. Chem., Int. Ed.* **2001**, *40*, 603; i) J.-I. Uenishi, D.Matsui, H.Ohmiya, *J. Organomet. Chem.* **2002**, *653*, 141.

[27] F.Quignard, S.Larbor, S.Goutodier, A.Chopin, *J. Chem. Soc., Dalton Trans.* **2002**, *6*, 1147.

[28] C.Ch.Tzschucke, Ch.Markert, H.Glatz, W, Bannwarth, *Angew. Chem., Int. Ed.* **2002**, *41*, 4500.

[29] A.Köllhofer, H.Plenio, *Chem. Eur. J.* **2003**, 9, 1416.

[30] T.Fujuyama, M.Shinmen, S.Nishitani, M.Sato, I.Ryu, *Org. Lett.* **2002**, *4*, 1691.

[31] B.M.Choudary, S.Madhi, N.S.Chowdari, M.J.Dantam, B.Sreedhar, *J. Am. Chem. Soc.* **2002**, *124*, 14127.

[32] L.Djakovitch, P.Rollet, *Tetrahedron Lett.* **2004**, *45*, 1367.

[33] a) J.K.Whiteshell, *Chem. Rev.* **1989**, *89*, 1581; b) R.L.Halterman, S.T.Jan, H.L.Nimmons, D.J.Standlee, M.A.Khan, *Tetrahedron* **1997**, *53*, 11257; c) K.S.Kim, J.I.Park, P.Ding, *Tetrahedron Lett.* **1998**, *39*, 6471; d) S.Superchi, M.Contursi, C.Rosini, *Tetrahedron* **1998,** *54*, 11247; e) J.A.Tuge, D.A.Gately, J.R.Norton, *J. Am. Chem. Soc.* **1999**, *121*, 4520; f) C.A.Ray, T.W.Wallance, R.A.Ward, *Tetrahedron Lett.* **2000**, *41*, 3501; g) M.B.Andrus, B.B.V.Soma Sekhar, E.L.Meredith, N.KDalley, *Org. Lett.* **2000**, *2*, 3035.

[34] a) K.Tomioka, *Synthesis* **1990**, 541; b) K.R.K.Prasad, N.N.Joshi, *Tetrahedron: Asymmetry* **1996**, *7*, 1957; c) M.Shindo, K.Koga, K.Tomioka, *J. Org. Chem.* **1998**, *63*, 9351; d) M.I.Donnoli, S.Superchi, C.Rosini, *J. Org. Chem.* **1998**, *63*, 9392; e) K.Ishimaru, K.Monda, Y.Yamamoto, K.Akiba, *Tetrahedron* **1998**, *54*, 727.

[35] a) M.E.Bruin, E.P.Kündig, *Chem. Commun.* **1998**, 2635; b) T.Suzuki, N.Yamagiwa, Y.Matsuo, S.Sakamoto, K.Yamaguchi, M.Shibasaki, R.Noyori, *Tetrahedron Lett.* **2001**, *42*, 4669.

[36] F.Dietl, A.Merz, R.Tomahogh, *Tetrahedron Lett.* **1982**, *23*, 5255; b) M.Kawashima, A.Hirayama, *Chem. Lett.* **1991**, 763.

[37] a) H.C.Kolb, M.S.VanNieywenhze, K.B.Sharpless, *Chem. Rev.* **1994**, *94*, 2483; b) H.Becker, K.B.Sharpless, *Angew. Chem., Int. Ed.* **1996**, *35*, 448.

[38] a) K.R.K.Prasad, N.N.Joshi, *J. Org. Chem.* **1996**, *61*, 3888; b) K.Murata, K.Okano, M.Miyagi, H.Iwane, R.Noyori, T.Ikariya, *Org. Lett.* **1999**, *1*, 1119.

[39] a) J.E.McMurry, *Chem. Rev.* **1989**, *89*, 1513; b) T.Wirth, *Angew. Chem., Int. Ed.* **1996**, *35*, 61.

[40] A.Catterjee, T.H.Bennur, N.N.Joshi, *J. Org. Chem.* **2003**, *68*, 5668.

[41] P.Binger, R.Köster, *Angew. Chem.* **1962**, *74*, 652.

[42] H.C.Brown, S.P.Rhodes, *J. Am. Chem. Soc.* **1966**, *91(15)*, 4306.

[43] J.A.Soderquist, R.Huertas, G.Leon-Colon, *Tetrahedron Lett.* **2000**, *41*, 4251.

[44] D.T.Carey, F.S.Mair, R.G.Pritchard, J.E.Warren R.J.Woods, *J. Chem. Soc. Dalton Trans.* **2003**, 3792.

[45] V.M.Dembitsky, H.A.Ali, M.Srebnik, *Applied Organomet. Chem.* **2003**, *17*, 327.

[46] S.Narashimhan, R.Balakumar, *Aldrichimica Acta* **1998**, *31(1)*, 19.

[47] T.C.Morrill, C.A.S'ouza, L.Yang, A.J.Sampugnaro, *J. Org. Chem.* **2002**, *67*, 2481.

[48] J.M.Brown, D.I.Hulmes, T.P.Layzell, *J. Chem. Soc., Chem. Commun.* **1993**, 1673.

[49] S.Pereira, M.Srebnik, *Tetrahedron Lett.* **1996**, *37*, 3283.

[50] a) T.Hayashi, Y.Matsumoto, Y.Ito, *Tetrahedron: Asymmetry.* **1991**, *2*, 601; b) H.Doucet, E.Fernández, P.T.Layzell, J.M.Brown, *Chem. Eur. J.* **1999**, *5*, 1320.

[51] J.M.Brown, H.Doucet, E.Fernández, H.E.Heeres, M.W.Hooper, D.I.Hulmes F.I.Dnight, T.P.Layzell, G.C.Lloyd-Jones, In *Organometallics in Organic Synthesis, Transition Metal Catalysed Reactions. A "Chemistry for the 21st Century" monograph;* S.I.Murahashi, S.G.Davies (Eds.), Blackwell Science: Oxford **1999**, 465.

[52] K.Sonogashira, In *Comprehensive Organic Synthesis*; B.M.Trost, I.Fleming (Eds.); Pergamon: New York **1991**, *3*, 521.

[53] E.Mas-Marza, A.M. Segarra, C.Claver, E.Peris, E.Fernandez, *Tetrahedron: Letters.* **2003**, *44*, 6495

[54] a) S.Thorand, N.Krause, *J. Org. Chem.* **1998**, *63*, 8551; b) H.F.Chow, Ch.W.Wan, K.H.Low, Y.Y.Yeung , *J. Org. Chem.* **2001**, *66*, 1910.

[55] R.Z.Ku, J.C.Huang, J.Y.Cho, F.M.Kiang, K.J.Reddy, Y.C.Chen, K.J.Lee, J.H.Lee, S.M.Peng, S.T.Liu, *Organometallics* **1999**, *18*, 2145.

[56] C.S.Chin, B.Lee, I.Yoo, T.Know, *J. Chem. Soc., Dalton Trans.* **1993**, 581.

[57] a) R.Margalef-Català, P.Salagre, P.Medina, J.Sueiras, C.Claver, E.Fernández, *J. Catal.* **2001**, *201*, 70; b) A.M.Segarra, R.Guerrero, C.Claver, E.Fernández, *Chem. Eur. J.* **2003**, *9*, 191.

[58] a) K.Burgess, W.A.van der Donk, S.A.Westcott, T.B.Marder, R.T.Baker, J.C.Calabrese, *J. Am. Chem. Soc.* **1992**, *114*, 9350; b) S.A.Westcott, H.P.Blom, T.B.Marder, R.T.Baker, J.C.Calabrese, *Inorg. Chem.* **1993**, *32*, 2175.

[59] J.Chatt, L.M.Venanzi, *J. Chem. Soc. Part VI* **1957**, 4735.

[60] M.D.Fryzyk, B.Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262.

[61] M.Green, S.H.Kuc, S.H.Taylor, *J. Chem. Soc.* **1971**, 2334.

[62] T.Tani, T.Akutagawa, H.Kumobayashi, T.Taketomi, H.Takaya, A.Miyashita, R.Noyori, S.Otsuka, *J. Am. Chem. Soc.* **1984**, *106*, 5208.

[63] a) www.aistgo.jp/RIODB/SDBS; b) C.Döbler, G.M.Mehltretter, U.Sundermeir, M.Beller, *J. Am. Chem. Soc.* **2000**, *122*, 10289.

List of Abbreviations

9-BBN	9-borabicyclo [3.3.1] nonane
B.E.T.	Brunnaruer, Emmet and Teller
bA	bentonite A
B_{ARF}	$B[C_6H_3(CF_3)_2$-3,5]
bB	bentonite B
BCat or HBcat	catecholborane
BDH	bentonite
BDPBzP	3-benzyl-2,4-bis(diphenylphosphino)pentane
BDPP	2,4-bis(diphenylphosphino)pentane
Binap	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BPin or HBPin	pinacolborane
Chiraphos	2,3-bis(diphenylphosphino)butane
cod	1,2-cyclooctadyene
Cp, Cp*	C_5H_5, C_5Me_5,
Cy	cyclohexyl
DFT	density functional theory
DIOP	4,5-bis(diphenylphosphino-methyl)-2,2-dimethyl-1,3-dioxolane
DiPAMP	Bis[(2-methoxyphenyl)phenylphosphino]ethane]
DMA	N,N-dimethylacetamide
DME	1,2-dimethoxyethane

d^n	electron configuration
dppb	1,2-bis(diphenylphosphino)butane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1'-bis(diphenylphosphino)ferrrocene
dppm	1,3-bis(diphenylphosphino)methylene)
dppp	1,3-bis(diphenylphosphino)propane)
e.e	enantiomeric excess
eq.	equivalent
GC	gas chromatography
HPLC	high performance liquid chromatography
^{i}Pr	iso-propil
IRTF	infrared fourier transform
LDH	layered double hydroxide
μ	descriptor for bridging
MK-10	montmorillonite K-10
MK-10_T	montmorillonite K-10 preheated
nbd	norbornardiene
NMR	nuclear magnetic resonance
OTf	triflate
p-	para-
Ph	phenyl

Pip	piperidine
PTA	phosphotugstic acid
Pyrr	pyrrolidine
QM/MM	quantum mechanics (methods) / molecular mechanics (methods)
Quinap	1-(2-diphenylphosphino-1-naphthyl)isoquinoline
SEM	scanning electron microscopy
SHB	supported hydrogen bounded
SP	square pyramid based
Solv.	solvent
Sulphos	$^{-}O_3S(C_6H_4)CH_2C(CH_2PPh_2)_3$
TBP	trigonal bipyramid based
THF	tetrahydrophurane
TMB	3,3,5,5-tetramethyl benzidine
TMS	tetramethylsilane

Abbreviations used in the description of spectra:

δ	chemical shift in part per million
s	singlet
d	doublet
t	triplet
q	quadruplet

dd	doublet of doublets
m	multiplet
br	broad
J	coupling constant

Agraïments (*acknowledgments)*.

La tesi. Escriure-la ha suposat anar 4 anys enrera, experiment per experiment. Un exercici retrospectiu d'anàlisi. Recuperar dades científiques, sí, però també reviure a través del record moments personals importants. Realment, tal com va dir en el seu moment el neuròleg Marcus Jacobson "la ciència pot descubrir el que és cert però no el que és bondadós, just i humà". És veritat, la ciència no pot. Però, el treball del científic, en equip, permet gaudir d'aquest factor humà: els companys. En aquest moment de la tesi (casi tocant el final) puc afirmar que ha estat una grata experiència, que m'ha permés, no només madurar com a científic, sinó també créixer com a persona. I són dos tresors meritoris d'un sincer agraïment. És injust només disposar d'un parell de fulls per exposar aquest aspecte més personal de la tesi profundament lligat a amics, companys i familiars, en front al gairabé dos-cents fulls on s'exposa la meva recerca. Ho intentaré, i espero ser capaç d'expressar la meva més SINCERA GRATITUD.

Oficialment a la Dra Elena Fernández, afectuosament a l'Elena. Hem viscut grans moments professionals i personals amb dificultats i amb èxits…i tots ens han unit. T'agraeixo moltíssim la confiança dipositada en mi, la química que m'has ensenyat juntament amb mil consells i necessàries correccions. T'agraeixo molt no només l'esforç (hem treballat moltíssim) sino també la humanitat que has dipositat en la meva tesi. Quatre anys, que en mi, han cristal·litzat en un profund afecte. Senzillament, gràcies Elena.

Vull agrair també a la Dra Carmen Claver, per haver-me permès formar part del seu grup de recerca, lloc on he pogut desenvolupar aquesta tesi. A més a més,no vull deixar de mencionar bons moments com els divertits sopars de Nadal juntament amb els orgànics a casa seva.

Arriba el moment dels companys de laboratori, apreciadíssims amics Alí, Amàia, Isabel, Rosa, Marta, Olga, Esther i Eugeni amb vosaltres he compartit intenses jornades de feïna amenitzades amb l'estoneta del cafè...quan arribava ('si, si ara vinc!'), reunions de grups, sopars, congressos, la confecció d'un àlbum de fotos,

canvis de parers, rialles....i en alguns casos una amistat que, espero, duri malgrat la distància. Sou genials!

No puc deixar de recordar el Pedro i el Lluís que, molt amablament, van donar-me un cop de mà en els meus inicis. I amb els qui vaig disfrutar d'estones molt divertides. Ni als que han vingut de passada pel laboratori deixant un inoblidable record com Jos, Serenella, Elisa i altres. Ni a la Raquel, sempre davant de l'ordinador al seminari des de primera hora del matí.

A tots agraeixo els vostres consells i el vostre ajut. Sincerament, us tinc una gran estima.

Jesús, molt bona sort en aquesta nova empresa: la teva tesi, que tot just ara comences juntament amb la Clara, la Bianca i la Yvette (també us desitjo el millor a vosaltres). Moltes gràcies per la teva paciència i col·laboració. Ha estat un plaer treballar amb tu. Som un equip!!!.

També voldria agrair a tots els doctors de l'àrea el seu suport per formar part del grup. Especialment, a l'Anna i l'Arantxa, amb les que he disfrutat de llargues xerrades i he disposat de la seva ajuda al laboratori i que no puc deixar d'agrair.

Al llarg de la tesi he tingut l'oportunitat de treballar amb l'Elias (l'home pacient) i l'Elena (l'energia personificada). M'ho he passat molt bé nois! i ha estat un plaer, gràcies per la vostra dedicació. Faig extensible la meva gratitud a en Carles Bó i al grup de Castelló (Macarena i Eduardo Peris).

Ramon i Francesc, sense la vostra feina aquesta tesi tampoc hagués anat enlloc. Us agraeixo la vostra paciència i disponibilitat. I admiro el vostre bon taranna. Gràcies amics.

I would like to thank Dr John M. Brown to allow me to work in your research group. I spent there a very wonderful period of my thesis and I have happy memory of all the members of your group, specially of Jasotha, Simona and Christophe with I am very grateful for.

Aprofito per agrair a tots els meus amics que tant s'han interessat per la meva feina sempre amb un bon consell. Especialment, a la Sílvia. I a la Tere, juntament amb el Jordi i la Núria, pels seus ànims.

Aquesta tesi no hagués tingut cap sentit per a mi sense el suport i l'estima dels meus pares i el meu germà. No tinc paraules per expressar tot el que sento. No

sé com expressar-vos l'emoció que tinc mentre escric aquestes línies. Sé que ja ho sabeu. GRÀCIES en majúscules per tot. Us estimo molt.

I finalment, moltíssimes gràcies a tu, Robert. Per la teva paciència i comprensió. Pels ànims. Per estar sempre quan et necessitava, tot i els moments més durs. Ho saps, oi?, jo també.

Disculpeu-me si m'he deixat algú. Una vegada més gràcies.

Anna

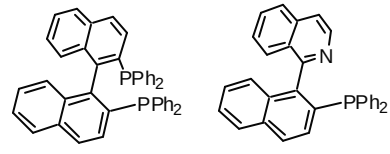
Chapter 2

Catalytic asymmetric hydroboration reaction of vinylarenes

Knowledge of the catalytic cycle of a reaction, makes it possible to understand the activity and selectivity of the catalytic system and the role of the substrates and reagents. For this reason, it is necessary to make an effort to find out more about the reaction mechanism. Unfortunately, this is not an easy task and it is sometimes difficult to acquire date, partly because of the low stability of intermediates. This chapter attempts to rationalise the unpredictability of the transition metal-catalysed asymmetric hydroboration of vinylarenes when the following elements are varied: the electronic nature of the precursor catalyst ([M(cod)(L,L)]BF_4, [M(μ-Cl)(cod)]$_2$/(L,L)), the ligand ((L,L)= (R)-Binap and (R)-Quinap), the metal (M=Rh and Ir) and the hydroborating reagent (catecholborane, pinacolborane). In addition, we investigate the origin of regio- and stereoselectivity on basis to multinuclear NMR spectroscopic studies in agreement with studies based on DFT calculations and QM/MM strategies [1].

1. Introduction

The catalytic asymmetric hydroboration reaction provides a way of transforming alkenes into many different types of C*-X and C*-R bonds via the optically enriched organoboron adduct C*-B. Burgess and Ohlmeyer developed the first catalytic asymmetric hydroboration of olefins in 1988, using rhodium catalyst complexes modified with various diphosphine chiral ligands [2]. However, the potential power of asymmetric catalysts for synthesizing added-value products justifies its development, which is of central importance in modern science and technology [3]. Stereochemical control is derived from the reagent rather than from the catalyst in very few cases. Only, when a reagent is readily and economically available in enantiomerically pure form, does reagent-controlled asymmetric catalysis become a reasonable objective [4]. Generally, asymmetric catalysts are based on transition metal complexes bearing chiral ligands [5]. Homotopic atropoisomeric-type ligands such as Binap (**25**) (Figure 1) [6], which are extremely valuable in a number of reactions, and heterotopic ligands, such as the (P,N) ligand Quinap (**28**) [7], (Figure 1), have made efficient enantioselective synthesis possible in several homogeneous catalytic reactions. Nevertheless, there is no general solution for dealing with asymmetric transformation, probably because of the dramatic effect on the enantioselectivity of the steric and/or electronic properties of the ligand, substrate and reagent.



25 **28**

Figure 1

The catalytic asymmetric hydroboration reaction of vinylarenes can occur with regiochemical and enantiochemical control [8] to give the corresponding chiral 2-aryl boronate esters. But this reaction is not an exception and, the stereoselectivity

depends mainly on the structure and electronic nature of the ligand coordinated to the metal in the catalytic complex, the substrate, and the hydroborating reagent. The effects provided by the structure of the ligand and the nature of the aryl substituents on the vinylarenes have been studied in an attempt to predict the relative importance of the steric and electronic effects [9], [10]. These studies have provided several conclusions that must be taken into account. One of them, suggests that if heterotopic P,N ligands [8b], [9], [11] modify the rhodium complexes, the enantioselectivity is higher than when homotopic P,P ligands are used [8a]. In addition, the cationic rhodium complexes modified with heterotopic P,N ligands in the asymmetric induction of the hydroboration of a model vinylarene such as styrene may or may not be temperature dependent [8e], [9], [11]. Finally, the electronic nature of the alkenes influences the stereoselectivity to the extent that e.e values seem to obey a linear free energy relationship with Hammett constants [9], [11].

As far as the hydroborating reagent is concerned, the catecholborane seems to be the borane source that has the most favourable effect on the experimental hydroboration reactions, although it is not yet clear exactly why. The following factors, however, may help to explain its performance. The fact that catecholborane is monomeric and coplanar means that it is spatially undemanding; therefore its addition to the metal is without hindrance. Also, the electronic nature of this borane is unusual. The five-ring heterocycle is aromatic and has a significant B-O double bond character, but B-H also shows a pronounced enhanced acidity. On the other hand, the principal problem is the disproportion to BH_3 and the catechol-bridged boronate ester $B_2(C_6H_4O_2)_3$ (**35**) [12].

Several fundamental questions about the source of chirality are largely unsolved: for example, how is chirality transferred to the reactive site and how much chirality is involved? Recently, Zhang et al. reported that the dihedral angles of chiral biaryl ligands influence the enantioselectivity of the asymmetric hydrogenation reaction [13]. Harada et al. found that there was a parabolic relationship between the e.e and the torsion angle of the two-biaryl moieties in the asymmetric Diels-Alder reaction of acrylates with cyclopentadiene using homotopic biaryldiol ligands [14]. In addition, Lipkowitz and col. were able to reproduce exactly the same e.e trend as the one observed by Harada through a measure of chirality content because of continuous

chirality metrics (CCM) [15], [16]. They introduced the idea of chiraphore, which is the part of the molecule responsible for stereoinduction. In fact, they established that a stereoselective catalyst is efficient when its maximum capacity to differentiate between two enantiomers occurs in the reaction site, where the substrate/catalyst interactions are able to discriminate between the reaction pathways leading to one enantiomer or the other.

The nature of the catalytic cycle of the alkene hydroboration using the Wilkinson catalyst $RhCl(PPh_3)_3$ was first reported by Männig and Nöth in 1985 [17], and has been addressed experimentally [18], by means of quantum chemistry methods [19]. It was reviewed recently [20] (Figure 2). They proposed that the catalysed reaction might proceed via oxidative addition of borane to the rhodium (I) centre followed by alkene coordination. Whether the following pathway could be alkene insertion into Rh-H or Rh-B is still controversial, however. In general, all authors seem to agree that the last sequence could be the reductive elimination of the arylboronate ester. Of all the steps considered in this catalytic cycle, the coordination of the alkene to the metal center could be the one controlling the regio- and enantioselectivity.

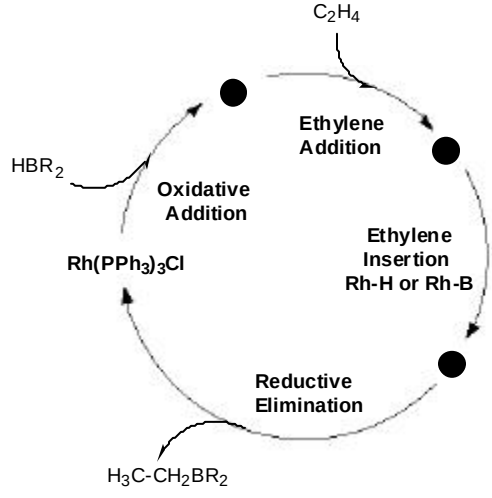


Figure 2

The combination of several techniques, (X-ray crystallography, kinetics and NMR) has enabled to draw a detailed picture of the reaction mechanism of asymmetric hydrogenation. This was partly made possible by the relative stability of some intermediates in the catalytic cycle, such as the key hydridealkylrhodium intermediate.

To the best of our knowledge, only few attempts have been made to characterise intermediates in the hydroboration reaction. These intermediates make it possible for their activity and selectivity to be rationalised. It appears that the true catalytic species are quite transient, at least when catecholborane is used as the hydroborating reagent. Brown et al. [21] proposed as a plausible intermediate a penta-coordinated complex H-Rh/Quinap/catecholborane/vinylarene based on X-ray structural data on the $PdCl_2$(Quinap) complex combined with Chem 3D structures of the borane and alkene. This model assumed that the hydride was in an axial position and coplanar with a coordinated C=C substrate, (Figure 3).

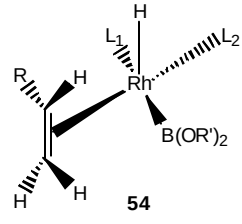


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Figure 3

In addition, this model suggested that the influence of electronic effects on the enantiomeric excess might arise from the potential π-stack formed between the aryl group of the substrate and a nearby P-aryl group of the ligand. Also recently, Chan et al. [11] have suggested that transition-state models, on the basis of the penta-coordinated Rh/H/Pyphos/catecholborane/vinylarene complexes, can explain the electronic effect of modified substrates and/or ligands in asymmetric hydroboration. The latter work, proposed that vinylarenes with electron-releasing substituents coordinate more strongly to the rhodium center than the vinylarenes with electron-withdrawing substituents. The authors speculated that electron-rich substrates may be

closer to the metal than their electron-poor analogues, thus improving stereochemical communication and providing higher enantioselectivity. Although, it is true that interactions between the substrates and the rhodium-ligand-catecholborane complex play an important role, their real nature is still unknown.

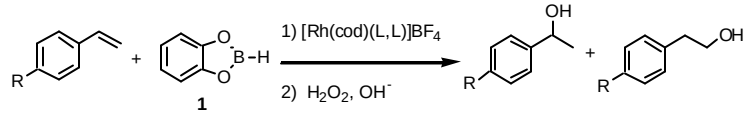
Finally it should be pointed out that the role of the ligand, the substrate and the hydroborating reagent need to be understood, if ligand design is to be free from trial and error approaches and the catalytic system is to perform more predictably after small variations in the reactants and catalysts. This chapter aims to provide more information about these influences and the intermediates involved in the asymmetric catalytic cycle.

2. Results and discussion

2.1. Role of the ligand

We made a comprehensive study of (R)-Binap and (R)-Quinap as ligands, to determine how they affect the hydroboration/oxidation of several electronically different vinylarenes. While the Binap is a homotopic atropoisomeric P,P ligand which chelates with the metal to form a seven-member ring, the heterotopic atropoisomeric P,N Quinap shares a six-member ring with the metal center. Comparing Quinap to its parent ligand Binap, the P,N ligand is less bulky in the region of the isoquinoline because it replaces one of the diphenylphosphinonapthalene moieties. This structural difference, in conjunction with the electronic features of the P,N ligand, may explain why the enantioselectivity in the hydroboration/oxidation of vinylarenes dramatically increases when Quinap is the modifying ligand of Rh(I), (Table 1). P,N ligands that are structurally very similar to Quinap, also behave in a similar way, [7], [8e], [9-10], [22]. The reaction with Binap requires low temperatures for a satisfactory e.e [8a].

Table 1. Influence of the ligand ((L,L)= (R)-Binap, (R)-Quinap) on the asymmetric hydroboration/oxidation of vinylarenes with cationic rhodium complexes.[a]



Conversion > 90%

Entry	Catalytic System	R	Branched	e.e [b] (%)
1	[Rh(cod)(R)-Binap]BF_4	H	99	57
2	[Rh(cod)(R)-Quinap]BF_4	H	95	88
3	[Rh(cod)(R)-Binap]BF_4	Me	99	58
4	[Rh(cod)(R)-Quinap]BF_4	Me	97	89
5	[Rh(cod)(R)-Binap]BF_4	F	99	57
6	[Rh(cod)(R)-Quinap]BF_4	F	96	80

[a] Standard conditions: substrate/borane/Rh complex = 1/1.1/0.01. Solvent: THF. T: 25^0C. Time: 1h. [b] (R) Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm.

In order to study the specific effects of the ligands on the catalytic hydroboration of electronically different vinylarenes, a model must be established for the rhodium intermediate that is responsible for the diastereoselection. Several theoretical studies into the catalysed olefin hydroboration reaction have used model ligands, (i.e. PH_3, and model hydroboration reagents, H-$B(OH)_2$ [19-20]), and dealt with whether the mechanism is *associative* or *dissociative* with regards to phosphine, and whether alkene is inserted through hydride or boryl migration. However, several studies agree that the first step in the catalytic cycle is the oxidative addition of H-$B(OR)_2$ to the Rh centre in $RhCl(PPh_3)_3$, yielding a penta-coordinated hydroboryl complex such as [$RhL_2HCl(B(OR)_2)$], where L=PH_3, PMe_3, P^iPr_3, PPh_3, (Figure 4), [17-18], [23].

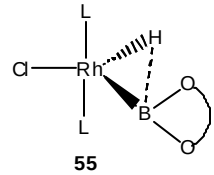


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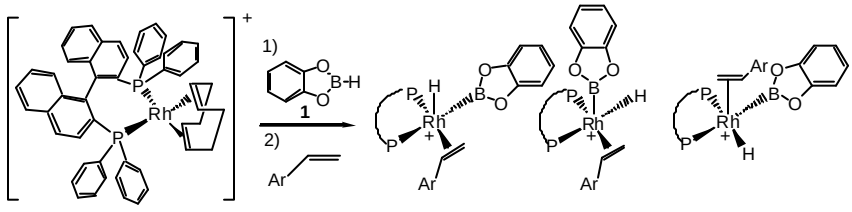
Figure 4

Very few of the metal-boryl complexes isolated from the oxidative addition of H-B(OR)$_2$ to metal complexes [24], have involved rhodium complexes [25]. In addition, there are serious difficulties in isolating rhodium intermediate species during the fast hydroboration reaction, where the chiral ligand, the hydride, the boryl and the olefin are coordinated to the metal. All these events have limited the determination of reaction intermediates in comparison with other metal complexes [26].

In an attempt to clarify the nature of the key intermediates in the hydroboration reaction, we performed a multinuclear NMR spectroscopic study of styrene and catecholborane addition to the catalyst precursor [Rh(cod)(L,L)]BF$_4$, where (L,L)= (R)-Binap and (R)-Quinap. When the ligand is Binap, several different isomers were formed from the stoichiometric addition of catecholborane and styrene to the [Rh(cod)(R)-Binap]BF$_4$ complex, (Scheme 1).



56 **57** **58** **59**

Scheme 1

Initially, the ^{1}H NMR spectra of free catecholborane carried out in CD_3CN showed a quadruplet centred at 4.25ppm ($J_{H\text{-}B}$=197.2Hz), due to the H bonded to B (spin 3/2, 80.4%, natural abundance, spin 3, 19.6%, natural abundance). After the borane reagent and styrene had been added to complex **56**, the resonances of the hydride ligand appeared as an upfield shift centred at δ=-14.51ppm as a double doublet of doublets, (Figure 5(a)). The three coupling constants, $J_{H\text{-}Rh}$=18Hz, $J_{H\text{-}P}$=14Hz, $J_{H\text{-}P}$= 9Hz, are indicative of the hydride position *cis* to two non-equivalent phosphorous nuclei. It is known that the hydride located *trans* to phosphorous is associated with higher coupling constant values ($J_{H\text{-}P(trans)}$=110-130Hz). A selective ^{31}P decoupling experiment significantly simplified the hydride signal in the ^{1}H NMR, which

showed a broad doublet centred at the same chemical shift δ=-14.51 ppm. The inequivalence of the phosphorous nuclei may be because one P is *trans* to the catecholboryl, while the other is *trans* to the styrene. The experiment suggests to us the plausible formation of isomer **57**, (Scheme 1). The ^{11}B and the ^{31}P NMR spectra confirm this arrangement. The initial doublet due to the B bonded to H in free catecholborane, (δ=28.88ppm, J_{H-B}=197.2Hz), was shifted upfield as a broad resonance (δ=21.40ppm) after catecholborane and styrene were added to the metal complex. $^{31}P\{^{1}H\}$ NMR spectra in d^{8}-THF, also showed a significant shift from the initial doublet centred at δ=26.15ppm (J_{P-Rh}=145.5Hz), in the [Rh(cod)(R)-Binap]BF_4 complex, to two new doublets centred at δ=46.93ppm (J_{P-Rh}=207.8Hz) and δ=46.70ppm (J_{P-Rh}=207.8Hz) (Figure 5(b)). Similar resonances have been observed in the literature by monitoring ^{1}H NMR and ^{31}P NMR spectroscopy after catecholborane oxidative addition reaction on [IrX(CO)(P,P)], (where (P,P)= dppe, chiraphos), [27].

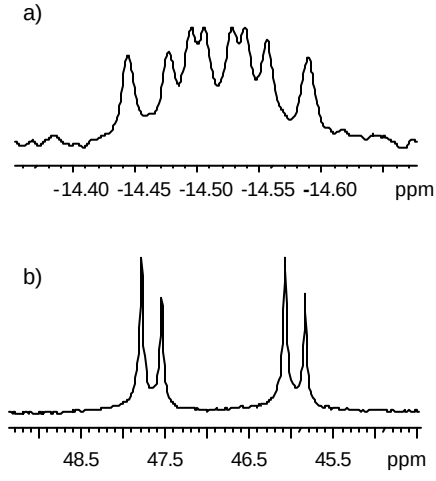
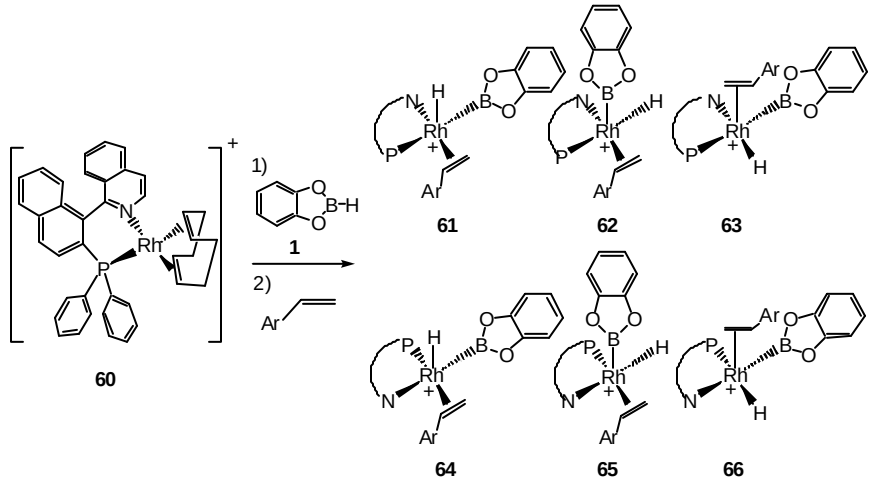


Figure 5.

New NMR signals appeared after catechol-borane and styrene had been added to complex **56** (a) hydride signal in ^{1}H NMR; (b) ^{31}P NMR.

Styrene coordination to rhodium was confirmed by the upfield shift of the alkene hydrogen signals from δ=5.22, 5.73ppm in free styrene to δ=4.82, 5.43ppm in the rhodium isomer formed.

What is more, the *cis* addition of catecholborane and styrene to [Rh(cod)(R)-Quinap]BF_4, may involve the formation of a larger number of isomers, (Scheme 2). We tried to monitor the ^{1}H, ^{11}B and ^{31}P NMR spectra of the *cis* addition of catecholborane and styrene on the [Rh(cod)(R)-Quinap]BF_4 complex, but no hydride signals appeared upfielded in the ^{1}H NMR spectra. The most significant features observed were, first, the slight shift in the initial doublet in the ^{31}P NMR, from δ=32.67ppm, ($J_{P\text{-}Rh}$=140.8Hz) in [Rh(cod)(R)-Quinap]BF_4, upfielded to δ=32.25ppm, ($J_{P\text{-}Rh}$=140.7Hz); and second, the displacement of both signals due to H and B nuclei from free catecholborane, which indicates that the borane reagent was no longer free. We suggest on the basis of literature precedent [24a], [28-29] that, alternatively, a three-centre bonding interaction between Rh-B-H might have taken place. Although we could not demonstrate that a particular isomer was formed after the *cis* addition of catecholborane and styrene to [Rh(cod)(R)-Quinap]BF_4, we assumed that the key intermediate could be any of the isomers shown in Scheme 2, by analogy with the Rh-Binap analogue catalytic system. Brown [9] and Chang [11] suggested that the key intermediate in this case, would probably be **61**.



Scheme 2

One must consider at this point the nature of the stereodefining step in the catalytic cycle. Brown et al. [9], proposed that the coordination step of the alkene to rhodium is not necessarily the stereodefining event but that the insertion step could be. Indeed, Rh-C bond formation is one of the most electronically and sterically demanding steps in the catalytic cycle, but unfortunately the insertion of the alkene through boryl and hydride migration is still not clear. Arguments in favour of boryl migration are given by Ziegler et al. [18c], [19a, c], although the new C-B coupling could provide undesired by products. In contrast, Evans et al. [18a, b], [19b], [30], suggest that hydride insertion is preferred and even favoured if sterically demanding electron-withdrawing ligands are used. In this context, we believe that the insertion step is not the key determining step for regio- and enantioselectivity. The stereochemistry of the final product is probably determined in a previous step such as the one in which the olefin coordinates to the metal and generates intermediates **61** and **57**. The complete picture for the asymmetric induction could involve the consecutive sequences for the alkene like coordination + insertion. For instance, a non prochiral alkene such as acenaphthene reacts enantioselectively (e.e = 86% with [Rh(cod)(S)-Quinap]BF_4, [9]) as a result of the different chemical environment in its approach to the metal center, (Figure 6).

As part of a joint project, the parallel studies made by Bo and Daura, using DFT calculations and QM/MM strategies, were in excellent agreement with the trend of our experimental results [1]. These calculations allow us to study the origin of regio- and stereoselectivity in the rhodium-catalyzed hydroboration reaction of vinylarenes, and the role of the steric and/or electronic features of the ligand. Although this theoretical study does not come within the scope of this thesis, their results complement our own experimental studies. Therefore, some of their most important results are also included in the present discussion.

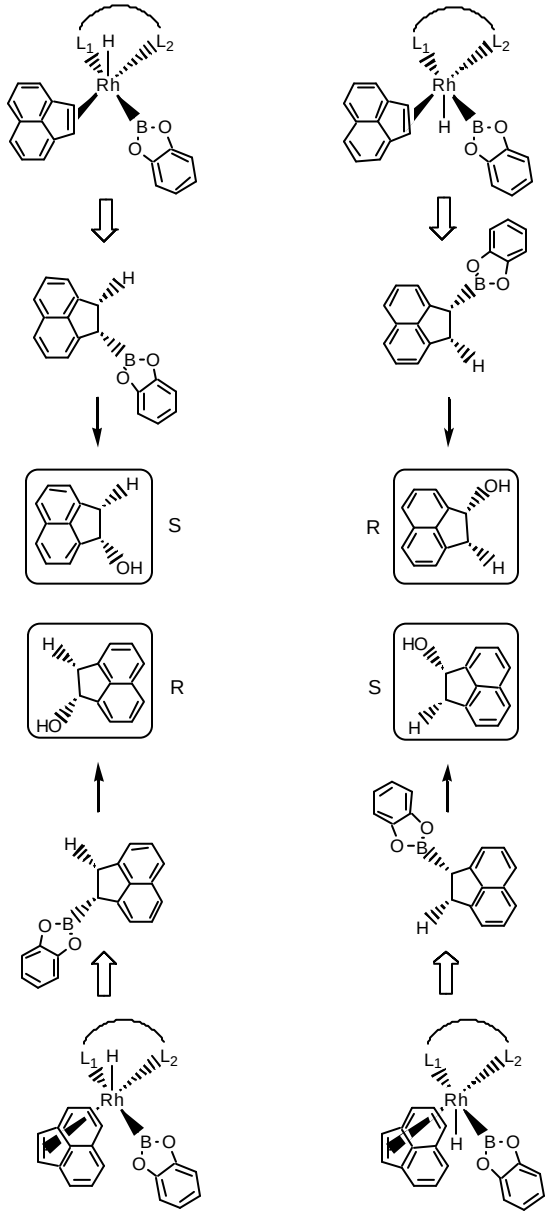


Figure 6

Bo and Daura assumed that the relative stability of the possible isomers was directly related to their population and, therefore, the most stable isomers were those that determined the reaction outcome. At this point, it should be pointed out that the isomers were distinguished by the different interactions between the substrate and the catalyst. The most stable isomer, then, should determine the reaction outcome, thus demonstrating that the coordination of the alkene to the metal center is the stereodefining step. On the basis of our experimental results from the NMR data, the computational modelling study was focused on the squared-pyramid based intermediates type **61** ((L,L) = Quinap) and **57** ((L,L)= Binap), where the hydrido ligand was located up side (Figure 7, Group A) or down side (Figure 7, Group B).

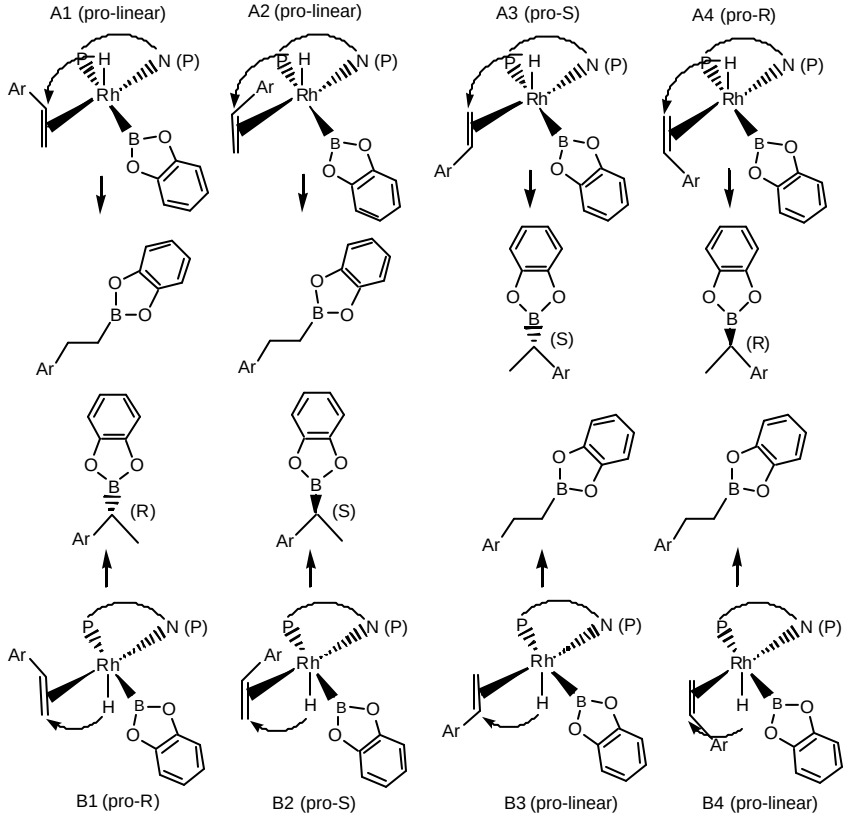


Figure 7

From all the eight isomers associated with the relative coordination of the alkene in relation to the Rh-hydride complex, pro-linear intermediates appeared at relative energy values that were higher than those of pro-branched intermediates, favouring the expected branched products. As far as the enantioselectivity is concerned, when (L,L)= Quinap and the alkene= styrene, the pro-R (B1) and pro-S (B2) isomers were the two most stable forms, with an energy difference of 4.1 kcal.mol^{-1}. However, when (L,L)= Binap, the second most stable isomer after the pro-R (B1) intermediate was found to be the pro-S (A3) with an energy difference of 0.3 kcal.mol^{-1}.

Such a small difference in energy has been shown by Bo and Daura to explain the lower stereodifferentiation of the P,P ligand. In addition, an analysis of the intermolecular interactions revealed that intermolecular π-π stacking interactions between the substrate and the ligand, the substrate and the hydroborating reagent, and the hydroborating reagent and the ligand, could be the reason for the relative stability of the key intermediates.

These theoretical predictions agree with the catalytic experimental data, and also with some of the data reported in the literature where stereodifferentiation becomes temperature dependent in related chiral P,N ligands, [1b]. This is the case for rhodium complexes modified with the atropoisomeric ligand Pyphos (**31**) [11], (2-(2'-diphenylphosphino-4',6'-di-*tert*-butyl-1'-phenyl)-3-methyl-pyridine), which requires temperatures around 0 ^{0}C to provide enantiomeric excess values comparable to the Rh-Quinap in the hydroboration/oxidation of vinylarenes, (Figure 8).

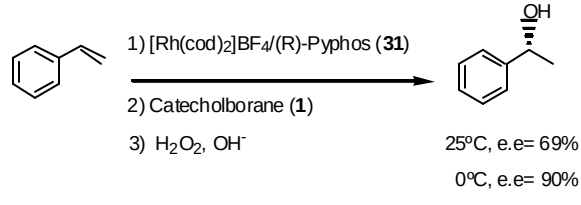
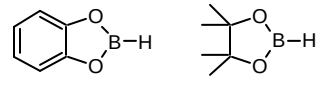


Figure 8

2.2. The role of the hydroborating reagent

The oxidative addition of the hydroborating reagent is considered to be one of the first steps in the catalytic cycle of the hydroboration reaction. Two events are essential to the success of this step: a basic ligand must modify the catalytic system, and the hydroborating reagent must have a boron atom that is sufficiently Lewis-acidic to be catalytically activated for the B-H addition. If we focus on the reagent, diorganyloxyboranes H-B(RO)$_2$ and in particular those which are cyclic compounds show an extremely high degree of Lewis acidity, [31]. In this context, catecholborane (**1**) (Figure 9), is one of the most commonly used, probably because it facilitates B-H addition to the metal and the boryl coordinated to the metal has a favourable steric profile. Although, catecholborane has proved to be the most versatile diorganyloxyborane so far, it is still far from ideal, because its intrinsic instability and degradation give rise to complex mixtures of highly active species that are responsible for a number of side reactions during the catalytic reaction, (for example alkene isomerisation, hydrogenation, vinylboronate ester formation [32] and BH_3 addition [12]). To avoid those difficulties, it is recommended to redistill catecholborane just before it is used and, for slow reactions to use solvents that are not sensitive to Lewis acids as toluene instead of tetrahydrofurane. Therefore, alternative hydroborating reagents have to be considered although very few have been isolated. The pinacolborane (**5**), (Figure 9), is another diorganyloxyborane with a five-member ring, but unlike catecholboronate, it is stable and insensitive to moisture. The pinacolborane has been qualitatively tested in the reactivity of transition metal-catalysed hydroboration of alkenes, [12], [33], although to the best of our knowledge its influence on the selectivity has not been reported yet.



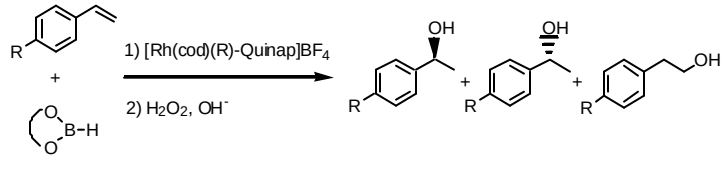
1 **5**

Figure 9

In the present study, we have expanded the scope of the asymmetric hydroboration/oxidation reaction of vinylarenes with pinacolborane as hydroborating reagent.

In general, we found that [Rh(cod)(R)-Quinap]BF_4 as precursor of catalyst, provided slightly higher percentages of the enantioselective branched product when catecholborane is used as hydroborating reagent instead of pinacolborane, (Table 2, entries 1 and 2). This trend is also observed for hydroboration/oxidation of substituted styrenes, such as electron-rich styrenes (Table 2, entries 3 and 4) but not so much for electron poor-styrenes (Table 2, entries 5 and 6).

Table 2. Asymmetric hydroboration/oxidation of vinylarenes towards (R)-(+)-*sec*-alcohol catalysed by [Rh(cod)(R)-Quinap]BF_4 complex and catechol-borane (**1**) or pinacolborane (**5**) as hydroboration reagent.[a]



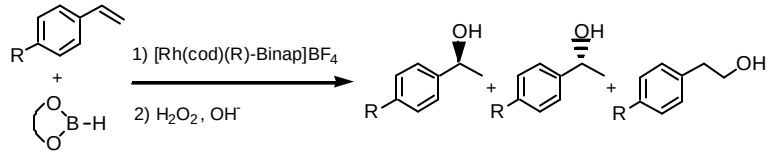
Entry	Borane	R	Yield (%)	Branched (%)	e.e [b] (%)
1	Catecholborane	H	99	95	88
2	Pinacolborane	H	99	75.5	73
3	Catecholborane	Me	98	97	89
4	Pinacolborane	Me	93	91.5	86
5	Catecholborane	F	97	96	80
6	Pinacolborane	F	93	93	83

[a] Standard conditions: substrate/borane/Rh complex = 1/1.1/0.01. Solvent: THF. T: 25^{0}C. Time: 1h. [b] (R) Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm.

When the chiral auxiliary ligand (R)-Binap modified the rhodium complex, the differences in the catalytic activity were notable, starting from the fact that the reactivity

was lower than for [Rh(cod)(R)-Quinap]BF_4. Our preliminary experiments indicated that the hydroboration/oxidation of styrene with pinacolborane provided similar percentages of the primary and the secondary alcohol. Furthermore, we observed a change in the absolute configuration of the branched alcohol when catecholborane was replaced by pinacolborane, which also indicated significant structural differences in the enantioselective step of the catalytic cycle, (Table 3, entries 1 and 2).

Table 3. Asymmetric hydroboration/oxidation of vinylarenes towards *sec*-alcohol catalysed by [Rh(cod)(R)-Binap]BF_4 complex and catecholborane (**1**) or pinacolborane (**5**) as hydroboration reagent.[a]



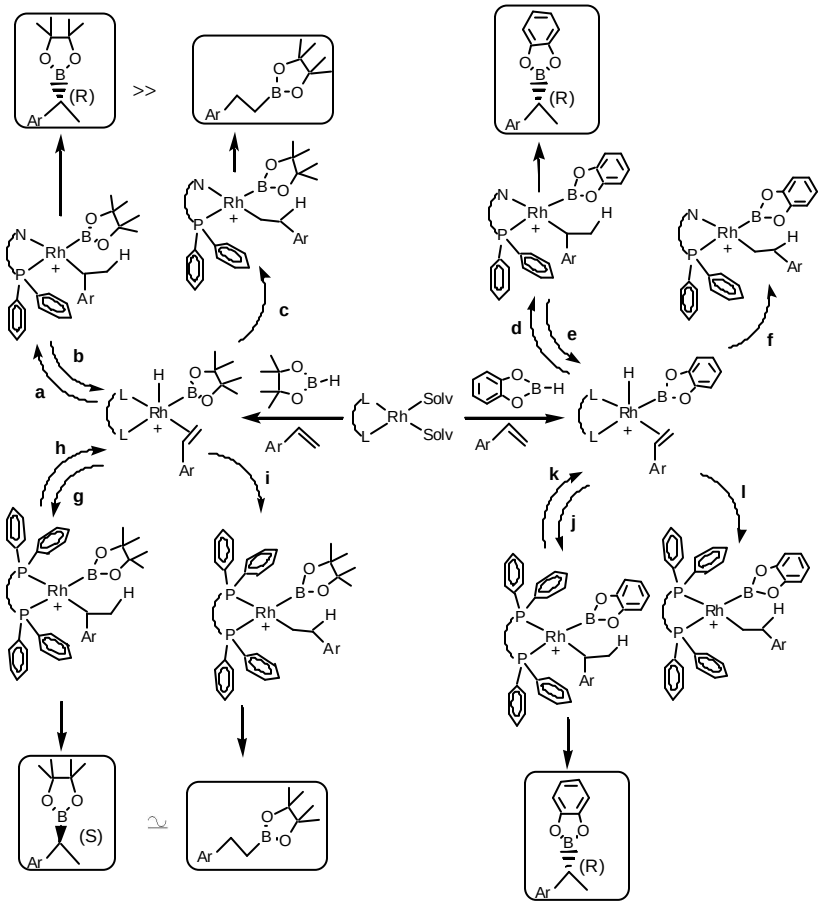
Entry	Borane	R	Yield (%)	Branched (%)	e.e [b] (%)
1	Catecholborane	H	92	99	57(R)
2	Pinacolborane	H	97	50	18(S)
3	Catecholborane	Me	87	99	58(R)
4	Pinacolborane	Me	54	41	16(S)
5	Catecholborane	F	91	99	57(R)
6	Pinacolborane	F	46	46	16(S)
7	Catecholborane	MeO	89	99	60(R)
8	Pinacolborane	MeO	46	58	38(S)
9[c]	Catecholborane	MeO	77	99	70(R)
10[d]	Catecholborane	MeO	25	99	77(R)
11	Catecholborane	Cl	93	99	65(R)
12	Pinacolborane	Cl	71	45	4(S)

[a] Standard conditions: substrate/borane/Rh complex = 1/1.1/0.01. Solvent: THF. T: 25^0C. Time: 1h; [b] Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm; [c] Temperature: 0^0C; [d] Temperature: -78^0C.

Because of these results, we explored the catalytic hydroboration/oxidation reaction of substituted styrenes, and we also observed attenuated regioselectivity and reversed enantioselectivity, (Table 3). Significant changes were observed for the corresponding *p*-MeO-styrene: e.e values were around 60% for the (R)-(+)-*sec*-alcohol with catecholborane and 38% for the (S)-(-)-*sec*-alcohol with pinacolborane, (Table 3, entries 7 and 8). The variation in the configuration is even more pronounced at low temperatures, where a more forced metal-complex is expected, (Table 3, entries 9 and 10).

In order to rationalise the influence of the hydroborating reagent on both reactivity and selectivity, we will again take into account the catalytic cycle. After the oxidative addition and alkene coordination steps, the rhodium intermediate complex accommodates both the hydroborating reagent and the alkene itself. One of the most striking differences between both reagents, the catecholborane (**1**) and the pinacolborane (**5**), is that the steric demand of the pinacolborane is higher. It seems that the more crowded environment around the rhodium center carries the lower reactivity and selectivity towards the secondary alcohol, (Scheme 3). The fact that the isoquinoline region of Quinap was more tolerant to the accommodation of pinacolborane meant that the catalytic activity was similar to when catecholborane was used, although small quantities of the primary alcohol were also formed. The favoured η^3-coordination of vinylarenes with the Rh/(R)-Quinap/pinacolborane intermediate, allowed mainly the migratory insertion towards the secondary-alkyl rhodium complex, which eventually provided the Markovnikov alcohol product via reductive elimination, (Scheme 3, path a). The primary insertion observed when pinacolborane is involved could be due to a β-H elimination, (Scheme 3, path b), followed by a primary reinsertion sequence, (Scheme 3, path c). On other hand, when catecholborane is the borane reagent in the Rh/(R)-Quinap intermediate, the almost exclusive formation of the secondary-alkyl complex may proceed at a faster rate than that of β-H elimination (Scheme 3, paths d and e). Analogous behaviour is observed with the use of catecholborane and Rh-(R)-Binap complex, (Scheme 3, path j, k, l). In the reaction of Rh-(R)-Binap and pinacolborane, vinylarenes presumably undergo a more facile β-H elimination (Scheme 3, path h), due to the very sterically congested secondary-alkylrhodium complex following a primary reinsertion sequence, (Scheme 3, path i).

However, we can not rule out the possibility of a direct initial primary insertion of the alkene because of the steric hindrance of the Rh/(R)-Binap/pinacolborane intermediate, followed by reductive elimination, which provides the primary product in competition with the favoured secondary boronate ester. The moderate reactivity of Rh-(R)-Binap/ /pinacolborane with substituted styrenes would be in agreement with this latter assumption.



Scheme 3

Plausible catalytic pathways: oxidative addition of the hydroborating reagent to the rhodium complex followed by the migratory insertion of the alkene into the M-H bond (the migratory insertion of the alkene into the M-B bond could also be considered) and reductive elimination of the alkylboronate esters.

As far as the enantioselectivity is concerned and taking into account the experimental data, the reversal in enantioselectivity between Rh/(R)-Quinap/ /pinacolborane and Rh/(R)-Binap/pinacolborane has to be highlighted. Therefore, the data must be analysed further if the influence of these hydroborating reagents on the asymmetric induction is to be understood.

Again, Bo's and Daura's parallel studies with DFT calculations and QM/MM strategies were in excellent agreement with the trend of our experimental results [1b]. As that used in the previous theoretical studies all eight possible isomers (Figure 7, A1-A4, B1-B4) were considered in the search for the most stable isomer of the metal complexes Rh/ligand/borane/styrene, (where the ligand was (R)-Quinap and (R)-Binap, and the borane was catecholborane and pinacolborane). Figure 10 shows the relative stability of the most stable isomeric forms in agreement with the experimental data, and it shows the following:

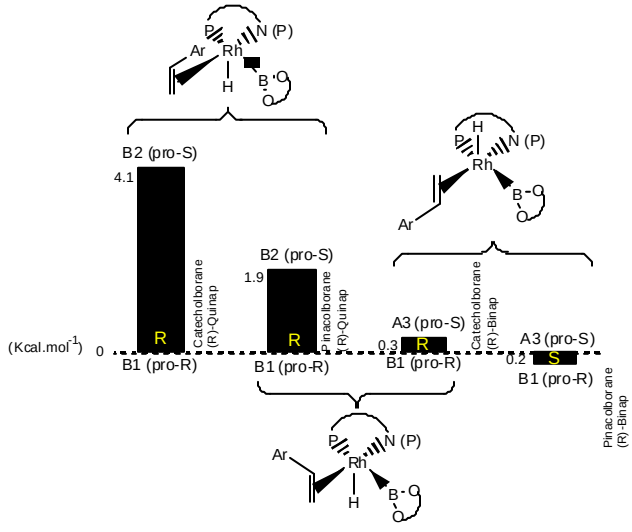


Figure 10

a) The difference between isomer B1 (pro-R) and B2 (pro-S) decreased from 4.1 to 1.9 when catecholborane was substituted with pinacolborane. This may explain the decrease in the enantiomeric excess observed with this hydroboration reagent exchange, in the hydroboration of styrene catalysed by Rh/(R)-Quinap.

b) For the Rh/(R)-Binap/styrene catalytic systems, the most stable isomer was B1 (pro R) when catecholborane was the hydroborating reagent and A3 (pro-S) when it was pinacolborane. These differences in the most stable isomer, may explain the reverse enantioselectivity observed. The low energy values between the first and the second most stable isomer, also agree with the low asymmetric induction obtained with Rh/(R)-Binap/borane catalytic systems.

Bo and Daura explained the different stabilisations of the isomers by the different π- π stacking interactions between the ligand, the hydroborating reagent and the substrate, [1].

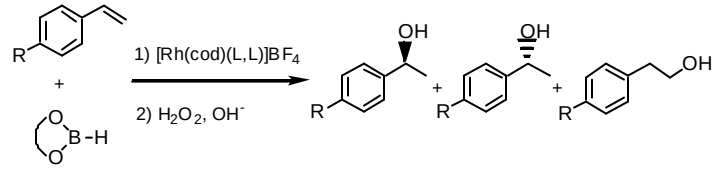
2.3. The role of the substrate

To complete the overall picture of the factors controlling the hydroboration reaction, we examined the reactivity of several other substituted vinylarenes to elucidate the role of substituents on the overall product distribution.

The enantioselectivity observed in the hydroboration/oxidation of substituted styrenes depends significantly on the aryl ring substituents. Brown et al., suggested a simple trend related to the inductive electronic effect of the substituents [9], for the rhodium catalyst complex modified with Quinap and other similar ligands and with catecholborane as the hydroborating reagent. For electron-releasing *para*-substituents, such as methyl, (Table 4, entry 1), enantiodifferentiation is higher than for the electron-withdrawing *para*-substituents, such as fluoride, (Table 4, entry 3). Therefore the enantiomeric excess increased as the electron-releasing character of substituents in styrene increased: *p*-F-styrene < styrene < *p*-Me-styrene.

On the basis of Brown's observation and in order to prove a general tendency associated to the electronic properties of the substrate, we analyzed the electronic effects induced by the *para* substituents of styrene on the Rh/ligand/borane intermediates, (where the ligand was (R)-Binap (**25**) and (R)-Quinap (**28**), and the borane was catecholborane (**1**) and pinacolborane (**5**)), (Table 4).

Table 4. Asymmetric hydroboration/oxidation of substituted vinylarenes towards *sec*-alcohol catalysed by $[Rh(cod)(L,L)]BF_4$ ((L,L)= (R)-Binap (**25**) and (R)-Quinap (**28**)) and catecholborane (**1**) or pinacolborane (**5**) as the hydroboration reagent.[a]



Entry	R	(L,L)	Borane	e.e [b] (%)
1	Me	(R)-Quinap	Catecholborane	89 (R)
2	H	(R)-Quinap	Catecholborane	88 (R)
3	F	(R)-Quinap	Catecholborane	80 (R)
4	Me	(R)-Quinap	Pinacolborane	86 (R)
5	H	(R)-Quinap	Pinacolborane	73 (R)
6	F	(R)-Quinap	Pinacolborane	83 (R)
7	Me	(R)-Binap	Catecholborane	58 (R)
8	H	(R)-Binap	Catecholborane	57 (R)
9	F	(R)-Binap	Catecholborane	57 (R)
10	Me	(R)-Binap	Pinacolborane	16 (S)
11	H	(R)-Binap	Pinacolborane	18 (S)
12	F	(R)-Binap	Pinacolborane	16 (S)

[a] Standard conditions: substrate/borane/Rh complex = 1/1.1/0.01. Solvent: THF. T: 25^0C. Time: 1h. [b] Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm.

A slight tendency in favour of higher asymmetric induction for electron-rich vinylarenes was observed irrespectively of whether catecholborane (Table 4, entries 1-

3) or pinacolborane (Table 4, entries 4-6) was added to [Rh(cod)(R)-Quinap]BF_4. However, at room temperature, the hydroboration carried out with [Rh(cod)(R)-Binap]BF_4 showed no trend when both hydroborating reagents were used. This might be because the Rh-(R)-Quinap complex favours π-π interactions between the more electronically-rich substrates and the ligand or catecholborane/pinacolborane reagent. However, when Rh-(R)-Binap complex is involved in any of these π-π interactions, the differentiation between the isomers of the key rhodium intermediates seems to diminish.

Bo and Daura undertook a deeper analysis [1], to reveal that the difference between the two most stable isomers B1 (pro-R) and B2 (pro-S), increased as the electron-withdrawing character of the styrene substituents decreased, (Figure 11.a).

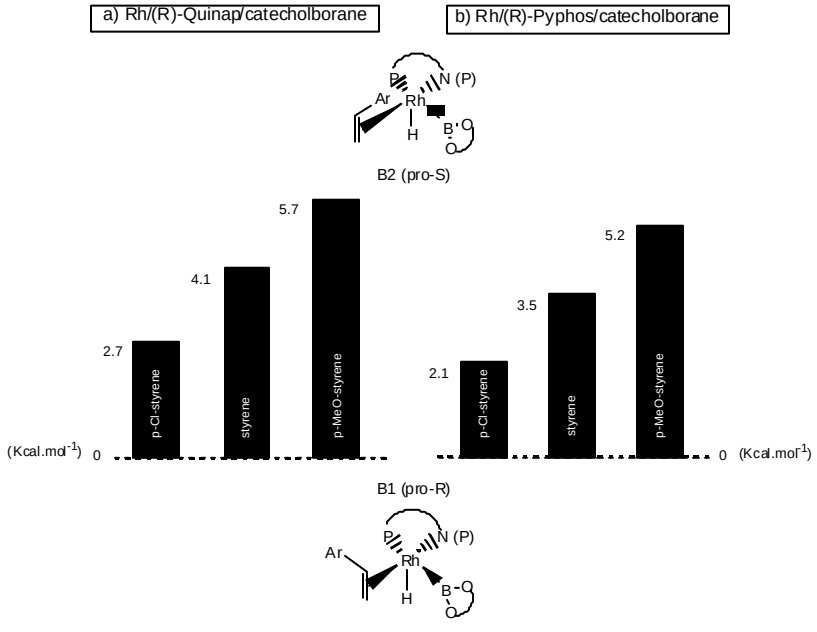


Figure 11

Like the enantiodifferentiation observed in the experimental data, the difference in the relative stability between B1 and B2 also seems to have a clear electronic origin and is therefore related to the nature and strength of the intermolecular π-π interactions observed in the key rhodium intermediates.

Bo and Daura also demonstrated [1] that enantiodifferentiation towards electronically different vinylarenes, may already be present in the rhodium key intermediates, in the hydroboration reaction with the catalytic system Rh-(R)-Pyphos [11]. Thus, the more enantioselective hydroboration/oxidation on the branched alcohol from *p*-Cl-styrene (e.e= 79%), styrene (e.e= 90%) to *p*-MeO-styrene (e.e= 94%), the higher increment in energies between B1 and B2, (Figure 11.b). However, the relative energy values in this series are lower than those for the Rh-(R)-Quinap catalytic system, which should also explain the temperature dependence (0^0C required) in the case of Rh-(R)-Pyphos [11].

2.4. The role of the metal

The catalytic hydroboration reaction is not limited to rhodium complexes [34]. However, the successful enantioselective transformation of vinylarenes, and to a lesser extent of norbornene, has long been restricted to the use of the cationic and neutral complexes of this particular transition metal. Recently, Bonin and Micouin et al. [35] reported an example of the complete reversal of enantioselectivity between Rh and Ir systems in the hydroboration reaction of *meso* hydrazine substrates. This made us wonder when the Ir-Binap catalytic system is also a suitable catalyst for the hydroboration of vinylarenes.

When complex [Ir(cod)(R)-Binap]BF_4 was used under the same hydroboration/oxidation reaction conditions as the analogous rhodium system, (substrate/catecholborane/Ir complex = 1/1.1/0.01, in THF, 25^0C, 1h), conversion was complete but regioselectivity was only about 30% for 1-phenylethanol. The most surprising fact is that enantioselectivity was, under those conditions, almost nil. The Ir/(R)-Binap complex did not seem to induce asymmetry at all and, in addition, there was also a dramatic decrease in the regioselectivity in favour of the linear product, due to the metal exchange.

On trying to rationalise the reversal of regioselectivity shown by the iridium complexes, we came back to the central question of whether the insertion step in the catalytic cycle takes place by hydride migration or boryl migration. In fact, experimental [36] and theoretical studies [29a] have proposed two main catalytic cycles: one of them involves a migratory insertion into the metal-H bond [18a, b], [19b], [30], and the other favours the migration of a boryl group [18c], [19b]. It has also been observed that these two pathways should lead to opposite regioisomers or, in the case of *meso* substrates, enantiomers. It has been postulated [35], that iridium catalysed hydroboration involves the Ir-B migratory insertion step while the rhodium catalysed hydroboration involves the Rh-H migratory insertion, (Figure 12). Those different mechanistic pathways could explain the opposite regioselectivity observed between Ir-Binap and Rh-Binap catalytic systems for our experimental hydroboration reaction.

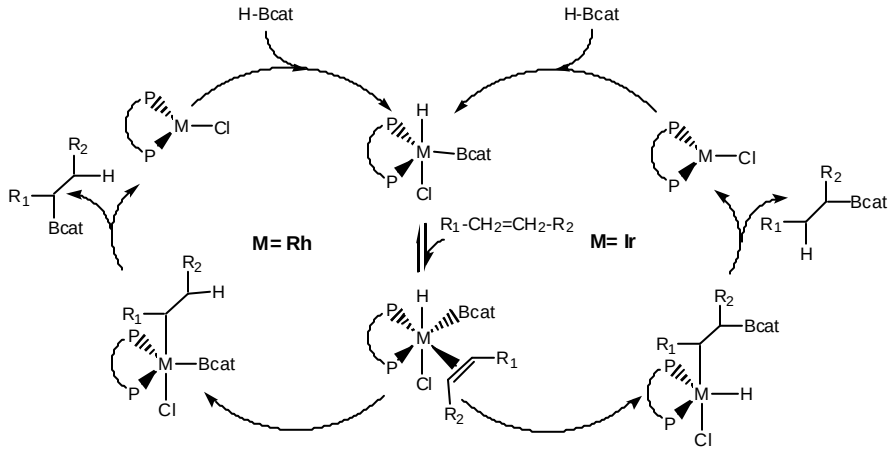


Figure 12

In order to establish why the enantioselectivity is so affected by the change in the metal of the catalytic system, Bo and Daura calculated that the relative stability of the B1 (pro-R) isomer and B2 (pro-S) isomer in both rhodium and iridium key intermediates were significantly different (Figure 13). Again, the nature of the π-π-

stacking interactions provides extra-stabilisation for the B2 isomer in Ir/(L,L) catalytic systems.

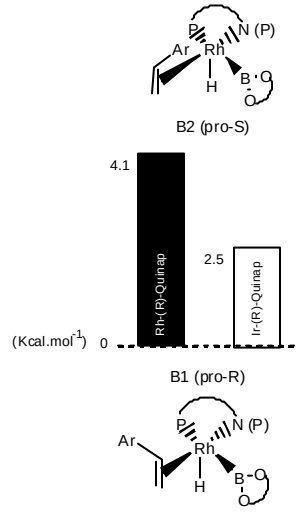


Figure 13

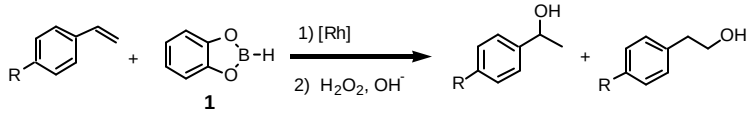
2.5. The influence of the electronic nature of the catalytic system

In view of the fact that both the regio- and the enantioselectivity of the hydroboration of vinylarenes depend heavily on the structural features of the catalysts applied, we felt that it could be interesting to focus on the electronic nature of the rhodium (I) source with a coordinated and non-coordinated counterion.

We made a comparative study of the asymmetric hydroboration of vinylarenes with [Rh(cod)(R)-Quinap]BF_4 and [Rh(μ-Cl)(cod)]$_2$/2eq.(R)-Quinap complexes, (Table 5). Like the cationic catalysts, we noticed a preferential secondary insertion of the styrene into the neutral rhodium complex formed from [Rh(μ-Cl)(cod)]$_2$/2eq.(R)-Quinap. However, the neutral catalytic system seems to have some additional influence and favours the enantioselectivity at values up to 94% for (R)-(+)-1-phenylethanol, (Table 5, entries 1 and 2). Electronically different vinylarenes were selected to study the scope of the neutral catalytic systems. In all cases, for styrenes

with electron-withdrawing and electron-releasing substituents, the neutral catalytic system increased enantioselectivity to values between 91.5% (*p*-F-styrene) and 96% (*p*-MeO-styrene), (Table 5, entries 3-6).

Table 5. Asymmetric hydroboration/oxidation of vinylarenes with catecholborane, towards (R)-sec-alcohol, catalysed by cationic and neutral rhodium complexes [a]



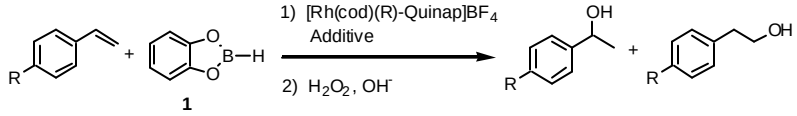
Entry	Catalytic System	R	Yield (%)	Branched (%)	e.e [b] (%)
1	[Rh(cod)(R)-Quinap]BF_4	H	92	95	88
2	[Rh(μ-Cl)(cod)]$_2$/(R)-Quinap	H	99	98	94
3	[Rh(cod)(R)-Quinap]BF_4	MeO	98	96	94
4	[Rh(μ-Cl)(cod)]$_2$/(R)-Quinap	MeO	92	99	96
5	[Rh(cod)(R)-Quinap]BF_4	F	97	96	80
6	[Rh(μ-Cl)(cod)]$_2$/(R)-Quinap	F	98	98	91.5
7	[Rh(cod)(R)-Quinap]BF_4	CF_3	77	95	38
8	[Rh(μ-Cl)(cod)]$_2$/(R)-Quinap	CF_3	72	90	66

[a] Standard conditions: substrate/borane = 1/1.1; cationic complex: 1 mol % [Rh(cod)(R)-Quinap]BF_4; neutral complex: 0.5 mol% [Rh(μ-Cl)(cod)]$_2$/ 2eq. (R)-Quinap. Solvent: THF. T: 25^{0}C. Time: 1h; [b] (R) Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm.

The increase in asymmetric induction was highest in the hydroboration of the electron-poor vinylarene *p*-CF_3-styrene, where the enantioselectivity went from 38% with the cationic system to 66% with the neutral system. One example of improved enantioselectivity with neutral rhodium catalysts is also found in the related literature on the hydroboration of alkenylboronic esters, although the cationic rhodium catalyst provided better yields [37]. Nevertheless, no explanations were provided for these facts.

The neutralizing influence of chlorine as a coordinated counterion was confirmed in a new experiment in which different amounts of the salt $BnMe_3NCl$ were added to the catalytic system [Rh(cod)(R)-Quinap]BF_4, and the products of the hydroboration of styrene were distributed in a very similar way to when the neutral catalytic system was used, (Table 6, entries 1-3). An excess of chlorine does not even seem to be necessary. To obtain more information about the role of the halide in the asymmetric hydroboration reaction of vinylarenes, different additives containing the halide Cl^-, Br^-, I^- were introduced in the hydroboration of *p*-F-styrene, (Table 6, entries 4-6).

Table 6. Influence of the halide on asymmetric hydroboration/oxidation of vinylarenes with catecholborane, towards the (R)-sec-alcohol, catalysed by [Rh(cod)(R)-Quinap]BF_4.[a]



Entry	Additive	R	Yield (%)	Branched (%)	e.e [b] (%)
1	$BnMe_3NCl$ (0.012 mmol)	H	96	95	91
2	$BnMe_3NCl$ (0.03 mmol)	H	98	96	91.5
3	$BnMe_3NCl$ (0.05 mmol)	H	94	96	93
4	$BnMe_3NCl$ (0.03 mmol)	F	95	95	91.5
5	$PhMe_3NBr$ (0.03 mmol)	F	85	97.5	92
6	$PhMe_3NI$ (0.03 mmol)	F	95	95	91.5
7	$BnMe_3NCl$ (0.03 mmol)	CF_3	88	97	74
8	$BnMe_3NCl$ (0.03 mmol)	OMe	89.5	99	98

[a] Standard conditions: substrate/borane/Rh complex = 1/1.1/0.01. Solvent: THF. T: 25°C. Time: 1h; [b] (R) Configuration determined by GC with chiral column FS-Cyclodex β-IP, 50m x 0.25mm.

In the three cases, the increase in enantioselectivity was the same, despite the different electronic and steric factors of the halide. In terms of enantioselectivity,

the benefits of the chloride in the reaction media are very clear in the hydroboration of *p*-CF_3-styrene and *p*-MeO-styrene, (Table 6, entries 7 and 8). When the substrate was *p*-CF_3-styrene, the e.e value was 74%, which is only comparable with the asymmetric induction provided by the cationic rhodium complex modified with the closely heterotopic P,N ligand (S)-(+)-1-(2-di(2-furyl)phosphine-1-naphthyl)isoquinoline [9]. As far as the substrate *p*-MeO-styrene is concerned, its corresponding secondary alcohol was obtained with the highest enantiomeric excess reported so far in the literature, (e.e= 98%).

What is the role of the halide in the asymmetric induction of the hydroboration reaction of vinylarenes? This question leads to other questions about the nature and the structure of the neutral intermediate metal species involved in the catalytic cycle, and their influence on the catalytic activity. Despite the questions that remain unresolved for the hydroboration catalytic cycle, there is general agreement that the oxidative addition of the hydroborating reagent to the rhodium centre could be one of the first steps. The first B-H activation from neutral rhodium complexes was observed by Kono and Ito in 1975. They isolated the hydride-η^1-borylrhodium adduct **32**, [$Rh(PPh_3)_2HCl(Bcat)$], (Figure 14, where Bcat=catecholborane), from Wilkinson's catalyst, [23a].

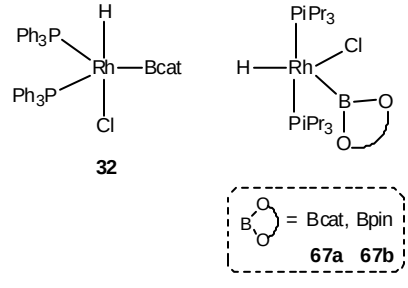


Figure 14

Recently, the relative location of the hydride and boryl in these neutral complexes was confirmed by the complete structural information provided by the analogue complexes [$Rh(P^iPr_3)_2HCl(Bcat)$] **67a** [23b] and [$Rh(P^iPr_3)_2HCl(Bpin)$] **67b**

[38] (Figure 14, where Bcat=catecholborane and Bpin=pinacolborane). However, to the best of our knowledge, the hydride-η^1-borylrhodium intermediates modified with chelating diphosphines have not been characterised and structurally determined. In this context and aimed to know the factors governing borane additions to Rh(I) centres, we studied the stoichiometric oxidative addition of catecholborane to the neutral catalytic system formed from $[Rh(\mu\text{-}Cl)(cod)]_2$ and 2eq. (L,L) (where (L,L)= Binap and Quinap). This study was conducted via multinuclear NMR techniques.

For the five coordinated, 16-electron hydride-η^1-borylrhodium complex formed, we can expect at least either a square-pyramid based (SP) or a trigonal bipyramid (TBP) geometry. However the resonances of the hydride ligand were shifted upfield and centred at δ = -15.82ppm as a double triplet, ($J_{H\text{-}Rh}$= 31.2Hz, $J_{H\text{-}P}$ = 16.2Hz), (Figure 15). This may indicate that the hydride position is cis to two equivalent phosphorous nuclei. The ^{31}P NMR agrees with the postulated equivalence of the phosphorous nuclei due to the unique doublet centered at 44.92ppm, ($J_{P\text{-}Rh}$= 197.8Hz), (Figure 15).

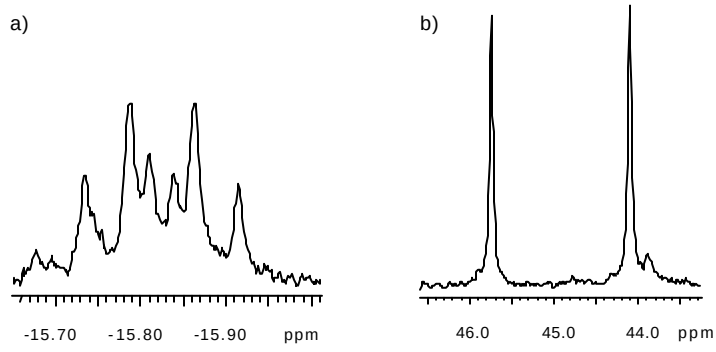


Figure 15.

(a) Hydride signal in the ^1H NMR of complex $[Rh(\mu\text{-}Cl)(cod)]_2$ after the addition of Binap and catecholborane; (b) ^{31}P NMR spectrum of the complex $[Rh(\mu\text{-}Cl)(cod)]_2$ after the addition of Binap and catecholborane.

This oxidative addition was confirmed by ^{11}B NMR, since the initial doublet due to the B bonded to H in free catecholborane (δ= 28.88ppm, $J_{B\text{-}H}$= 197.2Hz), was

shifted to a broad signal centred at δ= 23.20ppm. The equivalence of the phosphorous in the chelating diphosphine could be indicative of a TBP geometry where the bidentate ligand is located in the equatorial plane and the hydride ligand occupies the apical position. Since the hydride resonances are chemically shifted upfield and the oxidative addition of catecholborane is expected to be *cis*, we suggest a complete arrangement around the Rh(III) center, where the halide Cl^- is *trans* to the hydride and the boryl is in the equatorial plane, (Figure 16). Consistent spectroscopic values are also reported in a related study that describes the oxidative addition of catecholborane to [IrCl(CO)(L,L)] complexes, [27]. Taking into account that the following step in the catalytic cycle is the coordination of the alkene to the hydride-η^1-borylrhodium intermediate, we can envisage several different isomers with octahedral geometry. A systematic theoretical study, carried out by Bo and Daura, into the relative energies of these plausible isomers revealed that one of them could be the most stable.

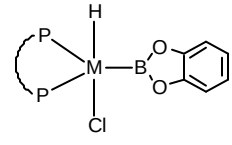


Figure 16

3. Conclusions

An NMR spectroscopic study of the stoichiometric addition of styrene and catecholborane addition to the catalyst precursor, $[Rh(cod)(L,L)]BF_4$ and $[Rh(cod)(\mu\text{-}Cl)]_2$/2eq (L,L), where (L,L)= (R)-Binap and (R)-Quinap, showed structural evidence for the intermediates that may be involved in the catalytic cycle.

A simple trend in the inductive electronic effect of the vinylarenes on the asymmetric induction is observed in the case the rhodium catalyst complex modified with (R)-Quinap and catecholborane or pinacolborane as a hydroborating reagent. The enantiomeric excess of the hydroborated/oxidised products increased as the electron withdrawing character of styrene substituents decreased: *p*-F-styrene < styrene < *p*-Me-styrene. However, this trend can not be extended to the rhodium complex modified with (R)-Binap.

Experimentally we found that the efficiency of the hydroborating reagent heavily depends on the steric factors of the catalytic systems. Thus, pinacolborane (stable and not sensitive to moisture) can be added to vinylarenes with selectivities similar to those of catecholborane, when the catalytic system is based on $[Rh(cod)(R)\text{-Quinap}]BF_4$. In contrast, a notable reversal of enantioselectivity can be achieved by using pinacolborane with $[Rh(cod)(R)\text{-Binap}]BF_4$.

The asymmetric hydroboration reaction catalysed by two transition metals (Rh and Ir), with the same *d* shell electronic configuration, shows considerable differences in both regio- and enantioselectivity. Cationic iridium complexes modified with (R)-Binap provide only 30% of the secondary alcohol with no enantiomeric excess. It would appear that, when the iridium complex is involved, significant steric influences come into play in the interaction between the metal complex, the substrate and the hydroborating reagent.

In addition to the efficiently catalysed hydroboration of vinylarenes by rhodium neutral systems, the enantioselectivity can be significantly enhanced. The beneficial neutralising effect of the coordinated chloride has been observed to come either from the catalyst precursor or from an additive such as R_3NCl. Similar benefits are observed when the nature of the halide is changed, from Cl^-, Br^-, to I^-. The increase in e.e values, which were as high as 98% for the hydroboration of *p*-MeO-styrene, were analysed in greater depth.

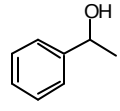
4. Experimental section

General comments. All reactions and handlings were carried out with standard vacuum line techniques under an atmosphere of dry nitrogen. All rhodium and iridium organometallic complexes were synthesised using standard Schlenk techniques. All organic solvents were distilled, stored over molecular sieve (0.4 nm Aldrich), and degassed with a nitrogen flow prior to use. The complexes $[M(\mu\text{-Cl})(cod)]_2$ [39], $[M(cod)_2]BF_4$ [40-41], $[M(cod)(R)\text{-Binap}]BF_4$ [42], (where M=Rh, Ir) and $[Rh(cod)(R)\text{-Quinap}]BF_4$ [9], were prepared as previously reported. They were characterized by elemental analysis, ^1H and ^{31}P NMR, and FTIR. NMR spectra were recorded on a Varian Gemini 300 and Mercury 400 spectrometer. Chemical shifts were reported relative to tetramethylsilane for ^1H as internal reference, 85% H_3PO_4 for ^{31}P and BF_3OEt_2 for ^{11}B as the external reference. Gas chromatographic analyses were performed on a Hewlett-Packard 5890 II with a flame ionisation detector equipped with a chiral column FSCyclodex β-IP, 50m x 0.25mm. Elemental analysis of organometallic complexes was carried out on a Carlo-Erba Microanalyzer EA 1108. IR spectra (range 4000-400cm^{-1}) were recorded on a FTIR MIDAC PROSPECT-IR spectrometer with KBr pellets.

Experimental NMR studies. The stoichiometric addition of styrene and catecholborane to the precursor of catalyst $[Rh(cod)(L,L)]BF_4$ and $[Rh(\mu\text{-Cl})(cod)]$/ 2eq. (L,L), where (L,L) = (R)-Binap and (R)-Quinap, was carried out in CD_3CN solvent and monitored by ^1H, ^{31}P and ^{11}B NMR. An orange solution of the catalyst precursor $[Rh(cod)(L,L)]BF_4$ (0.016 mmol) and $[Rh(\mu\text{-Cl})(cod)]$/2eq. (L,L) (0.08 mmol) in CD_3CN (0.7mL) was prepared under nitrogen in a NMR tube. It was monitored by ^1H and ^{31}P NMR. The styrene (0.016mmol, 1.8μL) was added to the solution of the catalyst precursor under nitrogen. ^1H, ^{31}P NMR spectra were observed. Freshly distilled catecholborane (0.016mmol) was added under nitrogen and then the solution changed colour from yelow to brown. The mixture was monitored by ^1H, ^{31}P and ^{11}B NMR. Previously, ^1H NMR spectrum of styrene and ^{11}B NMR spectrum of freshly distilled catecholborene were carried out in CD_3CN solvent.

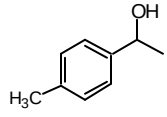
Homogeneous catalytic hydroboration/oxidation of vinylarenes with catecholborane. Vinylarene (2 mmol) was added to a solution of catalyst (1 mol%) inTHF (2 mL) under nitrogen. The solution was stirred for 5 min and freshly distilled catecholborane (2 mmol) was then added. The mixture was stirred at ambient temperature for 1h and then quenched with EtOH (2 mL). Work up was carried out carefully because of the risk of explosion by using peroxides with ether and THF. Afterwards, NaOH (2M, 2mL) and H_2O_2 (2 mL) were added and the mixture was stirred for several hours. The reaction mixture was extracted with Et_2O (3x20) and washed (NaOH 2M, H_2O, saturated brine). The organic extracts were dried over $MgSO_4$, and evaporated under reduced pressure. The products were characterised by NMR, and quantification was carried out by gas chromatography.

Phenylethanol [8a]



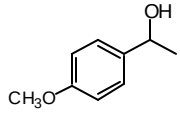
^{1}H RMN δ(ppm)= 7.50-7.20 (m ,5H), 4.55 (q ,$^3J_{H-H}$=6.7Hz, 1H), 1.80(br s, 1H), 1.50 (d ,$^3J_{H-H}$=6.6Hz, 3H).

1-(4-Methylphenyl)ethanol [9]



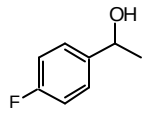
^{1}H RMN δ(ppm)= 7.29 (d ,$^3J_{H-H}$=8.2Hz, 2H), 7.19 (d, $^3J_{H-H}$= =8.2Hz, 2H), 4.86 (q ,$^3J_{H-H}$=6.6Hz, 1H), 2.36 (s, 3H), 1.80(br s, 1H), 1.48 (d ,$^3J_{H-H}$=6.6Hz, 3H).

1-(4-Methoxyphenyl)ethanol [9]



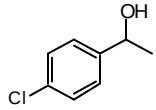
^{1}H RMN δ(ppm)= 7.31 (d ,$^3J_{H-H}$=8.2Hz, 2H), 6.9 (d ,$^3J_{H-H}$= =8.2Hz, 2H), 4.87 (q ,$^3J_{H-H}$=6.5Hz, 1H), 3.82 (s, 3H), 1.74(br s, 1H), 1.48 (d, $^3J_{H-H}$=6.5Hz,3H).

1-(4-Fluorophenyl)ethanol [9]



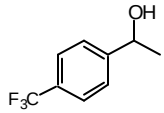
^{1}H RMN δ(ppm)= 7.40-7.10 (m, 4H), 4.86 (q ,$^{3}J_{H-H}$=6.4Hz, 1H), 1.90(br s, 1H), 1.48 (d , $^{3}J_{H-H}$=6.4Hz, 3H).

1-(4-Chlorophenyl)ethanol [9]



^{1}H RMN δ(ppm)= 7.40-7.10 (m, 4H), 4.85 (q ,$^{3}J_{H-H}$=6.6Hz, 1H), 1.70(br s, 1H), 1.47 (d , $^{3}J_{H-H}$=6.6Hz, 3H).

1-(4-Trifluoromethylphenyl)ethanol [9]



^{1}H RMN δ(ppm)= 7.7-7.4 (m, 4H), 4.97 (q ,$^{3}J_{H-H}$=6.6Hz, 1H), 1.80 (br s, 1H), 1.51 (d , $^{3}J_{H-H}$=6.5Hz, 3H).

References

[1] a) E.Daura-Oller, A.M.Segarra, J.M.Poblet, C.Claver, E.Fernández, C.Bo, *J. Org. Chem.* **2004**, *69(8)*, 2669; b) A.M.Segarra, E.Daura-Oller, C.Claver, J.M.Poblet, C.Bo, E.Fernández*, Chem. Eur. J.* **2004** (submitted).

[2] K.Burgess, M.J.Ohlmeyer, *J. Org.Chem.* **1988**, *53*, 5178.

[3] (a) H.B.Kagan, *Asymmetric Synthesis,* J.D.Morrison (Ed.), Academic Press: Orlando **1985**, *vol.5*, 1; (b) K.E.Koenig, *Asymmetric Synthesis,* J.D.Morrison (Ed.), Academic Press: Orlando **1985**, *vol.5*, 71; (c) R.Noyori, M.Kitamura, *Modern Synthetic Methods*, R.Schefford (Ed), Springer-Verlag: Berlin **1989**, *vol.5*, 115; (d) E.N.Jacobsen, A.Pfaltz, H.Yamamoto, (Eds) *Comprehensive Asymmetric Catalysis*, Springer: Berlin **1999**; (e) *Catalytic Asymmetric Synthesis*, Ojima I. (ed), VCH Publishers: New York **2000.**

[4] J.M.Brown, G.C.Lloyd-Jones, *Tetrahedron Asymmetry* **1990**, *1*, 869.

[5] (a) W.S.Knowles, W.C.Christopfel, K.E.Loenig, C.F.Hobbs, *Catalytic Aspects of Metal Phosphine Complex*, E.C.Alyea, D.W.Meek (Eds), American Chemical Society: Washington **1982**, 9325; (b) H.B.Kagan; M.Sasaki, in *The Chemistry of Organophosphorous Compounds*, F.R.Hartley, (Ed), Wiley: New York **1990**, *vol 1*, 53; (c) H.Brunner, *Top. Stereochem* . **1998**, *18*, 129.

[6] (a) A.Miyashita, A.Yasuda, H.Takaya, K.Toriumi, T.Ito, T.Souchi, R.Noyori, *J. Am. Chem. Soc*. **1980**, *102*, 7932; (b) A.Miyashita, H.Takaya, K.Toriumi, T.Souchi, R.Noyori, *Tetrahedron* **1984**, *40*, 1245; (c) H.Takaya, K,Mashima, K.Koyano, M.Yagi, H.Kumobayashi, T.Taketomi, S.Akutagawa, R.Noyori, *J. Org. Chem.* **1986**, *51*, 629; (d) H.Takaya, S.Akutagawa, R.Noyori, *Org. Synth.* **1988**, *67*, 20.

[7] N.W.Alcock, J.M.Brown, D.I.Hulmes, *Tetrahedron: Asymmetry* **1993**, *4*, 743.

[8] (a) T.Hayashi, Y.Matsumoto, Y.Ito, *Tetrahedron: Asymmetry* **1991**, *2*, 601; (b) J.M.Brown, D.I.Hulmes, T.P.Layzell, *J. Chem. Soc., Chem. Commun.* **1993**, 1673; (c) A.Schnyder, A.Togni, U.Wiesly, *Organometallics* **1997**, *16*, 255; (d) I.Beletskaya, A.Pelter, *Tetrahedron* **1997**, *53*, 5957; (e) M.McCarthy, M.Hooper, P.J.Guiry, *Chem. Commun*. **2000**, 1333; (f) S.Demay, F.Volant,

P.Knochel, *Angew. Chem. Int. Ed. Engl*. **2001**, *40*, 1235; (g) C.Bianchini, P.Barbaro, G.Scapacci, *J. Organomet. Chem.* **2001**, *621*, 26.

[9] H.Doucet, E.Fernández, P.T.Layzell, J.M.Brown, *Chem. Eur. J*. **1999**, *5*, 1320.

[10] M.McCarthy, P.J.Guiry, *Tetrahedron* **2001**, *57*, 3809.

[11] F.Y.Kwong, Q.Yang, T.C.W.Mak, A.S.C.Chan, K.S.Chan, *J. Org. Chem.* **2002**, *67*, 2769.

[12] S.A.Westcott, H.P.Blom, T.B.Marder, R.T.Baker, J.C.Calebrese, *Inorg.Chem.* **1993**, *32*, 2175.

[13] Z.Zhang, H.Qian, J.Longmire, X.Zhang, *J. Org. Chem.* **2000**, *65*, 6223.

[14] T.Harada, M.Takeuchi, M.Hatsuda, S.Ueda, A.Oku, *Tetrahedron: Asymmetry* **1996**, *7*, 2479.

[15] D.Gao, D.Schefzick, K.B.Lipkowitz, *J. Am. Chem. Soc.* **1999**, *121*, 9481.

[16] K.B.Lipkowitz, C.A.D'Hue, T.Sakamoto, J.N.Stack, *J. Am. Chem. Soc.* **2002**, *124*, 14255.

[17] D.Männig, H.Nörth, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 878.

[18] (a) D.A.Evans, G.C.Fu, *J. Org. Chem*. **1990**, *55*, 2280; (b) D.A.Evans, G.C.Fu, B.A.Anderson, *J. Am. Chem. Soc*. **1992**, *114*, 6679; (c) K.Burgess, W.A.V.D.Donk, S.A.Westcott, T.B.Marder, R.T.Baker, J.C.Calabrese, *J. Am. Chem. Soc*. **1992**, *114*, 9350.

[19] (a) D.G.Musaev, A.M.Mebel, K.Morokuma, *J. Am. Chem. Soc*. **1994**, *116*, 10693; (b) A.E. Dorigo, P.V.R.Schleyer, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 115; (c) C.Widauer, H.Grützmacher, T.Ziegler, *Organometallics* **2000**, *19*, 2097.

[20] *For review see*: X.Huang, Z.Y.Lin, in *Computational Modeling of Homogeneous Catalysis*, F.Maseras, A.Lledós, (Eds), Kluwer **2002**, 189.

[21] (a) J.M.Brown, H.Doucet, E.Fernández, H.E.Heeres, M.W.Hooper, D.I.Hulmes, F.I.Knight, T.P.Layzell, G.C.Lloyd-Jones, in *Transition Metal Catalysed Reactions*, S.I.Murahashi, S.G.Davies (Eds), Blackwell Science: Oxford **1999**, 465; (b) J.M.Brown, D.I.Hulmes, J.M.Long, J.M.Valk, S.Pearson, D.M.Bayston, A.Goeke, J.M.Muir, W.N.Alcock. http://www.ch.ic.ac.uk/ /ectoc/ectoc-3/.

[22] (a) P.M.Lacey, C.M.McDonell, P.J.Guiry, *Tetrahedron Lett*. **2000**, *41*, 2475; (b) K.Maeda, J.M.Brown, *Chem. Commun.* **2002**, 310; (c) A.Korostylev, I.Gridnev, J.M.Brown, *J. Organomet. Chem.* **2003**, *680*, 329; (d) D.Kiely, P.J.Guiry, *J. Organomet. Chem.* **2003**, *687*, 545; (e) D.Kiely, P.J.Guiry, *Tetrahedron Letters* **2002**, *43*, 9545.

[23] (a) K.Kono, K.Ito, Y.Nagari, *Chemistry Lett.* **1975**, 1095; (b) S.A.Westcott, N.J.Taylor, T.B.Marder, R.T.Baker, N.J.Jones, J.C.Calabrese, *J. Chem. Soc., Chem. Commun.* **1991**, 304.

[24] (a) R.T.Baker, D.W.Overnall, R.L.Harlow, S.A.Westcott; N.J.Taylor, T.B.Marder, *Organometallics* **1990**, *9*, 3028; (b) J.R.Knorr, J.S.Merola, *Organometallics* **1990**, *9*, 3008; (c) J.F.Hartwig, S.Huber, *J. Am. Chem. Soc.* **1993**, *115*, 4908; (d) P.Nguyen, H.P.Blom, S.A.Westcott, N.J.Taylor, T.B.Marder, *J. Am. Chem. Soc.* **1993**, *115*, 9329.

[25] W.H.Lam, S.Shimada, A.S.Batsanow, Z.Lin, T.B.Marder, J.A.Howand, *Organometallics* **1993**, *22*, 4557.

[26] K.Miki, O.Shiotani, Y.Kai, N.Kasai, H.Kanatani, H.Kurosawa, *Organometallics* **1983**, *2*, 585.

[27] B.P.Cleary, R.Eisenberg, *Organometallics* **1995**, *14*, 4525.

[28] R.T.Baker, D.W.Ovenall, J.C.Calabrese, *J. Am. Chem. Soc.* **1990**, *112*, 9399.

[29] (a) P.R.Rablen, J.F.Hartwig, S.P.Nolan, *J. Am. Chem. Soc.* **1994**, *116*, 4121; (b) J.F.Hartwig, S.R.De Gala, *J. Am. Chem. Soc.* **1994**, *116*, 3661; (c) S.Schlecht, J.F.Hartwig, *J. Am. Chem. Soc.* **2000**, *122*, 9435.

[30] D.A.Evans, G.C.Fu, *J. Am. Chem. Soc.* **1991**, *113*, 4042.

[31] A.Lang, H.Nörth, M.Thomann-Albach, *Chem. Ber.* **1997**, *130*, 363.

[32] J.M.Brown, G.C.Lloyd-Jones, *J. Am. Chem. Soc.* **1994**, *116*, 866.

[33] (a) S.Pereira, M.Srebnik, *Organometallics* **1995**, *14*, 3127, (b) S.Pereira, M.Srebnik, *Tetrahedron Letters* **1996**, *37*, 3283.

[34] (a) D.A.Evans, A.R.Muci, R.Stürmer, *J. Org. Chem.* **1993**, *58*, 5307; (b) K.Burgess, M.Jaspers, *Organometallics* **1993**, *12*, 4197; (c) K.N.Harrison, T.J.Marks, *J. Am. Chem. Soc.* **1992**, *114*, 9220.

[35] A.Perez Luna, M.Bonin, L.Micouin, H.Husson, *J. Am. Chem. Soc.* **2002**, *124*, 12098.

[36] H.Wadepohl, *Angew. Chem.* **1997**, *109*, 2547; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2441.

[37] Ch.Wiesauer, W.Weissensteiner, *Tetrahedron: Asymmetry* **1996**, *7*, 5.

[38] S.Shimada, A.S.Barsanov, J.A.Howard, T.B.Marder, *Angew. Chem. Int .Ed.* **2001**, *40(11)*, 2168.

[39] J.Chatt, L.M.Venanzi, *J. Chem. Soc. Part VI* **1957**, 4735.

[40] M.D.Fryzyk, B.Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262.

[41] M.Green, S.H.Kuc, S.H.Taylor, *J. Chem. Soc.* **1971**, 2334.

[42] T.Tani, T.Akutagawa, H.Kumobayashi, T.Taketomi, H.Takaya, A.Miyashita, R.Noyori, S.Otsuka, *J. Am. Chem. Soc.* **1984**, *106*, 5208.

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CERTIFICA:

Que la memòria que du per títol "CATALYTIC ASYMMETRIC HYDROBORATION REACTION OF ALKENES. RECYCLING OF A CATALYST", que presenta Anna M. Segarra González per a optar al grau de Doctor per la Universitat Rovira i Virgili, ha estat realitzada sota la meva direcció en el corresponent Departament de la Universitat Rovira i Virgili.

Tarragona, Abril del 2004

Dra Elena Fernández Gutiérrez