The Development of Enantioselective Rhodium-Catalysed Hydroboration of Olefins

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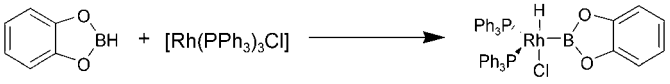
Abstract: Rhodium-catalysed enantioselective hydroboration of olefins is a valuable synthetic transformation, typically employing a chiral catalyst and an achiral borane source. The pertinent chemo-, regio- and enantioselectivity issues of this reaction are discussed. However, the main emphasis of this review is on the evolution of catalytic asymmetric hydroboration. This has primarily relied upon the development and application of chiral bidentate P,P and P,N ligands which have exhibited varying degrees of success in this transformation.

Keywords: asymmetric catalysis; hydroboration; P,N chiral ligands; P,P chiral ligands; mechanistic studies; rhodium

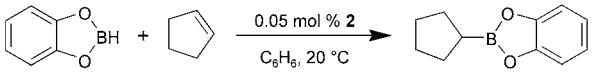
1 Introduction

Hydroboration, the addition of a boron-hydrogen bond across an unsaturated moiety, was first discovered by H. C. Brown in 1956.[1] Usually the reaction does not require a catalyst and the borane reagent, most commonly diborane (B_2H_6) or a borane adduct ($BH_3 \cdot THF$), reacts rapidly at room temperature to afford, after oxidation, the *anti*-Markovnikov alkene hydration product. However, when the boron of the hydroborating agent is bonded to heteroatoms, as is the case in catecholborane (1,3,2-benzodioxaborole; **1**), Scheme 1, the electron density at boron is increased and elevated temperatures are needed for hydroboration to occur.[2,3]



1 2

Scheme 1.



1 3 83%

Scheme 2.

The development of a catalytic hydroboration process was aided by the observation of Kono and Ito in 1975 that Wilkinson's catalyst [$Rh(PPh_3)_3Cl$] (**2**) undergoes oxidative addition when treated with catecholborane (**1**), Scheme 1.[4] Subsequently, Westcott et al. reported the isolation of the oxidative addition adduct with the triisopropylphosphine derivative and its characterisation by X-ray crystallography.[5]

It was another decade, however, before the idea of developing a rhodium-catalysed olefin hydroboration process came to fruition. This occurred in 1985 when Männig and Nöth reported the first examples of such a process.[6] They discovered that Wilkinson's catalyst (**2**) was effective for the addition of catecholborane (**1**) to a range of alkenes and alkynes, as exemplified by cyclopentene (**3**; Scheme 2).

This landmark discovery paved the way for the development of transition metal-catalysed hydroboration. The conversion of an alkene into an organoborane intermediate has made this a valuable synthetic technique, particularly since the development of enantioselective variants.[7,8] The organoboranes produced are important intermediates in many natural product and drug syntheses.[8,9] They serve as synthons for numerous functional

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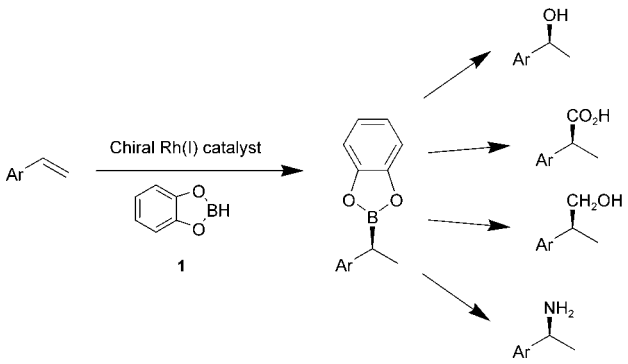
Pat Guiry was born in County Tipperary, Ireland and graduated with an Honours B.Sc. degree in Chemistry from University College Dublin in 1986. He stayed at University College Dublin for his Ph. D. working under the supervision of Professor Dervilla Donnelly on the application of aryllead triacetates to the synthesis of natural products. During his Ph. D. studies he also worked in Marseille in 1988 under the supervision of Dr. Jean-Pierre Finet (Cu-catalysed *N*-arylation) and at Texas A&M in 1989 with Professor Sir Derek Barton (mechanistic studies of arylation/phenol arylation). He received his Ph. D. degree in 1990 and moved to the group of Dr. John Brown FRS at the Dyson Perrins Laboratory, Oxford University for postdoctoral studies in the area of asymmetric catalysis. During this three year stay he was appointed in 1991 as a Tutorial Fellow at Wadham College Oxford and in 1992 as College Lecturer/Director of Studies at St Hughs College Oxford. He returned to University College Dublin as a College Lecturer in 1993 where he started his independent research. His research interests are the design and preparation of chiral ligands and their application in a broad range of asymmetric catalytic transformations. He was a visiting researcher in the group of Professor Andreas Pfaltz at the Max-Planck Institut für Kohlenforschung at Mülheim an der Ruhr (Germany) in 1996. He was the recipient of a President's Research Award in 1996 and a President's Teaching Award in 2000 from University College Dublin. He was promoted to Senior Lecturer in 2002 and to Professor in 2003. He was the Merck Frosst Visiting Professor at the University of Toronto in early 2004. He was appointed as the Chief Executive of the Conway Institute of Biomolecular and Biomedical Sciences at University College Dublin in 2004. A keen tennis player, he represented Ireland in 2005 in the Trabert Cup (ITF World Team Competition) in Perth where he was team captain.

Anne-Marie Carroll was born in County Wexford, Ireland. She studied at University College Dublin receiving her Honours B.Sc. degree in Chemistry in 2000 and was awarded the Eva Philbin and Hugh Ryan medals for obtaining the highest marks in her third and fourth years, respectively. Working in the group of Professor Pat Guiry she has recently completed her Ph. D. in which she researched the use of chiral P,N ligands in asymmetric metal-catalysed processes. She is currently employed in the pharmaceutical industry with GlaxoSmithKline in Cork, Ireland.

Tim O'Sullivan was born in County Kerry, Ireland. He studied at the University of Limerick receiving his Honours B.Sc. degree in Industrial Chemistry in 1997. He subsequently obtained a Ph. D. under the guidance of Professor Lewis Mander at the Research School of Chemistry at the Australian National University focusing on the total synthesis of diterpenoids. He returned to Ireland to work as a postdoctoral fellow with Dr. Mary Meegan in the Department of Pharmaceutical Chemistry, Trinity College Dublin. He is currently employed as a senior postdoctoral fellow at the Centre for Synthesis and Chemical Biology, University College Dublin in the research group of Professor Pat Guiry and is involved in the synthesis of novel Lipoxin analogues.

groups[10] and are often subject to a consecutive carbon-oxygen,[11,12] carbon-carbon,[13–20] boron-carbon,[21,22] boron-chlorine[3] or carbon-nitrogen[23] bond-forming reaction, Scheme 3. Critically, such further functionalisations occur with retention of stereochemistry.

Among recent examples that highlight the synthetic utility of this methodology are its direction towards a formal synthesis of the non-steroidal anti-inflammatory agents Ibuprofen™ and Naproxen™,[13,14,24] as well as the anti-depressant Sertraline.[25] Attempts to expand the range of substrates to include cyclopropenes[19] and norbornene-derived *meso*-bicyclic hydrazines[26] have



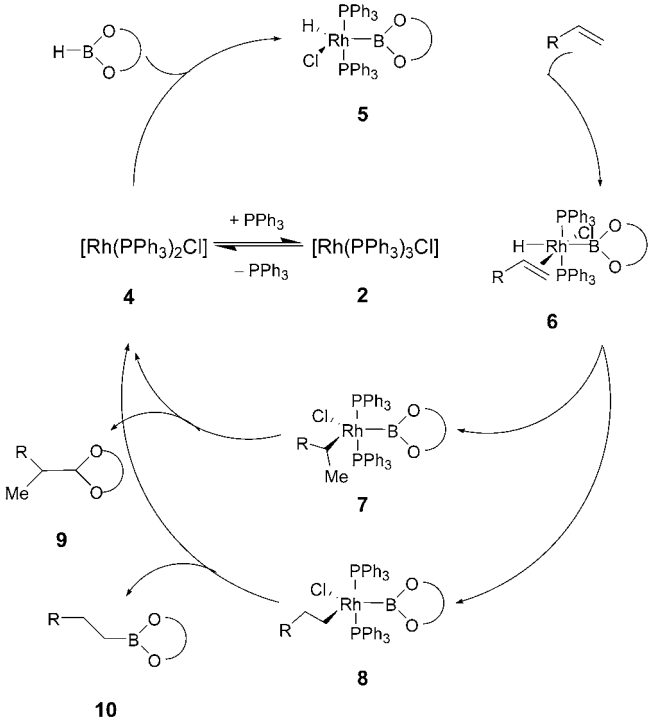
Scheme 3.

recently been reported. A further noteworthy contribution has been the development of a recyclable hydroboration process by the group of Fernández.[27–29] These and other approaches towards extending the synthetic scope of catalytic asymmetric hydroboration have been the subject of recent excellent reviews.[8,30]

Although many metals including lithium,[31] nickel,[32,33] palladium,[34–36] ruthenium,[37] iridium,[38–41] samarium,[42] lanthanum,[42–44] titanium[45] and zirconium[46–48] have been employed in this transformation with varying degrees of success, rhodium has remained the metal of choice. Indeed, it is enantioselective rhodium-catalysed olefin hydroboration that is the subject of this review, which covers the literature up to mid-2004. Firstly, the mechanism of rhodium-catalysed hydroboration will be presented, and the chemo-, regio- and enantioselectivity issues particular to this reaction then addressed. Thereafter, emphasis will be placed on the evolution of catalytic asymmetric hydroboration which has primarily relied upon the development and application of chiral bidentate P,P and P,N ligands.

2 Mechanism of Rhodium-Catalysed Hydroboration

The mechanism of rhodium-catalysed hydroboration, Scheme 4,[49] is thought to depend on the nature of the substrate, the catalyst, the ligand used and the reaction conditions employed.[2,50]



Scheme 4.

The dissociation of a triphenylphosphine ligand from Wilkinson's catalyst (**2**) generates the catalytically active species **4** to which the B–H bond of the borane reagent oxidatively adds to give **5**. The analogous complex with $P(i\text{-}Pr)_3$ rather than PPh_3 has been isolated and structurally characterised by Westcott and co-workers.[5] Coordination of the alkene *trans* to chlorine[51] generates **6**. The hydride and boryl ligands are *trans* in the reactive form of this complex.[52] Subsequent migratory insertion of the alkene into the rhodium-hydride bond produces the regioisomeric alkyl boronate esters **7** and **8**. Upon reductive elimination these give the *anti*-Markovnikov product **9** or the Markovnikov product **10**, respectively, and the catalytic species **4** is regenerated. Supporting evidence for this last step comes from stoichiometric studies of osmium boryl complexes by Roper and Wright.[53] Theoretical studies have suggested that reductive elimination is the slowest step in the overall transformation.[51,52]

Among efforts to elucidate the exact mechanism, Evans has proposed on the basis of deuterium labelling studies that certain steps in the catalytic cycle, namely olefin binding to the rhodium catalyst, as well as subsequent hydride migration, are reversible. However, the level of reversibility is highly substrate-dependent.[54] Parallel deuterium labelling studies by Burgess showed a disparity with the Evans' study,[55] but catalyst contamination by oxidised rhodium species was later shown to be responsible for the discrepancies between the two studies,[56,57] highlighting the critical importance of using freshly prepared catalyst.[58–60] Subsequent mechanistic investigations by Burgess,[49,61] as well as Marder and Baker[62] established that the catalytic cycle can be further complicated by the presence of degradation products of catecholborane, such as hydrogen and diborane for example. As a result, hydrogenation and uncatalysed hydroboration can compete with the potentially useful selectivities of the metal-catalysed variant.[45] Therefore, there have been considerable efforts to find alternative hydroborating agents. These include 4,4,6-trimethyl-1,3,2-dioxaborinane[6] (**11**) and pinacolborane[24,47,48,63–65] (**12**), with emphasis on boron hydrides bearing boron–oxygen bonds,[39] as well as borazine[66,67] (**13**, Figure 1). Despite these endeavours, catecholborane (**1**) is still the most useful borane and rhodium complexes the most useful catalysts for catalytic hydroboration.[68]

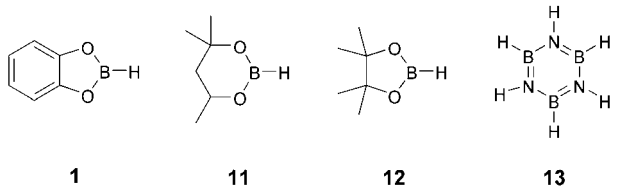


Figure 1.

The original mechanism proposed by Männig and Nöth,[6] and later supported by Evans and Fu,[57] analogous to that established for the corresponding hydrogenation process, is a dissociative mechanism. After oxidative addition of the borane, coordination of the alkene to **5**, Scheme 4, takes place with simultaneous dissociation of one of the PPh_3 ligands. Burgess and co-workers favoured an alternative associative mechanism[49] where the olefin and both PPh_3 ligands are bound to a six-coordinate Rh species **6**, Scheme 4. Hydroboration has also been studied by theoretical methods.[52] In addition, the nature of the catalytic cycle has been addressed experimentally and by means of quantum chemistry methods, and this has been reviewed recently.[69] Dorigo and Schleyer[70] conducted an *ab initio* study of the dissociative mechanism and categorically excluded the possibility of an associative mechanism while Musaev and coworkers favoured the latter process.[51]

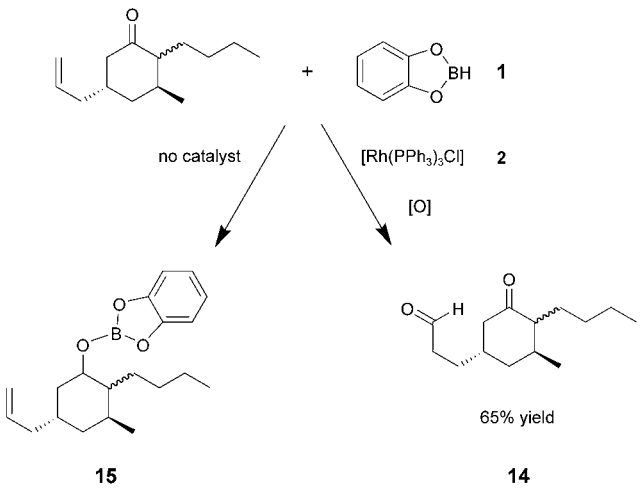
The formation of vinylboranes and vinylboronate esters during some metal-promoted hydroboration of alkenes has led to the suggestion of an alternative mechanistic pathway. Insertion of the alkene into the metal-boron bond of **6** occurs in preference to insertion into the metal-hydride bond.[51,71,72] In a competing side reaction to reductive elimination, β-H elimination from the resulting borylalkyl intermediate furnishes the vinylborane by-product.[73] There remains however a substantial body of evidence, both experimental[74,75] and theoretical,[52,70,76] that supports the idea that transfer of hydride to the coordinated alkene precedes transfer of the boryl fragment.[57]

3 Selectivity of Metal-Catalysed Hydroboration

The application of rhodium-catalysed hydroboration to the preparation of biologically active natural products[9] is a clear indication of its synthetic utility. A marked rate acceleration at room temperature in the presence of small amounts of a metal complex allows previously unreactive or thermally sensitive boranes to be employed. Furthermore, in many cases the chemo-, regio-, and stereoselectivities of the metal-catalysed variant are complementary or superior to those of uncatalysed processes.[45] Developments in this transformation have highlighted each of these facets.

3.1 Chemoselectivity

Männig and Nöth first demonstrated that the use of a catalyst can direct the course of the hydroboration reaction towards a different chemoselectivity than the uncatalysed variant.[6] The functional group selectivity of hydroboration was exploited in the total synthesis of the natural product, (+)-ptilocaulin, which displays antimicrobial activity against both Gram-positive and Gram-negative bacteria as well as significant cytotoxicity towards leukaemia cells.[77] In the presence of Wilkinson's catalyst (**2**), the terminal olefin is preferentially hydroborated over the ketone functionality with catecholborane (**1**) to furnish the desired product **14** in 65% overall yield after hydrogen peroxide and PCC oxidations, Scheme 5. In the absence of catalyst, the ketone is converted to the boronate **15** leaving the olefin unreacted.



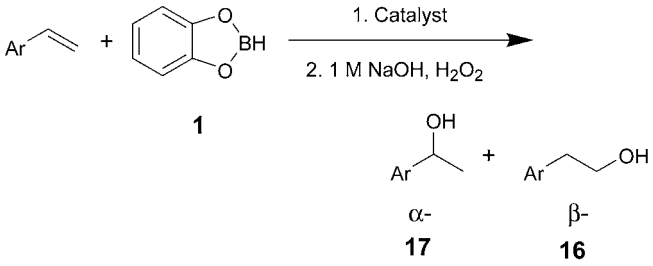
Scheme 5.

3.2 Regioselectivity

The uncatalysed hydroboration-oxidation of an alkene usually affords the *anti*-Markovnikov product while the catalysed version can be induced to produce either Markovnikov or *anti*-Markovnikov products. The regioselectivity obtained with a catalyst has been shown to depend on the ligands attached to the metal and also on the steric and electronic properties of the reacting alkene.[78] In the case of monosubstituted alkenes, (except for vinylarenes), the *anti*-Markovnikov alcohol is obtained as the major product in either the presence or absence of a metal catalyst. However, the difference is that the metal-catalysed reaction with catecholborane proceeds to completion within minutes at room temperature, while extended heating at 90 °C is required for the uncatalysed transformation.[39] It should be noted that there is a reversal of regioselectivity from Markovnikov B–H addition in unfunctionalised terminal olefins to the *anti*-Markovnikov manner in monosubstituted perfluoroalkenes, both in the achiral and chiral versions.[79,80]

In contrast, significant differences in regioselectivity are observed between the catalysed and uncatalysed hydroboration of vinylarenes with catecholborane (**1**; Table 1).

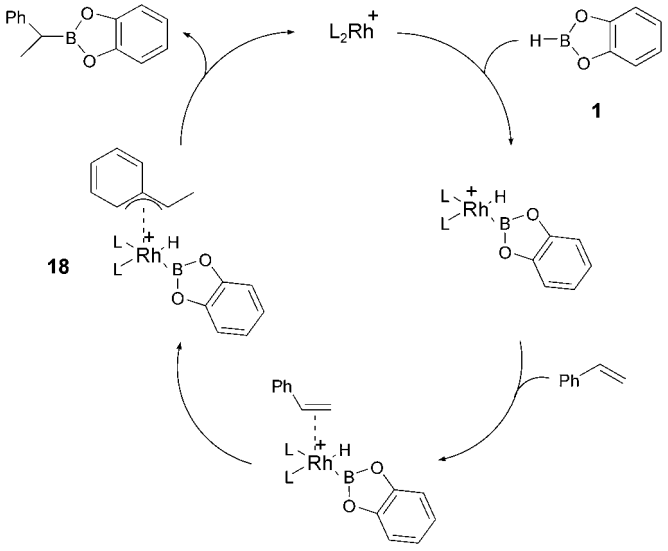
Table 1.



Entry	Catalyst	Substrate (Ar)	α:β
1[81]	None	Ph	8:92
2[82]	$Rh(PPh_3)_3Cl$	Ph	94:6
3[82]	$Rh(PPh_3)_3Cl$	4-Me-Ph	97:3
4[82]	$Rh(PPh_3)_3Cl$	4-Cl-Ph	99:1
5[11]	$Rh(COD)_2BF_4/PPh_3$	Ph	99:1
6[11]	$Rh(COD)_2BF_4$/dppb	Ph	99:1
7[11]	$Rh(COD)_2BF_4$/dppb	4-Cl-Ph	99:1
8[11]	$Rh(COD)_2BF_4$/dppb	4-OMe-Ph	99:1
9[11]	$Rh(COD)_2BF_4$/dppb	Mesityl	63:37
10[11]	$Rh(COD)_2BF_4$/dppb	2-Naphthyl	65:35
11[83]	None[a]	Ph	18:82
12[83]	$RhCl_3 \cdot n\ H_2O$[a]	Ph	17:83

[a] $BH_3 \cdot THF$ as borane source.

In the absence of an Rh catalyst, the linear *anti*-Markovnikov or β-alcohol **16** is formed as the major product, Table 1, entry 1.[81] However, the application of neutral or cationic rhodium complexes favoured the formation of the α-alcohol **17**, entries 2–10, complementary to that of the uncatalysed hydroboration-oxidation. The α-alcohol **17** was formed as the main product using Wilkinson's catalyst (**2**), entries 2–4,[82] although there were inconsistencies in the literature with regard to the product distribution obtained with this catalyst system.[11,54] However, this was resolved when contamination of the catalyst by oxidation was taken into account.[49,57] Using cationic phosphine-rhodium(I) catalysts, Hayashi showed that the regioselectivity was relatively insensitive to the electronic effects of substitution on the aryl ring, entries 5–8,[11] but was influenced by steric effects, entries 9–10.[11] Additionally, the choice of rhodium catalyst requires careful consideration since hydroboration with the rhodium(III) catalyst, $RhCl_3 \cdot n\ H_2O$, yielded the same product ratio as the uncatalysed reaction, entries 11 and 12.[83]



Scheme 6.

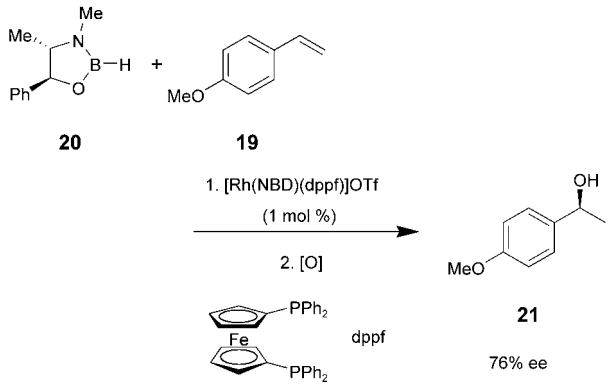
In order to account for the high regioselectivities observed in the rhodium-catalysed hydroboration of styrenes, Hayashi proposed a modified mechanism which proceeds through η^3-benzylrhodium complex **18** as a key intermediate, Scheme 6. Reductive elimination from this η^3-benzylrhodium complex **18** produces the secondary alkylborane regioselectivly.[11] A related η^3-benzylpalladium complex was recently isolated by Hartwig in studies on hydroamination.[84]

3.3 Enantioselectivity

The development of an asymmetric variant of rhodium-catalysed hydroboration was another significant milestone in the evolution of this transformation. The hydroboration-oxidation of substituted alkenes to regioselectively give the Markovnikov product can be used to introduce a chiral centre. In fact, the vast majority of catalytic hydroborations have been applied to the formal synthesis of enantiomerically enriched alcohols by oxidation of the initial catecholborane adduct with basic hydrogen peroxide,[23] although this synthetic scope has been extended to other functionalities.[8] The attractive feature of the catecholborane hydroboration-oxidation sequence is the facile removal of the catechol by-product by simple extraction with aqueous base.

Two methods have been used to incorporate enantiodiscrimination into rhodium-catalysed hydroboration. One such method, reported by J. M. Brown in 1990, involved the use of chiral hydroborating agents derived from ephedrine and pseudoephedrine in conjunction with an achiral catalyst.[85] The hydroboration of *para*-methoxystyrene (**19**) with a pseudoephedrine-derived borane **20** produced the most promising result: an enantiomeric excess of 76% after oxidation, with the α:β ratio 82% in favour of the secondary alcohol **21**, Scheme 7. In other cases, enantioselectivities close to 90% were observed using chiral boron sources, but the general utility of this procedure was limited by poor regiochemical control.[85] Neither did the use of chiral ligands in conjunction with the chiral borane reagents lead to significantly enhanced ees.

Instead, by far the most common approach towards catalytic asymmetric hydroboration is to use a chiral cat-



Scheme 7.

alyst and an achiral borane source. Both homobidentate P,P and heterobidentate P,N ligand classes have been employed in this transformation with varying degrees of success. As far as possible, these ligands will be grouped according to their chirality classification: axial, central or planar. However, divergence from this will unavoidably occur in an effort to chart the evolution of catalytic asymmetric hydroboration.

4 Chiral P,P Ligands

The development of chiral catalysts for use in enantioselective rhodium-catalysed hydroborations was pioneered by Burgess,[7] Suzuki[86] and Hayashi.[11,87] The chiral diphosphine ligands employed in their preliminary investigations, Figure 2, had previously been successfully applied in other catalytic asymmetric transformations.

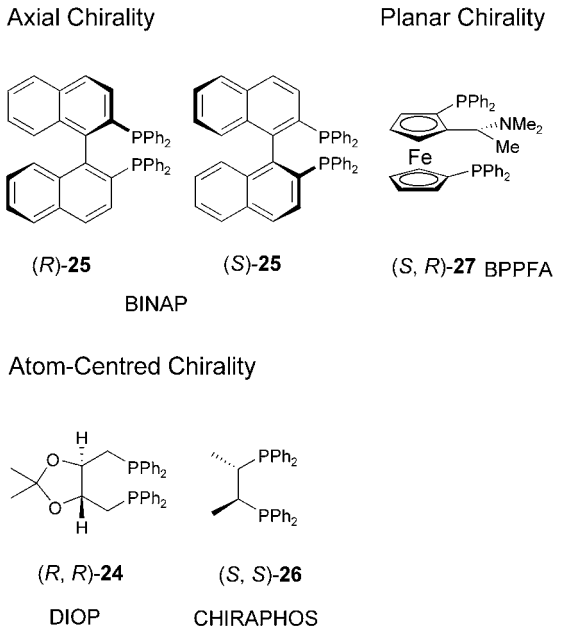
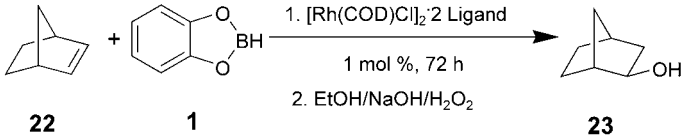


Figure 2.

Table 2.



Entry	Ligand	Temperature [°C]	Solvent	% ee[a]
1	(*R*,*R*)-**24**	40	C_6H_6	23
2	(*R*,*R*)-**24**	5	C_6H_6	31
3	(*R*,*R*)-**24**	−25	THF	57
4	(*R*,*R*)-**24**	−40	THF	55
5	(*R*)-**25**	5	C_6H_6	43
6	(*R*)-**25**	−25	THF	64

[a] Absolute configuration (1*R*,2*R*) in all cases.

Initial probings into enantioselective hydroboration by Burgess[7] centred on norbornene (**22**) as substrate where regioselectivity was not an issue and the results obtained were promising, Table 2.

exo-Norborneol (**23**) was consistently afforded in excellent yields (>90%) upon treatment of norbornene (**22**) with catecholborane (**1**) in the presence of a catalytic amount (1 mol %) of cationic Rh(I) complexes of centrally chiral (*R*,*R*)-DIOP (**24**)[88] or axially chiral (*R*)-BINAP (**25**),[89] Figure 2. Using the Rh/(*R*,*R*)-DIOP (**24**) catalyst system, Burgess found there was an inverse relationship between the asymmetry induced and the reaction temperature, entries 1–3. An initial 23% ee at 40 °C was increased to 31% and 57% ee on decreasing the reaction temperature to 5 and −25 °C, respectively. No significant increase in enantioselectivity was observed by further decreasing the temperature, entry 4, although

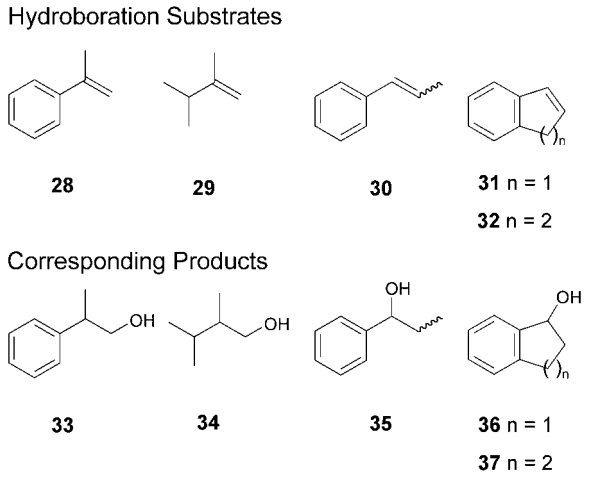


Figure 3.

Table 3.

Entry[a]	Substrate	Ligand[b]	Yield [%]	% ee (Config.)
1	**28**	(*S*,*S*)-**24**	27 (**33**)	38 (*S*)
2	**28**	(*S*)-**25**	73 (**33**)	38 (*S*)
3	**28**	(*S*,*S*)-**26**	31 (**33**)	16 (*S*)
4	**28**	(*S*,*R*)-**27**	23 (**33**)	7 (*R*)
5	**29**	(*S*,*S*)-**24**	29 (**34**)	12 (*S*)
6	(*Z*)-**30**	(*S*,*S*)-**24**	86 (**35**)	47 (*S*)
7	(*E*)-**30**	(*S*,*S*)-**24**	79 (**35**)	41 (*S*)
8	**31**	(*S*,*S*)-**24**	93 (**36**)	58 (*R*)
9	**32**	(*S*,*S*)-**24**	58 (**37**)	14 (*R*)

[a] All reactions were carried out in toluene with 1 mol % of Rh(I) complexes at $-5\,^{\circ}C$ for 72 h.
[b] The catalysts were prepared *in situ* from $[ClRh(ethene)_2]_2$ and 2 equivalents of diphosphine ligands.

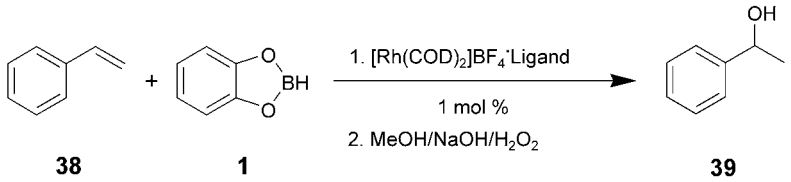
the reduced temperature had no adverse effect on chemical yield.[7] In the corresponding reactions with (*R*)-BINAP (**25**), an optimum enantioselectivity of 64% was obtained, entry 6. Overall, the latter catalyst system was more enantioselective than the Rh/(*R*,*R*)-DIOP (**24**) complex, entries 5 and 6.[7]

Suzuki expanded on Burgess' work, expanding the substrate scope and the chiral ligands employed.[86] In addition to (*S*,*S*)-DIOP (**24**) and (*S*)-BINAP (**25**), the ligands (*S*,*S*)-CHIRAPHOS (**26**)[90] and (*S*,*R*)-BPPFA (**27**),[91] Figure 2, were applied, invoking elements of central and planar chirality, respectively. 1,1-Disubstituted alkenes such as 2-phenylpropene (**28**) and 2,3,3-trimethylprop-1-ene (**29**), as well as internal alkenes like norbornene (**22**), (*Z*)- and (*E*)-1-phenyl-1-propene (**30**), indene (**31**) and 1,2-dihydronaphthalene **32** were among the substrates tested, which gave, after oxidation, the corresponding alcohols **33**–**37**, Figure 3 and Table 3.

Suzuki found that the rate of hydroboration depended on both the substitution pattern of the alkene, and the chiral ligands employed. In general, 1,1-disubstituted alkenes gave a lower yield of *anti*-Markovnikov alcohol after oxidation (<30%), entries 1 and 5, than did internal alkenes: 58–93% of Markovnikov product, entries 6–9, comparing results obtained with (*S*,*S*)-DIOP (**24**). All chiral diphosphine ligands employed were effective, irrespective of the type of chirality present, entries 1–4. However, (*S*,*S*)-DIOP (**24**) was found to induce the highest asymmetry: 58% ee for the hydroboration-oxidation of the cyclic alkene, indene (**31**), entry 8. This was later optimised to 74% ee when the reaction was carried out at $-30\,^{\circ}C$ for 120 h. However, application of the same catalyst system for the hydroboration-oxidation of the homologous cyclic alkene, 1,2-dihydronaphthalene (**32**), resulted in a more sluggish reaction and disappointing 14% ee, entry 9, highlighting the critical dependence on the nature of the alkene of the reaction outcome.

Nonetheless, with these encouraging results, the real breakthrough occurred when Hayashi carried out enantioselective hydroboration of vinylarenes with cationic diphosphine-rhodium complexes.[11,87] The most remarkable feature about Hayashi's work was the complete reversal in regioselectivity observed in the catalysed hydroboration relative to the uncatalysed variant, Section 3.2. Irrespective of the substitution pattern of the styrene, the regioselectivity of the alcohol after oxidation overwhelmingly (>99/1) favoured the Markovnikov alkene hydration product in a complementary regioselectivity to the uncatalysed process. Using the same

Table 4.

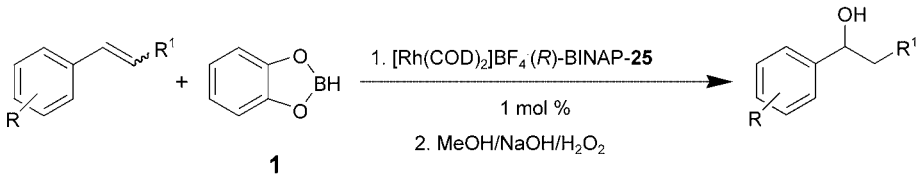


38 **1** **39**

Entry[a]	Ligand	Temp. [°C]	Solvent	Time [h]	Yield [%]	% ee (Config.)
1	(*R*)-**25**	25	THF	0.5	92	57 (*R*)
2	(*R*,*S*)-**27**	25	THF	0.5	77[b]	22 (*R*)
3	(*S*,*S*)-**26**	25	THF	0.5	98	16 (*S*)
4	(*R*,*R*)-**24**	25	THF	0.5	87	4 (*R*)
5	(*R*)-**25**	−30	THF	0.5	90	76 (*R*)
6	(*R*)-**25**	−50	THF	1	71	81 (*R*)
7[c]	(*R*)-**27**	−78	DME	2	91	96 (*R*)
8	(*R*)-**25**[d]	−78	DME	2	92	94 (*R*)

[a] Regioselectivity (α/β) >99/1 in all cases with the exception of entry 2.
[b] Regioselectivity (α/β) 95/5.
[c] Reaction with 2 mol % of the catalyst.
[d] Isolated BINAP/Rh complex, $[Rh(COD)((R)\text{-BINAP})]BF_4$ was used.

Table 5.



	40	41	19	42	43	44	30	45	28	31
R	4-Cl	4-Me	4-MeO	3-Cl	2-Cl	2-MeO	H	H	Ph	Indene
R^1	H	H	H	H	H	H	Me	Ph	Me	

Entry[a]	Substrate	Temp. [°C]	Solvent	Time [h]	Yield [%]	% ee (Config.)
1[b]	**40**	−78	DME	6	98	91 (*R*)
2[b]	**41**	−78	DME	2	77	94 (*R*)
3[b]	**19**	−78	THF/DME[c]	6	54	89 (*R*)
4[b]	**42**	−78	DME	2	99	85 (*R*)
5	**43**	−50	THF	1	30	72 (*R*)
6	**44**	−30	THF	0.5	84	82 (*R*)
7	(*E*)-**30**	25	THF	34	65	42 (*S*)
8	(*Z*)-**30**	25	THF	48	58	18 (*S*)
9	(*E*)-**45**	25	THF	50	48	16 (*S*)
10	**28**	25	THF	3.5	27[d]	19 (*S*)
11	**31**	25	THF	3	65[e]	13 (*S*)

[a] Regioselectivity (α/β) > 99/1 in all cases with the exception of entries 10 and 11.
[b] Reaction with 2 mol % of the catalyst.
[c] THF/DME = 1/3.
[d] Regioselectivity (α/β) 39/61.
[e] Regioselectivity (α/β) 93/7.

chiral diphosphine ligands as Suzuki, Figure 2, Hayashi firstly investigated the enantioselective hydroboration of styrene (**38**) with catecholborane (**1**), Table 4.

(*R*)-BINAP (**25**) was found to be the most effective chiral ligand, giving a high yield of 1-phenylethanol (**39**) in 57% ee after 30 minutes at room temperature, entry 1. Other diphosphine ligands, (*R*,*S*)-BPPFA (**27**), (*S*,*S*)-CHIRAPHOS (**26**) and (*R*,*R*)-DIOP (**24**), were all less enantioselective for this reaction (< 23% ee), despite the comparable catalytic activity of their cationic rhodium/ligand complexes to that of (*R*)-BINAP (**25**) entries 2–4. The cationic rhodium/(*R*)-BINAP (**25**) complex was highly active as a catalyst, the hydroboration of styrene (**38**) being completed in 30 minutes even at −30 °C with 1 mol % of the catalyst, entry 5. Like Burgess,[7] Hayashi found there was an inverse relationship between the asymmetry induced and the reaction temperature, entries 1, 5–8. Reactions at −78 °C were carried out in DME, entries 7 and 8, since catecholborane (**1**) was frozen and hence insoluble in THF at this temperature. Although other solvents including benzene, toluene and dichloromethane were employed, DME remained the solvent of choice. Furthermore, pre-formed phosphine-rhodium complex [Rh(COD)((*R*)-BINAP)]BF_4 showed almost the same enantioselectivity and catalytic activity as the catalyst formed *in situ* from [Rh(COD)$_2$]BF_4 and (*R*)-BINAP (**25**), entries 7 and 8.

With the proven catalytic activity of the cationic rhodium/(*R*)-BINAP (**25**) complex, Hayashi extended his study of asymmetric hydroboration-oxidation to the substituted styrene derivatives, **19**, **28**, **30**, **31**, **40**–**45**, Table 5.

Irrespective of their electronic properties, functional groups in the *para*-position (substrates **19**, **40** and **41**) did not appear to influence the enantioselectivity of

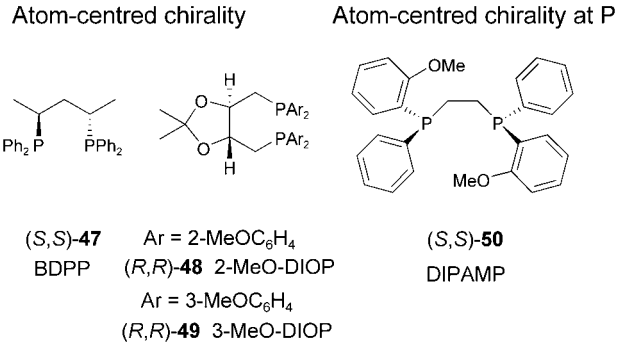
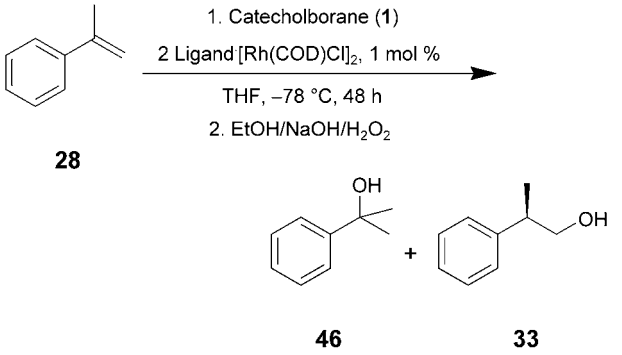


Figure 4.

Table 6.



Entry	Ligand	Rh : Ligand	**46 : 33**	% ee of **33**
1	(*S*,*S*)-**26**	1 : 1	1 : 19	25[a]
2	(*R*,*R*)-**50**	1 : 1	1 : 6	0
3	(*S*,*S*)-**47**	1 : 1	1 : 1	27
4	(*R*)-**25**	1 : 1	1 : 6	25
5	(*R*,*R*)-**24**	1 : 1	1 : 9	27
6	(*R*,*R*)-**24**	1 : 2	8 : 1	[b]
7	(*R*,*R*)-**48**	1 : 1	[b]	15
8[c]	(*R*,*R*)-49	1 : 1	4 : 1	15

[a] Absolute configuration (*R*) in all cases.
[b] Not determined.
[c] Ref.[94]

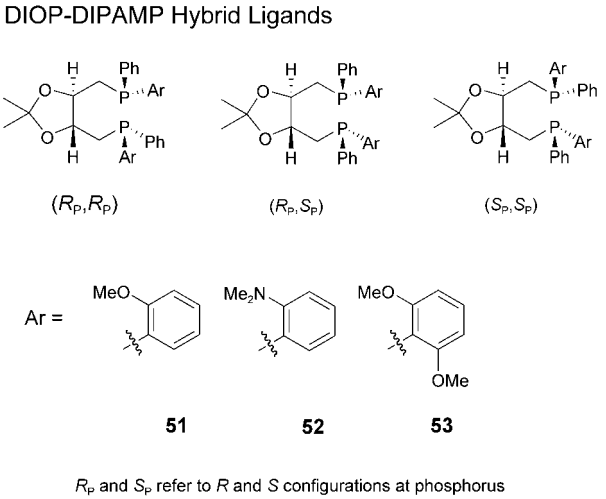


Figure 5.

the product alcohols obtained after oxidation (89–94% ee), entries 1–3. Similarly, reaction of *meta*-substituted styrene **42** also proceeded in high ee, entry 4, although the more sterically hindered *ortho*-substituted derivatives **43** and **44** showed somewhat lower enantioselectivity, entries 5 and 6. In all cases, the near-perfect regioselectivity (> 99/1) for the Markovnikov alkene hydration product was maintained. β-Substituted styrenes **30** and **45** were unreactive at low temperatures and required room temperature conditions for a reasonable rate of reaction to occur, but this compromise may in part have been responsible for the poor to modest asymmetry (16–42% ee) induced in their product alcohols, entries 7–9. α-Substituted styrene **28** also required reaction at room temperature, entry 10, but the *anti*-Markovnikov alkene hydration product **33**, Figure 3, was formed preferentially in both lower yield and enantiomeric purity than Suzuki had achieved with a $[ClRh(ethene)_2]_2 \cdot 2$ (*S*)-BINAP (**25**) catalyst system (38% ee).[86] Hydroboration-oxidation of indene (**31**), entry 11, to give the Markovnikov product **36**, Figure 3, also occurred in significantly lower selectivity (65% yield, 13% ee) compared to Suzuki's result with DIOP (**24**), (91% yield, 74% ee),[86] a result which merely serves to highlight the many control factors at play in catalytic asymmetric hydroboration.

At this juncture however, enantiomeric excesses above 95% had only been induced in rhodium-catalysed hydroborations of styrene and *para*-substituted styrene derivatives,[11,82] for which BINAP (**25**) was by far the single most effective chiral ligand. Further understanding of the factors which controlled enantioselective hydroboration was clearly necessary.

Burgess studied the possibility of a correlation between ligand chelate-ring size and hydroboration product distribution.[92] The hydroboration of 2-phenylpropene (**28**) to give, after oxidation, the Markovnikov product **46** or the *anti*-Markovnikov product **33**, was investigated with a broader range of diphosphine ligands, Table 6. As well as (*R*)-BINAP (**25**), an expanded class of C_2-symmetrical centrally chiral diphosphine ligands was employed, Figure 4. Among these were (*S*, *S*)-BDPP (**47**), the DIOP analogues (*R*,*R*)-2-MeO-DIOP (**48**) and (*R*,*R*)-3-MeO-DIOP (**49**), all of which have an asymmetric carbon backbone, and (*R*,*R*)-DIPAMP (**50**)[93] which is chiral at phosphorus.

(*S*,*S*)-CHIRAPHOS (**26**) and (*R*,*R*)-DIPAMP (**50**), entries 1 and 2, Table 6, form five-membered chelate ring structures. The ligand (*S*,*S*)-BDPP (**47**), entry 3, is structurally analogous to (*S*,*S*)-CHIRAPHOS (**26**) except that it chelates the metal in a six-membered ring. Both (*R*)-BINAP (**25**) and (*R*,*R*)-DIOP (**24**), entries 4 and 5, give seven-membered chelate rings, as do (*R*,*R*)-2-MeO-DIOP (**48**) and (*R*,*R*)-3-MeO-DIOP (**49**), entries 7 and 8. These results indicate that there is little correlation between chelate-ring size and product distribution. However, combined with data from the hydroboration-oxidation of norbornene (**22**) and indene (**31**) with the same seven diphosphine ligands as in Table 6, some general pointers for the rational design of more effective chiral ligands were garnered. In general, ligands that gave five-membered chelate rings were less enantioselective than those that gave six- or seven-membered chelates; for example, (*S*,*S*)-CHIRAPHOS (**26**) and (*R*,*R*)-DIPAMP (**50**), gave essentially racemic products for the hydroboration of norbornene (**22**). Howev-

Table 7.

Ligand	*exo*-Norborneol[a] (**23**)		1-Indanol[a] (**36**)		1-Phenylethanol[b] (**39**)	
	% ee	Config.	% ee	Config	% ee	Config.
(*R*,*R*)-**24**	60	1*R*	74	*S*	48	*R*
(S_P,S_P)-**51**	84	1*R*	49	*S*	13	*R*
(R_P,S_P)-**51**	80	1*R*	77	*S*	19	*R*
(R_P,R_P)-**51**	60	1*R*	54	*S*	~0	*R*

[a] Typical conditions: catecholborane (1), THF, −25 °C, 0.5 mol % 2 Ligand·[Rh(COD)Cl_2]$_2$.
[b] Catalyst is 1.0 mol % [Rh(COD)Ligand$_2$]BF_4, prepared *in situ*.

er, this reaction proceeded in 82% and 69% ee, respectively, for (*R*,*R*)-2-MeO-DIOP (**48**) and (*R*,*R*)-3-MeO-DIOP (**49**), highlighting that subtle stereoelectronic modifications of existing chiral ligands could have a pronounced effect on the degree of asymmetry induced. By comparison, (*R*,*R*)-DIOP (**24**) gave 60% ee for the same transformation.[92]

The data in Table 6 also reinforce how the nature of the ligand influences the regiochemistry of the reaction and highlights the importance of phosphine-to-rhodium ratios in enantioselective hydroborations.[82,94] When the phosphine-to-rhodium ratio was 1:1, four of the seven ligands preferentially gave, after oxidation, the primary alcohol **33**, entries 1, 2, 4 and 5. (*S*,*S*)-BDPP (**47**) gave an equal product distribution of both alcohols, entry 3, while (*R*,*R*)-3-MeO-DIOP (**49**) was the only ligand to give more tertiary alcohol **46**, entry 8. With (*R*,*R*)-DIOP (**24**) as ligand, the hydroboration of 2-phenylpropene (**28**) gave, after oxidation, a ratio of tertiary to primary alcohol, **46:33**, of 1:9, entry 5. However, increasing the phosphine-to-rhodium ratio from 1:1 to 2:1 for the same ligand caused a complete reversal of the regioselectivity to 8:1 in favour of the Markovnikov product **46**, entry 6, approaching the near complete regioselectivities previously observed by Hayashi in the rhodium-catalysed hydroboration of vinylarenes.[11,87] "Asymmetric amplification" experiments provided no evidence to suggest there was more than one phosphine ligand per catalyst molecule but did not conclusively rule out that possibility either.[94]

Subsequently, Burgess[95] prepared a series of hybrid ligands **51**–**53**, Figure 5, which were chiral not only in the carbon backbone like (*R*,*R*)-DIOP (**24**), but also at phosphorus, like DIPAMP (**50**).

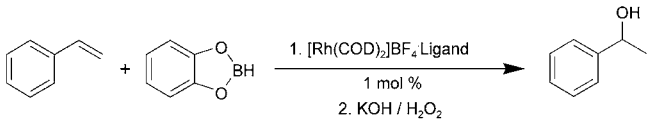
The best result with these ligands was in the hydroboration-oxidation of norbornene (**22**) which gave *exo*-norborneol (**23**) in 84% ee. In general, modest enantioselectivities were observed and this was believed to be due to puckering of the seven-membered metal chelates away from ideal C_2-conformations. Evidence for this deviation from ideal C_2-symmetrical behaviour came from X-ray crystallographic analysis of molybdenum tetracarbonyl complexes. Extending the range of hydroboration-oxidation substrates to include indene (**31**) and styrene (**38**) gave 1-indanol (**36**) and 1-phenylethanol (**39**), respectively, with the same sense of asymmetric induction irrespective of the chirality at phosphorus, showing that it was the chirality of the carbon backbone that controlled the asymmetry of the reaction, Table 7.[95] There was no correlation in these experiments between the chirality at phosphorus and that at carbon and attempts to produce "matched" and "mismatched" catalysts were not successful.

As a greater understanding has emerged of the control factors at play in enantioselective rhodium-catalysed hydroborations, an increased number of novel chiral diphosphine ligands has been reported in the chemical literature, Figure 6, the majority of these within the last five years.

Given the proven success of BINAP (**25**) in catalytic asymmetric hydroborations, it is perhaps surprising that so few BINAP analogues have been reported. One such ligand was the C_2-symmetrical, axially chiral diphosphine **54**, Figure 6, by Jendralla and co-workers.[96] Whereas the majority of phosphine ligands that had been tested in catalytic asymmetric synthesis were electron-rich, (more so than triphenylphosphine), among them DIOP (**24**), DIPAMP (**50**) and BINAP (**25**), there was nonetheless a literature precedent for enhancing catalyst performance by reducing the basicity of the phosphine.[96] To this end, the synthesis and resolution of the electron-poor (6,6′-difluorobiphenyl-2,2′-diyl)bis(diphenylphosphine) (**54**) was undertaken, which was also expected to offer handling advantages in that it would be less susceptible to oxidation than more electron-rich diphosphines. This ligand was applied in asymmetric hydroboration with excellent catalytic activity. The hydroboration of *para*-methoxystyrene (**19**) with an *in situ* formed rhodium(I) complex of (*R*)-**54** was near quantitiative within 1.5 h at 0 °C, Scheme 8. Oxidation gave a 78:22 preference for the secondary alcohol **21**, in a respectable 78% ee.

However, the vast majority of new, novel chiral diphosphines reported have possessed elements of either atom-centred or planar chirality. Included in the former class is the C_2-symmetrical diphosphine **55**, Figure 6, from the group of Flor.[97] This ligand may be regarded as a diphosphine containing two intramolecular solvent

Table 8.



Entry	Substituents	Ligand	Solvent	Temp [°C]	% ee (Config.)
1	R^1, R^2=H	(*R*,*R*)-**59**	Et_2O/CH_2Cl_2[b]	−60	65 (*R*)
2	R^1, R^2=H	(*R*,*R*)-**60**	Et_2O/CH_2Cl_2[b]	−60	65 (*S*)
3	R^1, R^2=H	(*R*,*R*)-**61**	DME	−35	92 (*S*)
4	R^1=H, R^2=F	(*R*,*R*)-**61**	DME	−35	93 (*S*)
5	R^1=H, R^2=OMe	(*R*,*R*)-**61**	DME	−35	93 (*S*)
6	R^1=Me, R^2=H	(*R*,*R*)-**61**	DME	−35	91 (*S*)

[a] Regioselectivity (α/β) > 99/1 in all cases.
[b] Et_2O/CH_2Cl_2 = 4/1.

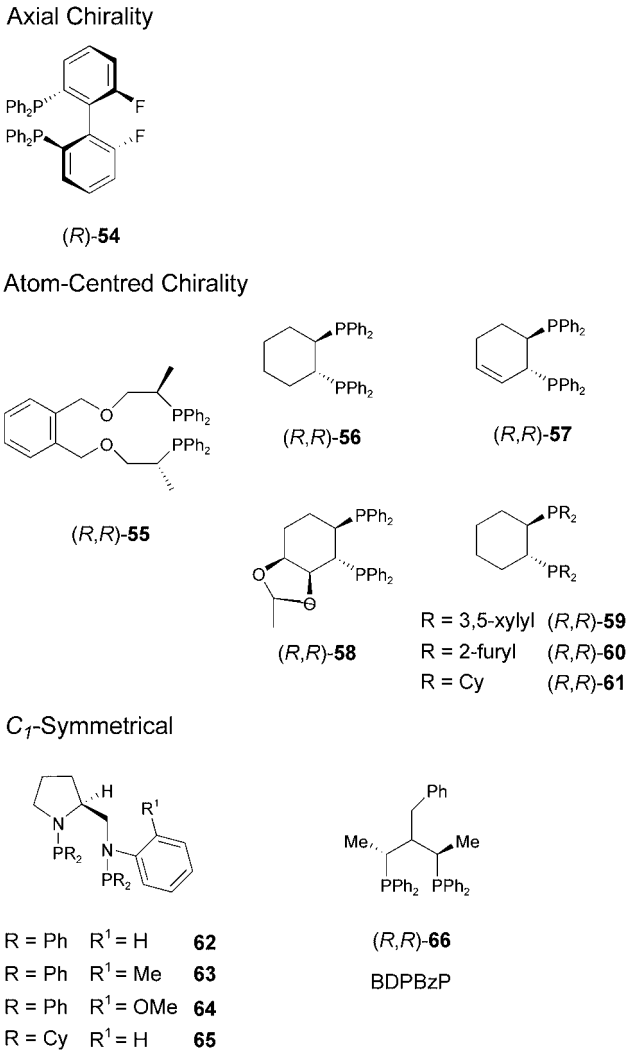
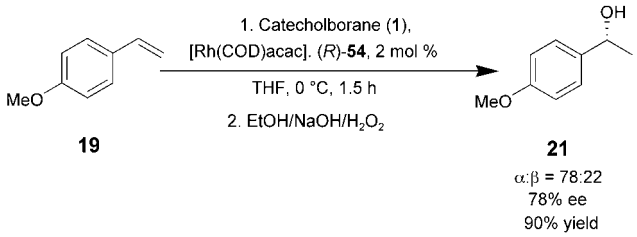


Figure 6.

molecules, due to the two hemilabile ether donor groups. The cationic Rh(I) complex of (*R*,*R*)-**55** was tested in the asymmetric hydroboration of styrene (**38**) with



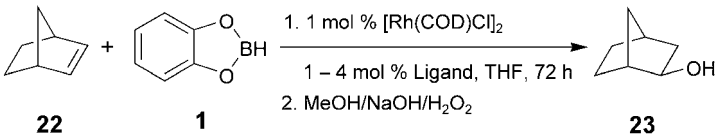
Scheme 8.

catecholborane (**1**), at both 20 °C and −25 °C. The catalyst system showed high activity and chemoselectivity (> 96%) at both temperatures. The regioselectivity for formation of the branched product, 1-phenylethanol (**39**), was 82% and 95% at 20 °C and −25 °C, respectively. Despite the high chemo- and regioselectivity, enantioselectivity was very poor: < 1% ee at 20 °C and an optimum 10% ee at the lower temperature.

Of greater success were Knochel's C_2-symmetrical diphosphine ligands **56**–**61**, Figure 6, which were employed in the hydroboration of styrene and substituted styrenes.[98] The corresponding 1-arylethanols was produced with excellent regioselectivity (> 99:1) and variable enantioselectivity after oxidation, Table 8.

The diphosphines **56**–**58** induced low asymmetries (8–15% ee) irrespective of the reaction conditions. The more electron-rich ligand (*R*,*R*)-**59** gave (*R*)-1-phenylethanol in a much-improved 65% ee, entry 1. Conversely, the application of the more electron-poor diphosphine (*R*,*R*)-**60** resulted in the (*S*)-enantiomer, but with the same level of enantioselection, entry 2, highlighting the importance of the electron density of the phosphorus centre on the sense of asymmetric induction. Optimum results with styrene were achieved with the most electron-rich diphosphine (*R*,*R*)-**61**, entry 3. With DME as solvent for 3 h at −35 °C, (*S*)-1-phenylethanol was afforded in 92% ee and near complete regioselectivity (> 99:1). No reaction occurred at lower temperatures while increasing the temperature resulted in

Table 9.



22 **1** **23**

Entry	Ligand (mol %)	Temp [°C]	Yield [%]	% ee
1[a]	(*R*,*R*)-**62** (2)	25	58	12
2	(*R*,*R*)-**62** (1)	−78	60	37
3	(*R*,*R*)-**62** (2)	−78	61	63
4	(*R*,*R*)-**62** (4)	−78	64	72
5	(*R*,*R*)-**63** (4)	−78	62	65
6	(*R*,*R*)-64 (4)	−78	57	60
7[a]	(*R*,*R*)-**65** (4)	25	60	31
8	(*R*,*R*)-**65** (4)	−78	86	77

[a]Reaction time = 24 h.

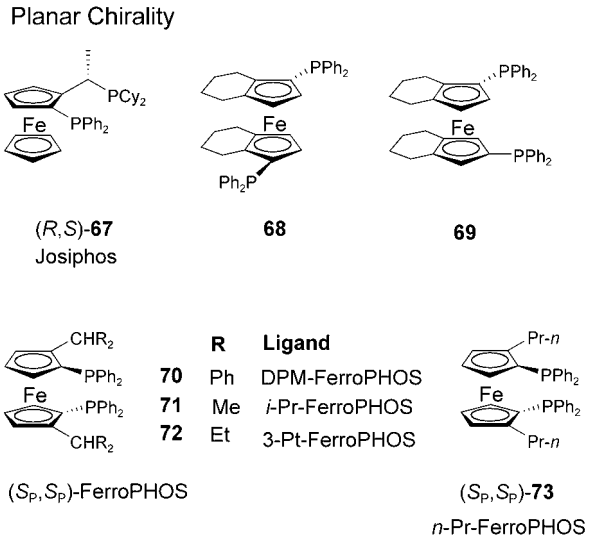


Figure 7.

both lower regio- and enantioselectivities. Under these optimum conditions, a number of *para*- and *meta*-substituted styrene derivatives were hydroborated with good to quantitative conversion (62–100%), excellent regioselectivity (>97:3) and good to excellent enantioselectivity (up to 93% ee), entries 4–6. Overall, the best result with ligand (*R*,*R*)-**61** was 93% ee and 100% conversion for the regioselective (>99:1) hydroboration of *para*-fluorostyrene. Using chiral diphosphine (*R*,*R*)-**60**, and a DME/toluene solvent system (3/2), a number of *ortho*-substituted styrene derivatives were hydroborated with relatively high levels of asymmetric induction (77–82% ee), similar regioselectivities and surprisingly high conversions (complete conversion after 1 h at −75 °C). On the whole, rhodium complexes of these ligands are among the most efficient catalyst systems for the hydroboration of styrene derivatives.

Although the vast majority of centrally chiral diphosphine ligands to be employed in enantioselective rhodium-catalysed hydroborations possess C_2-symmetry, there are a few examples of C_1-symmetrical diphosphine ligands. Buono prepared bis(aminophosphine) ligands **62**–**65**,[99] while Bianchini reported (*R*,*R*)-BDPBzP (**66**),[100] Figure 6.

Ligands **62**–**65** were applied in the hydroboration-oxidation of norbornene (**22**) with catecholborane (**1**), Table 9.[99] In all cases, *exo*-norborneol (**23**) was formed as the major product. As expected, decreasing the reaction temperature increased the enantioselectivity, entries 1, 3, 7 and 8. Like Burgess,[94] Buono found that the phosphine-to-rhodium ratio was a critical factor in the reaction. Increasing the amount of ligand led to an increase in ee, entries 2–4. Manipulation of the steric properties of (*R*,*R*)-**62** by increasing the steric hindrance on the amino-bound phenyl group did not improve the level of asymmetry induced; in fact, ees were lower, entries 5 and 6. However, tuning of the electronic properties of the donor phosphorus by substitution of a phenyl ring for a cyclohexyl group simultaneously resulted in both an optimum 86% yield and 77% ee with ligand (*R*,*R*)-**65**, entry 8. Interestingly, it was with the cyclohexyl-substituted diphosphine ligand (*R*,*R*)-**61** that Knochel also achieved the highest levels of asymmetric induction.[98]

Application of these ligands to the hydroboration-oxidation of styrene (**38**) proceeded with moderate yields and much lower enantioselectivities than for norbornene (**22**). The best result was with (*R*,*R*)-**65**, which afforded (*S*)-1-phenylethanol (**39**) in 61% yield and 42% ee. However, Bianchini's (*R*,*R*)-BDPBzP (**66**) was even less efficient for this substrate, and gave both poor yields (29%) and poor enantioselectivities (26% ee) for the hydroboration of styrene (**38**) at 0 °C.[101]

The third major class of diphosphine ligand employed in catalytic asymmetric hydroboration are those possessing planar chirality, Figure 7, in addition to which BPPFA (**27**), Figure 2, is also a member. These ligands are chiral by virtue of the non-symmetrical disubstitution of one of the cyclopentadienyl rings.

Togni prepared the ferrocenyldiphosphine Josiphos (**67**).[102] A catalyst (2 mol %) prepared *in situ* from $[Rh(NBD)_2]BF_4$ and (*R*,*S*)-**67** was applied to the hydroboration-oxidation of styrene (**38**) with catecholborane (**1**). With DME as solvent for 10 h at −78 °C, (*R*)-1-phenylethanol (**39**) was afforded in 65% yield, 92% ee and near perfect regioselectivity (>99:1), compared to 60% ee at room temperature. Unfortunately, styrene was the only substrate which reacted at low temperature. The hydroboration of more sterically demanding substrates such as indene (**31**) necessitated room temperature conditions to attain complete conversion within a reasonable time. Using the same catalyst (1 mol %), (*R*)-1-indanol (**36**) was formed in 42% ee after oxidation, albeit in good yield (70%). While the hydroboration-oxidation of norbornene (**22**) furnished (*R*)-*exo*-

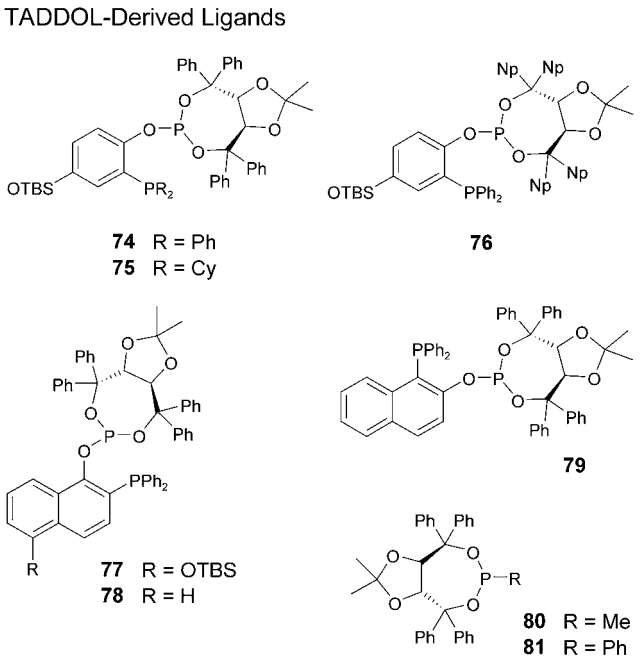


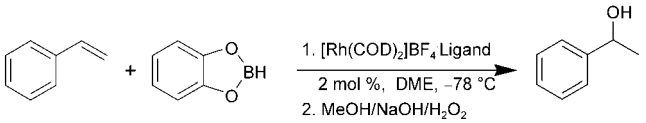
Figure 8.

norborneol (**23**) with complete regioselectivity, the asymmetry induced was very poor (7% ee). It was postulated that the reduced activity of Josiphos (**67**) in hydroborations compared to other chiral bis(diphenylphosphino) ligands reported, was due to increased basicity of the phosphine **67** compared to other ligands,[102] supporting the rationale behind Jendralla's synthesis of electron-poor biphenyl **54**.[96]

While Josiphos (**67**) also possessed an element of atom-centred chirality in the side chain, Reetz reported a new class of ferrocene-derived diphosphines which had planar chirality only: ligands **68** and **69** which have C_2- and C_1-symmetry, respectively.[103] Rh(I) complexes of ligands (−)-**68** and (−)-**69** were used *in situ* as catalysts (0.75 mol %) for the hydroboration of styrene (**38**) with catecholborane (**1**) for 12 h in toluene at −50 °C. The Rh/C_1-symmetrical (−)-**69** catalyst system was the more enantioselective of the two: (*S*)-1-phenylethanol (**39**) was afforded in 52% and 77% ee with diphosphines (−)-**68** and (−)-**69**, respectively. In both cases the regioselectivity was excellent (>99:1). With the same reaction time but using DME as solvent at lower temperature (−60 °C), the rhodium complex of **69** afforded the alcohol product **39** in an optimum 84% ee.

Kang and co-workers prepared the FerroPHOS ligands **70**–**73**, Figure 7, which are intriguingly described as possessing *cylindrical chirality* (defined as the chirality originating from the C_2-symmetricity of two identical planar chiralities).[104] The steric and electronic properties of these ligands were explored by changing the substituent in the *pseudo*-benzylic position. These highly air-stable ferrocenyldiphosphines were employed in

Table 10.



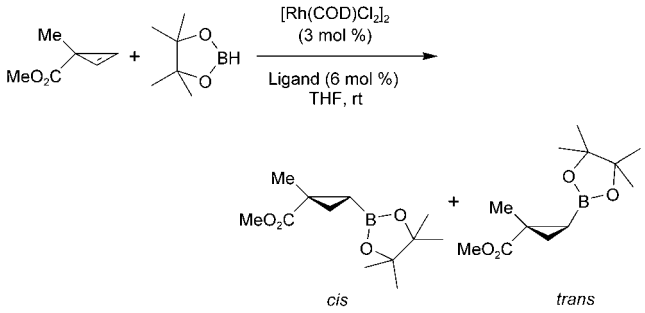
Entry	Ligand	Time [h]	Yield [%]	% ee (Config.)
1	**74**	2.5	98	81 (*R*)
2	**75**	2.5	92	49 (*S*)
3	**76**	2.5	24	87 (*R*)
4	**77**	3.5	97	88 (*R*)
5	**78**	3.5	63	91 (*R*)
6	**79**	3.5	7[b]	61 (*R*)

[a] Regioselectivity (α/β) > 94/6 in all cases with the exception of entry 6.
[b] Regioselectivity (α/β) 85/15.

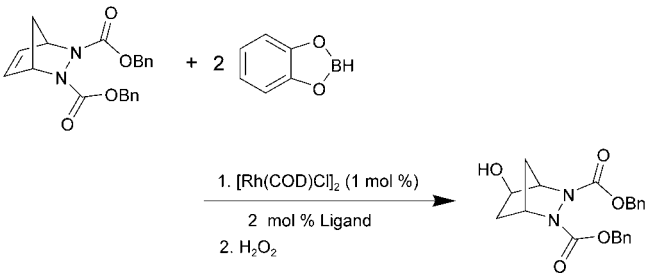
asymmetric hydroborations of styrene (**38**) and indene (**31**) using 2 mol % of a catalyst prepared *in situ* from the respective ligand and $Rh(COD)_2BF_4$. DPM-FerroPHOS (**70**) gave the best result: 85% ee, greater than 99% regioselectivity, and complete conversion for the hydroboration of styrene (**38**) in DME for 11 h at −78 °C. For the hydroboration of indene (**31**), 3-Pt-FerroPHOS (**72**) afforded 1-indanol (**36**) in an optimum 42% ee and 85% yield in THF at room temperature. In general however, decreasing the steric bulk of the side chain in ligands **71**–**73** resulted in lower asymmetric induction (23–77% ee), and reduced activity (15–85%) for both substrates. Not surprisingly therefore, the least efficient ligand was *n*-Pr-FerroPHOS (**73**) which possessed the least sterically demanding side chain, the linear *n*-propyl group. This diphosphine showed no enantioselectivity whatsoever for the hydroboration of indene (**31**) and a sluggish 15% conversion after 11 h for styrene (**38**; 23% ee).[104]

All the chelating bidentate P,P ligands presented thus far are chiral diphosphines. However, TADDOL-derived phosphine-phosphite ligands also represent an important sub-class of P,P ligands. Among these are ligands **74**–**79**, Figure 8, identified by screening a modular 20-component ligand library. (Ligand screening found that in general, TADDOL-derived ligands had superior activity to those derived from other chiral diols or amino alcohols).[105]

Schmalz and co-workers tested these ligands in the rhodium-catalysed hydroboration of styrene (**38**) with catecholborane (**1**), Table 10.[105] Small variations of the ligand framework led to significant and unpredictable differences in the performance of the rhodium complexes (2 mol %) generated *in situ* from $Rh(COD)_2BF_4$ and the respective ligand. For example, changing the diphenylphosphine group of ligand **74** to a bulkier, more electron-rich dicyclohexylphosphine in ligand **75**, gave



Scheme 9.



Scheme 10.

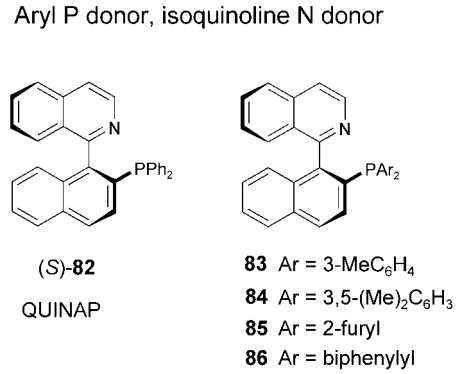


Figure 9.

rise to comparable catalytic activity but lowered and opposite asymmetric induction, entries 1 and 2. Tuning of the other phosphorus donor atom by exchanging the phenyl-TADDOL-derived phosphite **74** with the corresponding 2-naphthyl-TADDOL-derived **76** resulted in enhanced enantioselectivity (87% ee) but significantly attenuated catalytic activity (24% yield), perhaps due to steric crowding, entry 3.

Variation of the aromatic backbone of the ligand from hydroquinone derivatives **74**–**76** to the 1,5-naphthalenediol analogues **77**–**79** produced all-round better performances. This was postulated to be due to stronger pre-organisation arising from steric interaction between the proton in the 8-position of **77** and the phosphite core.[105] Ligand **77** gave the best overall result in terms of yield (97%) and enantioselectivity (88% ee), entry 4. Removal of the *tert*-butyldimethylsilyl-protected alcohol to give phosphite **78** led to a lower 63% yield but slightly enhanced 91% ee, entry 5. However, exchanging the positions of the phosphine and phosphite on the naphthalene backbone in **77** to afford the regioisomeric **79** had a significantly more deleterious effect on the selectivity (61% ee) and, in particular, the catalytic activity of this system (7% yield), entry 6, highlighting the sensitivity of this reaction to subtle changes in ligand structure.

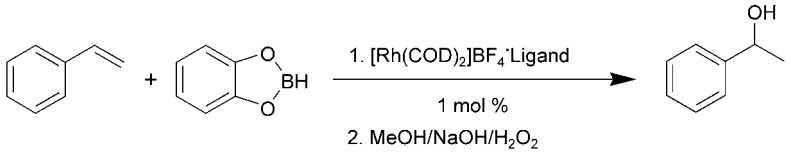
Finally, the group of Seebach has applied ***monodentate*** TADDOL-derived cyclic phosphonites **80** and **81**, Figure 8, to the hydroboration-oxidation of styrene (**38**) in DME at 0 °C.[106] The methyl phosphonite **80** regioselectively afforded (*R*)-1-phenylethanol (**39**) in 64% yield and 26% ee, while the phenyl analogue **81** gave the alcohol in an excellent 95% yield but with even lower – and opposite – asymmetric induction [16% (*S*)]. These results illustrate that while monodentate phosphorus(III) derivatives may indeed form highly catalytically active complexes with transition metals such as rhodium, in general asymmetric hydroboration is far more effective with bidentate ligands.

More recent work employing diphosphine ligands has focused on both new substrates for hydroboration and also new hydroborating agents. Specifically, Gevorgyan has successfully employed cyclopropenes as substrates with pinacolboranes as the borane source.[19] Impressive enantioselectivities were obtained with a range of diphosphines, e.g., with rhodium complexes of NORPHOS (>99% ee), PHANEPHOS (97% ee), BINAP (94% ee) and Tol-BINAP (96% ee), all with near perfect *cis*-selectivity, Scheme 9.

Micouin investigated rhodium-catalysed hydroboration as a means of desymmetrising *meso*-hydrazines in an important new application.[41] Enantiomeric excesses of up to 84% were obtained after screening diphosphines such as DIOP and BDPP, Scheme 10. Interestingly, they noted an unprecedented reversal of enantioselectivity by changing from rhodium to iridium.

Nonetheless, among the bidentate diphosphines and with the notable exception of BINAP (**25**),[11,87] there have been only sporadic examples of ligands whose rhodium complexes give enantioselectivities above 85% in hydroboration: Knochel's dicyclohexylphosphine **61**,[98] Togni's Josiphos **67**[102] and TADDOL derivatives **74**, **76**–**78**.[105] Even BINAP (**25**) is only effective at −78 °C. Not surprisingly, research groups began to look beyond the realm of chiral P,P ligands for catalytic asymmetric hydroboration and a parallel interest in the application of chiral heterobidentate chelates was generated. The phosphinamine ligand class has received the most attention. These ligands, as well as having the potential to induce asymmetry through steric factors, can also generate electronic asymmetry on the metal centre due to the combination of hard and soft donor atoms and the different reactivity associated with each.[107,108]

Table 11.



38 **1** **39**

Entry	Ligand	Vinylarene		Yield [%]	% ee
1[a]	(*S*)-**82**	R = R^1 = H	**38**	69	88 (*S*)
2[a]	(*S*)-**82**	R = 4-MeO; R^1 = H	**19**	57	94 (*S*)
3	(*R*)-**82**	R = 4-Me; R^1 = H	**41**	75	89 (*R*)
4[a]	(*S*)-**82**	R = 4-Cl; R^1 = H	**40**	56	78 (*S*)
5[a]	(*S*)-**82**	Indene	**31**	75	76 (*S*)
6[a]	(*S*)-**82**	Dihydronaphthalene	**32**	78	96 (*S*)
7	(*R*)-**82**	R = H; R^1 = (*Z*)-Me	(*Z*)-**30**	80	93 (*R*)
8	(*R*)-**82**	R = H; R^1 = (*E*)-Me	(*E*)-**30**	80	95 (*R*)
9	(*R*)-**82**	R = H; R^1 = (*Z*)-Ph	(*Z*)-**45**	86	91 (*R*)
10	(*R*)-**82**	R = 4-MeO; R^1 = Me	(*E*)-**88**	84	97 (*R*)
11	(*S*)-**83**	R = 4-Me; R^1 = H	**41**	79	88 (*S*)
12	(*S*)-**83**	R = 4-Cl; R^1 = H	**40**	72	65 (*S*)
13	(*S*)-**83**	Dihydronaphthalene	**32**	79	86 (*S*)
14	(*S*)-**84**	R = 4-Me; R^1 = H	**41**	77	79 (*S*)
15	(*S*)-**84**	R = 4-Cl; R^1 = H	**40**	77	54 (*S*)
16	(*S*)-**85**	R = 4-Me; R^1 = H	**41**	79	88 (*S*)
17	(*S*)-**85**	R = 4-Cl; R^1 = H	**40**	78	82 (*S*)
18	(*S*)-**85**	Indene	**31**	80	78 (*S*)
19	(*S*)-**85**	Dihydronaphthalene	**32**	81	82 (*S*)
20	(*S*)-**85**	R = 2,4-(Me)$_2$; R^1 = H	**89**	81	93 (*S*)
21	(*R*)-**86**	R = 4-Me; R^1 = H	**41**	76	71 (*R*)
22	(*R*)-**87**	R = R^1 = H	**38**	70	67 (*R*)
23	(*R*)-**87**	Indene	**31**	59	64 (*R*)
24	(*R*)-**87**	Dihydronaphthalene	**32**	69	84 (*R*)
25	(*R*)-**87**	R = H; R^1 = (*E*)-Me	(*E*)-**30**	60	91 (*R*)

[a] Reaction time = 1 h.

Chiral P,N Ligands

5.1 Axial Chirality

The first successful axially chiral phosphinamine ligand in asymmetric catalysis was QUINAP (**82**), Figure 9, reported by Brown in 1993[109,110] and the original synthesis has since been modified.[111] The donor nitrogen atom is incorporated in an isoquinoline unit to form a six-membered chelate ring.

Brown and co-workers tested cationic Rh(I) complexes of QUINAP (**82**) in the enantioselective hydroboration-oxidation of vinylarenes[12,112] which proceeded with excellent regioselectivities, in most cases > 95%, Table 11. The product configuration induced was the same as for BINAP (**25**)–rhodium complexes of the (*R*)-ligand gave rise to the (*R*)-secondary alcohol. In contrast to BINAP (**25**), the Rh/QUINAP (**82**) catalyst system was effective at ambient temperature. In fact, while the enantioselectivities unusually showed little change between 0 °C and −40 °C, the effect of further cooling was found to be deleterious. For best results, the rhodium complex was reprecipitated before use (THF/light petroleum ether) and the vinylarene substrates purified by distillation prior to reaction. Both the regio- and enantioselectivity were sensitive to the ligand-to-rhodium ratio, a finding also observed with diphosphine ligands.[94,99]

High asymmetries were induced with styrene (**38**; 88% ee), entry 1, and styrene derivatives **19** and **41** with electron-donating substituents in the *para*-position, (94% and 89% ee), entries 2 and 3, but electron-withdrawing substituents as in 4-chlorostyrene (**40**), entry 4, gave lower ee values (78%). Of importance, however, was the finding that cyclic vinylarenes, such as indene (**31**) and dihydronaphthalene (**32**), also gave high enantioselectivities (76% and 96%, respectively), entries 5 and 6. The hydroboration-oxidation of such sterically demanding substrates was far less successful when complexes of BINAP (**25**) were employed [19% ee for indene (**31**); dihydronaphthalene (**32**) has not been report-

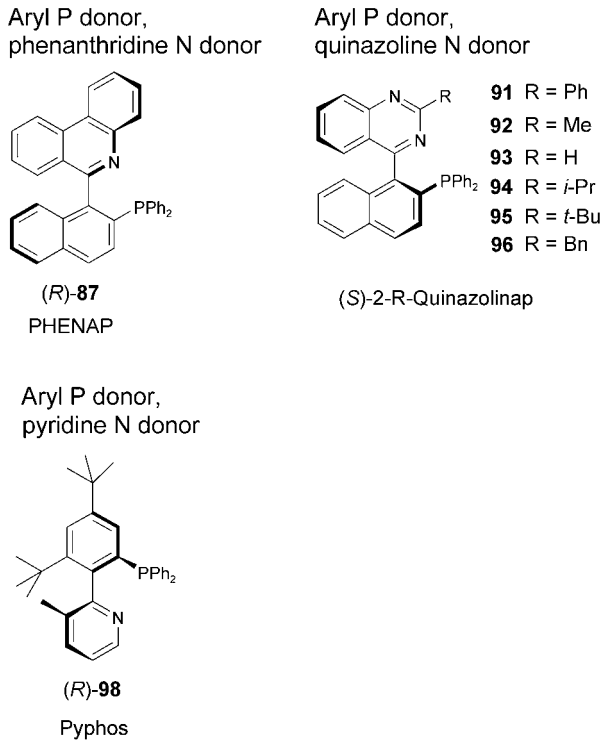


Figure 10.

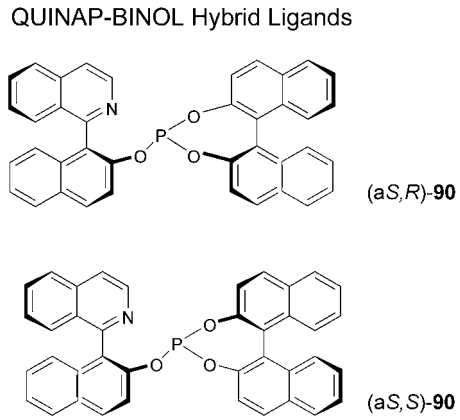


Figure 11.

ed].[11] In general, hydroborations catalysed by rhodium complexes of QUINAP (**82**) were tolerant of vinylarenes that had (*E*)- or (*Z*)-β-substituents but not α-substituents. This represented a considerable expansion of substrate scope as compared to previous P,P (or P,N) complexes employed, which were only effective for monosubstituted vinylarenes.[111] Specifically, the hydroboration of (*Z*)- and (*E*)-1-phenyl-1-propene (**30**), entries 7 and 8, proceeded with 93% and 95% ee, respectively, with QUINAP (**82**). The corresponding results with BINAP (**25**) were 18% and 42% ee in reactions run at ambient temperature.[11] The high yields unexpectedly afforded by both isomers of **30** suggested a high possibility of a rhodium hydride-driven *cis-trans* isomerisation,[112] and certainly the reaction with *trans*-stilbene (**45**) [45 turnovers in 20 h (85% ee)] was much slower than that of *cis*-stilbene (**45**), entry 9.

QUINAP (**82**) is amenable to structural variation at several points. Among these are the aryl groups on phosphorus which were systematically varied to examine the effect on the efficiency and enantiodifferentiating ability of the ligand. Thus the analogues **83**–**86**, Figure 9, were prepared and resolved[113] in a similar manner to QUINAP (**82**). Their rhodium complexes were subsequently applied in hydroboration-oxidation of vinylarenes, Table 11, entries 11–21, with comparable regioselectivities to QUINAP (**82**).[112] Enantioselectivities of up to 93% were observed, entry 20, compared with 97% for the parent catalyst system, entry 10. The key finding from this study was that the parent diphenylphosphino ligand QUINAP (**82**) gave superior results for electron-rich vinylarenes, whereas by making the donor phosphorus atom less electron-rich, as in the difurylphosphino ligand **85**, superior results for electron-poor vinylarenes were obtained. [For the hydroboration of an electron-rich substrate (4-methylstyrene; **41**) with ligands **82**–**86**, see entries 3, 11, 14, 16 and 21; for electron-poor 4-chlorostyrene (**40**), entries 4, 12, 15 and 17]. These QUINAP analogues were also effective for the hydroboration-oxidation of indene (**31**) and dihydronaphthalene (**32**), entries 18, 13 and 19.

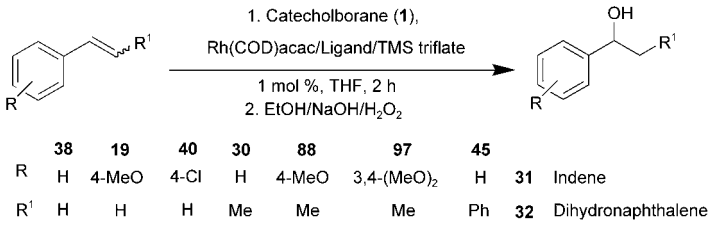
Gevorgyan also tested rhodium complexes of QUINAP employing cyclopropenes as substrates with pinacolboranes as the borane source.[19] In contrast to the high enantioselectivities obtained with a range of diphosphines, only a racemic mixture was formed in this case.

Micouin investigated rhodium-QUINAP complexes in the desymmetrisation of *meso*-hydrazines but obtained poor yields (11%) and only modest enantioselectivities (24% ee).[41]

It became apparent during a mechanistic investigation of the allylic alkylation process with QUINAP (**82**), involving both solution ^{1}H NMR and solid state studies, that the 3-H of the isoquinoline unit takes up a position in space near the metal that leads to critical ligand-reactant steric interactions thought to be significant for asymmetric induction.[114] This finding led to the design by Brown of the vaulted analogue PHENAP (**87**), Figure 10, where the donor nitrogen atom is part of a phenanthridine unit.

PHENAP (**87**) was prepared and resolved[115] in a similar manner to QUINAP (**82**) and tested in asymmetric rhodium-catalysed hydroboration-oxidations,[116] Table 11, entries 22–25. Regioselectivities were on a par with QUINAP (**82**).[116] Impressive enantioselectivities were obtained and the sterically demanding cyclic substrates were hydroborated in 64–84% ee, entries 23 and 24, as well as β-substituted vinylarene (*E*)-**30** with a similar enantioselectivity as with QUINAP (**82**). Com-

Table 12.



Entry	Ligand (R group)	Vinylarene	Temp. [°C]	Conv. [%]	α:β	% ee (Config.)
1	(*S*)-**92** (Me)	**38**	20	100	88:12	90 (*S*)
2	(*S*)-**96** (Bn)	**38**	0	100	84:16	87 (*S*)
3	(*S*)-**92** (Me)	**19**	20	99	88:12	95 (*S*)
4	(*S*)-**92** (Me)	**19**	0	97	70:30	91 (*S*)
5	(*S*)-**93** (H)	**40**	20	100	83:17	81 (*S*)
6	(*S*)-**93** (H)	**40**	0	100	75:25	64 (*S*)
7	(*S*)-**92** (Me)	(*E*)-**30**	0	96	94:6	95 (*S*)
8	(*S*)-**91** (Ph)	(*E*)-**30**	20	100	91:9	94 (*S*)
9	(*S*)-**92** (Me)	(*Z*)-**30**	0	100	99:1	97 (*S*)
10	(*S*)-**94** (*i*-Pr)	(*Z*)-**30**	20	100	96:4	96 (*S*)
11	(*S*)-**92** (Me)	(*E*)-**88**	0	89	88:12	97 (*S*)
12	(*S*)-**94** (*i*-Pr)	(*E*)-**88**	20	51	77:23	93 (*S*)
13	(*S*)-**92** (Me)	(*E*)-**97**	0	75	92:8	98 (*S*)
14	(*S*)-**92** (Me)	(*E*)-**45**	20	50	n.a.	87 (*S*)
15	(*S*)-**94** (*i*-Pr)	(*Z*)-**45**	20	84	n.a.	99 (*S*)
16	(*S*)-**92** (Me)	(*Z*)-**45**	20	96	n.a.	97 (*S*)
17	(*R*)-**95** (*t*-Bu)	(*Z*)-45	0	80	n.a.	97 (*R*)
18	(*S*)-**93** (H)	**31**	0	39	97:3	98 (*S*)
19	(*S*)-**92** (Me)	**31**	20	100	>99:1	99.5 (*S*)
20	(*S*)-**92** (Me)	**32**	0	90	>99:1	93 (*S*)

pared to the corresponding results obtained with diphosphine ligands, Section 4, it is clear that QUINAP (**82**), its structural relatives **83**–**86** and PHENAP (**87**), give superior results in the asymmetric rhodium-catalysed hydroboration of several vinylarenes, and are essentially the only practical solution for β-substituted alkenes.[117] The reasons for this are not well understood, but are thought to be due to the particular geometry of the P,N chelate which can accommodate the steric demand of substituents in the region of the alkene double bond. For QUINAP complexes the P,N chelate is a pronounced boat and there is reduced steric demand in the region of space around the isoquinoline nitrogen, certainly when compared to the aryl residues of BINAP (**25**).[112] This structural difference, coupled with the intrinsic electronic features of the P,N ligand, explain why the asymmetric induction is higher with chiral QUINAP (**82**) than with chiral BINAP (**25**).[112]

The lack of characterisation of reactive intermediates is a hindrance to further progress on understanding the mechanism but recent reports from the groups of Brown and Fernandez are steps in the right direction.[117–119] In particular, Brown has identified binuclear reactive intermediates by NMR when the hydroboration pre-catalyst was examined in the presence of catecholborane at low temperatures. Fernandez has reported a theoretical study of model systems from spectroscopically postulated Rh-BINAP and Rh-QUINAP intermediates in the catalytic cycle, concluding that the origin of regio- and enantioselectivity in hydroboration reactions of vinylarenes is related to the coordination step of the alkene instead of the migratory insertion. They have also extended the study to investigate the effect of the hydroborating agent, the metal and the counterion of the catalytic precursor in the catalytic asymmetric hydroboration of vinylarenes. Clearly, electronic tuning of the donor phosphorus atom by changing from PPh_2 in QUINAP (**82**) to $P(furyl)_2$ in ligand **85** was highly successful, rendering the latter ligand particularly effective for the hydroboration of electron-deficient vinylarenes.[112] In a new departure in the quest for QUINAP-type ligands with an electron-deficient phosphorus atom, a novel QUINAP-derived triaryl phosphite ligand **90**, Figure 11, was developed by Brown ten years after the parent ligand **82** was first reported.[117]

Ligand **90** was prepared directly from a single enantiomer of the corresponding naphthol of QUINAP (**82**), an early intermediate in the original synthesis, and both enantiomers of BINOL. Application in hydroboration showed that, in practice, only one of the cationic rhodium complexes of the diastereomeric pair proved effective, (a*S*,*S*)-**90**. While (a*S*,*S*)-**90** gave 68% ee for the

hydroboration of styrene (**38**; 70% yield), the diastereomer (a*S*,*R*)-**90** afforded the product alcohol after oxidation in an attenuated 2% ee (55% yield) and the same trend was apparent in the hydroboration of electron-poor vinylarenes. Indeed, even with (a*S*,*S*)-**90**, the asymmetries induced were very modest (31–51% ee). The hydroboration pre-catalyst was examined in the presence of catecholborane (**1**) at low temperatures and binuclear reactive intermediates were identified. However, when similar experiments were conducted with QUINAP (**82**), no intermediates of the same structural type were found.[117]

A series of axially chiral 2-substituted quinazoline-containing phosphinamine ligands, the "Quinazolinaps", **91**–**96**, Figure 10, has been prepared and resolved by our research group.[120–123] The naphthalene-quinazoline pivot was chosen as it would be inert to racemisation.[121] In light of the mechanistic observations on related ligand systems, the 2-position of the quinazoline [equivalent to the 3-position of QUINAP (**82**)] is believed to be important for asymmetric induction. Therefore, it was of interest to vary the substituent at the 2-position in an effort to investigate the effect of steric demand on the degree of enantioselection observed. Of interest also was the reduced basicity of the Quinazolinap donor nitrogen relative to QUINAP (**82**) (the pK_a values of simpler heteroaromatics related to **82** and **91** are 5.1 and 3.3, respectively).[121] It was hoped that variation of this electronic desymmetrisation, coupled with steric properties, would aid further understanding of the enantioselection process.

Cationic rhodium complexes of these ligands were prepared and applied in the enantioselective hydroboration-oxidation of a range of vinylarenes,[123,124] carefully chosen to highlight the effect on reactivity and enantioselectivity of different aryl substituents and β-substitution. A selection of these results, with the emphasis on the ligand which gave the highest enantioselectivity for each substrate, is shown in Table 12. Like QUINAP (**82**) and PHENAP (**87**), the (*S*)-ligand gave rise to the (*S*)-secondary alcohol.

The 2-substituted-Quinazolinap-derived rhodium complexes proved extremely efficient catalysts for the hydroboration-oxidation of vinylarenes. For styrene derivatives, in most cases quantitative conversions were obtained after just 2 h at the relevant temperature, entries 1–6. Higher enantioselectivities were afforded with a 4-methoxy substituent **19** (up to 95% ee, entry 3), compared to the 4-chloro **40** or unsubstituted **38** analogues, entries 5 and 1, a trend also observed in hydroboration with rhodium complexes of QUINAP (**82**). This highlights that both the electronic nature of the substrate combined with the inherent steric properties of the catalyst are important for high asymmetric induction. It is noteworthy that in most cases, optimum enantioselectivities were afforded by the less sterically demanding 2-methyl **92** and 2-unsubstituted analogues **93**, although the steric bulk of the 2-benzyl ligand **96** proved most effective for the hydroboration of styrene (**38**) at 0 °C, entry 2. In the Quinazolinap series as a whole, it was found that an electron-releasing substituent, as in **19**, had an adverse effect on regioselectivity compared to **38** and **40**.[123] In general, decreasing the reaction temperature had a deleterious effect on the regio- and enantioselectivity of the hydroboration. In contrast, low temperatures (−78 °C) were necessary to obtain high enantioselectivities for these substrates with BINAP (**25**).[11,87] While the asymmetry observed with this modular Quinazolinap series **91**–**96** is comparable, if not superior to other atropisomeric systems applied, they are limited in terms of regiochemical control.

Gratifyingly, a marked increase in regio- and enantioselectivity was observed when β-substituted substrates were employed, entries 7–17. On the whole, the hydroboration of (*Z*)-isomers proceeded with better conversions, regioselectivities and enantioselectivities than the hydroboration of the corresponding (*E*)-isomers. This is epitomised by the hydroborations of (*E*)- and (*Z*)-1-phenyl-1-propene (**30**), entries 7–10, and *cis*- and *trans*-stilbene (**45**), entries 14–17. For the hydroboration of (*Z*)-1-phenyl-1-propene (**30**), optimum enantiomeric excesses of 96% and 97% at room temperature and 0 °C, respectively, were obtained with (*S*)-2-methyl-Quinazolinap (**92**) and (*S*)-2-isopropyl-Quinazolinap (**94**), entries 9 and 10, the best results reported to date for this substrate. These two ligands were again to the fore for the hydroboration of *trans*-anethole (**88**), entries 11 and 12, although in comparison to (*E*)-1-phenyl-1-propene (**30**), regioselectivities were lower due to the additional 4-methoxy aromatic substituent. Surprisingly, a more favourable regiochemistry was obtained with *trans*-3,4-dimethoxy-β-methylstyrene (**97**) relative to *trans*-anethole (**88**), entry 13, and enantioselectivity was also excellent. Not for the first time, the steric influence of the 2-methyl analogue **92** proved optimal. The highest enantioselectivity to date for the hydroboration of *cis*-stilbene [(*Z*)-**45**, 99% ee] was achieved with the rhodium catalyst derived from (*S*)-2-isopropyl-Quinazolinap (**94**), entry 15. The 2-methyl and 2-*tert*-butyl ligands **92** and **95** were also highly effective in this transformation, entries 16 and 17. Furthermore, the cationic Quinazolinap/rhodium complexes proved excellent catalysts for the hydroboration of indene (**31**) and dihydronaphthalene (**32**), entries 18–20. While (*S*)-Quinazolinap (**93**) afforded 98% ee in the hydroboration of indene (**31**), entry 18, the introduction of a 2-methyl group into the ligand framework was striking, entry 19. As well as quantitative conversion and complete regioselectivity, an exceptional enantiomeric excess of 99.5% was observed; this remains the best result reported yet for the hydroboration of indene (**31**).

The group of Chan have reported the synthesis and resolution of the atropisomeric ligand Pyphos (**98**), Figure 10.[125,126] With the incorporation of the donor nitro-

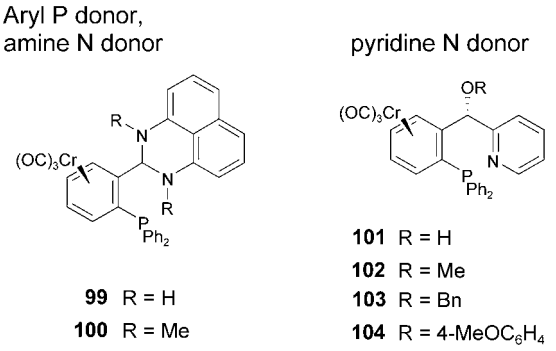


Figure 12.

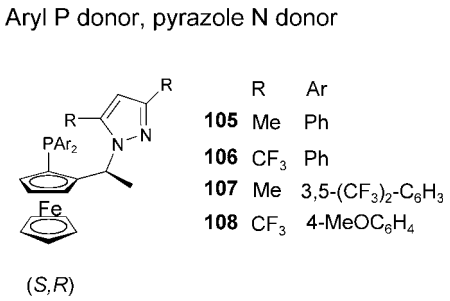
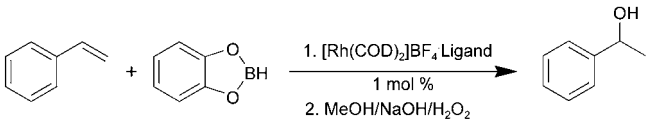


Figure 13.

gen atom in a pyridine moiety, an attractive feature of this system was the possibility of recycling the catalyst *via* phase separation (extraction of the ligand from the reaction mixture with hydrochloric acid). (*R*)-Pyphos (**98**) was applied in the enantioselective hydroboration of *para*-substituted vinylarenes and regioselectivities were excellent (>98:2 to 99:1) regardless of the substituent.[127] However, the reaction is only effective at low temperatures in contrast to other P,N ligands such as Quinap and the Quinazolinaps which induce high degrees of asymmetry, even at room temperature. Although the dihedral angle of (*R*)-Pyphos (**98**) (87°) is much larger than those of QUINAP (**82**), PHENAP (**87**) or the Quinazolinaps **91**–**96**, (65–67°) comparable asymmetries were induced. However, as in rhodium-catalysed hydroboration with these ligands, the enantioselectivity was dependent on the electronic properties of the *para*-substitutent. The enantiomeric excesses ranged from 79% for 4-chlorostyrene, 40% to 94% for 4-methoxystyrene (**19**), with 90% ee for the hydroboration of styrene (**38**). It was postulated that if the vinylarene always coordinates *trans* to nitrogen,[128] then for an electron-rich substrate, there is tighter coordination to cationic rhodium than for electron-poor analogues. Hence the electron-rich substrate is more strongly influenced by the chiral environment which gives rise to enhanced enantioselectivity.[127]

Table 13.



Entry[a]	Ligand	Yield [%]	α:β	% ee (Config.)
1	(*S*,*R*)-**105**	91	66:34	95 (*R*)
2	(*S*,*R*)-**106**	78	61:39	33 (*R*)
3	(*R*,*S*)-**107**	63	[b]	98.5 (*S*)
4	(*R*,*S*)-**108**	28	[b]	5 (*S*)

[a] Typical conditions: catecholborane (1) 1.0 mol % [Rh(COD)$_2$]BF$_4$·Ligand, THF, 20 °C, 3–5 h.
[b] Not quoted.

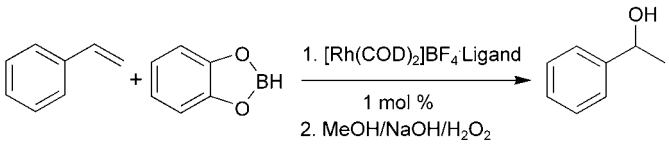
5.2 Planar Chirality

Chung and co-workers have developed a novel class of planar chiral (1,2-disubstituted arene)chromium tricarbonyl compounds which are amenable to facile steric and electronic tuning, Figure 12. Ligands **99** and **100**, which have a diamine and a phosphorus group in the two *ortho* benzylic positions, act as bi- and not tridentate ligands as determined by X-ray crystallography, and form a six-membered chelate ring.[129] Another modular series within this P,N class are ligands **101**–**104** which have an additional element of atom-centred chirality. The donor nitrogen is incorporated in a pyridine ring and thus gives rise to a seven-membered chelate.[130]

Rhodium complexes of these ligands were applied to the enantioselective hydroboration of styrenes.[129,130] Regioselectivities were excellent, regardless of the electronic nature of the substituent on the styrene. Ligands **99** and **103** were the best within each series. Ligand **99** induced moderate enantioselectivities (19–81% ee) at −15 °C. As the electron-donating ability of the *para*-substituent increases (Br < H < OMe), the ee increases simultaneously (19 < 53 < 62), a trend observed with QUINAP (**82**) and related P,N systems which also afforded higher ees for more electron-rich substrates. Curiously, the (superior) asymmetry induced by ligand **103** was not at all sensitive to the electronic effect of the substituent on the styrene ring. Enantiomeric excesses of 82% and 84% were afforded for 4-methoxy- and 4-bromostyrene, respectively. The highest ee for both ligands was in the hydroboration of 2,4-dimethylstyrene: 81% and 86% ee, for ligands **99** and **103**, respectively, where steric effects were the likely dominant factor.

The application of the diphosphine Josiphos (**67**), Figure 7, to the asymmetric hydroboration-oxidation of styrene (**38**) afforded 92% ee and excellent regioselectivity (>99:1) but this ligand was only effective at −78 °C, and only for this substrate.[102] By way of nucleophilic substitution with a pyrazole functionality at the

Table 14.



Entry[a]	Ligand	Time [h]	Conv. [%]	α:β	% ee[b]
1	**109**	19	74	97:3	57
2	**113**	14	54	84:16	80
3	**115**	16	>99	64:36	92

[a] Typical conditions: catecholborane (1), THF, −45 °C, 1.0 mol % $[Rh(COD)_2]BF_4$·2 Ligand.
[b] Absolute configuration (*S*) in all cases

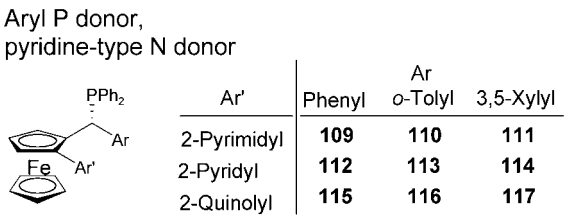


Figure 14.

pseudo-benzylic phosphine, Togni prepared a series of pyrazole-containing ferrocenyl ligands, Figure 13. These planar chiral ligands also possess an element of atom-centred chirality in the *pseudo*-benzylic position of the side chain. The simple synthetic approach allows for the preparation of a wide variety of analogues with easy modification of their stereoelectronic properties.

Rhodium complexes (1 mol %) prepared *in situ* from $[Rh(COD)_2]BF_4$ and the respective ligands **105**–**108** were employed in the enantioselective hydroboration-oxidation of styrene (**38**), Table 13.[131–133]

In contrast to the application of Josiphos (**67**) to the same transformation, these phosphinamine ligands were highly effective at ambient temperature. Ligand **105**, containing the 3,5-dimethylpyrazolyl fragment, afforded an excellent 95% ee for the hydroboration of styrene (**38**), entry 1. However, the ligands are limited in terms of regiochemical control, entries 1 and 2. Increasing the size of the pyrazole substituent from methyl to isopropyl resulted in a slightly lower 92% ee,[131] showing there was some dependence of the enantioselectivity on the steric properties of the ligand. However, the single most dominant influence was the electronic nature of the ligand. The different electronic properties of the pyrazole and phosphine moieties exert opposite influences and high asymmetries are induced when the combination exists such that nitrogen is a good σ-donor (electron-rich pyrazole) and phosphorus a good π-acceptor (electron-poor phosphine).[131]

To this end, while essentially conserving the steric bulk, replacement of the pyrazole methyl groups in **105** with the electron-withdrawing trifluoromethyl groups in **106** gave rise to a dramatic decrease in enantioselectivity, although the regioselectivity was largely unaffected, entry 2. However, when the CF_3 groups were placed on the phosphine instead in ligand **107**, thereby rendering the phosphine electron-deficient, an exceptional 98.5% ee was obtained, entry 3. This remains the best result reported yet for the hydroboration of styrene (**38**). In a striking illustration of the interplay of electronic effects and enantioselectivity, the combination of an electron-poor pyrazole and an electron-rich phosphine as in ligand **108** only afforded 5% ee, entry 4. The possibility that the low enantioselectivities in the case of electron-poor pyrazole ligands **106** and **108** was due to partial dissociation of the ligand from rhodium during catalysis was found to be unlikely and the pronounced effects on enantioselectivity therefore deemed largely electronic in nature.[131]

In terms of chiral ligands that incorporate both planar and atom-centred chirality, the ferrocenyl framework is unrivalled in its versatility. Moreover, the synthetic approach towards this ligand class allows for tailoring of the ligand through steric and electronic effects. The latter was in evidence in the electronic asymmetry of Togni's P,N ligands **105**–**108**. Recently, the group of Knochel has reported a set of nine new chiral ferrocenylphosphinamine ligands **109**–**117**, Figure 14. These ligands were tested in the rhodium-catalysed asymmetric hydroboration-oxidation of styrene (**38**), and representative results are shown in Table 14.[134]

Ligands **109**–**111** with a pyrimidyl group showed excellent regioselectivity but only moderate conversion and enantioselectivity, entry 1. In contrast, rhodium complexes of ligands **115**–**117** bearing a quinolyl group were highly efficient catalysts, inducing excellent enantioselectivity but at the expense of the regioselectivity, entry 3. The performance of the 2-pyridyl ligands **112**–**114**, lay in between these two extremes, entry 2. Optimal results were obtained with ligand **115** which gave 92% ee and almost quantitative conversion for the hydroboration of styrene (**38**), although with modest regioselectivity, entry 3.

6 Conclusion

In the two decades since Männig and Nöth paved the way for the development of a rhodium-catalysed olefin hydroboration process,[6] the subsequent enantioselective variant has become a valuable tool in catalytic asymmetric synthesis and a plethora of chiral ligands have been employed. Much of the early groundwork relied on the application of homobidentate P,P ligands. However, it has been the advent of heterobidentate P,N ligands in particular that has advanced the scope of this

reaction in terms of asymmetric induction. Even a brief glance at the results obtained underlines how the electronic and steric properties of each ligand must be finely tuned for individual substrates. To date, a ligand which provides the maximum reactivity and selectivity across a wide range of substrates remains elusive. Nevertheless, the future of enantioselective rhodium-catalysed hydroboration as an important synthetic transformation seems assured due to the high reactivity and impressive enantioselectivities thus far obtained.

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References

[1] H. C. Brown, B. C. Subba Rao, *J. Am. Chem. Soc.* **1956**, *78*, 2582.
[2] I. Beletskaya, A. Pelter, *Tetrahedron* **1997**, *53*, 4957.
[3] C. E. Tucker, J. Davidson, P. Knochel, *J. Org. Chem.* **1992**, *57*, 3482.
[4] H. Kono, K. Ito, Y. Nagai, *Chem. Lett.* **1975**, 1095.
[5] S. A. Westcott, N. J. Taylor, T. B. Marder, R. T. Baker, N. L. Jones, J. C. Calabrese, *J. Chem. Soc. Chem. Commun.* **1991**, 304.
[6] D. Männig, H. Nöth, *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 878.
[7] K. Burgess, M. J. Ohlmeyer, *J. Org. Chem.* **1988**, *53*, 5178.
[8] C. M. Crudden, D. Edwards, *Eur. J. Org. Chem.* **2003**, 4695.
[9] G. C. Fu, *Transition Metals for Organic Synthesis*, Vol. II, Wiley-VCH, Weinheim, **1998**.
[10] T. Hayashi, in: *Comprehensive Asymmetric Catalysis*, Vol. I, Springer, New York, **1999**.
[11] T. Hayashi, Y. Matsumoto, Y. Ito, *Tetrahedron: Asymmetry* **1991**, *2*, 601.
[12] J. M. Brown, D. I. Hulmes, T. P. Layzell, *Chem. Commun.* **1993**, 1673.
[13] A. Chen, L. Ren, C. M. Crudden, *Chem. Commun.* **1999**, 611.
[14] A. Chen, L. Ren, C. M. Crudden, *J. Org. Chem.* **1999**, *64*, 9704.
[15] L. Ren, C. M. Crudden, *Chem. Commun.* **2000**, 721.
[16] Y. Takaya, M. Ogasawara, T. Hayashi, *Tetrahedron Lett.* **1998**, *39*, 8479.
[17] S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angew. Chem. Int. Ed.* **2001**, *40*, 4544.
[18] A. Suzuki, *J. Organomet. Chem.* **2002**, 83.
[19] R. Rubina, M. Rubin, Gevorgyan, *J. Am. Chem. Soc.* **2003**, *125*, 7198.
[20] J.-P. Goddard, T. Le Gall, C. Mioskowski, *Org. Lett.* **2000**, *2*, 1455.
[21] M. J. O'Donnell, J. T. Cooper, M. M. Mader, *J. Am. Chem. Soc.* **2003**, *125*, 2370.
[22] G. A. Molander, T. Ito, *Org. Lett.* **2001**, *3*, 393.
[23] E. Fernandez, K. Maeda, M. W. Hooper, J. M. Brown, *Chem. Eur. J.* **2000**, *6*, 1840.
[24] C. M. Crudden, Y. B. Hleba, A. C. Chen, *J. Am. Chem. Soc.* **2004**, *126*, 9200.
[25] K. Maeda, J. M. Brown, *Chem. Commun.* **2002**, 310.
[26] A. Pérez Luna, M.-A. Ceschi, M. Bonin, L. Micouin, H.-P. Husson, *J. Org. Chem.* **2002**, *67*, 3522.
[27] A. M. Segarra, R. Guerrero, C. Claver, E. Fernandez, *Chem. Commun.* **2001**, 1808.
[28] A. M. Segarra, F. Guirado, C. Claver, E. Fernandez, *Tetrahedron: Asymmetry* **2003**, *14*, 1611.
[29] A. M. Segarra, R. Guerrero, C. Claver, E. Fernández, *Chem. Eur. J.* **2003**, *9*, 191.
[30] J. M. Brown, *Modern Rhodium Catalyzed Organic Reactions*, Wiley-VCH, Weinheim, **2004**.
[31] A. Arase, Y. Nunokawa, Y. Masuda, M. Hoshi, *J. Chem. Soc. Chem. Commun.* **1991**, 205.
[32] I. D. Gridnev, N. Miyaura, A. Suzuki, *Organometallics* **1993**, *12*, 589.
[33] G. W. Kabalka, C. Narayana, N. K. Reddy, *Synth. Commun.* **1994**, *24*, 1019.
[34] Y. Matsumoto, M. Naito, T. Hayashi, *Organometallics* **1992**, *11*, 2732.
[35] Y. Matsumoto, M. Naito, Y. Uozumi, T. Hayashi, *J. Chem. Soc. Chem. Commun.* **1993**, 1468.
[36] I. D. Gridnev, N. Miyaura, A. Suzuki, *J. Org. Chem.* **1993**, *58*, 5351.
[37] K. Burgess, M. Jaspars, *Organometallics* **1993**, *12*, 4197.
[38] R. H. Crabtree, M. W. Davis, *J. Org. Chem.* **1986**, *51*, 2655.
[39] D. A. Evans, G. C. Fu, A. H. Hoveyda, *J. Am. Chem. Soc.* **1992**, *114*, 6671.
[40] J. A. Brinkman, T. T. Nguyen, J. R. Sowa Jr., *Org. Lett.* **2000**, *2*, 981.
[41] A. Pérez Luna, M. Bonin, L. Micouin, H.-P. Husson, *J. Am. Chem. Soc.* **2002**, *124*, 12098.
[42] K. N. Harrison, T. J. Marks, *J. Am. Chem. Soc.* **1992**, *114*, 9220.
[43] D. A. Evans, A. R. Muci, R. Stürmer, *J. Org. Chem.* **1993**, *58*, 5307.
[44] G. A. Molander, D. Pfeiffer, *Org. Lett.* **2001**, *3*, 361.
[45] X. He, J. F. Hartwig, *J. Am. Chem. Soc.* **1996**, *118*, 1696.
[46] S. Pereira, M. Srebnik, *Organometallics* **1995**, *14*, 3127.
[47] S. Pereira, M. Srebnik, *Tetrahedron Lett.* **1996**, *37*, 3283.
[48] S. Pereira, M. Srebnik, *J. Am. Chem. Soc.* **1996**, *118*, 909.
[49] 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.
[50] K. Burgess, M. J. Ohlmeyer, *Chem. Rev.* **1991**, *91*, 1179.
[51] D. G. Musaev, A. M. Mebel, K. Morokuma, *J. Am. Chem. Soc.* **1994**, *116*, 10693.

[52] C. Widauer, H. Grützmacher, T. Ziegler, *Organometallics* **2000**, *19*, 2097.
[53] C. E. F. Rickard, W. R. Roper, A. Williamson, L. J. Wright, *Angew. Chem. Int. Ed.* **1999**, *38*, 1110.
[54] D. A. Evans, G. C. Fu, *J. Org. Chem.* **1990**, *55*, 2280.
[55] K. Burgess, W. A. van der Donk, A. M. Kook, *J. Org. Chem.* **1991**, *56*, 2949.
[56] K. Burgess, W. A. van der Donk, A. M. Kook, *J. Org. Chem.* **1991**, *56*, 7360.
[57] D. A. Evans, G. C. Fu, B. A. Anderson, *J. Am. Chem. Soc.* **1992**, *114*, 6679.
[58] J. M. Brown, D. A. Evans, A. P. James, *Org. Synth.* **1989**, *68*, 64.
[59] M. J. Burk, J. E. Feaster, W. A. Nugent, R. L. Harlow, *J. Am. Chem. Soc.* **1993**, *115*, 10125.
[60] I. D. Gridnev, M. Yasutake, N. Higashi, T. Imamoto, *J. Am. Chem. Soc.* **2001**, *123*, 5268.
[61] K. Burgess, M. Jaspars, *Tetrahedron Lett.* **1993**, *34*, 6813.
[62] S. A. Westcott, H. P. Blom, T. B. Marder, R. T. Baker, J. C. Calabrese, *Inorg. Chem.* **1993**, *32*, 2175.
[63] C. M. Vogels, P. G. Hayes, M. P. Shaver, S. A. Westcott, *Chem. Commun.* **2000**, 51.
[64] S. Colin, L. Vaysse-Ludot, J.-P. Lecouvé, J. Maddaluno, *J. Chem. Soc. Perkin Trans. 1* **2000**, 4505.
[65] T. Ohmura, Y. Yamamoto, N. Miyaura, *J. Am. Chem. Soc.* **2000**, *122*, 4990.
[66] P. J. Fazen, L. G. Sneddon, *Organometallics* **1994**, *13*, 2867.
[67] A. T. Lynch, L. G. Sneddon, *J. Am. Chem. Soc.* **1987**, *109*, 5867.
[68] E. Fernandez, M. W. Hooper, F. I. Knight, J. M. Brown, *Chem. Commun.* **1997**, 173.
[69] X. Huang, Z. Y. Lin, *Computational Modelling of Homogeneous Catalysis*, Kluwer, Dordrecht, **2002**.
[70] A. E. Dorigo, P. von Ragué Schleyer, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 115.
[71] R. T. Baker, J. C. Calabrese, S. A. Westcott, P. Nguyen, T. B. Marder, *J. Am. Chem. Soc.* **1993**, *115*, 4367.
[72] R. T. Baker, P. Nguyen, T. B. Marder, S. A. Westcott, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1336.
[73] G. R. Clark, G. J. Irvine, W. R. Roper, L. J. Wright, *Organometallics* **1997**, *16*, 5499.
[74] J. R. Knorr, J. S. Merola, *Organometallics* **1990**, *9*, 3008.
[75] J. M. Brown, G. C. Lloyd-Jones, *J. Am. Chem. Soc.* **1994**, *116*, 866.
[76] J. Liedtke, H. Ruegger, S. Loss, H. Grützmacher, *Angew. Chem. Int. Ed.* **2000**, *39*, 2478.
[77] J. Cossy, S. BouzBouz, *Tetrahedron Lett.* **1996**, *37*, 5091.
[78] M. R. Smith III, *Prog. Inorg. Chem.* **1999**, *48*, 505.
[79] P. V. Ramachandran, M. P. Jennings, H. C. Brown, *Org. Lett.* **1999**, *1*, 1399.
[80] A. M. Segarra, C. Claver, E. Fernandez, *Chem. Commun.* **2004**, 464.
[81] A. Pelter, K. Smith, in: *Comprehensive Organic Chemistry*, Vol. III, Pergamon Press, London, **1979**.
[82] J. Zhang, B. Lou, G. Guo, L. Dai, *J. Org. Chem.* **1991**, *56*, 1670.
[83] T. C. Morrill, C. A. D'Souza, L. Yang, A. J. Sampognaro, *J. Org. Chem.* **2002**, *67*, 2481.
[84] U. Nettekoven, J. F. Hartwig, *J. Am. Chem. Soc.* **2002**, *124*, 1166.
[85] J. M. Brown, G. C. Lloyd-Jones, *Tetrahedron: Asymmetry* **1990**, *1*, 869.
[86] M. Sato, N. Miyaura, A. Suzuki, *Tetrahedron Lett.* **1990**, *31*, 231.
[87] T. Hayashi, Y. Matsumoto, Y. Ito, *J. Am. Chem. Soc.* **1989**, *111*, 3426.
[88] H. B. Kagan, T. P. Dang, *J. Am. Chem. Soc.* **1972**, *94*, 6429.
[89] H. Takaya, K. Mashima, K. Koyano, M. Yagi, H. Kumobayashi, T. Taketomi, S. Akutagawa, R. Noyori, *J. Org. Chem.* **1986**, *51*, 629.
[90] M. D. Fryzuk, B. Bosnich, *J. Am. Chem. Soc.* **1977**, *99*, 6262.
[91] T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, S. Konishi, K. Yamamoto, M. Kumada, *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138.
[92] K. Burgess, W. A. van der Donk, M. J. Ohlmeyer, *Tetrahedron: Asymmetry* **1991**, *2*, 613.
[93] B. D. Vineyard, W. S. Knowles, M. J. Sabacky, G. L. Bachman, D. J. Weinkauff, *J. Am. Chem. Soc.* **1977**, *99*, 5946.
[94] K. Burgess, W. A. van der Donk, *Inorg. Chim. Acta* **1994**, *220*, 93.
[95] K. Burgess, M. J. Ohlmeyer, K. H. Whitmire, *Organometallics* **1992**, *11*, 3588.
[96] H. Jendralla, C. H. Li, E. Paulus, *Tetrahedron: Asymmetry* **1994**, *5*, 1297.
[97] J. L. Ruiz, T. Flor, J. Carles Bayón, *Inorg. Chem. Commun.* **1999**, *2*, 484.
[98] S. Demay, F. Volant, P. Knochel, *Angew. Chem. Int. Ed.* **2001**, *40*, 1235.
[99] J.-M. Brunel, G. Buono, *Tetrahedron Lett.* **1999**, *40*, 3561.
[100] C. Bianchini, P. Barbaro, G. Scapacci, F. Zanobini, *Organometallics* **2000**, *19*, 2450.
[101] C. Bianchini, P. Barbaro, G. Scapacci, *J. Organomet. Chem.* **2001**, *621*, 26.
[102] A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062.
[103] M. T. Reetz, E. W. Beuttenmüller, R. Goddard, M. Pastó, *Tetrahedron Lett.* **1999**, *40*, 4977.
[104] J. Kang, J. H. Lee, J. B. Kim, G. J. Kim, *Chirality* **2000**, *12*, 378.
[105] F. Blume, S. Zemolka, T. Fey, R. Kranich, H.-G. Schmalz, *Adv. Synth. Catal.* **2002**, *344*, 868.
[106] J.-I. Sakaki, W. B. Schweitzer, D. Seebach, *Helv. Chim. Acta* **1993**, *76*, 2654.
[107] P. J. Guiry, M. McCarthy, P. M. Lacey, C. P. Saunders, S. Kelly, D. J. Connolly, *Curr. Org. Chem.* **2000**, *4*, 821.
[108] C. P. Saunders, P. J. Guiry, *Adv. Synth. Catal.* **2004**, *346*, 497.
[109] N. W. Alcock, J. M. Brown, D. I. Hulmes, *Tetrahedron: Asymmetry* **1993**, *4*, 743.
[110] N. W. Alcock, J. M. Brown, D. I. Hulmes, *J. Chem. Soc. Chem. Commun.* **1995**, 395.

[111] C. W. Lim, O. Tissot, A. Mattison, M. W. Hooper, J. M. Brown, A. R. Cowley, D. I. Hulmes, A. J. Blacker, *Organic Process Research & Development* **2003**, *7*, 379.
[112] H. Doucet, E. Fernandez, T. P. Layzell, J. M. Brown, *Chem. Eur. J.* **1999**, *5*, 1320.
[113] H. Doucet, J. M. Brown, *Tetrahedron: Asymmetry* **1997**, *8*, 3775.
[114] J. M. Brown, D. I. Hulmes, P. J. Guiry, *Tetrahedron* **1994**, *50*, 4493.
[115] J.-M. Valk, T. D. W. Claridge, J. M. Brown, D. Hibbs, M. B. Hursthouse, *Tetrahedron: Asymmetry* **1995**, *6*, 2597.
[116] J.-M. Valk, G. A. Whitlock, T. P. Layzell, J. M. Brown, *Tetrahedron: Asymmetry* **1995**, *6*, 2593.
[117] A. Korostylev, I. Gridnev, J. M. Brown, *J. Organomet. Chem.* **2003**, *680*, 329.
[118] E. Daura-Oller, A. M. Segarra, J. M. Poblet, C. Claver, E. Fernandez, C. Bo, *J. Org. Chem.* **2004**, *69*, 2669.
[119] A. M. Segarra, E. Daura-Oller, C. Claver, J. M. Poblet, C. Bo, E. Fernandez, *Chem. Eur. J.* **2004**, *10*, 6456.
[120] M. McCarthy, P. J. Guiry, *Polyhedron* **2000**, *19*, 541.
[121] M. McCarthy, R. Goddard, P. J. Guiry, *Tetrahedron: Asymmetry* **1999**, *10*, 2797.
[122] P. M. Lacey, C. M. McDonnell, P. J. Guiry, *Tetrahedron Lett.* **2000**, *41*, 2475.
[123] D. J. Connolly, P. M. Lacey, M. McCarthy, C. P. Saunders, A.-M. Carroll, R. Goddard, P. J. Guiry, *J. Org. Chem.* **2004**, *69*, 6572.
[124] M. McCarthy, M. W. Hooper, P. J. Guiry, *Chem. Commun.* **2000**, 1333.
[125] F. Y. Kwong, K. S. Chan, *Organometallics* **2000**, *19*, 2058.
[126] F. Y. Kwong, K. S. Chan, *Organometallics* **2001**, *20*, 2570.
[127] F. Y. Kwong, Q. Yang, T. C. W. Mak, A. S. C. Chan, K. S. Chan, *J. Org. Chem.* **2002**, *67*, 2769.
[128] H. Kurosawa, I. Ikeda, *J. Organomet. Chem.* **1992**, *428*, 289.
[129] S. U. Son, H.-Y. Jang, I. S. Lee, Y. K. Chung, *Organometallics* **1998**, *17*, 3236.
[130] S. U. Son, H.-Y. Jang, J. W. Han, I. S. Lee, Y. K. Chung, *Tetrahedron: Asymmetry 1999*, *10*, 347.
[131] A. Schnyder, L. Hintermann, A. Togni, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 931.
[132] U. Burckhardt, L. Hintermann, A. Schnyder, A. Togni, *Organometallics* **1995**, *14*, 5415.
[133] A. Schnyder, A. Togni, U. Wiesli, *Organometallics* **1997**, *16*, 255.
[134] R. J. Kloetzing, M. Lotz, P. Knochel, *Tetrahedron: Asymmetry* **2003**, *14*, 255.

