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"Bár zord a harc, megéri a világ,
Ha az ember az marad, ami volt:
Nemes, küzdő, szabadlelkű diák."

Ady Endre - Üzenet egykori iskolámba

Pour ma fiancée,

Pour conclure, je voudrais plus particulièrement remercier ma fiancée, Hélène Guerrand, pour son soutien sans faille tout au long de ces années. Elle a toujours su me guider, et m'aider à distinguer ce qui a de la valeur et du sens de tout le reste. Ma thèse vient de s'achever mais ensemble nous continuons à écrire de très belles pages du livre de notre vie et cela suffit à me combler.

Bordeaux, France,
26 March 2012 Szalóki György

Abstract

Part I : Synthesis of Novel Purely Planar Chiral Ferrocenes for Asymmetric Synthesis

The first part of the thesis describes the design and synthesis of a series of 1,2-bidendate purely planar chiral ferrocenyl ligand (Ligand A, B, C). The planar chirality was established using Kagan's Directed *ortho* Metallation (D*o*M) strategy. Introduction of the desired *α*–cyclopentadienyl moiety proved to be difficult using nucleophilic substitution. This was circumvented by utilising Stone's fulvene formation method, followed by reduction of the corresponding fulvene. The synthesised ligands were then subjected to complexation studies. In general, the obtained complexes proved to be unstable. Despite the instability issue, their activity was tested in several asymmetric catalytic processes (Diels-Alder reaction, reconstitutive condensation, allylic substitution), however no enantio-induction was detected. In the course of extending the scope of the Stone method, it was applied to different cyclopentadienyl type (indenyl, fluorenyl, tetramethylcyclopentadienyl) systems successfully. In addition, the synthesis of a novel ferrocene linked dimer is given. This ligand showed moderate activity in allylic alkylation reaction.

Part II : Synthesis of Novel Azaferrocenylboronic Acids

Based on Whiting's preliminary report a novel azaferrocenylboronic acid structure was envisaged. The best synthetic approach consisted of two steps. The aryl functionality was introduced at the 2-position of the azaferrocene ring in a Negishi cross coupling reaction, which was followed by a lithium-halogen exchange/boronylation sequence. Boronylations under different conditions were tested, however, isolation of the target boronic acid was unsuccessful probably due to its instability. Introduction of the borane functionality was achieved by using a modified boronylating agent and the resulting azaferrocenylborane proved to be stable. A monohydroxyboronic acid was isolated, which might be a candidate for asymmetric direct amide bond forming reactions.

Abbreviations

AAA	asymmetric allylic alkylation
Ac	acetyl
Ar	aryl
ARCM	asymmetric ring closing metathesis
ATH	asymmetric transfer hydrogenation
BINAP	2,2’-bis(diphenylphosphino)-1,1’-binapthyl
Bn	benzyl
BSA	*N*,*O*-bis(trimethylsilyl)acetamide
^{t}Bu	*tert*-butyl
cat.	catalyst
CDI	1,1'-Carbonyldiimidazole
CDMT	2-chloro-4,6-dimethoxy-1,3,5-trazine
cond.	condition
conv.	conversion
Cp	cyclopentadienyl
$Cp_{sub.}$	substituted cyclopentadienyl ring of ferrocene derivatives
$Cp_{unsub.}$	unsubstituted cyclopentadienyl ring of ferrocene derivatives
CSA	camphor sulfonic acid
Cy	cyclohexyl
DABCO	1,4-diazabicyclo[2.2.2]octane
DCC	dicyclohexylcarbodiimide
DCM	dichloromethane
decomp.	decomposition
DG	directing group
DIBAL-H	diisobutylaluminium hydride
DIC	diisopropylcarbodiimide
DMAP	4-*N*,*N*-dimethylaminopyridine
DMF	*N*,*N*-dimethylformamide

DMM	dimethylmalonate
DMP	Dess-Martin Periodinane
DMSO	dimethylsulfoxide
D*o*M	Directed *ortho* Metallation
dppb	1,4-Bis(diphenylphosphino)butane
dr	diastereoisomer ratio
e	electron
E	electrode potential
E^+	electrophile
EDCI	1-ethyl-3-(3-dimethylaminopropyl) carbodiimide
EDG	electron donating group
ee	enantiomeric excess
EEDQ	*N*-Ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline
Et	ethyl
EWG	electron withdrawing group
FBC	fluorous bi-phasic catalysis
Flu.	fluorenyl
Fulv.	fulvenyl
h	hours
HOAt	1-Hydroxy-7-azabenzotriazole
HOBt	hydroxybenzotriazole
HRMS	high resolution mass spectrometry
HYP	hydroxyproline
Ind.	Indenyl
IR	infra red
kJ	kilojoules
L	ligand
LG	leaving group
L-Selectride®	$LiHB(^iPr)_3$
Me	methyl
MMA	methyl methacrylate
m.p.	melting point
Ms	methanesulfonyl or mesyl
MS	molecular sieve

NIS	*N*-Iodosuccinimide
NMR	nuclear magnetic resonance
Nu	nucleophile
Oxaz.	oxazoline
^{i}Pr	*iso*-propyl
Ph	phenyl
Phth.	phthalimido group
PPFA	*N*,*N*-dimethyl-1-[-2-(diphenylphosphino)ferrocenyl]ethylamine
Py	pyridine
Rf	retention factor
red.	reduction
refl.	reflux
r.t.	room temperature
solv.	solvent
Superhydride®	$LiHBEt_3$
T	temperature
TBAF	tetrabutylammonium fluoride
TBHP	*tert*-butyl hydroperoxide
TBS	tert-butyldimethylsilyl
TES	triethylsilane
Tf	trifluoromethanesulfonyl or triflate
THF	tetrahydrofuran
THP	tetrahydropyran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMCp	tetramethyl cyclopentadienyl
TMEDA	*N*,*N*,*N*,*N*-tetramethylethylenediamine
TMS	trimethylsilyl
Tol	toluene
TON	turnover number
Ts	tolylsulfonyl or tosyl
*p*TSA	*para*-toluenesulfonic acid
y	yield

Table of Contents

Part I

Part II

1. Asymmetric Synthesis and Catalysis

Synthesis of enantiomerically pure compounds is very important because enantiomer recognition plays an important role in many biological systems. There are different ways of obtaining single enantiomers with respect to the source of chiral information.

Chiral Pool Strategy. One can use natural building blocks, such as amino acids or sugars existing in nature, to incorporate their chirality into the product. Although this is a cheap way of establishing chirality, as these compounds are readily available from natural sources, it is limited often to only one of the two enantiomers.

Resolution. A racemic mixture can be resolved by formation of diastereomers. By using chiral compounds a mixture of diastereomers result which are possible to separate by crystalisation. The limitation of the process lies in the maximum 50% yield which makes it wasteful unless both enantiomers are useful. This approach is used in the commercial synthesis of (*S*)- and (*R*)-BINAP.

Chiral Auxiliaries. In this technique the stereochemical information of the auxiliary is transferred to the product. However, the auxiliary needs to be used in a stoichiometric amount and its introduction and removal adds two extra steps to the synthesis.

Organocatalysis. In 1971 Hajós, Parrish,[1] Eder, Sauer and Wiechert[2] found that (*S*)-Proline catalyses asymmetric aldol reactions. The value of these reactions was overlooked for a few decades and it was in the late 1990s when organocatalysis was re-invigorated. Since then the field has been expanding continously.[3] This method uses

catalytic or substoichiometric amounts of small organic chiral molecules to achieve asymmetric induction.

Asymmetric Catalysis. The most efficient way of performing asymmetric transformations is by asymmetric catalysis. The strong asymmetric inductive effect of a chiral catalyst is reflected in their high Turnover Number (TON). However, to date only a few really efficient processes exist (asymmetric hydrogenation, epoxidation, dihydroxylation). The importance of the field was acknowledged by awarding the Nobel Prize to Knowles, Noyori and Sharpless in 2001.

2. Coordination Chemistry

The use of chiral organometallic catalysts is a powerful strategy in asymmetric catalysis. In general these catalysts consist of a metal atom stabilised by electron donating ligands. For a metal complex to be synthetically useful it needs to be stable enough so that no decomposition occurs under the reaction conditions. On the other hand, it needs to be reactive enough once it is added into the reaction to enable the rate acceleration. Synthetically useful metal complexes exist in the intersection of these two features. The rule of thumb to the stability of these compounds is the 18-electron rule. According to this a metal complex is stable if it has the noble gas configuration (18 electron in the ligand field). The ligand field consists of the electrons from the valence shell of the metal and the additional number of electrons (required to reach 18) given by the surrounding ligands.[4] However, there are exceptions whereby metal complexes do not fit this rule ($MeTiCl_3$, 8e; WMe_6, 12e; $PdCl_2(NCMe)_2$, 16e; $CoCp_2$, 19e; $NiCp_2$, 20e). There are three main ligand types for coordination complexes:

1. Ligands like CO, NR_3, PR_3, halogen, OR_2 and SR_2 use their lone pair to coordinate to the metal.

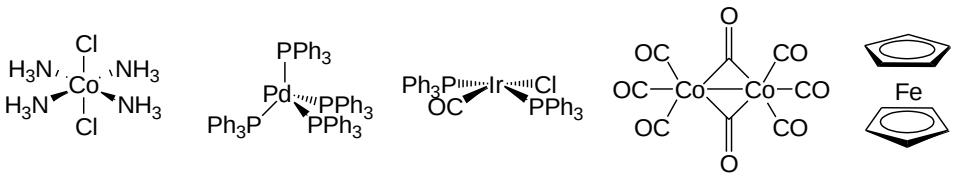
2. Molecules like ethylene, dienes, trienes, benzene and cyclopentadiene do not have lone pairs yet they bind strongly to some metals (**Pi Complexes**) using the electrons derived from the π-bonds or the aromatic system.

3. **Sigma Complexes** use the σ–bond of a molecule with the general structure H-Y (Y = H, C, Si, B, M). The latter (Y = M) is usually supported by strong backdonation from the non-bonding orbitals of the metal.

Ambidendate ligands (eg. CO, ethylene) can change their binding mode by using one of the 3 described above. Different ways of coordination are reflected in the hapto number (η) assigned to the ligand (number of atoms involved in binding to the metal).

3. Metallocenes

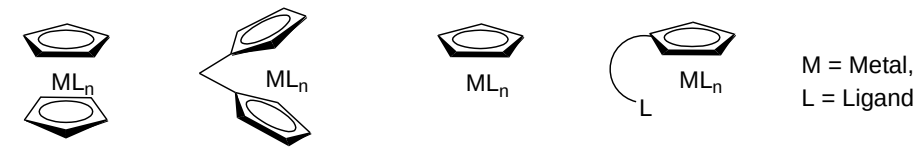
Metallocenes are classified as complexes having two Cp ligands coordinated to the metal centre. The discovery of ferrocene (**page 37**) made a great impact on organometallic chemistry. Its structure later had been deduced and the concept of π-bonding of a metal to an aromatic molecule has clearly revolutionalised the field describing classical Werner complexes until that point (**Figure 1**). The 'ene' terminus in the name metallocene refers to the aromatic group involved in the coordination. On the other hand the stability and aromatic reactivity of these compounds is also reflected in it. Since the birth of the field, a vast number of other metallocenes have been synthesised and today they make up 80% of all transition metal complexes.[5]



1 $Co(NH_3)_4Cl_2$ **2** $Pd(PPh_3)_4$ **3** Vaska's complex **4** $Co(CO)_4$ **5** Ferrocene

Figure 1: A few examples for classical Werner complexes (**1**, **2**, **3** and **4**) and a metallocene (ferrocene) **5**.

The advantages of Cp over other ligands comes from the fact that it is chemically relatively inert and also binds strongly to the metal. In addition modifications of the Cp unit alter the chemical properties of the coordinated metal therefore the catalytic activity of the metal complex can be fine tuned. Another way of changing the activity of the metal is to reduce the steric congestion caused by the bulky Cp-groups. 'Tying back' is used to create some extra space on the coordinaton sphere of the metal (**Figure 2**). These compounds are called *ansa*-metallocenes **7** (*ansa* comes from latin meaning 'bent handle'). If an even more accessible coordination sphere is needed one Cp-unit can be removed to give half-sandwich metallocenes **8**. Their tendancy to racemise under the reaction conditions can be circumvented by linking the metal to the Cp-group through a 'handle' (*ansa*-half sandwich metallocenes **9**). The chelate effect (chelate comes from greek meaning 'claw') makes the ligands less prone to displacement compared to those of the monodendate ligands of the same type.



6 metallocene **7** "tied back" *ansa*-metallocene **8** half sandwich metallocene **9** *ansa*-half sandwich metallocene

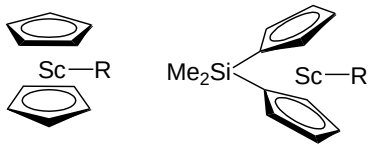
Figure 2: Main types of metallocenes (**6**, **7**, **8** and **9**).

3.1 Metallocenes in Synthesis

In 1957 Natta[6] and Breslow[7] found that bis(cyclopentadienyl)-titanium dichloride catalyses the polymerisation of ethylene. Today polymerisation remains the most important commercial application of metallocenes.

3.2 *Ansa*-Half Sandwich Metallocenes in Synthesis

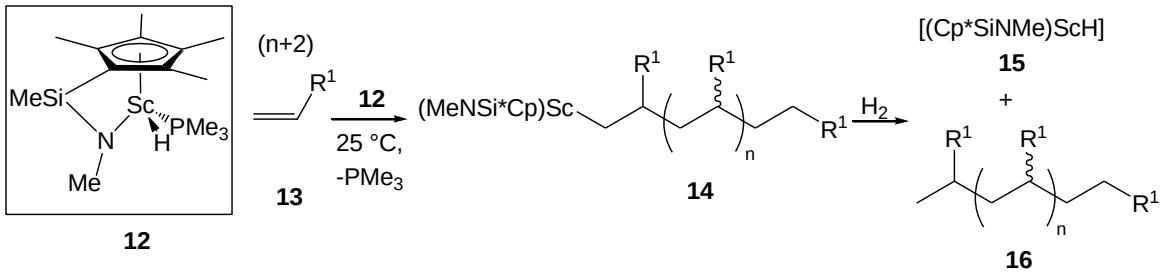
More than 30 years later *ansa*-half sandwich metallocenes found application in α–olefin polymerisation. In 1988 Bercaw found that complexes **10** and **11** undergo facile olefin insertion which makes them useful catalysts for polymerisation reactions (**Figure 3**).



10 **11**

Figure 3: Complexes **10** and **11** were found to undergo facile olefin insertion.

In an attempt to enhance the catalytic activity *ansa*-half sandwich scandocene **12** was synthesised and found to be active in the regioselective α–olefin polymerisation reaction (**Scheme 1**). It was anticipated that complex **12** was more reactive than **10** and **11** for two reasons. By changing the bulky Cp ligand to a PMe_3 group made the reactive metal centre more accessible and, secondly, the amido group is believed to make the metal more Lewis acidic.[8]

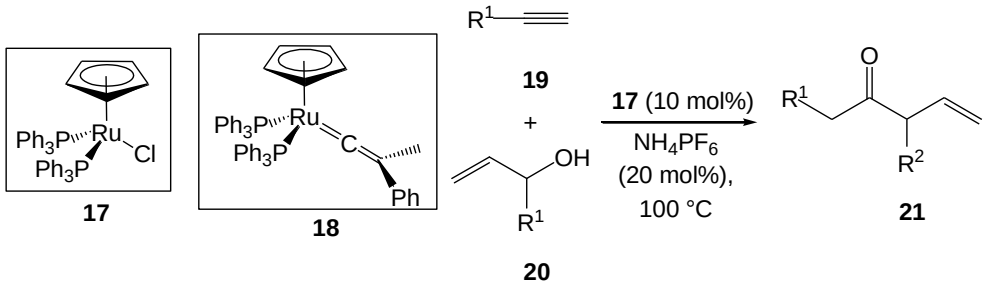


12 **13** **14** **16**

Scheme 1: Ansa-half scandocene **12** is active in regioselective α–polymerisation reaction.

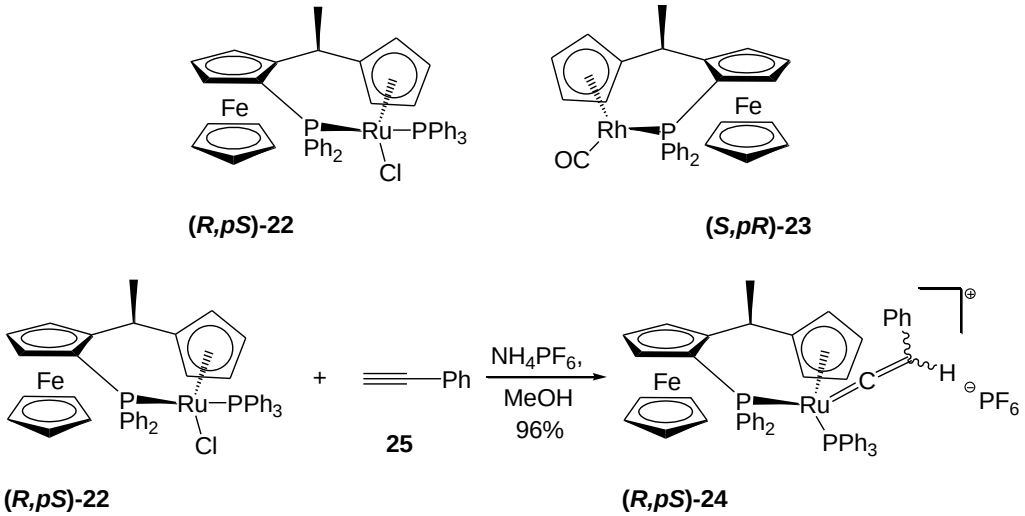
3.3 *Ansa*-Half Sandwich Metallocenes in Asymmetric Catalysis

In 1991 Trost investigated the reconstitutive condensation of allylic alcohols **20** and terminal alkynes **19** catalysed by Ru complex **17** (**Scheme 2**).[9] It was proposed that the reaction proceeds *via* a ruthenium vinylidene intermediate **18**.



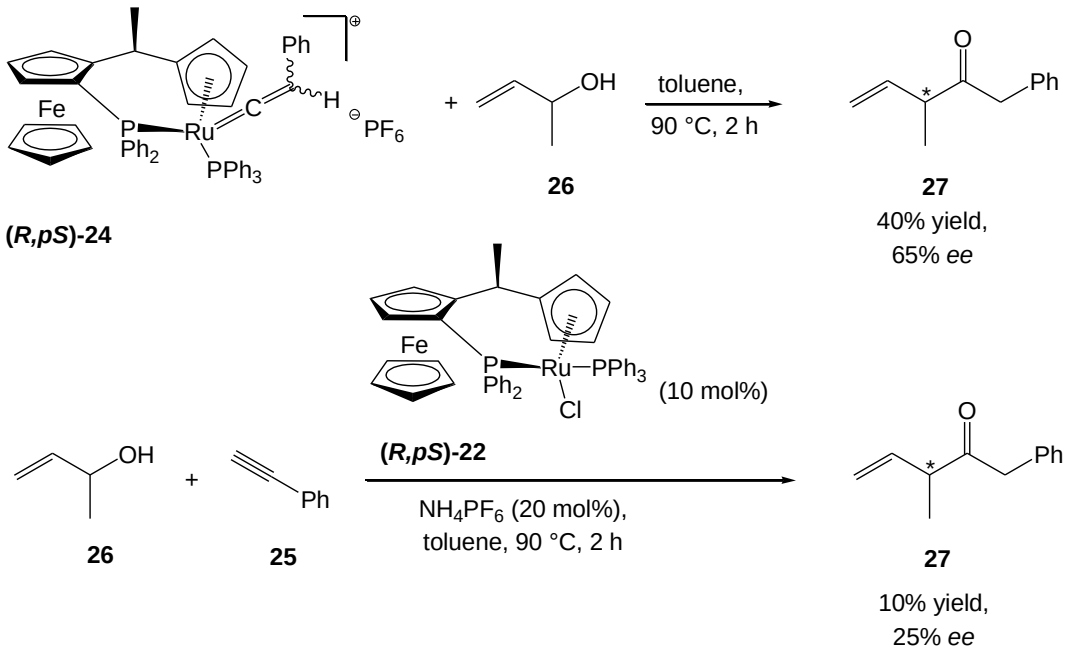
Scheme 2: Reconstitutive condensation of terminal alkynes **19** and allylic alcohols **20**.

This work was extended by Hidai in 1997, who synthesised planar chiral ferrocene complexes **(*R,pS*)-22** and **(*S,pR*)-23** and vinylidene **(*R,pS*)-24** (**Scheme 3**).[10] Vinylidene **(*R,pS*)-24** was obtained as a single diastereomer after recrystallisation.



Scheme 3: Ruthenium complexes synthesised by Hidai and co-workers.

When **(*R,pS*)-24** was reacted with allylic alcohol **25**, product **26** was obtained in 40% yield and 65% *ee*. Conducting the reaction under catalytic conditions (10 mol%), gave the product in 10% yield and 25% *ee* (**Scheme 4**). These results suggest that vinylidene **(*R,pS*)-24** is indeed involved in the reaction, however, stereospecific formation and regeneration of vinylidene **(*R,pS*)-24** does not occur under these reaction conditions. In fact, it was found that upon treatment of complex **(*R,pS*)-22** with excess phenylacetylene **25** gave **27** as mixture of diastereomers in 7/2/1 ratio.



Scheme 4: Reconstitutive condensation under stoichiometric and catalytic conditions.

Trost later proposed a catalytic cycle for the reaction (**Figure 4**).[11] First, the catalyst forms a vinylidene complex with the terminal alkyne **25**, thus activating it towards nucleophilic attack. Then the allylic alcohol coordinates to the ruthenium in exchange for a ligand. This is followed by nucleophilic attack of the hydroxyl at the α-position. After this a π–allyl complex is formed which in the last step gives the product **27** and liberates the catalyst for the next catalytic cycle.

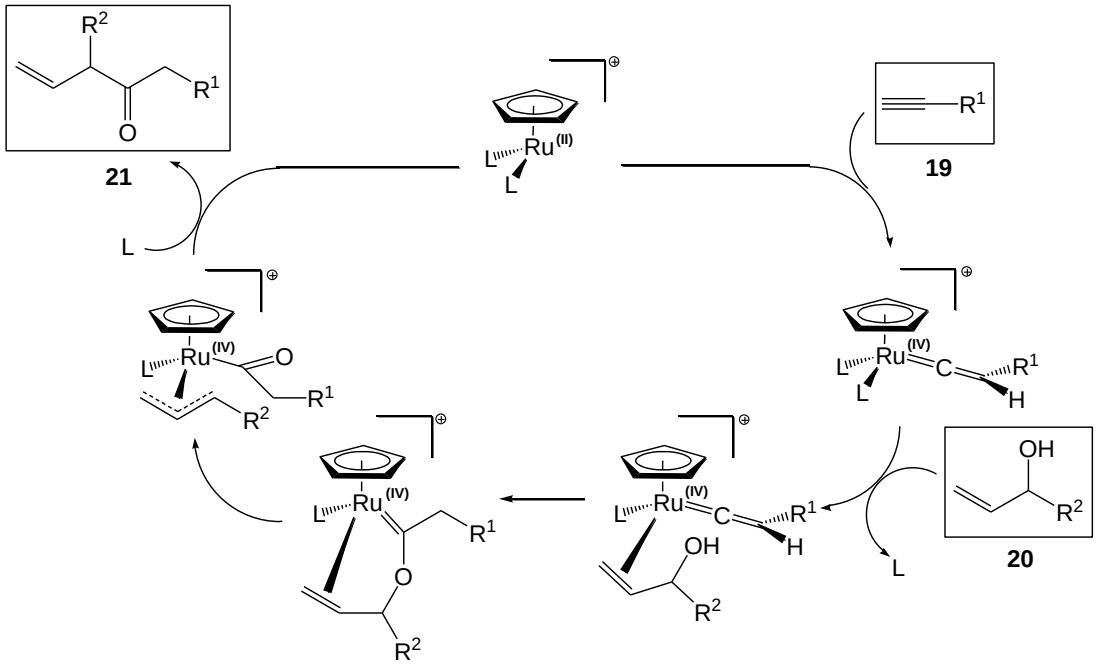
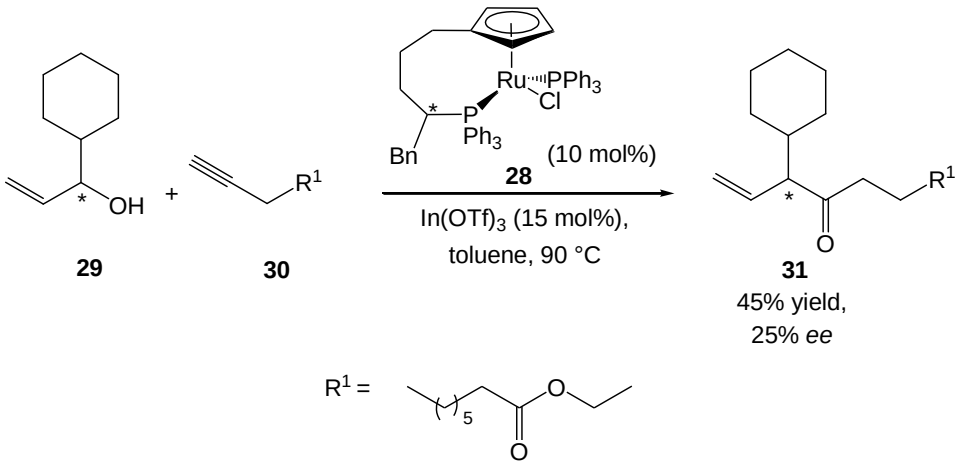


Figure 4: Catalytic cycle proposed by Trost for reconstitutive condensation.

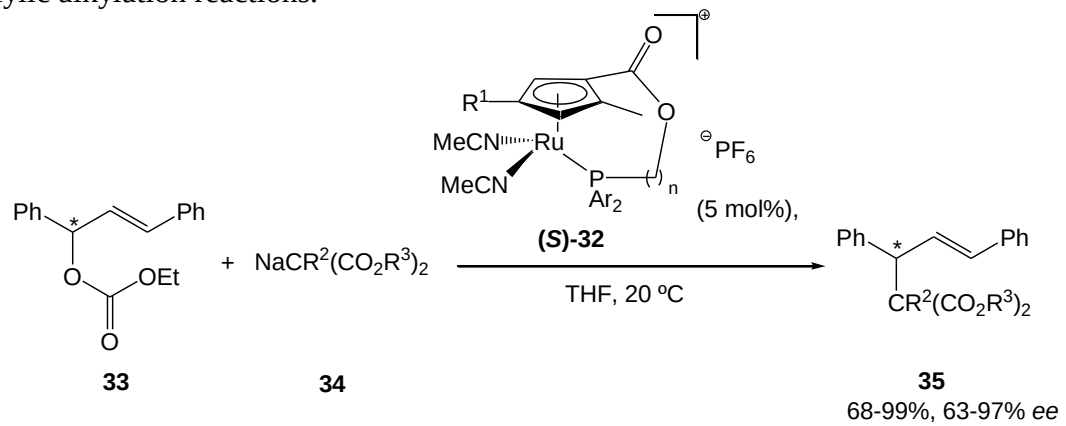
After testing several ligands, ruthenium complex **28** was found to be the most efficient in the condensation reaction (**Scheme 5**).



Scheme 5: Trost's most active ligand in the condensation reaction.

These examples suggest that controlling the stereochemical environment around the metal is essential to achieve high asymmetric induction in the condensation reaction. In 2001 Takahashi published the first asymmetric ruthenium catalysed allylic substitution (**Scheme 6**).[12] The synthesised half and *ansa*-half sandwich ruthanocenes **(*S*)-32** were

tested in asymmetric allylic amination and alkylation reactions (AAA). The activity was high in both cases, however, the asymmetric induction proved to be higher in the allylic alkylation reactions.



Scheme 6: Allylic alkylation catalysed by *ansa*-half sandwich ruthenocenes.

It was also found that tethering the phosphino function was crucial for the catalytic activity, as half sandwich ruthenocene **(*S*)-36** demonstrated only poor activity (3% yield, **Figure 5**).

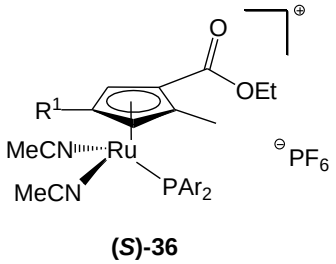
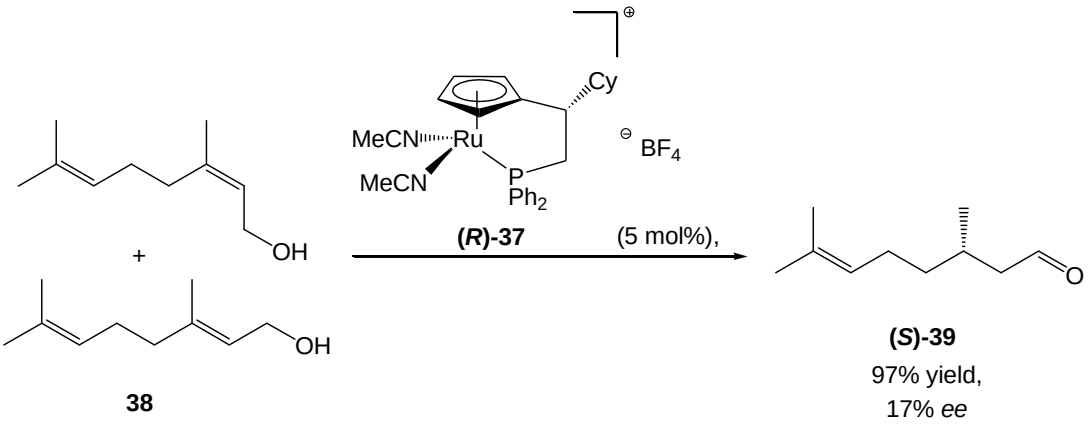


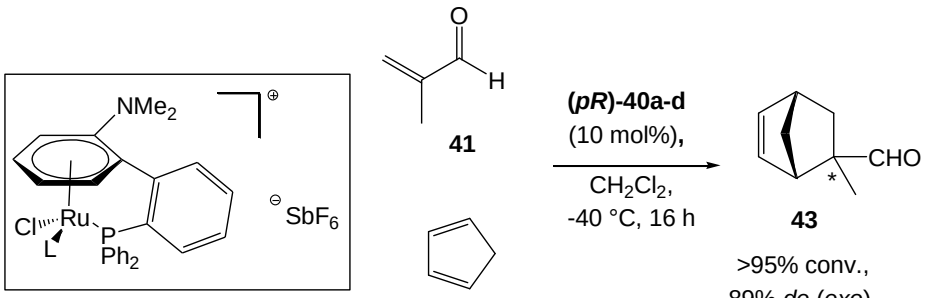
Figure 5: Half sandwich ruthenocene **(*S*)-36** was inactive in AAA.

In 2004 Salzer published the first asymmetric isomerisation by *ansa*-half sandwich ruthenocenes.[13] The most active catalyst **(*R*)-37** gave the product in 97% yield and 17% *ee* (**Scheme 7**).



Scheme 7: Isomerisation of geraniol **38** to citronellal **(*S*)-39**.

Faller developed novel arene tethered planar chiral ruthenocenes **(*pR*)-40a-d** which showed activity in asymmetric Diels-Alder reactions, giving the product **43** in excellent *endo*/*exo* selectivity and low *ee* (**Scheme 8**).[14]

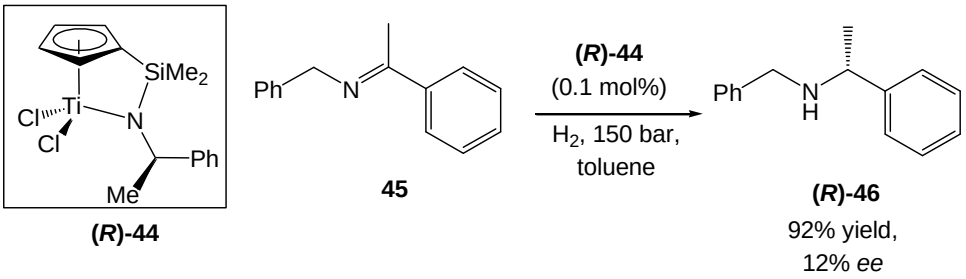


Entry	Complex	L	*endo/exo*	*ee* (%)
1	**(*pR*)-40a**	PPh_3	98/2	20
2	**(*pR*)-40b**	$PPhMe_2$	96/4	26
3	**(*pR*)-40c**	$P(OPh)_3$	97/3	13
4	**(*pR*)-40d**	PPh_2Cy	94/6	40

Scheme 8: Catalytic asymmetric Diels-Alder reaction.

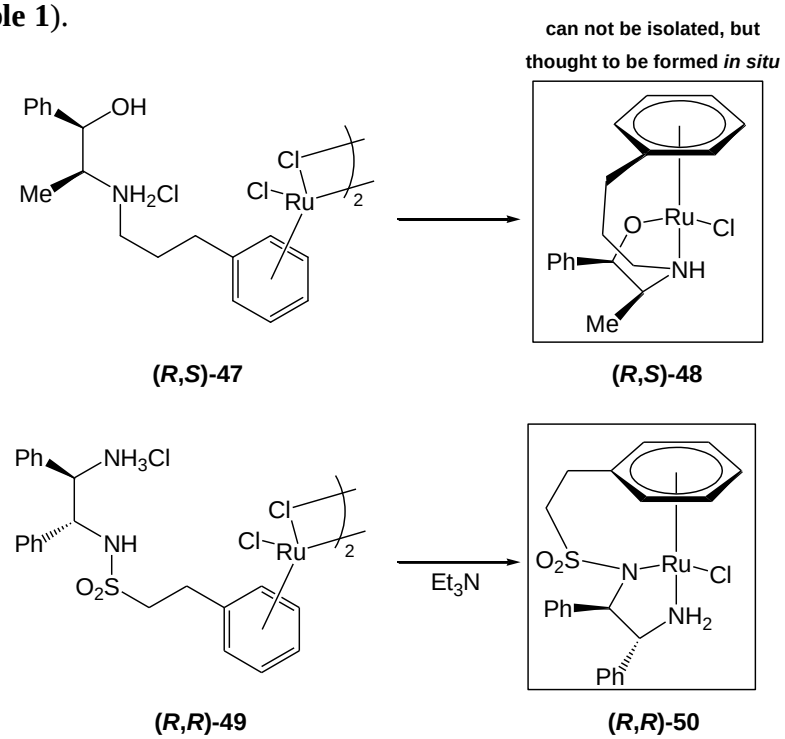
In complexes **(*pR*)-40a-d** the planar chirality is believed to establish a chiral environment around the metal which is responsible for the asymmetric induction.

The first homogenous catalytic asymmetric hydrogenation of imines was published by Okuda in 1996, where Ti complex **(*R*)-44** was used to give product **(*R*)-46** in low *ee* (12% *ee*, **Scheme 9**).[15]



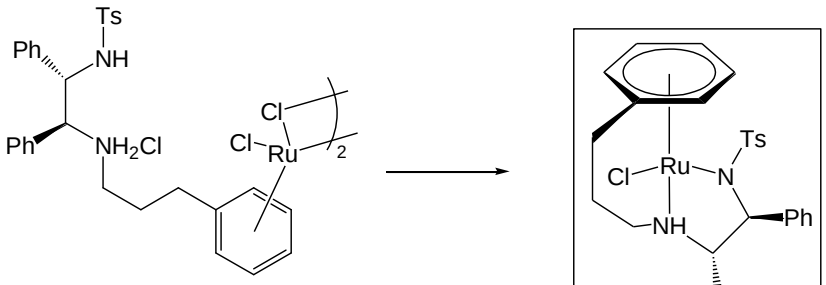
Scheme 9: Homogenous enantioselective hydrogenation by Okuda.

Wills synthesised several *ansa*-half sandwich ruthenocenes bearing a tethered diamine functionality (**Scheme 10**).[16] The three-point coordination to the metal is believed to increase stability of the complexes. Upon treatment of dimer **(*R*,*R*)-49** with a base (Et_3N) complex **(*R*,*R*)-50** was isolated, which gave excellent results (99% yield, 96% *ee*) in the Ru catalysed Asymmetric Transfer Hydrogenation (ATH) of acetophenone **53** (**entry 1**, **Table 1**).

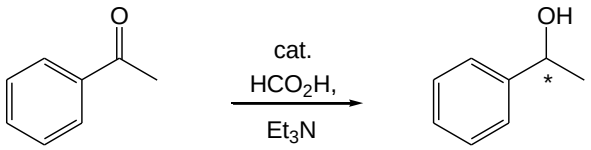


Scheme 10: Formation of complexes **(*R*,*S*)-45** and **(*R*,*R*)-47**.

Complex **(*R*,*S*)-48** could not be isolated, therefore, dimer **(*R*,*S*)-47** was tested under catalytic conditions to yield the product in 96% and 66% *ee* (**entry 2**, **Table 1**). This implied that the corresponding complex **(*R*,*S*)-48** is formed *in situ* in the reaction mixture. Dimer **(*R*,*R*)-49** proved to be more effective than dimer **(*R*,*S*)-47** (**entry 3**, **Table 1**). On the other hand, reaction time increased compared to those conducted with the preformed complex **(*R*,*R*)-50**. To further improve the catalytic activity of complex **(*R*,*R*)-50** (**Table 1**) the same group prepared the "reverse-tethered" complex **(*S*,*S*)-52**, which proved to be a very active and versatile catalyst for Asymmetric Transfer Hydrogenation (ATH) (**entry 4**, **Table 1**).[17] Complex **(*S*,*S*)-51** also proved to be very efficient even when forming the catalytically active complex **(*S*,*S*)-52** *in situ* (**entry 5**, **Table 1**).



(*S*,*S*)-51 **(*S*,*S*)-52**



53 **54**

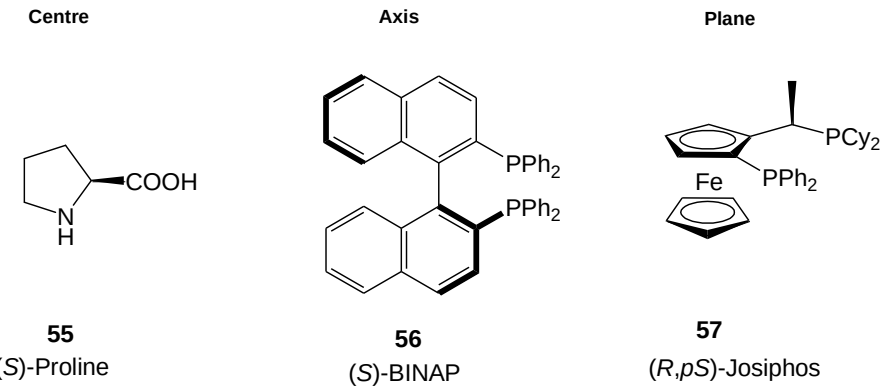
Entry	Catalyst	Loading (mol%)	T(°C)	time(h)	Y(%)	*ee*(%)
1	**(*R*,*R*)-50**	0.5	28	18	>99	96(*R*)
2	**(*R*,*S*)-47**	0.5	28	1	96	66(*R*)
3	**(*R*,*R*)-49**	0.5	28	21	>99	96(*R*)
4	**(*S*,*S*)-52**	0.5	28	3	100	96(*S*)
5	**(*S*,*S*)-51**	0.5	40	3	100	96(*R*)

Table 1: ATH reaction of acetophenone **53** catalysed by complexes **(*R*,*R*)-50**, **(*R*,*S*)-47**, **(*R*,*R*)-49**, **(*S*,*S*)-52** and **(*S*,*S*)-52**.

Ansa-half sandwich metallocenes have proven to catalyse a small number of reactions, however, they can not be applied widely due to the fact that they are only applicable to specific substrates. In these complexes the metal centres are responsible for the catalytic activity, while the chiral ligand is the source of the stereochemical information. Usually the stereochemical information is introduced somewhere on the linker which also has the role of tethering other Lewis basic function(s) to the Cp or Ar group, therefore helping to configurationally stabilise the molecule due to the chelate effect. In most of these complexes central chirality serves as the source of the stereochemical information. In the examples of Faller or Takahashi the stereochemical bias is created by planar chirality introduced on the Cp or Ar rings.

4. Chirality

The success of many asymmetric transformations relies upon how well the stereochemical information is transferred from a chiral reagent to the substrate. This information stems from the existance of some sort of chiral element in the molecule such as a centre, axis or plane (**Figure 6**).



55
(*S*)-Proline

56
(*S*)-BINAP

57
(*R*,*pS*)-Josiphos

Figure 6: Examples of different chiral elements (centre, axis and plane).

5. Planar Chirality

The term planar chirality was introduced by Cahn Ingold and Prelog describing the stereochemistry of cyclophanes and later was adopted by Schögl for metallocene structures. Metallocenes and a*nsa*-half metallocenes bearing at least two different substituents on the same ring have a plane of chirality in the molecule which gives existence to two possible enantiomeric forms ***pS*** and ***pR*** (**Figure 7**).

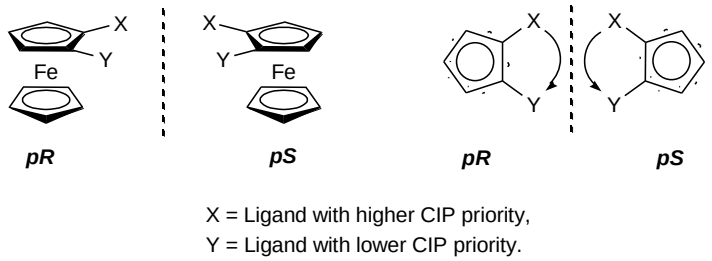


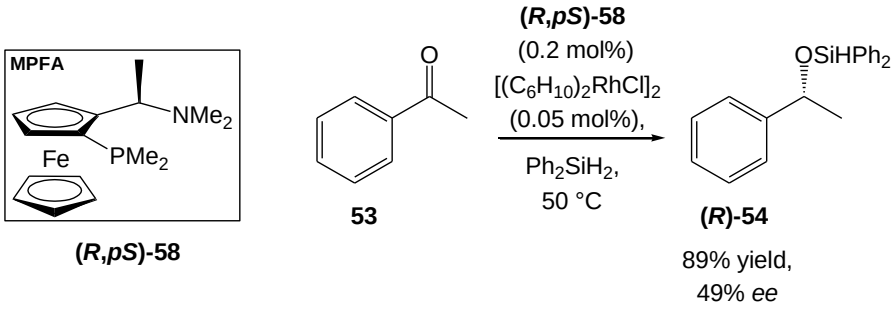
Figure 7: The ***pR*** and ***pS*** enantiomers and their stereochemical assignement.

6. Chiral Ferrocenes

The majority of planar chiral compounds known in the literature are planar chiral ferrocenes. Intensive research has been conducted on 1,2 disubstituted N/P, P/P and N/S ligands. These ligands have mainly been synthesised from Ugi's amine, ferrocenyl-oxazolines or sulfoxides, by diastereoselective Directed *ortho* Metallation (D*o*M) (**page 39**). These derivatives are easy to obtain and in most of the cases removal of the Directing Group (DG) is not performed. Therefore they bear two chiral elements, centre and plane.

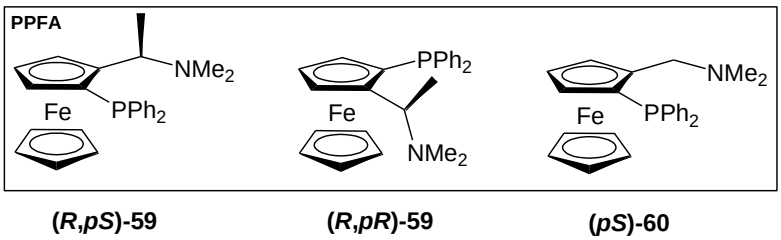
6.1 Chiral Ferrocene Phosphines

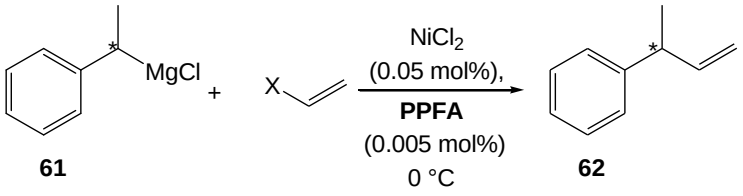
One of the earliest examples appeared in 1974 by the work of Kumada who synthesised MPFA **(*R*,*pS*)-58** and applied it to the asymmetric hydrosilylation of aromatic ketones (**Scheme 11**).[18]



Scheme 11: (*R*,*S*)-MPFA showed activity in the hydrosilylation of aromatic ketones.

The same group applied these type of ligands to cross-coupling reactions between alkyl Grignard reagents and vinyl halides.[19] Another interesting observation was made by inverting the stereochemistry of the planar chiral element which gave the product with the opposite stereochemistry **(*R*)-62** (**entry 2**, **Table 2**). The *ee* was lower, meaning that the level of stereoinduction in **(*R*,*pS*)-59** represented a mismatch between the planar and centre of chirality. By eliminating the central chiral element the reaction retained the same *ee* (**entry 3**, **Table 2**). From these results it is obvious that planar chirality has a powerful control over the stereochemistry of the product in this transformation.

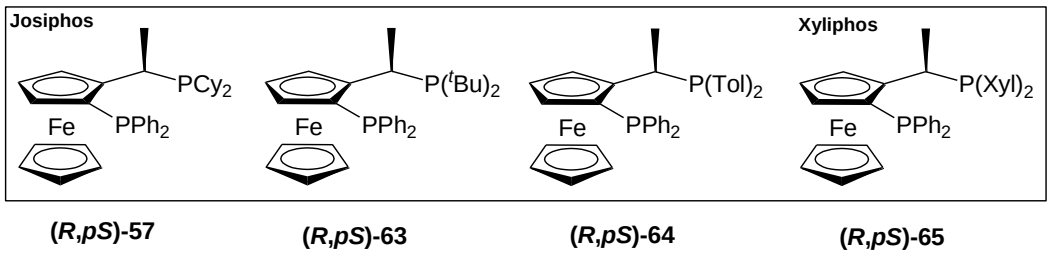




Entry	PPFA	Y(%)	% *ee*
1	(*R*,*pS*)-59	>95	68(*S*)
2	(*R*,*pR*)-59	>95	54(*R*)
3	(*pS*)-60	>95	65(*S*)

Table 2: Asymmetric cross-coupling reaction between alkyl Grignard reagents and vinyl halides.

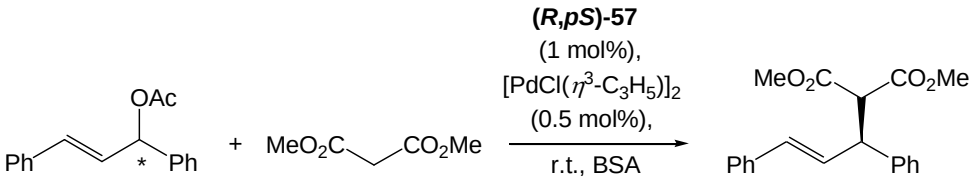
The first member of the Josiphos-type ligands was published by Togni in 1994.[20] These ligands showed activity in a wide range of reactions and they are probably the most successful 1,2-disubstituted planar chiral ferrocenyl ligands up date. By changing the substitution on the phosphines, the resulting ligand can be fine-"tuned" in order to maximise yields of a certain transformation. Their synthesis is straightforward, therefore, synthesis of new ligands only depend on the availability of the phosphines (**Figure 8**).

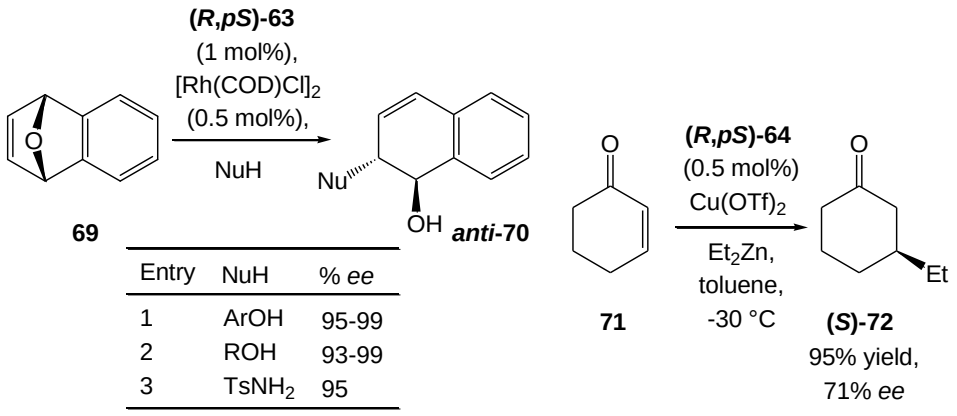


(*R*,*pS*)-57 (*R*,*pS*)-63 (*R*,*pS*)-64 (*R*,*pS*)-65

Figure 8: Few members of the Josiphos ligand family.

Josiphos type ligands have found applications in asymmetric hydrogenations of C=C, C=O, C=N bonds, allylic alkylation, ring opening and 1,4-addition reactions (**Scheme 12**).

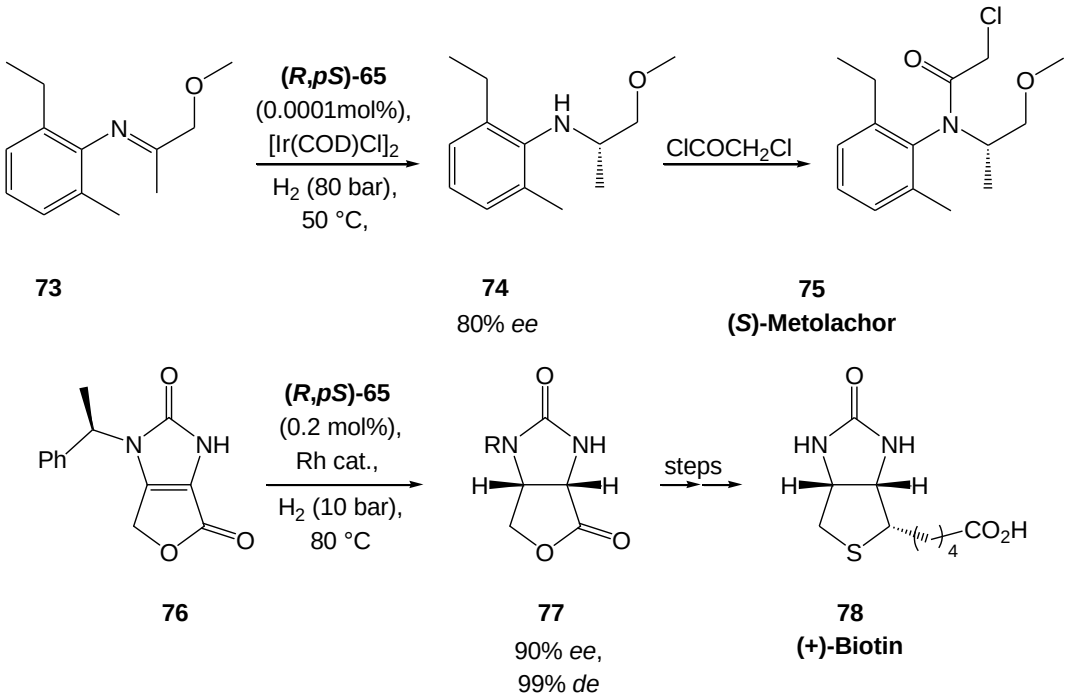




Entry	NuH	% *ee*
1	ArOH	95-99
2	ROH	93-99
3	$TsNH_2$	95

Scheme 12: Examples for the application of Josiphos-type ligands.

Some analogues were even found to be useful on industrial scale syntheses. (*S*)-Metholachor **75** is the active ingredient of Dual Magnum®, one of the most important herbicides for maize.[21] Xyliphos **(*R,pS*)-65**/$[Ir(COD)Cl]_2$ was found to be an active catalyst for the production of intermediate **74** with a substrate/catalyst (s/c) ratio of 10^6 which is one of the highest values known for enantioselective homogenous hydrogenations (**Scheme 13**). Compound **76** was employed in the synthesis of (+)-Biotin **78**. This homogenous system proved to be much more effective than the heterogenous Rh/Al_2O_3 system.



Scheme 13: Enantioselective hydrogenations of intermediates **74** and **77** are the key steps of the synthesis of (*S*)-Metolachor **75** and (+)-Biotin **78**.

Since the first report of Josiphos ligands, a great variety of P/P ligands have been synthesised and found application in many reactions, mostly for Ru/Rh catalysed enantioselective hydrogenations (**Figure 9**). Some of the important ones are Pigiphos (Togni; 1995),[22] TRAP (Kuwano; 1997),[23] FERRIPHOS (Knochel; 1998),[24] MandyPhos (Knochel; 1999),[25] Walphos (Spindler; 2002),[26] BoPhoz (Boaz; 2002),[27] Taniaphos (Knochel; 2003),[28] JoSPOphos (Pugin/Pfaltz; 2010)[29] and [5]ferrocenophane-type ligand (Šebesta; 2011).[30]

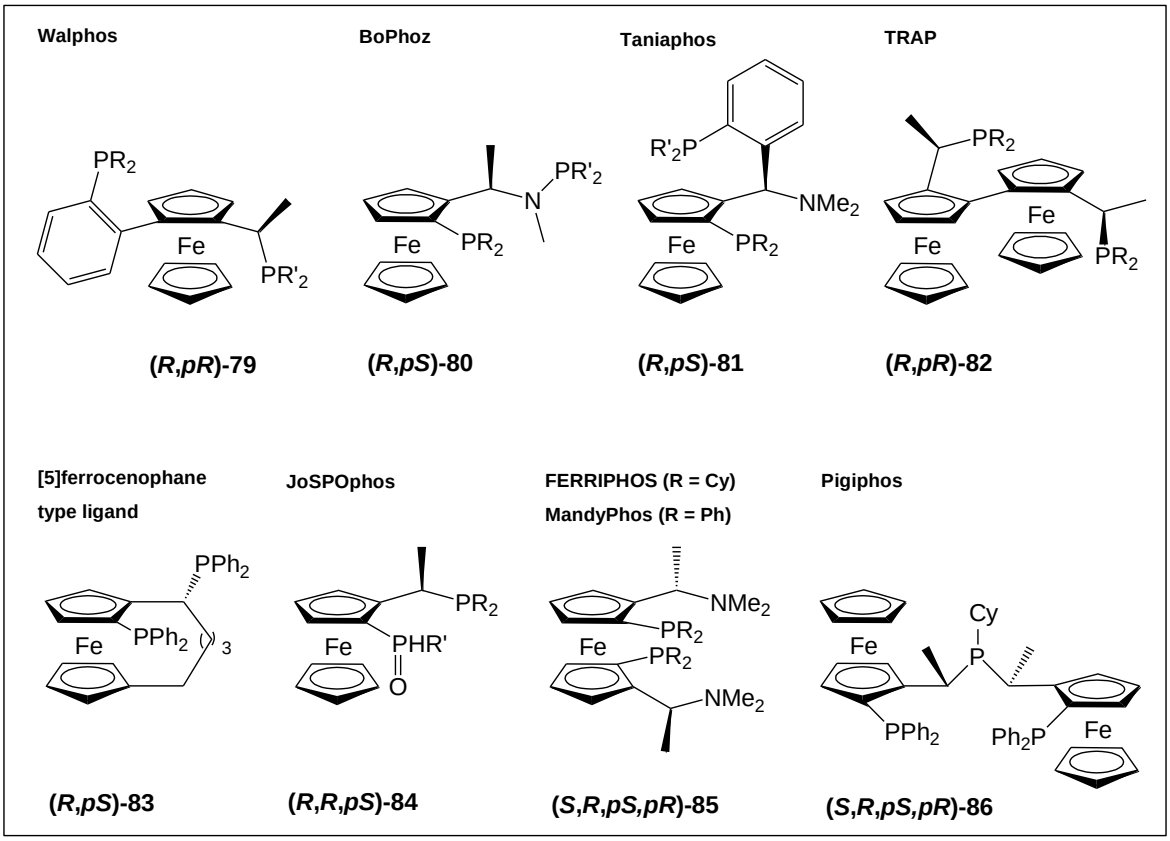
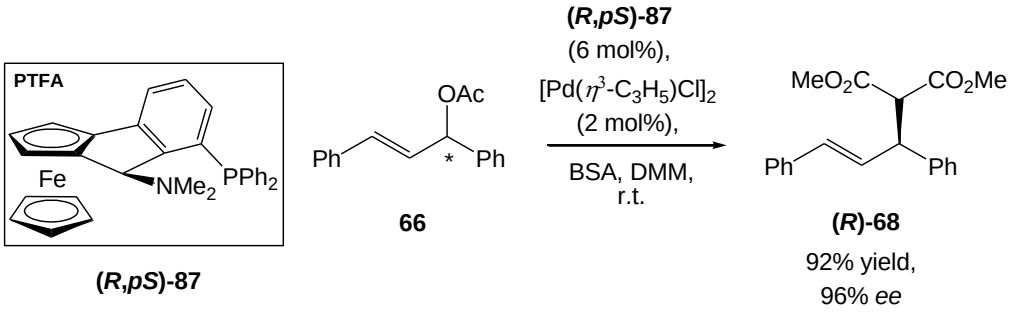


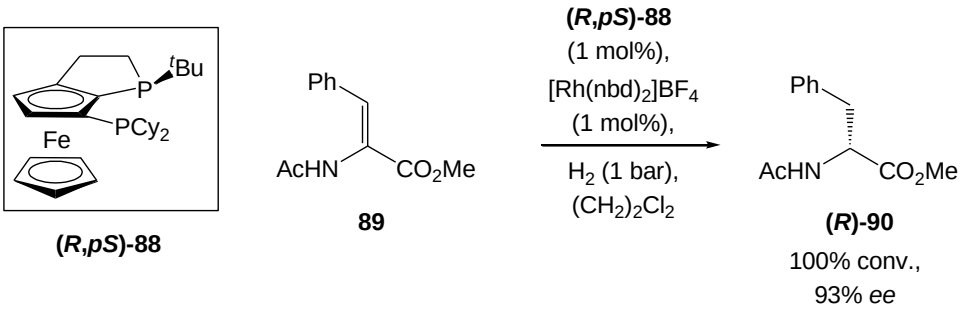
Figure 9: Some of the important members of the P/P ligand family.

In 2007 Fukuzawa published the synthesis of a modified version of PPFA-ligand ***(R, pS)*-59**.[31] PTFA ***(R, pS)*-87** was designed this way, in order to allow less conformational freedom, therefore, have enhanced stereoinduction. Ligand ***(R,pS)*-87** gave excellent *ee*s in AAA (**Scheme 14**).



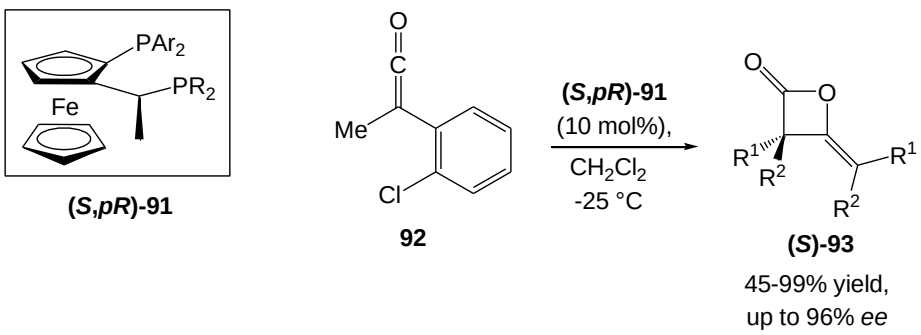
Scheme 14: Ligand **(*R*,*pS*)-87** is a sterically more rigid version of PPFA **(*R*,*pS*)-59**.

In another work, Pfaltz synthesised P-stereogenic ferrocenophospholane type ligands.[32] Similarly the aim was to cause a more pronounced stereochemical bias around the Rh-metal by two-point tether of the phosphorous to the same cyclopentadienyl ring. These ligands performed well in Rh catalysed asymmetric hydrogenation (**Scheme 15**).



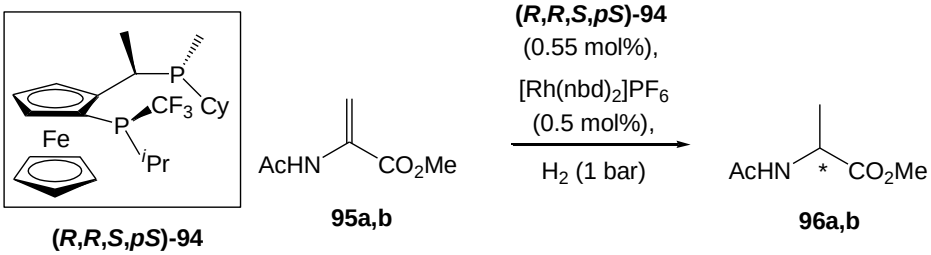
Scheme 15: P-stereogenic ferrocenophospholane ligand **(*R*,*pS*)-88** performed well in Rh catalysed enantioselective hydrogenation.

Recently, Josiphos-type ligands were applied to the homodimerisation of ketenes **89**.[33] Using **(*R*,*pS*)-91** instead of **(*S*,*pR*)-91** gave the product of the other antipode **(*R*)-93** (**Scheme 16**).



Scheme 16: Homodimerisation of ketoketenes catalysed by Josyphos type ligands **(*S*,*pR*)-91**.

Lately, Togni has published the synthesis of Josiphos type, doubly P-stereogenic ligands.[34] The Rh catalysed enantioselective hydrogenation was highly stereoselective using these ligands (**Scheme 17**).

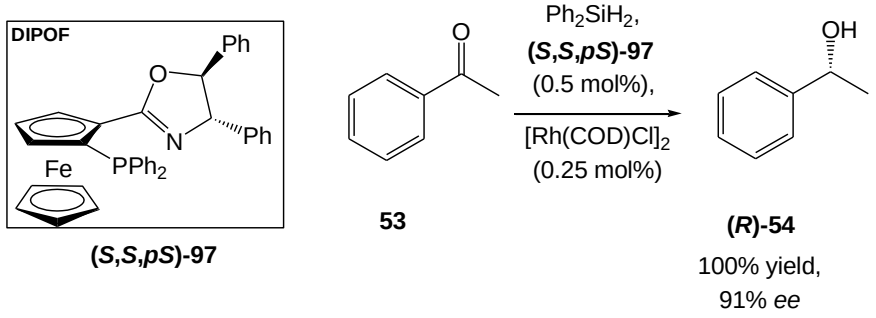


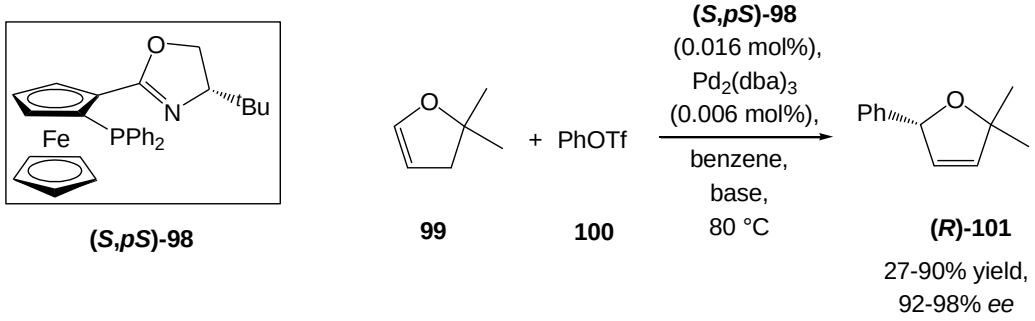
Entry	Subs.	R	Solv.	*ee*(%)
1	**95a**	NHAc	MeOH	>99
2	**95b**	CH_2CO_2Me	CF_3CH_2OH	>99

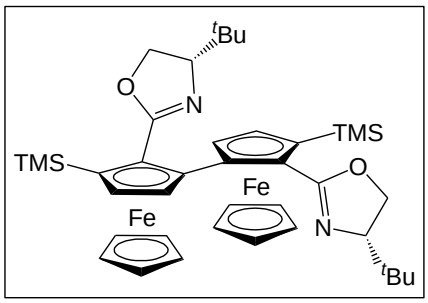
Scheme 17: Rh catalysed enantioselective hydrogenation using **(*R*,*R*,*S*,*pS*)-94**.

6.2 Chiral Ferrocene Oxazolines

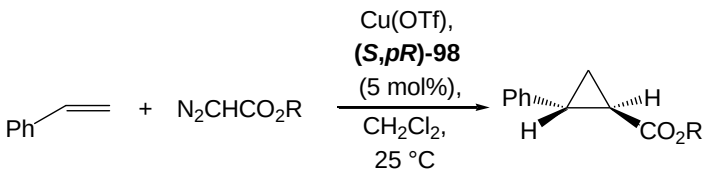
Chiral oxazoline based ligands were first applied to asymmetric catalytic reactions in 1986.[35] They found applications in the asymmteric hydrogenation of ketones (Uemura; 1995)[36], cyclopropanations (Ahn; 1997)[37] and Heck reactions (Guiry; 1998)[38] (**Scheme 18**).







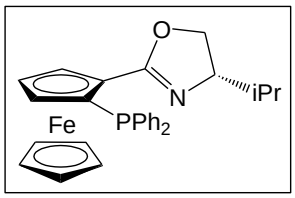
(*S*,*pR*)-102



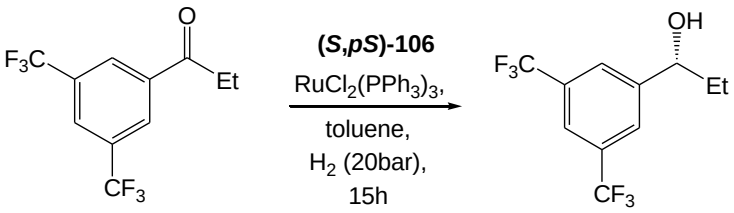
103 **104** R = *i*Menthyl **(*1R*,*2R*)-105** 64% yield, *E*/*Z* 77/33 90%/99% *ee*

Scheme 18: Reactions catalysed by ferrocenyl-oxazolinones.

Ligand **(*S*,*pS*)-106** proved to be an efficient catalyst for the Ru catalysed hydrogenation of **107** on a 4 L scale with a s/c ratio of 20 000.[39] Alcohol **(*R*)-108** is an important intermediate in the synthesis of an NK-1 receptor antagonist compound (**Scheme 19**).



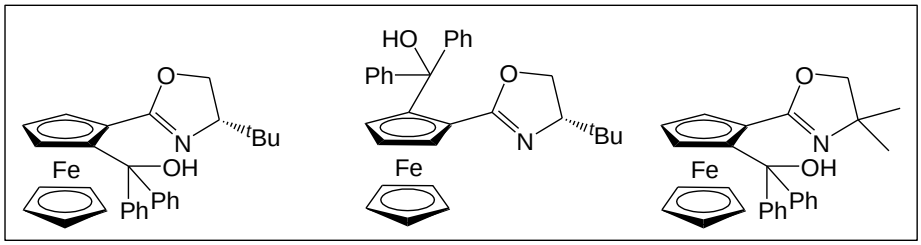
(*S*,*pS*)-106



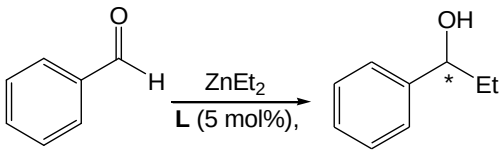
107 **(*R*)-108** 100% conv., 96% *ee*

Scheme 19: Enantioselective hydrogenation of arylketone **107**.

In 1998, Bolm utilised similar oxazolidinone compounds in asymmetric dialkylzinc additions to aromatic aldehydes.[40] Reversing the stereochemistry of the planar chiral element caused the stereoselectivity to drop dramatically (**entry 2**, **Table 3**). These results show that, although planar chirality is not solely responsible for the enantioselectivity in this process it clearly has a strong influence on it (**entry 3**, **Table 3**).



(*S*,*pR*)-109 **(*S*,*pS*)-109** **(*pR*)-110**

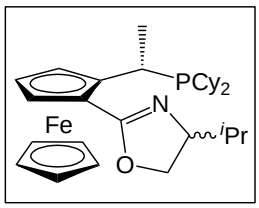


111 **112**

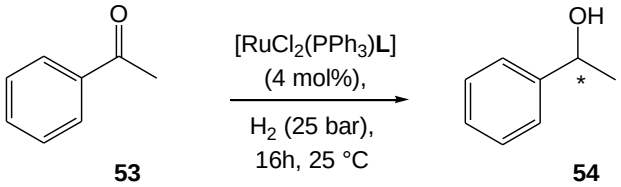
Entry	**L**	Y(%)	*ee*(%)
1	**(*S*,*pR*)-109**	99	94(*R*)
2	**(*S*,*pS*)-109**	55	35(*R*)
3	**(*pR*)-110**	97	51(*R*)

Table 3: Asymmetric diethylzinc addition catalysed by ferrocenyl oxazolidinones.

Weissensteiner and co-workers synthesised oxazolines **(*S*,*pR*)-113**.[41] Excellent stereoselectivity was observed in Ru catalysed enantioselective hydrogenation of acetophenone (94-99% *ee*). However, inverting the stereochemistry on the oxazoline ring obstructed the stereoinduction (43-58% *ee*). These mis-matched cases (**entries 2**, **4**, **6**, **Table 4**) are in accord with previous observations, that stereoinduction is exerted not by the centre of chirality alone (**Table 3**).



L = (*S*,*pR*)-113



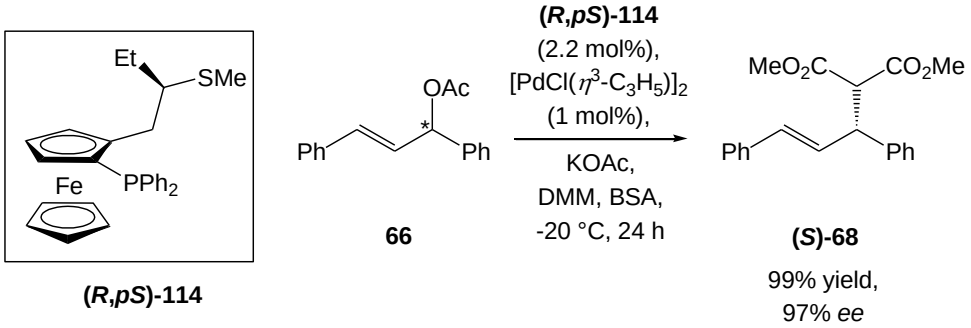
53 **54**

Entry	Solvent	Base	Conv. (%)	Oxaz.	*ee* (%)
1	toluene/H_2O	K_2CO_3	99	*R*	99(*S*)
2	toluene/H_2O	K_2CO_3	99	*S*	44(*R*)
3	toluene/H_2O	NaOH	99	*R*	97(*S*)
4	toluene/H_2O	NaOH	99	*S*	43(*R*)
5	^{i}PrOH	KO^{t}Bu	95	*R*	94(*S*)
6	^{i}PrOH	KO^{t}Bu	95	*S*	58(*R*)

Table 4: Ru catalysed enantioselective hydrogenation of acetophenone **53** using oxazoline ligand **(*S*,*pR*)-113**.

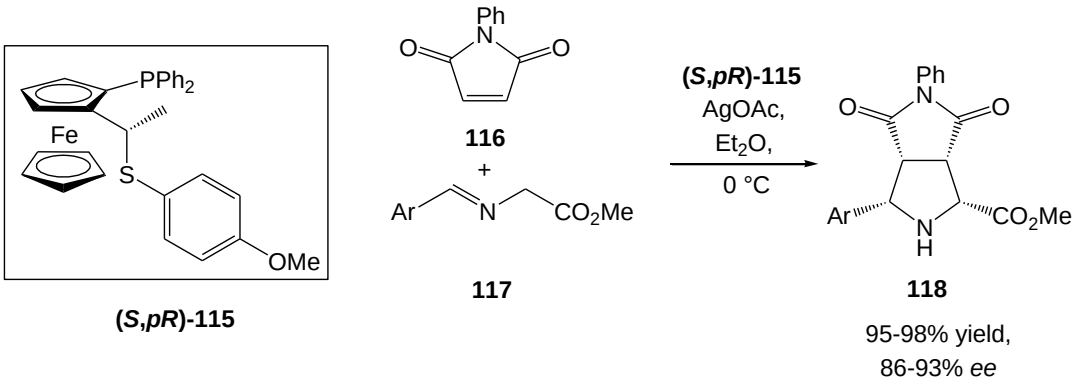
6.3 Chiral Ferrocene Sulfur Compounds

In 1999 Enders published the synthesis of novel P/S bidendate ligand family and investigated their activity in Pd catalysed allylic alkylation reaction.[42,43] They found that moving the central chiral element to the *β*–position had no effect on the stereochemical induction (**Scheme 19**).



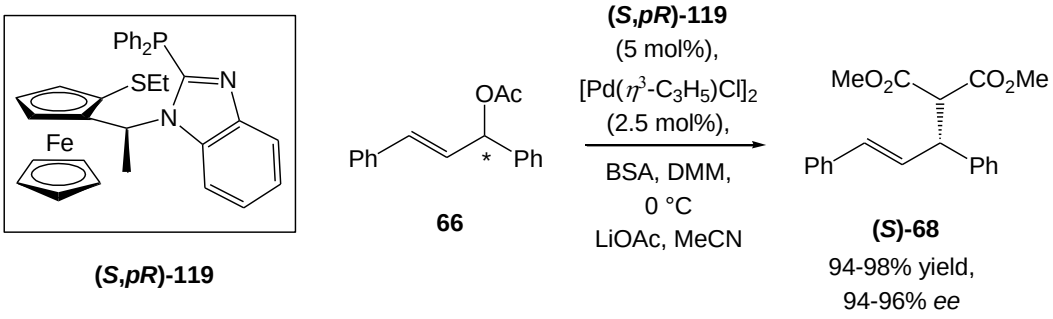
Scheme 19: Asymmetric Pd catalysed allylic alkylation using chiral ferrocene sulfur compounds.

Zhou demonstrated the first Ag catalysed asymmetric [3+2] cycloaddition of azomethine ylides using **(*S*,*pR*)-115** as a ligand (**Scheme 20**).[44]



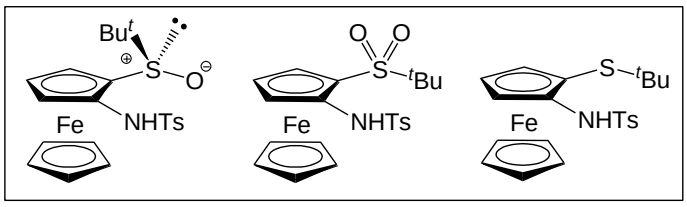
Scheme 20: Ag catalysed asymmetric [3+2] cycloaddition of azomethine ylide.

In 2009 Chan demonstrated the catalytic efficiency of S/P type bidendate ligands in AAA (**Scheme 21**).[45] As a result of starting their syntheses from Ugi's amine **(*S*)-190** (**page 39**) they bore a heterocyclic moiety onto which the diphenylphosphino group was introduced.

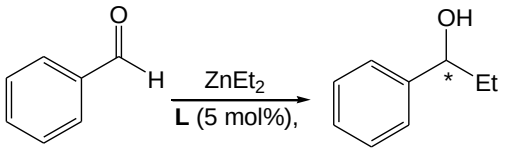


Scheme 21: Chan's S/P ligands performed well in AAA.

Carretero investigated the use of chiral sulfoxides as a source of chirality in the asymmetric diethylzinc addition to aromatic aldehydes.[46] They also investigated the stereoinductive strength of the planar chirality. Purely planar chiral sulfone **(*pR*)-121** and sulfide **(*pR*)-122** exerted slightly better stereocontrol than central chiral **(*S,pR*)-120** (**entries 2** and **3**, **Table 5**) which implies that in this transformation the stereocontrol is mainly governed by the planar chiral element.



(*S,pR*)-120 **(*pR*)-121** **(*pR*)-122**



111 **112**

Entry	**L**	Y(%)	*ee*(%)
1	**(*S,pR*)-120**	79	80 (*R*)
2	**(*pR*)-121**	82	82 (*R*)
3	**(*pR*)-122**	82	82 (*R*)

Table 5: Asymmetric diethylzinc addition catalysed by ferrocenyl sulfoxide, sulfone and sulfide.

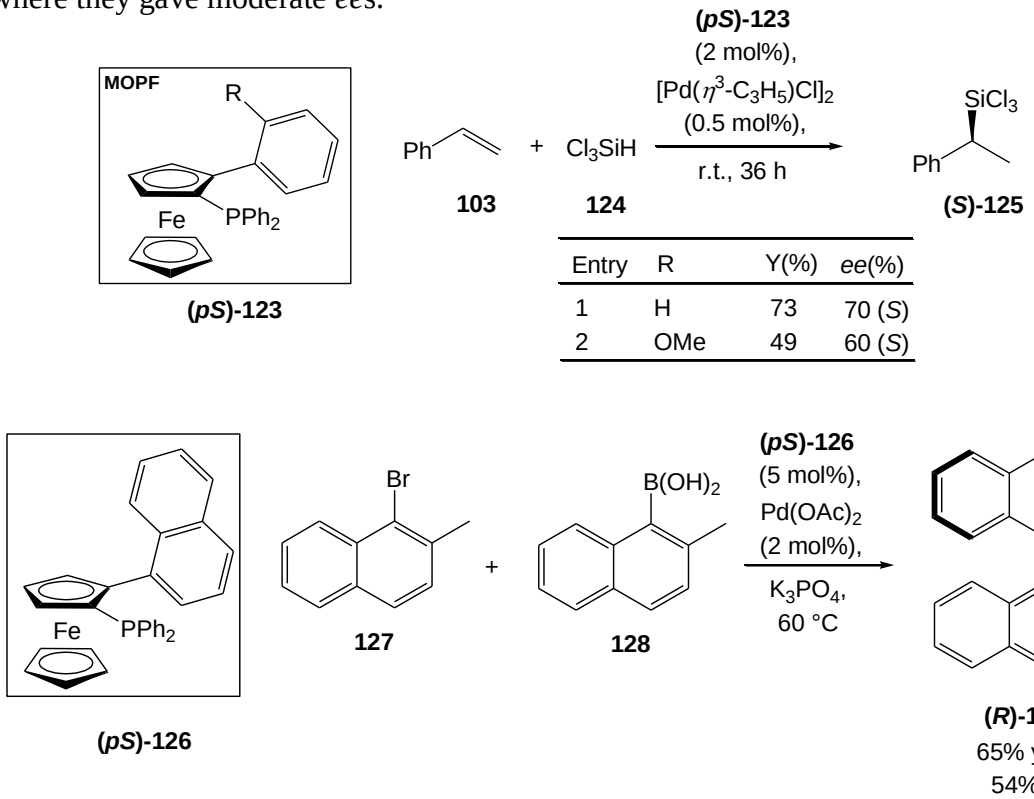
Most of the ligands found in the early examples in the literature bear other types (usually centre) of chirality in the molecule apart from the plane of chirality. The extent to which the stereochemical information of these two stereochemical elements (centre, plane) is transferred to the product is unknown, however, the strong stereoinductive

effect of planar chirality is clearly demonstrated. To date there has been only a small amount of research done using purely planar chiral ligands.

7. Purely Planar Chiral Ferrocenes in Asymmetric Catalysis

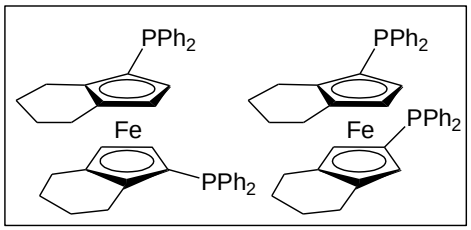
7.1 Phosphine ligands

In 1999, Johannsen's group published the synthesis of MOPF-type ligands **(*pS*)-123** which are easily accessible and can be derivatised.[47] The initial ligands were used in the enantioselective hydrosilylation of styrene (**Scheme 22**). This work was later extended and the ligands were used in Suzuki Cross-Coupling reactions of activated, as well as non-activated aryl chlorides. The ligands were also tested in an asymmetric coupling where they gave moderate *ee*s.[48]

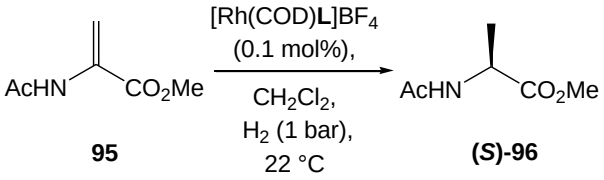


Scheme 22: Purely Planar Chiral monodendate phosphine ligands showed activity in asymmetric hydrosilylation and Suzuki Cross-Coupling reactions.

Reetz reported purely planar chiral bidendate P/P ligands used catalyse asymmetric hydrogenation.[49] Interestingly the doubly planar chiral **(*pS*,*pS*)-130** gave higher *ee* than the analogue **(*pS*)-131** bearing a single planar chiral element (**Scheme 23**).



(*pS*,*pS*)-130 **(*pS*)-131**

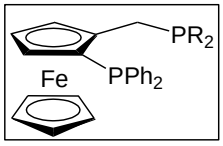


95 **(*S*)-96**

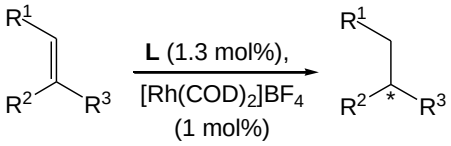
Entry	**L**	Y(%)	*ee*(%)
1	**(*pS*,*pS*)-130**	>95	96
2	**(*pS*)-131**	>95	64

Scheme 23: Asymmetric hydrogenation using purely planar chiral analogues **(*pS*,*pS*)-126** and **(*pS*)-127**.

Kagan synthesised purely planar chiral bidendate phosphines on the basis of Josiphos type ligands.[50] These ligands proved to be highly active in the Rh catalysed enantioselective hydrogenation of olefins or enamines (**Table 6**).



(*S*)-132 (R = Cy),
(*S*)-133 (R = Cyclopentyl)



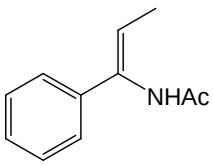
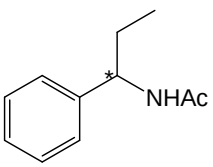
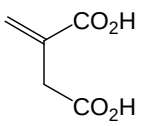
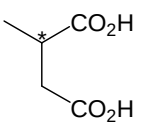
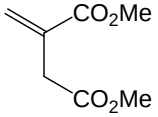
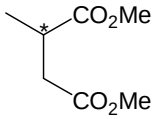
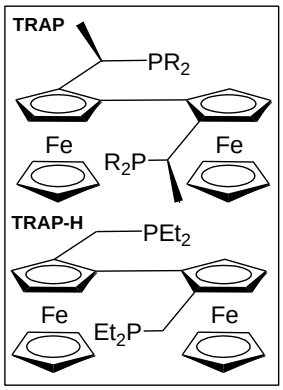
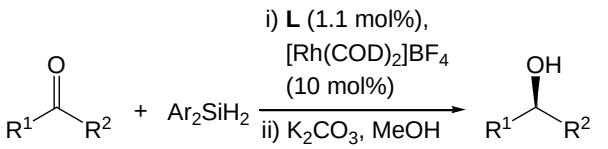
Entry	Substrate	Product	**L**	H_2(atm.)	Y(%)	*ee*(%)
1			**(*S*)-132**	10	95	82 (*S*)
2			**(*S*)-133**	1	92	93 (*S*)
3			**(*S*)-132**	1	95	92 (*S*)
4			**(*S*)-132**	1	94	98 (*S*)

Table 6: Rh catalysed enantioselective hydrogenation of olefins and enamines.

The purely planar chiral analogue of TRAP **(*pS*)-136** was synthesised by Ito in 2004 and was found to be more active in the enantioselective hydrosilylation of ketones than the parent TRAP ligand (**Table 7**).[51]



(S, *pS*)-134 (R = Et), **(S, *pS*)-135** (R = Bu), **(*pS*)-136**

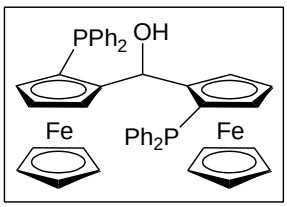


137 **138** **(*S*)-139**

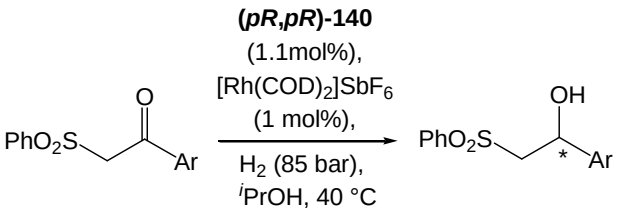
R^1	R^2	(*S*,*pS*)-136		(*S*,*pS*)-134		(*S*,*pS*)-135	
		Y(%)	*ee*(%)	Y(%)	*ee*(%)	Y(%)	*ee*(%)
Ph	Me	89	94	90	85	89	92
Ph	CH_2Me	96	80	-	-	73	62
Cy	Me	90	89	76	81	-	-
C_6H_{13}	Me	82	77	88	65	-	-

Table 7: Enantioselective hydrosilylation of ketones using TRAP-like ligands.

Hou and Dai synthesised a bis ferrocenyl structure **(*pR*,*pR*)-140** which showed excellent activity in the enantioselective hydrogenation of *β*–sulfonyl ketones (**Scheme 24**).[52]



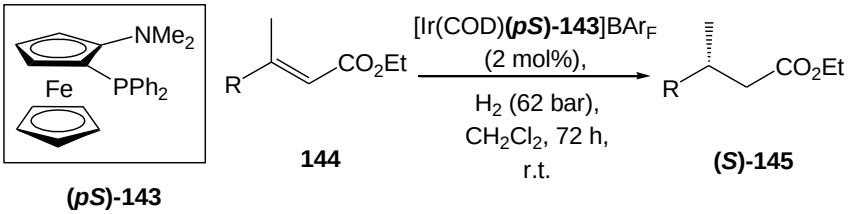
(*pR*,*pR*)-140



141 **142** >99% conv., 72-98% *ee*

Scheme 24: Enantioselective hydrogenation of *β*–sulfonyl ketones using **(*pR*,*pR*)-140**.

Recently Metallinos has demonstrated the strong influence of the planar chiral element on the stereoselectivity of the catalytic reaction by P/N bidendate ligand **(*pS*)-143** (**Scheme 25**).[53]



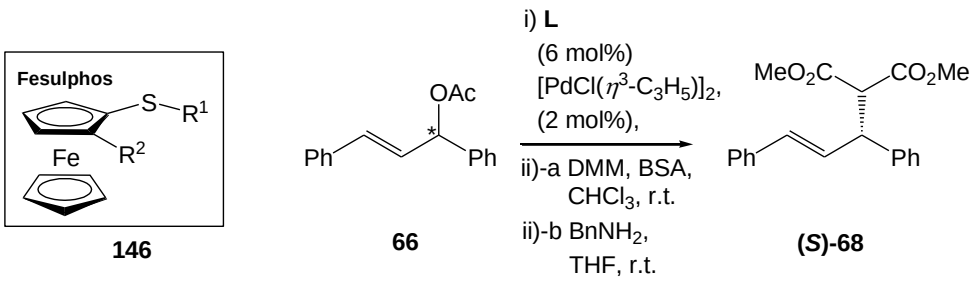
Entry	R	Y(%)	*ee*(%)
1	Ph	94	91
2	*p*MeOPh	99	92

Scheme 25: Ir-catalysed asymmetric hydrogenation using ligand **(*pS*)-143**.

7.2 Sulfur ligands

Kagan's D*o*M using chiral sulfoxides not only expanded the scope of the synthesis of purely planar chiral ligands but also introduced a new type of ligand family which bear a sulfur-functionality, as a Lewis basic function.

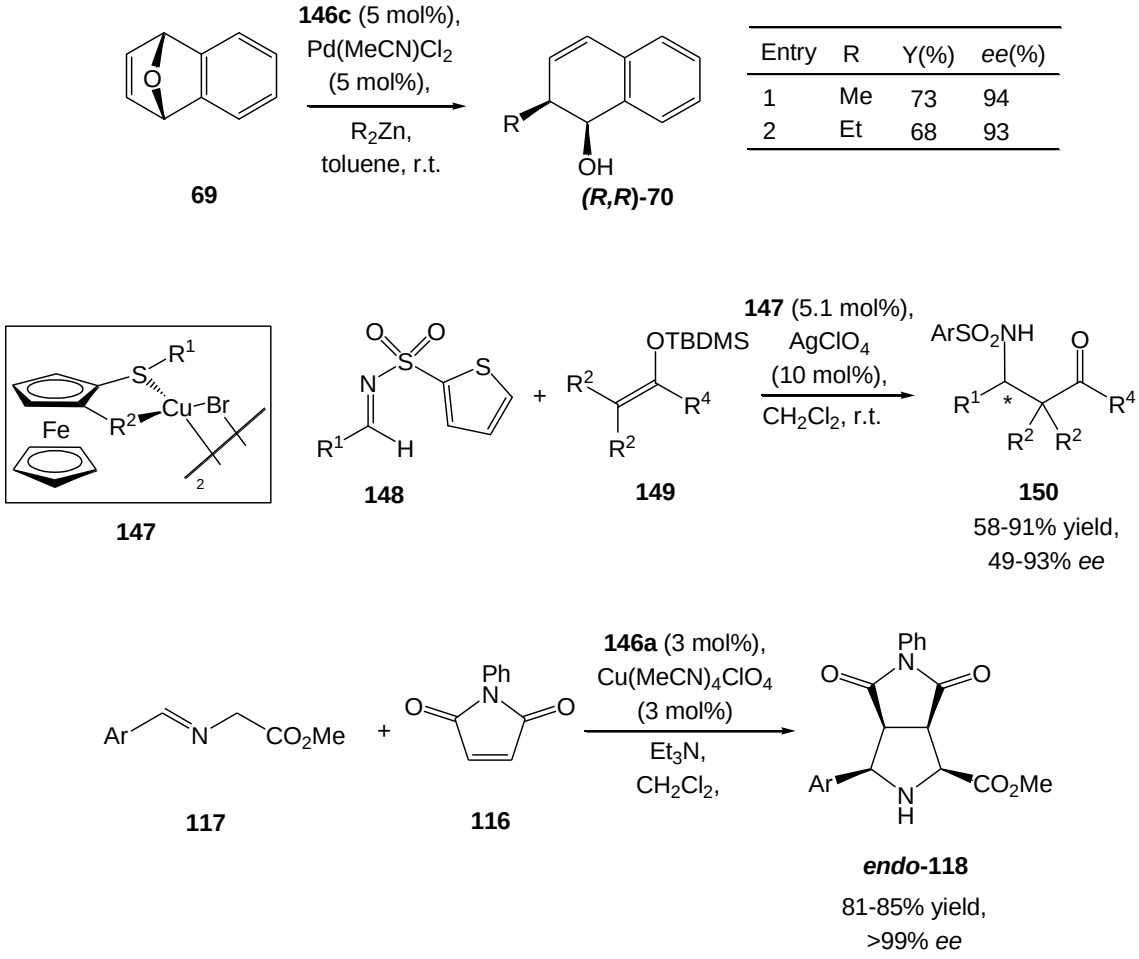
As a continuation of his work Carretero published the synthesis of several bidendate thioether phosphino ligands. These ligands were then applied to asymmetric allylic aminations (**Scheme 26**).[54]



Entry	L	R^1	R^2	ii-a		ii-b	
				Y(%)	*ee*(%)	Y(%)	*ee*(%)
1	**146a**	^{t}Bu	PPh_2	92	93	80	97
2	**146b**	^{t}Bu	$P(2\text{-Fur})_2$	60	90	60	94
3	**146c**	^{t}Bu	PCy_2	96	84	50	40
4	**146d**	^{t}Bu	$NH\text{-}PPh_2$	87	88	73	60
5	**146e**	^{t}Bu	CH_2PPh_2	91	85	72	98
6	**146f**	^{t}Bu	$P(^o\text{Tol})_2$	97	73	82	99.5
7	**146g**	^{p}Tol	PPh_2	92	40	73	60

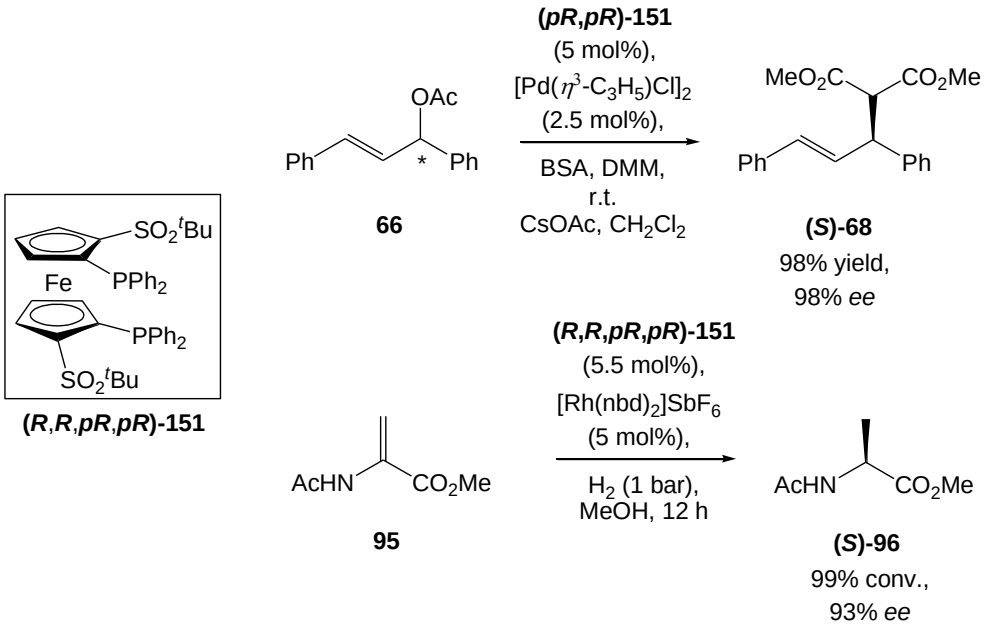
Scheme 26: Asymmetric allylic amination using Carretero's ligands.

The scope of applications was expanded during the following years to the desymmetrisation of meso oxabenzonorbornadiene,[55] Mannich-type additions[56], Cu catalysed dipolar cycloadditions of azomethine ylides[57] and formal aza-Diels-Alder reactions (**Scheme 27**).[58]



Scheme 27: Versatile application of Fesulphos derived ligands.

Zhang synthesised purely planar chiral S/S/P/P type ligand **(*R*,*R*,*pR*,*pR*)-151**, which showed excellent activity in AAA and asymmetric hydrogenation reactions (**Scheme 28**).[59] This also demonstrates the utility of Kagan's sulfoxide approach. After the directed *ortho* substitution the sulfoxide is oxidised to the corresponding sulfone therefore losing the chiral centre in the molecule to give purely planar chiral analogues.

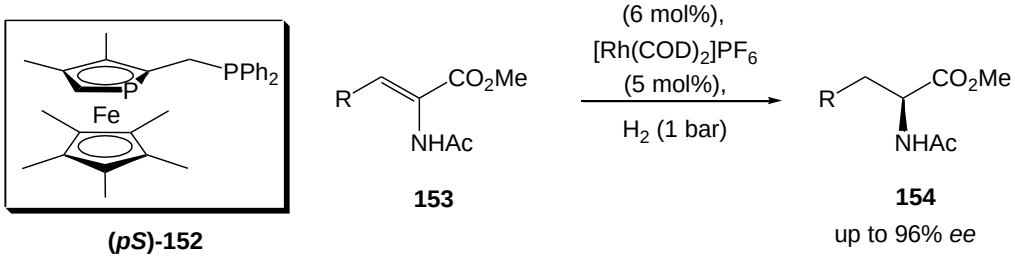


Scheme 28: Rh catalysed asymmetric hydrogenation and Pd catalysed AAA reactions using ligand **(*R*,*R*,*pR*,*pR*)-151**.

8. Heterocyclic ligands

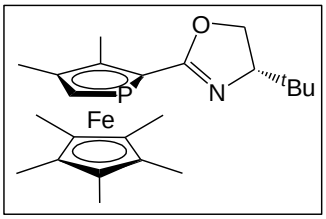
8.1 Phosphaferrocenes

Almost from the beginning of the history of metallocenes synthesis, characterisation and investigation of the catalytic activity of "heteroferrocenes" served as a basis for extensive research on the field.[60] The first phosphaferrocene was reported in 1977 by Mathey. The same group also showed that these ligands can coordinate to transition metals. The first really successful application was published by Fu and co-workers, where ligand **(*pS*)-152** was used in the enantioselective hydrogenation of enamines (**Scheme 29**).[61]

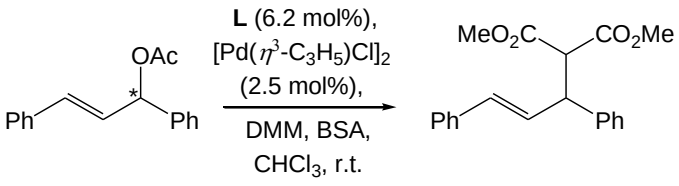


Scheme 29: Asymmteric alkylation using Fu's ligand.

Later on it was also shown that the stereocontrol in the reaction is mainly governed by the planar chiral element (**Scheme 30**).[62] In asymmetric alkylations, ligand **(*S*,*pS*)-155** gave product **(*R*)-68** in 73% *ee*. When the other diastereomer **(*S*,*pR*)-155** was used the product **(*S*)-68** with the opposite stereochemistry was isolated in 82% *ee*.



(*S*,*pS*)-155

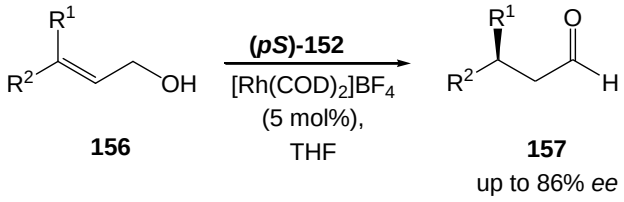


66 **68**

Entry	Ligand	*ee* (%)
1	**(*S*,*pS*)-155**	73(*R*)
2	**(*S*,*pR*)-155**	82(*S*)

Scheme 30: Effect of inverting planar chirality.

Ligand **(*pS*)-152** was also applied to the asymmetric isomerisation of allylic alcohols (**Scheme 31**). Furthermore the structure of the catalytically active species [Rh(COD)**(*pS*)-152**]PF_6 was determined using X-ray crystallography.[63]



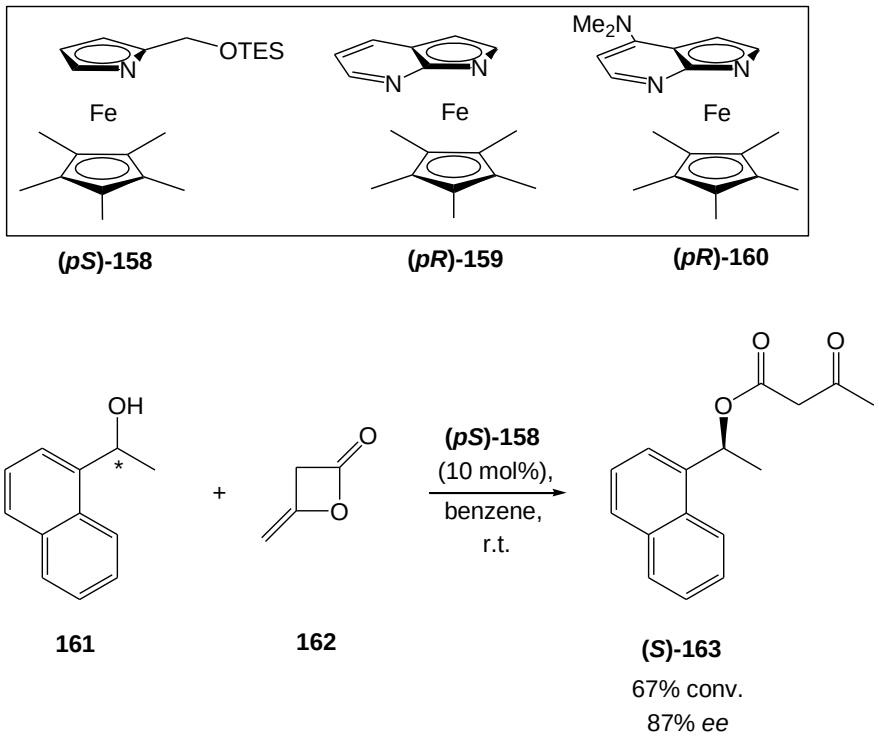
156 **157**
up to 86% *ee*

Scheme 31: Rh catalysed enantioselective isomerisation of alcohol **156** using **(*pS*)-152**.

8.2 Azaferrocenes

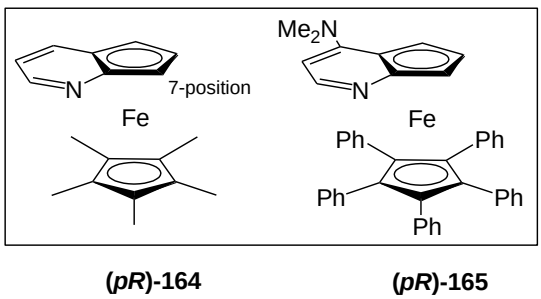
Far less attention has been focused on the nitrogen analogues of these heterocyclic ferrocenes.[64] Synthesis of azaferrocene was reported in 1964 independently by two research groups. The first optically active azaferrocene was reported by Schögl and co-workers in 1969.[65] But for almost 30 years the potential of optically active

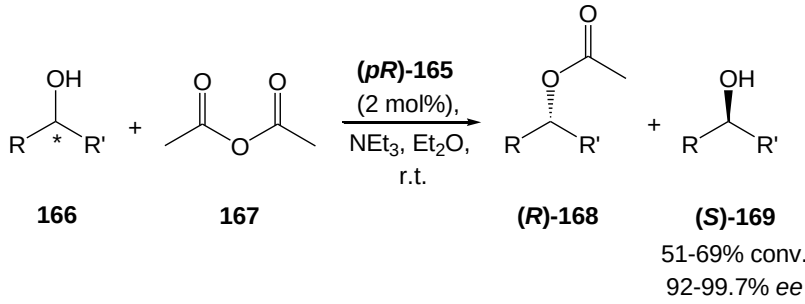
azaferrocenes was not explored further. In the course of designing an asymmetric nucleophilic catalyst for reactions such as the acylation of alcohols, cianosylilation of aldehydes and addition of alcohols to ketenes, Fu reported 1',2',3',4',5'-pentamethylazaferrocenes **(*pS*)-158**, **(*pR*)-159** and **(*pR*)-160** (**Scheme 32**).[66] Initial studies showed good activity in the kinetic resolution of secondary alcohols.



Scheme 32: Kinetic resolution of secondary alcohols using azaferrocene **(*pS*)-158**.

In order to increase the steric bulk around the catalytic site the 7-position was substituted. Changing the methyl substituents to phenyl on the Cp* ring significantly increased the efficiency of the catalyst (**Scheme 33**).[67]



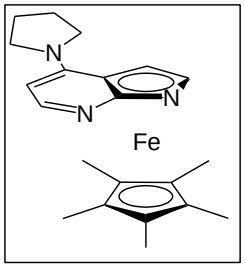


166 **167** **(*R*)-168** **(*S*)-169**

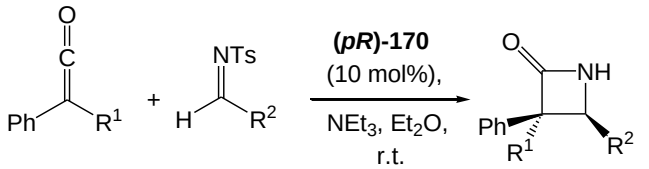
51-69% conv.
92-99.7% *ee*

Scheme 33: Kinetic resolution of secondary alcohols using azaferrocene **(*pR*)-165**.

Addition of different kinds of nucleophiles can also be performed in an asymmetric fashion with the use of nucleophilic catalysts. The Staudinger ketene cycloaddition is a useful way to form *β*–lactams which makes asymmetric Staudinger reactions highly important. Ligand **(*pR*)-170** proved to be a very efficient chiral inducer in the reaction of ketenes **171** and imines **172** (**Scheme 34**).[68]



(*pR*)-170

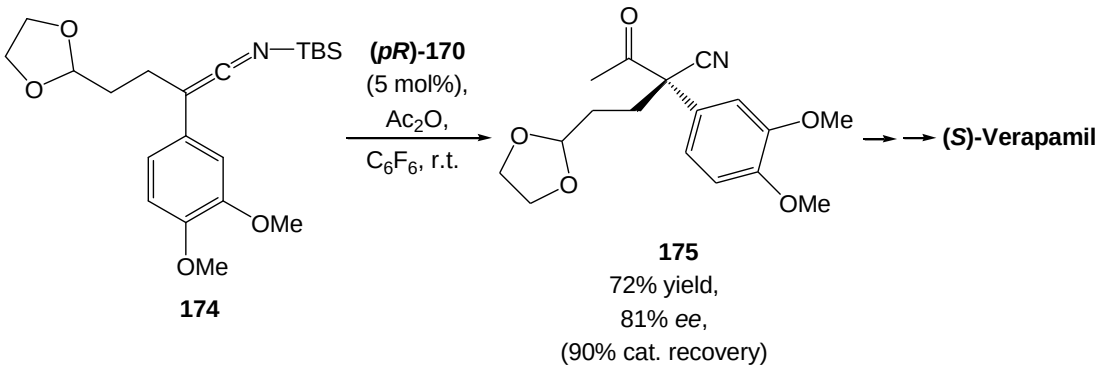


171 **172** **173**

88-98% conv.
89-98% *ee*

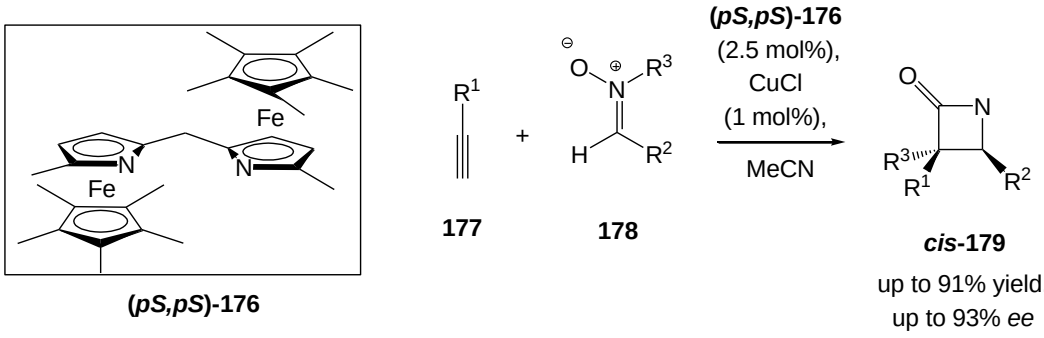
Scheme 34: Asymmetric catalytic Staudinger reaction.

This planar chiral analogue of DMAP also showed catalytic activity in other asymmetric catalytic processes such as the addition of 2-cyanopyrrole to ketenes, the kinetic resolution of amines and the acylation of silyl ketene acetals. The synthetic utility was demonstrated in the synthesis of (*S*)-Verapamil (**Scheme 35**).[69]



Scheme 35: Key step of Fu's (*S*)-Verapamil synthesis.

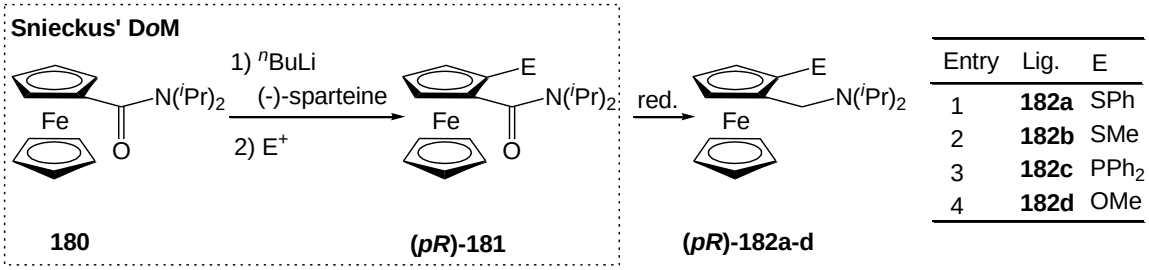
Bis(azaferrocene) analogue was found effective in the Cu catalysed coupling of alkynes and nitrones providing access to enantiomerically enriched *β*–lactams (**Scheme 36**).[70]



Scheme 36: Cu catalysed coupling of alkynes and nitrones using bis(azaferrocene) **(*pS*,*pS*)-176**.

9. Previous work within the group

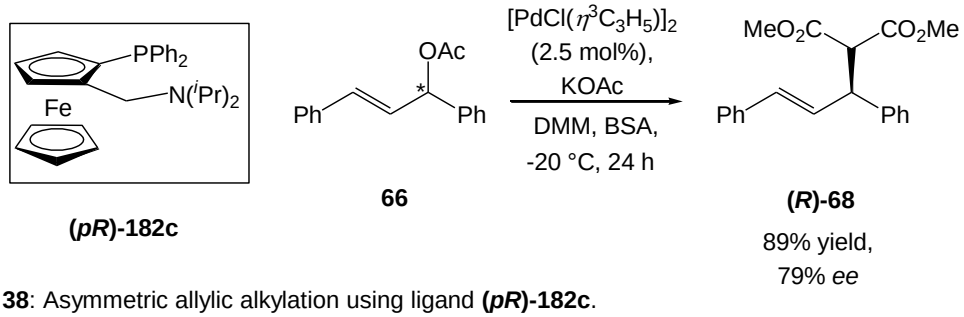
A series of novel purely planar chiral ferrocene anlogoues were synthesised following the Snieckus D*o*M protocol (**page 40**). These compounds were reduced to give a series of 1,2-disubstituted N/S, N/P and N/O ligands (**Scheme 37**).[71]



Entry	Lig.	E
1	**182a**	SPh
2	**182b**	SMe
3	**182c**	PPh_2
4	**182d**	OMe

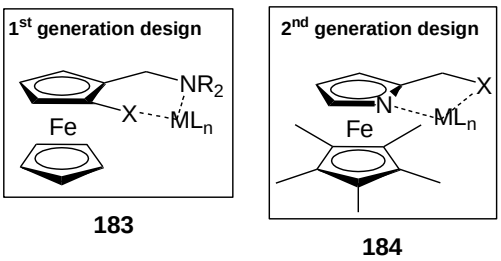
Scheme 37: Synthesis of novel bidendate ligands **(*pR*)-182a-d**.

These ligands showed moderate activity in Pd catalysed allylic alkylation reactions (**Scheme 38**).



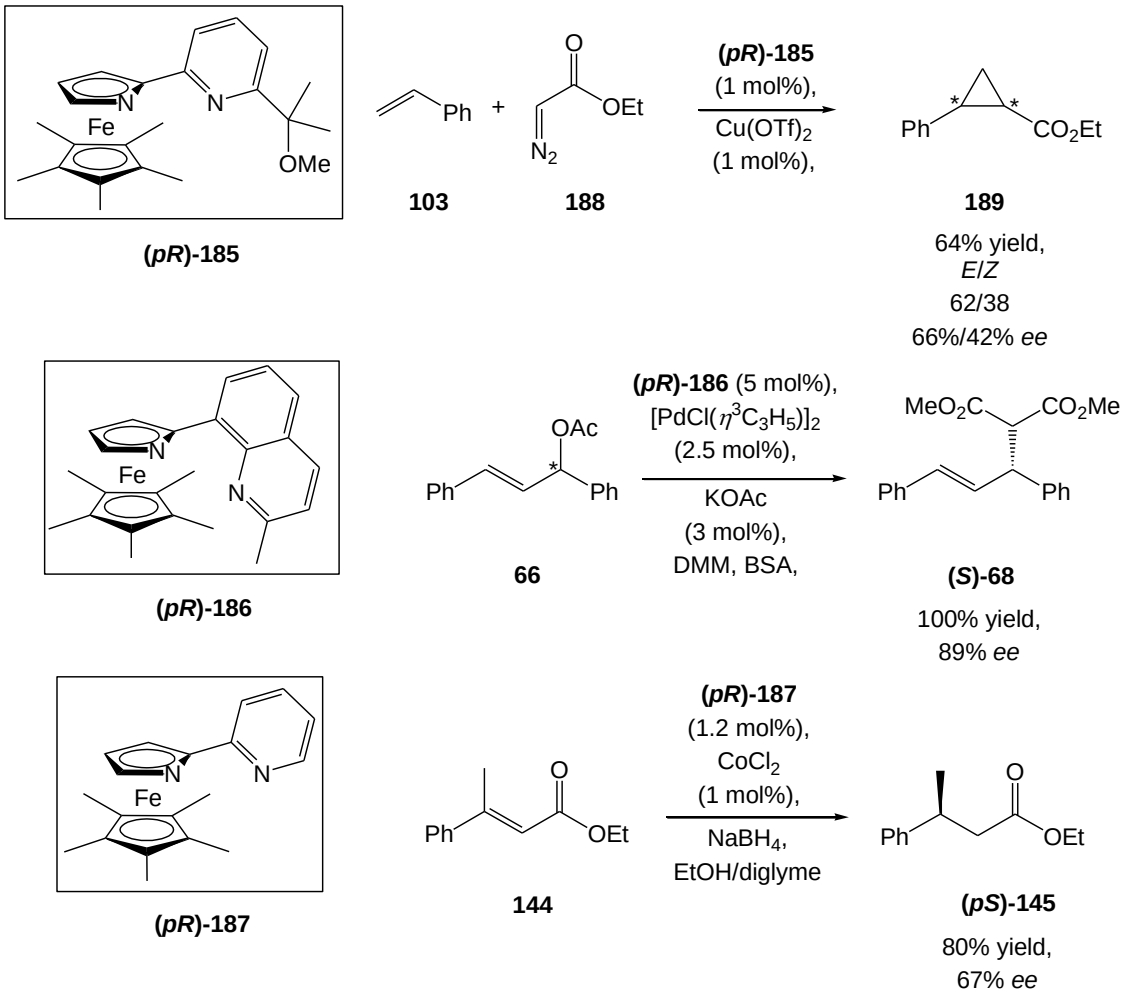
Scheme 38: Asymmetric allylic alkylation using ligand **(*pR*)-182c**.

It was hypothesised that the metallocene backbone is too far away from the catalytic site to exert its control over the reaction. Therefore the stereochemical information of the planar chirality was not transferred to the product efficiently. A second generation ligand design was devised (**Scheme 39**). The monosubstituted azaferrocene would serve as a bidendate ligand, exploiting the ability of the nitrogen lone pair to take part in metal-coordination. Purely planar chiral ligands can be obtained by enantioselective functionalisation of the azaferrocene.[72]



Scheme 39: 1st and 2nd generation ligand design.

Several analogues were synthesised following this general ligand design and some of them proved to be active in reactions like asymmetric allylic alkylations, cyclopropanations and allylic oxidations (**Scheme 40**).



Scheme 40: Some analogues of 2nd generation ligands showed activity in certain asymmetric transformations.

These examples clearly show that planar chirality is a useful source of chirality which can be efficiently transferred to the product with careful ligand design. Planar chiral ferrocenes show activity in numerous asymmetric transformations (hydrogenation, hydrosilylation, reconstitutive condensation, Diels-Alder reaction, allylic substitution, kinetic resolution, nucleophilic catalysis, Mannich-type additions, Cu catalysed dipolar cycloadditions of azomethine ylides and formal aza-Diels-Alder reactions)

10. Ferrocenes

The first synthesis of ferrocene was reported by Pauson and Kealy 1951. They reported the isolation of a compound which is highly stable and undergoes Friedel-Crafts reactions. The proposed structure was corrected by Wilkinson[73] in 1953 who obtained the Nobel Prize for his work in 1973 along with Ernst Otto Fischer. The expression ”sandwich”-structure was introduced by Dunitz in 1956.[74] These unique compounds possess great value due to :

- The strong iron-cyclopentadienyl bond (381 ± 13 kJ mol^{-1}), which prevents iron-cyclopentadienyl dissociation and therefore racemisation,

- Air and moisture stability,

- Commercial availability, low cost,

- The cyclopentadienyl ring bears high electrodensity which increases the rate of electrophilic substitution reactions on it. Ferrocene is approximately 3×10^6 times more reactive toward electrophiles than benzene,

- It is possible to control the reactivity of the metal centre by switching the redox state of the ferrocene,

- Ferrocene has an ability to stabilise an adjacent positive charge. The “α-effect” is believed to involve indirect stabilisation by electrondensity transfer to the π-system of the Cp ring, which then overlaps with the vacant p-orbital, as well as direct stabilisation by one of the three iron non-bonding orbitals and the vacant p-orbital in

the α-position (**Figure 10**). This has the effect of accelerating substitution reactions at this position.

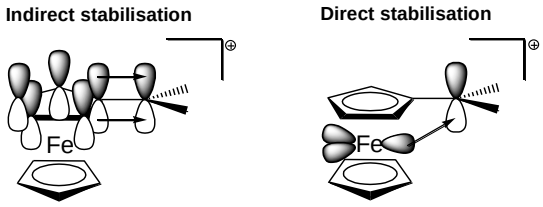


Figure 10: Indirect and direct stabilisation of α–ferrocenyl cation.

Both theories help to explain the retention of configuration in nucleophilic substitution reactions when the α-position is chiral.[75] The latter explanation is widely favoured due to the tilting of the Cp-rings that was predicted by theoretical calculations and confirmed by X-ray structural analysis (**Figure 11**). [76]

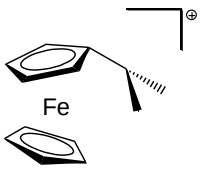


Figure 11: X-ray analysis supports the direct stabilisation hypothesis.

As a result of these features (adjustable steric and tunable electronic properties) sandwich Cp systems have long been recognised as useful asymmetric catalysts. The ease of derivatisation makes ferrocene a very attractive building block for ligand synthesis.

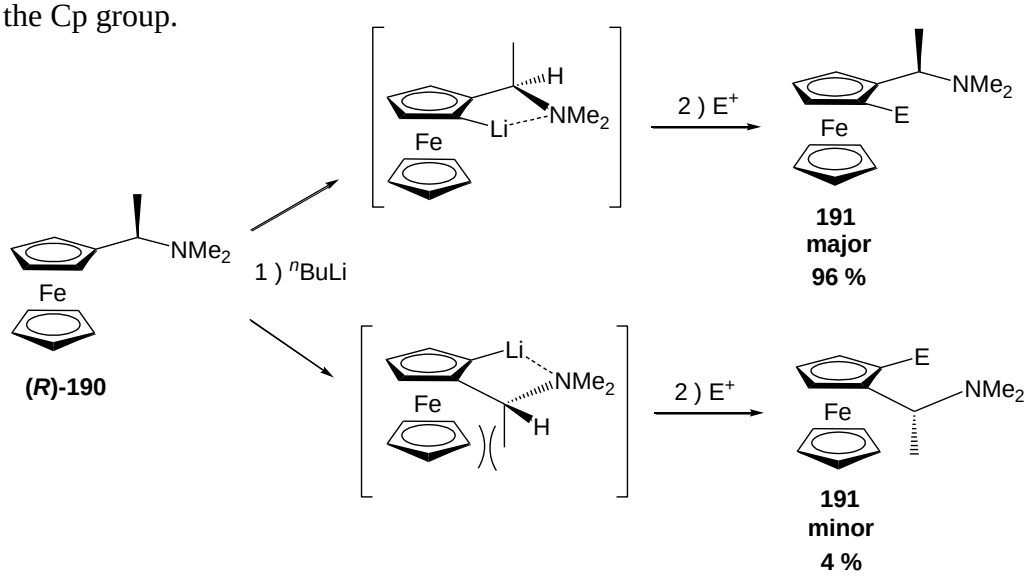
10.1 Synthesis of Planar Chiral Ferrocenes

Although synthesis of optically active planar chiral ferrocenes was achieved more than 50 years ago, there was not any straight forward methods available for the synthesis of these compounds until 1970.[77] Ugi described the first diastereoselective Directed *ortho* Metallation (D*o*M).[78] This provided access to a great variety of planar chiral ferrocene

derivatives and extensive research started after this point. In 1993 Kagan published another method using chiral sulfoxides as Directing Groups (DG).[79] This triggered a renaissance of the field and was followed by several groups publishing alternative DGs such as oxazolines (Kagan; 1993)[80] and oxazolidines (Richards[81]/Sammakia[82]/Uemura[83]/Ahn[84]; 1995). To date, three main approaches have been established:

1. Diastereoselective D*o*M

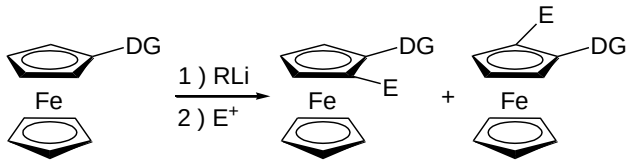
This method uses a chiral DG as a source of the stereochemical information to achieve diastereoselective deprotonation on the ferrocene ring. In the case of Ugi's amine one diastereomer is formed with 96% diastereoselectivity (**Scheme 41**). The formation of the other diastereomer is obstructed by the steric repulsion between the methyl group and the Cp group.



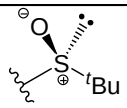
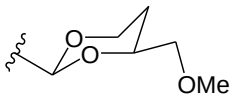
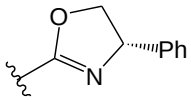
Scheme 41: Diastereoselective D*o*M of Ugi's amine **(*R*)-190**.

It is possible to further derivatise the product by nucleophilic substitution at the *α*–position. This approach provided many of the most efficient planar chiral ligands such as Josiphos, Walphos, BoPhoz, Pigiphos and TRAP (**page 18**). Other methods using

alternative DGs (sulfoxides, oxazolines and oxazolidines) give similar diastereoselectivities (**Scheme 42**).



192 **193** **194**

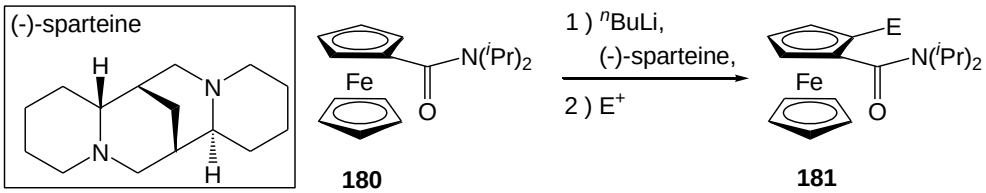
Entry	DG	193	194
1		2	98
2		99	1
3		99	1

Scheme 42: Diastereoselective D*o*M performed using different DGs.

It is worth noting that sulfoxide DGs are particulary useful as they provide access to purely planar chiral analogues if needed (reduction to sulfide, or transmetallation-electrophilic trapping). Apart from these main approaches several other methods have been developed based on DGs such as azepines, pyrrolidines, hydrazones, sulfoximines, *o*-methylephedrine, imidazolines, phosphine oxides and oxaphospholidines.

2. Enantioselective D*o*M

Following the attempts by Nozaki[85] and Simpkins[86] to develope an enantioselective approach for the asymmetric functionalisation of monosubstituted ferrocenes, in 1996 Snieckus published the first efficient D*o*M yielding purely planar chiral ferrocenes using (-)-sparteine as a chiral additive (**Scheme 43**).[87]

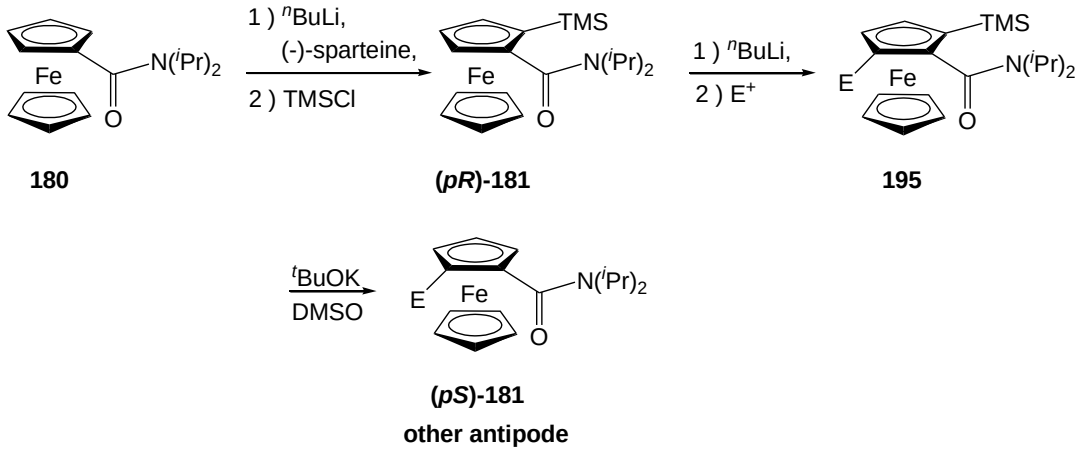


Entry	Prod.	E
1	**(*pR*)-181**	TMS, SPh, SePh, PPh_2,
2	**(*pS*)-181**	Me, $B(OH)_2$

Scheme 43: Snieckus' enantioselective D*o*M.

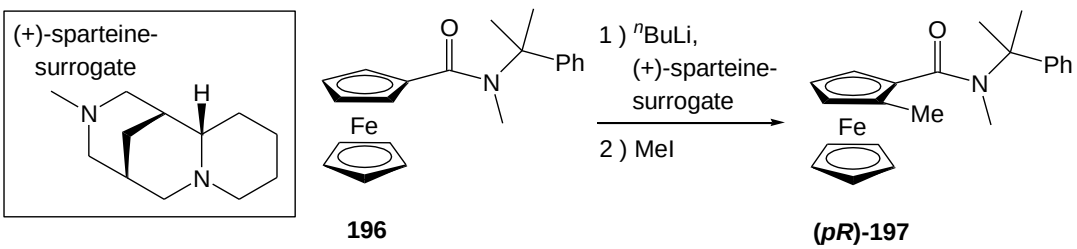
Later the cumyl amide derivative was found to be easier to derivatise further.[88] The drawback of this method is the fact that only one enantiomer of sparteine is available. This can be circumvented in two ways.

By using the "TMS-trick", first a TMS group is introduced in an asymmetric fashion (**Scheme 44**). The TMS derivative **(*pR*)-181** is then subjected to another *ortho*-lithiation, electrophilic trapping sequence. In the last step the TMS group is removed leaving a 1,2-disubstituted analogue **(*pS*)-181**.



Scheme 44: "TMS-trick".

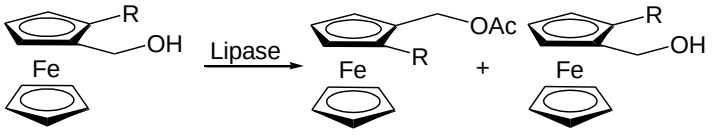
In 2006, O'Brien published the synthesis of a (+)-sparteine-surrogate starting from a natural product. By substituting (-)-sparteine with a (+)-sparteine-surrogate the other antipode **(*pR*)-197** could be accessed which can be synthesised from a natural product in a few steps (**Scheme 45**).[89]



Scheme 45: Using (+)-sparteine-surrogate as a chiral inducer.

3. Resolution

Enzymatic resolution methods started to appear in the late 1980s. The first efficient method was reported by Nicolosi, which used a lipase to resolve the racemic mixture of **(+/-)-198**.[90,91]The other enantiomer is available by hydrolysis of the acetate **(*pS*)-199** (**Table 8**).



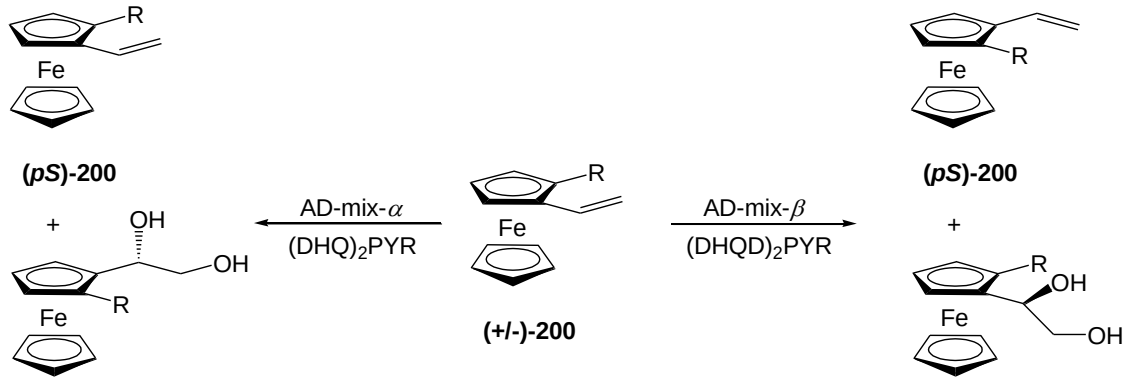
(+/-)-198 **(*pS*)-199** **(*pR*)-198**

	CCL		Novozyme®	
R	**(*pS*)-199**	**(*pR*)-198**	**(*pS*)-199**	**(*pR*)-198**
SMe	36% conv.	n.g.	32% conv.	n.g.
	76% *ee*	42% *ee*	90% *ee*	48% *ee*
I	25% conv.	n.g.	25% conv.	n.g.
	70% *ee*	28% *ee*	96% *ee*	32% *ee*

n.g. = not given
CCL = Candida Cylindracea
Novozyme® = Candida antarctica

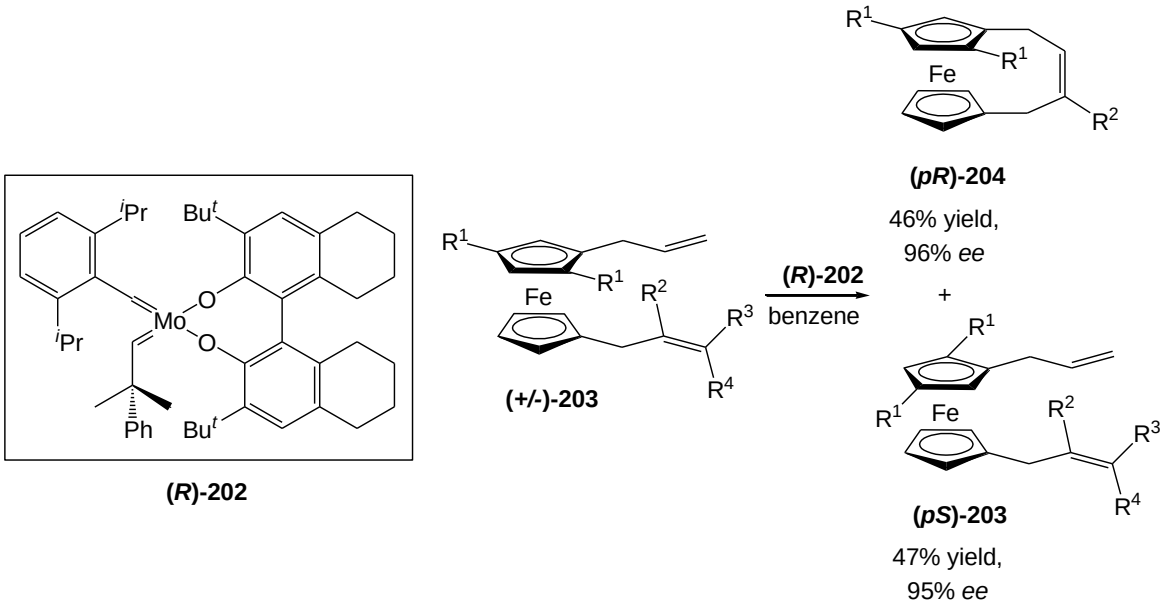
Table 8: Enzymatic resolution using Lipases.

The first chiral catalyst mediated kinetic resolution was reported by Moyano in 2006. The corresponding products **(*S*,*pS*)-201** and **(*R*,*pR*)-201** were isolated in good yield and *ee*. The stereochemical outcome agrees with the general rule for Asymmetric Dihydroxylation reactions (**Scheme 46**).[92]



Scheme 46: Kinetic resolution using Asymmetric Dihydroxylation.

Ogasawara also published a catalytic kinetic resolution protocol performing Asymmetric Ring Closing Metathesis (ARCM) on a racemic mixture of ferrocene derivative **(+/-)-203** using a molybdenum catalyst **(*R*)-202** (**Scheme 47**).[93]



Scheme 47: Kinetic resolution using Asymmetric Dihydroxylation.

11. Ligand Design

Conceptually, to design catalysts for the stereocontrolled formation of new σ–bonds to a pro-chiral molecule we require a metal possessing 4 quadrants of differing size (**Figure 12**). Upon coordination of a prochiral substrate the least sterically congested complex should result. With the prochiral face of the unsaturated system differentiated, hydrogenation, addition of HY (Y = NR_2, SiR_3, BR_2, CN) or polymerisation will form new stereocentres in a contolled fashion.

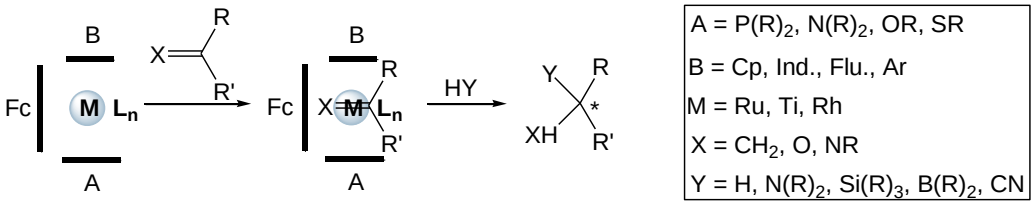


Figure 12: General concept.

Some earlier work done within the group synthesised potential ligands based on alignments **1** and **2** were synthesised (**Figure 13**).[72] These ligands showed activity in Pd catalysed AAA, Cu catalysed cyclopropanation, and allylic reduction reactions with moderate to good *ee*s. **(page 35**).

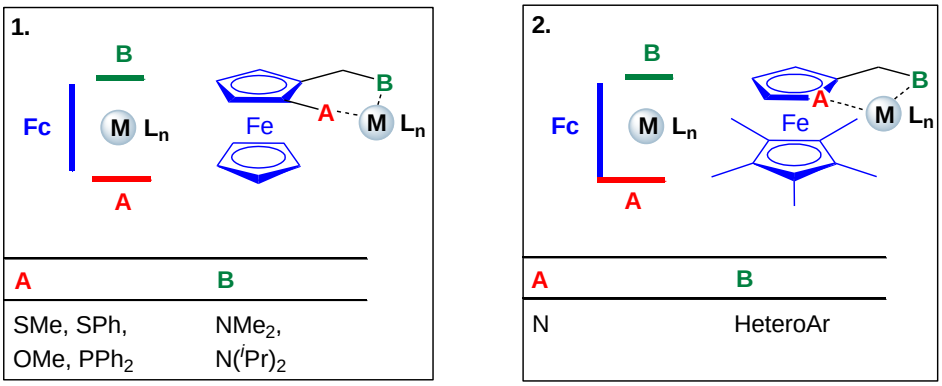


Figure 13: Previous work following the general ligand design.

Some of the most recent work has involved the synthesis of analogues (**alignment 3**, **Figure 14**) to mimic *ansa*-half sandwich metallocenes, where the source of chiral information is originated from the planar chirality provided by the ferrocene unit.[94] These complexes however proved to be highly unstable. Despite this instability issue complexation studies were attempted, but gave no positive results. This was most probably due to the lack of stability of the desired complexes.

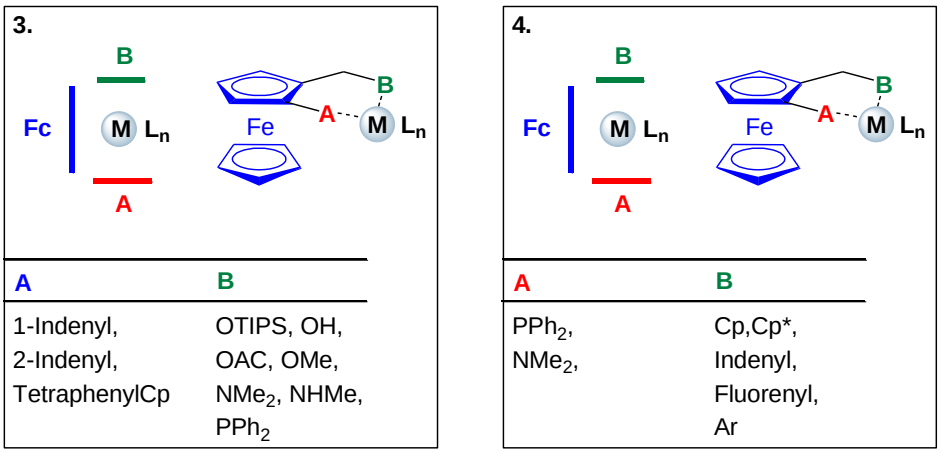


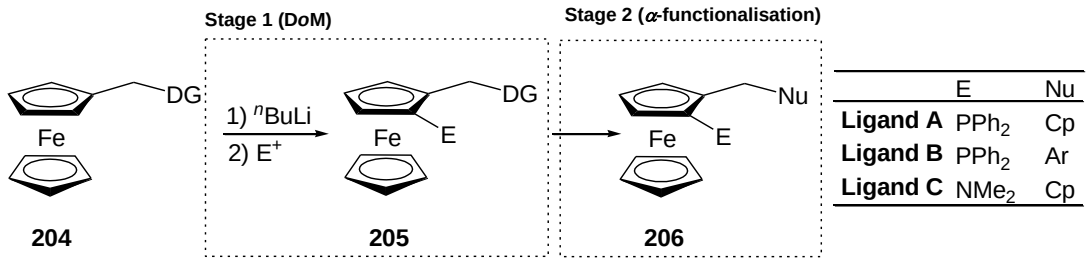
Figure 14: Alignments **3** and **4**.

There are several factors which affect the stability of ferrocenes.[95] EWGs close to the ferrocene unit weaken the Fe-Cp bond and result in lower thermal stability of the compounds. On the other hand EDGs make the ferrocene unit sensitive to oxidation. Analogues bearing a partial positive charge at the α–position are photochemically unstable. Certain chlorinated solvents increase the photoinstability of ferrocenes. Another reason for instability might arise from the activated nature of the doubly benzylic position between the ferrocene and indenyl units.

Our latest ligand design and the aim of this work was to synthesise ligands based on alignment **4**. We get to alignment **4** by exchanging A and B groups. Therefore the cyclopentadienyl-like moiety is in the α–position while the Lewis basic functionality is placed right onto the ring (alignment **4**, **Figure 14**). By moving the Cp unit into the α–position we were hoping to avoid having an activated α–doubly benzylic position.

1. General Considerations

Approaches to synthesise 1,2-disubstituted planar chiral ferrocenes generally consists of two main steps.[96] In the first stage a mono-substituted ferrocene **204** is substituted to give a 1,2-disubstituted analogue **205**. For regiocontrol, this method exploits the directing ability of the first group already in place and is called Directed *ortho* Metallation (D*o*M). In the second stage the directing group is converted to the desired moiety (**Scheme 48**). Our synthetic work included the synthesis of three analogoues (**Ligand A**-**C**) based on the general ligand structure **206**.



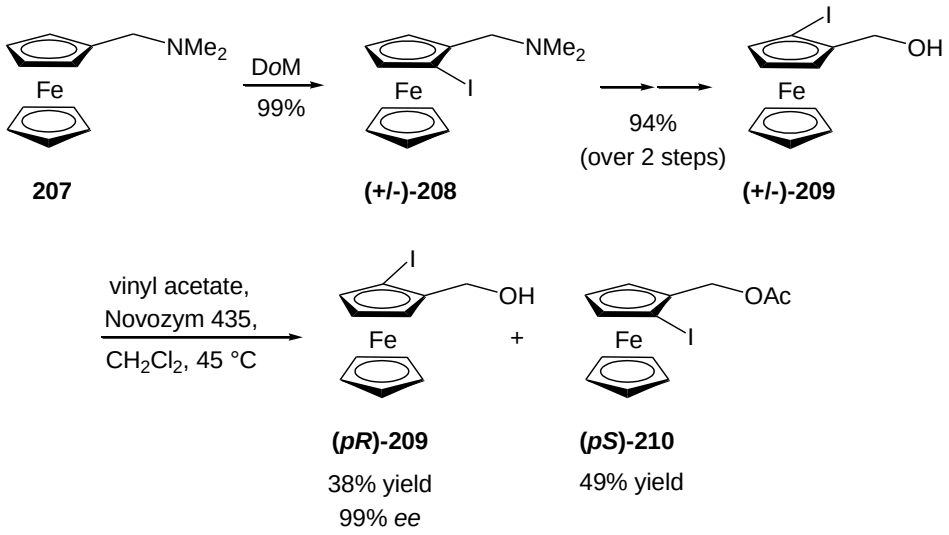
	E	Nu
Ligand A	PPh_2	Cp
Ligand B	PPh_2	Ar
Ligand C	NMe_2	Cp

Scheme 48: General scheme of the 2-step strategy used to synthesise 1,2-disubstituted planar chiral ferrocenes **206**.

2. Previous Work

Previous work within our group established a route to 1,2-disubstituted purely planar chiral ferrocenes.[93] Racemic **(+/-)-208** was obtained by the D*o*M of **207**. In the following steps the dimethylamine group was converted to an alcohol group and the racemic material was then resolved enzymatically to give enantiomerically pure ***(pR)*-**

209 (**Scheme 49**).[89] It seemed convenient to adopt this sequence as a starting point for our synthesis.



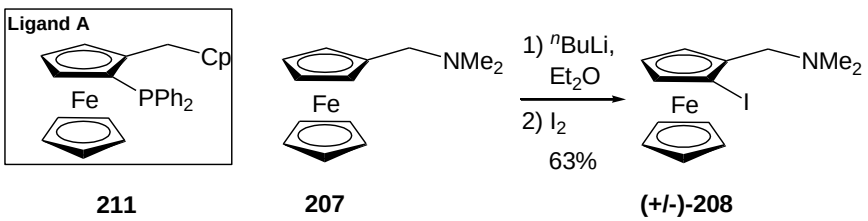
Scheme 49: Synthesis of 1,2-disubstituted purely planar chiral ferrocenes **(*pR*)-209** and **(*pS*)-210**.

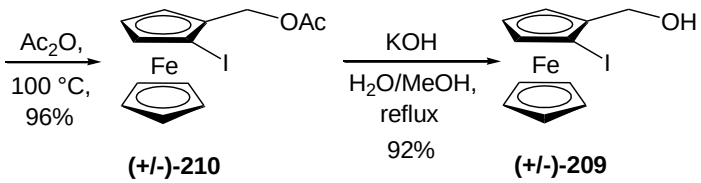
3. Ligand A

3.1 Synthesis of Ligand A

3.1.1 First Stage (*ortho*-functionalisation)

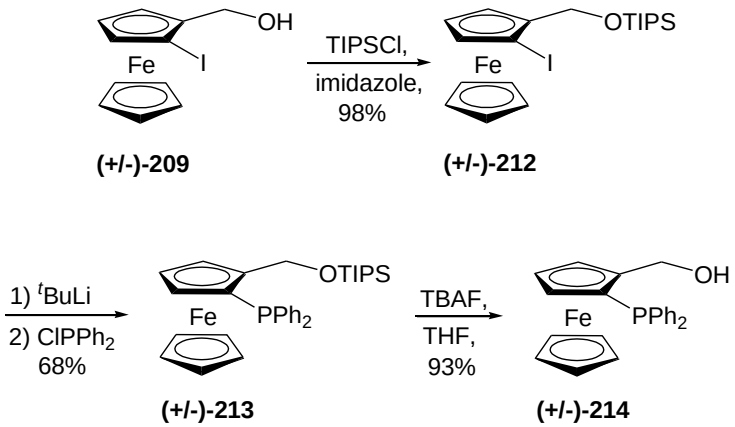
In the first step commercially available or synthesised *N*,*N*-dimethylaminomethylferrocene was subjected to D*o*M using iodine as an electrophile to give racemic amine **(+/-)-208.**[199] The amine functionality was then converted to the corresponding alcohol *via* acetate **(+/-)-210** (**Scheme 50**). At this stage of the project the enzymatic resolution was not performed and the synthesis was further developed using the racemic material.





Scheme 50: Synthesis of 2-hydroxymethyl-1-iodoferrocene **(+/-)-209**.

The alcohol functionality was protected as its silylether **(+/-)-212**. Iodide **(+/-)-212** was then subjected to lithium-halogen exchange and upon quenching the reaction mixture with $ClPPh_2$, diphenylphosphino derivative **(+/-)-213** was isolated. In the last step silylether **(+/-)-213** was deprotected to give alcohol **(+/-)-214** (**Scheme 51**).



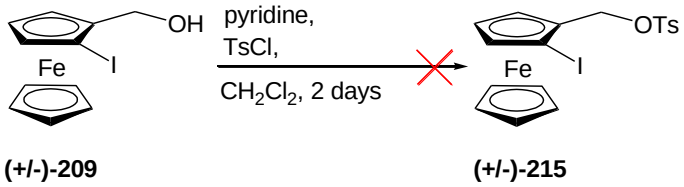
Scheme 51: Synthesis of 1-diphenylphosphino-2-hydroxymethylferrocene **(+/-)-214**.

3.1.2 Second Stage (*α*-functionalisation)

Having the desired diphenylphosphino group in place we focused on introducing the cyclopentadienyl functionality into the *α*-position. On the basis of the general strategy described earlier (**page 46**), for this conversion a S_N2 reaction was envisaged. Therefore, formation of a suitable leaving group in *α*-position was first attempted.

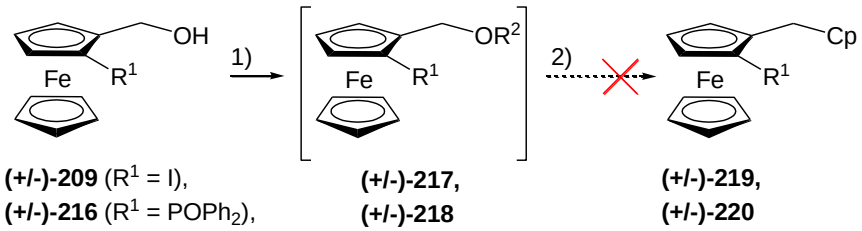
Sulfonate

Tosylation of alcohol **(+/-)-209** was attempted,[97] however even after two days the reaction contained only unreacted starting material (**Scheme 52**).



Scheme 52: Attempted synthesis of tosylate **(+/-)-215**.

In order to generate the corresponding sulfonates **(+/-)-217** and **(+/-)-218** from alcohols **(+/-)-209** and **(+/-)-216** *in situ*, a set of alternative conditions were tested (**Table 9**).[98] In these reactions only unreacted starting material **(+/-)-209** and **(+/-)-216** was observed.



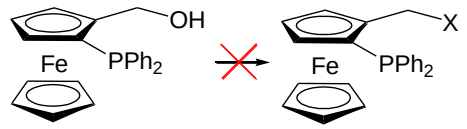
Entry	Subs.	R^1	R^2	Conditions
1	**209**	I	Ms	1) MsCl, DIPEA, 2) LiCp
2	**209**	I	Ms	1) NaH, TsCl, 2) LiCp
3	**216**	$POPh_2$	Ts	1) NaH, TsCl, 2) LiCp

Table 9: Attempts for *in situ* generation of sulfonates **(+/-)-217**, **(+/-)-218**.

Halide

All attempts to form halides **(+/-)-221a**, **(+/-)-221b** and **(+/-)-221c** were unsuccessful (**Scheme 53**).[99,100] This was mainly attributed to the lone pair of the

phosphorus which might cause side-reactions. The highly unstable C-X bond might be another reason for the formation of by-products.



(+/-)-214

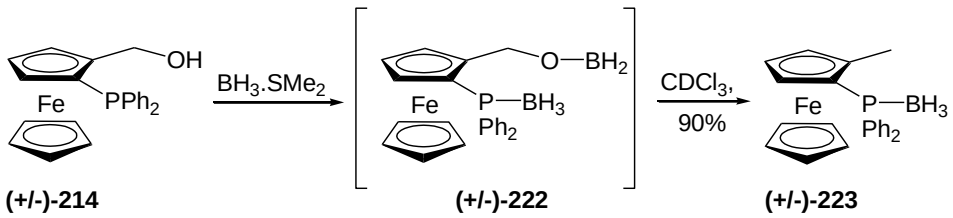
(+/-)-221a, (X = Cl),
(+/-)-221b, (X = Br),
(+/-)-221c, (X = I),

Entry	Subs.	Conditions
1	**(+/-)-221a**	$(COCl)_2$, DMF (cat.), CH_2Cl_2, r.t.
2	**(+/-)-221b**	PBr_3, CH_2Cl_2, -78 °C
3	**(+/-)-221c**	PPh_3, I_2, imidazole, CH_2Cl_2, r.t.

Scheme 53: Attempted *α*–substitutions to give halogenides **(+/-)-221a**, **(+/-)-221b** and **(+/-)-221c**.

Protection of phosphorus

There are different methods in the literature for the protection of the ferrocenyl-phosphine moiety. Treating a phosphine with borane gives a fairly stable coordination compound which can be deprotected later by using other Lewis basic functionalities such as amines.[101] Treatment of phosphine **(+/-)-214** with $BH_3.SMe_2$ gave a yellow solid **(+/-)-222**. Upon redissolution of this solid in CH_2Cl_2 or $CDCl_3$, methylferrocene **(+/-)-223** was isolated (**Scheme 54**).

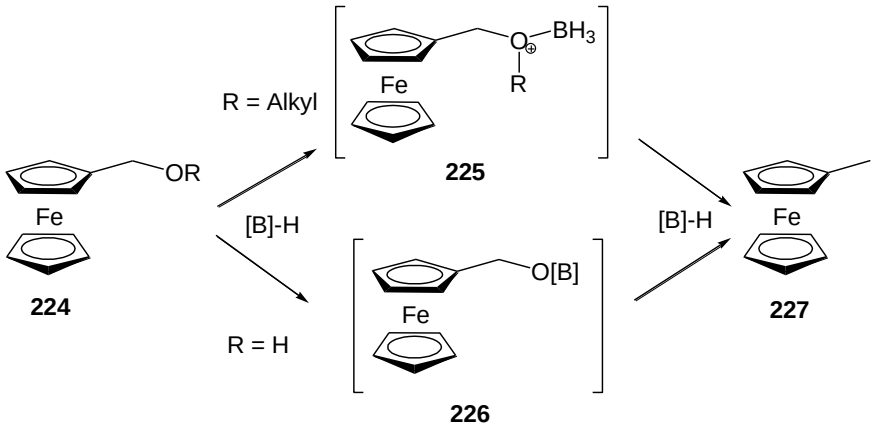


(+/-)-214 **(+/-)-222** **(+/-)-223**

Scheme 54: Protection of diphenylphosphine led to methylferrocene **(+/-)-223**.

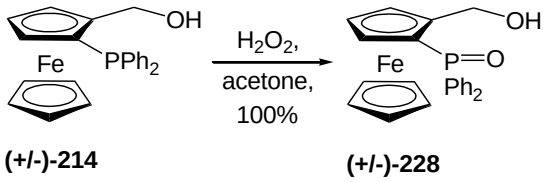
One literature precedent was found which showed that borane as a SMe_2 or THF complex can reduce a range of *α*–ferrocenyl compounds **224** (aldehydes, ketones, carboxylic acids, esters, acetals, alcohols, ethers) to the corresponding methyl derivative **227** under mild conditions.[102] The reduction of alcohols is believed to

proceed via a borate-intermediate **226**, but complexation of borane to oxygen **225** could also be responsible for the activation of the C-O bond (**Scheme 55**).



Scheme 55: Proposed mechanism of reduction of *α*–ferrocenyl ethers/alcohols **224** to methylferrocene **227**.

Oxidation of phosphines to phosphine oxides is also used in ferrocene chemistry as a means of protection.[103] The corresponding phosphine oxides are more stable due to the covalent character of the protection. Oxidation of diphenylphosphine **(+/-)-214** with H_2O_2 gave the corresponding phosphine oxide **(+/-)-228** quantitatively (**Scheme 56**).

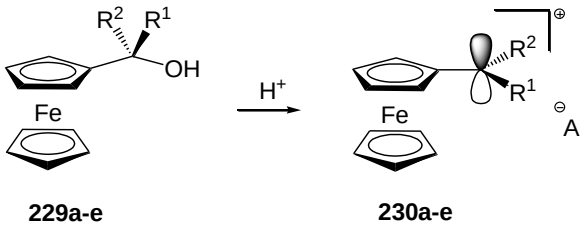


Scheme 56: Protection of the diphenylphosphine moiety as a phosphine oxide.

Making hydroxyl a better LG (S_N1-mechanism)

After protection of the phosphine moiety, further manipulation of the hydroxy group in the *α*–position was attempted. The substitution reactions at the *α*–position are believed to proceed *via* carbocation intermediates. The surprisingly high stability of these

species is due to the *α*–effect (**page 38**), which enables the characterisation[104,105] and/or isolation[106,107] of these species in some cases at low temperatures (**Scheme 57**).



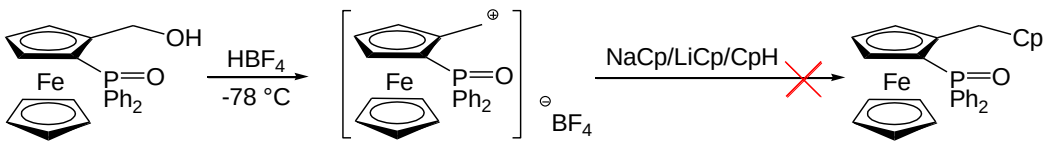
229a-e **230a-e**

Entry	Subs.	R^1	R^2
1	**230a**	H	H
2	**230b**	H	Me
3	**230c**	H	Ph
4	**230d**	Me	Me
5	**230e**	Ph	Ph

Scheme 57: Formation of *α*–ferrocenylcarbocations **230a-e**.

The stability of these carbocations can be related to their pK_R^+, obtained from solvolysis experiments of the corresponding alcohols in AcOH or H_2SO_4. Their stability increases in the following order: **230a**<**230b**<**230d**<**230c**<**230e**. Coordinating solvents also help to stabilise the cations. The stabilising effect of the solvents, which is paralleled with their basicity, increases in the following order: MeO^tBu, THF, Et_2O.

Alcohol **(+/-)-228** was treated with HBF_4 and then a variety of cyclopentadienyl salts were added to the reaction mixture. None of the isolated compounds turned out to be the desired product (**Scheme 58**). This might be due to the fact that primary *α*–carbocation **(+/-)-231** is the least stabilised among *α*–substituted carbocations.

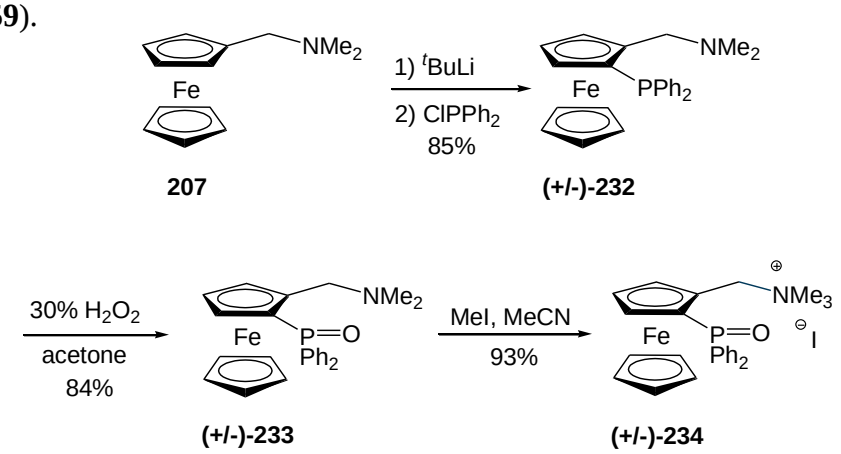


(+/-)-228 **(+/-)-231** **(+/-)-220**

Scheme 58: Attempted *in situ* formation and reaction of ferrocenyl *α*-carbocation **(+/-)-231**.

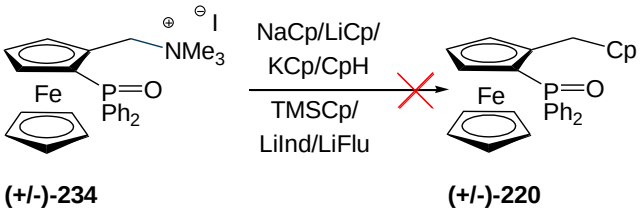
Trialkyl-amino LG

Following the unsuccessful *α*–substitution we investigated the use of different leaving groups. Trialkyl-amino groups are also known to be good leaving groups in nucleophilic substitution reactions. Moreover analogous approaches have already been used in ferrocene chemistry to synthesise similar *α*–amino,[4] or *α*–cyclopentadienyl derivatives.[108] The corresponding tetraalkyl-ammonium salt **(+/-)-234** was synthesised. First the diphenylphosphino-group was introduced into the *ortho*-position of *N*,*N*-(dimethylaminomethyl)ferrocene **207** by D*o*M. This was followed by the oxidation of phosphine **(+/-)-232** to phosphine oxide **(+/-)-233** in 84% yield. Finally treating amine **(+/-)-233** with MeI gave the desired tetraalkyl-ammonium salt **(+/-)-234** in a good yield (**Scheme 59**).



Scheme 59: Synthesis of tetraalkyl-ammonium salt **(+/-)-234**.

In this way, the unreliable *in situ* formation of the reactive *α*-carbocation intermediate was circumvented by the formation of the stable tetraalkyl-ammonium salt **(+/-)-234**. This compound was then reacted with a great variety of cyclopentadienyl/indenyl/fluorenyl-derivatives, however, it turned out to be unreactive (**Scheme 60**). Upon forcing conditions decomposition of the starting material occured in each case.

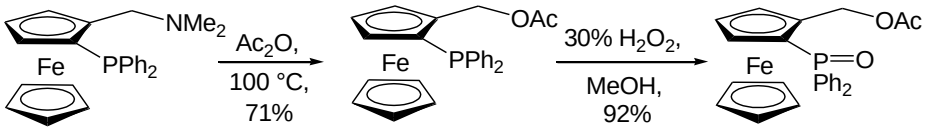


(+/-)-234 **(+/-)-220**

Scheme 60: Unsuccessful *α*-substitution of tetraalkyl-ammonium salt **(+/-)-234**.

Acetate LG

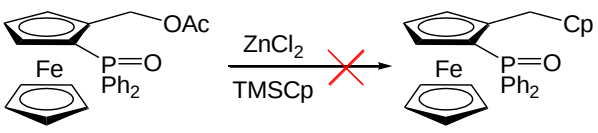
According to literature precedent, *α*-carbocations generated from the corresponding acetates react with π-nucleophiles such as allylsilanes, allylstannates, silylenol ethers and hydride donors.[109] Synthesis of acetate **(+/-)-236** was realised in two steps. Diphenylphosphinoferrocene **(+/-)-232** was treated with Ac_2O to give acetate **(+/-)-235**. In the last step the diphenylphosphine was protected as the phosphine oxide **(+/-)-236** (**Scheme 61**).



(+/-)-232 **(+/-)-235** **(+/-)-236**

Scheme 61: Synthesis of acetate **(+/-)-236**.

Acetate **(+/-)-236** was reacted with TMSCp in the presence of a Lewis acid at low temperature. Product formation was not observed and raising the temperature to r.t. led to decomposition of the starting material (**Scheme 62**).



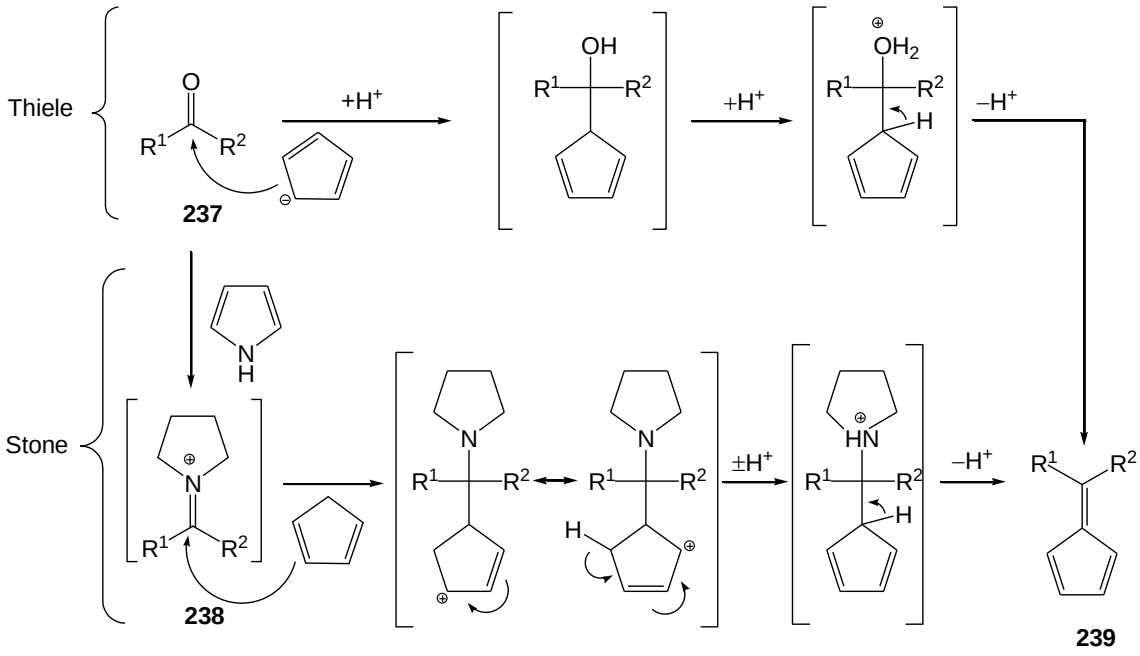
(+/-)-236 **(+/-)-220**

Scheme 62: Unsuccessful *α*-substitution of acetate **(+/-)-236**.

It was considered probable that the nature of the Cp nucleophile was the key to the success of the desired substitution reaction.

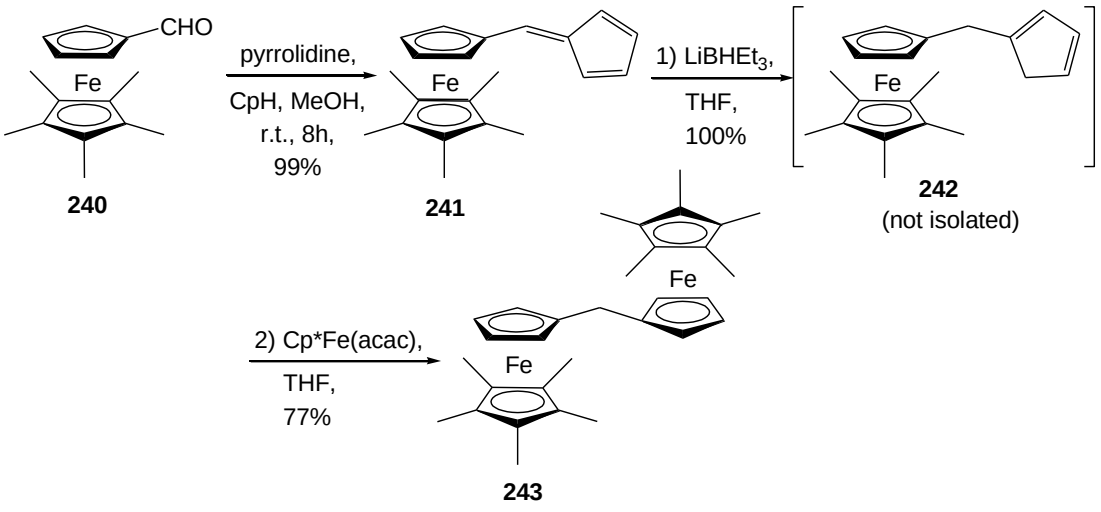
Cyclopentadiene as a nucleophile

There are two main methods to prepare fulvenes from ketones and aldehydes. In 1900 Thiele found that reacting cyclopentadiene with a carbonyl compound **237** in protic solvents (MeOH) in the presence of a strong base (MeONa) gave rise to the corresponding fulvene **239**.[110] Somewhat later Stone and Little observed that the same transformation takes place when mixing cyclopentadiene and the carbonyl compound **237** in the presence of pyrrolidine.[111] The authors imply that pyrrolidine acts on one hand as a carbonyl activating agent by means of iminium salt **238** formation. On the other hand serves as a base for the fulvene formation (**Figure 15**).[112]



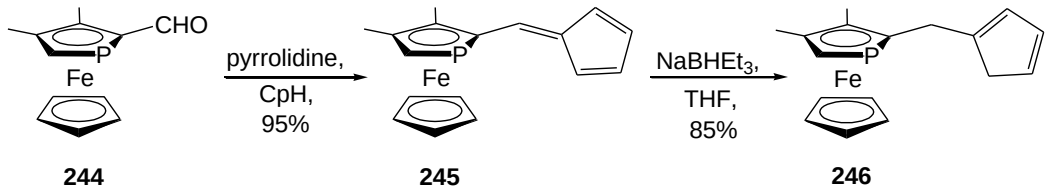
Scheme 15: Suggested mechanism for reactions of ketone **237** with CpH under Thiele- and Stone-conditions.

The Stone-method was first successfully applied in ferrocene chemistry by Bildstein in order to convert ferrocenyl-aldehyde **240** to the cyclopentadiene derivative **242** *via* the corresponding fulvene **241** (**Scheme 63**).[113]



Scheme 63: Synthesis of ferrocenyl-cyclopentadiene **242** *via* fulvene **241**.

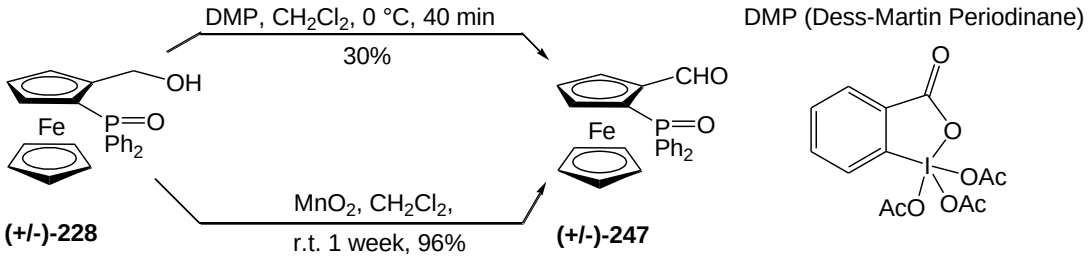
The Stone method was later utilised by Ganter to synthesise phosphaferrocenyl-cyclopentadiene derivative **246** (**Scheme 64**).[114]



Scheme 64: Synthesis of phosphaferrocenyl-cyclopentadiene derivative **246** using the Stone-method.

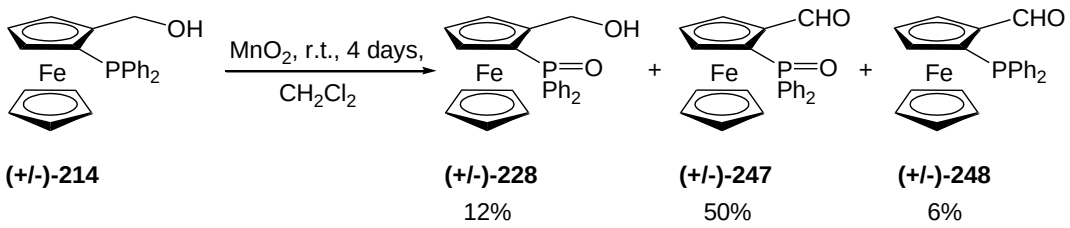
This two step sequence seemed convenient for our purposes. On one hand, the first step is performed under mild conditions to give the fulvene quantitatively. On the other hand, the second step exploits the reactivity of the activated sp^2 α–carbon against nucleophilic attack (hydride, alkyl), which has been also well documented.[115,116,117]

To adopt the Stone-method to our synthesis first we needed to synthesise aldehyde **(+/-)-247**. Reaction of alcohol **(+/-)-228** with Dess-Martin periodinane gave aldehyde **(+/-)-247** along with some starting material. Purification of the aldehyde proved to be difficult due to the small difference in Rf-values (**Scheme 65**). Oxidation of alcohol **(+/-)-228** with MnO_2[118] was sluggish but gradually progressed to give the product **(+/-)-247** almost quantitatively after a week. The purification was also easier in this case.



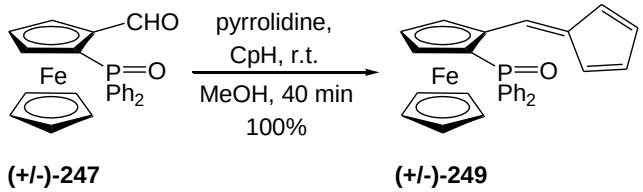
Scheme 65: Oxidation of alcohol **(+/-)-228** to aldehyde **(+/-)-247**.

In an attempt to synthesise aldehyde **(+/-)-247** from phosphine **(+/-)-214** in one single step, by oxidation using MnO_2, a mixture of oxidised products **(+/-)-228**, **(+/-)-247** and **(+/-)-248** were isolated (**Scheme 66**).



Scheme 66: Oxidation of phosphine **(+/-)-214** gave a mixture of products.

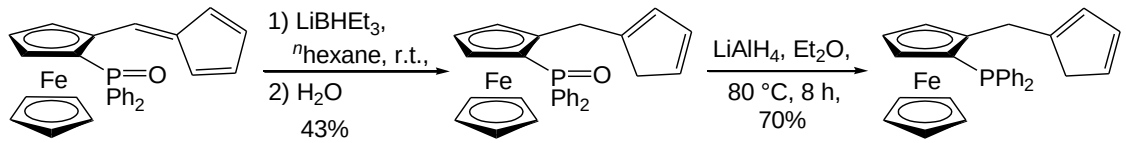
The reaction of aldehyde **(+/-)-247** and cyclopentadiene in the presence of pyrrolidine gave the corresponding fulvene **(+/-)-249** quantitatively after 40 minutes at r.t. (**Scheme 67**).



(+/-)-247 **(+/-)-249**

Scheme 67: Formation of fulvene **(+/-)-249** from aldehyde **(+/-)-247**.

Fulvene **(+/-)-249** was then converted to cyclopentadiene **(+/-)-220**, which in the final step was reduced to phosphine **(+/-)-211** (**Scheme 68**).



(+/-)-249 **(+/-)-220** **(+/-)-211**

Scheme 68: Two step reduction of diphenylphosphinoxi-fulvene **(+/-)-249**.

The steps however were not easily reproducible. Possible reasons are the polar nature of diphenylphosphine oxides **(+/-)-249** and **(+/-)-220**, which made the purification more difficult compared to the diphenylphosphine analogues. In the last step reasonable yields were only achieved when elevated temperatures were used, which also led to side-reactions and/or decomposition. Furthermore, alcohol **(+/-)-214** inpurities from the oxidation step further complicated column chromatography.

3.1.3 Kagan's D*o*M

Stone's method provided a convenient finish for the synthesis, however some steps needed to be improved/eliminated. After consideration, a different sequence was devised. One of the D*o*Ms developed by Kagan uses a masked aldehyde directing group, to synthesise 1,2-disubstituted planar chiral ferrocenes (**page 40**).[80] At the end of the sequence it might be possible to get to our final compound in two steps under mild conditions, without the need of phosphorus protection/deprotection (**Figure 16**).

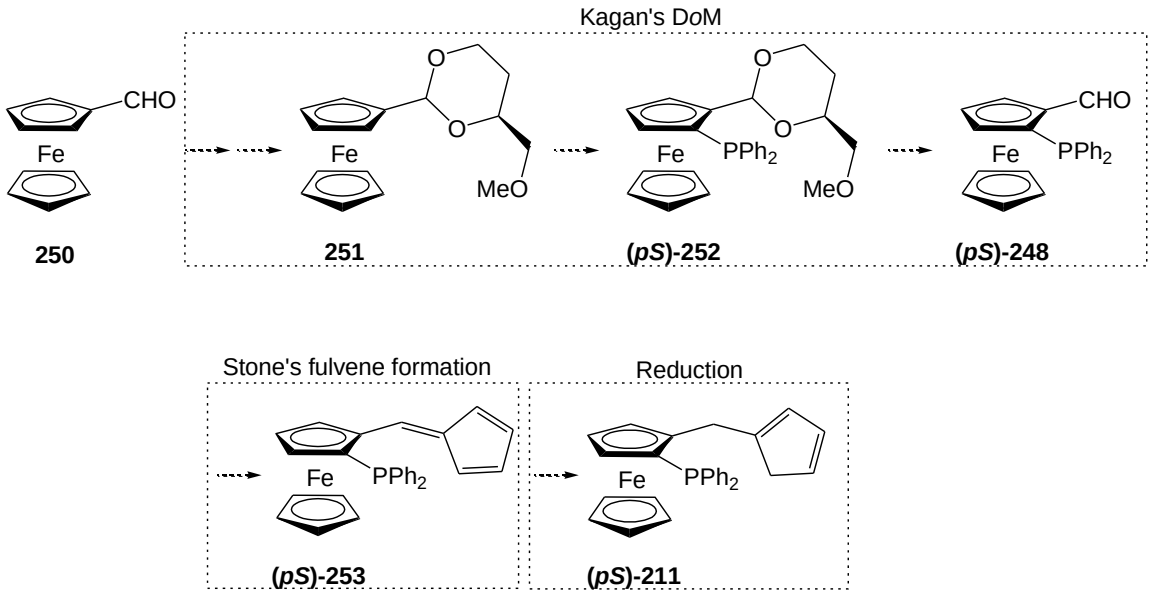
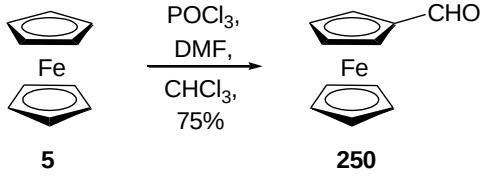


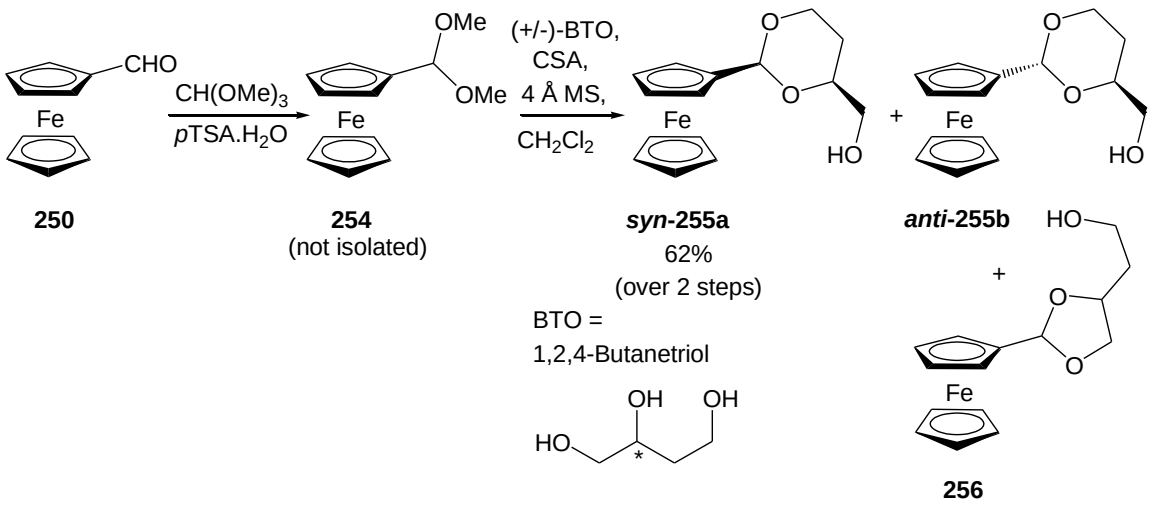
Figure 16: Proposed synthetic sequence to obtain ligand **(*pS*)-211**.

First, formylferrocene **250** was synthesised according to a literature precedent, using a Vilsmeier-Haack formylation reaction (**Scheme 69**).[119]



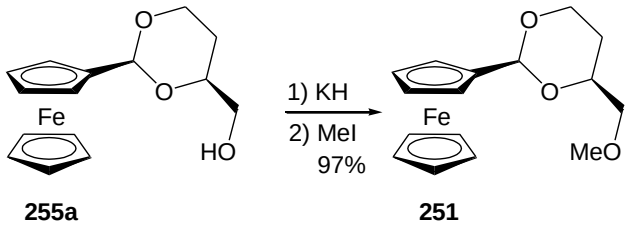
Scheme 69: Synthesis of formylferrocene **250**.

Incorporation of the cyclic acetal directing group was accomplished in two steps (**Scheme 70**). In the second step a mixture of acetals was formed. One of the diastereomers ***syn*-255a** could be separated from this mixture. The rest formed as an inseparable mixture of compounds. Based on NMR data, this mixture is believed to contain the other diastereomer ***anti*-255b** and a 5-membered acetal **256**. Diastereomer ***syn*-255a** was later found to give high yields in the *ortho*-substitution step while the other acetals showed ***anti*-255b** and **256** less *ortho*-directing effect, resulting in lower yields. Therefore, careful separation was performed at this point to avoid carrying monosubstituted acetals ***anti*-255b** and **256** throughout the synthesis.



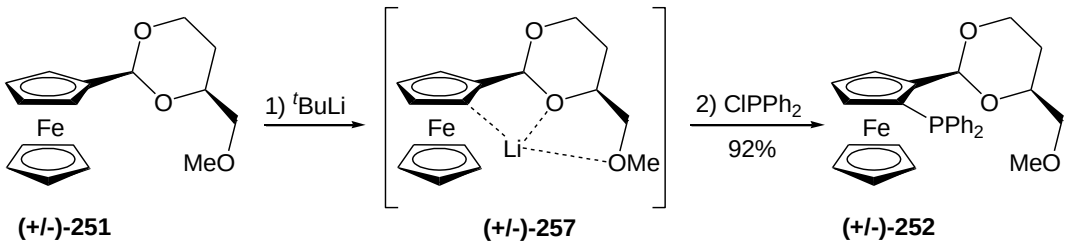
Scheme 70: Incorporation of acetal directing group.

In the next step acetal **255a** was protected as its methyl ether **251** (**Scheme 71**).



Scheme 71: Protection of the hydroxyl-group.

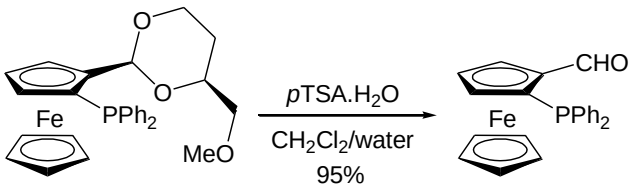
This was followed by *ortho*-lithiation and reaction with $ClPPh_2$ to give the 1,2-disubstituted planar chiral ferrocene **(+/-)-252** in 92% yield (**Scheme 72**). Incorporation of (*S*)-1,2,4-butanetriol in the acetalisation step can give access to **(*pS*)-252** in 98% *ee* according to Kagan's results.[80]



(+/-)-251 **(+/-)-257** **(+/-)-252**

Scheme 72: Directed *ortho* Metallation (DoM).

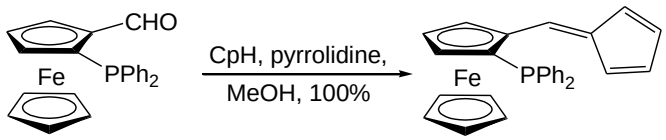
After introduction of the diphenylphosphine-functionality the acetal group was removed (**Scheme 73**). At first, inconsistent yields were obtained. This was attributed to the facile oxidation of the diphenylphsophino moiety, therefore degassed solvents were used in all subsequent steps in order to maximise the yields. Purification of **(+/-)-248** by column chromatography was further simplified by its intense colour and a large difference in Rf to **(+/-)-252**. Therefore the crude material was usually passed through a short plug of silica and concentrated under reduced pressure immediately to give **(+/-)-248** in excellent yield.



(+/-)-252 **(+/-)-248**

Scheme 73: Deprotection of acetal **(+/-)-252**.

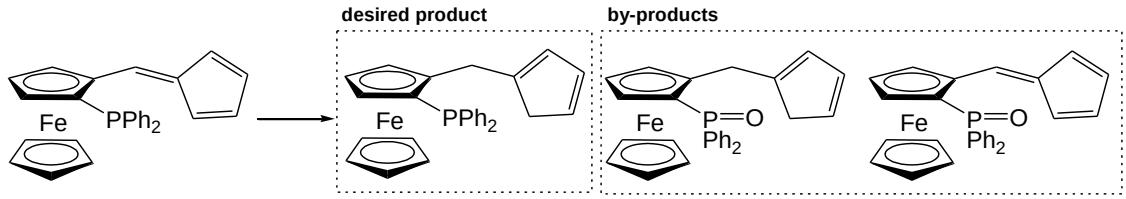
Aldehyde **(+/-)-248** was reacted with cyclopentadiene in the presence of pyrrolidine to give fulvene **(+/-)-253** in quantitative yield (**Scheme 74**).



(+/-)-248 **(+/-)-253**

Scheme 74: Formation of fulvene **(+/-)-253**.

Reduction of fulvene was first attempted using Superhydride® ($LiBHEt_3$). This reagent gave a mixture of cyclopentadiene **(+/-)-211** and oxide **(+/-)-220** (**entry 1**, **Table 10**). It was proposed that BEt_3 formed during the reaction might form a complex with the diphenylphosphino group, retarding the reaction and giving rise to the oxide **(+/-)-220** by-product. To test this hypothesis DABCO was added to the reaction mixture to liberate the complexed diphenylphosphino moiety. In this reaction the mixture of the cyclopentadiene **(+/-)-211** and oxide **(+/-)-220** was isolated (**entry 2**, **Table 10**). Performing the reaction in a ^{n}hexane mainly the oxide **(+/-)-220** was isolated (**entry 3**, **Table 10**). In order to protect the diphenylphosphine moiety before hydride-addition $BH_3.SMe_2$ was added to fulvene **(+/-)-253** followed by addition of Superhydride®. This resulted in oxide **(+/-)-220** formation (**entry 4**, **Table 10**). In the course of seeking an effectice hydride-source for the reaction, next we tried L-Selectride®. However mostly the formation of the oxide **(+/-)-220** was observed (**entry 5**, **Table 10**). Other non-boron based reducing agents were tested such as LiH and DIBAL (**entries 6**, **7**, **Table 10**). These reagents did not reduce fulvene **(+/-)-253** and formation of some **(+/-)-249** was shown by TLC. Fortunately $LiAlH_4$ seemed to react with fulvene **(+/-)-253** in a fast and quite clean reaction (76% yield, **entry 8**, **Table 10**). Formation of small amounts of oxide **(+/-)-220** and some decomposition were still observed.



(+/-)-253 **(+/-)-211** **(+/-)-220** **(+/-)-249**

Entry	H^--source	Amount (eq.)	Solv.	Time	**(+/-)-211** (%)	**(+/-)-220** (%)	Comments
1	Superhydride®	1	THF	1 h	21	42	-
2	Superhydride®	1.5	THF	4 days	36	25	DABCO
3	Superhydride®	1.5	*n*hexane	1.5 h	-	65	-
4	Superhydride®	1.5	THF	30 min	-	N.D.[a]	BH_3
5	L-Selectride®	excess	THF	8 h	-	N.D.[a]	-
6	LiH	excess	THF	3 h	-	-	N.D.[b]
7	DIBAL	1.5	THF	4 days	-	-	N.D.[b]
8	$LiAlH_4$	1.5	THF	8 h	76	-	-

N.D. = not determined, a = mainly **(+/-)-220**, b = **(+/-)-253** and **(+/-)-249**.

Table 10: Optimisation of the reduction step.

After optimisation of the last step we established a synthetic sequence to obtain our target ligand **(+/-)-211** in 42% overal yield over 7 steps. The asymmetric sequence, to give enantiomerically pure cyclopentadiene **(*pS*)-211** could also be carried on the basis of Kagan's procedure.[80] For preliminary complexation studies racemic ligands were used.

3.2 Complexation studies with Ligand A

3.2.1 Reconstitutive condensation

As previously discussed in details (**page 6**), Trost investigated the Ru catalysed asymmetric condensation between terminal alkynes and allylic alcohols.[9] As an extension of his work Hidai and co-workers reported planar chiral ferrocene complexes **(*R,pS*)-22** and **(*R,pS*)-24**.[10] They exerted moderate asymmetric induction in the asymmetric condensation reactions. With Ligand A **(*pS*)-211** in hand, we aimed to

synthesised the corresponding complexes **(*pS*)-258** and **(*pS*)-259** and test their catalytic activity in the asymmetric condensation (**Figure 17**). This would also give a better picture of the effect of the planar chiral element on the stereoinduction in this transformation. For initial complexational studies racemic ligand **(+/-)-211** was used.

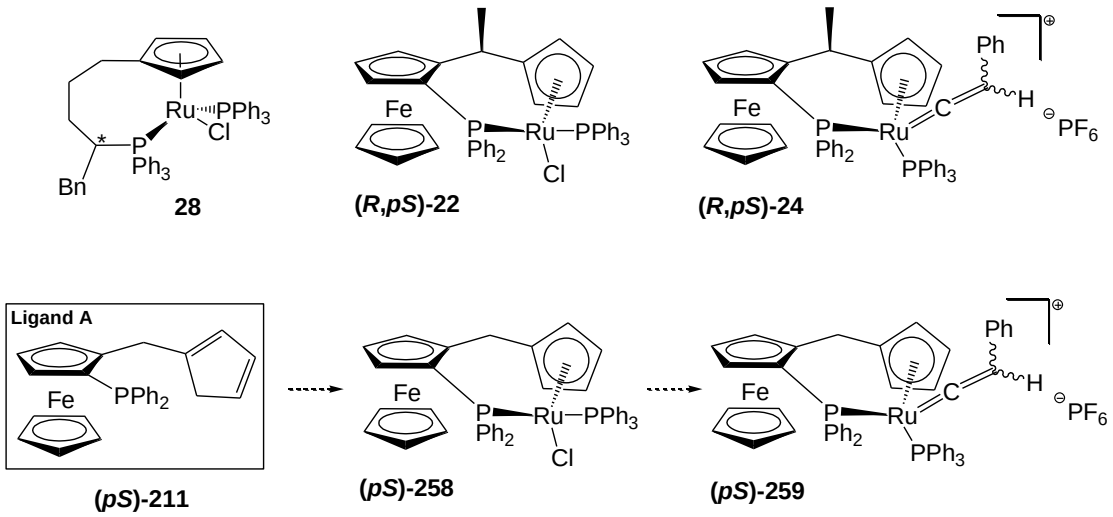
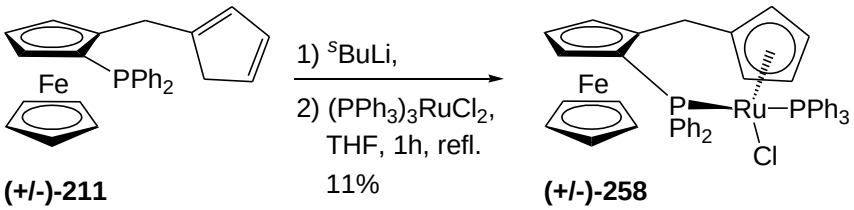


Figure 17: Trost's complex: **28**. Hidai's complexes: **(*R*,*pS*)-22** and **(*R*,*pS*)-24**. Ligand A: **(*pS*)-211**. Target complexes **(*pS*)-258** and **(*pS*)-259**.

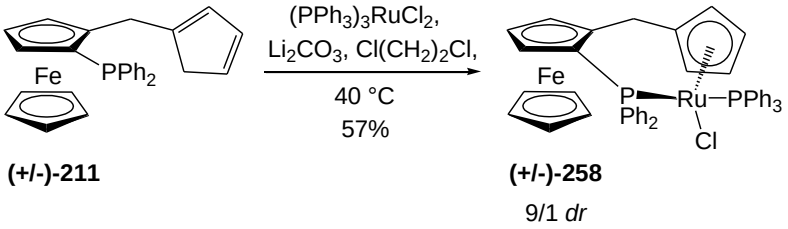
First, Hidai's conditions were tried but gave unsatisfactory results.[10] The product **(+/-)-258** was isolated only in low yield and contained high amounts of triphenylphosphine and triphenylphosphine oxide, which could not be removed by chromatography or recrystallisation (**Scheme 75**).



Scheme 75: Synthesis of complex **(+/-)-258**.

Following Trost's work we found that these complexes formed under milder conditions, at ambient temperature without the need to deprotonate the cyclopentadiene

group beforehand.[9] After optimisation, a reproducible procedure was found by which complex **(+/-)-258** was obtained as an unseparable mixture of diastereomers in 9/1 ratio (**Scheme 76)**.

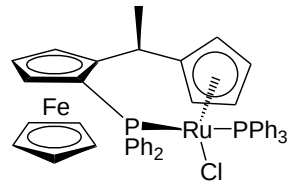


(+/-)-211 **(+/-)-258**

9/1 *dr*

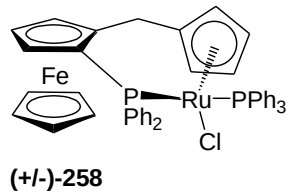
Scheme 76: Optimised conditions to obtain complex **(+/-)-258**.

Complex **(+/-)-258** proved to be unstable, therefore full characterisation was not possible. Several unsuccessful attempts were made to obtain single crystals good enough for X-ray characterisation. Structure **(+/-)-258** is based on NMR data compared with the one available in literature for complex **(*R*,*pS*)-22** (**Table 11**).[10]



(*R*,*pS*)-22

^{1}H NMR δ(ppm), *J*(Hz)	
1.33 (3H, d, *J* = 7.0, CH_3)	4.48 (1H, m)
3.04 (1H, m)	4.57 (1H, m)
3.51 (1H, m)	5.20 (1H, m)
3.94 (1H, m)	6.44 (2H, m, CH-PPh_2)
4.12 (5H, s, CH-$Cp_{unsub.}$)	6.87 (2H, m, CH-PPh_2)
4.29 (1H, m)	7.00-8.10 (21H, m)
4.30 (1H, m)	
^{31}P NMR δ(ppm), *J*(Hz)	
28.5 (d, *J* = 41)	45.5 (d, *J* = 41)



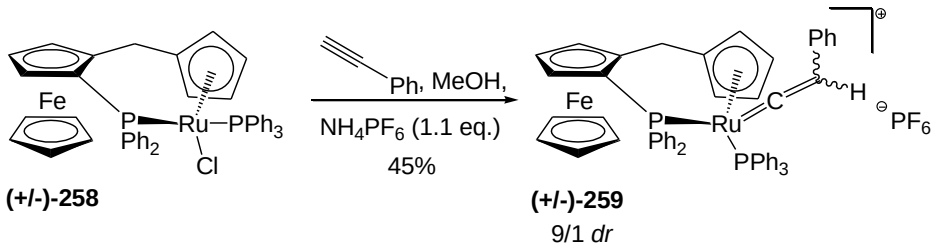
(+/-)-258

major diastereomer

^{1}H NMR δ(ppm), *J*(Hz)	
2.68 (1H, d, *J* = 16.9, CH_2)	4.40 (1H, m, CH-$Cp_{sub.}$)
3.14 (1H, m, CH)	5.13 (1H, m, CH)
3.44 (1H, d, *J* = 16.9, CH_2)	5.38 (1H, m, CH)
3.90 (1H, m, CH-$Cp_{sub.}$)	6.50 (2H, m, CH-PPh_2)
3.96 (5H, CH-$Cp_{unsub.}$)	6.78 (2H, m, CH-PPh_2)
4.26 (1H, m, CH)	6.89-7.46 (19H, m, CH-PPh_2)
4.35 (1H, t, *J* = 2.5, CH)	8.16 (2H, t, *J* = 8.5, CH-PPh_2)
^{31}P NMR δ(ppm), *J*(Hz)	
32.65 (d, *J* = 40.8)	44.0 (d, *J* = 40.8)

Table 11: Chemical shifts of literature compound **(*R*,*pS*)-22** and complex **(+/-)-258** from our experiment.

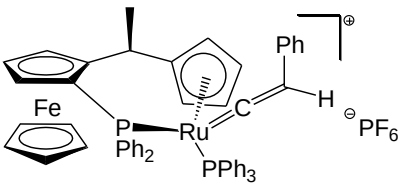
Complex **(+/-)-258** was reacted with phenylacetylene according to Hidai's work and the vinylidene complex **(+/-)-259** was isolated in 47% yield, 9/1 *dr* (**Scheme 77**).[10]



(+/-)-258 **(+/-)-259** 9/1 *dr*

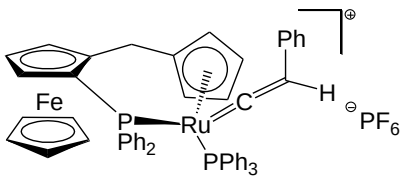
Scheme 77: Formation of vinylidene complex **(+/-)-259**.

This compound also turned out to be unstable which prevented us from getting full analytical data on it. NMR data is given in (**Table 12**).



(*RpS*)-24

^{1}H NMR δ(ppm), *J*(Hz)	
1.45 (3H, d, *J* = 7.0, CH_3)	5.13 (1H, m)
3.07 (1H, m)	5.27 (1H, m)
3.97 (5H, s, CH-$Cp_{unsub.}$)	5.35 (1H, m)
4.19 (1H, m)	5.74 (1H, m)
4.30 (1H, m)	6.89 (2H, m, CH-PPh_2)
4.67 (1H, m)	6.80-7.40 (28H, m)
4.86 (1H, m)	
^{31}P NMR δ(ppm), *J*(Hz)	
31.8 (d, J = 27)	44.9 (d, J = 27)



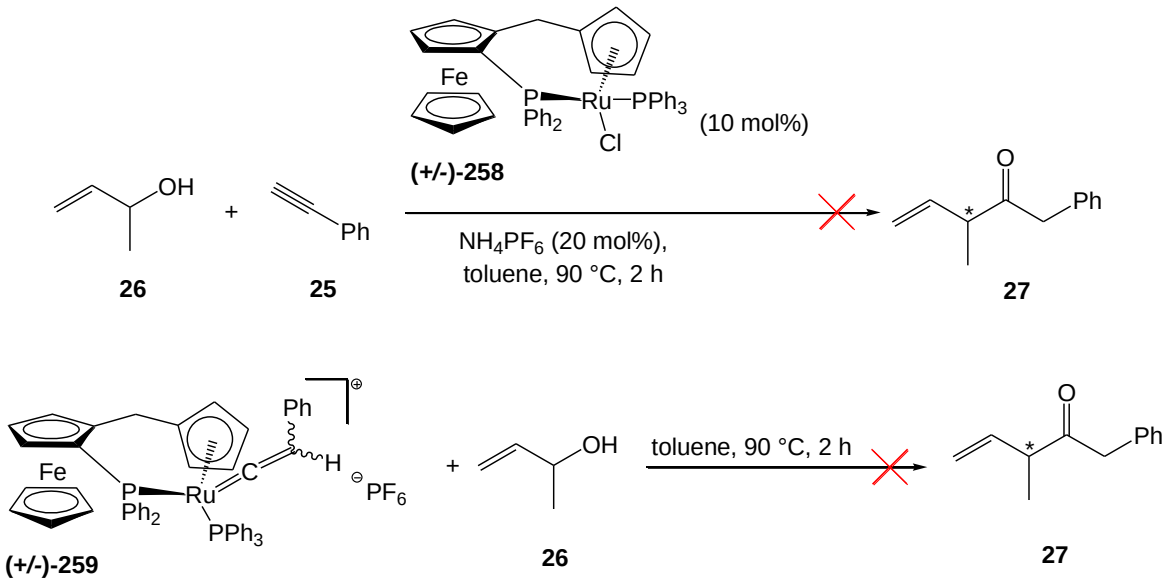
(+/-)-259

major diastereomer

^{1}H NMR δ(ppm), *J*(Hz)	
3.20 (1H, d, *J* = 16.2, CH_2)	4.38 (5H, CH-$Cp_{unsub.}$)
3.34 (1H, m, CH)	4.84 (1H, m, CH)
3.56 (1H, m, CH)	5.23 (1H, m, CH)
3.72 (1H, d, *J* = 16.6, CH_2)	6.39 (2H, t, *J* = 8.2, CH-PPh_2)
4.23 (1H, t, *J* = 2.4, CH-$Cp_{sub.}$)	6.84-7.46 (25H, m, CH-PPh_2)
4.34 (1H, m, CH-$Cp_{sub.}$)	7.53 (2H, t, *J* = 8.8, CH-PPh_2)
4.37 (1H, m, CH-$Cp_{sub.}$)	8.34 (2H, t, *J* = 8.5, CH-PPh_2)
^{31}P NMR δ(ppm), *J*(Hz)	
38.3 (d, *J* = 35.3)	53.8 (d, *J* = 35.3)

Table 12: Chemical shifts of literature compound **(*R*,*pS*)-24** and complex **(+/-)-259** from our experiment.

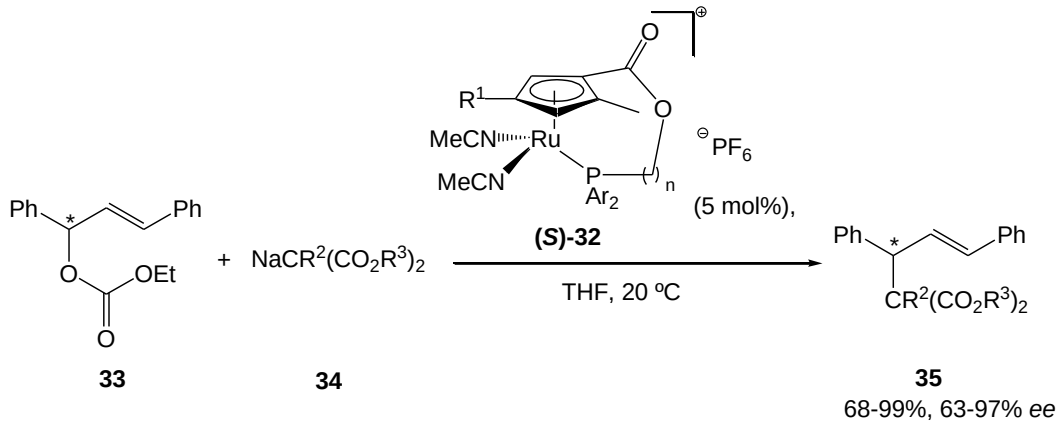
Regardless of their instability, the catalytic activity of complexes **(+/-)-258** and **(+/-)-259** was tested in the condensation reaction under catalytic and stoichiometric conditions. The racemic product **27** was synthesised beforehand according to literature precedent.[120] The reactions were monitored by GC analysis, however formation of the desired product **27** was not observed (**Scheme 78**).



Scheme 78: Attempted condensation reactions.

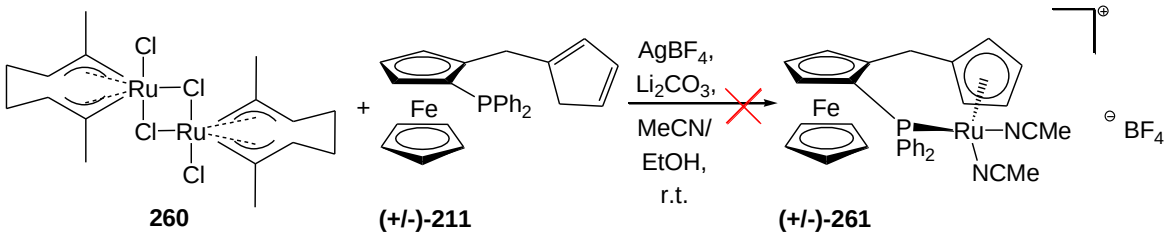
3.2.2 Allylic substitution

Transition metal catalysed allylic substitution is a powerful method for constructing complex organic molecules. Palladium is the most widely used among the transition metals and gives excellent results. However, to expand the scope of this transformation studies utilising other transition metals have been investigated. Takahashi used planar chiral, ruthenium (II) *ansa*-half sandwich metallocenes to catalyse allylic substitution reactions (**Scheme 79**).[12]



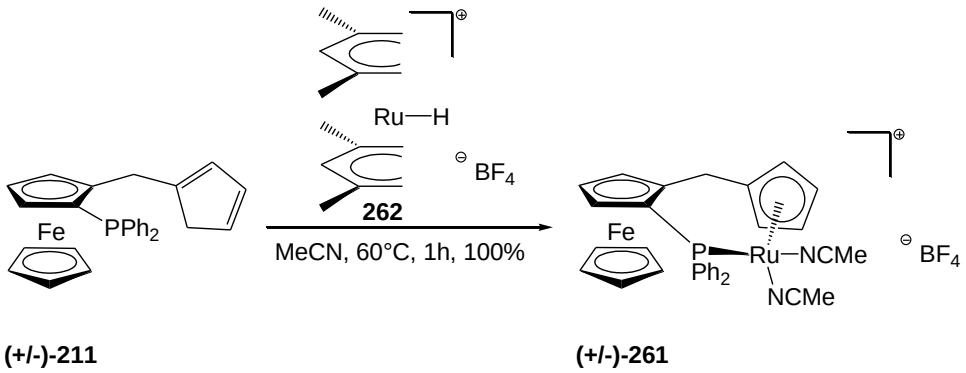
Scheme 79: Allylic substitution using ruthenium (II) *ansa*-half sandwich metallocene catalyst **(*S*)-32**.

On the basis of this work, we planned to synthesise similar ruthenium (II) complexes.[121,122a,b] Ligand A **(+/-)-211** was reacted with **260** in order to form complex **(+/-)-261**.[123] This reaction led mostly to the decomposition of the starting material. A small amount of product **(+/-)-261** formation was observed but isolation was not possible as it turned out to be unstable (**Scheme 80**).



Scheme 80: Attempted complexation of Ligand A **(+/-)-211**.

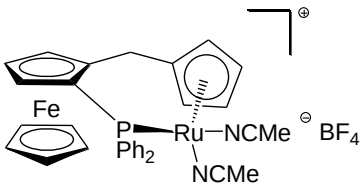
The formation of complex **(+/-)-261** under different conditions was attempted.[124] Ligand A **(+/-)-211** was consumed in less then an hour at r.t (**Scheme 81**). After one hour the crude material was passed through neutral alumina and concentrated under reduced pressure to give complex **(+/-)-261**.



(+/-)-211 **(+/-)-261**

Scheme 81: Successful complexation of Ligand A **(+/-)-211**.

Full characterisation of complex **(+/-)-261** was not possible due to instability issues, the molecular ion was not found in the mass spectrum of the crude material. Structure **(+/-)-261** is based on the NMR data of the isolated material (**Table 13**).

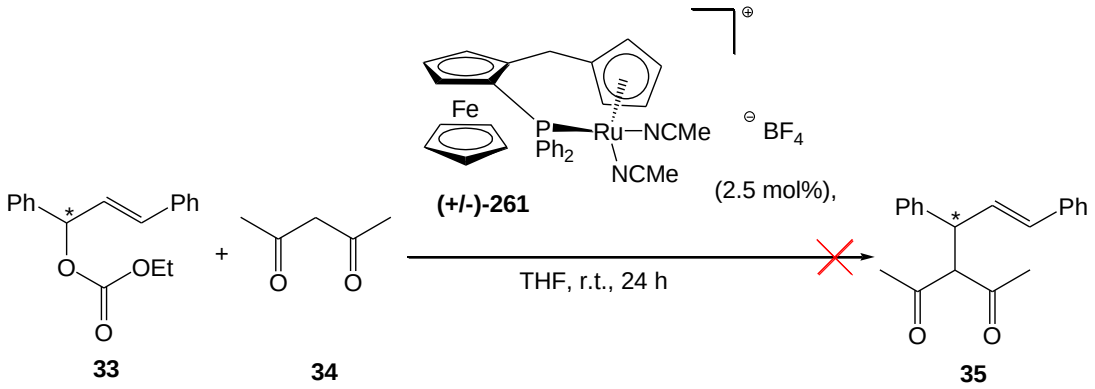


(+/-)-261

^{1}H NMR δ(ppm), *J*(Hz)	
1.68 (3H, d, J_{HP} = 1.1, CH_2)	4.52 (1H, bs, CH)
2.26 (3H, d, J_{HP} = 1.1, CH_2)	4.83 (1H, bs, CH)
2.84 (1H, d, *J* = 17.2, CH_2)	5.12 (1H, m, CH)
3.34 (1H, d, *J* = 17.1, CH_2)	5.17 (1H, bs, CH)
3.78 (5H, CH-$Cp_{unsub.}$)	6.86 (2H, m, CH-PPh_2)
4.27 (1H, m, CH-$Cp_{sub.}$)	7.31 (3H, m, CH-PPh_2)
4.46 (1H, m, CH-$Cp_{sub.}$)	7.56 (3H, m, CH-PPh_2)
4.46 (1H, t, *J* = 2.5, CH-$Cp_{sub.}$)	7.76 (2H, m, CH-PPh_2)
^{31}P NMR δ(ppm), *J*(Hz)	
43.6	

Table 13: Chemical shifts of isolated complex **(+/-)-261**.

Despite this instability issue, the catalytic activity of complex **(+/-)-261** was tested in an allylic substitution reaction. Complex **(+/-)-261** turned out to be catalytically inactive in the allylic substitution reaction of carbonate **33** with dimethyl malonate **34** (**Scheme 82**).



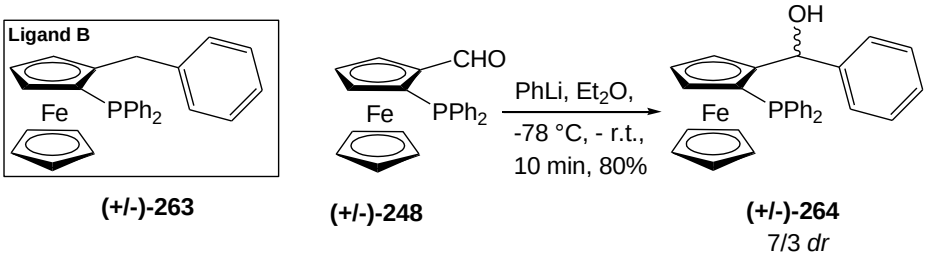
Scheme 82: Testing the catalytic activity of complex **(+/-)-261**.

At this point in our research, catalytic inactivity was attributed to the instability and therefore, decomposition of complexes **(+/-)-258**, **(+/-)-259** and **(+/-)-261** under the reaction conditions. To address this issue, other ligands were synthesised based on the general ligand structure **206**.

4. Ligand B

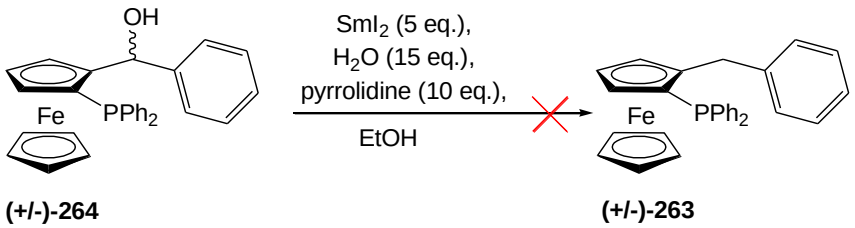
4.1 Synthesis of Ligand B

In the course of synthesising other ligands based on the general structure **300**, we decided to change the cyclopentadienyl group to an aryl functionality. Similar *ansa*-half, aryl complexes have been described in the literature.[14] The previously synthesised phosphine **(+/-)-248** was reacted with phenyllithium (**Scheme 83**). In this reaction two diastereomers of **(+/-)-264** were formed in a 7/3 ratio.



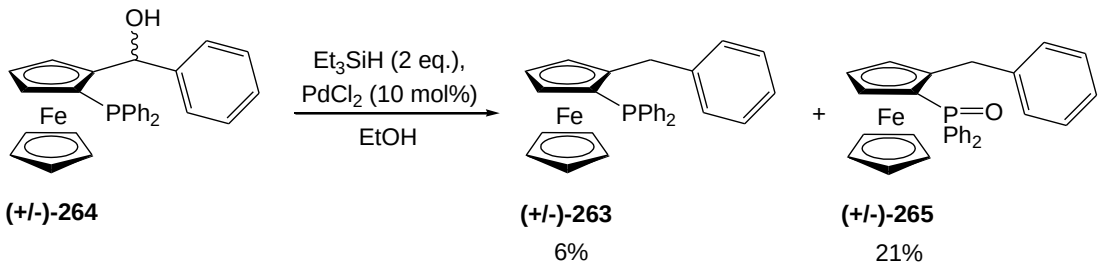
Scheme 83: Reaction of aldehyde **(+/-)-248** with phenyllithium.

For the dehydroxylation reaction a number of different conditions were tested. The first reaction, using SmI_2, gave a mixture of two unidentifiable compounds (**Scheme 84)**.[125]



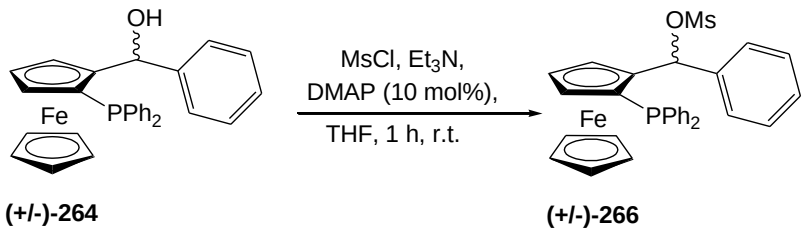
Scheme 84: Dehydroxylation reaction using SmI_2.

Reaction with Et_3SiH gave a mixture of the desired product **(+/-)-263** (6%) and phosphineoxide **(+/-)-265** (21%) (**Scheme 85**).[126]



Scheme 85: Dehydroxylation reaction using Et_3SiH.

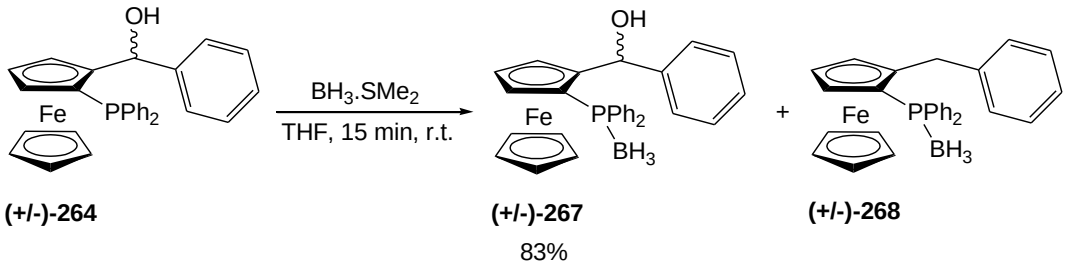
Mesylation of alcohol **(+/-)-264** was then attempted by with MsCl in THF in the presence of Et_3N and DMAP. This reaction resulted in the formation of a mixture of unidentifiable compounds (**Scheme 86**).



(+/-)-264 **(+/-)-266**

Scheme 86: Attempted formation of mesylate **(+/-)-266**.

During the synthesis of Ligand A **(+/-)-211** it was found that α–hydroxyferrocene underwent facile dehydroxylation in the presence of borane. Therefore alcohol **(+/-)-264** was reacted with $BH_3.SMe_2$ in THF at r.t. resulting in the formation of borane **(+/-)-267** in 84% yield. A small amount of dehydroxylated borane **(+/-)-268** was observed by TLC (**Scheme 87**).

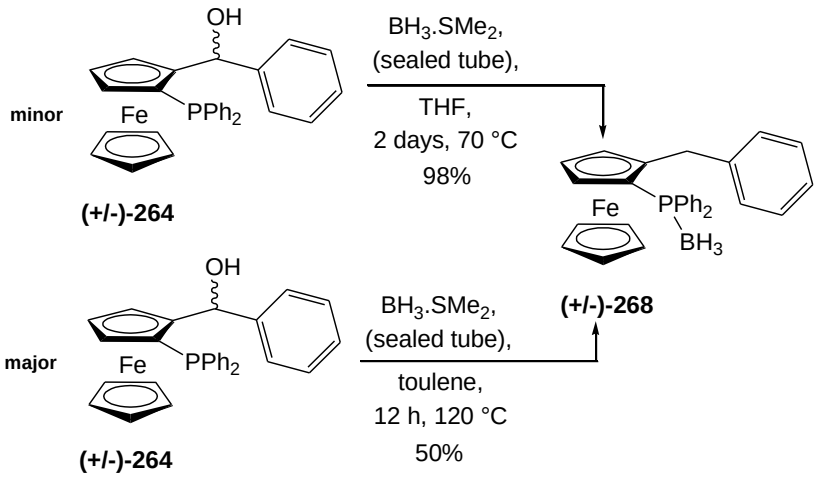


(+/-)-264 **(+/-)-267** 83% **(+/-)-268**

Scheme 87: Dehydroxylation of alcohol **(+/-)-264** with borane.

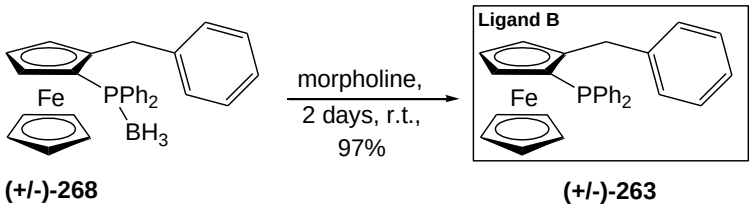
The experiment was repeated at elevated temperatures to yield the desired dehydroxylated borane **(+/-)-268**. It was also found that reaction of major diastereomer **(+/-)-264a** with borane was sluggish, therefore more forcing conditions were used

(**Scheme 88)**. This observation suggest that the major diastereomer is in a conformation which makes the α–position less accessible.



Scheme 88: Dehydroxylation of **(+/-)-264-major** and **(+/-)-264-minor**.

In the last step of the synthesis the borane group was removed from the molecule using morpholine under mild conditions to give Ligand B **(+/-)-263** in excellent yield (**Scheme 89**).

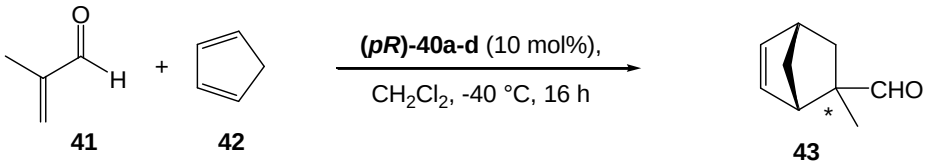


Scheme 89: Removal of borane group.

4.2 Complexation studies of Ligand B

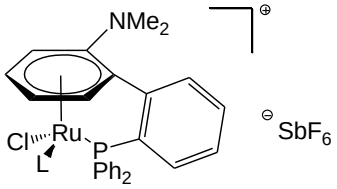
4.2.1 Diels Alder reaction

Chiral transition metal *ansa*-half sandwich complexes have been utilised as Lewis acids in catalytic Diels-Alder and Mukaiyama-Aldol reactions. One major drawback of these complexes is the possible racemisation of the metal centre. Faller investigated the catalytic activity of transition metal *ansa*-half sandwich complexes bearing tethered donor ligands which were thought to be less prone to racemisation (**page 10**).[14] The complexes were tested in a catalytic asymmetric Diels-Alder reaction (**Scheme 90**).



41 **42** **43**

conversion >95%,

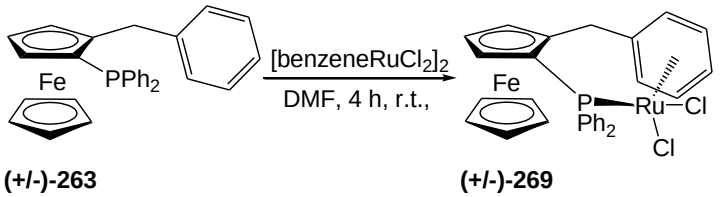


(*pR*)-40a-d

Entry	Cat.	L	*endo/exo*	*ee* (%)
1	**(*pR*)-40a**	PPh_3	98/2	20
2	**(*pR*)-40b**	$PPhMe_2$	96/4	26
3	**(*pR*)-40c**	$PO(Ph)_3$	97/3	13
4	**(*pR*)-40d**	PPh_2Cy	94/6	40

Scheme 90: Asymmetric Diels-Alder reaction catalysed by ruthenium (II) *ansa*-half sandwich metallocene complexes **(*pR*)-40a-d**.

Ligand B **(+/-)-263** was reacted with $[benzeneRuCl_2]_2$ in DMF.[127,128] After 4 hours phosphine **(+/-)-263** was consumed and the product **(+/-)-269** was formed along with some decomposition (**Scheme 91**). After removal of the solvent under reduced pressure, complex **(+/-)-269** was isolated. Complex **(+/-)-269** was recrystallised from chloroform/^{n}hexane to give the clean product in 9% yield. Under the (unoptimised) recrystallisation conditions serious amount of decomposition took place. Product **(+/-)-269** also seemed quite unstable in solution, however, it could be stored as a solid.



(+/-)-263 **(+/-)-269**

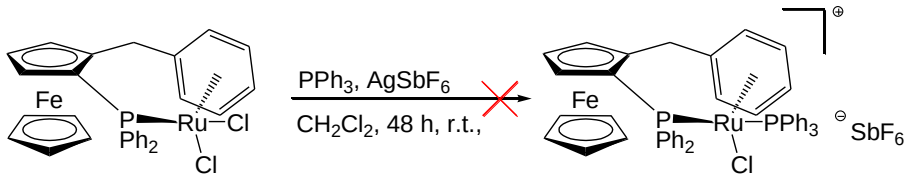
Isolated yield 100%
Recrystallised yield 9%

^{1}H NMR δ(ppm), *J*(Hz)	
3.26 (1H, d, *J* = 15.7, CH_2)	4.83 (1H, m)
3.37 (1H, d, *J* = 15.4, CH_2)	7.04 (3H, m)
3.93 (5H, s, CH-$Cp_{unsub.}$)	7.36-7.53 (8H, m)
4.05 (1H, m)	7.69 (2H, m)
4.44 (1H, m)	8.29 (2H, m)

HRMS (EI) $C_{29}H_{25}PCl_2FeRu$ calcd. 631.94574, found 631.94679.

Scheme 91: Formation of ruthenium (II) complex **(+/-)-269**.

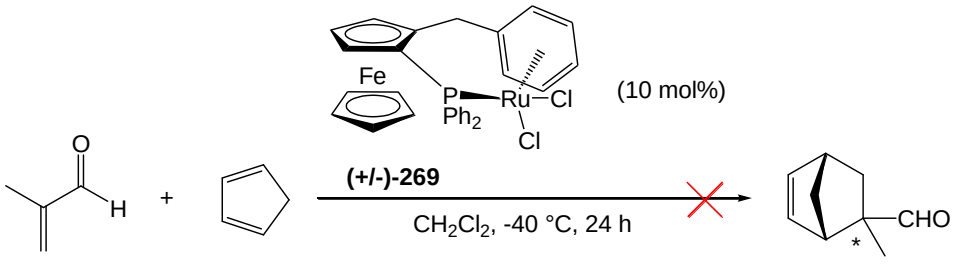
Complex **(+/-)-269** was reacted with triphenylphosphine in the presence of silver-hexafluoroantimonate.[28] After two days the starting material was reisolated along with another unknown compound which was not the desired product (**Scheme 92**).



(+/-)-269 **(+/-)-270**

Scheme 92: Unsuccessful formation of complex **(+/-)-270**.

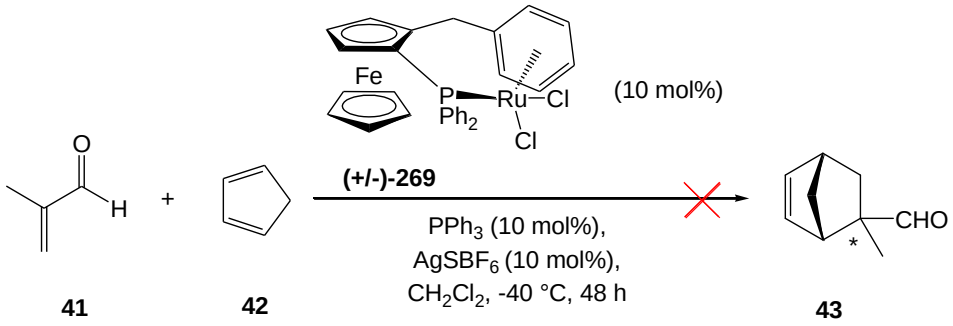
The catalytic activity of complex **(+/-)-269** was tested in the Diels-Alder reaction of cyclopentadiene with 2-methylacrolein **41**. The reaction, however, did not yield any of the desired product **43** (**Scheme 93**).



41 **42** **43**

Scheme 93: Testing the catalytic activity of complex **(+/-)-269**.

In the next reaction we tried to form complex **(+/-)-270** *in situ* (**Scheme 94**). Unfortunately formation of the desired product **43** was not observed.



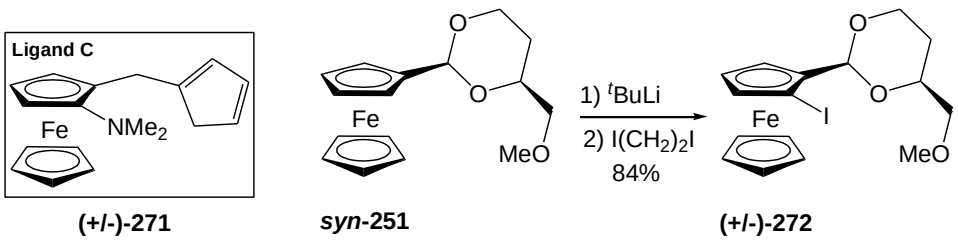
Scheme 94: Attempted *in situ* formation of complex **(+/-)-270**.

In the course of seeking a more stable complex we moved on and synthesised another member of the ligand family.

5. Ligand C

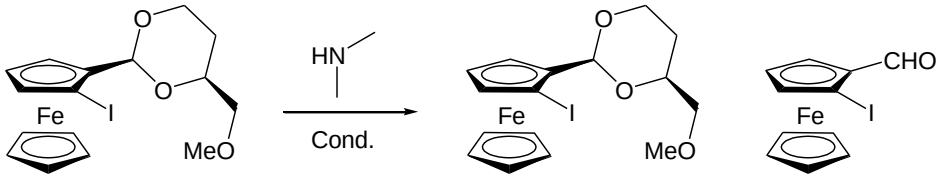
5.1 Synthesis of Ligand C

The synthesis of Ligand C **(+/-)-271** was devised where the ferrocene is substituted by a different Lewis basic functionality (NMe_2 instead of PPh_2). Synthesis of Ligand C started from protected acetal **251** which was first *ortho*-substituted to give iodide **(+/-)-272** (**Scheme 95**).



Scheme 95: *Ortho*-substitution of acetal **251**.

Due to the high electron density accomodated on the aromatic cyclopentadienyl rings in ferrocenyl systems, introduction of new functionality is more easily achieved by electrophilic aromatic substitution. Although there are different methods available for the synthesis of aminoferrocene overall yields are low. The azide introduction/reduction sequence was avoided due to the explosive character of the intermediates.[129] Recently, there have been a lot of improvements in transition metal catalysed carbon-heteroatom couplings. Reaction under Ullmann type[130] and Buchwald-conditions[131] were tried but none of them gave the desired product (**Table 14**).



(+/-)-272 **(+/-)-272** **(+/-)-273**

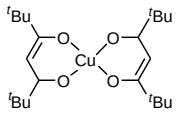
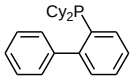
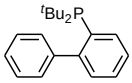
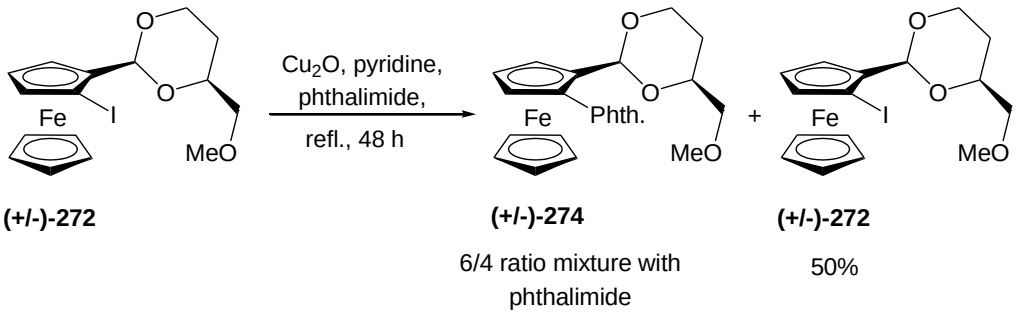
Catalyst	Base	Solvent	Temp. (°C)	Time	Result
	KO^{t}Bu	toluene	120	8 h	**(+/-)-272**, 80%
Pd_2dba_3  **Cy-JohnPhos**	NaO^{t}Bu	toluene	80	8 h,	**(+/-)-272**, 23%, **(+/-)-273**, 66%,
Pd_2dba_3  **JohnPhos**	NaO^{t}Bu	toluene	80	8 h,	**(+/-)-272/ (+/-)-273** ~1/1 ratio

Table 14: Reaction of iodide **(+/-)-272** under Ullmann and Buchwald-conditions.

Another way of intoducing amine functionality by a substitution of a LG, was developed by Siegmund Gabriel in 1887.[132] The Gabriel Synthesis utilises potassium phthalimide to couple with alkyl halides. Arylhalides must bear several electron withdrawing groups on them to enable the coupling. Aromatic systems lacking EWGs can be coupled with phthalimide in the presence of Cu(I) salts.[133] In the second step of

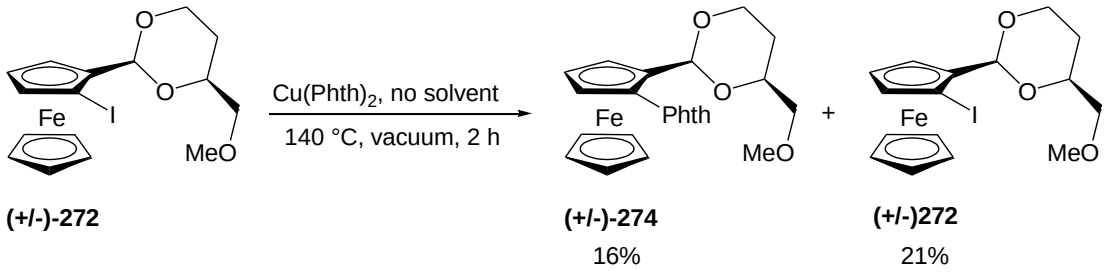
the process the amine functionality is released under acidic/basic conditions. Another modification uses hydrazine-hydrate (Ing-Manske procedure) to achieve removal of the phthaloyl functionality under neutral conditions.[134]

First a general procedure was tested, however, this reaction gave back the starting material **(+/-)-272** (50%) and an inseparable mixture of the product **(+/-)-274** and phthalimide (~6/4) (**Scheme 96**).[135]



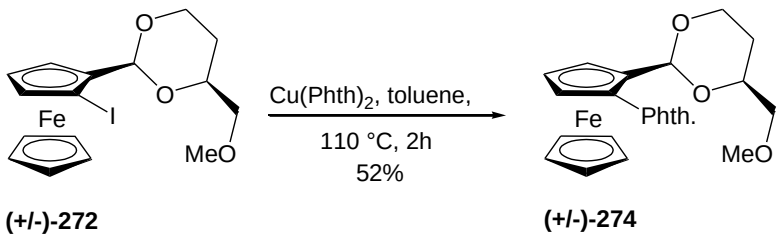
Scheme 96: Reaction of iodide **(+/-)-272** with phthalimide in pyridine.

According to another procedure the corresponding phthalimido derivative could be obtained by heating the starting material under vacuum with $Cu(Phth)_2$.[136] The desired product **(+/-)-274** was isolated in 16% yield under these conditions along with some recovered starting material **(+/-)-272** (21%) (**Scheme 97**).



Scheme 97: Reaction of iodide **(+/-)-272** with $Cu(Phth)_2$.

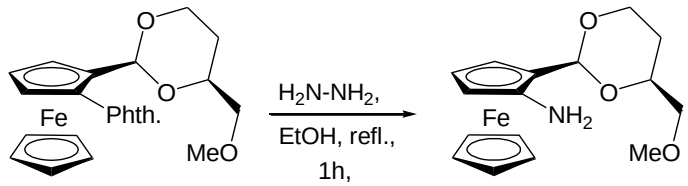
Performing the reaction in refluxing toluene increased the yield to 52% (**Scheme 98**).



(+/-)-272 **(+/-)-274**

Scheme 98: Reaction of iodide **(+/-)-272** with $Phth_2Cu$ in refluxing toluene.

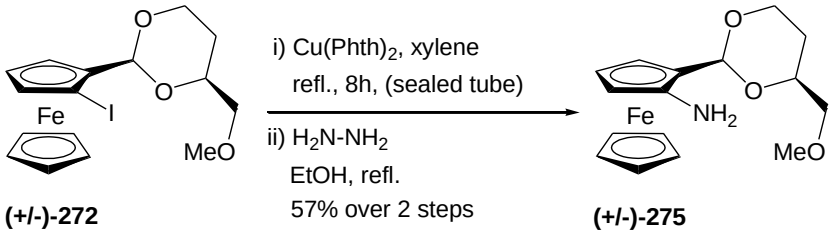
Phthalimide **(+/-)-274** was hydrolysed using hydrazine-hydrate in refluxing ethanol to give amine **(+/-)-275** in 84% yield (**Scheme 99**).



(+/-)-274 **(+/-)-275**

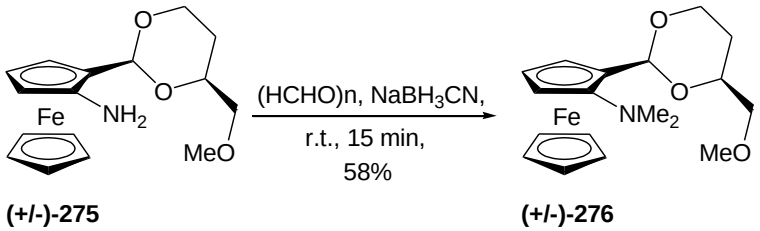
Scheme 99: Hydrolysis of phthalimide **(+/-)-274**.

Purification of phthalimide **(+/-)-274** was cumbersome due to the phthalimide by-product formed during the reaction. Therefore a two-step procedure was devised in which the crude material from the phthalimide formation was passed through a pad of silica and transferred to the next step. After the next step the purification of the product amine **(+/-)-275** was more easily achieved. In order to further improve yields the first step was carried out in a sealed tube to prevent the iodide **(+/-)-272** from subliming out of the reaction (**Scheme 100**).



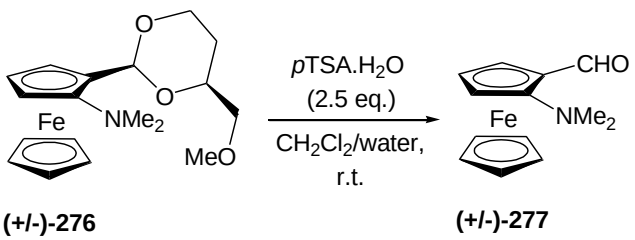
Scheme 100: Improved two step procedure to obtain amine **(+/-)-275**.

Before the deprotection of acetal functionality the amine moiety had to be methylated. Amine **(+/-)-275** was subjected to reductive amination[137] to give dimethylamine **(+/-)-276** (**Scheme 101)**.



Scheme 101: Reductive amination of amine **(+/-)-275**.

Deprotection of the acetal **(+/-)-276** took place significantly faster than in the case of the diphenylphosphine analogue, which was attributed to the better solubility of amine **(+/-)-276**. However, yields were lower possibly due to isolation problems which comes from the same feature of amine. Decreasing the amount of water used and eliminating the aqueous work up increased the isolated yields (**Table 15**).

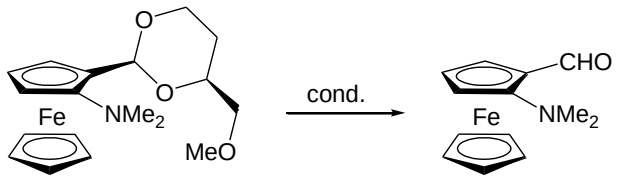


Entry	CH_2Cl_2/water	Work-up	**(+/-)-277**, Y(%)	**(+/-)-276**, Y(%)
1	1/1	extraction, column chrom.	N.A.	N.I.
2	4/1	extraction, column chrom.	31	N.I.
3	8/1	removal of solvent under reduced pressure, column chrom.	39	21
4	24/1	removal of solvent under reduced pressure, column chrom.	45	N.I.

N.I. = not isolated

Table 15: Hydrolysis of acetal **(+/-)-276** using *p*TSA.H_2O.

In an attempt to improve the isolated yields of amine **(+/-)-277** different protocols were tested (**Scheme 102**).[138-141]

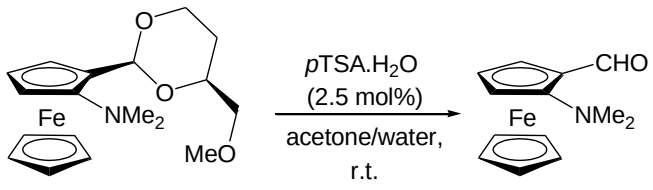


(+/-)-276 **(+/-)-277**

Entry	Reagent	Solvent	Temp.	Time	Result
1	$FeCl_3.6H_2O$	CH_2Cl_2	r.t.	2 days	decomp.
2	Montmorillonite K10	CH_2Cl_2	refl.	2 days	unreacted **(+/-)-276**
3	Amberlyst 15®	$CHCl_3$	r.t.	2 days	unreacted **(+/-)-276**
4	$TiCl_4$	Et_2O	r.t.	20 h	unreacted **(+/-)-276**, decomp.

Scheme 102: Attempted hydrolysis of acetal **(+/-)-276** under different conditions.

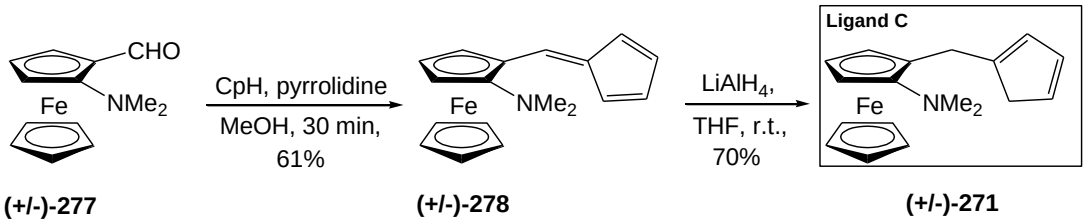
As these protocols gave no significant improvement of the yield, the original protocol was optimised further. The solvent system was switched to acetone/water, while the amount of *p*TSA.H_2O was reduced from 2.5 eq. to 2.5 mol%, to give the aldehyde **(+/-)-277** in 61% yield (**Scheme 103**).[142]



(+/-)-276 **(+/-)-277**
crude yield 100%,
isolated yield 61%

Scheme 103: Improved procedure for hydrolysis of acetal **(+/-)-276**.

To get to our target Ligand C **(+/-)-271**, the previously used Stone-fulvene formation, reduction sequence was adopted (**Scheme 104**). We obtained our ligand in 43% (unoptimised) yield over two steps.



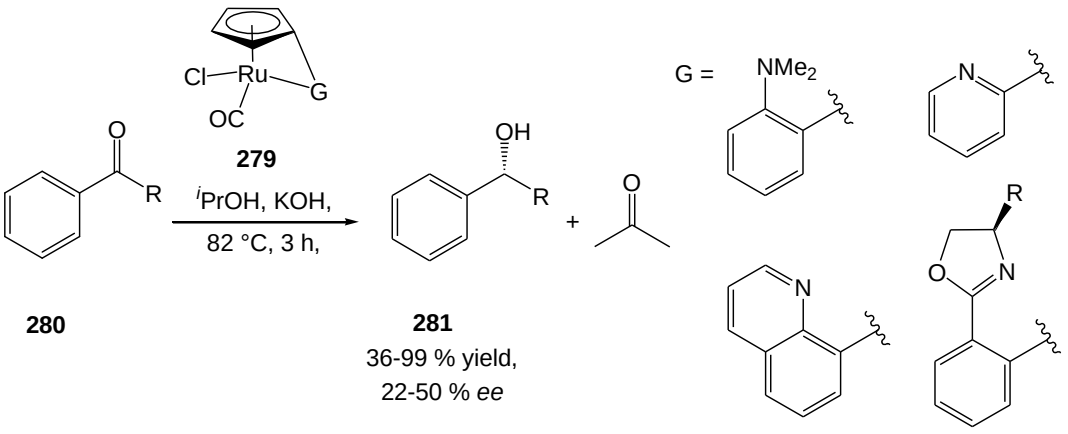
(+/-)-277 **(+/-)-278** **(+/-)-271**

Scheme 104: Synthesis of cyclopentadiene **(+/-)-271** from aldehyde **(+/-)-277** in two steps.

5.2. Complexation studies of Ligand C

5.2.1 Transfer Hydrogenation

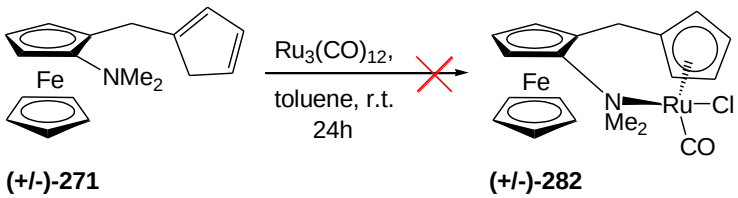
Recently Dyker synthesised a few ruthenium (II) *ansa*-half sandwich metallocene complexes and investigated their catalytic activity in transfer hydrogenation reaction (**Scheme 105**). [143]



280 **281**
36-99 % yield,
22-50 % *ee*

Scheme 105: Ruthenium (II) *ansa*-half sandwich complexes **279** used in asymmetric catalytic transfer hydrogenation reaction by Dyker.

Reaction of Ligand C **(+/-)-271** with $Ru_3(CO)_{12}$ resulted in the reisolation of amine **(+/-)-271**. Forcing conditions led to the decomposition of the starting material (**Scheme 106**).



(+/-)-271 **(+/-)-282**

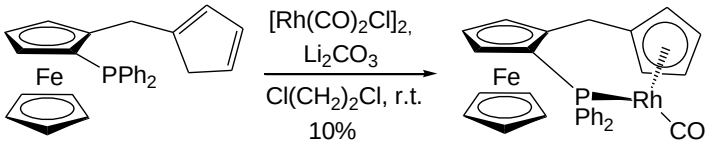
Scheme 106: Unsuccessful formation of complex **(+/-)-282**.

6. Other transition metal complexes

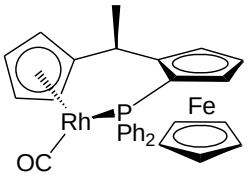
The syntheses of 1,2-disubstituted ferrocene based transition metal *ansa*-half sandwich metallocene complexes **28**, **(*S*)-32** and **279** were based on similar metal complexes described in the literature. The catalytic activity of complexes were tested in catalytic asymmetric transformations without success. A vast number of other *ansa*-half sandwich metallocene complexes have been described in the literature without the investigation of their catalytic activity. We thought, the synthesis of analogous 1,2-disubstituted ferrocene based transition metal *ansa*-half sandwich metallocene complexes would provide useful information on the structure and stability of these complexes.

6.1 Rh-complex (+/-)-283

Ligand A **(+/-)-211** was reacted with $[Rh(CO)_2Cl]_2$ in CH_2Cl_2 to give complex **(+/-)-283** in 10% isolated yield (**Table 16**).[10] Complex **(+/-)-283** was fairly stable as a solid, but proved to be unstable in solution.

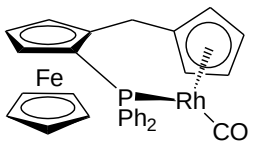


(+/-)-211 **(+/-)-283**



(*S*,*pR*)-23

^{1}H NMR δ(ppm), *J*(Hz)	
1.19 (3H, d, *J* = 7.0, CH_3)	5.27 (1H, m)
3.65 (1H, m)	5.46 (1H, m)
3.93 (5H, s, CH-$Cp_{unsub.}$)	5.61 (1H, m)
3.95 (1H, m)	5.76 (1H, m)
4.18 (1H, m)	6.2-7.9 (10H, m)
4.42 (1H, m)	
^{31}P NMR δ(ppm), *J*(Hz)	
45.7 (d, *J* = 197)	



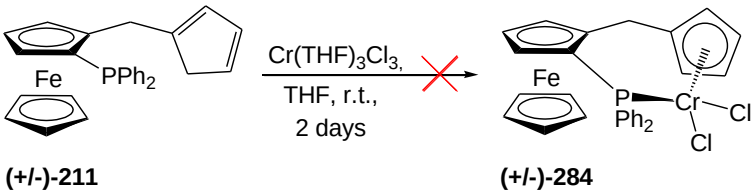
(+/-)-283

^{1}H NMR δ(ppm), *J*(Hz)	
3.06 (1H, d, *J* = 16.3, CH_2)	5.58 (1H, bs, CH)
3.43 (1H, dd, *J* = 16.3, 4.1, CH_2)	5.73 (1H, bs, CH)
3.95 (1H, m, CH-$Cp_{sub.}$)	7.18 (2H,m, CH-PPh_2)
4.00 (5H, CH-$Cp_{unsub.}$)	7.25 (3H,m, CH-PPh_2)
4.41 (2H, m, CH-$Cp_{sub.}$)	7.48 (3H,m, CH-PPh_2)
5.14 (1H, bs, CH)	7.91 (2H,m, CH-PPh_2)
5.46 (1H, bs, CH)	
^{31}P NMR δ(ppm), *J*(Hz)	
48.1 (d, *J* = 196)	

Table 16: Chemical shifts of isolated complex **(+/-)-283**.

6.2 Cr-complex (+/-)-284

In the reaction of Ligand A **(+/-)-211** with $Cr(THF)_3Cl_3$ only decomposition and oxidation of the starting material was observed (**Scheme 107**).[144]

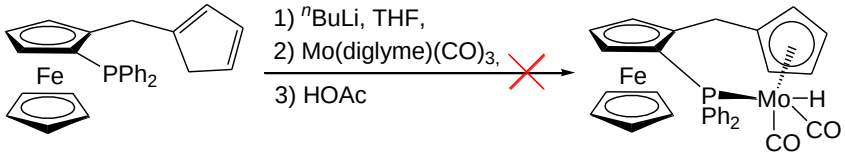


(+/-)-211 **(+/-)-284**

Scheme 107: Unsuccessful formation of complex **(+/-)-284**.

6.3 Mo-complex (+/-)-285

Reaction of $Mo(diglyme)(CO)_3$ with Ligand A **(+/-)-211** gave no reaction apart from oxidation of the phosphine functionality to some extent (**Scheme 108**).[145]

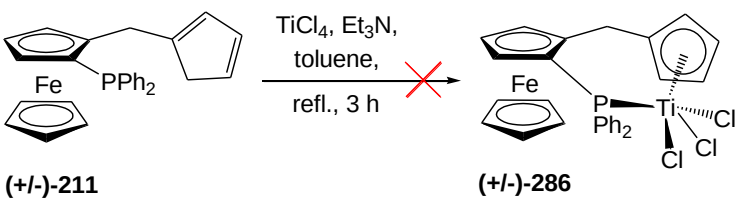


(+/-)-211 **(+/-)-285**

Scheme 108: Unsuccessful formation of complex **(+/-)-285**.

6.4 Ti-complex (+/-)-286

The same result was observed in the reaction of Ligand A **(+/-)-211** with $TiCl_4$ (**Scheme 109**).



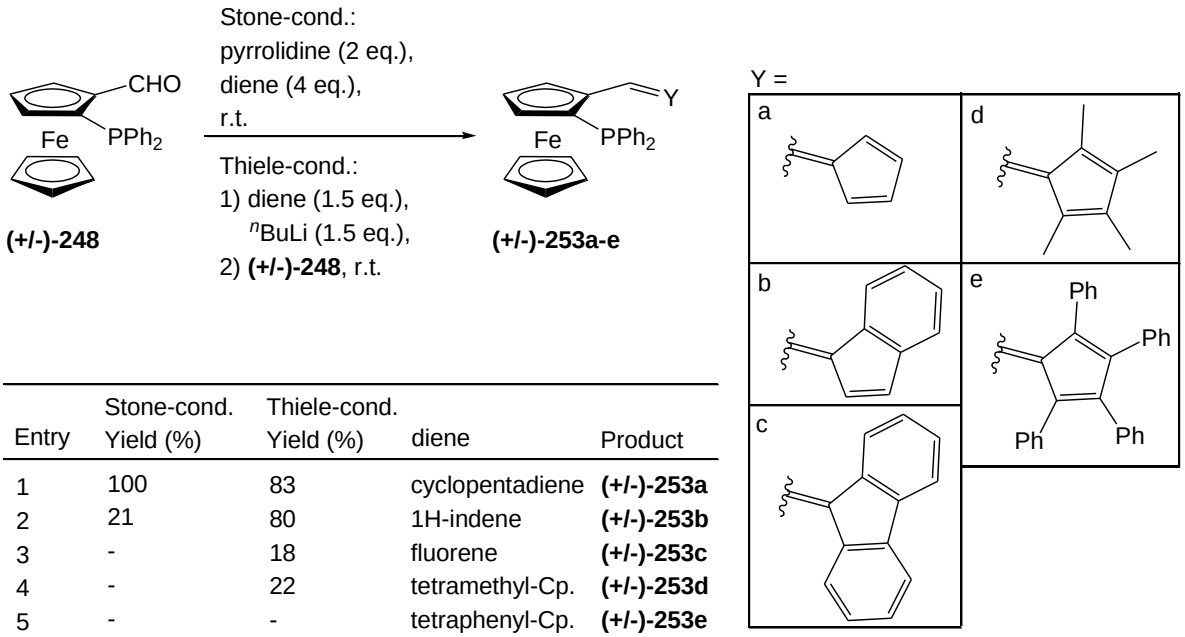
(+/-)-211 **(+/-)-286**

Scheme 109: Unsuccessful formation of complex **(+/-)-286**.

7. Other ligands

7.1 Expanding the scope of fulvene formation

To expand the scope of our synthetic route we tried to synthesise other cyclopentadiene derivatives such as indene **(+/-)-253b**, fluorene **(+/-)-253c**, tetramethyl cyclopentadiene **(+/-)-253d** and tetraphenyl cyclopentadiene **(+/-)-253e**. Using the Stone- and Thiele-conditions (**page 109**, **Table 17**).[109,110]

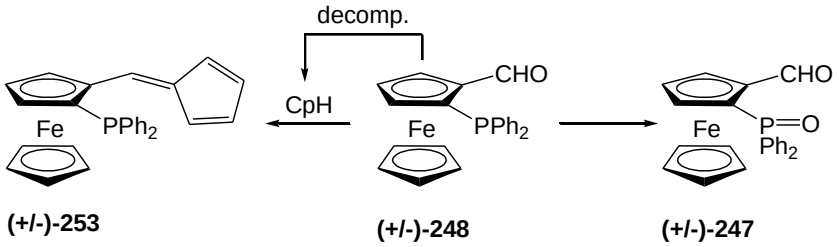


Entry	Stone-cond. Yield (%)	Thiele-cond. Yield (%)	diene	Product
1	100	83	cyclopentadiene	**(+/-)-253a**
2	21	80	1H-indene	**(+/-)-253b**
3	-	18	fluorene	**(+/-)-253c**
4	-	22	tetramethyl-Cp.	**(+/-)-253d**
5	-	-	tetraphenyl-Cp.	**(+/-)-253e**

Table 17: Fulvene formation under Stone- and Thiele-conditions.

In general, steric congestion seemed to affect both methods, however the Stone method turned out to be more sensitive to steric effects (**entries 3**, **4**, **5**, **Table 17**). Reactions under Thiele conditions gave the products (**entries 3**, **4**, **Table 17**), even in the case when the Stone method failed and proceeded much quicker, although gave less clean products. This was attributed to the fact that under these conditions side reactions may

compete with the fulvene formation. Under the Stone conditions the usual by-products were oxide **(+/-)-247** and cyclopentadiene **(+/-)-253** (**entries 2**, **4**, **Table 17**). The formation of oxide **(+/-)-247** is a result of long reaction times. Cyclopentadiene **(+/-)-253** forms by the reaction of aldehyde and cyclopentadiene, which could be originated from the decomposition of aldehyde **(+/-)-248 (Scheme 110)**. The formation of cyclopentadiene was also observed in other reactions using ferrocene based compounds.



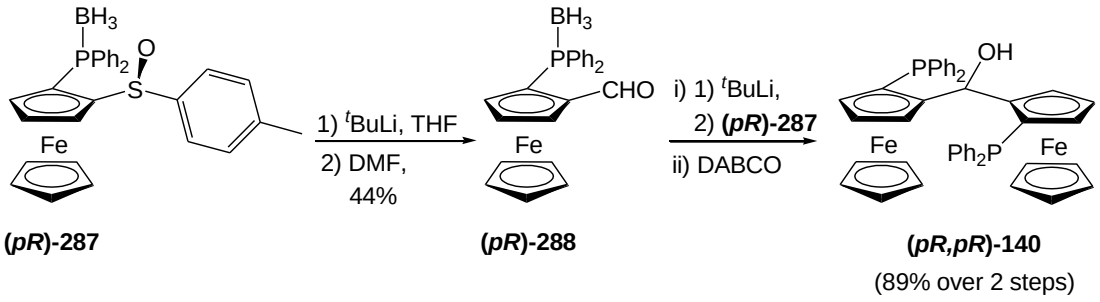
Scheme 110: By-product observed under Stone-conditions

These fulvenes can be subjected to reduction to give the corresponding cyclopentadienes. These compounds could serve as ligands for the formation of 1,2-disubstituted ferrocene based *ansa*-half sandwich metallocene complexes. By different substitution on the diene component steric congestion could be altered around the metal.

7.2 Dimerisation of Ligand A

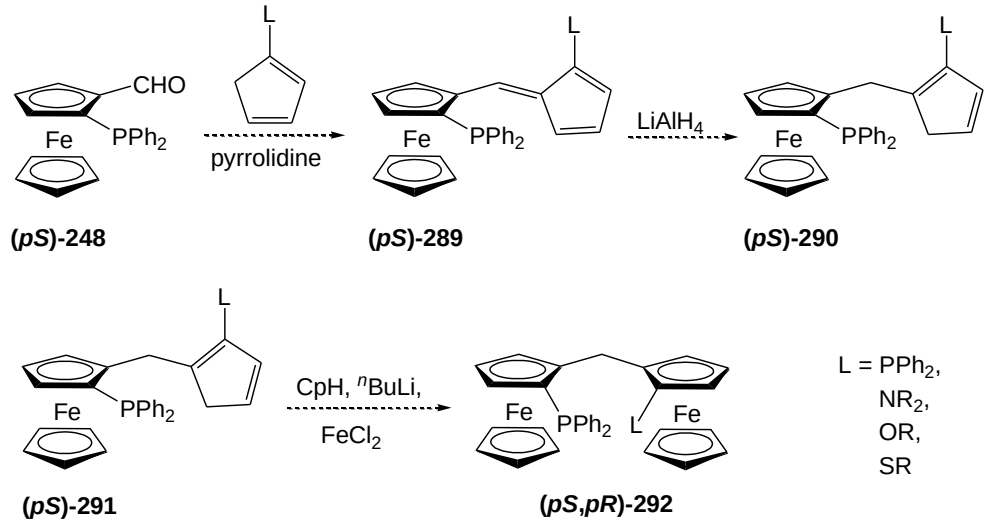
To further expand the utility of Stone fulvene formation, we thought it might be useful for the synthesis of bis-ferrocene type ligands. Hou and Dai developed a bis-ferrocene ligand **(*pR,pR*)-140** for the rhodium catalysed asymmetric hydrogenation of *β*–keto

sulfones (**page 27**).[52] The main step of the synthesis is a dimerisation reaction which gave the **(*pR,pR*)-140** enantiomer from enantiomericaly pure **(*pR*)-288** (**Scheme 111**).



Scheme 111: Synthesis of Hou and Dai's bis ferrocenyl ligand **(*pR*,*pR*)-140**.

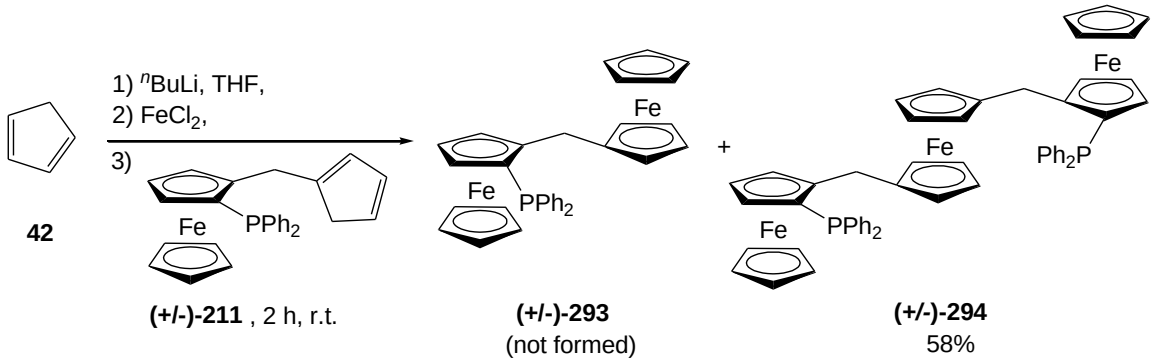
We devised a synthetic route via fulvene derivatives, leading to bis-ferrocene ligands with mixed stereochemistry **(*pS,pR*)-292** (**Scheme 112**).



Scheme 112: Proposed sequence leading to ligand **(*pS*,*pR*)-292**.

We assumed that the analogeous Stone-method and the following reduction would be likely to work. Therefore preliminary experiments were performed to test the ability of cyclopentadiene **(+/-)-211** to form bis-ferrocenyl structure **(+/-)-293**. Surprisingly, it

was not possible to form bis-ferrocenyl structure **(+/-)-293** by this method. Instead, the ferrocene linked dimeric ligand **(+/-)-294** was isolated from the reaction mixture in moderate yield (58%, **Scheme 113**).

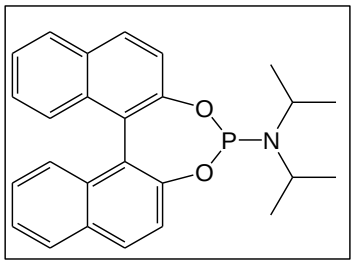


Scheme 113: Synthesis of dimer **(+/-)-294**.

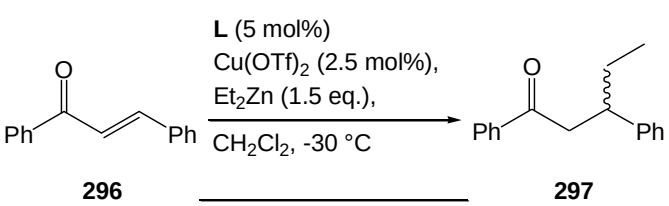
Ferrocene linked dimer **(+/-)-294** proved to be fairly stable and therefore, seemed to be an interesting ligand to try in catalytic asymmetric reactions. The catalytic activity of dimer **(+/-)-294** was tested in three different reactions known to be catalysed by bidendate phosphine ligands.

7.2.1 Conjugate-addition

Dimer **(+/-)-294** was found to be inactive in the $Cu(OTf)_2$ catalysed 1,4 addition of Et_2Zn to chalcone **296** (**entry 2**, **Table 18**).[146]



(+/-)-295



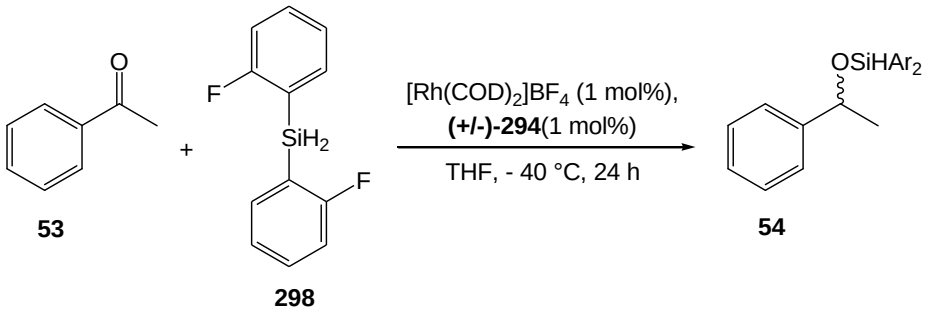
296 **297**

Entry	L	Y(%)
1	**(+/-)-295**	49
2	**(+/-)-294**	0
3	-	0

Table 18: 1,4-Adddition of Et_2Zn onto chalcone **296**.

7.2.2 Hydrosilylation

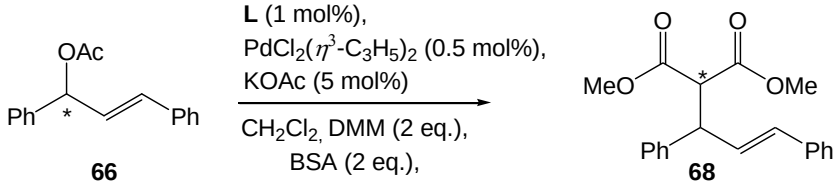
Dimer **(+/-)-294** was also found inactive in the rhodium catalysed hydrosilylation of acetophenone **53** (**Scheme 114**).[51]



Scheme 114: Hydrosilylation of acetophenone **53**.

7.2.3 Allylic substitution

Although (+/-)-BINAP proved to be superior in terms of catalytic activity (**entry 1**, **Table 19**), dimer **(+/-)-294** did catalyse the allylic substitution of acetate **66** with dimethyl malonate **68**.[147] The reaction gradually progressed and reached 100% yield in around 16 hours (**entry 2**, **Table 19**).



Entry	L	Temp(°C)	Time(h)	Y(%)
1	**(+/-)-BINAP**	25	4	100
2	**(+/-)-294**	40	16	100
3	**-**	40	24	0

Table 19: Allylic substitution of acetate **66** with dimethyl malonate **67**.

8. Conclusions

Apart from one example **(*R,pS*)-22** there are no 1,2-disubstituted ferrocene based *ansa*-half sandwich metallocene complexes reported in the literature. Complex **(*R,pS*)-22** served as a basis for the synthesis of **(+/-)-258** and **(+/-)-259**. Synthesis of other examples **(+/-)-269**, **(+/-)-261** and **(+/-)-283** were based on *ansa*-half sandwich metallocene structure **299** (**column 1**, **Figure 18**).

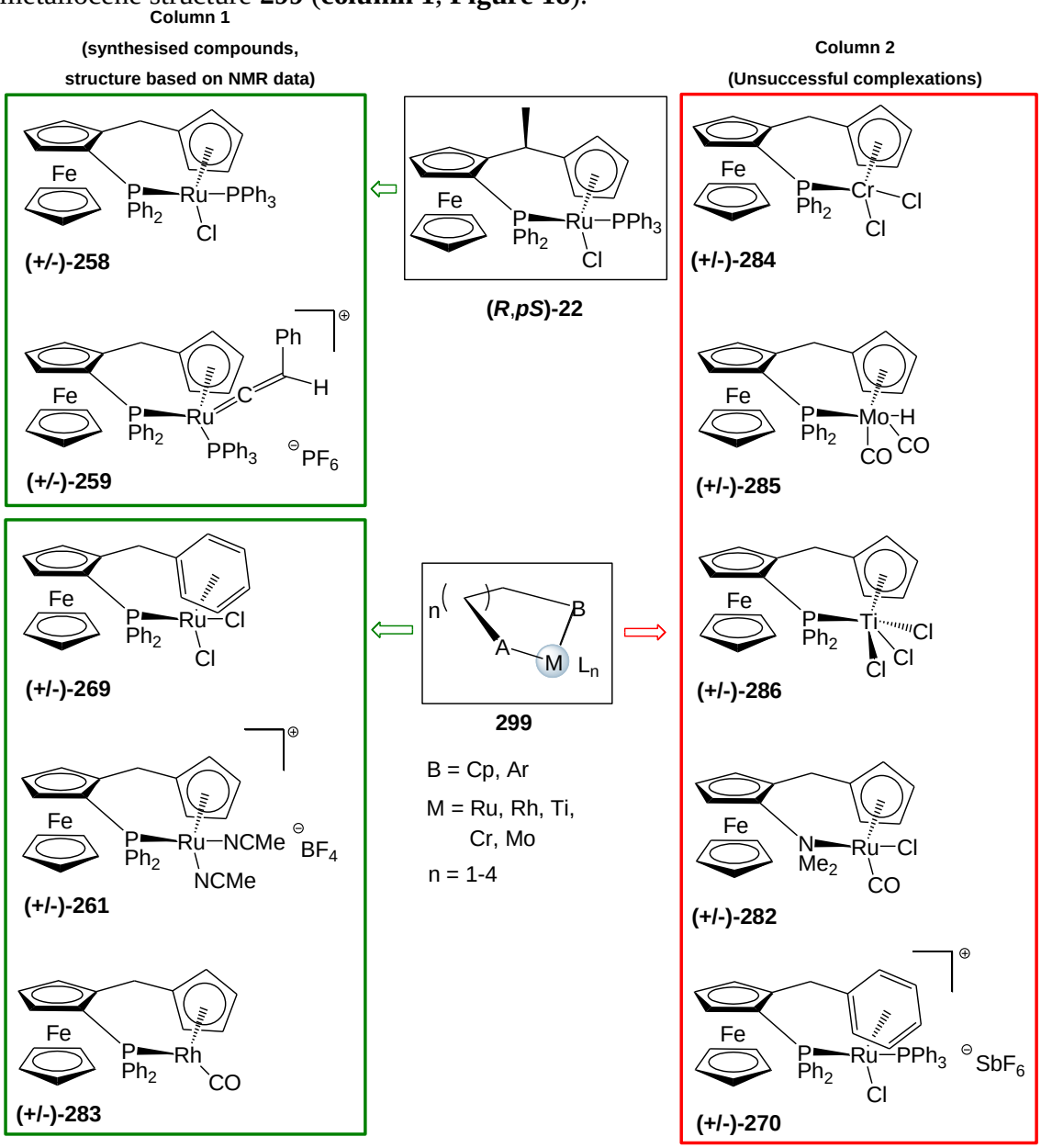


Figure 18: Successful (**column 1**) and unsuccessful (**column 2**) complexations.

Structures were assigned on the basis of comparing NMR data to similar compounds known in the literature. These complexes were tested in catalytic asymmetric reactions (reconstitutive condensation, Diels-Alder reaction, allylic substitution). They proved to be catalytically inactive which was attributed to their instability under the reaction conditions. Synthesis of other complexes **(+/-)-282**, **(+/-)-284**, **(+/-)-285**, **(+/-)-286** and **(+/-)-270** was attempted but remained unsuccessful (**column 2**, **Figure 18**). This was also believed to be in connection with stability issues. A novel, P/P bidendate ligand **(+/-)-294** was isolated in moderate yield (58%, **Figure 19**). Ferrocene linked dimer **(+/-)-294** showed activity in the Pd catalysed Asymmetric Allylic Alkylation (AAA).

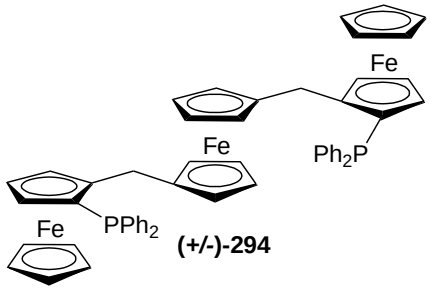


Figure 19: Ferrocene linked dimer **(+/-)-294** was synthesised in 58% yield.

8.1 Possible reasons for instability

8.1.1 Oxidation of diphenylphosphine moiety

In the case of diphenylphosphino functionalised ligands, facile oxidation of the diphenylphosphino moiety must be taken into account. The affinity of these compounds for oxidation was observed during their synthesis. Although, this process seemed to be slow and could be minimised by using deoxygenated solvents, it could occur to complexes **(+/-)-258**, **(+/-)-259**, **(+/-)-261** and **(+/-)-269** during asymmetric catalytic reaction.

8.1.2 Sterics

Two main differences between the *ansa*-half sandwich metallocene complexes **299** and our general ligand structure **300** are the additional ferrocene unit and the size of the linker connecting the cyclopentadienyl functionality with the tethered Lewis basic functionality (**Figure 20**). The additional bulky ferrocene unit intoduced onto the linker, might cause steric congestion between the ligands coordinated to the transition metal. Changing the size of the linker can also be related to steric congestion caused in the ligand field around the metal.

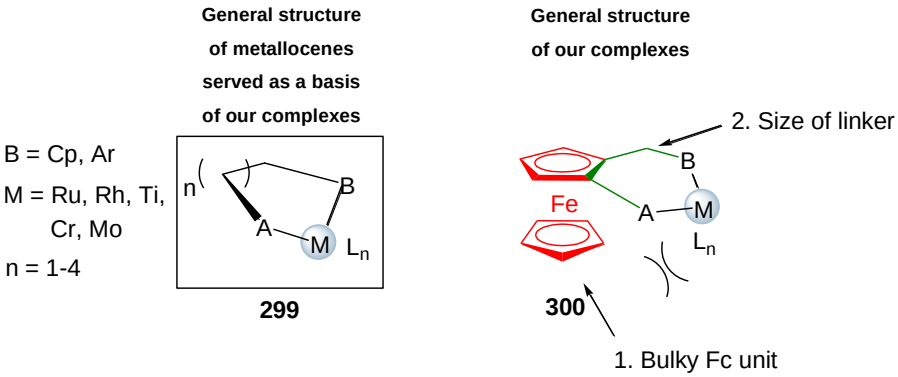
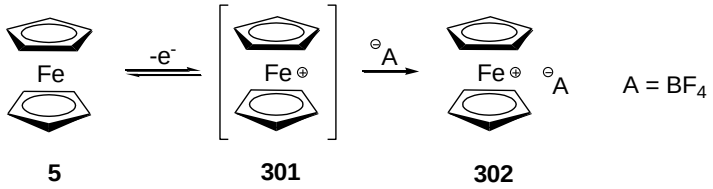


Figure 20: Steric factors: Additional ferrocene unit and size of linker.

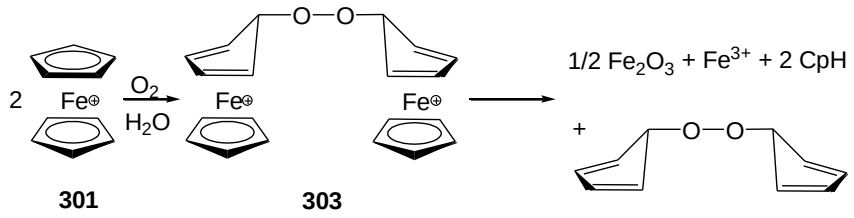
8.1.3 Redox side-reactions

Ferrocene **5** undergoes reversible, one electron oxidation (**Scheme 115**). The resulting ferrocenium cation **301** is fairly stable and can be isolated as a salt **302**. In fact, ferrocenium tetrafluoroborate **302** is commercially available and sometimes used as a one electron oxidising agent.



Scheme 115: Ferrocenium cation **301** formed in a reversible redox reaction from ferrocene **5**.

Ferrocenium **301** decomposes under certain conditions. The mode of decomposition is not fully understood, but possibly involves molecular oxygen as proposed by Zotti (**Scheme 116**). This is supported by the observation that during cyclic voltammetry experiments, the presence of oxygen rendered the ferrocene/ferrocenium oxidation irreversible.[148]



Scheme 116: Oxygen catalysed decomposition of ferrocenium cation **301**.

EDGs such as methyl groups, shift the electrode potential (E) of ferrocene **5** to a cathodic direction (negative E value), therefore make it more prone to oxidation. This connection between E values and the electron rich nature of the Fc system can be nicely seen by the E values of the corresponding ferrocene **5** and bis(pentamethyl)ferrocene **304** (**Figure 21**).

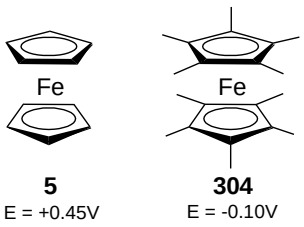
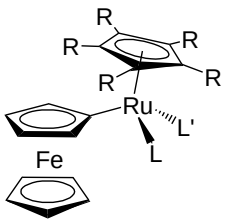


Figure 21: E values nicely correlate with the electronic character of the ferrocenyl system.

In more complex systems such as **305** (**Table 20**) or **306** (**Figure 22**) (involving two or more metals) the electronic interaction between the Ru and the Fc unit is illustrated by the fact that inductive effects on the Ru affect the redox potential (E) of the Fc group

(**Table 20**).[149] In additon in this example the Ru centered oxidation was irreversible and subsequent chemical decomposition took place.



305

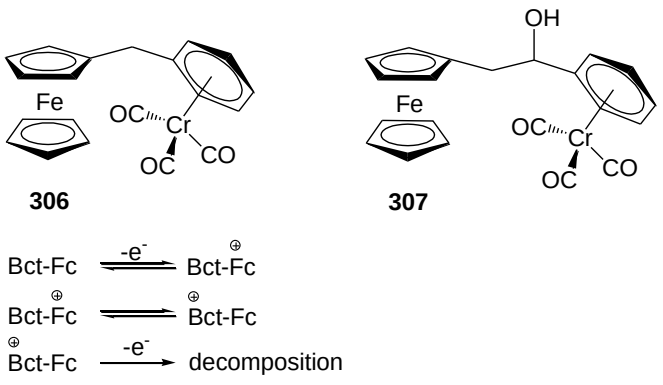
306					
Entry	R	L	L'	**E_1(V)**	**E_2(V)**
1	H	CO	CO	+0.13	+1.3
2	H	PPh_3	PPh_3	-0.10	+0.9
3	H	CN^tBu	CN^tBu	-0.2	+0.5
4	Me	CO	CO	+0.07	+1.5
5	Me	PPh_3	PPh_3	-0.17	+1.0
6	Me	CN^tBu	CN^tBu	-0.24	+0.5

E_1 = Ferrocenyl-centered oxidation

E_2= Ruthenium-centered oxidation

Table 20: Inductive effect exerted by adjacent metal (Ru).

An even more apparent example shows the strong electronic interaction of the two metals (Fe and Cr) in complex **306** (**Figure 22**). Oxidation of complex **306** took place in two steps, but was found to involve intramolecular oxidation of the benzenechromiumtricarbonyl (Bct), by the ferrocenium (Fc) cation. This oxidation proved to be irreversible and resulted in decomposition. However as the metal fragments get far enough away from each other, such as in the case of comple **307**, two reversible, one electron oxidation occured.



306 **307**

Figure 22: Electrochemical interaction between Cr and Fe atoms in complex **306**.

On the basis of these examples it can be assumed that in our complexes (**page 91**) there is a subtle electrochemical relationship between the metals. In addition Lewis basic functionalities (PPh_2, NMe_2) further lower E values. In combination of the previous with the latter effect, E values of these complexes are expected to be lower compared to ferrocene itself. Lower E values in turn, can be closely related to sensitivity of complexes towards oxidation (**Figure 21**). Despite using deoxygenated solvents in our experiments decomposition occurred in certain cases. Therefore other, non-oxidative mechanisms might be in operation for the decomposition of these compounds.

9. Summary

We established a divergent synthetic sequence by which it was possible to access a wide variety of Ligands. For the incorporation of the cyclopenatdienyl moiety, the fulvene formation/reduction two step sequence proved to be the most convenient. Three members of the ligand family were synthesised (Ligand A, B and C). Complexation studies were carried out based on literature precedents. The complexes **(+/-)-258**, **(+/-)-259**, **(+/-)-261** and **(+/-)-269** showed instability, therefore full characterisaton was not possible (**column 1**, **Figure 18**). Nevertheless they were tested in asymmetric transformations but unfortunately showed no activity.

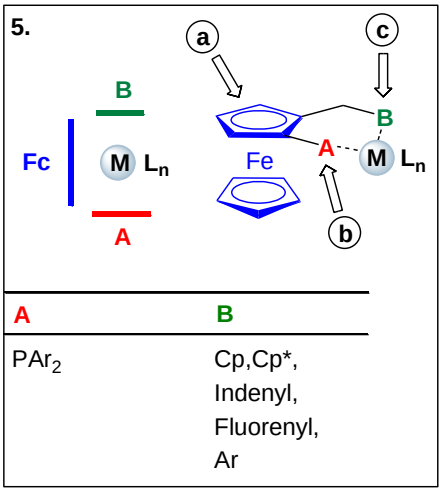
This work was continued by expanding the scope of the fulvene formation, which could lead to other Ligand structures. Synthesis of complexes **(+/-)-282**, **(+/-)-284**, **(+/-)-285**, **(+/-)-286** and **(+/-)-270** were attempted. These complexation reactions however either led to no product formation or gave unstable products (**column 2**, **Figure 18**). In the course of synthesising different ligands dimer **(+/-)-294** was synthesised which proved to be stable, and showed moderate activity in Pd catalysed allylic alkylation.

10. Future Work

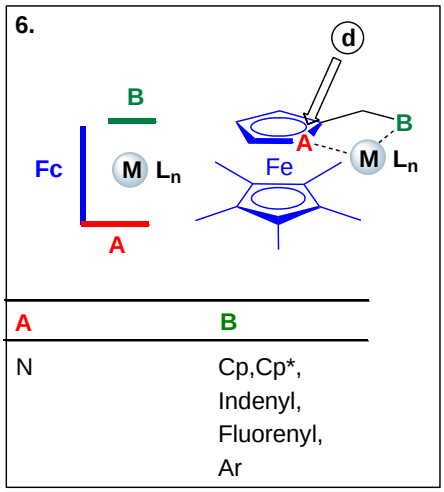
The main hurdle yet to overcome is the instability of these ligands. The main reason that makes ferrocene a popular scaffold for ligand synthesis lies in its stability. The stability is affected by the character of any substituents. In general, electron withdrawing groups increase the electron density on the ferrocene backbone therefore make it prone to oxidation. In addition, in complexes involving two metals, the subtle inductive electronic relationship between the metals (Fe and Ru/Rh/Cr/Mo/etc.) further complicates electronic distribution within these systems. In our opinion, the overall stability of these complexes is the key to their successful catalytic asymmetric applications. Cyclic voltammetry studies on our synthesised complexes, might give a useful insight to their stability. Electrode potential values could give an idea of the overall electron density of the complex. Electron density might be altered by introducing electron withdrawing groups in our system. The electron withdrawing groups could be introduced at several points (**Figure 23**):

a. Introduction of an electron withdrawing groups onto the ferrocene,
b. Introduction of an electron withdrawing groups onto the Lewis basic functionality (concept introduced by Togni for the electronic "tuning" of Josiphos type ligands)
c. Introduction of an electron withdrawing groups onto α–cyclopentadienyl or aryl moiety.

d. Introduction of an electron withdrawing atom into the ferrocene ring (eg. azaferrocene-systems are known to be more electron deficient than ferrocene-systems)



A, B or/and Fc could be substituted with an electron withdrawing group.



A, such as nitrogen could be placed into the ring. Azaferrocenes known to be more electron deficient than Fc.

Figure 23: Alignment **5** and **6** illustrate the possible ways of decreasing the electron density in our system.

The electron density of these synthesised ligands could be compared to those based on the original ligand structure, with the help of cyclic voltammetry measurements. Then the most stable (possibly lower electron density) ligands should be subjected to complexation. We believe that for successful future applications the issues of stability should be addressed first.

1. The Amide Bond

The amide bond is one of the most fundamental linkages in nature from, simple peptides or enzymes, through to polyketides, cyclopeptides, antibiotics and pharmaceuticals. In addition, they are commonly used as directing/protecting groups and in functional group interconversions. Nature has developed enzymes for the efficient formation of such bonds for millions of years. Although there are processes based on enzymatic carboxamidations, due to the limited substrate tolerance of these enzymes they are not widely utilised. A recent study based on the synthesis of drug candidates showed that around 9.1% of all reactions were amide bond forming reactions.[150] It was also revealed that 25% of known pharmaceuticals contained at least one amide bond.[151]

2. Amide Bond Formation

2.1 "Traditional" methods

Amide bond formation is formally a condensation reaction. When mixing carboxylic acids **308** and amines **309** an ammonium salt **310** is formed first and further reaction to give an amide is disfavoured. In nature enzymes help to overcome this barrier. Otherwise, direct amide bond formation needs high temperature (160-180 °C) which is very often too harsh for other functionalities to bear. Therefore, carboxylic acids must be activated prior to the formation of the amide bond (**Figure 24**). By activation

different kind of LGs are accommodated onto the carbonyl group, facilitates the aminolysis, while the salt formation is also avoided.

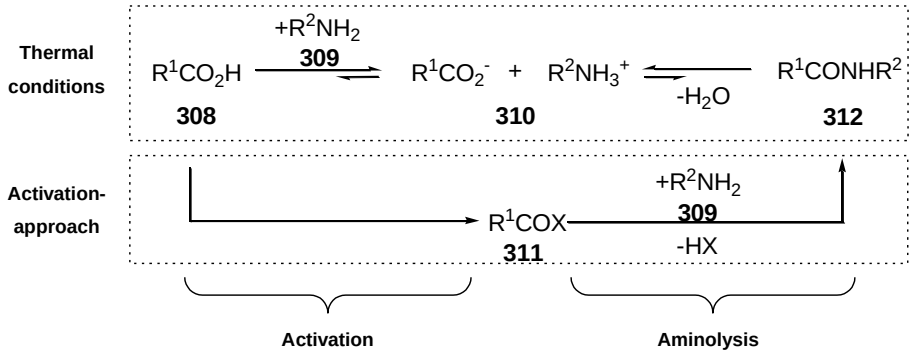


Figure 24: Carboxamidation under thermal conditions and activation of carboxylic acids.

An exhaustive discussion of these traditional methods are beyond the scope of this introduction and will not be addressed here. There are several reviews covering the literature to date.[152,153] In 2005 the ACS Green Chemistry Institute Pharmaceutical Roundtable voted amide bond forming reactions the highest priority among those being used by the pharmaceutical industry, but better methods would be preferred.[1] Common disadvantages are:

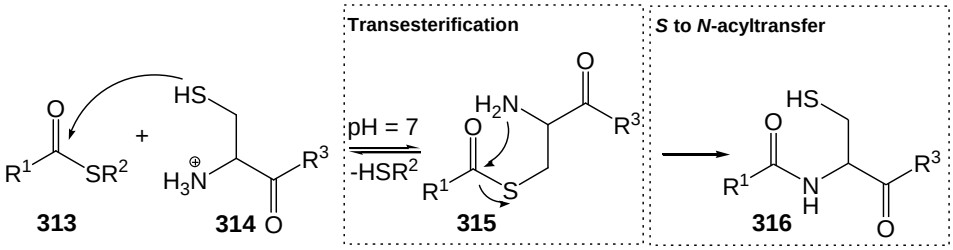
1. Poor atom/redox economy
2. Health issues (toxic or carcinogenic compounds involved at some point in the synthesis)
3. Harsh conditions (give rise to racemisation and incompatibility with certain groups, protecting groups)
4. High substrate dependence (even robust existing methods might fail with sterically demanding or more complex substrates)

Bearing these in mind, it is not surprising that the field of amide bond formation has been subject to intensive research the past decade. Some of the emerging methods will be discussed in the following section.

2.2 Alternative methods

2.2.1 Native Chemical Ligation

Native chemical ligation utilises a cysteine residue at the *N*-terminus of a desired peptide **314**, to couple with another peptide **313** having a thioester functionality at its *C*-terminus.[154] The method consists of a reversible thiol-thioester exchange, followed by an irreversible *S* to *N*-acyltransfer (**Scheme 117**). The reaction takes place in aqueous media at neutral pH. Limiting factors are the compulsory cysteine residue which remains in the product **316** and the low yield of *C*-terminus thioester formation in some cases.

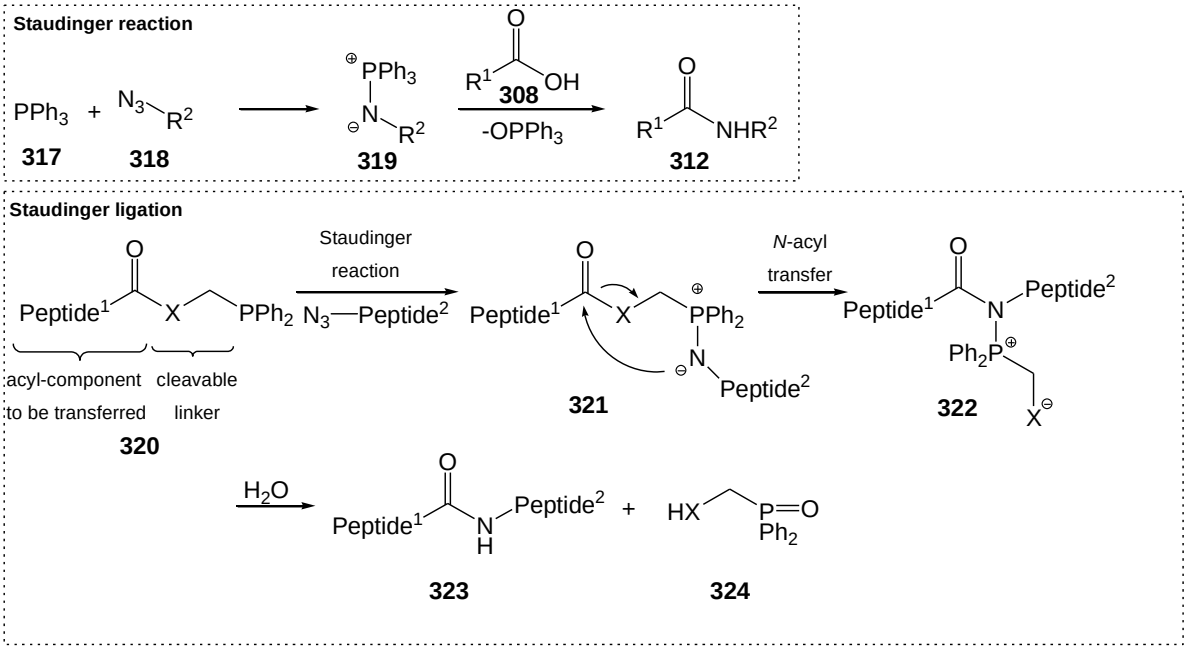


Scheme 117: Native Chemical Ligation.

2.2.2 Staudinger Ligation

In the classic Staudinger reaction an azide **318** is reacted with a phosphine **317** giving an aza ylide (or iminophosphorane) **319**. This intermediate is reacted *in situ* with electrophiles such as carboxylic acid derivatives, carbonyl or thiocarbonyl compounds. Amides **312** can be obtained by using carboxylic acid **308** for electrophilic trapping (**Scheme 118**). In 2000, Bertozzi published a highly chemoselective ligation procedure,

which exploited the exceptional affinity of phosphine towards azides.[155] This rendered the procedure useful in the presence of other functional groups or complex biomolecules. The phosphine was linked to the *C*-terminal part of a peptide **320**. The *N*-terminal part was introduced in a Staudinger reaction. *N*-acyl transfer gave amidophosphonium salt **322** which was hydrolysed at the end of the sequence to give peptide **323**.



Scheme 118: Staudinger reaction and Staudinger-ligation.

Several linkers **325-328** were developed by the same group to improve utility of the protocol (**Figure 25**).[156]

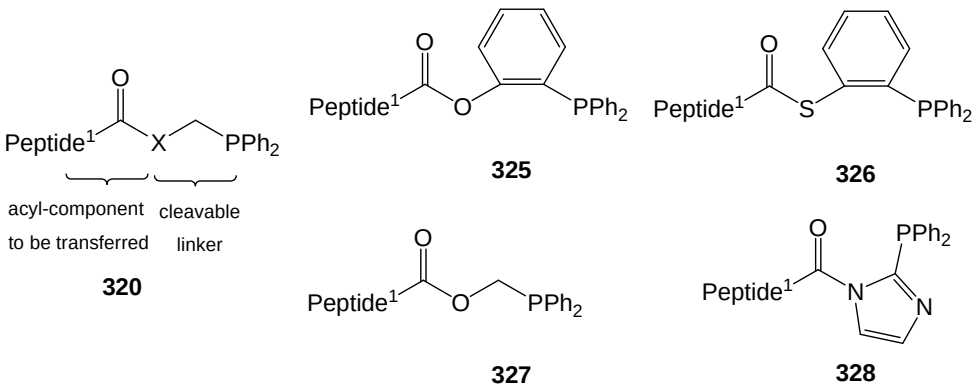
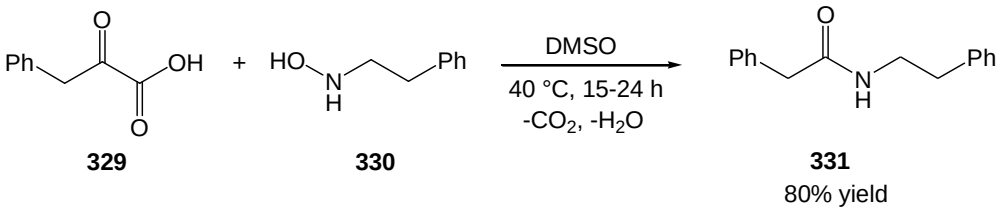


Figure 25: Cleavable linkers for Staudinger-ligation.

2.2.2 Ligation using *α*–ketoacids hydroxylamines

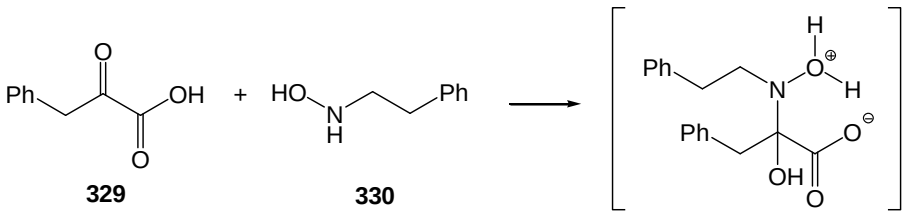
Another ligation method utilised *α*–ketoacids **329** and hydroxylamines **330** to obtain amides **331**.[157] The reaction proceeded at 40 °C without the use of any catalyst and the only by-products are CO_2 and water (**Scheme 119**). The method also worked for short (2-3 membered) peptides (58-80% yields).



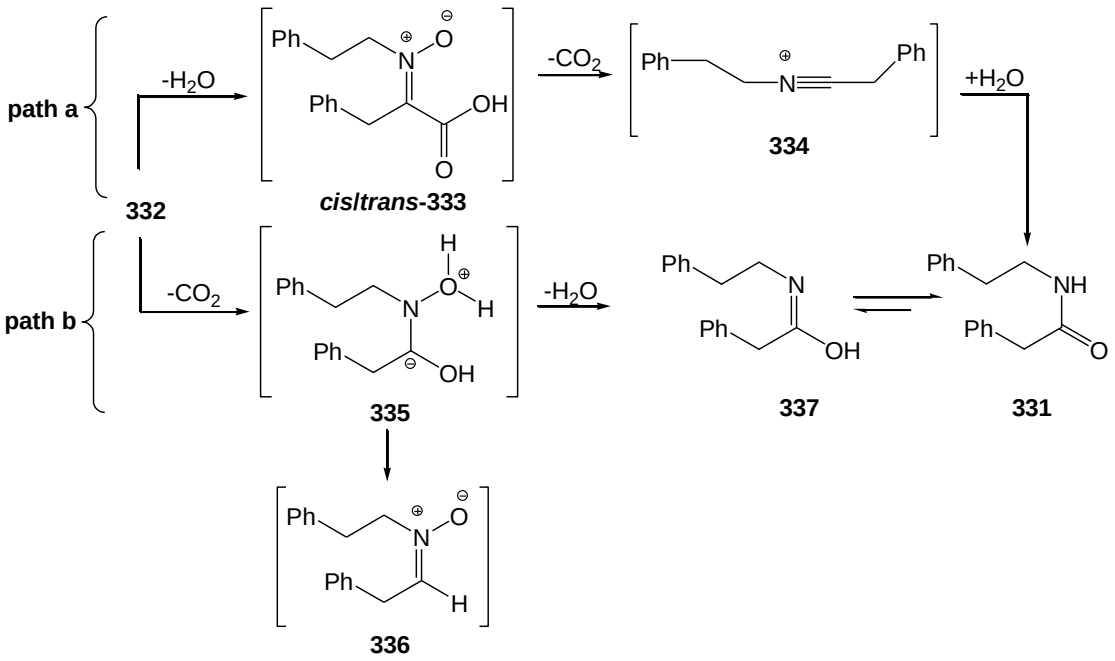
329 **330** **331**
80% yield

Scheme 119: Decarboxylative condenstaion of *N*-alkylhydroxylamines **330** and α–ketoacids **329**.

The reaction most likely proceeded through decarboxylation of the tetrahedral intermediate **332** (**path b**, **Scheme 120**). This was supported by the fact that nitrone **336** was isolated from the reaction. Although nitrones ***cis*-333** and ***trans*-333** (**path a**) formed rapidly in the beginning of the reaction, nitrilum ion **334** was not observed nor could it be trapped. Therefore the reaction seemed less likely to follow **path a**.



329 **330** **332**



Scheme 120: Possible reaction pathways.

2.2.3 Hydrative amide synthesis (umpolung)

Recently, Johnston reported an unconventional hydrative approach to amides.[158] This umpolung concept of using a nucleophilic acyl donor **340** and an electrophilic amine acceptor **341** was in contrast to conventional condensation approaches using electrophilic acyl acceptor **338** and nucleophilic amine donor **339** (**Figure 26**).

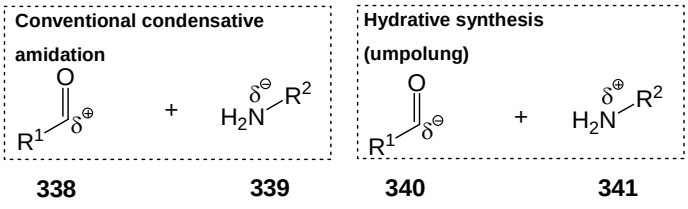
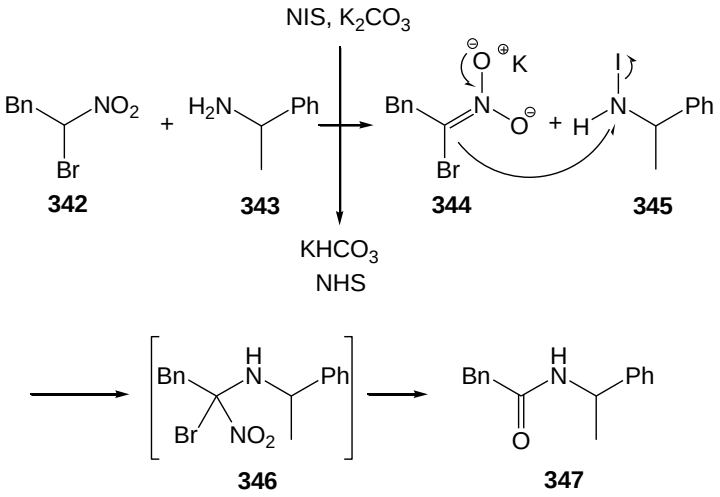


Figure 26: General and Umpolung concepts of hydrative amide synthesis.

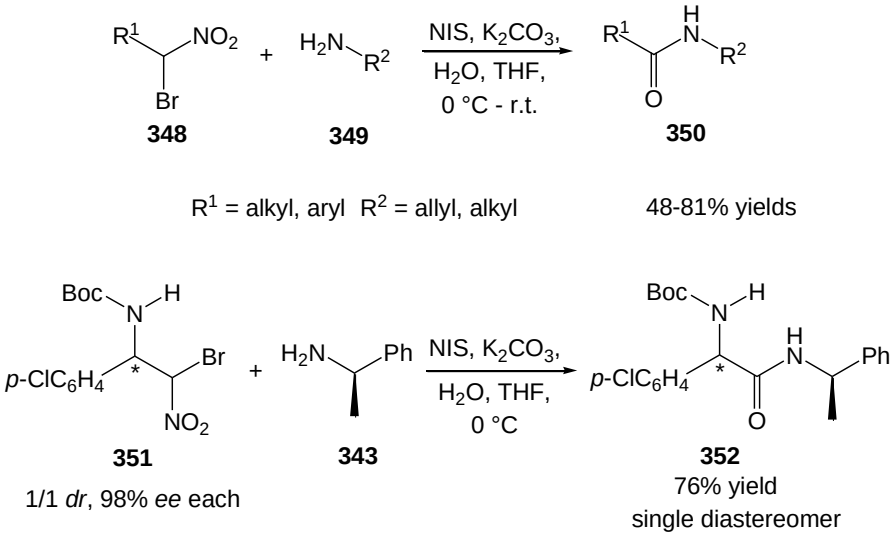
The proposed mechanism is depicted in (**Scheme 121**). Acccording to this the nitronate **344** attacked the *N*-halo amine **345** to give tetrahedral intermediate **346**. This was then

hydrolysed in the final step. Other pathways going *via* the aldehyde (Nef reaction), acyl-chloride or active ester were ruled out.



Scheme 121: Mechanistic proposal for the hydrative amide synthesis.

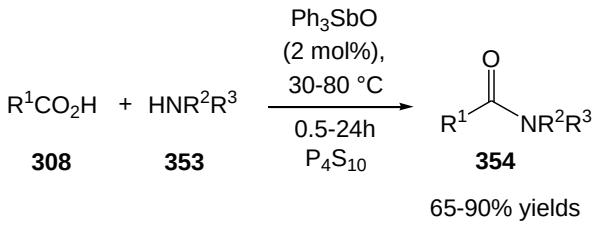
Under optimised conditions amides **350** were obtained in moderate to good yields. The method did not work for aryl amines such as aniline. Upon testing these conditions on enantiomerically pure substrates **351** no racemisation took place (**Scheme 122**). In addition the protocol showed good functional group tolerance (hydroxyl, acetal).



Scheme 122: The scope of hydrative coupling.

2.3 Catalytic methods

In 1986 Nomura published a catalytic amidation method using triphenylantimony oxide **355**.[159] Under optimised conditions carboxylic acids were successfully coupled with different mono/di-alkyl amines, anilines and even peptides in pyridine at elevated temperatures (30-80 °C) in the presence of P_4S_{10} using triphenylantimony oxide **355** in catalytic amount (2 mol%) (**Scheme 123**).[160]



Scheme 123: Optimised procedure for triphenylantimony oxide **355** catalysed direct carboxamidation.

First organoantimony carboxylate **356** was formed, which was then reacted *in situ* with different amines **353** to yield the product **354** and regenerate oxide **355** (**Figure 27**). The major disadvantages of this method lay in the high toxicity of antimony and tetraphosphorus decasulfide.

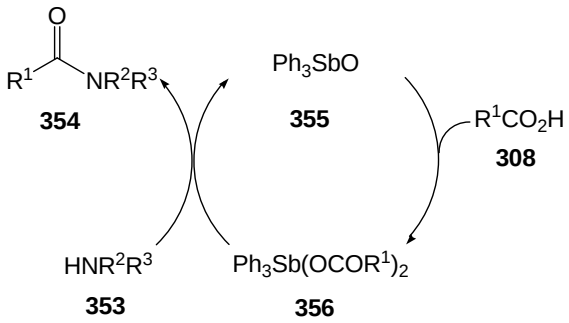
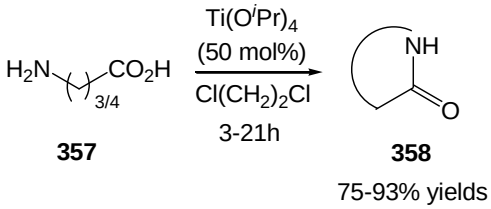


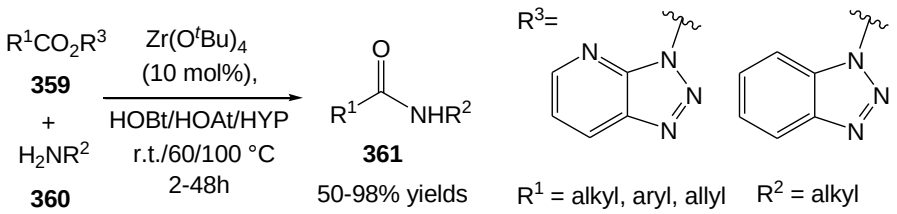
Figure 27: Catalytic cycle proposed by Nomura for the triphenylantimony oxide **355** catalysed direct carboxamidation.

Early transition metals, such as titanium(IV) have been found to be active in esterification/amidation reactions. Based on these reports Helquist investigated $Ti(O^iPr)_4$ catalysed lactamisations.[161] It was found that substoichiometric amounts (50 mol%) of $Ti(O^iPr)_4$ (50 mol%) affected these reactions and the corresponding 5/6-membered lactams **358** were formed in good yields (**Scheme 124**).



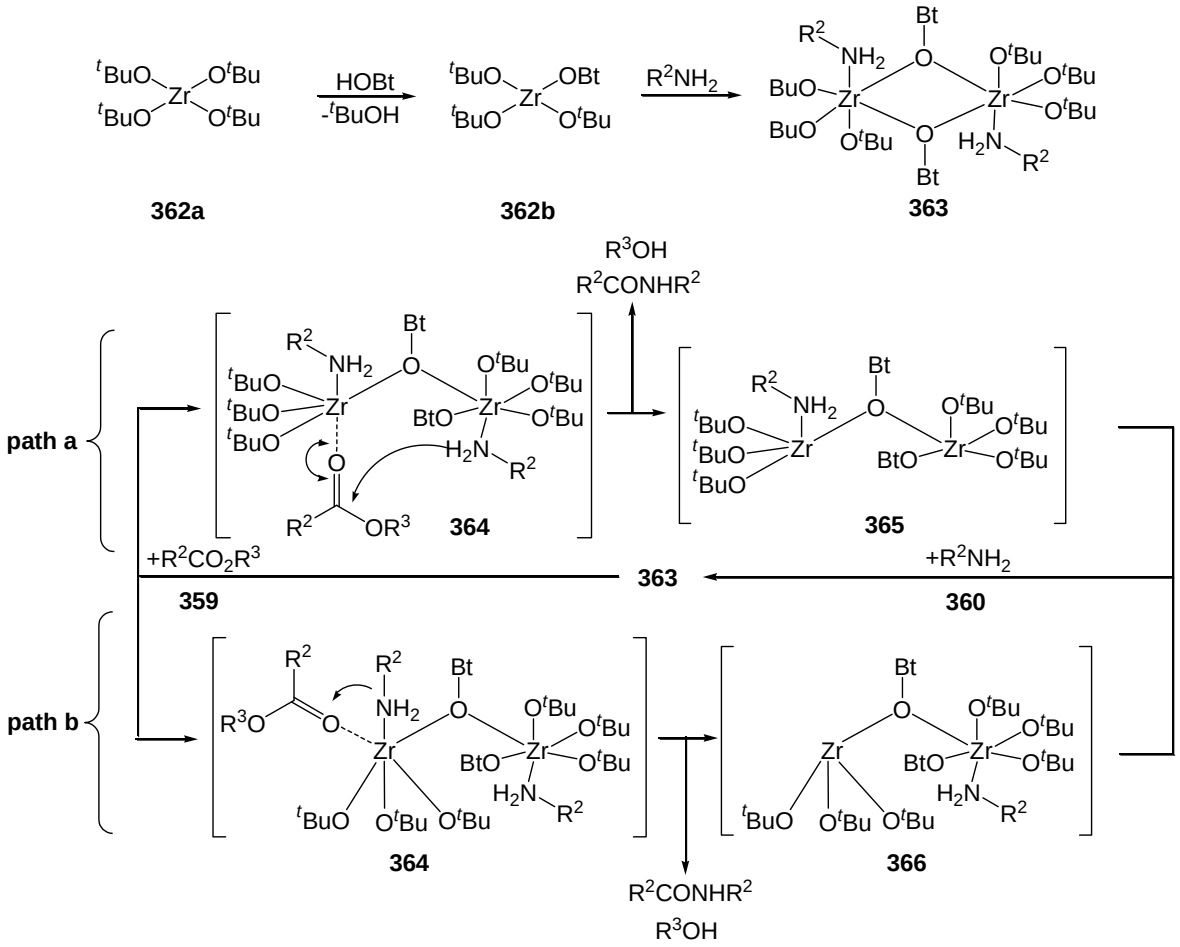
Scheme 124: $Ti(O^iPr)_4$ catalysed direct lactamisation.

Porco investigated the application of group (IV) metals such as Ti, Zr and Hf, in catalytic ester-amide exchange reactions.[162] Additives such as HOAt, HOBt or HYP accelerated the reaction (**Scheme 125**).



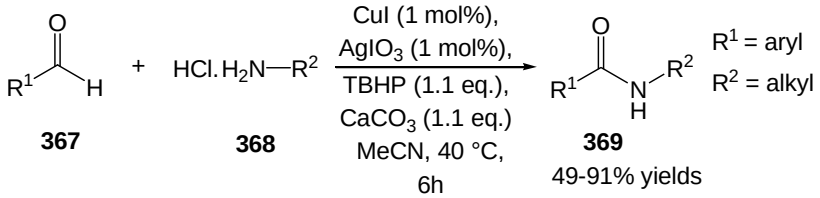
Scheme 125: Zr catalysed carboxamidation of esters **359**.

Upon mixing $Zr(O^tBu)_4$ **362a** the additive and the amine **360,** complex **363** was isolated (**Scheme 126**). The mechanistic rationale involved coordination of the ester **359** to the metal which was then attacked by the amine **360** giving product **361**. Whether the reacting substrates **359** and **360** were coordinated to the same metal was unknown (**path a** or **path b**). The method could be used for acid/base sensitive or very complex substrates.



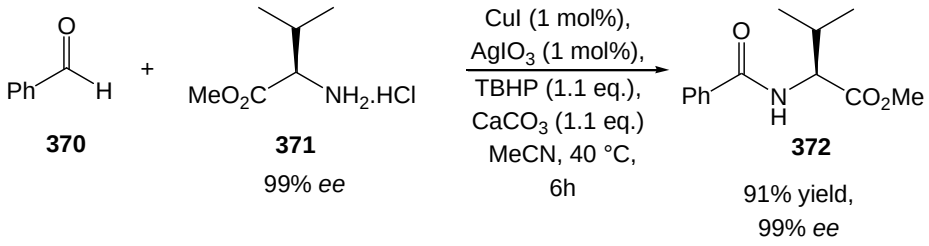
Scheme 126: Proposed mechanism of Zr catalysed ester-amide exchange. Dimeric species **363** is possibly involved in the reaction.

Late transition metals have also been successfully applied to catalytic amide bond formations. Li established a highly efficient oxidative coupling of aldehydes **367** and amine hydrochloride salts **368** (**Scheme 127**).[163] The procedure utilised catalytic amounts of CuI and $AgIO_3$ (1 mol%) in addition to the oxidant (TBHP).



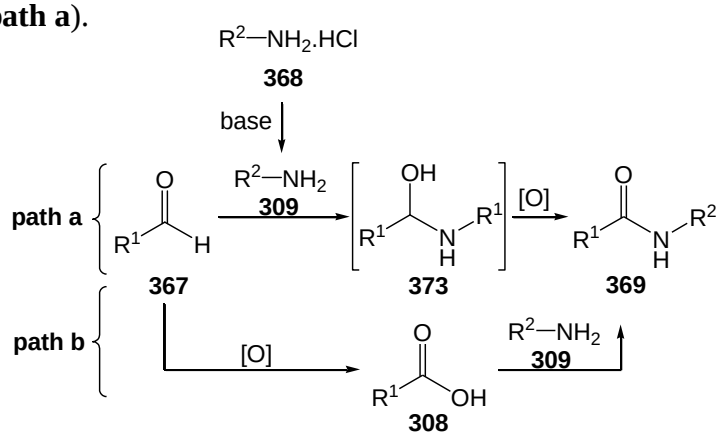
Scheme 127: Cu catalysed oxidative amidation.

Performing the reactions with optically active amine **371** gave amide **372** in good yield without loss of the enantiomeric purity (**Scheme 128**).



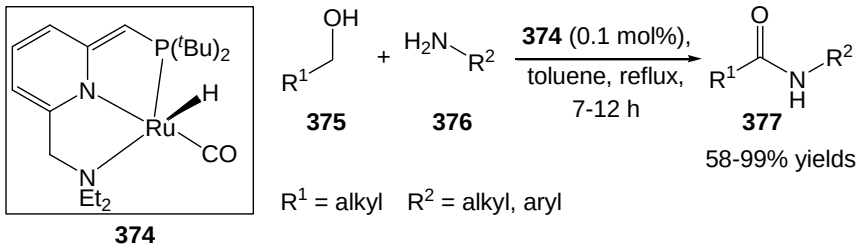
Scheme 128: Under these conditions no racemisation was observed.

The possible mechanism involved the formation of hemiaminal **373**, which is oxidised *in situ* to the product **369** (**path a**, **Scheme 129**). On the other hand formation of product **62** might have arisen from the carboxylic acid **308** by a transamidation reaction (**path b**). The reaction of benzoic acid (instead of benzaldehyde) under the optimised conditions gave no product **369**. Therefore, the reaction more likely proceeded through hemiaminal **373** (**path a**).



Scheme 129: Tentative mechanism of oxidative amidation of aldehydes **367** with amine hydrochloride salts **368**.

In 2007, Milstein reported a very active catalytic system for the direct synthesis of amides from alcohols and amines with the liberation of H_2.[164] PNN pincer type ligand **374** was utilised in only 0.1 mol% but unfortunately the method was only applicable to primary amines **376** and primary alkyl alcohols **375** (**Scheme 130**).



Scheme 130: Ru catalysed synthesis of amides form alcohols and amines.

In the first step alcohol **375** added onto the dearomatised complex **374** (**Figure 28**). This was followed by the elimination of aldehyde **379**. Aldehyde **379** reacted with amine **376** to give hemiaminal **380** which then added to the pincer complex **374**. In the final step the product **377** was expelled during the formation of dihydrogenated complex **382**.

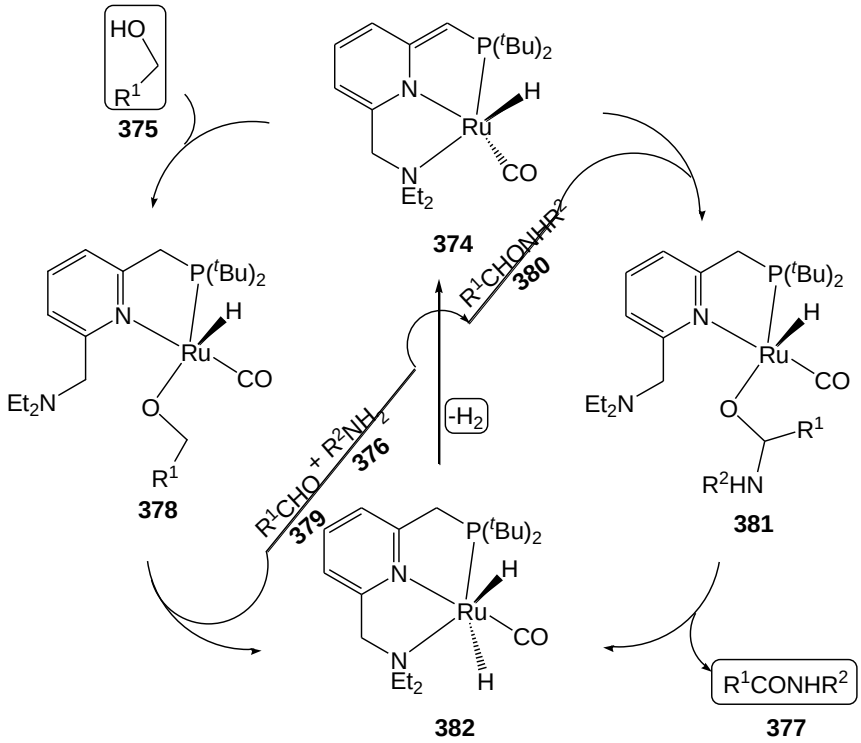


Figure 28: Catalytic cycle proposed for the direct synthesis of amides from alcohols and amines.

In principle the reaction could proceed through hemiaminal **380** (**path a**, **Figure 29**) or hemiacetal **383** (**path b**). Ester **384** did not react with amine **376** under the same conditions in the presence or absence of catalyst **374**. Therefore **path b** could be ruled out.

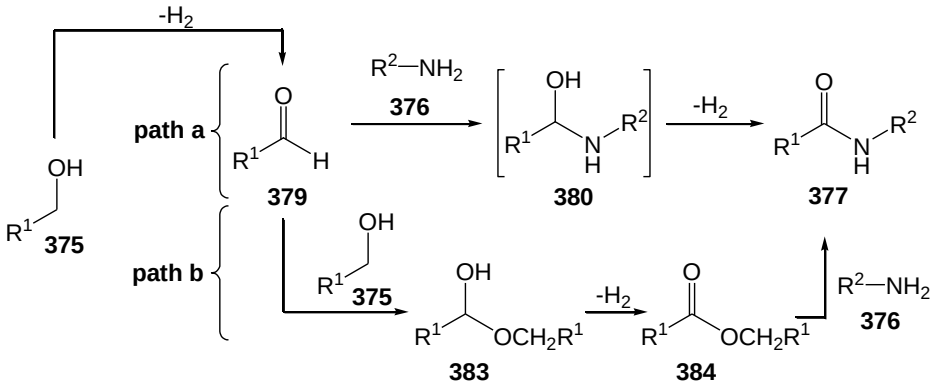
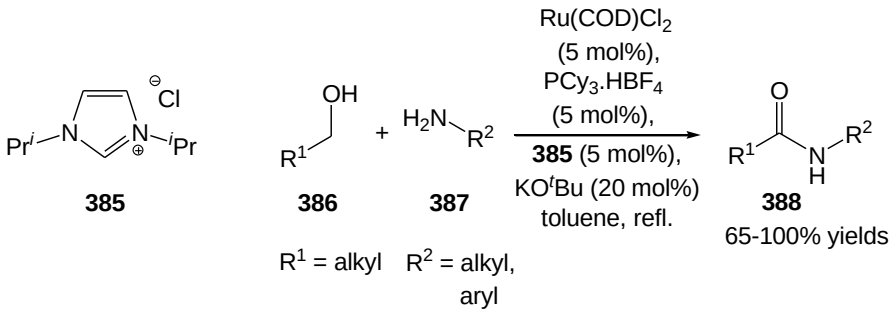


Figure 29: Reaction is believed to proceed through hemiaminal **374** (**path a**).

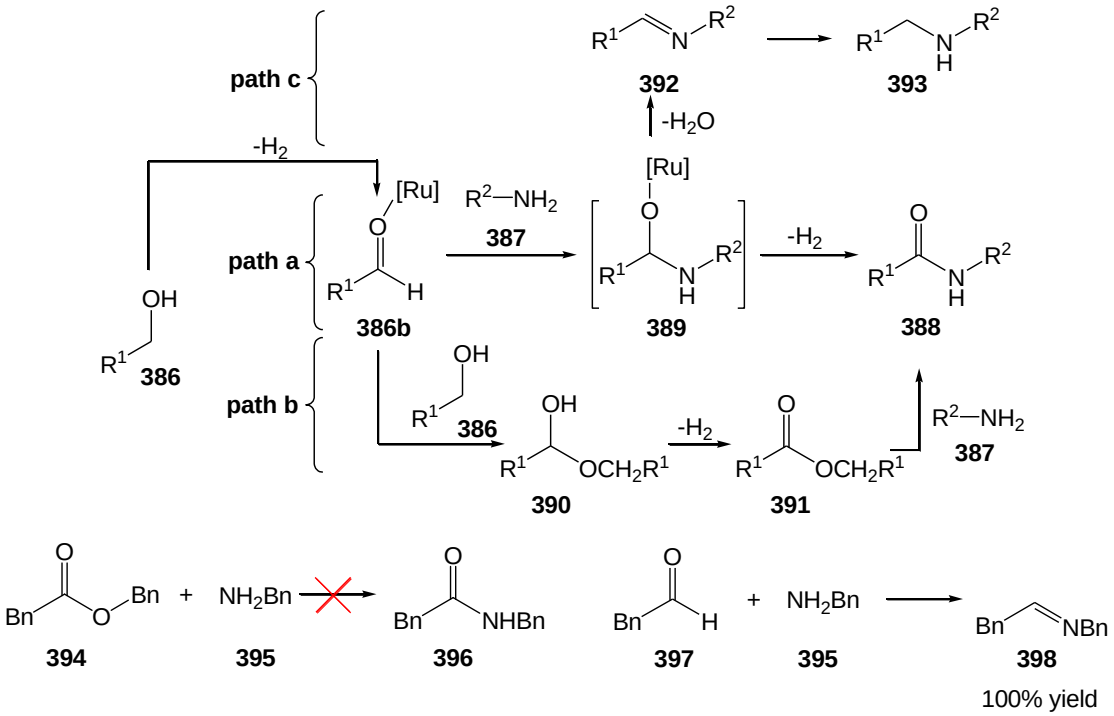
Another Ru based catalyst system was published by Madsen, which coupled primary alkyl alcohols **386** with primary alkyl and aryl amines **384** (**Scheme 131**).[165] The only example using a secondary amine a gave lower yield (40%) under harsher conditions (163 °C in mesitylene).



Scheme 131: Synthesis of amides form alcohols **386** and amines **387** using Madsen's catalyst system.

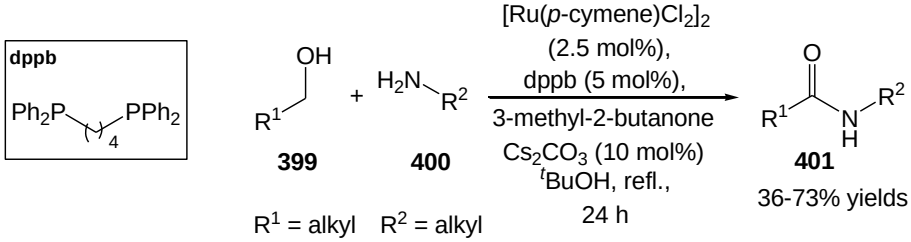
Although the catalytically active complex was not isolated or proposed. The reaction path most probably involved a hemiaminal **389** intermediate (**path a**, **Scheme 132**). Control experiments between ester **394** and amine **395** confirmed this (**path b**). In the

reaction between benzaldehyde **397** and **395** benzylamine under the same conditions, the corresponding imine **398** was isolated (**path c**). In the reaction of alcohols **386** and amines **387**, imine **392** formation was not observed. Therefore it was proposed that during the reaction the aldehyde **388** and hemiaminal **389** stayed coordinated to the [Ru] and were released only at the end of the reaction (**path a**).



Scheme 132: The reaction was proposed to proceed through **path a**.

In the course of investigating the alkylation of amines with alcohols, Williams observed the formation of amide by-products in specific cases (**Scheme 133**).[166] Under optimised conditions primary alkyl alcohols **399** were coupled with primary alkyl amines **400** with varying yields (36-73%). The only example using a secondary amine (morpholine) gave low yield (31%).



Scheme 133: Oxidative Coupling of alcohols and amines under hydrogen transfer condtitions.

An oxidative process was proposed, coupled with Hydrogen Transfer catalysis. However, no mechanistic investigations were conducted (**Figure 30**).

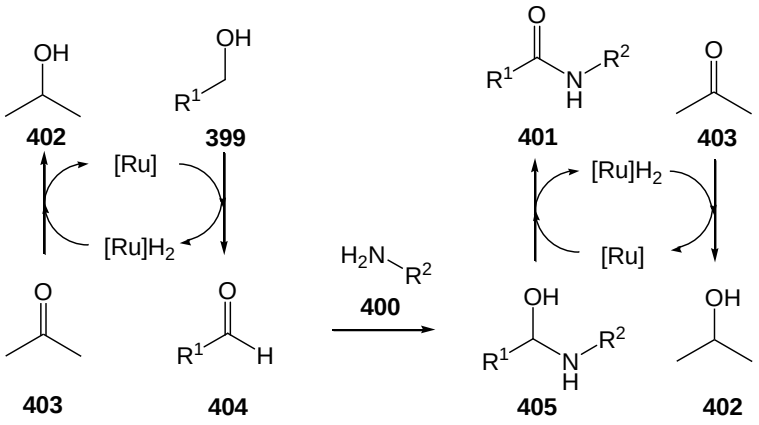
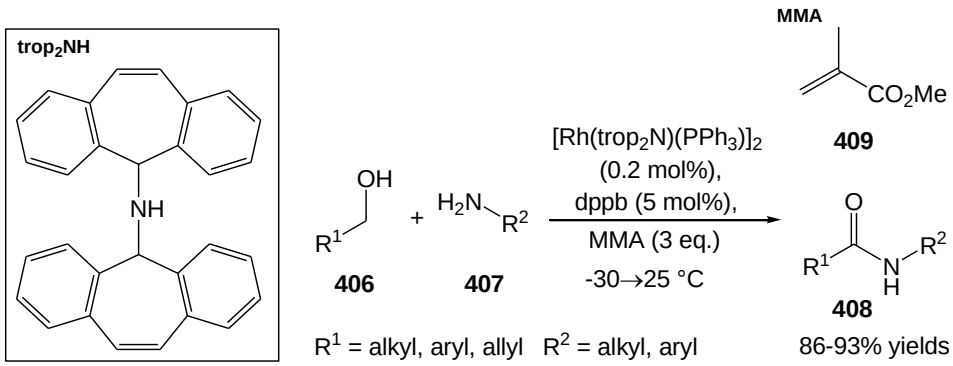


Figure 30: Oxidative coupling of alcohols and amines using hydrogen transfer catalysis.

Grützmacher developed a Rh catalysed dehydrogenative coupling protocol (**Scheme 134**).[167] Although there were only five examples reported involving amines **407** and alcohols **406**, the coupling worked well for water and ammonia as well as other coupling partners, resulting in the corresponding carboxylic acid and amide products.



Scheme 134: Rh catalysed dehydrogenative coupling.

The simplified catalytic cycle is depicted in (**Figure 31)**. Because of stability issues amido complex **411a** was generated *in situ*. For the optimised conditions MMA **409** was used as a terminal H_2-acceptor.

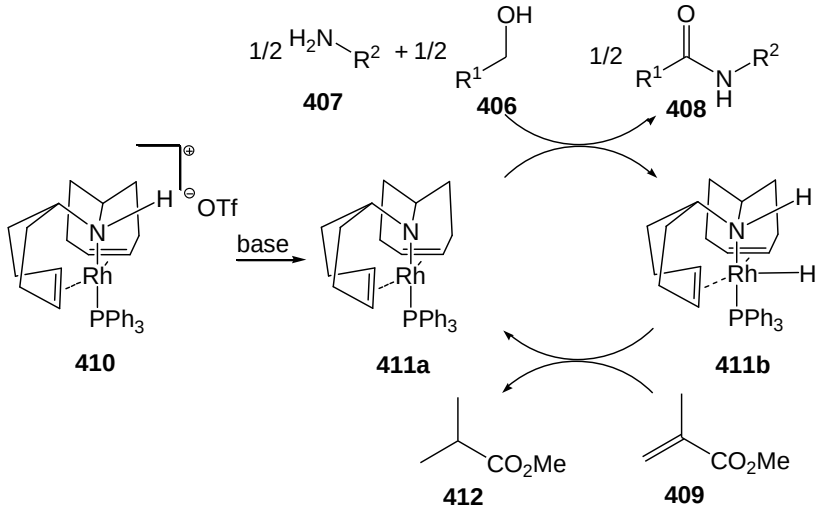


Figure 31: Simplified mechanism of Dehydrogenative Coupling (DHC) of amines **407** and alcohols **406**.

3. Boronic Acids in Direct Carboxamidation

A recent survey showed that the majority of the existing methods used by pharmaceutical companies for the synthesis of amides, had very poor atom economy.[168] These methods were categorised by three main features such as wide utility, scalability and greenness (**Figure 32**).

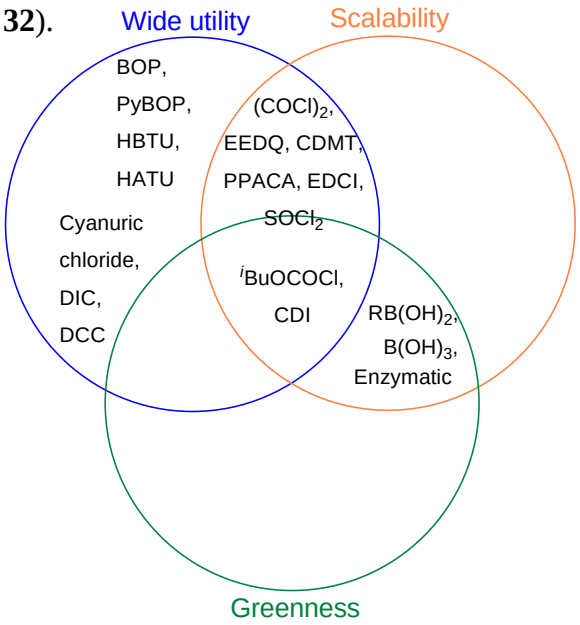
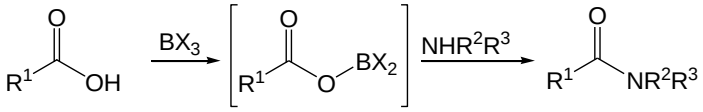


Figure 32: Venn diagram of amide formation from acids (examples which are not prone to racemisation). Adopted with changes from, with the permission of the Royal Society of Chemistry.[162]

Methods outside the greenness-zone had serious health issues and/or bad atom/redox economy. Therefore, they have been avoided more and more in the pharmaceutical industry. All reagents being widely used are applied in stoichiometric quantities. The application of boronic acids and enzymes are among the emerging methods aiming to render direct carboxamidation catalytic. Enzymatic catalysis has not yet gained wide utility, due to the poor substrate tolerance of enzymes available. Intensive research has been done on the field of boronic acid catalysed direct amide bond formation.

Several boron reagents such as $ClB(OMe)_2$,[169] $HB(OR)_2$, $H_3B.NR_3$,[170] $F_3B.Et_2O$[171] and catecholborane[172] were shown to react with carboxylic acids to form acyloxyboronate/borane compounds **413** (**Scheme 135**). These activated intermediates then reacted with amines to afford amides **354**. However, even under harsh conditions, the rate of these reactions was low.



308 **413** **354**

BX_3 = $Cl(OMe)_2$, $HB(OR)_2$, $H_3B.NR_3$, $F_3B.Et_2O$, catecholborane

Scheme 135: Activation of carboxylic acids **308** with different kind of boron reagents.

In 1996, the first direct carboxamidation was published by Yamamoto, using a catalytic amount (5 mol%) of arylboronic acid.[173] The reason for placing EWGs on the phenyl group was twofold. Electron poor arylboronic acids were less likely to undergo protodeboronation, which might destroy the catalyst at higher temperature. On the other hand they served as a better LG, therefore accelerating the aminolysis step. The same group isolated and characterised mono(acyloxy)boronic acid **415**. On the basis of this result a catalytic cycle was proposed in which the carboxylic acid **308** was activated by

forming intermediate **415** (**Figure 33**). The experimental results also suggested that formation of intermediate **415** was the rate-determining step.

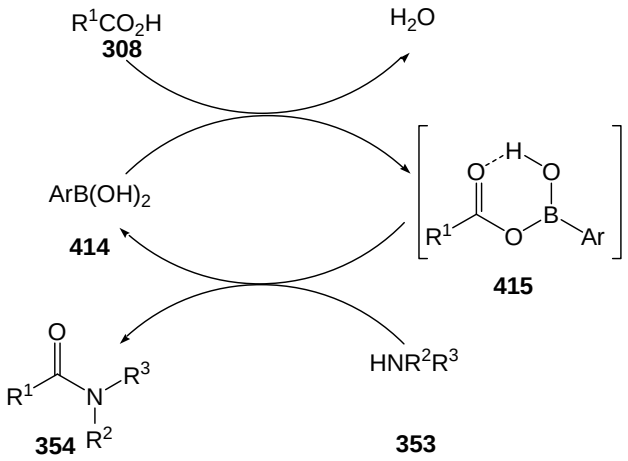
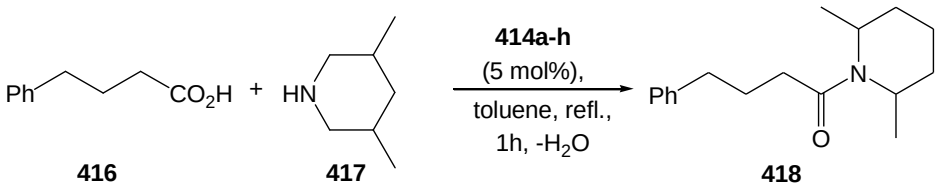


Figure 33: Catalytic cycle proposed for direct carboxamidation.

A wide range of electron deficient arylboronic acids **414a-h** were tested (**Table 21**). Yields under thermal conditions were minimal.



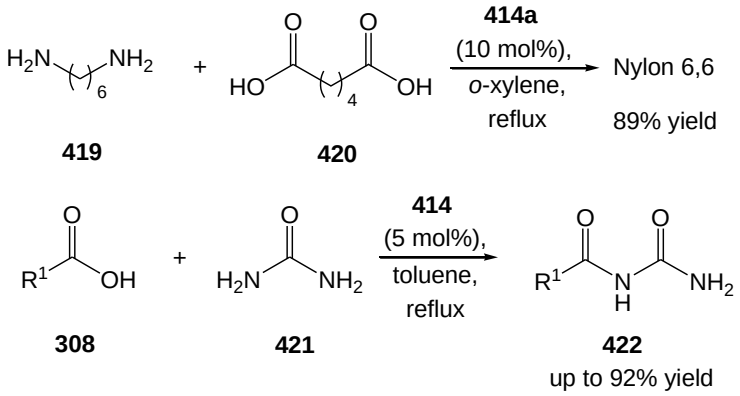
Entry	**414**	Ar	Y(%)	Entry	**414**	Ar	Y(%)
1	a	3,4,5-$F_3C_6H_2$	74	5	e	C_6H_5	23
2	b	3-$NO_2C_6H_4$	60	6	f	2,4,6-$(CF_3)_3C_6H_2$	21
3	c	3,5-$(CF_3)_2C_6H_3$	56	7	g	2,3,4,5-F_4C_6H	11
4	d	4-$CF_3C_6H_4$	54	8	h	no catalyst	<2

414a-h = $ArB(OH)_2$

Table 21: Direct amidation using electron deficient arylboronic acids.

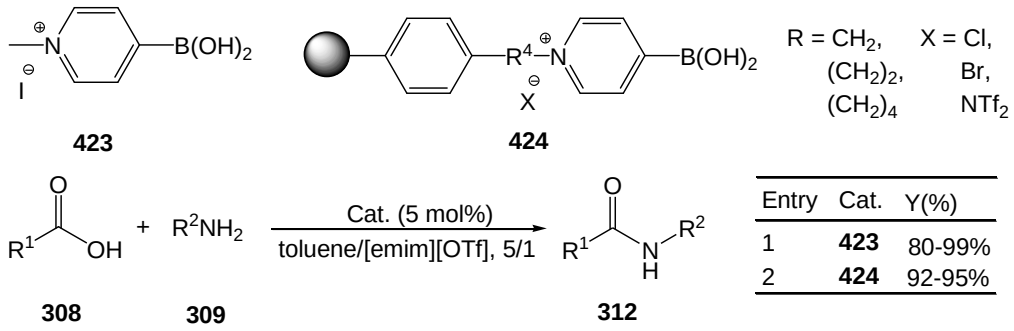
The scope of the method was tested on a variety of different amines and carboxylic acids with good yields (up to 99%). In addition amidation of optically active carboxylic acids proceeded with only a small loss of enantiomeric purity (<2% *ee*). As an extension of their work the same group applied these arylboronic acids to direct

polycondensation of dicarboxylic acids **420** and diamines **419** (**Scheme 136**).[174] Less reactive coupling partners such as ureas **421** gave *N*-acylureas **422** in good yield.[175]



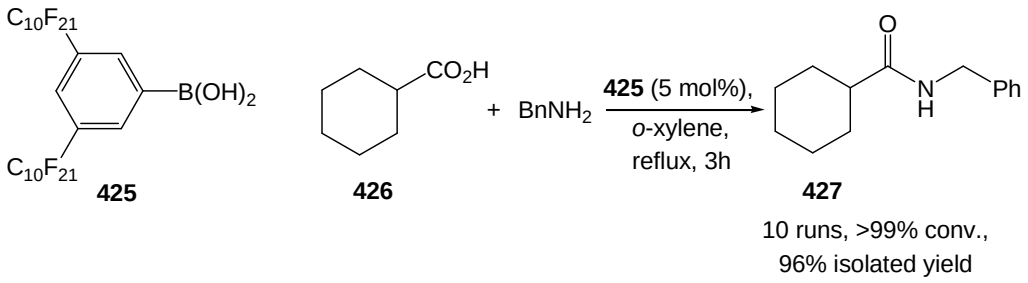
Scheme 136: Boronic acid catalysed synthesis of Nylon 6,6 and N-acylureas **422**.

In 2000 Ishihara and co-workers synthesised *N*-alkyl-4-boronopyridinium salt **423** which proved to be an efficient, reusable catalyst for direct carboxamidations. This catalyst tolerated polar solvents as well (**Scheme 137**). Later polymer-bound analogues of 4-boronopyridinium salts **424** were developed and used successfully in direct carboxamidations. These catalysts were thermally stable and reusable (no change in the yield after three consecutive runs).[176]



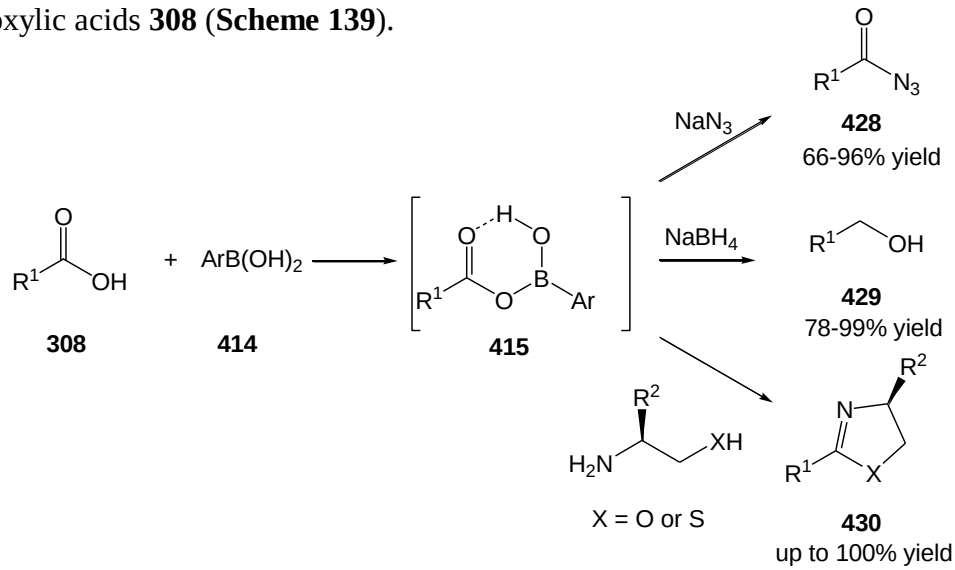
Scheme 137: 4-Boronopyridinium salts **424** were reusable.

The same group designed arylboronic acids bearing fluorous ponytails.[177] Compound **425** was successfully applied to fluorous bi-phasic catalysis (FBC) (**Scheme 138**).



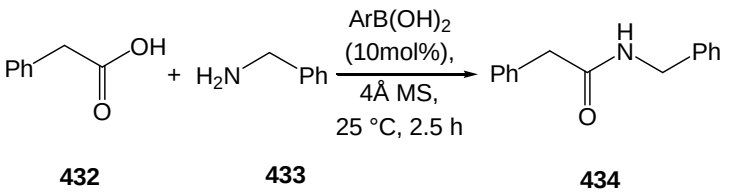
Scheme 138: Boronic acid **425** was successfully applied to FBC.

Electron deficient arylboronic acids **414** were also successfully applied to the synthesis of acyl azides **428**,[178] oxazolines/thiazolines **430**,[179] and alcohols **429**,[180] from carboxylic acids **308** (**Scheme 139**).



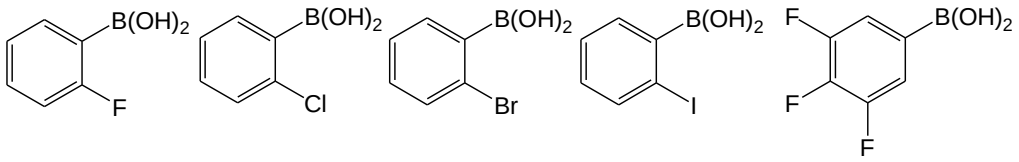
Scheme 139: Other synthetically useful compounds **428**, **429** and **430** can be accessed under boronic acid catalysed conditions.

Later, Hall investigated direct carboxamidations using 45 different *ortho*-functionalised arylboronic acids.[181] The reactions were run at ambient temperature with equimolar amounts of carboxylic acid **432** and amine **433**. The activity of halo-derivatives decrease in the order of **431d**>**431c**>**431b**>**431a** which suggests that inductive effects can not alone be responsible for the activity of these compounds (**Table 22**).



432 **433** **434**

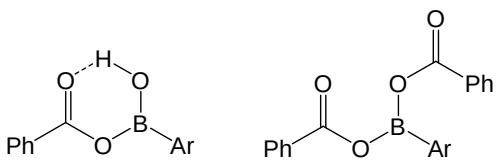
Entry	$ArB(OH)_2$	Y(%) THF	Y(%) CH_2Cl_2
1	**414a**	22	42
2	**431a**	27	41
3	**431b**	47	64
4	**431c**	49	76
5	**431d**	71	91



431a **431b** **431c** **431d** **414a**

Table 22: Direct carboxamidation catalysed by arylboronic acids.

The corresponding intermediate **415** proposed originally by Yamamoto was isolated from the reaction mixture, although diacylboronate **435** might also be involved in the reaction (**Figure 34**).



415 **435**

Figure 34: Mono(acyloxy)boronic acid intermediate **415** was isolated from the reaction.

In addition, they envisaged that in a similar fashion, *α,β*-unsaturated carboxylic acids **436** might be activated by the formation of acyloxyboronic acids. Therefore these arylboronic acids **431a-e** were tested in other very synthetically useful transformations such as 1,4-addition or Diels-Alder reactions (**Figure 35**).[182]

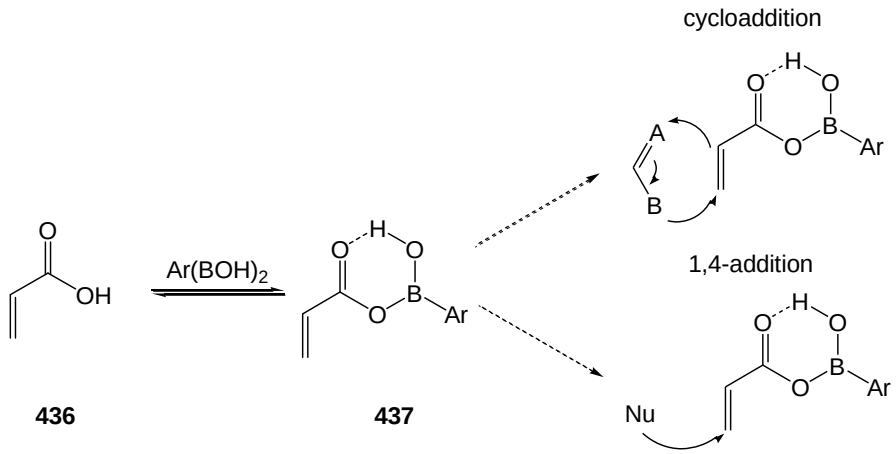


Figure 35: LUMO-lowering activation of *α*,*β*-unsaturated carboxylic acids.

The structure of the active intermediate was further discussed by Marcelli in 2011, who used density functional theory (DFT) to identify the reaction going through the lowest energy transition states.[183] The calculations supported the intermediacy of **415** proposed by Yamamoto. Reaction *via* diacylboronate intermediate **446** proposed by Whiting (*vide supra*) was found to have a significantly higher overall energy barrier. Hemiaminal dehydration was the rate determining step with formation of *cis*-amide significantly favoured (**Figure 36**). The high activity of *ortho*-haloarylboronic acids was elucidated in terms of Lewis basicity of the substituting halogens (I>Br>Cl>F). This ability helps to stabilise the intermediate **438**, therefore lowering the energy of the transition state.

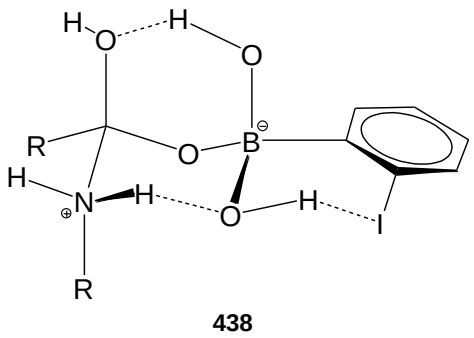


Figure 36: Lowest energy structure of the transition state in the rate-determining step.

Houston *et al*. applied boric acids to the selective formation of esters from *α*–hydroxy carboxylic acids under mild conditions (ambient temperature).[184] Under these conditions *β*–hydroxy carboxylic acid or simple carboxylic acid moieties were left untouched within the same molecule. Based on this observation the proposed mechanism involved cyclic boronate ester intermediates **441** or **442** (**Figure 37**). Whether the attack of the alcohol is inter- or intramolecular is not clear.

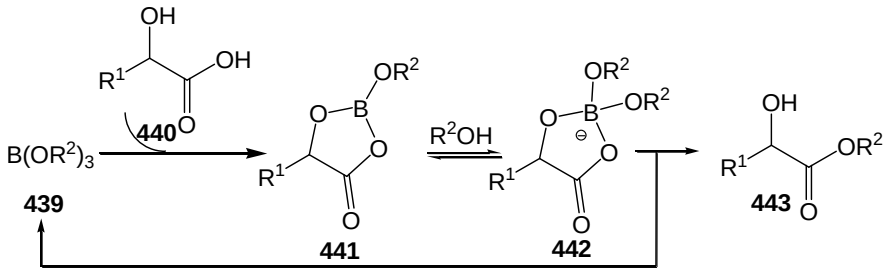


Figure 37: Catalytic cycle proposed by Houston for the boric acid **439** assisted esterification of *α*–hydroxy carboxylic acids **440**.

In 2006, Whiting published their results on catalytic direct carboxamidation using bifunctional arylboronic acids **444a**,**b** (**Figure 38**).[185] Diisopropyl derivative **444a** was more active, which can be explained by the obstructed intramolecular B-N coordination of the more hindered nitrogen. Their aim was to make the conditions of this transformation milder. Therefore the reactions were conducted in refluxing fluorobenzene (84 °C). In addition, they wanted to get a better picture of the degree of the competing thermal amide formation. At lower temperatures catalysts **444a**,**b** gave better results than arylboronic acid **414a**.

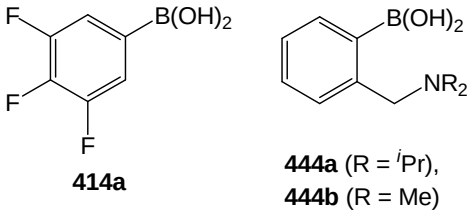


Figure 38: Catalysts **444a** and **444b** gave better yields at lower temperatures.

Under these conditions, the thermal background-reaction was found to be minimal. The bifunctional nature of the catalyst is believed to be important, however, its mode of action is not fully understood. In accordance with Yamamoto's results, derivatives bearing EWGs on the phenyl ring such as **444c-f** gave better yields **(Figure 39**).[186] The difference in activity of **444a,b** and **444c-f** is not substantial, therefore, commercial availability of **444a,b** makes it more attractive at the moment.

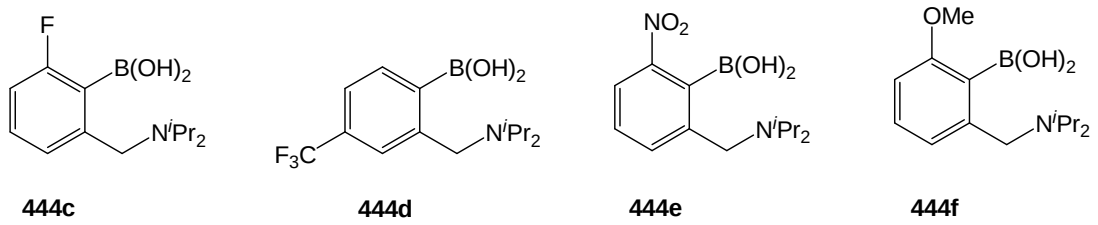


Figure 39: Bifunctional derivatives bearing EWGs.

Using soft ionisation electrospray mass spectrometry showed the existence of species **445**, **446** and **447** (**Figure 40**). The corresponding intermediate **415** (proposed by Yamamoto) was not observed.

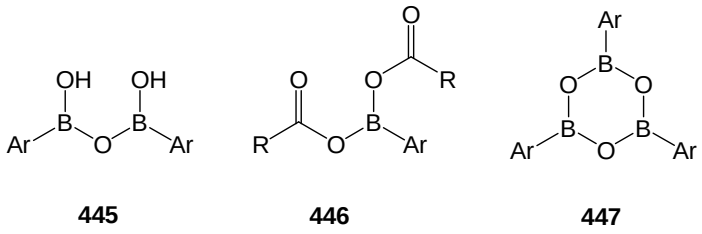
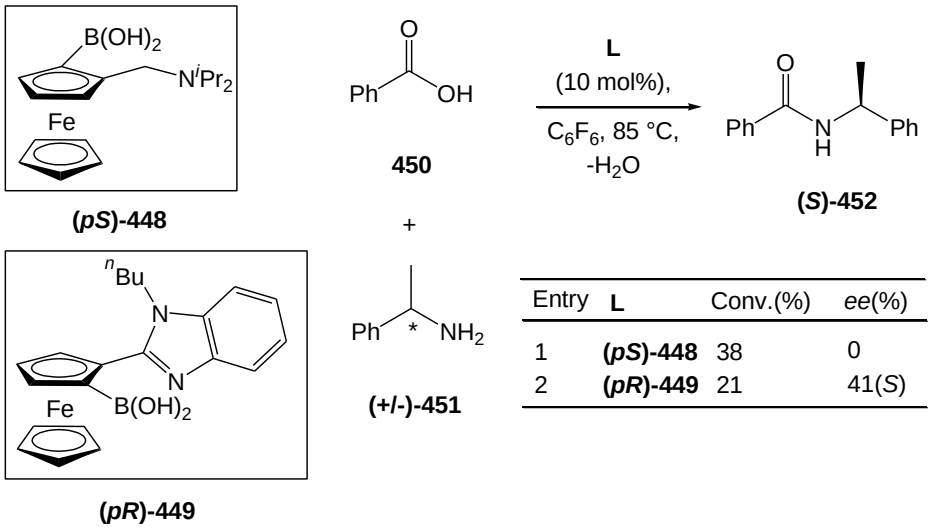


Figure 40: Intermediates detected by soft ionisation electrospray mass spectrometry.

4. Asymmetric Amide Bond Formation

Direct amide formation has been known and utilised for 150 years. Asymmetric direct amide formation has been much less investigated until recent years. In 2008, Whiting reported an asymmetric direct carboxamidation protocol using bifunctional catalysts.[187,188] Planar chirality served as a source of stereochemical information in these molecules. Although ligand **(*pS*)-448** did not show activity, boronic acid **(*pR*)-449** gave the product in 41% *ee* (**Scheme 140**).



Entry	L	Conv.(%)	*ee*(%)
1	**(*pS*)-448**	38	0
2	**(*pR*)-449**	21	41(*S*)

Scheme 140: Asymmetric direct carboxamidation using planar chiral **(*pR*)-449**.

The observed asymmetric induction was explained on the basis of the benzimidazole group acting not as a steric block but more as a Lewis basic functionality. The ligand could bind to the amine **(*pR*)-449** by H-bonding, therefore, one of the enantiomers to the activated diacylboronate **(*pR*)-453** (**Figure 41**). In the case of **(*pS*)-448** the more basic dialkyl amine functionality acted more as a base. After protonation, differentiation between the enantiomers of the incoming nucleophile was not possible.

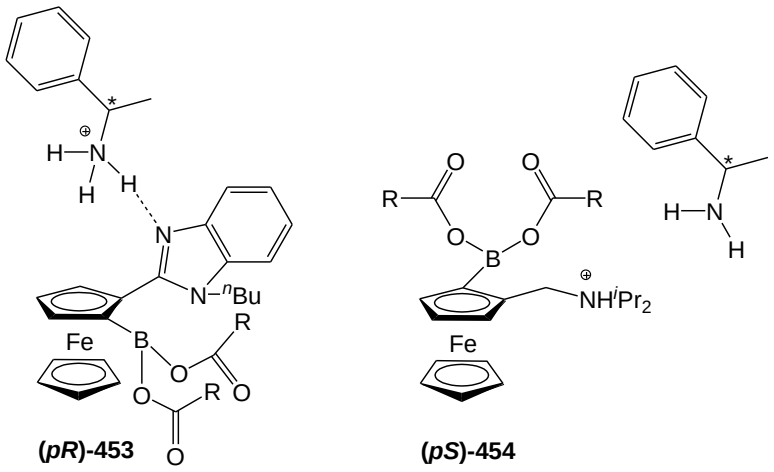
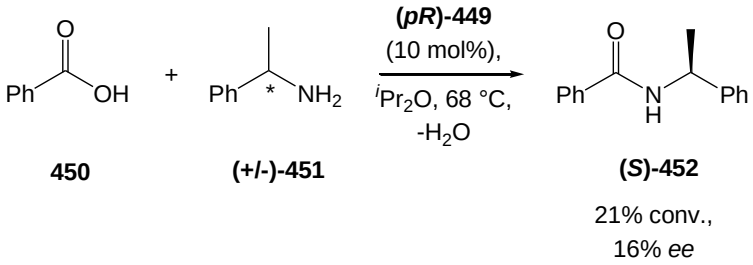


Figure 41: H-bonding is believed to be responsible for asymmetric induction.

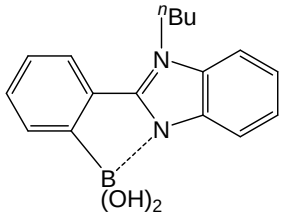
The background reaction might have an effect on the low *ee*. Catalyst **(*pR*)-449** underwent proto-deboronation under the reaction conditions to a certain extent. The boronic acid produced is known to enhance the rate of direct carboxamidations at elevated temperatures and probably acted as a non-asymmetric catalyst in this case. Although by conducting the experiment at 68 °C in $^{i}Pr_2O$ the background reaction was supressed, surprisingly it did not result in improvement of the *ee* (16%, **Scheme 141**).



Scheme 141: Lowering the temperature resulted in lower asymmetric induction.

In the course of looking for a more active catalyst, benzimidazole **455** was synthesised (**Figure 42**). It showed no activity in the reaction. This result was explained by the N-B chelation in these compounds, which is supported by ^{11}B NMR. The distance between

the nitrogen and the boron atoms is shorter than in ferrocenyl derivative which was probably responsible for a higher level of N-B chelation.



455

Figure 42: Inactivity of benzimidazole **455** is explained by B-N chelation.

Despite the transfer of stereochemical information in this process not being fully understood, the distance of boron and nitrogen atoms seemed crucial for the efficient asymmetric induction.

5. Ligand design

On the basis Whiting's work, we aimed to synthesise bifunctional azaferrocenylboronic acid **457** (**Figure 43**). In our ligand **457**, planar chirality would serve as a source of stereochemical information. The basicity of the protonated azaferrocenyl nitrogen (pKa = 4.65) should not allow high amounts of deprotonation under amidation conditions, therefore, leaving the nitrogen lone pair free for H-bonding. On the other hand, the ability of azaferrocenes to form coordination complex such as **458** is well documented. By altering the steric environment around the boron and nitrogen atoms (Cp*) the level of B-N chelation could be controlled.

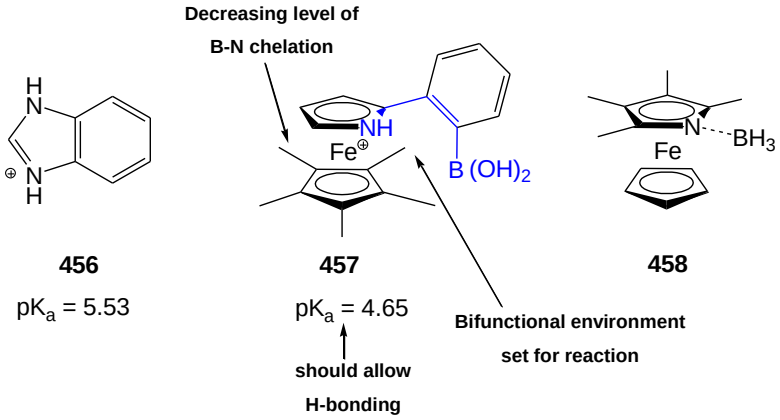
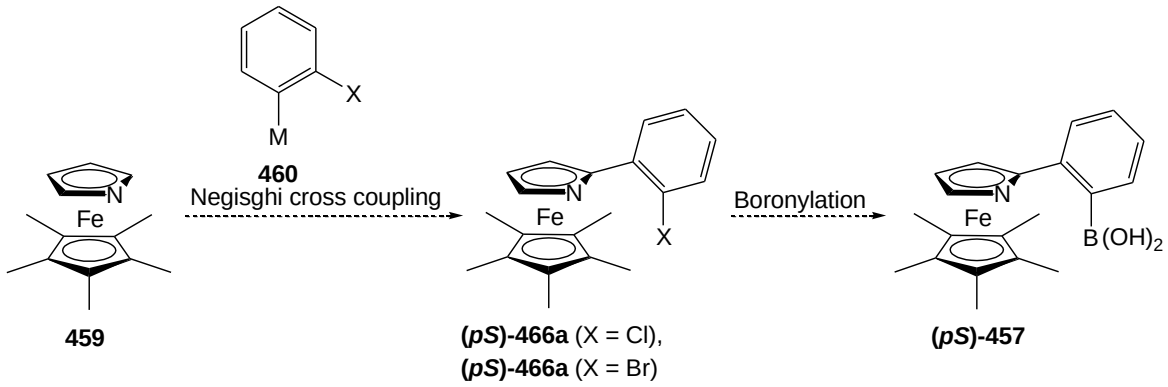


Figure 43: Benzimidazole **456**. Our target ligand **457** and azaferrocenyl borane **458**.

Taking advantage of the previous work done on the field of azaferrocenes (**page 35**) within the group we planned to synthesise the desired compound by the route depicted in (**Scheme 142**).[72]



Scheme 142: Devised synthetic route to azaferrocenylboronic acid **(*pS*)-457**.

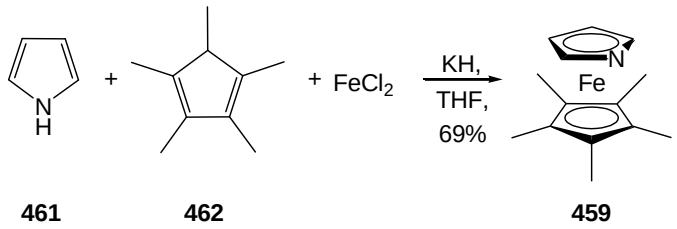
This simple two step sequence would give access to **(*pS*)-457** which we plan to use in asymmetric direct carboxamidation reactions.

1. Synthesis of 1',2',3',4',5'-pentamethylazaferrocene

Azaferrocene **152** was synthesised according to Fu's procedure (**Scheme 143**).[66]

Yields were also improved from 53 to 69% after optimisation. Three factors seemed to be crucial for the isolation of the product in high yield. This procedure was reproducible on a 5 gram scale.

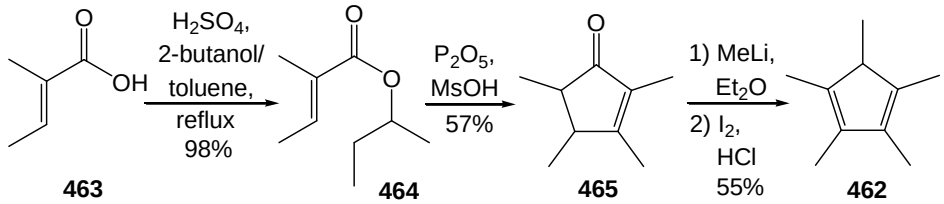
- $FeCl_2$ was dried under vacuum at 100 °C overnight prior to the reaction. Vigorous stirring also helped to grind the $FeCl_2$ lumps into a fine powder.
- During workup the bulk amount of the THF was removed under reduced pressure at 40 °C.
- Filtration was performed using EtOAc which seemed to dissolve much less unreacted $FeCl_2$, therefore making the column chromatography easier.



461 **462** **459**

Scheme 143: Synthesis of 1',2',3',4',5'-pentamethylazaferrocene **459**.

Pentamethyl cyclopentadiene **462** was synthesised by the following route (**Scheme 144**).[189]

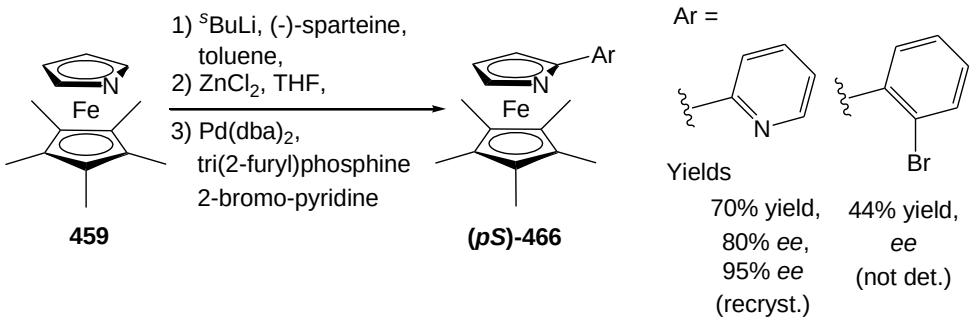


463 **464** **465** **462**

Scheme 144: Synthesis of 1,2,3,4,5-pentamethyl cyclopentadiene **462**.

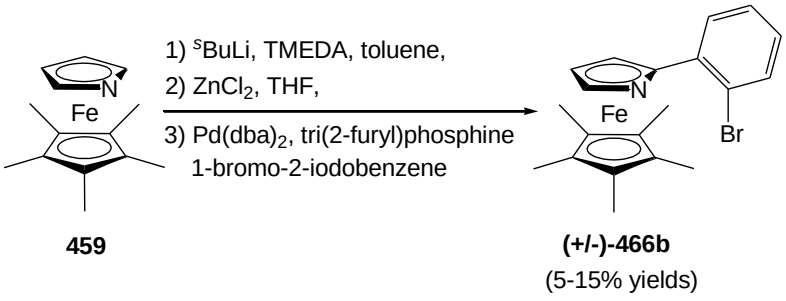
2. Introduction of the aromatic functionality

The aromatic functionality was introduced by a Negishi cross coupling reaction. This procedure was developed by the Anderson group previously.[72] In the course of this work several other conditions were tested but Negishi cross coupling gave the best yields. With the utilisation of (-)-sparteine, enantioselective deprotonation was posssible on azaferrocenes **459** allowing access to the aryl derivatives **(*pS*)-466** in enantiomerically enriched form. The *ee*s could be further improved by recrystallisation (**Scheme 145**).



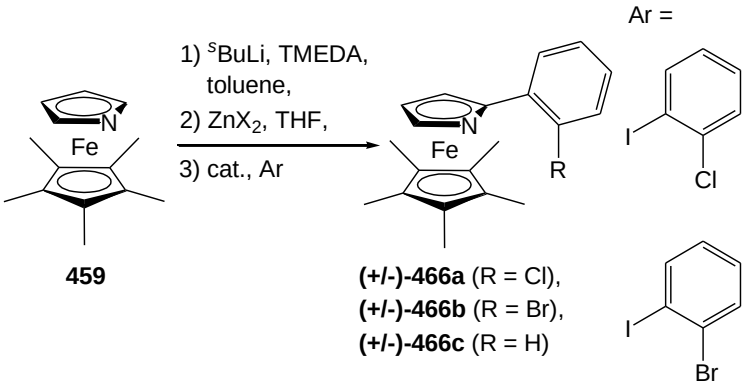
Scheme 145: Synthesis of **(*pS*)-153** by asymmetric deprotonation, followed by a Negishi cross coupling.

Initially, experiments were carried out under racemic conditions. The reaction was extremely sensitive to moisture and the $ZnCl_2$ had to be dried (under vacuum) prior to the reaction and used as a THF solution. Altogether the reaction gave lower yield for **(+/-)-466b** (5-15%) and the yields were variable (**Scheme 146**).

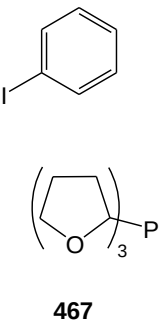


Scheme 146: Synthesis of bromide **(+/-)-466b** by Negishi cross coupling.

Our attempts to further develop the procedure gave no significant improvement in the yield. Zinc bromide gave higher yields than $ZnCl_2$ (**entries 5**, **6**, **7** and **8**, **Table 23**), however, preparation of anhydrous $ZnBr_2$ solution is more difficullt due to the higher melting point of $ZnBr_2$. Commercially available $ZnCl_2$ solution gave no product. On the other hand 2-chloro-1-iodobenzene gave better yields than 2-bromo-1-iodobenzene (**entries 5**, **6**, **7** and **8**, **Table 23**). Iodobenzene gave 43% (unoptimised, **entry 9**, **Table 23**) yield. Regarding the catalyst, the $Pd(dba)_2$, tri(2-furyl)phosphine **467** combination proved to be the most efficient, however, yields were still variable and seemed to depend significantly on the quality of the prepared THF solution of ZnX_2 (**Table 23**).



Entry	ZnX_2	cat.	Ar	Y (%)
1	$ZnCl_2$	$Pd[P(^tBu)_3]_2$	**I/Br**	-
2	$ZnCl_2$	$Pd(PPh_3)_4$	**I/Br**	-
3	$ZnCl_2$	$Pd(dba)_2$+dppf	**I/Br**	-
4	$ZnCl_2$	$PdCl_2(PPh_3)_2$	**I/Br**	6
5	$ZnCl_2$	$Pd(dba)_2$, **467**	**I/Br**	17
6	$ZnCl_2$	$Pd(dba)_2$, **467**	**I/Cl**	30
7	$ZnBr_2$	$Pd(dba)_2$, **467**	**I/Br**	30
8	$ZnBr_2$	$Pd(dba)_2$, **467**	**I/Cl**	49
9	$ZnCl_2$	$Pd(PPh_3)_4$	**I**	43

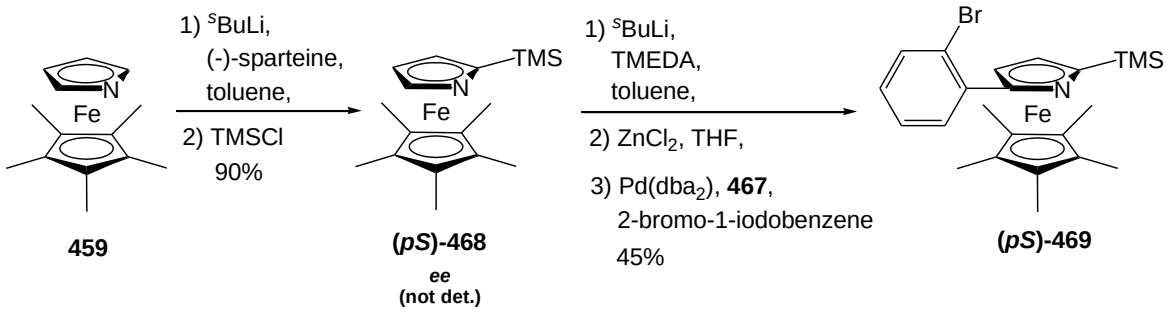


467

Table 23: Optimisation of Negishi cross coupling.

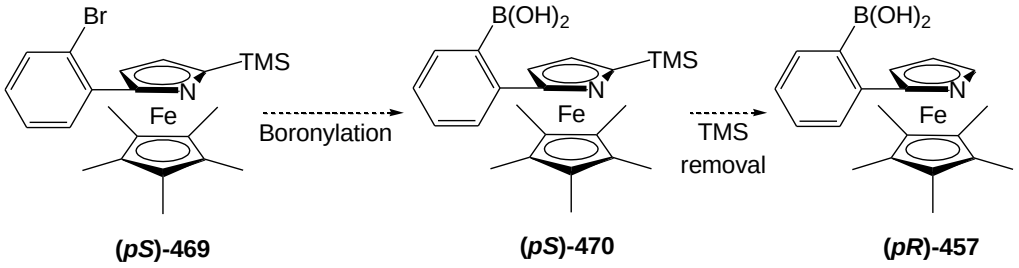
We were not entirely sure which other factors affected the yield. However TMS-substituted azaferrocene was found to give the bromo substituted derivative **(*pS*)-469** in slightly better yield (45%, unoptimised), when using $ZnCl_2$ as a metallating agent (**Scheme 147**). The presence of an EDG on the azaferrocene ring seemed to affect the

yield of the cross coupling reaction. In addition the TMS group blocks one of the acidic sites which might be exploited in the next (boronylation) step. The TMS group might be beneficial to get to the **(*pR*)**-series of these azaferrocene derivatives (see TMS-trick, **page 41**).



Scheme 147: Synthesis and reaction of TMS derivative **(*pS*)-468**.

This TMS-substitution method can be a useful approach to get to our target compound **(*pS*)-457**, as long as the removal of the TMS group can be achieved in a good yield (**Scheme 148**).



Scheme 148: Devised synthestic sequence to boronic acid **(*pS*)-457**.

At this point of our research we focused on the introduction of the boronic acid functionality into the *α*–position of the aromatic group (*vide supra*). Due to lack of time, this route (**Scheme 146** and **147**) was not further investigated.

3. Introduction of the boronic acid functionality

Three main approaches exist for boronylation: electrophilic borate trapping, transition metal-catalysed coupling using diboronyl reagents and transmetallation of arylsilanes or arylstannanes (**Figure 44**).[190]

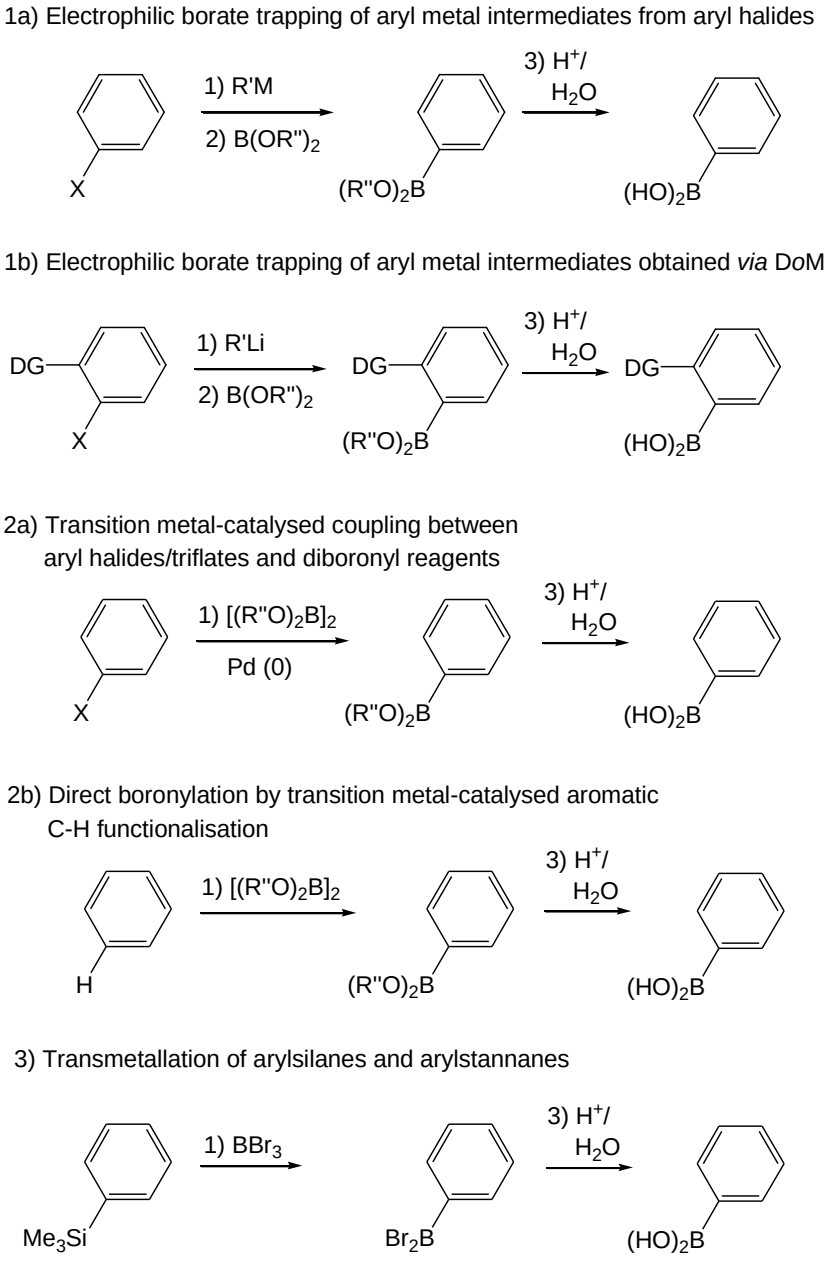
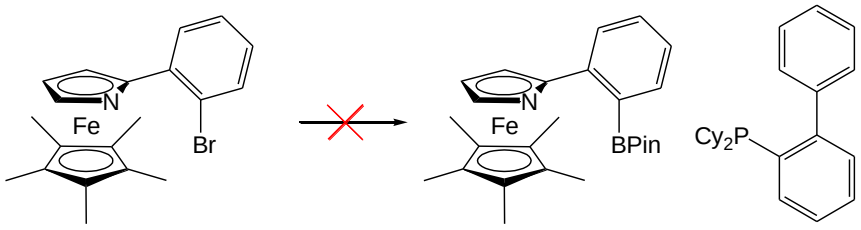


Figure 44: Common methods for synthesising arylboronic acids.

3.1 Transition metal-catalysed coupling

In 1995, Miyaura found that tetraalkoxydiboron compounds could be coupled with aromatic halides in the presence of catalytic amount of $PdCl_2$(dppf) to give aryl-boronic esters.[191]

Reactions attempted using Miyaura conditions did not give the desired product **(+/-)-471**.[4,192] The reactions resulted in decomposition of the starting material and isolation of some other unidentified by-products (**Table 24**).



(+/-)-466b **(+/-)-471** **472**

Entry	cat.	Base	B.agent	Solvent	T(°C)	Y (%)
1	$PdCl_2$(dppf) (3 mol%),	KOAc	HBPin	DMSO	80	-
2	$PdCl_2$(dppf) (3 mol%),	KOAc	$BPin_2$	DMSO	80	-
3	$Pd(OAc)_2$ (5 mol%), **472** (20 mol%)	Et_3N	HBPin	Dioxane	80	-

Table 24: Unsuccessful Miyaura-borylations.

3.2 Transmetallation of arylsilanes

Arylsilanes are known to react with boronylating reagents such as BBr_3. The driving force for this transformation relies on the stability of the C-B (356 kJ/mol), Si-Br (310 kJ/mol) bonds compared to those in the substrates C-Si (318 kJ/mol), B-Br (377 kJ/mol).[189] The reaction possibly passing through intermediates **474** and **475** where Si stabilises the α–positive charge (**Figure 45**).

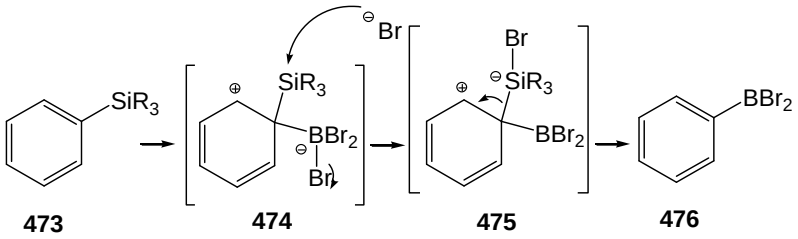
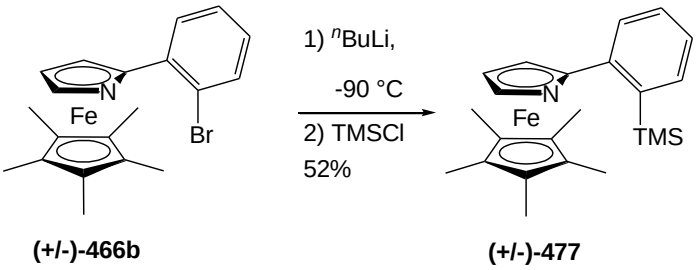


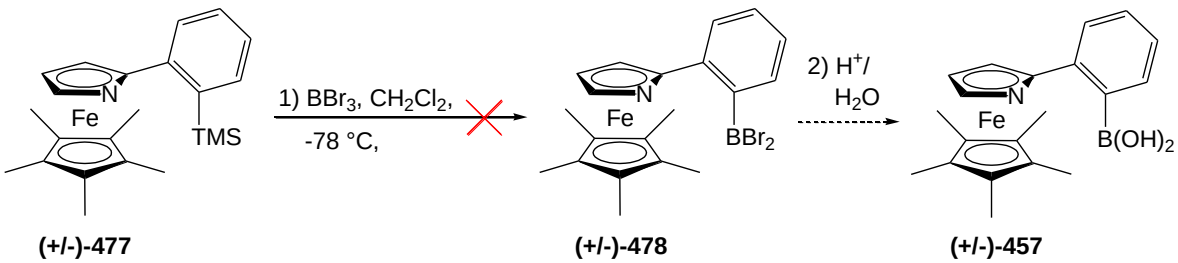
Figure 45: Reaction mechanism of transmetallation of arylsilanes **473**.

TMS derivative **(+/-)-477** was synthesised from bromide **(+/-)-466b** by lithium-halogen exchange, followed by electrophilic trapping, in 52% (unoptimised) yield. It is also worth mentioning that other TMS-substituted by-products were also formed, which might be the result of the TMS-trapping of intermediates formed by competing deprotonation adjacent to pyrrolyl N or methyl group of Cp* even at -90 °C (**Scheme 149**).



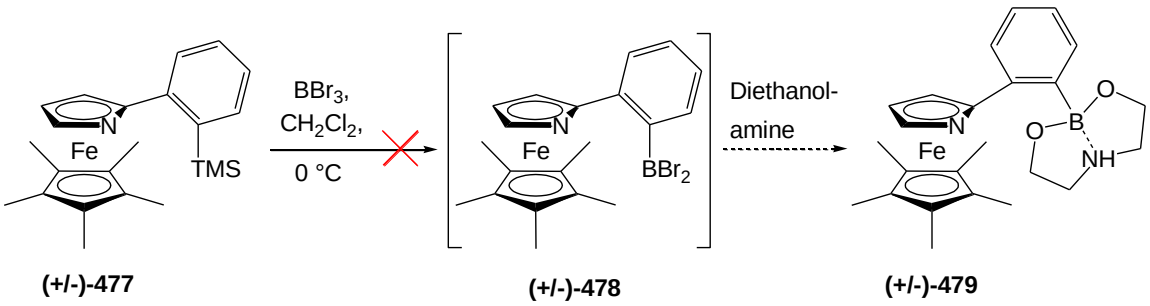
Scheme 149: Synthesis of TMS derivative **(+/-)-477**.

TMS derivative **(+/-)-477** was then reacted with BBr_3.[193] This reaction resulted in rapid decomposition of the starting TMS derivative **(+/-)-477** (**Scheme 150**).



Scheme 150: Attempted boronylation of TMS deivative **(+/-)-477**.

In another reaction, diethanolamine was added to the mixture before the addition of BBr_3 in order to *in situ* trap the intermediate **(+/-)-478** as a borate ester **(+/-)-479**. This reaction also led to decomposition of the starting material (**Scheme 151**).

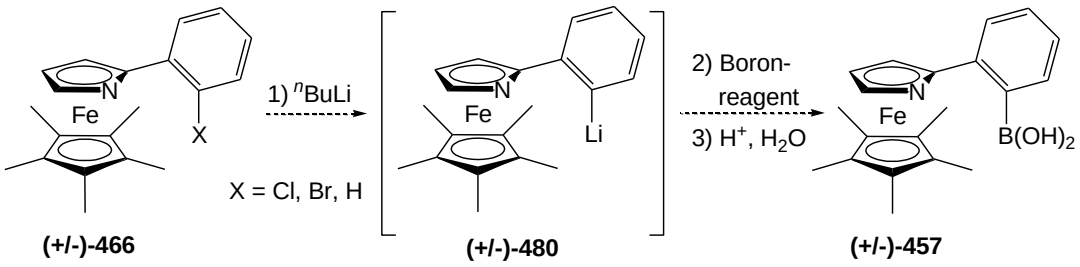


(+/-)-477 **(+/-)-478** **(+/-)-479**

Scheme 151: Attempted *in situ* formation and trapping of borane **(+/-)-478**.

3.3 Electrophilic borate trapping

To introduce the boronic acid functionality, first the *ortho*-position must be metallated (deprotonation, or halogen-metal exchange) which can be then quenched with an electrophilic boron reagent (**Scheme 152**).



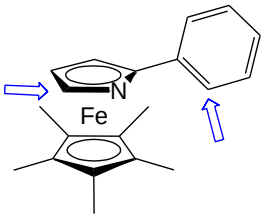
(+/-)-466 **(+/-)-480** **(+/-)-457**

Scheme 152: Approach to introduce boron functionality.

3.3.1 DoM by Deprotonation

Azaferrocenes can be *ortho*-substituted without bearing a DG. This is due to the fact that the nitogen exerts a directing effect, therefore, facilitating the deprotonation in the

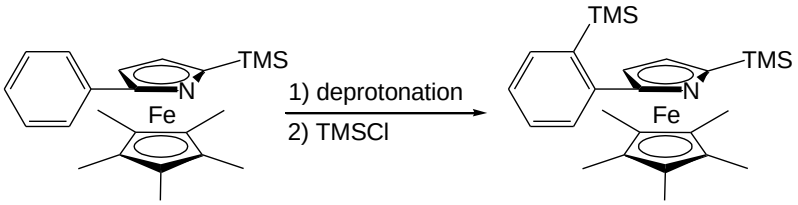
ortho-position, adjacent to the N-atom. We were wondering whether this can be exploited in order to deprotonate the neighbouring phenyl group at the *ortho*-position (**Figure 46**).



(+/-)-466c

Figure 46: Possible positions for deprotonation.

To find out the difference between the ease of deprotonation at the azaferrocenyl-*ortho*- and the phenyl-*ortho*-positions a set of different conditions were tried. Having only one possible position to deprotonate TMS derivative **(*pS*)-469b** was treated with ^{s}BuLi in the presence of TMEDA (**entry 1**, **Table 25**). The starting material did not react under these conditions. Then TMEDA was omitted which was thought to decrease the activity of ^{s}BuLi (**entry 2**, **Table 25**). In another experiment a longer deprotonation time was used (**entry 3**, **Table 25**) but again no reaction was observed.

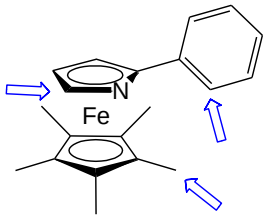


(*pS*)-469b **(*pS*)-481**

Entry	Base	Additive	Time	Solvent	Y (%)
1	^{s}BuLi	TMEDA	1h	THF	-
2	^{s}BuLi	-	1h	THF	-
3	^{s}BuLi	-	4h	THF	-
4	^{t}BuLi	-	5h	^{n}hexane	-

Table 25: Deprotonation studies of TMS derivative **(*pS*)-469b**.

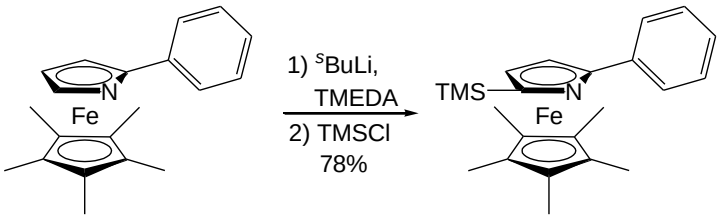
Deprotonation using ^{t}BuLi (**entry 4**, **Table 25**) gave an inseparable mixture of products which most probably consisted of the mono- and polysubstituted derivatives. In fact, substitution on the Cp*-ring has previously been reported.[64] Although the nitrogen has been shown to have directing ability it does not allow selective deprotonation in these systems (**Figure 47**).



(+/-)-466c

Figure 47: Positions, where deprotonation can occur.

Another experiment showed that monosubstituted azaferrocene **(+/-)-466c** is substituted primarily at azaferrocenyl-*ortho* position (**Scheme 153**).



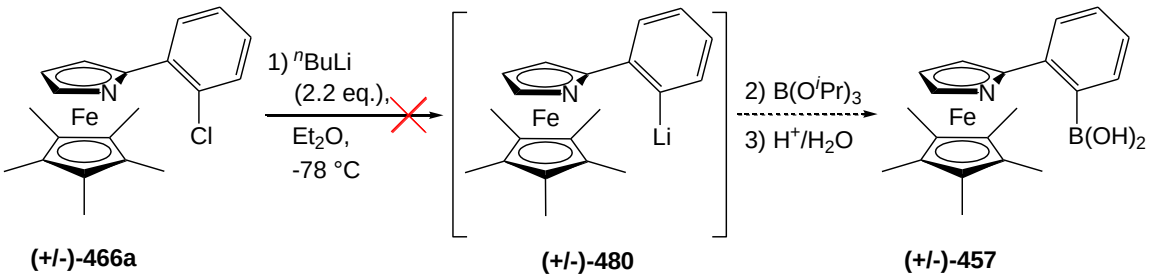
(+/-)-466c **(+/-)-469b**

Scheme 153: Substitution occured in azaferrocenyl-*ortho* position.

This turned our attention towards possible functionalisation of the phenyl group by lithium-halogen exchange.

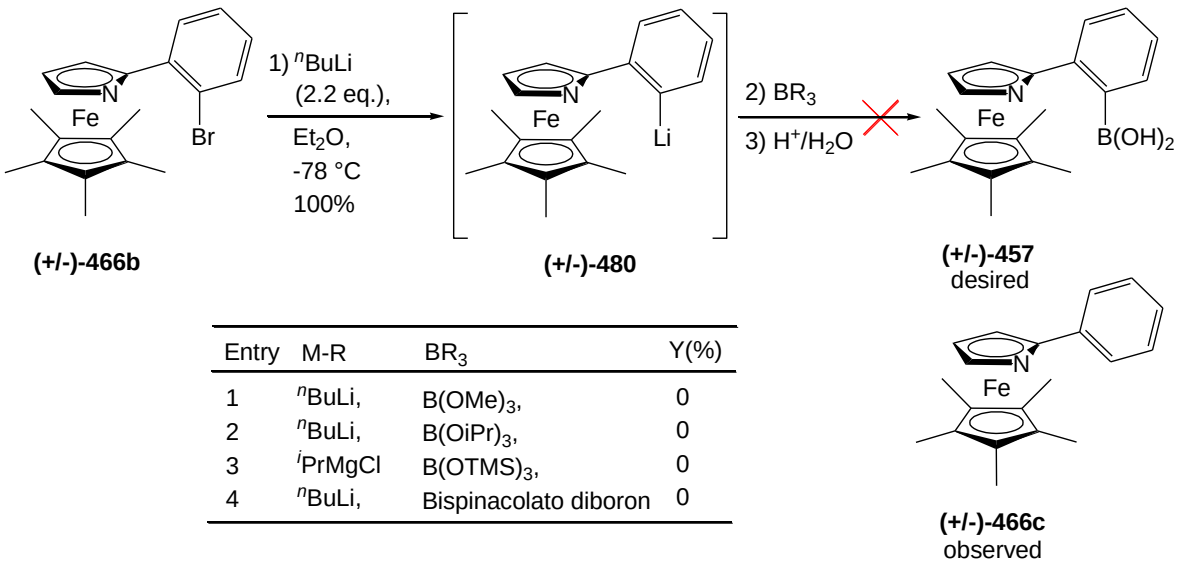
3.3.2 *Do*M by lithium-halogen exchange

Lithium halogen exchange seemed a more selective way of *ortho*-metallation. The nitrogen of the azaferrocene could potentially aid this transmetallation process. Chloro derivative **(+/-)-466a** failed to undergo lithium-halogen exchange (**Scheme 154**).



Scheme 154: Attempted lithium-halogen exchange of chloride **(+/-)-466a**.

On the other hand, bromo derivative **(+/-)-466b** gave the lithiated product almost quantitatively after 2 hours (judged by TLC) at -78 °C. Quenching the reaction mixture with $B(OMe)_3$ did not give the desired product **(+/-)-457**. In a series of reactions some other boronylating agents ($B(O^iPr)_3$,[194] $B(OTMS)_3$,[195] and bis((pinacolato)diboron) were tested (**Scheme 155**).



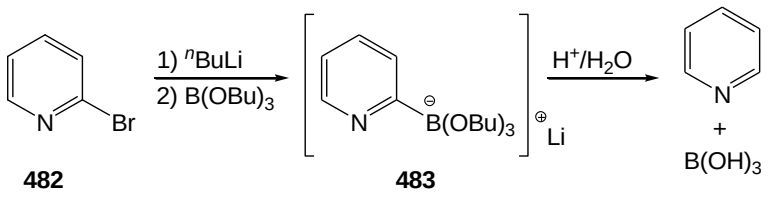
Entry	M-R	BR_3	Y(%)
1	^{n}BuLi,	$B(OMe)_3$,	0
2	^{n}BuLi,	$B(OiPr)_3$,	0
3	^{i}PrMgCl	$B(OTMS)_3$,	0
4	^{n}BuLi,	Bispinacolato diboron	0

Scheme 155: Boronylating agents failed to give boronic acid **(+/-)-457**.

In each of these reactions only the phenyl derivative **(+/-)-466c** was observed by TLC as a result of proton-quench of the intermediate lithium species **(+/-)-480**. It was hypothised that boronic acid **(+/-)-457** or the corresponding borate might be present in the reaction mixture, however, being extremely reactive, neither is observed nor can be isolated.

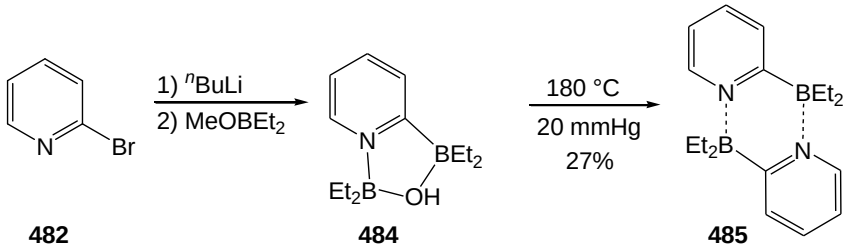
3.3.3 Alternative boronylating reagents

Despite the utility of heterocyclic boronic acids as building blocks for biologically active molecules they are employed less frequently than their non-heterocyclic analogues.[196] This stems from the fact that their synthesis can be difficult in some cases. Pyridinylboronic acids **482** for example have proven to be difficult to synthesise. The synthesis of 2-pyridinylboronic acid is still unresolved. The lithium borate salt **483** has been synthesised but proved to be unstable in protic solvent, giving back pyridine and boric acid as a result of proto-deboronation (**Scheme 156**).[197]



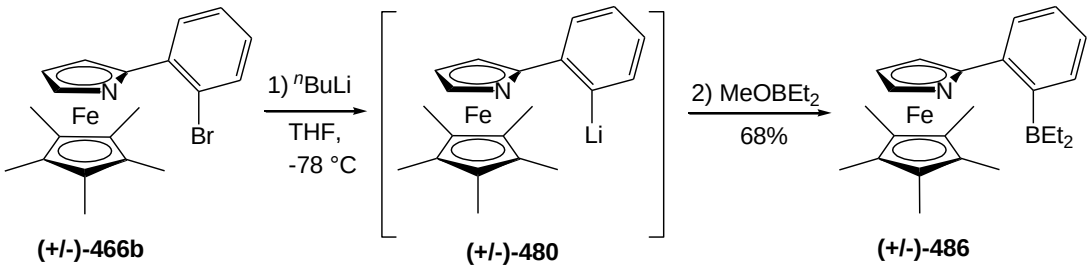
Scheme 156: Boronate **483** showed instability under protic conditions.

Using $MeOBEt_2$ as a boronylating agent borane **484** was isolated which proved to be stable to acidic work up.[198] This adduct at elevated temperature and under vacuum formed a stable compound which turned out to be a dimer **485**. The structure was later determined by X-ray crystallography (**Scheme 157**).[199]



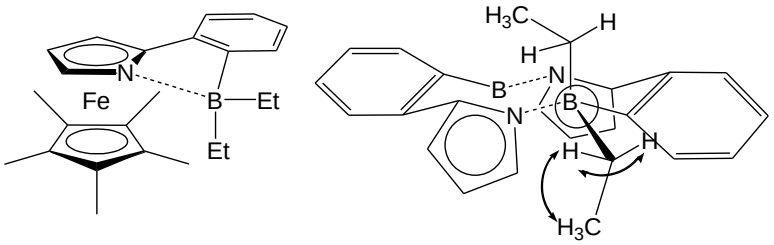
Scheme 157: Formation of dimer **485**.

After treating bromo derivative **(+/-)-466b** with ^{n}BuLi, $MeOBEt_2$ was added to the reaction. After two hours at r.t. borane **(+/-)-486** formed in good yield. This compound has improved stability compared to those of the parent bromo derivative **(+/-)-466b** or azaferrocene **459** itself, possibly due to C-N chelation (**Scheme 158**).



Scheme 158: Synthesis of borane **(+/-)-486**.

The NMR showed the ethyl groups to be diastereotopic. This has led us to a dimeric structure **(+/-)-486b**, or a 5-membered chelate structure **(+/-)-486a** for borane (**Figure 48**). On **Figure 48** in dimeric structure **(+/-)-486b** the azaferrocene units are omitted for clarity, but assumed to take an *exo* position. The two ethyl groups are more or less fixed between the *exo* azaferrocene unit and the phenyl group. Therefore rotation around the B-C bond is obstructed. This results in the chemical shifts of the methylene units and the methyl groups being different.



(+/-)-486a or **(+/-)-486b**

^{1}H NMR δ(ppm), *J*(Hz)
-0.01 (1H, dq, *J* = 13.2, 7.2, CH_2)
0.15 (3H, t, *J* = 7.4, CH_3)
0.32 (1H, dq, *J* = 13.3, 7.4, CH_2)
0.65 (1H, dq, *J* = 13.8, 7.6 CH_2)
0.78 (1H, dq, *J* = 13.6, 7.9 CH_2)
1.08 (3H, t, *J* = 7.5, CH_3)

Figure 48: NMR data suggest structures **(+/-)-486a** or **(+/-)-486a**.

According to the general mechanism proposed by Yamamoto (**page 116**) boron must bear hydroxyl functionalities in order to form activated mono(acyloxy)boronic ester **415** (**Figure 49**). The formation of di(acyloxy)boronic ester **435** was suggested by Whiting on the basis of soft ionisation electrospray mass spectrometry (**page 122**). Based on this mechanistic rational borane **(+/-)-486** is not suitable to catalyse direct amide bond formation. However it might find applications as a Frustrated Lewis Pair (FLP) (**page 147**).

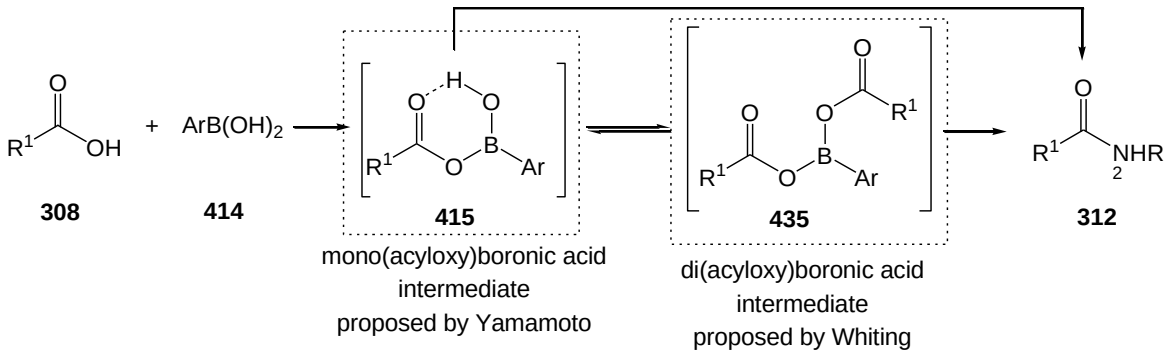
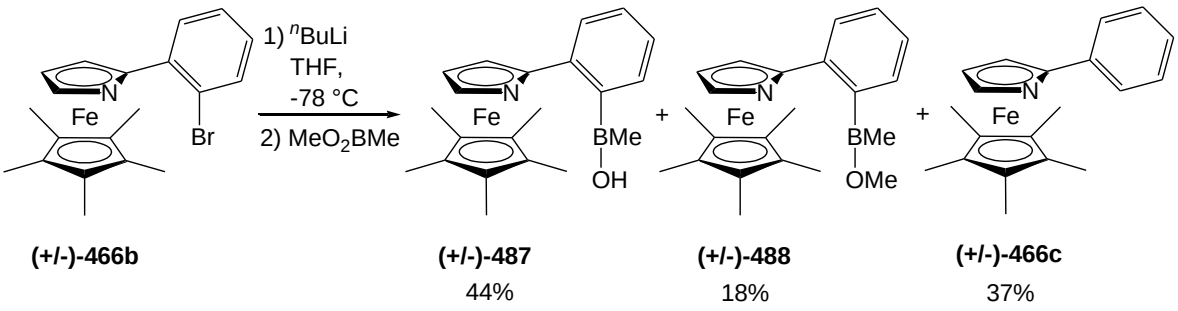


Figure 49: Proposed mechanism of direct carboxamidation catalysed by boronic acids.

By using a different kind of boronylating agent, we tried to get to boronic acid **(+/-)-487** or boronic ester **(+/-)-488**. In theory boronic acid **(+/-)-487** could catalyse direct amide bond formation as it has at least one hydroxyl group on the boron atom. The

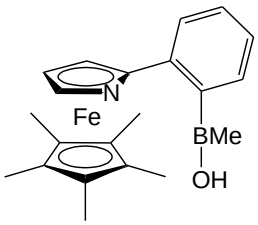
boronylating agent ($(MeO)_2BMe$) was synthesised according to the procedure of Dahlhoff (**Scheme 159**).[200]



(+/-)-466b **(+/-)-487** 44% **(+/-)-488** 18% **(+/-)-466c** 37%

Scheme 159: Boronylation of bromo derivative **(+/-)-487** using $(MeO)_2BMe$.

From the reaction boronic ester **(+/-)-488** was isolated as a mixture (~1/1) with an unidentifiable compound. Some impure starting material **(+/-)-466b** was also isolated. A third compound which was believed to be the desired product **(+/-)-487** was obtained in 44% yield. Structure depicted in **Scheme 158** are based on NMR data (**Table 26**).



(+/-)-487

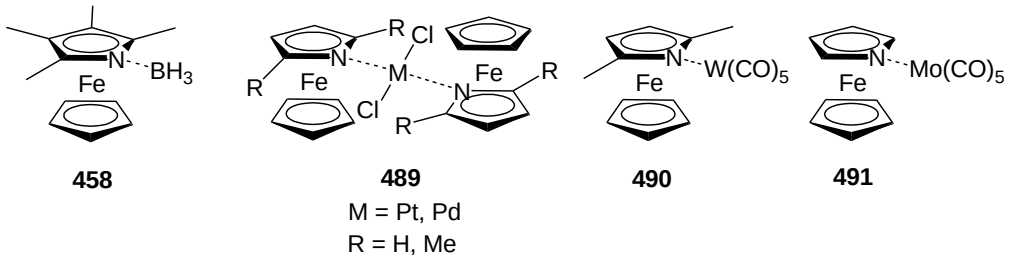
^{1}H NMR δ(ppm), *J*(Hz)	
-0.11 (3H, bs, B-CH_3)	5.30 (1H, bs, CH-$Cp_{sub.}$)
1.71 (15H, s CH_3-Cp*)	7.26 (2H, m, CH-Ar)
4.53 (1H, bs, CH-$Cp_{sub.}$)	7.43 (1H, m, CH-Ar)
4.57 (1H, bs, CH-$Cp_{sub.}$)	7.52 (1H, m, CH-Ar)
^{11}B NMR δ(ppm), *J*(Hz)	
4.5	

Table 26: NMR data of boronic acid **(+/-)-487**.

However, the reaction would need to be repeated and optimised in order to obtain more material. Due to lack of time we were unable to investigate this any further.

4. Protection of Nitrogen

Azaferrocenes have a different reactivity compared to those of the analogous ferrocene derivatives. Azaferrocenes for example fail to undergo Friedel-Crafts acylation which is related to the fact of having an electronegative, deactivating nitrogen in the ring. This feature highly resembles the reactivity of pyridines. Azaferrocenes react with electrophiles on the nitrogen atom, which further deactivates the pyrrolyl ring.[201] Azaferrocenes behave as a relatively strong σ–donor and a rather weak π–acceptor when forming a coordination complexes (**Figure 50**).[64]



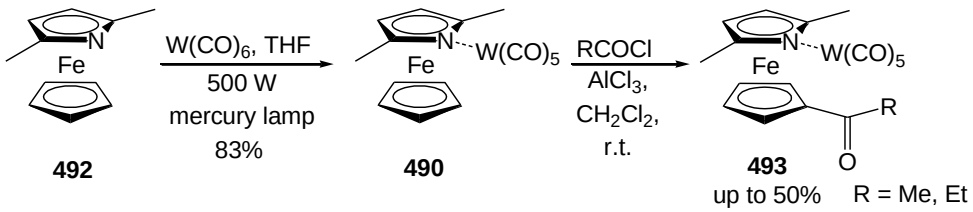
458 **489** **490** **491**

M = Pt, Pd
R = H, Me

Figure 50: Coodination complexes formed by azaferrocenes.

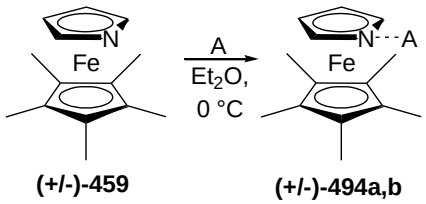
In our case, N-M (M = Zn or Pd) coordination might occur during the Negishi coupling which would retard the reaction. Secondly, taking the N-B chelation into account, it is reasonable to assume that strong adducts might form between the nitrogen and the boronylating agent.

This coordinating ability was first exploited by Kowalski in 2005 to synthesise acylated azaferrocenes **493**.[202] The neutral $W(CO)_6$ was coordinated to the azaferrocene in order to protect the lone pair of the nitrogen. By this method it was possible to isolate acylated azaferrocenes **493** for the first time (**Scheme 160**). There was no comment on removal of the $W(CO)_5$ fragment following the acylation.



Scheme 160: Acylation of protected azaferrocene **490**.

Recently, an X-ray crystal structure was published of 1',2',3',4',5'-pentamethylazaferrocene and the corresponding BH_3 **(+/-)-494a** and BF_3 **(+/-)-494b** adducts (**Scheme 161**).[203]



Entry	A	Reagent	Y(%)	Product
1	BH_3,	BH_3.THF	70	**(+/-)-494a**
2	BF_3	$BF_3.Et_2O$	52	**(+/-)-494b**

Scheme 161: Complexation of 1',2',3',4',5'-pentamethylazaferrocene **459** with BH_3 and BF_3.

In order to investigate the potential of a protection-deprotection approach, preliminary studies were made to form complexes **(+/-)-494** (**Figure 51**).

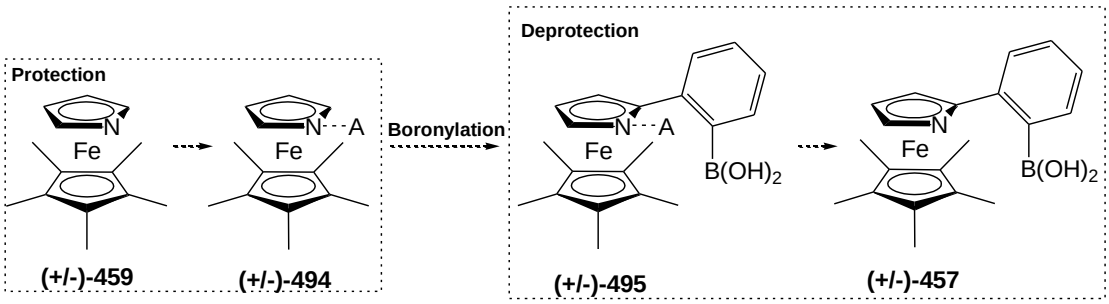
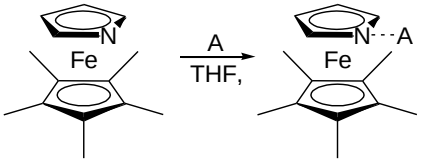


Figure 51: Approach using N-protection/deprotection.

Preliminary studies were made to form coordination complexes **(+/-)-494a**, **(+/-)-494c** and **(+/-)-494c** (**Scheme 162**). Irradiation during the formation of metal complexes

494c and **(+/-)-494d** seemed more efficient when an UV-lamp (254 nm) was used instead of a 500 W mercury-lamp.[204] Even under these conditions we were unable to reach the yields (**Scheme 161**) published for this procedure. In addition, complexes **(+/-)-494c** and **(+/-)-494d** showed instability. Upon treatment of azaferrocene **459** with BH_3.THF complex **(+/-)-494a** formed quickly.

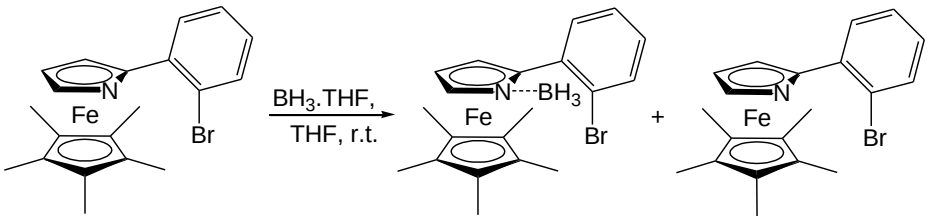


(+/-)-459 **(+/-)-494a,c,d**

Entry	$M(CO)_6$	Cond.	Y(%)	Product
1	$Mo(CO)_6$,	hν, 7 days,	29	**494c**
2	$W(CO)_6$,	hν, 7 days,	42	**494d**
3	BH_3.THF	0 °C, 45 min	66	**494a**

Scheme 162: Different methods tried for nitrogen-protection.

Protected BH_3-complex **(+/-)-494a** seemed more convenient regarding the short reaction time and higher yield, therefore, formation of complex **(+/-)-496** was attempted. In this reaction a mixture of product **(+/-)-496** and starting material **(+/-)-466b** was present and the reaction did not go to completion. Furthermore, after isolation, product **(+/-)-496** proved to loose BH_3 rapidly in solution giving back the starting material **(+/-)-466b** (**Scheme 163**).



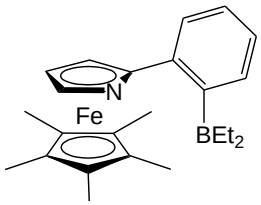
(+/-)-466b **(+/-)-496** 25% **(+/-)-466b** 57%

Scheme 163: Complexation of bromo derivative **(+/-)-466b** with BH_3.

Due to this observed instability of complexes **(+/-)-496**, **(+/-)-494a**, **(+/-)-494c** and **(+/-)-494c** this route was not investigated further.

5. Conclusions

In the course of this project several azaferrocenes were synthesised. Synthesis of aryl-derivatives **(+/-)-466** were achieved. Among the several different approaches tested D*o*M by lithium-halogen exchange, coupled with electrophilic trapping by a boronylating agent was the most successful method for the introduction of the boronic acid moiety. However, it was assumed that instability of the desired product **(+/-)-457** posed a problem in its isolation. This hypothesis was supported by the fact that upon treatment of lithiated intermediate **(+/-)-480** with a different kind of boronylating agent, such as $MeOBEt_2$, isolation of **(+/-)-486** was possible (**Figure 52**).



(+/-)-486

Figure 52: Borane **(+/-)-486** proved to be stable.

Borane **(+/-)-486** might not be suitable to catalyse direct amide bond forming reactions, however, it might still be useful as a Frustrated Lewis Pair (FLP).[205] FLPs are molecules bearing both Lewis acidic and basic functionalities that, for steric reasons can not form a Lewis acid-base pair. They have demonstrated new reactivity which might lead to new approaches in catalysis and asymmetric catalysis (metal-free).

Phosphino-borane **499** was used to the catalyse reduction of imines (**Figure 53**). Although the number of imines that undergo reduction under these conditions is limited, this example clearly shows the potential of this method.

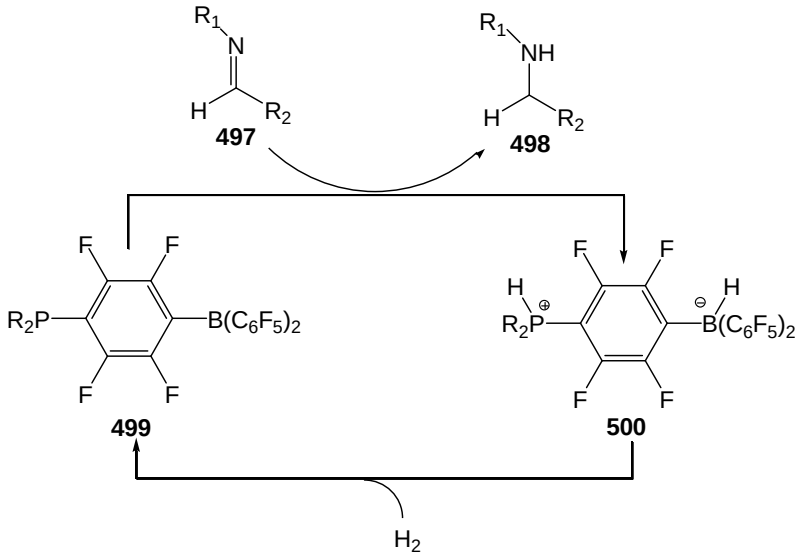


Figure 53: Catalytic cycle devised for the reduction of imines **497**.

In theory, the reduction could be done asymmetrically. In our case planar chirality might serve as a source of stereochemical information.

Synthesis of borane **(+/-)-487** was not completed due to lack of time, however preliminary experiments showed that formation of borane **(+/-)-487** occurs using MeO_2BMe as a boronylating agent. After optimisation this reaction could be the final step to our altered azaferrocenylboronic acid **(+/-)-487** in 13% (unoptimised) yield over two steps from 1',2',3',4',5'-pentamethylazaferrocene (**Figure 54**).

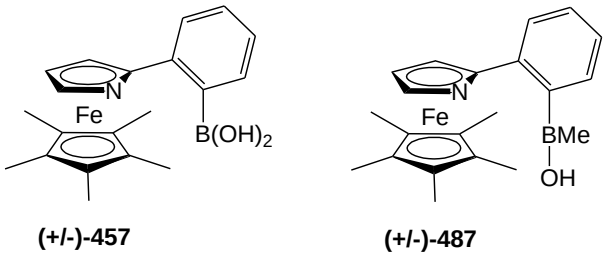


Figure 54: Synthesised azaferrocenylboronic acid **(+/-)-487**.

This compound might be a useful catalyst for direct amide bond forming reactions. This two step sequence also provides access to planar chiral derivative **(*pS*)-487** which could be tested in an asymmetric amide bond forming reaction.

6. Summary and Future Work

Although the target compound **(+/-)-457** could not be synthesised, we established a two step sequence starting from 1',2',3',4',5'-pentamethylazaferrocene to borane **(+/-)-486** and monohydroxylboronic acid **(+/-)-487** (**Figure 55**).

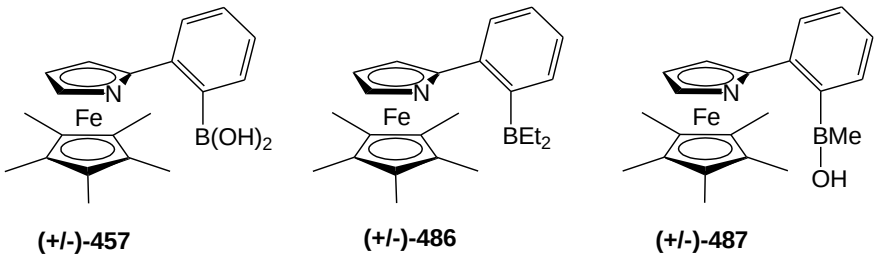
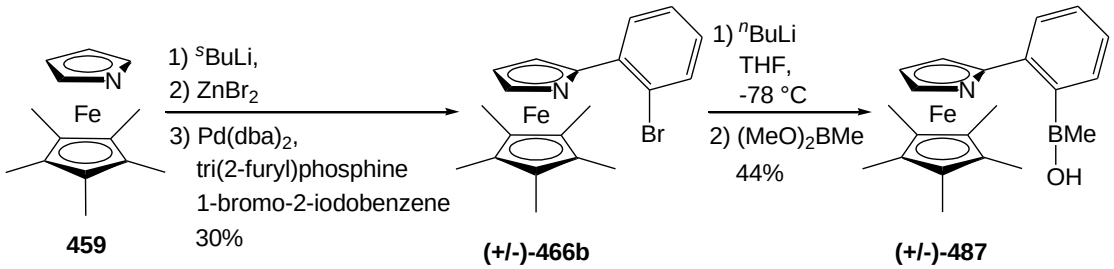


Figure 55: Target boronic acid **(+/-)-457** could not be synthesised.

Based on the mechanistic proposals for the direct amide bond forming reactions, the former is not suitable to catalyse this transformation, lacking the essential hydroxyl group(s) on the boron. However, borane **(+/-)-486** may find applications as a frustrated lewis pair (FLP). This direction chould be further investigated. Based on the intermediates proposed by Whiting, monohydroxylboronic acid **(+/-)-487** is likely to catalyse direct carboxamidations. Testing its activity in this transformation should be addressed. In case of success, the current two step protocol would need to be optimised to enable synthesis of **(+/-)-487** on a larger scale (**Scheme 164**).



Scheme 164: Two step protocol developed for the synthesis of **(+/-)-487**.

General Experimental

All reaction were carried out under positive pressure of argon using a Schlenk apparatus unless otherwise stated. Air sensitive compounds were handled using Glove box. For all non-aqueous chemistry, glassware was rigorously flame-dried. All reaction temperatures refer to values recorded for an external bath. Room temperature implies temperature in the range 20-25 °C. Cryogenic conditions were achieved using a solid carbon dioxide-acetone (-78 °C) or EtOH (-90 °C) baths. Degassing of solutions were carried out by freezing the solution using liquid N_2, subjecting the flask to vacuum, followed by slowly warming (closed reaction vessel) to room temperature. This was repeated three times Reactions were monitored by thin layer chromatography (TLC) performed on Polygram ALOX N/UV254 aluminium backed plates, which then were visualised using ultraviolet light (254nm) and/or $KMnO_4$ solution. Flash column chromatography was performed using Geduran® silica gel 60, 40-63 μm. For filtrations Celite was used.

Purification of Solvents and Reagents

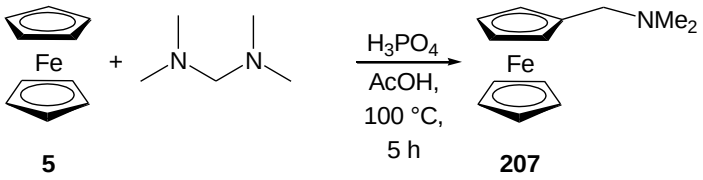
Dry solvents were freshly distilled or used obtained from a solvent tower, where the degassed solvents were passed through two columns of activated alumina and a 7 micron filter under 4 bar pressure. Amines such as pyrrolidine, pyrrole, triethylamine, TMEDA, (-)-sparteine, diisopropylethylamine were distilled from CaH and stored

under argon at -20 °C. Acetic anhydride, iodobenzene, 1-bromo-2-iododbenzene, $POCl_3$, TMSCl, $ClPPh_2$ were distilled prior to use. Cylopentadiene was cracked freshly prior to use but also could be stored at -20 °C for several weeks without dimerisation. Dry solutions of $ZnCl_2$ and $ZnBr_2$ were prepared by the following procedure: the salt was fused under vacuum until bubbling had stopped. Then it was let to cool to ambient temperature and dissolved in THF (1M). Finally it was filtered under Schlenk conditions using a pad of Celite and stored at r.t. under argon. $FeCl_2$ (Riedel de Haan) was dried under vacuum at 100 °C using vigorous stirring overnight and stored in the Glovebox. KH in mineral oil was washed with ^{n}hexane three times under Schlenk conditions and dried for 10 min under vacuum prior to use. Activation of 4 Å molecular sieves was achieved by heating under high vacuum. All solutions of organo-lithium reagents were standardised with diphenyl acetic acid.

Characterisation

Melting Points are uncorrected and were recorded on a Stuart Scientific SMP3 apparatus. Infrared spectra were recorded on a Perkin-Elmer 1600 FTIR instrument as a solid or oil and are reported in cm^{-1}. 1H NMR spectra were recorded on a Bruker AMX/ Bruker AVANCE III spectrometer at 600, 500, 400 and 300 MHz (stated at each individual spectra) in a solution in $CDCl_3$ unless otherwise stated. Chemical shifts are reported in ppm relative to the solvent standard $\delta = 7.27$ for ^{1}H NMR and $\delta = 77.2$ for ^{13}C NMR. Coupling constants are reported in Hz and rounded to the nearest 0.1 Hz. The multiplicity of eash signal is described by the following abbreviations: bs (broad singlet), s (singlet), d (doublet, t (triplet), q (quartet), m (multiplet), dd (doublet of

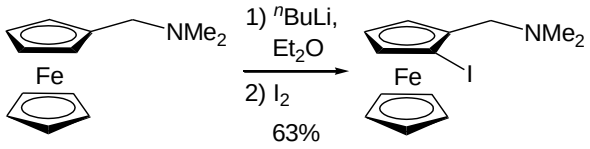
doublet), dt (doublet of triplet) etc. The chemical shifts of multiplets corresponding to a single proton are quoted as a point, representing the centre of the multiplet. Where appropriate, HMQC, COSY, HMBC, NOESY experiments were carried out to aid assignment. Mass spectra were acquired on Thermo Finnigan Mat900xp **(**EI/CI) VG-70se (FAB) and Waters LCT Premier XE (ES) instruments. Elemental analysis was performed on an Exeter Analytical Inc. EA440 horizontal load analyser.



5 **207**

***N*,*N*-Dimethylaminomethylferrocene** (**207**).

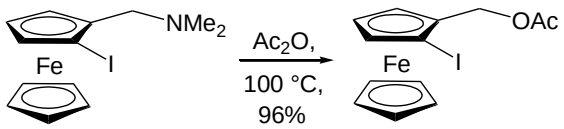
Ferrocene (17.2 g, 92.5 mmol) was added to a stirred solution of *N*,*N*,*N*',*N*'-tetramethylmethylenediamine (16.0 g, 156 mmol, 1.70 eq.) and H_3PO_4 (16.0 g, 163 mmol, 1.77 eq.) in AcOH (150 mL) and the resulting mixture was stirred at 100 °C for 5 h. The mixture was let to cool to r.t. and was diluted with water (200 mL) and extracted with Et_2O (3 × 120 mL). To the aqueous phase NaOH (90 g) was added when the product separated from the aqueous phase. The mixture was extracted with Et_2O (3 × 190 mL), dried ($MgSO_4$) concentrated under *vacuo* to give *N*,*N*-dimethylaminomethylferrocene (17.6 g, 78%) as an orange oil. Rf 0.25 (CH_2Cl_2/MeOH, 10/1); ^{1}H NMR (300 MHz) δ 2.15 (6H, s, N($C\underline{H}_3$)$_2$), 3.25 (2H, s, $C\underline{H}_2$), 4.08 (7H, s, $C\underline{H}$-$Cp_{sub.}$, $C\underline{H}$-$Cp_{unsub.}$), 4.14 (2H, s, $C\underline{H}$-$Cp_{sub.}$); ^{13}C NMR (75 MHz) δ 44.8 (N($\underline{C}H_3$)$_2$), 59.2 ($\underline{C}H_2$), 68.0 ($\underline{C}H$-$Cp_{sub.}$), 68.4 ($\underline{C}H$-$Cp_{unsub.}$), 70.1 ($\underline{C}H$-$Cp_{sub.}$), 83.4 (H_2C-$\underline{C}$-$Cp_{sub.}$). ^{1}H NMR and ^{13}C NMR agreed with literature data.[200]



207 **(+/-)-208**

1-[*N*,*N*-(Dimethylamino)methyl]-2-iodo-ferrocene (**(+/-)-208**).

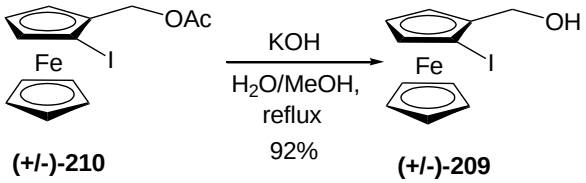
A solution of *N*,*N*-dimethylaminomethylferrocene (0.50 mL, 2.48 mmol) in Et_2O (7.5 mL) was treated with ^{n}BuLi (1.45 mL, 3.64 mmol, 1.47 eq.) at -78 °C and the solution was stirred at r.t. for 4 h. Then a solution of I_2 (0.74 g, 2.90 mmol, 1.17 eq.) in THF (2.0 mL) was added at -78 °C and the mixture was stirred at -78 °C for 1 h and another 30 min at r.t. The reaction was quenched with water (5 mL), extracted with Et_2O (2 × 5 mL), dried ($MgSO_4$) and concentrated. The resulting dark brown oil was purified by flash column chromatography (^{n}hexane/Et_2O/Et_3N, 10/10/1) to afford 1-[(dimethylamino)methyl]-2-iodo-ferrocene (576 mg, 63%) as an oil. Rf 0.37 (^{n}hexane/Et_2O/Et_3N, 10/10/1); ^{1}H NMR (400 MHz) δ 2.21 (6H, s, N(C$\underline{H}_3$)$_2$), 3.33 (2H, s, C$\underline{H}_2$), 4.08 (5H, s, C$\underline{H}$-Cp$_{unsub.}$), 4.18 (1H, t, *J* = 2.5 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.26 (1H, dd, *J* = 2.6, 1.4 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.40 (1H, dd, *J* = 2.4, 1.4 Hz, C$\underline{H}$-Cp$_{sub.}$); ^{13}C NMR (100 MHz) δ 45.3 (N(C$\underline{H}_3$)$_2$), 46.4 (I-C$\underline{-}$Cp$_{sub.}$), 58.7 (C$\underline{H}_2$), 68.8 (C$\underline{H}$-Cp$_{sub.}$), 69.1 (C$\underline{H}$-Cp$_{sub.}$), 71.6 (C$\underline{H}$-Cp$_{unsub.}$), 74.8 (C$\underline{H}$-Cp$_{sub.}$), 85.0 (H_2C-C$\underline{-}$Cp$_{sub.}$). ^{1}H NMR and ^{13}C NMR agreed with literature data.[201]



(+/-)-208 **(+/-)-210**

1-[(Acetoxy)methyl]-2-iodo-ferrocene (**(+/-)-210**).

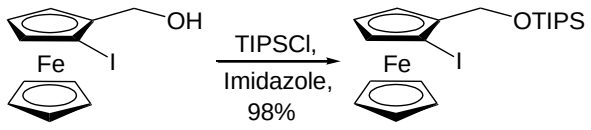
A solution of 1-[(dimethylamino)methyl]-2-iodo-ferrocene (2.54 g, 6.87 mmol) in Ac_2O (76 mL) was heated to 100 °C for 3 h. Then saturated K_2CO_3 was added carefully at 0 °C and stirring was continued for another 30 min at r.t. The mixture then was extracted with Et_2O (2 × 50 mL). The organics were washed with saturated $NaHCO_3$ (40 mL), dried ($MgSO_4$) and concentrated to give 1-[(acetoxy)methyl]-2-iodo-ferrocene (2.53 mg, 96%) as a brown oil which was used in the next step without further purification. Rf 0.78 (^{n}hexane/Et_2O/Et_3N, 10/10/1); ^{1}H NMR (400 MHz) δ 2.05 (3H, s OCOC$\underline{H}_3$), 4.18 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.27 (1H, t, *J* = 2.5 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.38 (1H, dd, *J* = 2.5, 1.3 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.50 (1H, dd, *J* = 2.3, 1.3 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.88 (1H, d, *J* = 12.2 Hz, C$\underline{H}_2$-OAc), 5.05 (1H, d, *J* = 12.2 Hz, C$\underline{H}_2$-OAc); ^{13}C NMR (100 MHz) δ 21.1 (OCO$\underline{C}H_3$), 44.9 (I-$\underline{C}$-$Cp_{sub.}$), 62.9 ($\underline{C}H_2$), 69.2 ($\underline{C}$H-$Cp_{sub.}$), 69.7 ($\underline{C}$H-$Cp_{sub.}$), 71.7 ($\underline{C}$H-$Cp_{unsub.}$), 75.5 ($\underline{C}$H-$Cp_{sub.}$), 82.8 (H_2C-$\underline{C}$-$Cp_{sub.}$), 170.6 (O$\underline{C}$OCH$_3$). ^{1}H NMR agreed with literature data.[202]



(+/-)-210 **(+/-)-209**

1-(Hydroxymethyl)-2-iodo-ferrocene (**(+/-)-209**).

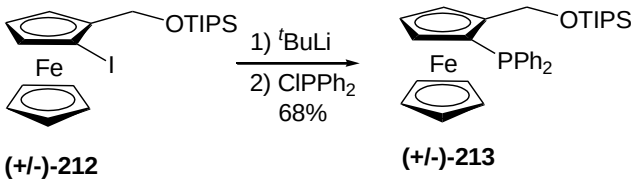
A solution of 1-[(acetoxy)methyl]-2-iodo-ferrocene (3.60 g, 9.37 mmol) and KOH (21.0 g, 375 mmol, 40.0 eq.) was refluxed in a mixture of H_2O (245 mL) and MeOH (245 mL) overnight. The mixture was concentrated in *vacuo* and extracted with Et_2O (3 × 150 mL). The organics were washed with brine (1 × 80 mL), dried ($MgSO_4$) and concentrated to give 1-(hydroxymethyl)-2-iodo-ferrocene (2.94 g, 92%) as a yellow solid (m.p. 76-78 °C, lit. m.p. 81-83 °C). Rf 0.30 (^{n}hexane/Et_2O, 1/1); ^{1}H NMR (400 MHz) δ 1.69 (1H, s, O<u>H</u>), 4.18 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.25 (1H, t, *J* = 2.5 Hz, C<u>H</u>-$Cp_{sub.}$), 4.33 (1H, dd, *J* = 2.6, 1.4 Hz, C<u>H</u>-$Cp_{sub.}$), 4.38 (1H, d, *J* = 12.4 Hz, C<u>H</u>$_2$), 4.48 (1H, dd, *J* = 2.4, 1.4 Hz, C<u>H</u>-$Cp_{sub.}$), 4.50 (1H, d, *J* = 12.4 Hz, C<u>H</u>$_2$); ^{13}C NMR (100 MHz) δ 43.9 (I-<u>C</u>-$Cp_{sub.}$), 61.4 (<u>C</u>H_2), 67.8 (<u>C</u>H-$Cp_{sub.}$), 69.1 (<u>C</u>H-$Cp_{sub.}$), 71.4 (<u>C</u>H-$Cp_{unsub.}$), 75.1 (<u>C</u>H-$Cp_{sub.}$), 88.2 (H_2C-<u>C</u>-$Cp_{sub.}$). ^{1}H NMR agreed with literature data.[89]



(+/-)-209 **(+/-)-212**

1-(Triisopropylsilylethermethyl)-2-iodoferrocene (**(+/-)-212**).

To a solution of 1-(hydroxymethyl)-2-iodo-ferrocene (4.96 g, 14.5 mmol) in DMF (50 mL) (^{i}Pr)$_3$SiCl (4.10 mL, 17.4 mmol, 1.20 eq.) and imidazole (2.47 g, 36.3 mmol, 2.50 eq.) was added and the solution was stirred at r.t. overnight. The reaction was quenched with water (32 mL), extracted with Et_2O (2 × 30 mL), dried ($MgSO_4$), concentrated and purified by flash column chromatography (^{n}hexane/Et_2O, 95/5) to give 1-(triisopropylsilylethermethyl)-2-iodoferrocene (4.30 g, 98%) as an orange oil. Rf 0.86 (^{n}hexane/Et_2O, 95/5); IR υ_{max} 2942 (CH), 2865 (CH), 1462, 1105 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.14 (21H, m, O(C<u>H</u>(C<u>H</u>$_3$)$_2$)$_3$), 4.16 (5H, s, C<u>H</u>-Cp$_{unsub.}$), 4.19 (1H, t, *J* = 2.5 Hz, C<u>H</u>-Cp$_{sub.}$), 4.35 (1H, dd, *J* = 2.6, 1.4 Hz, C<u>H</u>-Cp$_{sub.}$), 4.41 (1H, dd, *J* = 2.4, 1.4 Hz, C<u>H</u>-Cp$_{sub.}$), 4.58 (2H, s, C<u>H</u>$_2$); ^{13}C NMR (75 MHz) δ 11.9 (O(<u>C</u>H(CH$_3$)$_2$)$_3$), 18.0 (O(CH(<u>C</u>H$_3$)$_2$)$_3$), 42.7 (I-<u>C</u>-Cp$_{sub.}$), 62.0 (<u>C</u>H$_2$), 67.0 (<u>C</u>H-Cp$_{sub.}$), 68.1 (<u>C</u>H-Cp$_{sub.}$), 71.3 (<u>C</u>H-Cp$_{unsub.}$), 74.1 (<u>C</u>H-Cp$_{sub.}$), 88.8 (H$_2$C-<u>C</u>-Cp$_{sub.}$); m/z (ES+) 521 (100%, M+Na), 498 (8%, M); HRMS $C_{20}H_{31}FeIOSi$ calcd. 498.0533, found 498.0519; Anal. Calcd. For $C_{20}H_{31}FeIOSi$: C, 48.21; H, 6.27. Found C, 47.75; H, 6.25%.

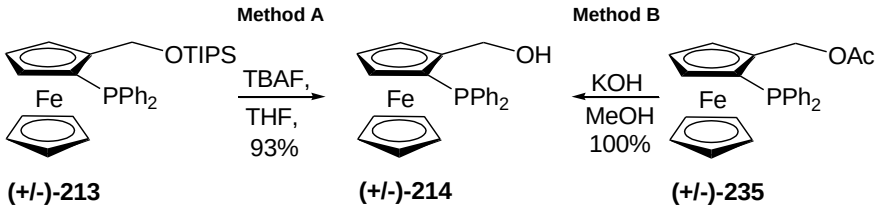


(+/-)-212 **(+/-)-213**

1-(Triisopropylsilylethermethyl)-2-diphenylphosphinoferrocene (**(+/-)-213**).

To a solution of *rac*-1-(triisopropylsilylethermethyl)-2-iodoferrocene (4.30 g, 8.65 mmol) in Et_2O (40 mL) ^{t}BuLi (10.8 mL, 17.3 mmol, 2.00 eq.) was added at -78 °C and the reaction mixture was stirred at r.t. for 1 h. Then $ClPPh_2$ (2.40 mL, 13 mmol, 1.50 eq.) was added at 0 °C and the mixture was stirred for another hour at r.t. The reaction was quenched with saturated $NaHCO_3$ (30 mL) at 0 °C, extracted with Et_2O (2 × 20 mL). The organics were washed with water (1 × 20 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography (^{n}hexane/Et_2O, 98/2) and recrystallised from EtOH to afford 1-(triisopropylsilylethermethyl)-2-diphenylphosphinoferrocene (3.30 g, 68%) as an orange solid (m.p. 95-97 °C). Rf 0.50 (^{n}hexane/Et_2O, 98/2); IR υ_{max} 3012 (CH), 2944 (CH), 2866 (CH), 1602 (Ar), 1464 (P-Ph), 1240 (Si-C), 1106 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.02 (21H, m, O(C<u>H</u>(C<u>H</u>$_3$)$_2$)$_3$), 3.71 (1H, dt, J = 2.4 Hz, $J_{HH/HP}$ = 1.2 Hz, C<u>H</u>-Cp$_{sub.}$), 4.01 (5H, s, C<u>H</u>-Cp$_{unsub.}$), 4.26 (1H, t, J = 2.4 Hz, C<u>H</u>-Cp$_{sub.}$), 4.55 (1H, dt, J = 2.3 Hz, $J_{HH/HP}$ = 1.4 Hz, C<u>H</u>-Cp$_{sub.}$), 4.65 (2H, s, C<u>H</u>$_2$), 7.15-7.59 (10H, m, C<u>H</u>-PPh$_2$); ^{13}C NMR (100 MHz) δ 12.0 (O(<u>C</u>H(CH$_3$)$_2$)$_3$), 18.1 (O(CH(<u>C</u>H$_3$)$_2$)$_3$), 60.5 (d, J = 11.3 Hz, <u>C</u>H$_2$), 69.1 (<u>C</u>H-Cp$_{sub.}$), 69.5 (<u>C</u>H-Cp$_{unsub.}$), 71.0 (d, J = 3.8 Hz, <u>C</u>H-Cp$_{sub.}$), 71.3 (d, J = 3.6 Hz, <u>C</u>H-Cp$_{sub.}$), 75.2 (d, J = 7.9 Hz, Ph$_2$P-<u>C</u>-Cp$_{sub.}$), 93.6 (d, J = 23.3 Hz, H$_2$C-<u>C</u>-Cp$_{sub.}$), 127.6 (*p*-<u>C</u>H-PPh$_2$), 127.9 (d, J = 5.8 Hz, *m*-<u>C</u>H-PPh$_2$), 128.1 (d, J = 7.7 Hz, *m*-<u>C</u>H-PPh$_2$), 129.1 (*p*-<u>C</u>H-PPh$_2$), 132.3 (d, J

= 17.7 Hz, *o*-CH-PPh_2), 135.1 (d, *J* = 21.1 Hz, *o*-CH-PPh_2), 137.6 (d, *J* = 8.8 Hz, *i*-C-PPh_2), 140.0 (d, *J* = 9.9 Hz, *i*-C-PPh_2); ^{31}P NMR (162 MHz) δ -22.6 (t, J_{PSi} = 6.7 Hz); m/z (ES+) 556 (11%, M), 384 (8%, M-OTIPS); HRMS $C_{32}H_{41}FeOPSi$ calcd. 556.2014, found 556.2026; Anal. Calcd. for $C_{32}H_{41}FeOPSi$: C, 69.06; H, 7.43. Found C, 68.74; H, 7.42%.



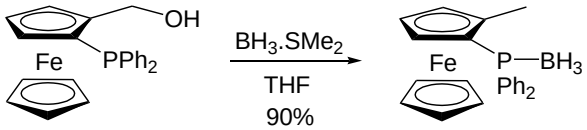
(+/-)-213 **(+/-)-214** **(+/-)-235**

1-(Diphenylphosphino)-2-(hydroxymethyl)-ferrocene (**(+/-)-214**).

Method A: To a solution of 1-(triisopropylsilylethermethyl)-2-iodoferrocene (2.84 g, 5.10 mmol) in THF (400 mL) Bu_4NF (10.2 mL, 10.2 mmol, 2.00 eq.) was added and the reaction was stirred at r.t. overnight. The mixture was quenched with water (50 mL) and extracted with CH_2Cl_2 (2 × 150 mL), dried ($MgSO_4$) and concentrated in *vacuo* to give 1-(diphenylphosphino)-2-(hydroxymethyl)-ferrocene (1.90 g, 93%) as an orange solid (m.p. 146-148 °C, lit.: 146 °C). The crude material was clean enough but if needed could be purified by flash column chromatography (^{n}hexane/EtOAc, 7/3). Rf 0.48 (^{n}hexane/EtOAc, 7/3).

Method B: A suspension of 1-[(acetoxy)methyl]-2-(diphenylphosphino)-ferrocene (2.10 g, 4.75 mmol) and 3M KOH (13.1 g, 78.0 mmol, 16.0 eq.) in MeOH (156 mL) was refluxed for 6 h. Then water (300 mL) was added to the mixture and the precipitate was filtered off giving 1-(diphenylphosphino)-2-(hydroxymethyl)-ferrocene (1.89 g, 100%) as an orange solid; IR υ_{max} 3012 (CH), 1602 (Ar), 1478 (P-Ph), 1434 (P-Ph),

1240 (Si-C) cm^{-1}; ^{1}H NMR (400 MHz) δ 1.43 (1H, dt, J = 6.3 Hz, J_{HP} = 1.4 Hz, O<u>H</u>), 3.75 (1H, dt, J = 2.4 Hz, $J_{HH/HP}$ = 1.0 Hz, C<u>H</u>-$Cp_{sub.}$), 4.10 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.30 (1H, t, J = 2.4 Hz, C<u>H</u>-$Cp_{sub.}$), 4.40 (1H, dd, J = 12.4 Hz, J_{HO} = 6.4 Hz, C<u>H</u>$_2$), 4.52 (1H, m, C<u>H</u>-$Cp_{sub.}$), 4.54 (1H, ddd, J = 12.4, J_{HO} = 6.0 Hz, J_{HP} = 1.8 Hz, C<u>H</u>$_2$), 7.18-7.56 (10H, m, C<u>H</u>-PPh_2); ^{13}C NMR (100 MHz) δ 60.0 (d, J = 9.7 Hz, <u>C</u>H_2), 69.5 (<u>C</u>H-$Cp_{unsub.}$), 69.6 (<u>C</u>H-$Cp_{sub.}$), 71.6 (d, J = 3.7 Hz, <u>C</u>H-$Cp_{sub.}$), 71.7 (d, J = 3.5 Hz, <u>C</u>H-$Cp_{sub.}$), 76.1 (d, J = 7.1 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 92.6 (d, J = 22.9 Hz, H_2C-<u>C</u>-$Cp_{sub.}$), 128.3 (d, J = 6.5 Hz, *m*-<u>C</u>H-PPh_2), 128.3 (*p*-<u>C</u>H-PPh_2), 128.4 (d, J = 6.1 Hz, *m*-<u>C</u>H-PPh_2), 129.3 (*p*-<u>C</u>H-PPh_2), 132.4 (d, J = 18.3 Hz, *o*-<u>C</u>H-PPh_2), 134.8 (d, J = 20.7 Hz, *o*-<u>C</u>H-PPh_2), 136.9 (d, J = 8.7 Hz, *i*-<u>C</u>-PPh_2), 139.7 (d, J = 10.0 Hz, *i*-<u>C</u>-PPh_2); ^{31}P NMR (162 MHz) δ -23.2; m/z (EI) 401 (7%, M+H), 400 (25%, M); HRMS $C_{23}H_{21}FeOP$ calcd. 400.06740, found 400.06791; Anal. Calcd. for $C_{23}H_{21}FeOP$: C, 69.00; H, 5.28. Found C, 68.57; H, 5.23%. ^{1}H NMR agreed with literature data.[203]

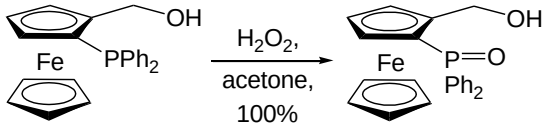


(+/-)-214 **(+/-)-223**

[1-(Diphenylphosphino)-2-methylferrocene]trihydro-boron (**(+/-)-223**).

To a solution of 1-(diphenylphosphino)-2-(hydroxymethyl)-ferrocene (100 mg, 0.26 mmol) in THF (4.0 mL) $BH_3.SMe_2$ (0.06 mL, 0.65 mmol, 2.50 eq.) was added dropwise and stirred at r.t. for 15 min. The mixture was concentrated in *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 95/5) to give [1-(diphenylphosphino)-2-methylferrocene]trihydro-boron (53.0 mg, 90%) as an orange solid (m.p. 170-172 °C). Rf 0.86 (^{n}hexane/EtOAc, 95/5); IR υ_{max} 2919 (CH), 1433 (P-

Ph), 1106, 1060 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.04 (3H, s, C<u>H</u>$_3$), 3.78 (1H, dt, *J* = 2.4 Hz, $J_{HH/HP}$ = 1.6 Hz, C<u>H</u>-Cp$_{sub.}$), 4.25 (5H, s, C<u>H</u>-Cp$_{unsub.}$), 4.30 (1H, t, *J* = 2.4 Hz, C<u>H</u>-Cp$_{sub.}$), 4.44 (1H, dt, *J* = 2.3 Hz, $J_{HH/HP}$ = 1.5 Hz, C<u>H</u>-Cp$_{sub.}$), 7.37-7.71 (10H, m, C<u>H</u>-PPh$_2$); ^{13}C NMR (100 MHz) δ 14.8 (C<u>H</u>$_3$), 68.7 (d, *J* = 65.8 Hz, Ph$_2$P-<u>C</u>-Cp$_{sub.}$), 69.3 (d, *J* = 6.8 Hz, <u>C</u>H-Cp$_{sub.}$), 70.4 (<u>C</u>H-Cp$_{unsub.}$), 73.0 (d, *J* = 6.4 Hz, <u>C</u>H-Cp$_{sub.}$), 74.3 (d, *J* = 7.7 Hz, <u>C</u>H-Cp$_{sub.}$), 88.9 (d, *J* = 13.3 Hz, H$_3$C-<u>C</u>-Cp$_{sub.}$), 128.3 (d, *J* = 10.1 Hz, *m*-<u>C</u>H-PPh$_2$), 128.5 (d, *J* = 10.0 Hz, *m*-<u>C</u>H-PPh$_2$), 130.6 (d, *J* = 36.7 Hz, *i*-<u>C</u>-PPh$_2$), 130.8 (d, *J* = 2.3 Hz, *p*-<u>C</u>H-PPh$_2$), 130.9 (d, *J* = 2.3 Hz, *p*-<u>C</u>H-PPh$_2$), 131.2 (d, *J* = 33.7 Hz, *i*-<u>C</u>-PPh$_2$), 132.7 (d, *J* = 9.3 Hz, *o*-<u>C</u>H-PPh$_2$), 133.1 (d, *J* = 9.4 Hz, *o*-<u>C</u>H-PPh$_2$); ^{31}P NMR (162 MHz) δ 16.1 (d, J_{PB} = 69.1 Hz); m/z (EI) 399 (4%, M+H), 398 (10%, M), 384 (M-BH$_3$); HRMS $C_{23}H_{24}FeBP$ calcd. 398.10526, found 398.10656; Anal. Calcd. for $C_{23}H_{24}FeBP$: C, 69.40; H, 6.08. Found C, 69.35; H, 6.37%.

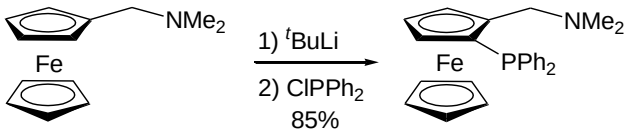


(+/-)-214 **(+/-)-228**

1-(Diphenylphosphinyl)-2-(hydroxymethyl)-ferrocene (**(+/-)-228**).

To a solution of 1-(diphenylphosphino)-2-(hydroxymethyl)-ferrocene (158 mg, 0.39 mmol) in acetone (6.0 mL) 30% aq. H_2O_2 (54μL, 0.53 mmol, 4.23 eq.) was added dropwise and stirred at r.t. for 30 min while an orange solid precipitated. Then saturated $Na_2S_2O_3$ (5 mL) was added to the suspension at 0 °C, and the mixture was extracted with CH_2Cl_2 (2 × 6 mL), washed with water (1 × 4 mL), dried ($MgSO_4$) and concentrated in *vacuo* to result 1-(diphenylphosphinyl)-2-(hydroxymethyl)-ferrocene (160 mg, 100%) as a yellow solid (m.p. 190-191 °C). Rf 0.49 (CH_2Cl_2/MeOH, 10/1);

IR υ_{max} 3308 (OH), 3000 (CH), 1438 (P-Ph), 1151 (P=O) cm^{-1}; ^{1}H NMR (400 MHz) δ 3.94 (1H, dt, *J* = 2.4 Hz, $J_{HH/HP}$ = 1.6 Hz, C<u>H</u>-$Cp_{sub.}$), 4.17 (1H, dd, *J* = 13.1, *J* = 10.5 Hz, C<u>H</u>$_2$), 4.26 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.33 (1H, dd, *J* = 13.1, *J* = 2.9 Hz, C<u>H</u>$_2$) 4.34 (1H, t, *J* = 2.4 Hz, C<u>H</u>-$Cp_{unsub.}$), 4.54 (1H, dt, *J* = 2.3 Hz, $J_{HH/HP}$ = 1.5 Hz, C<u>H</u>-$Cp_{sub.}$), 5.50 (1H, dd, *J* = 10.4, 2.8 Hz, O<u>H</u>), 7.36-7.86 (10H, m, C<u>H</u>-PPh_2); ^{13}C NMR (100 MHz) δ 58.7 (<u>C</u>H$_2$), 69.6 (d, *J* = 115.1 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 69.7 (d, *J* = 11.1 Hz, <u>C</u>H-$Cp_{sub.}$), 70.2 (<u>C</u>H-$Cp_{unsub.}$), 73.1 (d, *J* = 15.0 Hz, <u>C</u>H-$Cp_{sub.}$), 74.1 (d, *J* = 9.8 Hz, <u>C</u>H-$Cp_{sub.}$), 95.5 (d, *J* = 11.1 Hz, H_2C-<u>C</u>-$Cp_{sub.}$), 128.3 (d, *J* = 12.3 Hz, *m*-<u>C</u>H-PPh_2), 128.5 (d, *J* = 12.2 Hz, *m*-<u>C</u>H-PPh_2), 131.4 (d, *J* = 10.34 Hz, *o*-<u>C</u>H-PPh_2), 131.6 (d, *J* = 10.0 Hz, *o*-<u>C</u>H-PPh_2), 131.8 (d, *J* = 2.8 Hz, *p*-<u>C</u>H-PPh_2), 132.0 (d, *J* = 2.7 Hz, *p*-<u>C</u>H-PPh_2), 132.4 (d, *J* = 108.6 Hz, *i*-<u>C</u>-PPh_2), 134.3 (d, *J* = 106.1 Hz, *i*-<u>C</u>-PPh_2); ^{31}P NMR (162 MHz) δ 33.5; m/z (ES+) 856 (30%, Dimer+H+Na), 855 (62%, Dimer+Na), 439 (100%, M+Na), 417 (1.3%, M+H); HRMS (M+H) $C_{23}H_{22}FeO_2P$ calcd. 417.0704, found 417.0701; Anal. Calcd. for $C_{23}H_{21}FeO_2P$: C, 66.37; H, 5.09. Found C, 65.30; H, 5.05%. ^{1}H NMR agreed with literature data.[203]

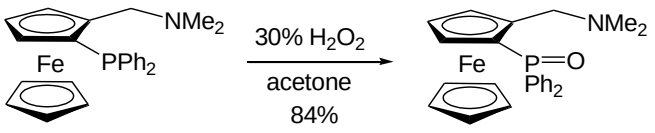


207 **(+/-)-232**

1-[(Dimethylamino)methyl]-2-(diphenylphosphino)-ferrocene (**(+/-)-232**).

To a solution of *N*,*N*-dimethylaminomethylferrocene (3.00 mL, 14.9 mmol) in Et_2O (30 mL) ^{t}BuLi (9.61 mL, 16.3 mmol, 1.10 eq.) was added at -78 °C. The mixture was stirred at r.t. for 1 h. Then $ClPPh_2$ (5.30 mL, 29.7 mmol, 2.00 eq.) was added at 0 °C

and the reaction was refluxed for 2 h. Then saturated $NaHCO_3$ (30 mL) was added at 0 °C and the mixture was extracted with Et_2O (2 × 30 mL). The organics were washed with water (20 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography on basic alumina using (^{n}hexane/EtOAc, 5/1) and recrystallised from EtOH to afford 1-[(dimethylamino)methyl]-2-(diphenylphosphino)-ferrocene (5.42 g, 85%) as an orange solid (m.p. 100-102 °C). Rf 0.45 (^{n}hexane/EtOAc, 5/1); IR υ_{max} 3059 (CH), 2930 (CH), 2817 (N-CH_3), 2769 (N-CH_3), 1454 (P-Ph), 1434 (P-Ph), 1234 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.02 (6H, s, N(C$\underline{H}_3$)$_2$), 3.43 (1H, d, *J* = 13.0 Hz , C$\underline{H}_2$), 3.50 (1H, dd, *J* = 13.0 Hz, J_{HP} = 2.4 Hz, C$\underline{H}_2$), 3.87 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 3.94 (5H, s, C$\underline{H}$-$Cp_{unub.}$), 4.31 (1H, t, *J* = 2.4 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.54 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 7.19-7.64 (10H, m, C$\underline{H}$-PPh_2); ^{13}C NMR (100 MHz) δ 45.1 (N(C$\underline{H}_3$)$_2$), 57.9 (d, *J* = 9.1 Hz, C$\underline{H}_2$), 69.7 (C$\underline{H}$-$Cp_{sub.}$), 69.7 (C$\underline{H}$-$Cp_{unsub.}$), 71.5 (d, *J* = 4.6 Hz, C$\underline{H}$-$Cp_{sub.}$), 72.7 (d, *J* = 4.1 Hz, C$\underline{H}$-$Cp_{sub.}$), 76.3 (d, *J* = 8.6 Hz, Ph_2P-C$\underline{-}$$Cp_{sub.}$), 90.7 (d, *J* = 25.5 Hz, H_2C-C$\underline{-}$$Cp_{sub.}$), 127.7 (d, *J* = 10.3 Hz, *m*-C$\underline{H}$-PPh_2), 127.8 (*p*-C$\underline{H}$-PPh_2) 128.1 (d, *J* = 8.0 Hz, *m*-C$\underline{H}$-PPh_2), 129.0 (*p*-C$\underline{H}$-PPh_2), 132.5 (d, *J* = 18.2 Hz, *o*-C$\underline{H}$-PPh_2), 135.2 (d, *J* = 21.6 Hz, *o*-C$\underline{H}$-PPh_2), 138.1 (d, *J* = 9.5 Hz, *i*-C$\underline{-}$$PPh_2$), 140.2 (d, *J* = 8.8 Hz, *i*-C$\underline{-}$$PPh_2$); ^{31}P NMR (162 MHz) δ -23.0; m/z (ES+) 428 (15%, M+H), 427 (4%, M), 399 (100%, M-2 × Me); HRMS (M+H) $C_{25}H_{27}FeNP$ calcd. 428.1231, found 428.1241; Anal. Calcd. for $C_{25}H_{26}FeNP$: C, 70.27; H, 6.13; N, 3.28. Found C, 70.19; H, 6.13; N, 3.29%.

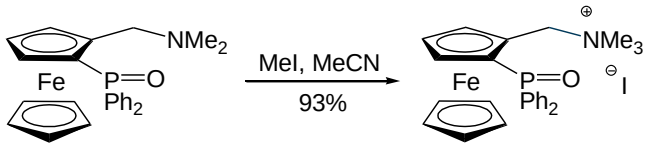


(+/-)-232 **(+/-)-233**

1-[(Dimethylamino)methyl]-2-(diphenylphosphinyl)-ferrocene (**(+/-)-233**).

To a solution of 1-[(dimethylamino)methyl]-2-(diphenylphosphino)-ferrocene (4.00 g, 9.36 mmol) in acetone (60 mL) 30% aq. H_2O_2 (24 mL, 231 mmol, 24.7 eq.) was added dropwise and the reaction mixture was stirred at r.t. for 30 min. Then saturated $Na_2S_2O_3$ (60 mL) was added to the solution at 0 °C, and the mixture was extracted with CH_2Cl_2 (2 × 50 mL), washed with water (40 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography on basic alumina using EtOAc to give 1-[(dimethylamino)methyl]-2-(diphenylphosphinyl)-ferrocene (3.50 g, 84%) as an orange solid (m.p. 140-142 °C). Rf 0.21 (Et_2O/MeOH, 99/1); IR υ_{max} 3079 (CH), 2931 (N-CH_3), 2763 (N-CH_3), 1438 (P-Ph), 1192 (P=O), 1106 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.93 (6H, s, N(C$\underline{H}_3$)$_2$), 3.35 (1H, d, *J* = 13.5 Hz, C$\underline{H}_2$), 3.60 (1H, d, *J* = 13.4 Hz, C$\underline{H}_2$), 3.92 (1H, m, C$\underline{H}$-Cp$_{sub.}$), 4.21 (5H, s, C$\underline{H}$-Cp$_{unsub.}$), 4.33 (1H, m, C$\underline{H}$-Cp$_{sub.}$), 4.60 (1H, m, C$\underline{H}$-Cp$_{sub.}$), 7.32-7.88 (10H, m, C$\underline{H}$-PPh$_2$); ^{13}C NMR (150 MHz) δ 45.1 (N($\underline{C}H_3$)$_2$), 57.4 ($\underline{C}H_2$), 70.1 (d, *J* = 10.6 Hz, $\underline{C}$H-Cp$_{sub.}$), 70.5 ($\underline{C}$H-Cp$_{unsub.}$), 72.3 (d, *J* = 114.5 Hz, Ph$_2$OP-$\underline{C}$-Cp$_{sub.}$), 73.6 (d, *J* = 15.0 Hz, $\underline{C}$H-Cp$_{sub.}$), 73.9 (d, *J* = 9.9 Hz, $\underline{C}$H-Cp$_{sub.}$), 89.9 (d, *J* = 10.6 Hz, H$_2$C-$\underline{C}$-Cp$_{sub.}$), 128.0 (d, *J* = 12.4 Hz, *m*-$\underline{C}$H-PPh$_2$), 128.1 (d, *J* = 12.1 Hz, *m*-$\underline{C}$H-PPh$_2$), 131.3 (d, *J* = 2.7 Hz, *p*-$\underline{C}$H-PPh$_2$), 131.4 (d, *J* = 2.6 Hz, *p*-$\underline{C}$H-PPh$_2$), 131.5 (d, *J* = 6.1 Hz, *o*-$\underline{C}$H-PPh$_2$), 131.7 (d, *J* = 10.0 Hz, *o*-$\underline{C}$H-PPh$_2$), 134.3 (d, *J* = 105.5 Hz, *i*-$\underline{C}$-PPh$_2$), 135.1 (d, *J* = 106.2 Hz, *i*-$\underline{C}$-PPh$_2$); ^{31}P NMR (162 MHz) δ 29.5;

m/z (EI) 444 (13%, M+H), 443 (55%, M), 428 (62%, M-O), 400 (35%, M-NMe_2), 399 (78%, M-NMe_2-H), 243 (15%, M-PPh_2), 242 (100%, M-PPh_2-H); HRMS $C_{25}H_{26}FeNOP$ calcd. 443.10959, found 443.10981; Anal. Calcd. for $C_{25}H_{26}FeNOP$: C, 67.73; H, 5.91; N, 3.16. Found C, 67.82; H, 5.92; N, 3.95%.

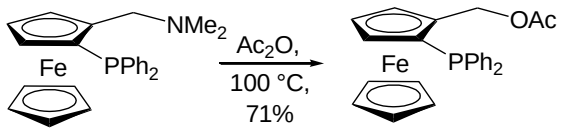


(+/-)-233 **(+/-)-234**

1-[(Trimethylamino)methyl]-2-(diphenylphosphinyl)-ferrocenyl iodide (**(+/-)-234**).

To a solution of 1-[(dimethylamino)methyl]-2-(diphenylphosphinyl)-ferrocene (3.50 g, 7.89 mmol) in acetonitrile (30 mL) MeI (26.0 mL, 0.41 mmol, 52.6 eq.) was added at 0 °C and the solution was stirred at r.t. for 1 h. The mixture was concentrated in *vacuo* to afford 1-[(trimethylamino)methyl]-2-(diphenylphosphinyl)-ferrocenyl iodide (4.30 g, 93%) as a brown solid (m.p. 168-170 °C). Rf 0.29 (CH_2Cl_2/MeOH, 10/1); IR υ_{max} 3005 (CH), 1620, 1474 (P-Ph), 1436 (P-Ph), 1162 (P=O), 1114 (P=O) cm^{-1}; ^{1}H NMR (400 MHz) δ 3.00 (9H, bs, N($C\underline{H}_3$)$_3$), 4.08 (5H, bs, C$\underline{H}$-$Cp_{unsub.}$), 4.30 (1H, bs, C$\underline{H}$-$Cp_{sub.}$), 4.66 (1H, bs, C$\underline{H}$-$Cp_{sub.}$), 5.16 (1H d, *J* = 13.1 Hz, C$\underline{H}_2$), 5.18 (1H, bs, C$\underline{H}$-$Cp_{sub.}$), 5.34 (1H, d, *J* = 12.7 Hz, C$\underline{H}_2$), 7.27-7.78 (10H, m, C$\underline{H}$-PPh_2); ^{13}C NMR (100 MHz) δ 52.4 (N($\underline{C}H_3$)$_3$), 64.7 ($\underline{C}H_2$), 71.5 (C$\underline{H}$-$Cp_{unsub.}$), 71.7 (d, *J* = 111.6 Hz, Ph_2OP-$\underline{C}$-$Cp_{sub.}$), 74.2 (d, *J* = 10.5 Hz, C$\underline{H}$-$Cp_{sub.}$), 74.5 (d, *J* = 12.9 Hz, C$\underline{H}$-$Cp_{sub.}$), 77.2 (d, *J* = 13.3 Hz, C$\underline{H}$-$Cp_{sub.}$), 116.6 (d, *J* = 2.7 Hz, H_2C-$\underline{C}$-$Cp_{sub.}$), 128.4 (d, *J* = 12.1 Hz, *m*-$\underline{C}$H-PPh_2), 128.8 (d, *J* = 11.9 Hz, *m*-$\underline{C}$H-PPh_2), 130.4 (d, *J* = 9.9 Hz, *o*-$\underline{C}$H-PPh_2), 130.6 (d, *J* = 10.2 Hz, *o*-$\underline{C}$H-PPh_2), 132.0 (*p*-$\underline{C}$H-PPh_2), 132.1 (*p*-$\underline{C}$H-PPh_2), 133.2 (d, *J* = 107.4 Hz, *i*-$\underline{C}$-

PPh_2), 134.3 (d, J = 102.9 Hz, *i*-C-PPh_2); ^{31}P NMR (162 MHz) δ 30.7; m/z (ES+) 459 (4%, M+H), 458 (10%, M), 400 (23%, M-NMe_3), 399 (100%, M-NMe_3-H); HRMS (M-I) $C_{26}H_{29}FeNOP$ calcd. 458.1336, found 458.1326; Anal. Calcd. for $C_{26}H_{29}FeINOP$: C, 53.36; H, 4.99; N, 2.39. Found C, 52.72; H, 5.09; N, 3.30%.

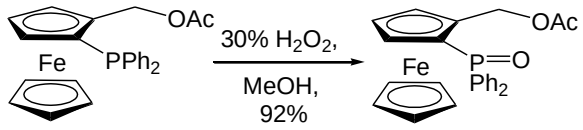


(+/-)-232 **(+/-)-235**

1-[(Acetoxy)methyl]-2-(diphenylphosphino)-ferrocene (**(+/-)-235**).

A solution of 1-[(dimethylamino)methyl]-2-(diphenylphosphino)-ferrocene (6.35 g, 14.9 mmol) in Ac_2O (15 mL) was heated to 100 °C for 2 h. The mixture was let to cool to r.t. and was kept in the freezer overnight. After filtration, washing with cold MeOH (2 × 10 mL) 1-[(acetoxy)methyl]-2-(diphenylphosphino)-ferrocene was obtained (4.93 g, 75%) as an orange solid (m.p. 173-175 °C) which was used in the next step without further purification. Rf 0.68 (^{n}hexane/Et_2O/Et_3N, 10/10/1); IR υ_{max} 3048 (CH), 1732 (C=O), 1436 (P-Ph), 1248 (C-O) cm^{-1}; ^{1}H NMR (400 MHz) δ 1.61 (3H, s, OCOC$\underline{H}_3$), 3.79 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.09 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.33 (1H, t, J = 2.4 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.54 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.98 (1H, d, J = 11.9 Hz, C$\underline{H}_2$), 5.18 (1H, dd, J = 11.9 Hz, J_{HP} = 2.3 Hz, C$\underline{H}_2$), 7.12-7.59 (10H, m, C$\underline{H}$-PPh_2); ^{13}C NMR (100 MHz) δ 20.5 (OCO$\underline{C}H_3$), 61.8 (d, J = 9.7 Hz, $\underline{C}H_2$), 69.7 ($\underline{C}$H-$Cp_{unsub.}$), 70.1 ($\underline{C}$H-$Cp_{sub.}$), 72.4 (d, J = 3.8 Hz, $\underline{C}$H-$Cp_{sub.}$), 73.1 (d, J = 3.3 Hz, $\underline{C}$H-$Cp_{sub.}$), 77.8 (d, J = 9.1 Hz, Ph_2P-$\underline{C}$-$Cp_{sub.}$), 86.3 (d, J = 24.6 Hz, H_2C-$\underline{C}$-$Cp_{sub.}$), 127.9 (*p*-$\underline{C}$H-PPh_2), 128.0 (d, J = 6.2 Hz, *m*-$\underline{C}$H-PPh_2), 128.2 (d, J = 7.7 Hz, *m*-$\underline{C}$H-PPh_2), 129.2 (*p*-$\underline{C}$H-PPh_2), 132.5 (d, J = 18.3 Hz, *o*-

C<u>H</u>-PPh_2), 135.0 (d, *J* = 20.9 Hz, *o*-C<u>H</u>-PPh_2), 137.1 (d, *J* = 8.6 Hz, *i*-<u>C</u>-PPh_2), 139.7 (d, *J* = 10.1 Hz, *i*-<u>C</u>-PPh_2), 170.6 (O<u>C</u>OCH_3); ^{31}P NMR (162 MHz) δ -22.1; m/z (EI) 443 (17%, M+H), 442 (60%, M); HRMS $C_{25}H_{23}FeO_2P$ calcd. 442.07796, found 442.07831; Anal. Calcd. for $C_{25}H_{23}FeO_2P$: C, 67.89; H, 5.24. Found C, 67.83; H, 5.23%.

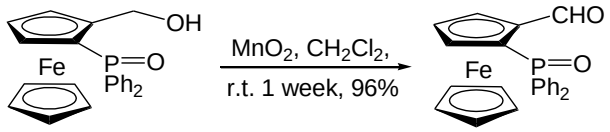


(+/-)-235 **(+/-)-236**

1-[(Acetoxy)methyl]-2-(diphenylphosphinoxy)-ferrocene (**(+/-)-236**).

To a solution of 1-[(acetoxy)methyl]-2-(diphenylphosphino)-ferrocene (450 mg, 1.02 mmol) in MeOH (30 mL) 30% aq. H_2O_2 (0.12 mL, 1.17 mmol, 1.15 eq.) was added dropwise at 0 °C and the mixture was stirred for 30 min at r.t. Then saturated $Na_2S_2O_3$ (15 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 20 mL) washed with water (10 mL) dried ($MgSO_4$) and concentrated in *vacuo* to give (433 mg, 92%) as an orange solid (m.p. 150-152 °C). Rf 0.07 (^{n}hexane/Et_2O/Et_3N, 10/10/1); IR υ_{max} 3074 (CH), 1723 (C=O), 1437 (P-Ph), 1238 (C-O) cm^{-1}; ^{1}H NMR (400 MHz) δ 1.63 (3H, s, OCOC<u>H</u>$_3$), 3.94 (1H, m, C<u>H</u>-Cp$_{sub.}$), 4.31 (5H, s, C<u>H</u>-Cp$_{unsub.}$), 4.39 (1H, dd, *J* = 2.4, 2.2 Hz, C<u>H</u>-Cp$_{sub.}$), 4.61 (1H, dt, *J* = 2.3 Hz, $J_{HH/HP}$ = 1.4 Hz, C<u>H</u>-Cp$_{sub.}$), 5.10 (1H, d, *J* = 11.9 Hz, C<u>H</u>$_2$), 5.21 (1H, d, *J* = 11.8 Hz, C<u>H</u>$_2$), 7.35-7.84 (10H, m, C<u>H</u>-PPh_2); ^{13}C NMR (100 MHz) δ 20.5 (OCO<u>C</u>H$_3$), 61.4 (<u>C</u>H$_2$), 70.3 (<u>C</u>H-Cp$_{unsub.}$), 70.9 (d, *J* = 10.9 Hz, <u>C</u>H-Cp$_{sub.}$), 73.4 (d, *J* = 112.9 Hz, Ph_2P-<u>C</u>-Cp$_{sub.}$), 74.5 (d, *J* = 9.3 Hz, <u>C</u>H-Cp$_{sub.}$), 74.9 (d, *J* = 14.4 Hz, <u>C</u>H-Cp$_{sub.}$), 85.1 (d, *J* = 10.4 Hz, H_2C-<u>C</u>-Cp$_{sub.}$), 128.0 (d, *J* = 4.5

Hz, *m*-CH-PPh_2), 128.2 (d, *J* = 4.4 Hz, *m*-CH-PPh_2), 131.3 (*p*-CH-PPh_2), 131.4 (*p*-CH-PPh_2), 131.6 (d, *J* = 10.2 Hz, *o*-CH-PPh_2), 131.7 (d, *J* = 10.3 Hz, *o*-CH-PPh_2), 133.5 (d, *J* = 117.2 Hz, *i*-C-PPh_2), 134.9 (d, *J* = 117.2 Hz, *i*-C-PPh_2), 170.5 ($OCOCH_3$); ^{31}P NMR (162 MHz) δ 29.7; m/z (EI) 459 (3%, M+H), 458 (10%, M), 394 (22%, M+H-Cp), 393 (100%, M-Cp); HRMS $C_{25}H_{23}FeO_3P$ calcd. 458.07287, found 458.07326; Anal. Calcd. for $C_{25}H_{23}FeO_3P$: C, 65.52; H, 5.06. Found C, 65.24; H, 5.06%.

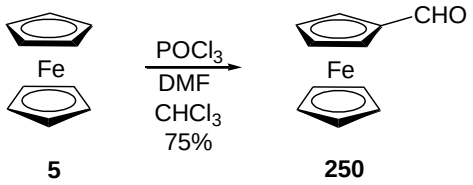


(+/-)-228 **(+/-)-247**

2-(Diphenylphosphinoxy)-ferrocenecarboxaldehyde (**(+/-)-247**).

To a solution of 1-(diphenylphosphino)-2-(hydroxymethyl)-ferrocene (1.17 g, 2.81 mmol) in CH_2Cl_2 (120 mL), MnO_2 (3.26 g, 33.7 mmol, 12.0 eq.) was added and the reaction was stirred at r.t. for a week. Then the mixture was filtered through Celite and the CH_2Cl_2 was removed in *vacuo* to give 2-(diphenylphosphinoxy)-ferrocenecarboxaldehyde (1.11 g, 96%) as an orange solid (m.p. 190 °C-decomp. lit.: 176-177 °C). Rf 0.63 (CH_2Cl_2/MeOH, 10/1); IR υ_{max} 3091 (CH), 2871 (CHO), 1663 (C=O), 1401 (P-Ph), 1247 (P=O), 1193 (C-O), 1164 (C-O) cm^{-1}; ^{1}H NMR (600 MHz) δ 4.25 (1H, m, CH-$Cp_{sub.}$), 4.41 (5H, s, CH-$Cp_{unsub.}$), 4.78 (1H, m, CH-$Cp_{sub.}$), 5.24 (1H, m, CH-$Cp_{sub.}$), 7.38-7.84 (10H, m, CH-PPh_2), 10.40 (1H, s, CHO); ^{13}C NMR (150 MHz) δ 71.6 (CH-$Cp_{unsub.}$), 71.7 (CH-$Cp_{sub.}$), 74.6 (d, *J* = 10.7 Hz, CH-$Cp_{sub.}$), 77.1 (d, *J* = 109.9 Hz, Ph_2P-C-$Cp_{sub.}$), 77.4 (CH-$Cp_{sub.}$), 78.9 (d, *J* = 13.3 Hz, CH-$Cp_{sub.}$), 82.8 (d, *J* = 9.8 Hz, H_2C-C-$Cp_{sub.}$), 128.5 (d, *J* = 12.2 Hz, *m*-CH-PPh_2), 128.7 (d, *J* = 12.2

Hz, *m*-CH-PPh_2), 131.6 (d, *J* = 15.3 Hz, *o*-CH-PPh_2), 131.7 (d, *J* = 15.2 Hz, *o*-CH-PPh_2), 132.1 (d, *J* = 2.8 Hz, *p*-CH-PPh_2), 132.1 (d, *J* = 2.8 Hz, *p*-CH-PPh_2), 132.9 (d, *J* = 107.3 Hz, *i*-C-PPh_2), 134.5 (d, *J* = 107.4 Hz, *i*-C-PPh_2); ^{31}P NMR (162 MHz) δ 27.8; m/z (EI) 415 (27%, M+H), 414 (100%, M), 387 (18%, M+H-CH_2-CHO), 386 (72%, M-CH_2-CHO), 349 (36%, M-Cp), 321 (39%, M-CH_2-CHO-Cp); HRMS $C_{23}H_{19}FeO_2P$ calcd. 414.04666, found 414.04726. Lit.: *Eur. J. Org. Chem*. **2009**, *5*, 716.

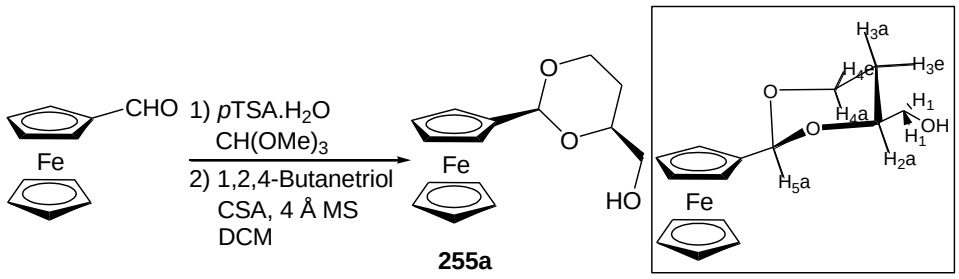


5 **250**

Ferrocenecarboxaldehyde (**250**).

To a solution of ferrocene (37.2 g, 0.20 mol) in $CHCl_3$ (150 mL) Dimethylformamide (30.8 mL, 0.40 mol, 2.00 eq.) was added. Then freshly distilled $POCl_3$ (61.2 g, 0.40 mol, 2.00 eq.) was added dropwise and the reaction was stirred at 60 °C for 20 h. The solvent was removed under reduced pressure and the mixture was poured onto ice. The unreacted ferrocene was filtered off and Na_2CO_3 was added in portions to the purple coloured solution which turned brown upon setting the pH to 9. This brown suspension was extracted with Et_2O (3 × 200 mL) and the organics were washed with water (1 × 150 mL), dried ($MgSO_4$) concentrated in *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 9/1) to give the product (31.9 g, 75%) as a deep red solid (m.p. 67-70 °C, lit.: 123-124 °C). Rf 0.16 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 3090 (CH), 1675 (CO), 1660 (CO), 1452, 1244 (CO) cm^{-1}; ^{1}H NMR (400 MHz) δ 4.29 (5H, s, CH-$Cp_{unsub.}$), 4.62 (2H, s, CH-$Cp_{sub.}$), 4.81 (2H, s, CH-$Cp_{sub.}$), 9.97 (1H, s, CHO); ^{13}C

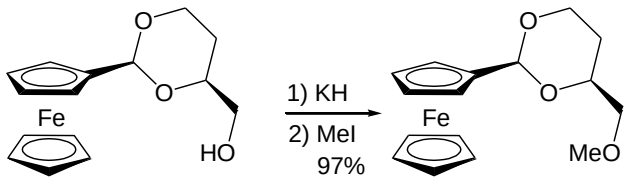
NMR (100 MHz) δ 69.7 (CH-$Cp_{unsub.}$ & CH-$Cp_{sub.}$), 73.2 (CH-$Cp_{sub.}$), 79.4 (C-CHO), 193.5 (CHO); m/z (EI) 215 (13%, M+H), 214 (35%, M), 187 (6%, Fc+H), 186 (50%, Fc), 121 (Fc-Cp); HRMS $C_{11}H_{10}FeO$ calcd. 214.00756, found 214.00823; Anal. Calcd. For $C_{11}H_{10}FeO$: C, 61.73; H, 4.71. Found C, 61.74; H, 4.67%. ^{1}H NMR and ^{13}C NMR agreed with literature data.[204]



4-(Hydroxymethyl)-2-ferrocenyl-1,3-dioxane (**255a**).

To a solution of ferrocenecarboxaldehyde (10.0 g, 56.7 mmol) in trimethyl orthoformate (60 mL), was added a catalytic amount of *p*TSA.H_2O (440 mg, 2.31 mmol, 0.05 eq.) and the solution was stirred at 80 °C overnight. Anhydrous K_2CO_3 (3 g) was then added and the solution was allowed to cool while the stirring was maintained. The mixture then was filtered through Celite and the filter cake was washed with Et_2O (2 × 50 mL). The filtrate was concentrated to give a dark brown oil which was dried for 6 h under *vacuo* and used directly in the next step. 1,2,4-butanetriol (4.96 g, 46.7 mmol, 1.00 eq.) was weighed in a flask and dried by mixing with toluene, removing the toluene on a rotary evaporator (3 times) and finally left under *vacuo* overnight. Camphorsulfonic acid (530 mg, 2.30 mmol, 0.05 eq.) and 4 Å Molecular sieves (10 g) was also dried under *vacuo* overnight. Crude product then was mixed with the camphorsulfonic acid, the 4 Å Molecular sieves and the 1,2,4-butanetriol in CH_2Cl_2

(50 mL), and stirred at r.t. overnight. Anhydrous K_2CO_3 was then added and the mixture then was filtered through Celite and the filter cake was washed with CH_2Cl_2 (2 × 50 mL), concentrated and purified by flash column chromatography on silica gel using (^{n}hexane/EtOAc, 1/1) to afford 4-(hydroxymethyl)-2-ferrocenyl-1,3-dioxane (8.69 g, 62%) as a yellow solid (m.p. 89-90 °C). Rf 0.40 (^{n}hexane/EtOAc, 1/1); IR υ_{max} 3311 (OH), 3088 (CH), 2851 (CO), 1658 (Ar), 1407 (OH), 1316 (OH), 1239 (CO), 1102 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 1.40 (1H, dtd, $J_{gem.}$ = 13.2 Hz, $J_{3}e\text{-}_{4}a_{\&3}e\text{-}_{2}a$ = 2.6 Hz, $J_{3}e\text{-}_{4}e$ = 1.3 Hz, $\underline{H}_3$e), 1.84 (1H, dddd, $J_{gem.}$ = 13.1 Hz, $J_{3}a\text{-}_{4}a$ = 12.4 Hz, $J_{3}a\text{-}_{2}a$ = 11.5 Hz, $J_{3}a\text{-}_{4}e$ = 5.2 Hz, $\underline{H}_3$a), 2.14 (1H, dd, $J_{O\underline{H}\text{-}1}$ = 7.9 Hz, $J_{O\underline{H}\text{-}1}$ = 5.2 Hz, O$\underline{H}$), 3.63 (1H, ddd, $J_{gem.}$ = 11.7 Hz, $J_{1\text{-}2}a$ = 6.7 Hz, $J_{1\text{-}O\underline{H}}$ = 5.2 Hz, $\underline{H}_1$), 3.68 (1H, ddd, $J_{gem.}$ = 11.7 Hz, $J_{1\text{-}O\underline{H}}$ = 7.9 Hz, $J_{1\text{-}2}a$ = 3.3 Hz, $\underline{H}_1$), 3.92 (1H, ddd, $J_{4}a\text{-}_{3}a$ = 12.6 Hz, $J_{gem.}$ = 11.4 Hz, $J_{4}a\text{-}_{3}e$ = 2.6 Hz, $\underline{H}_4$a), 3.96 (1H, m, $\underline{H}_2$a), 4.15 (2H, m, C$\underline{H}$-$Cp_{sub.}$), 4.18 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.24 (1H, ddd, $J_{gem.}$ = 11.3 Hz, $J_{4}e\text{-}_{3}a$ = 5.1 Hz, $J_{4}e\text{-}_{3}e$ = 1.4 Hz, $\underline{H}_4$e), 4.33 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.34 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 5.42 (1H, s, $\underline{H}_5$a); ^{13}C NMR (150 MHz) δ 27.0 ($\underline{C}_3$), 65.9 ($\underline{C}_1$), 66.6 ($\underline{C}$H-$Cp_{sub.}$), 66.6 ($\underline{C}_4$), 66.8 ($\underline{C}$H-$Cp_{sub.}$), 68.2 (2 × $\underline{C}$H-$Cp_{sub.}$), 69.0 ($\underline{C}$H-$Cp_{unsub.}$), 77.3 ($\underline{C}_2$), 85.9 (HC-$\underline{C}$-$Cp_{sub.}$), 100.3 ($\underline{C}_5$); m/z (EI) 302 (12%, M), 186 (35%, Fc), 121 (100%, Cp+Fe); HRMS $C_{15}H_{18}FeO_3$ calcd. 302.05998, found 302.05925; Anal. Calcd. For $C_{15}H_{18}FeO_3$: C, 59.63; H, 6.00. Found C, 59.35; H, 5.97%. ^{1}H NMR and ^{13}C NMR agreed with literature data.[205]

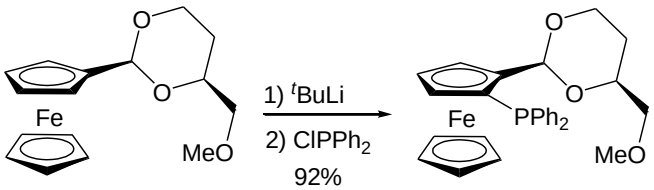


255a **251**

4-(Methoxymethyl)-2-ferrocenyl-1,3-dioxane (**251**).

A flask was charged with KH (6.92 g, 43.1 mmol, 1.50 eq.) in mineral oil. The KH was washed with ^{n}hexane (3 × 5 mL) then dried under vacuum. To the solution of KH in THF (80 mL) 4-(hydroxymethyl)-2-ferrocenyl-1,3-dioxane (8.69 g, 28.8 mmol) was added in THF (35 mL) at 0 °C. The mixture was stirred at for 30 min then MeI (2.68 mL, 43.1 mmol, 1.50 eq.) was added and the mixture was stirred for 1 h at r.t. Water (50 mL) and MeOH (30 mL) was then added to the reaction at 0 °C. The mixture was extracted with Et_2O (3 × 60 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography (Et_2O) to give 4-(methoxymethyl)-2-ferrocenyl-1,3-dioxane (8.59 g, 97%) as a yellow solid (m.p. 45-47 °C). Rf 0.56 (^{n}hexane/EtOAc, 7/3); IR υ_{max} 3095 (CH), 2889 (CO), 2848 (CO), 1650 (Ar), 1496, 1237 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 1.50 (1H, dm, $J_{gem.}$ = 13.3 Hz, $\underline{H}_3$e), 1.79 (1H, dddd, $J_{gem.}$ = 13.3 Hz, J_3a-$_4a$ = 12.4 Hz, J_3a-$_2a$ = 11.5 Hz, J_3a-$_4e$ = 5.1 Hz, $\underline{H}_3$a), 3.43 (1H, dd, $J_{gem.}$ = 10.3 Hz, $J_{1-2}a$ = 4.6 Hz, $\underline{H}_1$), 3.44 (3H, s, O-C$\underline{H}_3$), 3.55 (1H, dd, $J_{gem.}$ = 10.4 Hz, $J_{1-2}a$ = 6.1 Hz, $\underline{H}_1$), 3.91 (1H, ddd, J_{4a-3a} = 12.4 Hz, $J_{gem.}$ = 11.5 Hz, J_4a-$_3e$ = 2.7 Hz, $\underline{H}_4$a), 4.00 (1H, m, $\underline{H}_2$a), 4.12 (2H, m, C$\underline{H}$-$Cp_{sub.}$), 4.18 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.24 (1H, ddd, $J_{gem.}$ = 11.4 Hz, J_4e-$_3a$ = 5.1 Hz, J_4e-$_3e$ = 1.4 Hz, $\underline{H}_4$e), 4.34 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.36 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 5.39 (1H, s, $\underline{H}_5$a); ^{13}C NMR (150 MHz) δ 28.2 ($\underline{C}_3$), 59.6 (OC$\underline{H}_3$), 66.8 ($\underline{C}_4$), 66.9 (2 × C$\underline{H}$-$Cp_{sub.}$), 68.0 (C$\underline{H}$-$Cp_{sub.}$), 68.1 (C$\underline{H}$-$Cp_{sub.}$), 69.0 (C$\underline{H}$-$Cp_{unsub.}$), 75.8 ($\underline{C}_1$), 76.21 ($\underline{C}_2$), 86.1 (HC-$\underline{C}$-$Cp_{sub.}$), 100.3 ($\underline{C}_5$); m/z (EI) 317 (19%, M+H), 316 (100%, M),

214 (25%, Fc-CHO), 186 (49%, Fc), 121 (37%, Cp+Fe); HRMS $C_{16}H_{20}FeO_3$ calcd. 316.07564, found 316.07455; Anal. Calcd. For $C_{16}H_{20}FeO_3$: C, 60.78; H, 6.38. Found C, 60.55; H, 6.29%. ^{1}H NMR and ^{13}C NMR agreed with literature data. [205]

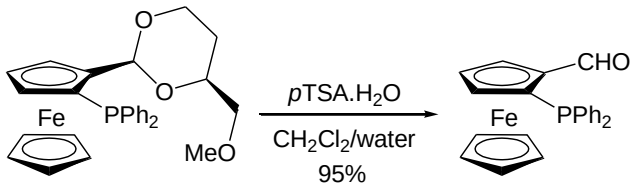


(+/-)-251 **(+/-)-252**

4-(Methoxymethyl)-2-[α-(diphenylphosphino)-ferrocenyl]-1,3-dioxane ((+/-)-252).

To a solution of 4-(methoxymethyl)-2-ferrocenyl-1,3-dioxane (8.00 g, 25.3 mmol) in Et_2O (90 mL) ^{t}BuLi (18.5 mL, 27.8 mmol, 1.10 eq.) was added at -78 °C and the mixture was stirred for 1 h at r.t. After $ClPPh_2$ (5.45 mL, 30.4 mmol, 1.20 eq.) was added at -78 °C and the mixture was stirred for 4 h at r.t. Water (40 mL) then 2M NaOH (10 mL) was added to the reaction mixture, the phases were separated, the water phase was extracted with Et_2O (2 × 40 mL). The combined organic phase was washed with brine (40 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography using (^{n}hexane/EtOAc, 7/3) to give 4-(methoxymethyl)-2-[α-(diphenylphosphino)-ferrocenyl]-1,3-dioxane (11.6 g, 97%) as a brown solid (m.p. 100-103 °C). Rf 0.46 (^{n}hexane/EtOAc, 7/3); IR υ_{max} 3049 (CH), 2952 (CH), 2875 (CH), 1432 , 1242 (CO), 1100 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 1.44 (1H, dm, $J_{gem.}$ = 13.4 Hz, $\underline{H}_3$e), 1.74 (1H, dddd, $J_{gem.}$ = 13.3 Hz, $J_{3}a$-$_{4}a$ = 12.6 Hz, $J_{3}a$-$_{2}a$ = 11.4 Hz, $J_{3}a$-$_{4}e$ = 5.2 Hz, $\underline{H}_3$a), 2.93 (2H, dd, $J_{gem.}$ = 10.2 Hz, $J_{1\text{-}2}a$ = 5.4 Hz, $\underline{H}_1$), 3.07 (3H, s, O-C$\underline{H}_3$), 3.70 (1H, dt, J = 2.4 Hz, $J_{HH/HP}$ = 1.2 Hz, C$\underline{H}$-Cp$_{sub.}$), 3.76 (1H, ddt, $J_{2}a$-$_{3}a$ = 11.4 Hz, $J_{2a\text{-}1}$ = 5.2 Hz, $J_{2}a$-$_{3}e$ = 2.4 Hz, $\underline{H}_2$a), 3.93 (1H, ddd, $J_{4}a$-$_{3}a$ = 12.5 Hz, $J_{gem.}$ = 11.6 Hz,

J_4a-$_{3e}$ = 2.7 Hz, $\underline{H}_4$a), 4.08 (5H, s, C$\underline{H}$-Cp$_{unsub.}$), 4.28 (1H, t, J = 2.6 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.28 (1H, ddd, $J_{gem.}$ = 11.4 Hz, J_4e-$_3a$ = 5.0 Hz, J_4e-$_3e$ = 1.4 Hz, $\underline{H}_4$e), 4.71 (1H, dt, J = 2.6 Hz, $J_{HH/HP}$ = 1.4 Hz, C$\underline{H}$-Cp$_{sub.}$), 5.69 (1H, d, J_{HP} = 2.3 Hz, $\underline{H}_5$a), 7.19-7.59 (10H, m, C$\underline{H}$-PPh$_2$); ^{13}C NMR (150 MHz) δ 28.4 ($\underline{C}_3$), 59.1 (OC$\underline{H}_3$), 67.1 ($\underline{C}_4$), 69.3 (d, J = 3.7 Hz, $\underline{C}$H-Cp$_{sub.}$), 69.5 ($\underline{C}$H-Cp$_{sub.}$), 70.1 ($\underline{C}$H-Cp$_{unsub.}$), 71.9 (d, J = 4.1 Hz, $\underline{C}$H-Cp$_{sub.}$), 74.8 ($\underline{C}_1$), 75.0 (d, J = 9.7 Hz, Ph$_2$P-$\underline{C}$-Cp$_{sub.}$), 75.6 ($\underline{C}_2$), 90.8 (d, J = 21.3 Hz, HC-$\underline{C}$-Cp$_{sub.}$), 100.0 (d, J = 9.7 Hz, $\underline{C}_5$), 127.7 (*p*-$\underline{C}$H-PPh$_2$), 127.7 (d, J = 6.2 Hz, *m*-$\underline{C}$H-PPh$_2$), 128.2 (d, J = 7.7 Hz, *m*-$\underline{C}$H-PPh$_2$), 129.2 (*p*-$\underline{C}$H-PPh$_2$), 132.7 (d, J = 18.1 Hz, *o*-$\underline{C}$H-PPh$_2$), 135.3 (d, J = 32.4 Hz, *o*-$\underline{C}$H-PPh$_2$), 137.5 (d, J = 7.9 Hz, *i*-$\underline{C}$-PPh$_2$), 140.0 (d, J = 8.9 Hz, *i*-$\underline{C}$-PPh$_2$); ^{31}P NMR δ -21.3; m/z (EI) 501 (4%, M+H), 500 (13%, M), 316 (12%, M-PPh$_2$), 186 (6%, Fc), 121 (5%, Cp+Fe); HRMS $C_{28}H_{29}FeO_3P$ calcd. 500.11982, found 500.11827; Anal. Calcd. For $C_{28}H_{29}FeO_3P$: C, 67.21; H, 5.84. Found C, 66.79; H, 5.89%. ^{1}H NMR and ^{13}C NMR agreed with literature data.[203]

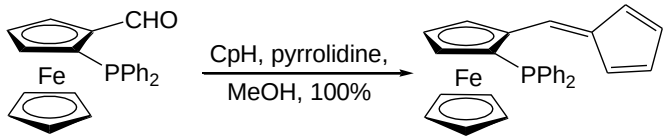


(+/-)-252 **(+/-)-248**

2-(Diphenylphosphino)-ferrocenecarboxaldehyde (**(+/-)-248**).

To a biphasic solution of 4-(methoxymethyl)-2-[α-(diphenylphosphino)-ferrocenyl]-1,3-dioxane (500 mg, 0.10 mmol) and *p*TSA.H_2O (475 mg, 2.50 mmol, 2.50 eq.) in CH_2Cl_2/Water (degassed) (17.5 mL/7.5 mL) was stirred vigorously for 8 h at r.t. The phases were separated and the wa ter-phase was extracted with CH_2Cl_2 (5 mL). Organics were concentrated in *vacuo* and purified by flash column chromatography

(CH_2Cl_2/EtOAc, 98/2) to give 2-(diphenylphosphino)-ferrocenecarboxaldehyde (380 mg, 95%) as an orange-red solid (m.p. 206-208 °C). Rf 0.69 (CH_2Cl_2/EtOAc, 98/2); IR υ_{max} 3053 (CH), 2837 (CH), 1664 (CO), 1428, 1249 (CO) cm^{-1}; ^{1}H NMR (400 MHz) δ 4.07 (1H, dt, J = 2.5 Hz, $J_{HH/HP}$ = 1.3 Hz, C<u>H</u>-$Cp_{sub.}$), 4.23 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.71 (1H, t, J = 2.6 Hz, C<u>H</u>-$Cp_{sub.}$), 5.11 (1H, dt, J = 2.6 Hz, $J_{HH/HP}$ = 1.2 Hz, C<u>H</u>-$Cp_{sub.}$), 7.14-7.59 (10H, m, C<u>H</u>-PPh_2), 10.23 (1H, d, J_{HP} = 2.8 Hz, C<u>H</u>O); ^{13}C NMR (100 MHz) δ 70.9 (<u>C</u>H-$Cp_{unsub.}$), 71.5 (d, J = 2.1 Hz, <u>C</u>H-$Cp_{sub.}$), 74.0 (<u>C</u>H-$Cp_{sub.}$), 76.4 (d, J = 4.3 Hz, <u>C</u>H-$Cp_{sub.}$), 80.7 (d, J = 16.9 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 83.4 (d, J = 14.0 Hz, OHC-<u>C</u>-$Cp_{sub.}$), 128.3 (d, J = 1.4 Hz, *m*-<u>C</u>H-PPh_2), 128.4 (d, J = 0.8 Hz, *m*-<u>C</u>H -PPh_2), 128.46 (*p*-<u>C</u>H-PPh_2), 129.5 (*p*-<u>C</u>H-PPh_2), 132.2 (d, J = 18.6 Hz, *o*-<u>C</u>H-PPh_2), 135.0 (d, J = 21.2 Hz, *o*-<u>C</u>H-PPh_2), 136.5 (d, J = 10.6 Hz, *i*-<u>C</u>-PPh_2), 139.1 (d, J = 10.5 Hz, *i*-<u>C</u>-PPh_2), 193.4 (d, J = 11.2 Hz, CHO); ^{31}P NMR (162 MHz) δ -23.0; m/z (EI) 399 (3%, M+H), 398 (13%, M), 186 (1%, Fc); HRMS $C_{23}H_{19}FeOP$ calcd. 398.05175, found 398.04978; Anal. Calcd. For $C_{23}H_{19}FeOP$: C, 69.37; H, 4.81. Found C, 69.08; H, 4.65%. ^{1}H NMR and ^{13}C NMR agreed with literature data.[203]

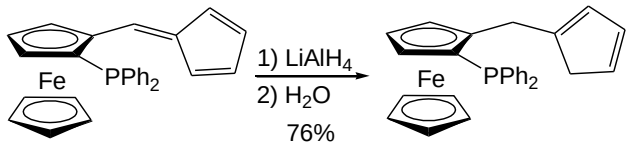


(+/-)-248 **(+/-)-253**

1-(Diphenylphosphino)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene ((+/-)-253).

2-(Diphenylphosphino)-ferrocenecarboxaldehyde (100 mg, 0.25 mmol), pyrrolidine (0.04 mL, 0.50 mmol, 2.00 eq.) and freshly cracked cyclopentadiene (0.08 mL, 1.00 mmol, 4.00 eq.) was stirred in degassed MeOH (10 mL) at r.t. for 3.5 h. The reaction was concentrated in *vacuo*, dried for few hours under vacuum and purified by flash column chromatography on silica using (^{n}hexane/EtOAc, 9/1) to give 1-(diphenylphosphino)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (113 mg, 100%) as a red-purple solid (m.p. 147-149 °C). Rf 0.64 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 3068 (CH), 1615 (C=C), 1606 (C=C), 1420 cm^{-1}; ^{1}H NMR (400 MHz) δ 4.07 (1H, m, C<u>H</u>-$Cp_{sub.}$), 4.11 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.69 (1H, t, *J* = 2.6 Hz, C<u>H</u>-$Cp_{sub.}$), 5.14 (1H, m, C<u>H</u>-$Cp_{sub.}$), 6.31 (1H, dt, *J* = 5.0, 1.7 Hz, C<u>H</u>-Fulv.), 6.45 (1H, dm, *J* = 5.0 Hz, C<u>H</u>-Fulv.), 6.63 (1H, ddt, *J* = 5.1, 1.6, 1.9 Hz, C<u>H</u>-Fulv.), 6.72 (1H, dm, *J* = 5.3 Hz, C<u>H</u>-Fulv.), 7.13-7.27 (5H, m, C<u>H</u>-PPh_2), 7.43-7.47 (3H, m, C<u>H</u>-PPh_2), 7.48 (1H, d, *J* = 3.1 Hz, Fc-C<u>H</u>=Fulv.), 7.60-7.67 (2H, m, C<u>H</u>-PPh_2); ^{13}C NMR (100 MHz) δ 71.0 (<u>C</u>H-$Cp_{unsub.}$), 71.1 (d, *J* = 2.4 Hz, <u>C</u>H-$Cp_{sub.}$), 73.0 (<u>C</u>H-$Cp_{sub.}$), 74.3 (d, *J* = 3.8 Hz, <u>C</u>H-$Cp_{sub.}$), 80.6 (d, *J* = 10.3 Hz, PPh_2-<u>C</u>-$Cp_{sub.}$), 85.5 (d, *J* = 20.7 Hz, Fulv.-<u>C</u>-$Cp_{sub.}$), 119.8 (<u>C</u>H-Fulv.), 126.9 (<u>C</u>H-Fulv.), 128.0 (*p*-<u>C</u>H-PPh_2), 128.3 (d, *J* = 9.7 Hz, *m*-<u>C</u>H-PPh_2), 128.4 (d, *J* = 11.9 Hz, *m*-<u>C</u>H-PPh_2), 128.9 (<u>C</u>H-Fulv.), 129.5 (*p*-<u>C</u>H-PPh_2), 132.0 (d, *J* = 17.7 Hz, *o*-<u>C</u>H-PPh_2), 133.4 (<u>C</u>H-Fulv.), 132.0 (d, *J* = 21.3 Hz, *o*-<u>C</u>H-PPh_2), 137.0 (d,

J = 8.1 Hz, *i*-C-PPh_2), 138.1 (d, *J* = 14.9 Hz, Fc-CH-Fulv.), 139.4 (d, *J* = 9.8 Hz, *i*-C-PPh_2), 142.4 (CH=C-Fulv.); ^{31}P NMR (162 MHz) δ -23.0; m/z (EI) 447 (28%, M+H), 446 (100%, M), 121 (4%, Cp+Fe); HRMS $C_{28}H_{23}FeP$ calcd. 446.08813, found 446.08852; Anal. Calcd. For $C_{28}H_{23}FeP$: C, 75.35; H, 5.19. Found C, 74.66; H, 5.10%.



(+/-)-253 **(+/-)-211**

1-(Diphenylphosphino)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (**(+/-)-211**).

To a solution of 1-(diphenylphosphino)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (50.0 mg, 0.11 mmol) in THF (5.0 mL) $LiAlH_4$ was added (0.08 mL, 0.17 mmol, 1.50 eq., 2M in THF) and the resulting solution was stirred at r.t. overnight. Water (4 mL) was added and the mixture was extracted with CH_2Cl_2 (2 × 3 mL), washed with water (1 × 2 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 9/1) to yield 1-(diphenylphosphino)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (38.0 mg, 76%) as a yellow solid (m.p. 114-116 °C) which consisted of 2 unseparable isomers in 6/4 ratio. Rf 0.66 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 3062 (CH), 3046 (CH), 2898 (CH), 2872, 1609 (C=C), 1583, 1475, 1430, 1362, 1172, 1105 cm^{-1}.

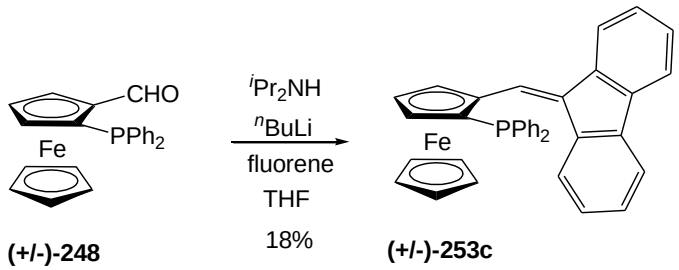
Major isomer:

^{1}H NMR (600 MHz) δ 2.48 (1H, dm, $J_{gem.}$ = 24.2 Hz, CH_2-Cp'), 2.69 (1H, dm, $J_{gem.}$ = 24.3 Hz, CH_2-Cp'), 3.54 (1H, dm, $J_{gem.}$ = 15.6 Hz, Fc-CH_2-Cp'), 3.71 (1H, m, CH-

$Cp_{sub.}$), 3.72 (1H, dm, $J_{gem.}$ = 15.2 Hz, Fc-C<u>H</u>$_2$-Cp'), 4.03 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.24 (1H, m, C<u>H</u>-$Cp_{sub.}$), 4.42 (1H, m, C<u>H</u>-$Cp_{sub.}$), 5.77 (1H, m, C<u>H</u>-Cp'), 6.25 (1H, m, C<u>H</u>-Cp'), 6.33 (1H, m, C<u>H</u>-Cp'), 7.03-7.60 (10H, C<u>H</u>-PPh_2); ^{13}C NMR (150 MHz) δ 29.5 (d, *J* = 10.2 Hz, <u>C</u>H$_2$-Cp'), 41.1 (Fc-<u>C</u>H$_2$-Cp'), 69.0 (<u>C</u>H-$Cp_{sub.}$), 69.8 (<u>C</u>H-$Cp_{unsub.}$), 71.0 (d, *J* = 4.2 Hz, <u>C</u>H-$Cp_{sub.}$), 71.9 (d, *J* = 4.0 Hz, <u>C</u>H-$Cp_{sub.}$), 75.3 (d, *J* = 6.3 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 92.9 (d, *J* = 25.7 Hz, H$_2$C-<u>C</u>-$Cp_{sub.}$), 127.4 (*p*-<u>C</u>H-PPh_2), 127. 8 (d, *J* = 6.1 Hz, *m*-<u>C</u>H-PPh_2), 128.0 (d, *J* = 3.1 Hz, <u>C</u>H-Cp'), 128. 2 (d, *J* = 7.8 Hz, *m*-<u>C</u>H-PPh_2), 129.1 (*p*-<u>C</u>H-PPh_2), 132.5 (d, *J* = 18.4 Hz, *o*-<u>C</u>H-PPh_2), 133.6 (<u>C</u>H-Cp'), 134.5 (<u>C</u>H-Cp'), 135.2 (d, *J* = 21.0 Hz, *o*-<u>C</u>H-PPh_2), 137.8 (d, *J* = 8.2 Hz, *i*-<u>C</u>-PPh_2), 139.7 (d, *J* = 9.1 Hz, *i*-<u>C</u>-PPh_2), 145.3 (H$_2$C-<u>C</u>-Cp'); ^{31}P NMR (162 MHz; $CDCl_3$) δ -23.1.

<u>Minor isomer</u>:

^{1}H NMR (600 MHz) δ 2.63 (1H, dm, $J_{gem.}$ = 22.1 Hz, C<u>H</u>$_2$-Cp'), 2.69 (1H, dm, $J_{gem.}$ = 22.3 Hz, C<u>H</u>$_2$-Cp'), 3.61 (1H, dm, $J_{gem.}$ = 15.8 Hz, Fc-C<u>H</u>$_2$), 3.73 (1H, m, C<u>H</u>-$Cp_{sub.}$), 3.75 (1H, dm, $J_{gem.}$ = 15.0 Hz, Fc-C<u>H</u>$_2$), 4.03 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.24 (1H, , C<u>H</u>-$Cp_{sub.}$), 4.39 (1H, m, C<u>H</u>-$Cp_{sub.}$), 5.94 (1H, m, C<u>H</u>-Cp'), 6.08 (1H, m, C<u>H</u>-Cp'), 6.18 (1H, m, C<u>H</u>-Cp'), 7.03-7.60 (10H, C<u>H</u>-PPh_2); ^{13}C NMR (150 MHz) δ 29.9 (d, *J* = 10.5 Hz, <u>C</u>H$_2$-Cp'), 43.3 (Fc-<u>C</u>H$_2$-Cp'), 69.1 (<u>C</u>H-$Cp_{sub.}$), 69.9 (<u>C</u>H-$Cp_{unsub.}$), 70.9 (d, *J* = 4.2 Hz, <u>C</u>H-$Cp_{sub.}$), 71.7 (d, *J* = 3.9 Hz, <u>C</u>H-$Cp_{sub.}$), 75.4 (d, *J* = 6.0 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 93.7 (d, *J* = 25.9 Hz, H$_2$C-<u>C</u>-$Cp_{sub.}$), 127.4 (*p*-<u>C</u>H-PPh_2), 127.8 (d, *J* = 6.6 Hz, *m*-<u>C</u>H-PPh_2), 128.0 (d, *J* = 3.1 Hz, <u>C</u>H-Cp'), 128.2 (d, *J* = 7.8 Hz, *m*-<u>C</u>H-PPh_2), 129.1 (*p*-<u>C</u>H-PPh_2), 130.7 (<u>C</u>H-Cp'), 132.2 (<u>C</u>H-Cp'), 132.5 (d, *J* = 18.1 Hz, *o*-<u>C</u>H-PPh_2), 135.1 (d, *J* = 21.0 Hz, *o*-<u>C</u>H-PPh_2), 137.8 (d, *J* = 8.2 Hz, *i*-<u>C</u>-PPh_2), 139.6 (d, *J* = 9.2 Hz, *i*-<u>C</u>-PPh_2), 148.1 (H$_2$C-<u>C</u>-Cp'); ^{31}P NMR (162 MHz; $CDCl_3$) δ -23.4; m/z (EI) 449 (3%, M+H), 448 (11%, M); HRMS $C_{28}H_{25}FeP$ calcd. 448.10378, found 448.10252.

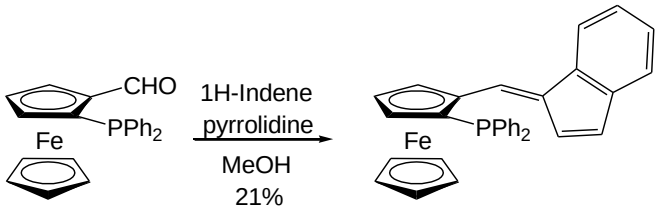


(+/-)-248 **(+/-)-253c**

1-(Diphenylphosphino)-2-[(9H-fluoren-9-ylidene)methyl]-ferrocene (**(+/-)-253c**).

To a solution of $^{i}Pr_2NH$ (0.07 mL, 0.50 mmol, 1.00 eq.) in THF (6.0 mL) ^{n}BuLi (0.24 mL, 0.60 mmol, 1.20 eq.) was added at -78 °C and the temperature was let to rise to r.t. during 30 min. Fluorene (83.0 mg, 0.50 mmol, 1.00 eq.) was added to the mixture at -78 °C and further stirred for another 30 min at -78 °C. 2-(diphenylphosphino)-ferrocenecarboxaldehyde (200 mg, 0.50 mmol) was then added in once and the reaction was stirred for 48 h. The mixture was extracted with Et_2O (2 × 4 mL) washed with water (1 × 4 mL), dried ($MgSO_4$) concentrated in *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 95/5) to give 1-(diphenylphosphino)-2-((9H-fluoren-9-ylidene)methyl)-ferrocene (50.0 mg, 18 %) as a red solid (m.p. 174-176 °C). Rf 0.57 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 3056 (CH), 1625 (C=C), 1602 (C=C), 1432, 1258, 1170 cm^{-1}; ^{1}H NMR (600 MHz) δ 4.04 (1H, bs, C<u>H</u>-$Cp_{sub.}$), 4.13 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.55 (1H, t, *J* = 2.4 Hz, C<u>H</u>-$Cp_{sub.}$), 5.05 (1H, bs, C<u>H</u>-$Cp_{sub.}$), 7.09-7.22 (12H, m, C<u>H</u>-PPh_2 & C<u>H</u>-Flu.), 7.61-7.65 (2H, m, C<u>H</u>-PPh_2), 7.68 (1H, d, *J* = 6.9 Hz, C<u>H</u>-Flu.), 7.71 (1H, d, *J* = 7.5 Hz, C<u>H</u>-Flu.), 7.72 (1H, s, Fc-CH=Flu.), 7.80 (1H, d, *J* = 7.3 Hz, C<u>H</u>-Flu.), 8.14 (1H, d, *J* = 7.8 Hz, C<u>H</u>-Flu.); ^{13}C NMR (150 MHz) δ 70.6 (<u>C</u>H-$Cp_{sub.}$), 70.7 (<u>C</u>H-$Cp_{unsub.}$), 72.4 (d, *J* = 2.6 Hz, <u>C</u>H-$Cp_{sub.}$), 73.4 (<u>C</u>H-$Cp_{sub.}$), 80.2 (d, *J* = 8.8 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 87.3 (d, *J* = 21.3 Hz, CH-<u>C</u>-$Cp_{sub.}$), 119.6 (<u>C</u>H-Flu.), 119.8 (<u>C</u>H-Flu.), 120.3 (<u>C</u>H-Flu.), 124.3 (<u>C</u>H-Flu.), 125.1 (d, *J* = 10.7 Hz, Ferr.-<u>C</u>H-Flu.), 126.6 (<u>C</u>H-Flu.),

126.9 (CH-Flu.), 127.6 (CH-Flu.), 127.9 (*p*-CH-PPh_2), 127.9 (*p*-CH-PPh_2), 128.2 (d, *J* = 5.8 Hz, *m*-CH-PPh_2), 128.4 (d, *J* = 7.8 Hz, *m*-CH-PPh_2), 129.5 (CH-Flu.), 132.1 (d, *J* = 17.5 Hz, *o*-CH-PPh_2), 135.2 (C-Flu.), 135.2 (d, *J* = 20.9 Hz, *o*-CH-PPh_2), 137.1 (C-Flu.), 137.4 (d, *J* = 8.2 Hz, *i*-C-PPh_2), 138.3 (C-Flu.), 139.4 (d, *J* = 10.5 Hz, *i*-C-PPh_2), 139.9 (C-Flu.), 140.9 (C-Flu.); ^{31}P NMR (162 MHz) δ -21.0; m/z (EI) 547 (2%, M+H), 546 (11%, M), 426 (31%, M-Fe-Cp), 425 (100%, M-Fe-Cp-H); HRMS $C_{36}H_{27}FeP$ calcd. 546.11943, found 546.11936.



(+/-)-248 **(+/-)-253b**

1-(Diphenylphosphino)-2-(1H-inden-1-ylidene)methyl)-ferrocene (**(+/-)-253b**).

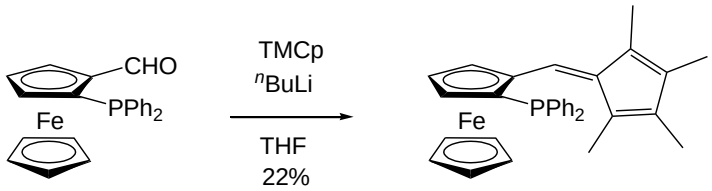
The solution of 2-(diphenylphosphino)-ferrocenecarboxaldehyde (50.0 mg, 0.13 mmol), pyrrolidine (0.02 mL, 0.25 mmol, 2.00 eq.) and 1H-indene (0.06 mL, 0.50 mmol, 4.00 eq.) in MeOH (5.0 mL) was stirred at r.t. overnight while the colour of the reaction changed from light orange to brown. The mixture was concentrated under *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 9/1) to give 1-(diphenylphosphino)-2-(1H-inden-1-ylidene)methyl)-ferrocene (13.0 mg, 21%) as a dark red solid (m.p. 70-72 °C) which consisted of two unsepar able isomers in 8/2 ratio. Rf 0.63 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 2922 (CH), 2852 (CH), 1619 (C=C), 1458, 1258, 1016 cm^{-1}.

Major isomer:

^{1}H NMR (600 MHz) δ 4.02 (1H, m, CH-Cp$_{sub.}$), 4.10 (5H, s, CH-Cp$_{unsub.}$), 4.64 (1H, t, *J* = 2.5 Hz, CH-Cp$_{sub.}$), 5.10 (1H, m, CH-Cp$_{sub.}$), 6.97 (1H, dd, *J* = 5.5 Hz, 1.0 Hz, olefinic-CH-indene), 7.04 (1H, d, *J* = 5.5 Hz, olefinic-CH-indene), 7.12-7.70 (17H, m, CH-PPh$_2$ & aromatic-CH-indene & Fc-CH=C); ^{13}C NMR (150 MHz) δ 70.9 (CH-Cp$_{unsub.}$), 71.0 (d, *J* = 2.8 Hz, CH-Cp$_{sub.}$), 72.4 (CH-Cp$_{sub.}$), 73.9 (d, *J* = 3.0 Hz, CH-Cp$_{sub.}$), 79.9 (d, *J* = 9.6 Hz, Ph$_2$P-C-Cp$_{sub.}$), 86.2 (d, *J* = 22 Hz, CH-C-Cp$_{sub.}$), aromatic region is ambiguous, therefore could not be assigned; ^{31}P NMR (162 MHz) δ -22.6.

Minor isomer:

^{1}H NMR (600 MHz) δ 4.04 (1H, m, CH-Cp$_{sub.}$), 4.11 (5H, s, CH-Cp$_{unsub.}$), 4.59 (1H, t, *J* = 2.5 Hz, CH-Cp$_{sub.}$), 5.11 (1H, m, CH-Cp$_{sub.}$), 6.53 (1H, d, *J* = 5.3 Hz, olefinic-CH-indene), 6.74 (1H, d, *J* = 5.3 Hz, olefinic-CH-indene), 7.12-7.70 (17H, m, CH-PPh$_2$ & aromatic-CH-indene & Fc-CH=C); ^{13}C NMR (150 MHz) δ 70.9 (CH-Cp$_{unsub.}$), 71.1 (CH-Cp$_{sub.}$), 72.0 (d, *J* = 2.7 Hz, CH-Cp$_{sub.}$), 73.6 (d, *J* = 2.7 Hz, CH-Cp$_{sub.}$), 80.5 (d, *J* = 9.2 Hz, Ph$_2$P-C-Cp$_{sub.}$), 86.8 (d, *J* = 22 Hz, CH-C-Cp$_{sub.}$), aromatic region is ambiguous, therefore could not be assigned; ^{31}P NMR (162 MHz) δ -21.6; m/z (EI) 497 (35%, M+H), 496 (100%, M), 431 (3%, M-Cp); HRMS $C_{32}H_{25}FeP$ calcd. 496.10378, found 496.10335.

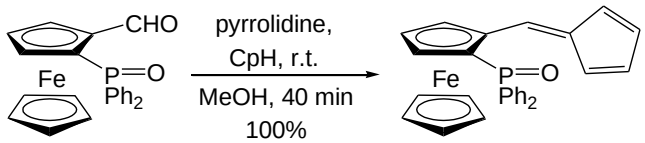


(+/-)-248 **(+/-)-253d**

1-(Diphenylphosphino)-2-((2,3,4,5-tetramethylcyclopenta-2,4-dienylidene)methyl)-ferrocene (**(+/-)-253d**).

To a solution of TMCp (46 mg, 0.38 mmol, 1.50 eq.) in THF (2.0 mL), ^{n}BuLi (0.15 mL, 0.38 mmol, 1.50 eq.) was added at 0 °C and the solution was stirred for 30 min at 0 °C. This solution was added to a solution of 2-(diphenylphosphino)-ferrocenecarboxaldehyde (100 mg, 0.25 mmol) in THF (2.0 mL) at 0 °C. The mixture was stirred overnight at r.t. The reaction was evaporated onto silica gel and purified by flash column chromatography (^{n}hexane/EtOAc, 95/5) to give 1-(diphenylphosphino)-2-((2,3,4,5-tetramethylcyclopenta-2,4-dienylidene)methyl)-ferrocene (27 mg, 22%) as an orange solid (m.p. 95-97 °C). Rf 0.70 (^{n}hexane/EtOAc, 95/5); IR υ_{max} 2912 (CH), 1615 (C=C), 1432, 1200, 1165, 1106 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.82 (3H, s, C$\underline{H}_3$), 1.84 (3H, s, C$\underline{H}_3$), 1.92 (3H, s, C$\underline{H}_3$), 2.01 (3H, s, C$\underline{H}_3$), 3.92 (1H, m, C$\underline{H}$-Cp$_{sub.}$), 4.08 (5H, s, C$\underline{H}$-Cp$_{unsub.}$), 4.45 (1H, t, *J* = 2.4 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.80 (1H, m, C$\underline{H}$-Cp$_{sub.}$), 7.12 (2H, m, *o*-C$\underline{H}$-PPh$_2$), 7.19 (3H, m, *p*-C$\underline{H}$-PPh$_2$ & *m*-C$\underline{H}$-PPh$_2$), 7.21 (1H, s, Fc-C$\underline{H}$=TMCp), 7.41 (3H, m, *p*-C$\underline{H}$-PPh$_2$ & *m*-C$\underline{H}$-PPh$_2$), 7.58 (2H, m, *o*-C$\underline{H}$-PPh$_2$); ^{13}C NMR (150 MHz) δ 10.1 (C$\underline{H}_3$), 11.4 (C$\underline{H}_3$), 11.5 (C$\underline{H}_3$), 13.9 (C$\underline{H}_3$), 70.3 (C$\underline{H}$-Cp$_{sub.}$), 70.6 (C$\underline{H}$-Cp$_{ubsub.}$), 73.2 (d, *J* = 2.7 Hz, C$\underline{H}$-Cp$_{sub.}$), 73.2 (d, *J* = 2.6 Hz, C$\underline{H}$-Cp$_{sub.}$), 80.0 (d, *J* = 8.2 Hz, PPh$_2$-C$\underline{H}$-Cp$_{sub.}$), 87.7 (d, *J* = 22.5 Hz, CH-C$\underline{H}$-Cp$_{sub.}$), 122.0 (C$\underline{H}$-TMCp), 126.0 (C$\underline{H}$-TMCp), 127.9 (*p*-C$\underline{H}$-PPh$_2$), 128.2 (d, *J* = 6.0 Hz, *m*-C$\underline{H}$-PPh$_2$), 128.2 (*p*-C$\underline{H}$-PPh$_2$),

128.3 (d, *J* = 7.8 Hz, *m*-CH-PPh_2), 129.3 (CH=TMCp), 132.2 (d, *J* = 17.7 Hz, *o*-CH-PPh_2), 135.2 (d, *J* = 20.8 Hz, *o*-CH-PPh_2), 135.6 (C-TMCp), 137.6 (d, *J* = 8.4 Hz, *i*-C-PPh_2), 139.6 (d, *J* = 10.3 Hz, *i*-C-PPh_2), 141.3 (C-TMCp), 145.5 (C-TMCp); ^{31}P NMR (162 MHz) δ -23.0; m/z (EI) 503 (5%, M+H), 502 (11%, M); HRMS $C_{32}H_{31}FeP$ calcd. 446.08813, found 446.08852.

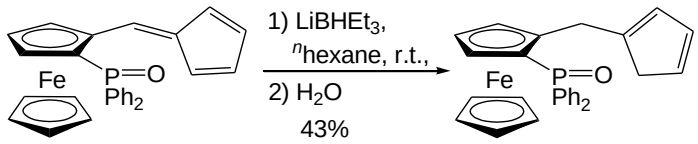


(+/-)-247 **(+/-)-249**

1-(Diphenylphosphinoxy)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene ((+/-)-249).

To a solution of 2-(diphenylphosphinoxy)-ferrocenecarboxaldehyde (50.0 mg, 0.12 mmol) in MeOH (5.0 mL) pyrrolidine (0.02 mL, 0.20 mmol, 1.70 eq.) and freshly cracked cyclopentadiene (0.04 mL, 0.48 mmol, 4.00 eq.) was added and the reaction was stirred at r.t. for 40 min. The mixture was concentrated under *vacuo* and purified by flash column chromatography (CH_2Cl_2/MeOH, 10/1) to yield 1-(diphenylphosphinoxy)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (56 mg, 100%) as a deep red solid (m.p. 88-90 °C). Rf 0.39 (CH_2Cl_2/MeOH); IR υ_{max} 3057 (CH), 2203, 1618 (C=C), 1608 (C=C), 1436 (P-Ph), 1256 (P=O), 1171, 1105; ^{1}H NMR (600 MHz) δ 4.12 (1H, dt, *J* = 2.5 Hz, $J_{HH/HP}$ = 1.4 Hz, CH-$Cp_{sub.}$), 4.33 (5H, s, CH-$Cp_{unsub.}$), 4.69 (1H, q, $J_{HH/HP}$ = 2.5 Hz, CH-$Cp_{sub.}$), 5.13 (1H, dt, *J* = 2.1, $J_{HH/HP}$ = 1.1 Hz, CH-$Cp_{sub.}$), 6.25 (1H, dt, *J* = 5.1, 1.8 Hz, CH-$Cp_{sub.}$), 6.40 (1H, dm, *J* = 5.1 Hz, CH-$Cp_{sub.}$), 6.58 (1H, ddt, *J* = 5.2, 1.9, 1.2 Hz, CH-$Cp_{sub.}$), 6.62 (1H, dm, *J* = 5.3 Hz,

C<u>H</u>-Cp$_{sub.}$), 7.33-7.37 (2H, m, C<u>H</u>-PPh$_2$), 7.41-7.46 (1H, m, C<u>H</u>-PPh$_2$), 7.49-7.60 (5H, m, C<u>H</u>-PPh$_2$), 7.68 (1H, s, Fc-C<u>H</u>=Fulv.), 7.77-7.82 (2H, m, C<u>H</u>-PPh$_2$); ^{13}C NMR (150 MHz) δ 71.7 (<u>C</u>H-Cp$_{unsub.}$), 72.2 (d, *J* = 8.7 Hz, <u>C</u>H-Cp$_{sub.}$), 73.4 (d, *J* = 11.2 Hz, <u>C</u>H-Cp$_{sub.}$), 76.1 (d, *J* = 112.2 Hz, OPPh$_2$-<u>C</u>-Cp$_{sub.}$), 77.1 (d, *J* = 14.5 Hz, <u>C</u>H-Cp$_{sub.}$), 84.5 (d, *J* = 9.9 Hz, Fulv.-<u>C</u>-Cp$_{sub.}$), 119.7 (<u>C</u>H-Fulv.), 127.3 (<u>C</u>H-Fulv.), 128.3 (d, *J* = 9.9 Hz, *m*-<u>C</u>H-PPh$_2$O), 128.5 (d, *J* = 12.2 Hz, *m*-<u>C</u>H-PPh$_2$O), 129.2 (<u>C</u>H-Fulv.), 131.7 (d, *J* = 10.2 Hz, *o*-<u>C</u>H-PPh$_2$O), 131.8 (d, *J* = 2.7 Hz, *p*-<u>C</u>H-PPh$_2$O), 131.8 (d, *J* = 10.2 Hz, *o*-<u>C</u>H-PPh$_2$O), 131.9 (d, *J* = 3.1 Hz, *p*-<u>C</u>H-PPh$_2$O), 133.4 (d, *J* = 106.7 Hz, *i*-<u>C</u>-PPh$_2$O), 133.8 (<u>C</u>H-Fulv.), 134.5 (d, *J* = 106.8 Hz, *i*-<u>C</u>-PPh$_2$O), 137.8 (Fc-<u>C</u>H-Fulv.), 143.2 (<u>C</u>-Fulv.); ^{31}P NMR (121 MHz) δ 30.6; m/z (EI) 463 (11%, M+H), 446 (31%, M), 398 (17%, M+H-Cp), 398 (65%, M-Cp); HRMS $C_{28}H_{23}FeOP$ calcd. 462.08305, found 462.08243.



(+/-)-249 **(+/-)-220**

1-(Diphenylphosphinoxy)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (**(+/-)-220**).

To a solution of 2-(diphenylphosphinoxy)-ferrocenecarboxaldehyde (40.0 mg, 0.09 mmol) in ^{n}hexane (2.0 mL) Superhydride® (0.30 mL, 0.30 mmol, 3.33 eq., 1M in THF) was added and the mixture was stirred at r.t. for 2 h. Water (1.5 mL) was added to the reaction at 0 °C and the mixture was extracted with CH_2Cl_2 (2 × 2 mL), dried ($MgSO_4$), concentrated under *vacuo* and purified by flash column chromatography (CH_2Cl_2/MeOH, 98/2) to give 1-(diphenylphosphinoxy)-2-[(cyclopenta-1,3-

dienyl)methyl]-ferrocene (17.0 mg, 43%) as a brown solid which consisted of two unseparable isomers in 6/4 ratio (m.p. 105-107 °C); IR υ_{max} 3368, 3052 (CH), 2919 (CH), 2217, 1482, 1435 (P-Ph), 1194, 1115, 1106 cm^{-1};

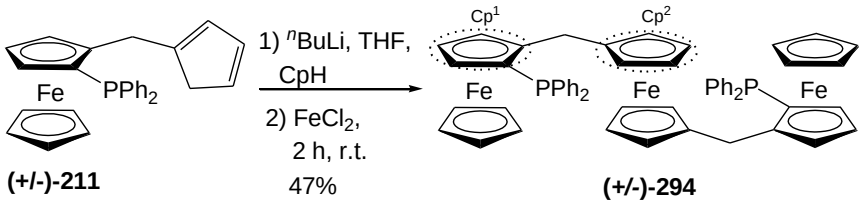
Major isomer:

^{1}H NMR (600 MHz) δ 2.50 (1H, dm, *J* = 23.5 Hz, C$\underline{H}_2$-Cp'), 2.61 (1H, dm, *J* = 23.1 Hz, C$\underline{H}_2$-Cp'), 3.58 (1H, dm, *J* = 16.6 Hz, Fc-C$\underline{H}_2$-Cp'), 3.80 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 3.86 (1H, dm, *J* = 16.6 Hz, Fc-C$\underline{H}_2$-Cp'), 4.27 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.28 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.44 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 5.81 (1H, m, C$\underline{H}$-Cp'), 6.03 (1H, m, C$\underline{H}$-Cp'), 6.12 (1H, m, C$\underline{H}$-Cp'), 7.28-7.32 (2H, m, C$\underline{H}$-PPh_2), 7.37-7.42 (1H, m, C$\underline{H}$-PPh_2), 7.46-7.55 (5H, m, C$\underline{H}$-PPh_2), 7.75-7.81 (2H, m, C$\underline{H}$-PPh_2); ^{13}C NMR (150 MHz) δ 29.8 (Fc-$\underline{C}H_2$-Cp'), 43.6 ($\underline{C}H_2$-Cp'), 69.8 (d, *J* = 11.1 Hz, $\underline{C}$H-$Cp_{sub.}$), 70.4 ($\underline{C}$H-$Cp_{unsub.}$), 71.9 (d, *J* = 114.4 Hz, Ph_2P-$\underline{C}$-$Cp_{sub.}$), 73.2 (d, *J* = 9.9 Hz, $\underline{C}$H-$Cp_{sub.}$), 73.6 (d, *J* = 15.5 Hz, $\underline{C}$H-$Cp_{sub.}$), 92.2 (d, *J* = 11.1 Hz, H_2C-$\underline{C}$-$Cp_{sub.}$), 128.0 ($\underline{C}$H-Cp'), 128.2 (d, *J* = 12.0 Hz, 2 × *m*-$\underline{C}$H-PPh_2), 130.7 ($\underline{C}$H-Cp'), 131.3 (d, *J* = 2.7 Hz, *p*-$\underline{C}$H-PPh_2), 131.5 (d, *J* = 2.9 Hz, *p*-$\underline{C}$H-PPh_2), 131.6 (d, *J* = 9.6 Hz, *o*-$\underline{C}$H-PPh_2), 131.6 (d, *J* = 11.0 Hz, *o*-$\underline{C}$H-PPh_2), 132.2 ($\underline{C}$H-Cp'), 134.0 (d, *J* = 105.6 Hz, *i*-$\underline{C}$-PPh_2), 134.6 (d, *J* = 105.8 Hz, *i*-$\underline{C}$-PPh_2), 147.8 (H_2C-$\underline{C}$-Cp'); ^{31}P NMR (162 MHz) δ 28.6.

Minor isomer:

^{1}H NMR (600 MHz) δ 2.50 (1H, d, *J* = 23.5 Hz, C$\underline{H}_2$-Cp'), 2.66 (1H, d, *J* = 23.1 Hz, C$\underline{H}_2$-Cp'), 3.55 (1H, dm, *J* = 17.0 Hz, Fc-C$\underline{H}_2$-Cp'), 3.80 (1H, dm, *J* = 16.8 Hz, Fc-C$\underline{H}_2$-Cp'), 3.80 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.27 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.28 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 4.46 (1H, m, C$\underline{H}$-$Cp_{sub.}$), 5.70 (1H, m, C$\underline{H}$-Cp'), 6.21 (1H, m, C$\underline{H}$-Cp'), 6.26 (1H, m, C$\underline{H}$-Cp'), 7.28-7.32 (2H, m, C$\underline{H}$-PPh_2), 7.37-7.42 (1H, m, C$\underline{H}$-PPh_2), 7.46-7.55 (5H, m,

C<u>H</u>-PPh_2), 7.75-7.81 (2H, m, C<u>H</u>-PPh_2); ^{13}C NMR (150 MHz) δ 29.1 (Fc-<u>C</u>H_2-Cp'), 41.1 (<u>C</u>H_2-Cp'), 69.7 (d, *J* = 10.3 Hz, <u>C</u>H-$Cp_{sub.}$), 70.4 (<u>C</u>H-$Cp_{unsub.}$), 71.6 (d, *J* = 114.7 Hz, Ph_2P-<u>C</u>-$Cp_{sub.}$), 73.3 (d, *J* = 9.9 Hz, <u>C</u>H-$Cp_{sub.}$), 73.7 (d, *J* = 16.1 Hz, <u>C</u>H-$Cp_{sub.}$), 91.7 (d, *J* = 10.9 Hz, H_2C-<u>C</u>-$Cp_{sub.}$), 128.0 (<u>C</u>H-Cp'), 128.0 (d, *J* = 12.2 Hz, *m*-<u>C</u>H-PPh_2), 128.1 (d, *J* = 12.0 Hz, *m*-<u>C</u>H-PPh_2), 131.2 (d, *J* = 2.7 Hz, *p*-<u>C</u>H-PPh_2), 131.4 (d, *J* = 3.4 Hz, *p*-<u>C</u>H-PPh_2), 131.6 (d, *J* = 6.1 Hz, *o*-<u>C</u>H-PPh_2), 131.7 (d, *J* = 9.4 Hz, *o*-<u>C</u>H-PPh_2), 133.3 (<u>C</u>H-Cp'), 134.1 (d, *J* = 102.8 Hz, *i*-<u>C</u>-PPh_2), 134.6 (<u>C</u>H-Cp'), 134.8 (d, *J* = 103.2 Hz, *i*-<u>C</u>-PPh_2), 145.0 (H_2C-<u>C</u>-Cp'); ^{31}P NMR (162 MHz) δ 28.8; m/z (EI) 465 (35%, M+H), 464 (100%, M), 263 (15%, M-OPPh_2-H), 121 (35%, Fe+Cp); HRMS $C_{28}H_{25}FePO$ calcd. 464.09868, found 464.09983.

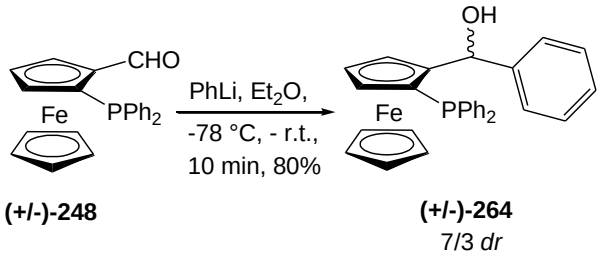


(+/-)-211 **(+/-)-294**

1,1'-[Di(α-(diphenylphosphino)-methylferrocenyl]ferrocene (**(+/-)-294**).

To a solution of 1-(diphenylphosphino)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (250 mg, 1.11 mmol) in THF (10.0 mL), ^{n}BuLi (0.36 mL, 1.22 mmol, 1.10 eq.) was added at 0 °C and the mixture was stirred at 0 °C for 30 min while the colour changed from yellow to orange-brown. Then $FeCl_2$ (92.0 mg, 1.44 mmol, 1.30 eq.) was added at once which was followed by stirring for 1.5 h at r.t. After this time the mixture was concentrated in *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 95/5) to yield 1,1'-[di(α-(diphenylphosphino)-methylferrocenyl]ferrocene (125 mg, 47%) as an orange solid (m.p. 75-77 °C). Rf 0.27 (^{n}hexane/EtOAc, 95/5); IR υ_{max} 3058

(CH), 2930 (CH), 1968, 1477 (P-Ph), 1432 (P-Ph), 1171, 1105 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 3.48 (2H, ddd, $J_{gem.}$ = 15.1, 6.7 Hz, J_{HP} = 1.6 Hz, C$\underline{H}_2$), 3.53 (2H, d, $J_{gem.}$ = 15.2, 5.6 Hz, C$\underline{H}_2$), 3.57 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 3.61 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 3.67 (2H, m, C$\underline{H}$-$Cp^{1}_{sub.}$), 3.71 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 3.73 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 3.87 (2H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 3.96 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 3.98 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.00 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 4.02 (1H, m, C$\underline{H}$-$Cp^{2}_{sub.}$), 4.16 (2H, dd, J = 2.3, 2.2 Hz, C$\underline{H}$-$Cp^{1}_{sub.}$), 4.16 (2H, m, C$\underline{H}$-$Cp^{1}_{sub.}$), 7.10 (4H, m, *o*-C$\underline{H}$-PPh_2), 7.21 (6H, m, *p*-C$\underline{H}$-PPh_2 & *m*-C$\underline{H}$-PPh_2), 7.39 (6H, m, *p*-C$\underline{H}$-PPh_2 & *m*-C$\underline{H}$-PPh_2), 7.57 (4H, m, *o*-C$\underline{H}$-PPh_2); ^{13}C NMR (150 MHz) δ 28.9 (d, J = 6.2 Hz, $\underline{C}H_2$), 28.9 (d, J = 6.1 Hz, $\underline{C}H_2$), 68.0 ($\underline{C}$H-$Cp^{2}_{sub.}$), 68.0 ($\underline{C}$H-$Cp^{2}_{sub.}$), 68.1 ($\underline{C}$H-$Cp^{2}_{sub.}$), 68.1 ($\underline{C}$H-$Cp^{2}_{sub.}$), 69.0 (2 × $\underline{C}$H-$Cp^{1}_{sub.}$), 69.2 ($\underline{C}$H-$Cp^{2}_{sub.}$), 69.3 ($\underline{C}$H-$Cp^{2}_{sub.}$), 69.7 ($\underline{C}$H-$Cp_{unsub.}$), 69.8 ($\underline{C}$H-$Cp_{unsub.}$), 69.8 (2 × $\underline{C}$H-$Cp^{2}_{sub.}$), 70.6 ($\underline{C}$H-$Cp^{1}_{sub.}$), 70.6 ($\underline{C}$H-$Cp^{1}_{sub.}$), 71.3 (d, J = 2.5 Hz, $\underline{C}$H-$Cp^{1}_{sub.}$), 71.3 (d, J = 2.6 Hz, $\underline{C}$H-$Cp^{1}_{sub.}$), 74.5 (d, J = 6.0 Hz, Ph_2P-$\underline{C}$-$Cp_{sub.}$), 74.6 (d, J = 6.0 Hz, Ph_2P-$\underline{C}$-$Cp_{sub.}$), 87.5 (H_2C-$\underline{C}$-$Cp^{2}_{sub.}$), 87.6 (H_2C-$\underline{C}$-$Cp^{2}_{sub.}$), 95.2 (d, J = 2.9 Hz, H_2C-$\underline{C}$-$Cp^{1}_{sub.}$), 95.3 (d, J = 2.9 Hz, H_2C-$\underline{C}$-$Cp^{1}_{sub.}$), 127.8 (*p*-$\underline{C}$H-PPh_2), 128.1 (d, J = 5.8 Hz, *m*-$\underline{C}$H-PPh_2), 128.2 (d, J = 7.9 Hz, *m*-$\underline{C}$H-PPh_2), 129.2 (*p*-$\underline{C}$H-PPh_2), 132.5 (d, J = 17.7 Hz, *o*-$\underline{C}$H-PPh_2), 132.6 (d, J = 17.7 Hz, *o*-$\underline{C}$H-PPh_2), 135.3 (d, J = 21.1 Hz, *o*-$\underline{C}$H-PPh_2), 137.8 (d, J = 7.9 Hz, *i*-$\underline{C}$-PPh_2), 139.0 (d, J = 9.1 Hz, *i*-$\underline{C}$-PPh_2), 140.0 (d, J = 9.1 Hz, *i*-$\underline{C}$-PPh_2); ^{31}P NMR (400 MHz) δ -23.2, -23.11; m/z (ES+) 951 (100%, M+H), 950 (30%, M); HRMS (M+H) $C_{56}H_{49}Fe_3P_2$ calcd. 951.1358, found 951.1382; Anal. Calcd. for $C_{56}H_{48}Fe_3P_2$: C, 70.77; H, 5.09. Found C, 70.02; H, 5.20%.



(+/-)-248 **(+/-)-264**
7/3 *dr*

Phenyl(2-(α-diphenylphosphino)ferrocenyl)methanol (**(+/-)-264**).

To a suspension of 2-(diphenylphosphino)-ferrocenecarboxaldehyde (100 mg, 0.25 mmol) in Et_2O (2.0 mL) phenyllithium (0.14 mL, 0.28 mmol, 1.10 eq., 2M in THF) was added at -78 °C. Then the reaction temperature was let to raise to r.t. while the colour has changed from orange to yellow. After 10 min at r.t. water (5 mL) was added then the mixture was extracted with Et_2O (2 × 3 mL), washed with brine (1 × 3 mL), dried ($MgSO_4$) concentrated under *vacuo*. The crude material consisted of 2 diastereomers in a 7/3 ratio, which were separated by flash column chromatography (CH_2Cl_2) to give phenyl(2-(α-diphenylphosphino)ferrocenyl)methanol (96 mg, 80%) as a yellow solid (m.p.$_{(major)}$ 147-149 °C, m.p.$_{(minor)}$ 132-134 °C). Rf$_{(major)}$ 0.38, Rf$_{(minor)}$ 0.50 (CH_2Cl_2); IR υ_{max} 3329 (OH), 3052 (CH), 1432 (P-Ph), 1159, 1080, 1026 cm^{-1}.

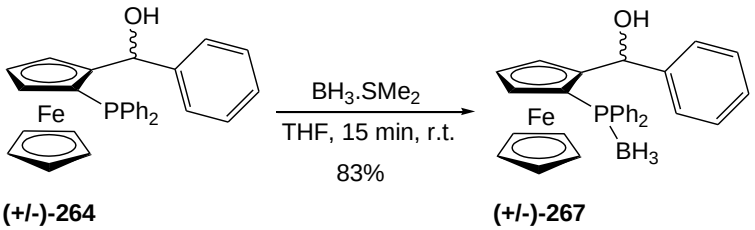
Major diast.:

^{1}H NMR (600 MHz) δ 2.65 (1H, t, $J_{HH\&HP}$ = 1.6 Hz, O<u>H</u>), 3.82 (1H, m, C<u>H</u>-Cp$_{sub.}$), 4.17 (5H, s, C<u>H</u>-Cp$_{unsub.}$), 4.32 (1H, t, *J* = 2.5 Hz, C<u>H</u>-Cp$_{sub.}$), 4.62 (1H, m, C<u>H</u>-Cp$_{sub.}$), 5.79 (1H, t, $J_{HH\&HP}$ = 2.2 Hz, Fc-C<u>H</u>(OH)-Ph), 6.82-7.59 (15H, m, C<u>H</u>-PPh$_2$ & C<u>H</u>-Ph); ^{13}C NMR (150 MHz) δ 68.3 (d, *J* = 3.6 Hz, <u>C</u>H-Cp$_{sub.}$), 69.5 (<u>C</u>H-Cp$_{sub.}$), 69.7 (<u>C</u>H-Cp$_{unsub.}$), 71.1 (d, *J* = 10.8 Hz, Fc-<u>C</u>H(OH)-Ph), 71.6 (d, *J* = 4.4 Hz, <u>C</u>H-Cp$_{sub.}$), 75.1 (d, *J* = 8.9 Hz, Ph$_2$P-<u>C</u>-Cp$_{sub.}$), 100.2 (d, *J* = 23.0 Hz, HC-<u>C</u>-Cp$_{sub.}$), 126.8 (*o*-<u>C</u>H-Ph),

127.4 (*p*-CH-Ph), 127.8 (*p*-CH-PPh_2), 127.9 (d, *J* = 5.9 Hz, *m*-CH-PPh_2), 128.0 (*m*-CH-Ph), 128.3 (d, *J* = 7.9 Hz, *m*-CH-PPh_2), 129.4 (*p*-CH-PPh_2), 132.3 (d, *J* = 17.9 Hz, *o*-CH-PPh_2), 135.3 (d, *J* = 21.0 Hz, *o*-CH-PPh_2), 137.0 (d, *J* = 8.0 Hz, *i*-C-PPh_2), 138.6 (d, *J* = 7.8 Hz, *i*-C-PPh_2), 142.6 (*i*-C-Ph) ^{31}P NMR (162 MHz) δ -23.8.

Minor diast.:

^{1}H NMR (600 MHz) δ 2.76 (1H, t, $J_{HH\&HP}$ = 5.3 Hz, OH), 3.87 (1H, m, CH-$Cp_{sub.}$), 3.97 (5H, s, CH-$Cp_{unsub.}$), 4.33 (1H, t, *J* = 2.4 Hz, CH-$Cp_{sub.}$), 4.35 (1H, m, CH-$Cp_{sub.}$), 5.82 (1H, dd, *J* = 5.1 Hz, J_{HP} = 1.5 Hz, Fc-CH(OH)-Ph), 7.07-7.62 (15H, m, CH-PPh_2 & CH-Ph) ^{13}C NMR (150 MHz) δ 69.9 (CH-$Cp_{unsub.}$), 70.0 (CH-$Cp_{sub.}$), 71.3 (d, *J* = 4.4 Hz, CH-$Cp_{sub.}$), 72.0 (d, *J* = 3.6 Hz, CH-$Cp_{sub.}$), 72.8 (d, *J* = 6.1 Hz, Fc-CH(OH)-Ph), 74.1 (d, *J* = 8.4 Hz, Ph_2P-C-$Cp_{sub.}$), 97.4 (d, *J* = 22.1 Hz, CH-C-$Cp_{sub.}$), 126.6 (*o*-CH-Ph), 127.3 (*p*-CH-Ph), 128.0 (*m*-CH-Ph), 128.1 (*p*-CH-PPh_2), 128.2 (d, *J* = 6.0 Hz, *m*-CH-PPh_2), 128.3 (d, *J* = 7.09 Hz, *m*-CH-PPh_2), 129.5 (*p*-CH-PPh_2), 132.4 (d, *J* = 17.7 Hz, *o*-CH-PPh_2), 135.2 (d, *J* = 21.2 Hz, *o*-CH-PPh_2), 137.0 (d, *J* = 6.8 Hz, *i*-C-PPh_2), 139.3 (d, *J* = 7.2 Hz, *i*-C-PPh_2), 143.2 (*i*-C-Ph); ^{31}P NMR (162 MHz) δ -23.3; m/z (EI) 477 (26%, M+H), 476 (76%, M), 460 (5%, M-OH), 339 (11%, M-Cp-Fe); HRMS $C_{29}H_{25}FeOP$ calcd. 476.09870, found 476.09784.

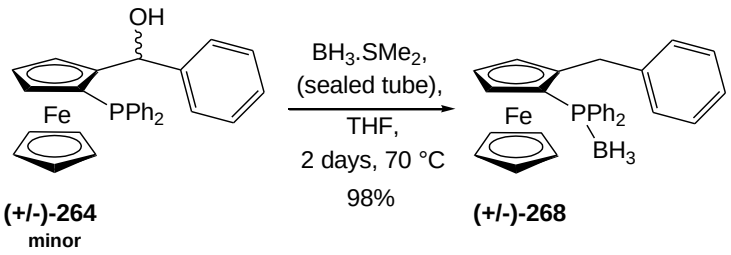


(+/-)-264 **(+/-)-267**

[1-(Diphenylphosphino)-2-(2-hydroxy-2-phenyl)]trihydro-boron (**(+/-)-267**).

To a solution of phenyl(2-(α-diphenylphosphino)ferrocenyl)methanol (100 mg, 0.21 mmol) in THF (2.0 mL) $H_3B.SMe_2$ (0.06 mL, 0.63 mmol, 3.00 eq.) was added and the mixture was stirred at r.t. for 3 h. The reaction was concentrated in *vacuo* and purified by flash column chromatography (CH_2Cl_2) to give [1-(diphenylphosphino)-2-(2-hydroxy-2-phenyl)]trihydro-boron (80 mg, 83%) as a yellow solid (m.p. 145-147 °C). Rf 0.31 (CH_2Cl_2); IR υ_{max} 3540 (OH), 3055 (CH), 2410 (BH), 2345 (BH), 2356 (BH), 1484, 1435 (P-Ph), 1154, 1105, 1070, 1018 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.58 (1H, d, *J* = 2.4 Hz, O<u>H</u>), 3.78 (1H, dt, *J* = 2.4 Hz, $J_{HH/HP}$ = 1.6 Hz, C<u>H</u>-$Cp_{sub.}$), 4.41 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.42 (1H, t, *J* = 2.5 Hz, C<u>H</u>-$Cp_{sub.}$), 4.80 (1H, dt, *J* = 2.2 Hz, $J_{HH/HP}$ = 1.6 Hz, C<u>H</u>-$Cp_{sub.}$), 6.00 (1H, d, *J* = 2.1 Hz, Fc-C<u>H</u>(OH)-Ph), 6.94-7.70 (15H, m, C<u>H</u>-PPh_2 & C<u>H</u>-Ph); ^{13}C NMR (125 MHz) δ 68.4 (d, *J* = 63.4 Hz, PPh_2-<u>C</u>-$Cp_{sub.}$), 69.4 (Fc-<u>C</u>H(OH)-Ph), 70.0 (d, *J* = 6.2 Hz, <u>C</u>H-$Cp_{sub.}$), 70.5 (<u>C</u>H-$Cp_{unsub.}$), 70.6 (<u>C</u>H-$Cp_{sub.}$), 73.6 (d, *J* = 3.8 Hz, <u>C</u>H-$Cp_{sub.}$), 98.9 (d, *J* = 14.0 Hz, <u>C</u>-CH(OH)-Ph), 126.9 (*o*-<u>C</u>H-Ph), 127.3 (*p*-<u>C</u>H-Ph), 127.9 (*m*-<u>C</u>H-Ph), 128.1 (d, *J* = 10.0 Hz, *m*-<u>C</u>H-PPh_2), 128.3 (d, *J* = 10.2 Hz, *m*-<u>C</u>H-PPh_2), 129.8 (d, *J* = 57.6 Hz, *i*-<u>C</u>-PPh_2), 130.3 (d, *J* = 61.2 Hz, *i*-<u>C</u>-PPh_2), 130.6 (d, *J* = 2.5 Hz, *p*-<u>C</u>H-PPh_2), 131.1 (d, *J* = 2.4 Hz, *p*-<u>C</u>H-PPh_2), 132.5 (d, *J* = 9.5 Hz, *o*-<u>C</u>H-PPh_2), 133.3 (d, *J* = 9.5 Hz, *o*-<u>C</u>H-PPh_2), 142.4 (*i*-<u>C</u>-Ph); ^{31}P NMR (162 MHz) δ 14.1 (d, J_{PB} = 51.4 Hz); ^{11}B NMR (160 MHz) δ -37.15; m/z (EI) 491 (2%,

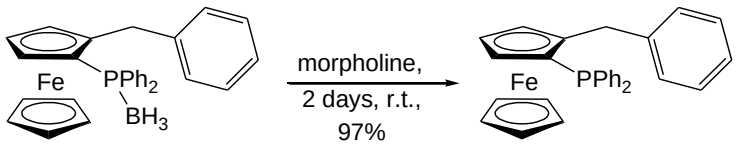
M+H), 490 (7%, M), 477 (34%, M+H-BH_3), 476 (100%, M-BH_3), 339 (5%, M-OH-Cp-Fe-BH_3); HRMS $C_{29}H_{28}FeBOP$ calcd. 490.13148, found 490.13216.



[1-(Diphenylphosphino)-2-(phenylmethyl)]trihydro-boron (**(+/-)-268**).

To a solution of [1-(diphenylphosphino)-2-(2-hydroxy-2-phenyl)]trihydro-boron (109 mg, 0.23 mmol), in THF (10 mL) $H_3B.SMe_2$ (0.65 mL, 6.87 mmol, 30.0 eq.) was added and the reaction was refluxed in a Schlenk-tube for 24 h. The mixture was concentrated in *vacuo* and purified by flash column chromatography (CH_2Cl_2) to give [1-(diphenylphosphino)-2-(phenylmethyl)]trihydro-boron (106 mg, 98%) as a yellow solid (m.p. 168-170 °C). Rf 0.78 (CH_2Cl_2); IR υ_{max} 3075 (CH), 2397 (BH), 2257 (BH), 1435 (P-Ph), 1105, 1064 cm^{-1}; ^{1}H NMR (600 MHz) δ 3.77 (1H, m, C<u>H</u>-$Cp_{sub.}$), 3.81 (1H, d, *J* = 15.4 Hz, Fc-C<u>H</u>$_2$-Ph), 3.92 (1H, d, *J* = 15.4 Hz, Fc-C<u>H</u>$_2$-Ph), 4.25 (5H, s, CH-$Cp_{unsub.}$), 4.33 (1H, t, *J* = 2.5 Hz, C<u>H</u>-$Cp_{sub.}$), 4.38 (1H, m, C<u>H</u>-$Cp_{sub.}$), 6.99-7.71 (15H, m, C<u>H</u>-PPh_2 & C<u>H</u>-Ph); ^{13}C NMR (150 MHz) δ 34.5 (Fc-<u>C</u>H$_2$-Ph), 68.5 (d, *J* = 65.2 Hz, PPh_2-<u>C</u>-$Cp_{sub.}$), 69.9 (d, *J* = 6.6 Hz, <u>C</u>H-$Cp_{sub.}$), 70.6 (<u>C</u>H-$Cp_{unsub.}$), 73.3 (d, *J* = 5.3 Hz, <u>C</u>H-$Cp_{sub.}$), 73.7 (d, *J* = 7.6 Hz, <u>C</u>H-$Cp_{sub.}$), 93.1 (d, *J* = 14.3 Hz, CH_2-<u>C</u>-Ph), 125.9 (*p*-<u>C</u>H-Ph), 128.0 (*m*-<u>C</u>H-Ph), 128.3 (d, *J* = 8.2 Hz, *m*-<u>C</u>H-PPh_2), 128.4 (d, *J* = 8.3 Hz, *m*-<u>C</u>H-PPh_2), 128.9 (*o*-<u>C</u>H-Ph), 130.6 (d, *J* = 57.1 Hz, *i*-<u>C</u>-PPh_2), 130.7 (d, *J* = 60.5 Hz, *i*-<u>C</u>-PPh_2), 130.7 (d, *J* = 2.3 Hz, *p*-<u>C</u>H-PPh_2), 131.0 (d, *J* = 2.2 Hz, *p*-<u>C</u>H-PPh_2), 132.8

(d, J = 9.4 Hz, *o*-CH-PPh_2), 133.3 (d, J = 9.4 Hz, *o*-CH-PPh_2), 140.4 (*i*-C-Ph); ^{31}P NMR (162 MHz) δ 15.1 (d, J_{PB} = 55.7 Hz); ^{11}B NMR (160 MHz) δ -37.03; m/z (EI) 475 (3%, M+H), 474 (9%, M), 460 (30%, M+H-BH_3), 460 (100%, M-BH_3), 385 (16%, M+H-BH_3-PPh_2), 384 (53%, M-BH_3-PPh_2); HRMS $C_{29}H_{28}FeBP$ calcd. 474.13656, found 474.13733.

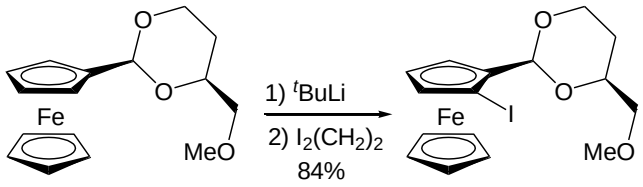


(+/-)-268 **(+/-)-263**

1-(Diphenylphosphino)-2-(phenylmethyl)ferrocene (**(+/-)-263**).

[1-(diphenylphosphino)-2-(phenylmethyl)]trihydro-boron (115 mg, 0.24 mmol) was stirred in Morpholine (4.0 mL) at r.t. for 2 days. The mixture was concentrated in *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 95/5) to give 1-(diphenylphosphino)-2-(phenylmethyl)ferrocene (108 mg, 97%) as a yellow solid (m.p. 150-152 °C). Rf 0.35 (^{n}hexane/CH_2Cl_2, 6/4); IR υ_{max} 3070 (CH), 3032 (CH), 2357, 1977, 1474, 1431 (P-Ph), 1307, 1237, 1176, 1106 cm^{-1}; ^{1}H NMR (600 MHz) δ 3.74 (1H, m, CH-$Cp_{sub.}$), 3.84 (1H, d, J = 15.1 Hz, Fc-CH_2-Ph), 3.89 (1H, d, J = 15.1 Hz, Fc-CH_2-Ph), 4.02 (5H, CH-$Cp_{unsub.}$), 4.24 (1H, t, J = 2.3 Hz, CH-$Cp_{sub.}$), 4.37 (1H, m, CH-$Cp_{sub.}$), 6.98-7.61 (15H, m, CH-PPh_2 & CH-Ph); ^{13}C NMR (150 MHz) δ 35.1 (d, J = 9.1 Hz, CH_2), 69.2 (CH-$Cp_{sub.}$), 69.8 (CH-$Cp_{unsub.}$), 71.1 (d, J = 4.1 Hz, CH-$Cp_{sub.}$), 71.8 (d, J = 4.0 Hz, CH-$Cp_{sub.}$), 75.4 (d, J = 6.3 Hz, Ph_2P-C-$Cp_{sub.}$), 94.1 (CH_2-C-$Cp_{sub.}$), 125.8 (*p*-CH-Ph), 127.7 (*p*-CH-PPh_2), 127.9 (d, J = 6.1 Hz, *m*-CH-PPh_2), 128.0 (*o*-CH-Ph), 128.2 (d, J = 7.8 Hz, *m*-CH-PPh_2), 128.8 (*m*-CH-Ph), 129.2 (*p*-CH-PPh_2), 132.4 (d, J =

18.1 Hz, *o*-CH-PPh_2), 135.2 (d, *J* = 21.0 Hz, *o*-CH-PPh_2), 137.7 (d, *J* = 8.2 Hz, *i*-C-PPh_2), 139.5 (d, *J* = 9.1 Hz, *i*-C-PPh_2), 141.0 (*i*-C-Ph); ^{31}P NMR (162 MHz) δ -23.1; m/z (EI) 461 (29%, M+H), 460 (100%, M); HRMS $C_{29}H_{25}FeP$ calcd. 460.10378, found 460.10426; Anal. Calcd. for $C_{29}H_{25}FeP$: C, 75.67; H, 5.47. Found C, 75.59; H, 5.50%.

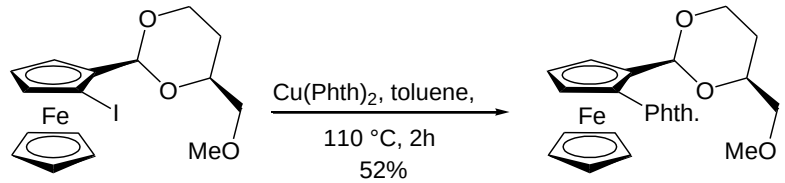


251 **(+/-)-272**

4-(Methoxymethyl)-2-[α-(iodo) ferrocenyl]-1,3-dioxane (**(+/-)-272**).

To a solution of 4-(methoxymethyl)-2-ferrocenyl-1,3-dioxane (1.50 g, 4.74 mmol) in Et_2O (15 mL), ^{t}BuLi (3.00 mL, 5.20 mmol, 1.10 eq.) was added at -78 °C and the reaction was stirred at r.t. for 1h. After this period 1,2-diiodoethane (1.60 g, 5.69 mmol, 1.20 eq.) was added in Et_2O (10.0 mL) at -78 °C and the reaction was stirred at r.t. for 5 h. Water (10 mL), then 2M NaOH (10 mL) was added to the reaction. After 10 min stirring the mixture was extracted with Et_2O (2 × 10 mL) washed with brine (1 × 10 mL), dried ($MgSO_4$) concentrated in *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 7/3) to give 4-(methoxymethyl)-2-[α-(iodo) ferrocenyl]-1,3-dioxane (1.75 g, 84%) as a yellow solid (m.p. 74-76 °C). Rf 0.50 (^{n}hexane/EtOAc, 7/3); IR υ_{max} 3104 (CH), 2935 (CH), 2880 (CH), 2824 (CH), 1784 (Ar), 1717 (Ar), 1466, 1361, 1240, 1135, 1122, 1105, 1080, 1050 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.54 (1H, dm, $J_{gem.}$ = 13.3 Hz, H_{3e}), 1.83 (1H, dddd, $J_{gem.}$ = 13.4 Hz, J_{3a-4a} = 12.5 Hz, J_{3a-2a} = 11.3 Hz, J_{3a-4e} = 5.2 Hz, H_{3a}), 3.39 (3H, s, O-CH_3), 3.40 (1H, dd, $J_{gem.}$ = 10.3 Hz, J_{1-2a} = 5.0 Hz, H_1), 3.52 (1H, dd, $J_{gem.}$ = 10.2 Hz, J_{1-2a} = 5.6 Hz, H_1), 4.01 (1H, ddd, J_{4a-3a} = 12.4 Hz, $J_{gem.}$ =

11.5 Hz, $J_{4a\text{-}3e}$ = 2.7 Hz, $\underline{H}_{4a}$), 4.05 (1H, dddd, $J_{2a\text{-}3a}$ = 11.2 Hz, $J_{2a\text{-}1}$ = 5.6, 5.0 Hz, $J_{2a\text{-}3e}$ = 2.4 Hz, $\underline{H}_{2a}$), 4.18 (5H, s, CH-$Cp_{unsub.}$), 4.21 (1H, t, J = 2.5 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.32 (1H, ddd, $J_{gem.}$ = 11.5 Hz, $J_{4e\text{-}3a}$ = 5.2 Hz, $J_{2a\text{-}3e}$ = 1.4 Hz, $\underline{H}_{4e}$), 4.41 (1H, dd, J = 2.5, 1.4 Hz, C$\underline{H}$-$Cp_{sub.}$), 4.45 (1H, dd, J = 2.5, 1.4 Hz, C$\underline{H}$-$Cp_{sub.}$), 5.42 (1H, s, $\underline{H}_5$); ^{13}C NMR (150 MHz) δ 28.2 ($\underline{C}_3$), 31.7 (I-$\underline{C}$-$Cp_{sub.}$), 59.5 ($\underline{C}H_3$), 66.3 ($\underline{C}$H-$Cp_{sub.}$), 67.2 ($\underline{C}_4$), 68.9 ($\underline{C}$H-$Cp_{sub.}$), 72.0 ($\underline{C}$H-$Cp_{unsub.}$), 75.0 ($\underline{C}$H-$Cp_{sub.}$), 75.5 ($\underline{C}_1$), 76.4 ($\underline{C}_2$), 86.1 (HC-$\underline{C}$-$Cp_{sub.}$), 101.1 ($\underline{C}_5$); m/z (EI) 443 (19%, M+H), 442 (100%, M), 316 (M-I); HRMS $C_{16}H_{19}FeO_3I$ calcd. 441.97228, found 441.97194; Anal. Calcd. For $C_{16}H_{19}FeO_3I$: C, 43.47; H, 4.33. Found C, 44.28; H, 4.39%.

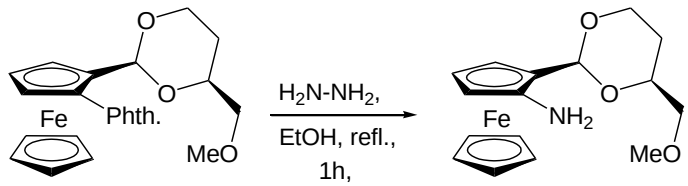


(+/-)-272 **(+/-)-274**

4-(Methoxymethyl)-2-[α-(phthalimido)-ferrocenyl]-1,3-dioxane (**(+/-)-274**).

A solution of 4-(methoxymethyl)-2-[α-(iodo)-ferrocenyl]-1,3-dioxane (50.0 mg, 0.11 mmol) and copper diphthalimide (100 mg, 0.28 mmol, 2.50 eq.) in toluene (2.0 mL) was refluxed for 24 h. The reaction was concentrated under *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 7/3) to give 4-(methoxymethyl)-2-[α-(phthalamido)-ferrocenyl]-1,3-dioxane (27.0 mg, 52%) as an orange solid (m.p. 144-146 °C). Rf 0.19 (^{n}hexane/EtOAc, 7/3); IR υ_{max} 2922 (CH), 2858 (CH), 1780 (Ar), 1714 (Ar), 1459, 1371, 1262, 1208 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 1.37 (1H, dm, $J_{gem.}$ = 13.3 Hz, $\underline{H}_{3e}$), 1.66 (1H, dddd, $J_{gem.}$ = 13.3 Hz, $J_{3a\text{-}4a}$ = 12.5 Hz, $J_{3a\text{-}2a}$ = 11.7 Hz, $J_{3a\text{-}4e}$ = 5.2 Hz, $\underline{H}_{3a}$), 2.93 (3H, s, O-C$\underline{H}_3$), 3.12 (2H, d, $J_{1\text{-}2a}$ = 5.4 Hz, $\underline{H}_1$), 3.83 (1H,

ddt, J_{2a-3a} = 11.3 Hz, J_{2a-1} = 5.3 Hz, J_{2a-3e} = 2.5 Hz, $\underline{H}_{2a}$), 3.90 (1H, ddd, J_{4a-3a} = 12.3 Hz, $J_{gem.}$ = 11.7 Hz, J_{4a-3e} = 2.6 Hz, $\underline{H}_{4a}$), 4.14 (1H, ddd, $J_{gem.}$ = 11.5 Hz, J_{4e-3a} = 5.1 Hz, J_{4e-3e} = 1.4 Hz, $\underline{H}_{4e}$), 4.21 (1H, t, J = 2.6 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.34 (5H, s, C$\underline{H}$-Cp$_{unsub.}$), 4.49 (1H, dd, J = 2.6, 1.6 Hz, C$\underline{H}$-Cp$_{sub.}$), 4.55 (1H, dd, J = 2.6, 1.6 Hz, C$\underline{H}$-Cp$_{sub.}$), 5.77 (1H, s, H_5), 7.75 (2H, dd, J = 5.4, 3.0 Hz, C$\underline{H}_7$), 7.89 (2H, dd, J = 5.4, 3.0 Hz, C$\underline{H}_8$); ^{13}C NMR (150 MHz) δ 28.0 ($\underline{C}_3$), 59.1 ($\underline{C}H_3$), 64.8 ($\underline{C}$H-Cp$_{sub.}$), 65.2 ($\underline{C}$H-Cp$_{sub.}$), 66.5 ($\underline{C}_4$), 67.0 ($\underline{C}$H-Cp$_{sub.}$), 70.7 ($\underline{C}$H-Cp$_{unsub.}$), 75.5 ($\underline{C}_1$), 75.6 ($\underline{C}_2$), 79.8 (CH-$\underline{C}$-Cp$_{sub.}$), 85.0 (Phth.-$\underline{C}$-Cp$_{sub.}$), 99.5 ($\underline{C}_5$), 123.2 ($\underline{C}_7$), 132.5 ($\underline{C}_6$), 134.0 ($\underline{C}_8$), 167.3 ($\underline{C}$O); m/z (EI) 462 (28%, M+H), 461 (100%, M), 359 (8%, M-Acetal), 294 (27%, M-Acetal-Cp), 266 (16%, M-Acetal-Cp-CHO); HRMS $C_{24}H_{23}FeNO_5$ calcd. 461.09200, found 461.09294; Anal. Calcd. For $C_{24}H_{23}FeNO_5$: C, 62.49; H, 5.03; N, 3.04 Found C, 61.83; H, 5.17; N, 2.78%.

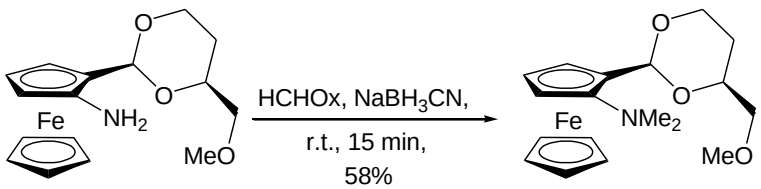


(+/-)-274 **(+/-)-275**

4-(Methoxymethyl)-2-[α-(amino)-ferrocenyl]-1,3-dioxane (**(+/-)-275**).

A solution of 4-(methoxymethyl)-2-[α-(phthalimido)-ferrocenyl]-1,3-dioxane (27.0 mg, 0.06 mmol) and hydrazine hydrate (0.20 mL, 2.67 mmol, 44.5 eq.) was refluxed for 1h in EtOH (1.0 mL). Water (3 mL) was added and the mixture was extracted with Et_2O (2 × 3 mL), dried ($MgSO_4$) to give 4-(methoxymethyl)-2-[α-(amino)-ferrocenyl]-1,3-dioxane (16.0 mg, 84%) as a dark orange solid (m.p. 85-87 °C). Rf 0.27 (EtOAc); IR υ_{max} 3423 (NH_2), 3343 (NH_2), 3097 (CH), 2950 (CH), 2901 (CH), 2867 (CH), 2823

(CH), 1620 (NH_2), 1496, 1362, 1197 (CO) cm^{-1}; ^1H NMR (600 MHz) δ 1.52 (1H, dm $J_{gem.}$ = 13.2 Hz, H_{3e}), 1.84 (1H, dddd, $J_{gem.}$ = 13.2 Hz, J_{3a-4a} = 12.6 Hz, J_{3a-2a} = 12.4 Hz, J_{3a-4e} = 5.2 Hz, $\underline{H}_{3a}$), 3.06 (2H, bs, $N\underline{H}_2$), 3.47 (3H, s, O-$C\underline{H}_3$), 3.49 (1H, dd, $J_{gem.}$ = 10.4 Hz, J_{1-2a} = 4.5 Hz, H_1), 3.58 (1H, dd, $J_{gem.}$ = 10.4 Hz, J_{1-2a} = 6.2 Hz, H_1), 3.79 (1H, bs, $C\underline{H}$-$Cp_{sub.}$), 3.93 (1H, ddd, J_{4a-3a} = 12.6 Hz, $J_{gem.}$ = 11.6 Hz, J_{4a-3e} = 2.5 Hz, H_{4a}), 3.97 (2H, bs, $C\underline{H}$-$Cp_{sub.}$), 4.05 (1H, m, H_{2a}), 4.12 (5H, s, $C\underline{H}$-$Cp_{unsub.}$), 4.24 (1H, dd, $J_{gem.}$ = 11.6 Hz, J_{4e-3a} = 5.1 Hz, $\underline{H}_{4e}$), 5.42 (1H, s, $\underline{H}_{5a}$); ^{13}C NMR (150 MHz) δ 28.1 ($\underline{C}_3$), 58.5 ($\underline{C}H$-$Cp_{sub.}$), 59.6 ($\underline{C}H_3$), 62.1 ($\underline{C}H$-$Cp_{sub.}$), 63.2 ($\underline{C}H$-$Cp_{sub.}$), 66.7 ($\underline{C}_4$), 69.9 ($\underline{C}H$-$Cp_{unsub.}$), 73.3 (H_2N-$\underline{C}$-$Cp_{sub.}$), 75.2 ($\underline{C}_1$), 76.2 ($\underline{C}_2$), 101.1 ($\underline{C}_5$), 104.9 (CH-$\underline{C}$-$Cp_{sub.}$); m/z (EI) 332 (6%, M+H), 331 (30%, M), 229 (5%, M-Acetal); HRMS $C_{16}H_{21}FeNO_3$ calcd. 331.08654, found 331.08632; Anal. Calcd. For $C_{16}H_{21}FeNO_3$: C, 58.02; H, 6.39; N, 4.23 Found C, 57.86; H, 6.40; N, 4.05%.

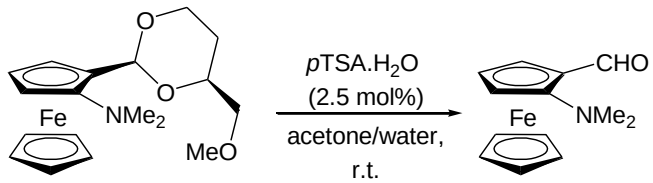


(+/-)-275 **(+/-)-276**

4-(Methoxymethyl)-2-[α-(*N*,*N*-dimethyl)-ferrocenyl]-1,3-dioxane (**(+/-)-276**).

To a suspension of 4-(methoxymethyl)-2-[α-(amino)-ferrocenyl]-1,3-dioxane (300 mg, 0.91 mmol) and paraformaldehyde (272 mg, 9.06 mmol, 10.0 eq.) in acetonitrile (15 mL) $NaBH_3CN$ (85.0 mg, 1.36 mmol, 1.50 eq.) was added and the mixture was stirred for 10 min at r.t. while the colour changed from orange to yellow. The suspension was concentrated in *vacuo* and purified by column chromatography (^{n}hexane/EtOAc, 2/8) to give 4-(methoxymethyl)-2-[α-(*N*,*N*-dimethyl)-ferrocenyl]-1,3-dioxane (190 mg, 58%)

as a yellow solid (m.p. 81-83 °C). Rf 0.41 (^{n}hexane/EtOAc, 2/8); IR υ_{max} 3094 (CH), 2946 (CH), 2871 (CH), 2843 ($N(CH_3)_2$), 2816 ($N(CH_3)_2$), 2771 ($N(CH_3)_2$), 1483, 1453, 1421, 1319, 1115 (CO), 1100 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 1.51 (1H, d, $J_{gem.}$ = 13.0 Hz, $\underline{H}_{3e}$), 1.79 (1H, dd, $J_{gem.}$ = 13.0 Hz, J_{3a-4e} = 5.0 Hz, $\underline{H}_{3a}$), 2.64 (6H, s, N-C$\underline{H}_3$), 3.34 (3H, s, O-C$\underline{H}_3$), 3.35 (1H, m, $\underline{H}_1$), 3.47 (1H, dd, $J_{gem.}$ = 9.5 Hz, J_{1-2a} = 6.3 Hz, $\underline{H}_1$), 3.92 (1H, s, C$\underline{H}$-$Cp_{sub.}$), 3.95 (1H, s, C$\underline{H}$-$Cp_{sub.}$), 4.00 (2H, m, $\underline{H}_{2a}$ & $\underline{H}_{4a}$), 4.18 (5H, s, C$\underline{H}$-$Cp_{unsub.}$), 4.25 (1H, s, C$\underline{H}$-$Cp_{sub.}$), 4.30 (1H, dd, $J_{gem.}$ = 10.9 Hz, J_{4e-3a} = 4.3 Hz, $\underline{H}_{4e}$), 5.59 (1H, s, $\underline{H}_5$); ^{13}C NMR (150 MHz) δ 28.2 ($\underline{C}_3$), 45.6 ($N(\underline{C}H_3)_2$), 56.5 ($\underline{C}$H-$Cp_{sub.}$), 59.3 ($O\underline{C}H_3$), 63.2 ($\underline{C}$H-$Cp_{sub.}$), 64.0 ($\underline{C}$H-$Cp_{sub.}$), 67.1 ($\underline{C}_4$), 69.3 ($\underline{C}$H-$Cp_{unsub.}$), 75.6 ($\underline{C}_1$), 76.0 ($\underline{C}_2$), 79.6 (H_2N-$\underline{C}$-$Cp_{sub.}$), 99.8 ($\underline{C}_5$), 112.8 (CH-$\underline{C}$-$Cp_{sub.}$); m/z (EI) 360 (4%, M+H), 359 (18%, M); HRMS $C_{18}H_{25}FeNO_3$ calcd. 359.11784, found 359.11792; Anal. Calcd. For $C_{18}H_{25}FeNO_3$: C, 60.18; H, 7.01; N, 3.90 Found C, 59.06; H, 6.88; N, 4.27%.

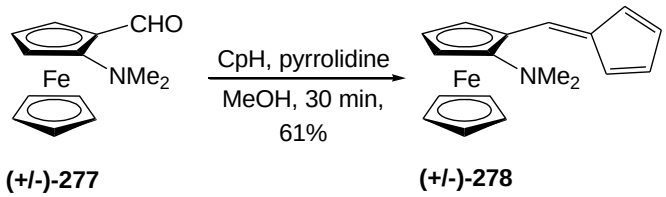


(+/-)-276 **(+/-)-277**

2-(*N*,*N*-dimethyl)-formylferrocene (**(+/-)-277**).

A solution of 4-(methoxymethyl)-2-[α-(*N*,*N*-dimethyl)-ferrocenyl]-1,3-dioxane (405 mg, 1.13 mmol) and *p*TSA.H_2O (10.0 mg, 0.06 mmol, 0.05 eq.) in acetone/water (4.0 mL/4.0 mL) was refluxed for 3.5 h. CH_2Cl_2 (5 mL) was added and the mixture was washed with $NaHCO_3$ (1 × 2 mL), and brine (1 × 2 mL), dried ($MgSO_4$) concentrated in *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 9/1) to yield 2-

(*N*,*N*-dimethyl)-formylferrocene (178mg, 61%) as a red oil. Rf 0.32 (^{n}hexane/EtOAc, 7/3); IR υ_{max} 3094 (CH), 2950 (CH), 2846 (CH), 2786 ($N(CH_3)_2$), 1666 (C=O), 1501, 1423, 1106 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 2.71 (6H, s, $N(C\underline{H}_3)_2$), 4.29 (6H, s, C<u>H</u>-$Cp_{sub.}$ & C<u>H</u>-$Cp_{unsub.}$), 4.42 (1H, s, C<u>H</u>-$Cp_{sub.}$), 4.63 (1H, s, C<u>H</u>-$Cp_{sub.}$), 10.15 (1H, s, C<u>H</u>O); ^{13}C NMR (150 MHz) δ 45.8 ($N(\underline{C}H_3)_2$), 60.4 (<u>C</u>H-$Cp_{sub.}$), 66.4 (<u>C</u>H-$Cp_{sub.}$), 68.0 (<u>C</u>H-$Cp_{sub.}$), 69.7 (<u>C</u>H-$Cp_{unsub.}$), 72.0 $(H_3C)_2N$-<u>C</u>-$Cp_{sub.}$), 117.7 (OHC-<u>C</u>-$Cp_{sub.}$), 193.0 (<u>C</u>HO); m/z (EI) 258 (14%, M+H), 257 (100%, M), 186 (22%, M-CHO-NMe_2), 121 (M-CHO-NMe_2-Cp); HRMS $C_{13}H_{15}FeNO$ calcd. 257.04976, found 257.04910.

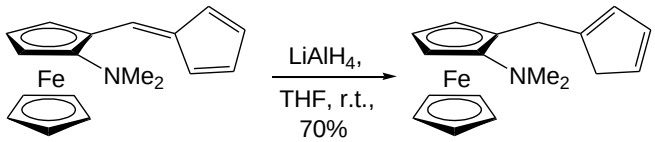


(+/-)-277 **(+/-)-278**

1-(*N*,*N*-Dimethyl)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (**(+/-)-278**).

To a solution of 2-(*N*,*N*-dimethyl)-formylferrocene (120 mg, 0.47 mmol) in MeOH (20 mL), pyrrolidine (0.08 mL, 0.93 mmol, 2.00 eq.), freshly cracked cyclopentadiene (0.02 mL, 1.86 mmol, 4.00 eq.) was added and the reaction was stirred for 30 min. The mixture was concentrated in *vacuo* and purified by flash column chromatography (CH_2Cl_2) to give 1-(*N*,*N*-dimethyl)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (86.0 mg, 61%) as a deep-purple-red oil. Rf 0.31 (CH_2Cl_2); IR υ_{max} 3096 (CH), 2943 (CH), 2821 (CH), 2778 ($N(CH_3)_2$), 1621 (C=C), 1609 (C=C), 1484, 1451, 1431, 1106 (CO) cm^{-1}; ^{1}H NMR (600 MHz) δ 2.65 (6H, s, $N(C\underline{H}_3)_2$), 4.18 (5H, s, C<u>H</u>-$Cp_{unsub.}$), 4.26 (1H, dd, *J* = 2.6, 1.3 Hz, C<u>H</u>-$Cp_{sub.}$), 4.38 (1H, t, *J* = 2.7 Hz, C<u>H</u>-$Cp_{sub.}$), 4.66 (1H, dd, *J* = 2.5, 1.1 Hz, C<u>H</u>-$Cp_{sub.}$), 6.36 (1H, dt, *J* = 5.0, 1.7 Hz, C<u>H</u>-Fulv.), 6.50 (1H, dt, *J*

= 5.0, 1.5 Hz, CH-Fulv.), 6.61 (1H, ddd, *J* = 5.1, 1.7, 1.5 Hz, CH-Fulv.), 6.65 (1H, dm, *J* = 5.2 Hz, CH-Fulv.), 7.37 (1H, s, Fc.-CH-Fulv.); ^{13}C NMR (150 MHz) δ 46.2 ($N(\underline{C}H_3)_2$), 58.0 (CH-$Cp_{sub.}$), 65.4 (CH-$Cp_{sub.}$), 66.7 (CH-$Cp_{sub.}$), 70.4 (CH-$Cp_{unsub.}$), 76.0 (Fulv.-C-$Cp_{sub.}$), 117.4 ($(H_3C)_2N$-C-$Cp_{sub.}$), 120.0 (CH-Fulv.), 126.7 (CH-Fulv.), 128.7 (CH-Fulv.), 132.8 (CH-Fulv.), 138.4 (Fc.-CH-Fulv.), 141.1(C-Fulv.); m/z (EI) 306 (4%, M+H), 305 (15%, M); HRMS $C_{18}H_{19}FeN$ calcd. 305.08614, found 305.08703.



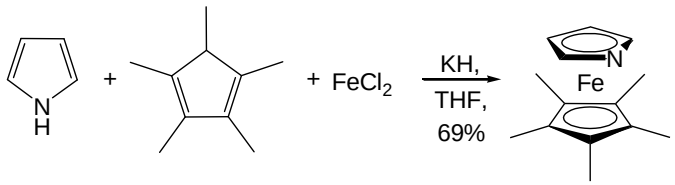
(+/-)-278 **(+/-)-271**

1-(Dimethylamino)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (**(+/-)-271**).

To a solution of 1-(dimethylamino)-2-[(cyclopenta-2,4-dienylidene)methyl]-ferrocene (70.0 mg, 0.23 mmol) in THF (15 mL) $LiAlH_4$ (0.14 mL, 0.28 mmol, 1.20 eq., 2M in THF) was added and the reaction was stirred for 3 h. Water (10 mL) was then added to the mixture at 0 °C and the mixture was extracted with Et_2O (2 × 15 mL). The combined organics were dried ($MgSO_4$), concentrated under *vacuo* and purified by flash column chromatography (CH_2Cl_2/EtOAc, 99/1) to give 1-(dimethylamino)-2-[(cyclopenta-1,3-dienyl)methyl]-ferrocene (49.0 mg, 70%) as a yellow solid (m.p. 52-54 °C), which consisted of 2 inseparable isomers in a 55/45 ratio. Rf 0.17 (CH_2Cl_2/EtOAc, 99/1); IR (solid) 3093 (CH), 2890 (CH), 2826 (CH), 2785 (CH), 1604 (C=C), 1490, 1417, 1101 cm^{-1};

Major isomer: ^{1}H NMR (600 MHz) δ 2.57 (6H, s, N(C<u>H</u>$_3$)$_2$), 2.92 (2H, s, C<u>H</u>$_2$-Cp'), 3.51 (1H, d, $J_{gem.}$ = 16.5 Hz, Fc-C<u>H</u>$_2$-Cp'), 3.70 (1H, d, $J_{gem.}$ = 16.7 Hz, Fc-C<u>H</u>$_2$-Cp'), 3.89 (1H, m, C<u>H</u>-Cp$_{sub.}$), 3.92 (1H, m, C<u>H</u>-Cp$_{sub.}$), 3.96 (1H, m, C<u>H</u>-Cp$_{sub.}$), 4.14 (5H, m, C<u>H</u>-Cp$_{unsub.}$), 6.09 (1H, s, C<u>H</u>-Cp'), 6.25 (1H, d, *J* = 4.7 Hz, C<u>H</u>-Cp'), 6.39 (1H, d, *J* = 3.8 Hz, C<u>H</u>-Cp'); ^{13}C NMR (150 MHz) δ 30.0 (Fc-<u>C</u>H$_2$), 43.7 (<u>C</u>H$_2$-Cp'), 45.4 (N(<u>C</u>H$_3$)$_2$), 56.0 (<u>C</u>H-Cp$_{sub.}$), 62.2 (<u>C</u>H-Cp$_{sub.}$), 66.9 (<u>C</u>H-Cp$_{sub.}$), 69.0 (<u>C</u>H-Cp$_{unsub.}$), 80.3 (CH$_2$-<u>C</u>-Cp$_{sub.}$), 112.6 ((H$_3$C)$_2$N-<u>C</u>-Cp$_{sub.}$), 127.4 (<u>C</u>H-Cp'), 130.9 (<u>C</u>H-Cp'), 132.4 (<u>C</u>H- Cp'), 149.1 (H$_2$C-<u>C</u>-Cp').

Minor isomer: ^{1}H NMR (600 MHz) δ 2.58 (6H, s, N(C<u>H</u>$_3$)$_2$), 2.95 (2H, s, C<u>H</u>$_2$-Cp'), 3.49 (1H, d, $J_{gem.}$ = 16.1 Hz, Fc-C<u>H</u>$_2$-Cp'), 3.62 (1H, d, $J_{gem.}$ = 16.4 Hz, Fc-C<u>H</u>$_2$-Cp'), 3.89 (1H, m, C<u>H</u>-Cp$_{sub.}$), 3.92 (1H, m, C<u>H</u>-Cp$_{sub.}$), 3.96 (1H, m, C<u>H</u>-Cp$_{sub.}$), 4.14 (5H, m, C<u>H</u>-Cp$_{unsub.}$), 5.96 (1H, s, C<u>H</u>-Cp'), 6.42 (1H, d, *J* = 4.4 Hz, C<u>H</u>-Cp'), 6.50 (1H, d, *J* = 4.2 Hz, C<u>H</u>-Cp'); ^{13}C NMR (150 MHz) δ 29.1 (Fc-<u>C</u>H$_2$), 41.3 (<u>C</u>H$_2$-Cp'), 45.4 (N(<u>C</u>H$_3$)$_2$), 56.1 (<u>C</u>H-Cp$_{sub.}$), 62.1 (<u>C</u>H-Cp$_{sub.}$), 66.8 (<u>C</u>H-Cp$_{sub.}$), 68.9 (<u>C</u>H-Cp$_{unsub.}$), 79.8 (CH$_2$-<u>C</u>-Cp$_{sub.}$), 112.6 ((H$_3$C)$_2$N-<u>C</u>-Cp$_{sub.}$), 127.0 (<u>C</u>H-Cp'), 133.8 (<u>C</u>H-Cp'), 134.9 (<u>C</u>H-Cp'), 146.4 (H$_2$C-<u>C</u>-Cp'); m/z (EI) 308 (23%, M+H), 307 (100%, M), 242 (M-Cp), 199 (M-Cp-NMe$_2$); HRMS C$_{18}$H$_{21}$FeN calcd. 307.10179, found 307.10158; Anal. Calcd. For C$_{18}$H$_{21}$FeN: C, 70.34; H, 6.89; N, 4.56 Found C, 70.21; H, 6.88; N, 4.49%.



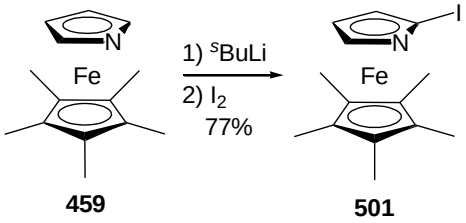
461 **462** **459**

1',2',3',4',5'-Pentamethylazaferrocene (**459**).

To a solution of KH (4.72 g, 29.4 mmol, 1.00 eq.) in THF (80 mL), freshly distilled pyrrole (2.3 mL, 33.2 mmol, 1.13 eq.) was added dropwise at 0 °C. The solution was refluxed for 8.5 h. The THF was removed by cannula filtration and the resulting tan solid was washed with THF (1 × 15 mL). The $FeCl_2$ was dried overnight before the reaction under vacuum at 120 °C. Vigorous stirring helps to grind the solid into a fine powder. To a solution of 1,2,3,4,5-pentamethylcyclopentadiene (4.0 g, 29.4 mmol) in THF (100 mL) ^{n}BuLi (11.8 mL, 29.4 mmol, 1.00 eq.) was added at 0 °C while a white-yellow slurry formed. The mixture was stirred at r.t. for 30 min before it was added by cannula to a suspension of $FeCl_2$ (3.72 g, 29.4 mmol, 1.00 eq.) in THF (40 mL) at 0 °C. The resulting green suspension was stirred at 0 °C for 30 min. To this mixture the previously prepared suspension of the potassiumpyrrolide in THF (40 mL) was added via cannula at r.t. The reaction was then stirred at r.t. for 2 h while the colour of the reaction turned from green to brown then black. Most of the THF was removed under *vacuo*, the mixture was filtered through a pad of silica gel and washed with EtOAc (until the silica has orange colour). The mixture was concentrated under *vacuo* and purified by flash column chromatography (PE/EtOAc/Et_3N, 90/5/5) to give 1',2',3',4',5'-pentamethylazaferrocene (5.12 g, 68%) as an orange solid (m.p. 90-93 °C). Rf 0.27 (^{n}hexane/EtOAc); IR υ_{max} 2970 (CH), 1548, 1422, 1376, 1064 cm^{-1}; ^{1}H

NMR (600 MHz) δ 1.95 (15H, s, C<u>H</u>$_3$-Cp*), 4.14 (2H, s, C<u>H</u>-Pyrrole), 4.95 (2H, s, C<u>H</u>-Pyrrole); ^{13}C NMR (150 MHz) δ 11.1 (<u>C</u>H$_3$-Cp*), 74.1 (2 × <u>C</u>H-Pyrrole), 80.8 (H$_3$C-<u>C</u>-Cp*), 91.8 (2 × <u>C</u>H-Pyrrole); m/z (EI) 258 (16%, M+H), 257 (100%, M), 191 (2%, Cp*Fe); HRMS $C_{14}H_{19}FeN$ calcd. 257.08614, found 257.08625; Anal. Calcd. For $C_{14}H_{19}FeN$: C, 65.39; H, 7.45; N, 5.45. Found C, 65.05; H, 7.49; N, 5.32%. ^{1}H NMR and ^{13}C NMR agreed with literature data.[66]

During column chromatography bis(1,2,3,4,5-pentamethylcyclopentadienyl)-iron was also isolated (789 mg, 16%) as a yellow solid (m.p. 90 °C decomp.). Rf 0.99 (PE/EtOAc/Et$_3$N, 90/5/5); IR υ_{max} 2964, 2892 2851 1473, 1425, 1372, 1026 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.95 (30 H, s, C<u>H</u>$_3$-Cp*); ^{13}C NMR (150 MHz) δ 9.78 (<u>C</u>H$_3$-Cp*), 78.5 (H$_3$C-<u>C</u>-Cp*); m/z (EI) 327 (20%, M+H), 326 (100%, M); HRMS $C_{20}H_{30}Fe$ calcd. 326.16913, found 326.16864; Anal. Calcd. For $C_{14}H_{19}FeN$: C, 73.62; H, 9.27. Found C, 73.57; H, 9.42%

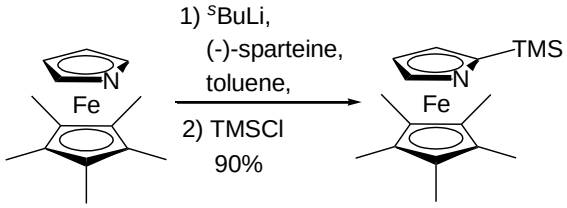


459 **501**

2-Iodo-1',2',3',4',5'-pentamethylazaferrocene (**501**)

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (500 mg, 1.94 mmol) and (-)-sparteine (0.54 mL, 2.33 mmol, 1.20 eq.) in Et_2O (8.0 mL) ^{s}BuLi (1.66 mL, 2.33 mmol, 1.20 eq.) was added at -78 °C and the reaction was stirred for 4 h at -78 °C. After a solution of iodine (296 mg, 2.33 mmol, 1.20 eq.) in Et_2O (23 mL) was added dropwise to the reaction. The reaction was stirred at r.t. for 1 h. The reaction mixture was evaporated onto silica gel and purified by flash column chromatography

(PE/EtOAc/Et_3N, 85/10/5) to give 2-iodo-1',2',3',4',5'-pentamethylazaferrocene (575 mg, 77%) as an orange solid (m.p. 68-70 °C). Rf 0.78 (^{n}hexane/EtOAc 1/1); IR υ_{max} 2906 (CH), 1542, 1425, 1377, 1069, 1027 cm^{-1}; ^1H NMR (600 MHz) δ 1.88 (15H, s, C<u>H</u>$_3$-Cp*), 4.11 (1H, s, C<u>H</u>-Pyrrole), 4.25 (1H, s, C<u>H</u>-Pyrrole), 4.92 (1H, s, C<u>H</u>-Pyrrole); ^{13}C NMR (100 MHz) δ 10.3 (<u>C</u>H$_3$-Cp*), 64.5 (I-<u>C</u>-Pyrrole), 76.0 (<u>C</u>H-Pyrrole), 80.1 (<u>C</u>H-Pyrrole), 82.3 (H_3C-<u>C</u>-Cp*), 92.9 (<u>C</u>H-Pyrrole); m/z (EI) 384 (16%, M+H), 383 (100%, M); HRMS $C_{14}H_{18}FeIN$ calcd. 382.98279, found 382.98299; Anal. Calcd. For $C_{14}H_{18}FeIN$: C, 43.90; H, 4.74; N, 3.66. Found C, 43.65; H, 4.74; N, 3.55%.

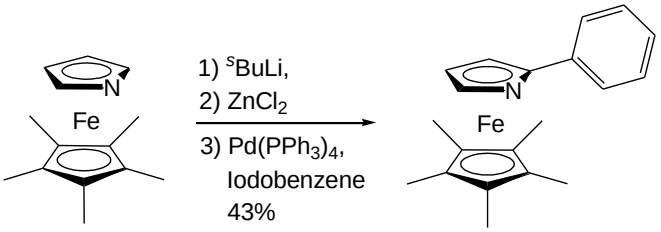


459 **468**

2-Trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (**468**).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (500 mg, 1.94 mmol) and (-)-sparteine (0.54 mL, 2.33 mmol, 1.20 eq.) in Et_2O (8.0 mL) ^{s}BuLi (1.66 mL, 2.33 mmol, 1.20 eq.) was added at -78 °C and the reaction was stirred for 4 h at -78 °C. After a solution of TMSCl (0.29 mL, 2.33 mmol, 1.20 eq.) in Et_2O (23 mL) was added dropwise to the reaction. The reaction was stirred at r.t. for 15 min. The reaction mixture was evaporated onto silica gel and purified by flash column chromatography (^{n}hexane/EtOAc, 1/1) to give 2-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (580 mg, 90%) as an orange solid (m.p. 190 °C decomp.). Rf 0.51 (^{n}hexane/EtOAc 1/1); IR υ_{max} 2957 (CH), 1708, 1545, 1420, 1066 cm^{-1}; ^1H NMR (600 MHz) δ 0.31 (9H, s, Si(C<u>H</u>$_3$)$_3$), 1.91 (15H, s, C<u>H</u>$_3$-Cp*), 4.06 (1H, s, C<u>H</u>-Pyrrole), 4.27 (1H, s, C<u>H</u>-

Pyrrole), 5.19 (1H, s, CH-Pyrrole); ^{13}C NMR (150 MHz) δ -0.7 ((H$_3$C)$_3$-Si), 11.4 (H$_3$C-Cp*), 76.9 (CH-Pyrrole), 79.0 (CH-Pyrrole), 80.4 (H$_3$C-C-Cp*), 96.7 (CH-Pyrrole), 97.3 ((CH$_3$)$_3$Si-C-Cp); m/z (EI) 330 (26%, M+H), 329 (100%, M); HRMS $C_{17}H_{27}FeNSi$ calcd. 329.12567, found 329.12608.

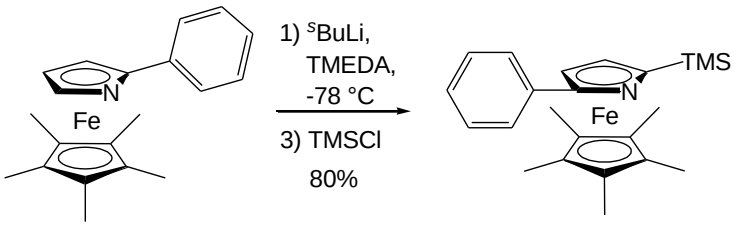


459 **(+/-)-466c**

2-Phenyl-1',2',3',4',5'-pentamethylazaferrocene (**(+/-)-466c**).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (500 mg, 1.94 mmol) and (-)-sparteine (0.54 mL, 2.33 mmol, 1.20 eq.) in toluene (8.0 mL) ^{s}BuLi (1.66 mL, 2.33 mmol, 1.20 eq.) was added at -78 °C and the mixture was stirred for 4 h at -78 °C. A solution of $ZnCl_2$ (7.70 mL, 7.77 mmol, 4.00 eq., 1M in THF) was then added to the reaction dropwise over 15 min at -78 °C, and the temperature was let to raise to r.t. During this time a premixed solution of $Pd(PPh_3)_4$ (112 mg, 0.09 mmol, 5 mol%) and Iodobenzene (0.33 mL, 2.92 mmol, 1.50 eq.) in THF (8.0 mL) was prepared and stirred for 15 min. This solution was added to the reaction and the mixture was stirred for 2 h. The reaction was diluted with CH_2Cl_2 (15 mL) and poured onto NH_4Cl (10 mL). This then was extracted with CH_2Cl_2 (2 × 10 mL), washed with $NaHCO_3$ (1 × 10 mL), brine (1 × 10 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography (PE/EtOAc/Et_3N, 85/10/5) to give 2-phenyl-1',2',3',4',5'-pentamethylazaferrocene (280 mg, 43%) as an orange-red solid (m.p. 97-99 °C). Rf 0.71 (PE/EtOAc/Et_3N, 85/10/5); IR υ_{max} 2961 (CH), 2908 (CH), 1602, 1509, 1452,

1375, 1032 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.70 (15H, s, C<u>H</u>$_3$-Cp*), 4.33 (1H, d, *J* = 1.7 Hz, C<u>H</u>-Pyrrole), 4.57 (1H, d, *J* = 2.1 Hz, C<u>H</u>-Pyrrole), 5.12 (1H, s, C<u>H</u>-Pyrrole), 7.26 (1H, t, *J* = 7.4 Hz, *p*-C<u>H</u>-Ph), 7.39 (1H, t, *J* = 7.6 Hz, *m*-C<u>H</u>-Ph), 7.69 (1H, t, *J* = 7.5 Hz, *o*-C<u>H</u>-Ph); ^{13}C NMR (150 MHz) δ 10.3 (<u>C</u>H$_3$-Cp*), 69.9 (<u>C</u>H-Pyrrole), 76.3 (<u>C</u>H-Pyrrole), 81.2 (H$_3$C-<u>C</u>-Cp*), 92.5 (<u>C</u>H-Pyrrole), 102.1 (Ph-<u>C</u>-Pyrrole), 125.3 (*o*-<u>C</u>H-Ph), 126.5 (*p*-<u>C</u>H-Ph), 128.4 (*m*-<u>C</u>H-Ph), 135.6 (*i*-<u>C</u>-Ph); m/z (EI) 334 (25%, M+H), 333 (100%, M), 198 (5%, AFc-Cp*); HRMS $C_{20}H_{23}FeN$ calcd. 333.11744, found 333.11694. ^{1}H NMR and ^{13}C NMR data agreed with literature data.[72]

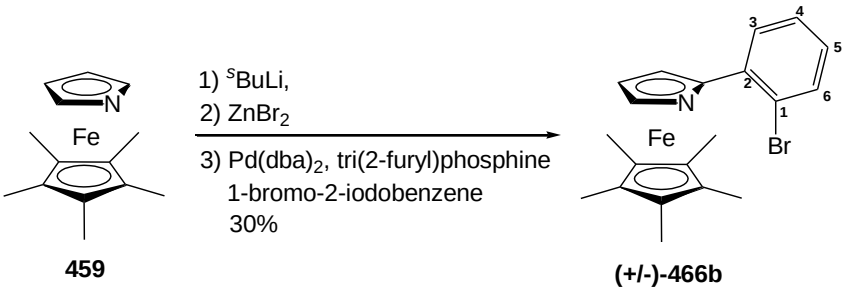


(+/-)-466c **(+/-)-469b**

2-Phenyl-5-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (**(+/-)-469b**).

To a solution of 2-phenyl-1',2',3',4',5'-pentamethylazaferrocene (150 mg, 0.45 mmol) in THF (10 mL) ^{s}BuLi (2.22 mL, 2.66 mmol, 6.00 eq.) and TMEDA (0.40 mL, 2.66 mmol, 6.00 eq.) was added at -78 °C and the solution was stirred for 1 h at -78 °C. TMSCl (0.56 mL, 1.98, 4.40 eq.) was then added and the reaction was stirred for 1 h at -78 °C. The solution was evaporated onto silica gel and purified by flash column chromatography (^{n}hexane/EtOAc/Et$_3$N, 90/5/5) to give 2-phenyl-5-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (147 mg, 80%) as an orange-red solid (m.p. 85-87 °C). Rf 0.91 (^{n}hexane/EtOAc/Et$_3$N, 85/10/5); IR υ_{max} 2957 (CH), 2903 (CH), 1605, 1452, 1373, 1242, 1023 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.37 (9H, s, Si(C<u>H</u>$_3$)$_3$), 1.64 (15H, s, C<u>H</u>$_3$-Cp*), 4.22 (1H, d, *J* = 2.3 Hz, C<u>H</u>-Pyrrole), 4.62 (1H, d, *J* = 2.4 Hz, C<u>H</u>-

Pyrrole), 7.26 (1H, t, *J* = 7.4 Hz, *p*-C<u>H</u>-Ph), 7.38 (1H, t, *J* = 7.4 Hz, *m*-C<u>H</u>-Ph), 7.77 (1H, t, *J* = 7.1 Hz, *o*-C<u>H</u>-Ph); ^{13}C NMR (100 MHz) δ -0.5 ((H$_3$<u>C</u>)$_3$-Si), 10.5 (<u>C</u>H$_3$-Cp*), 72.3 (<u>C</u>H-Pyrrole), 80.5 (<u>C</u>-Cp*), 80.9 (<u>C</u>H-Pyrrole), 100.0, 106.6, 126.1 (*o*-<u>C</u>H-Ph), 126.5 (*p*-<u>C</u>H-Ph), 128.3 (*m*-<u>C</u>H-Ph), 136.2 (*i*-<u>C</u>-Ph); m/z (EI) 406 (32%, M+H), 405 (100%, M); HRMS $C_{23}H_{31}FeNSi$ calcd. 405.15697, found 405.15694; Anal. Calcd. for $C_{23}H_{31}FeNSi$: C, 68.14; H, 7.71; N, 3.45. Found C, 67.20; H, 7.73; N, 3.40%.

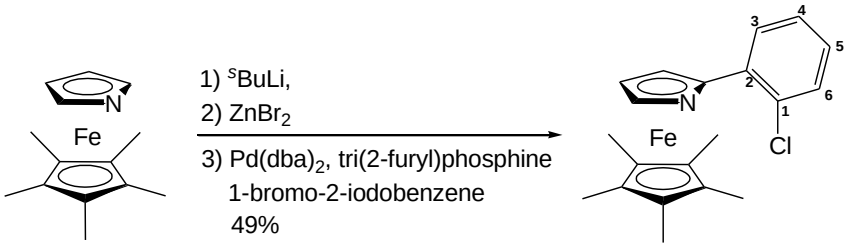


459 **(+/-)-466b**

2-(*α*-Bromo-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (**(+/-)-466b**).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (300 mg, 1.17 mmol) and TMEDA (0.21 mL, 1.40 mmol, 1.40 eq.) in toluene (6.0 mL) ^{s}BuLi (1.07 mL, 1.40 mmol, 1.20 eq.) was added at -78 °C and the mixture was stirred for 4 h at -78 °C. A solution of $ZnBr_2$ (4.66 mL, 4.66 mmol, 4.00 eq., 1M in THF) was then added to the reaction dropwise over 15 min at -78 °C and the temperature was let to raise to r.t. During this time a premixed solution of $Pd(dba)_2$ (16.7 mg, 0.03 mmol, 2.5 mol%), tri(2-furyl)phosphine (27.0 mg, 0.12 mmol, 10 mol%) and 1-bromo-2-iodobenzene (0.22 mL, 1.75 mmol, 1.50 eq.) in THF (4.0 mL) was prepared and stirred for 15 min. This solution was added to the reaction and the mixture was refluxed for 3 h. The reaction was diluted with CH_2Cl_2 (10 mL) and poured onto NH_4Cl (8 mL). This then was extracted with CH_2Cl_2 (2 × 8 mL), washed with $NaHCO_3$ (1 × 8 mL), brine (1 × 8 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column

chromatography subsequently (PE/EtOAc/Et_3N, 85/10/5; ^{n}hexane/EtOAc, 9/1) to give 2-(*α*-bromo-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (146 mg, 30%) as an orange-red solid (mp. 98-100 °C). Rf 0.49 (PE/EtOAc/Et_3N, 85/10/5); IR υ_{max} 2967 (CH), 2906 (CH), 1590, 1483, 1373, 1028, 1005 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.74 (15H, s, C<u>H</u>$_3$-Cp*), 4.39 (1H, s, C<u>H</u>-Pyrrole), 5.13 (1H, s, C<u>H</u>-Pyrrole), 5.50 (1H, s, C<u>H</u>-Pyrrole), 7.09 (1H, t, *J* = 7.4 Hz, C<u>H</u>^{5}-Ar), 7.34 (1H, t, *J* = 7.4 Hz, C<u>H</u>^{4}-Ar), 7.63 (1H, d, *J* = 7.8 Hz, C<u>H</u>^{6}-Ar), 8.17 (1H, d, *J* = 7.6 Hz, C<u>H</u>^{3}-Ar); ^{13}C NMR (100 MHz) δ 10.4 (<u>C</u>H$_3$-Cp*), 74.4 (<u>C</u>H-Pyrrole), 77.5 (<u>C</u>H-Pyrrole), 81.3 (H$_3$C-<u>C</u>-Cp*), 92.1 (<u>C</u>H-Pyrrole), 99.2 (Ph-<u>C</u>-Pyrrole), 126.6 (H<u>C</u>^{4}-Ar), 127.0 (H<u>C</u>^{5}-Ar), 129.8 (H<u>C</u>^{3}-Ar), 130.9 (H<u>C</u>^{6}-Ar), 130.9 (<u>C</u>^{1}-Ar), 134.1 (<u>C</u>^{2}-Ar); m/z (EI) 415 (10%, M(^{81}Br)+H), 414 (52%, M(^{81}Br)), 413 (90%, M(^{79}Br)+H), 411 (100%, M(^{79}Br)), 333 (4%, AFc-Br); HRMS $C_{20}H_{22}FeBrN$ calcd. 411.02796, found 411.02830; Anal. Calcd. for $C_{20}H_{22}FeBrN$: C, 58.28; H, 5.38; N, 3.40. Found C, 58.38; H, 5.35; N, 3.29%. ^{1}H NMR and ^{13}C NMR data agreed with literature data.[72]

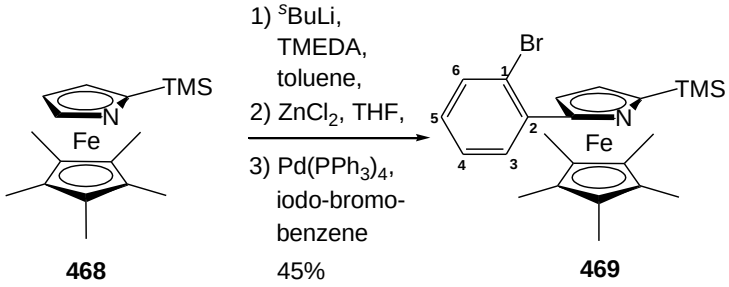


459 **(+/-)-466a**

2-(*α*-Chloro-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (**(+/-)-466a**).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (300 mg, 1.17 mmol) and TMEDA (0.21 mL, 1.40 mmol, 1.40 eq.) in toluene (6.0 mL) ^{s}BuLi (1.07 mL, 1.40 mmol, 1.20 eq.) was added at -78 °C and the mixture was stirred for 4 h at -78 °C. A solution of $ZnBr_2$ (4.66 mL, 4.66 mmol, 4.00 eq., 1M in THF) was then added to the

reaction dropwise over 15 min at -78 °C and the temperature was let to raise to r.t. During this time a premixed solution of $Pd(dba)_2$ (16.7 mg, 0.03 mmol, 2.5 mol%), tri(2-furyl)phosphine (27.0 mg, 0.12 mmol, 10 mol%) and 1-chloro-2-iodobenzene (0.22 mL, 1.75 mmol, 1.50 eq.) in THF (4.0 mL) was prepared and stirred for 15 min. This solution was added to the reaction and the mixture was refluxed for 3 h. The reaction was diluted with CH_2Cl_2 (10 mL) and poured onto NH_4Cl (8 mL). This then was extracted with CH_2Cl_2 (2 × 8 mL), washed with $NaHCO_3$ (1 × 8 mL), brine (1 × 8 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography subsequently (PE/EtOAc/Et_3N, 85/10/5; ^{n}hexane/EtOAc, 9/1) to give 2-(*α*-chloro-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (210 mg, 49%) as an orange solid (m.p. 104-107 °C). Rf 0.72 (PE/EtOAc/Et_3N, 85/10/5); IR υ_{max} 3060 (CH), 2967 (CH), 2906 (CH), 1593, 1486, 1373, 1264, 1093, 1031 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.73 (15H, s, C$\underline{H}_3$-Cp*), 4.39 (1H, s, C$\underline{H}$-Pyrrole), 5.11 (1H, s, C$\underline{H}$-Pyrrole), 5.31 (1H, s, C$\underline{H}$-Pyrrole), 7.16 (1H, t, *J* = 7.3 Hz, C$\underline{H}^5$-Ar), 7.29 (1H, t, *J* = 7.5 Hz, C$\underline{H}^4$-Ar), 7.42 (1H, d, *J* = 8.0 Hz, C$\underline{H}^6$-Ar), 8.16 (1H, d, *J* = 7.8 Hz, C$\underline{H}^3$-Ar); ^{13}C NMR (150 MHz) 10.5 ($\underline{C}H_3$-Cp*), 74.5 ($\underline{C}$H-Pyrrole), 77.6 ($\underline{C}$H-Pyrrole), 81.4 (H_3C-$\underline{C}$-Cp*), 92.2 ($\underline{C}$H-Pyrrole), 99.3 (Ph-$\underline{C}$-Pyrrole), 126.7 (H$\underline{C}^4$-Ar), 127.2 (H$\underline{C}^5$-Ar), 129.8 (H$\underline{C}^3$-Ar), 131.0 (H$\underline{C}^6$-Ar), 131.1 ($\underline{C}^1$-Ar), 134.2 ($\underline{C}^2$-Ar); m/z (EI) 370 (8%, M(^{37}Cl)+H), 369 (35%, M(^{37}Cl)), 368 (26%, M(^{35}Cl)+H), 367 (100%, M(^{35}Cl)), 331 (63%, M(^{35}Cl)-Cl); HRMS $C_{20}H_{22}FeClN$ calcd. 367.07847, found 367.07777; Anal. Calcd. for $C_{20}H_{22}FeClN$: C, 65.33; H, 6.03; N, 3.81. Found C, 64.71; H, 6.10; N, 3.65%.

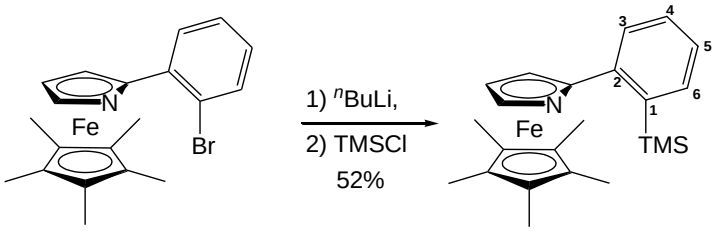


468 **469**

2-(*α*-Bromo-phenyl)-5-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (**469**).

To a solution of 2-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (500 mg, 1.5 mmol) and TMEDA (0.27 mL, 1.80 mmol, 1.20 eq.) in toluene (10 mL) ^{s}BuLi (1.50 mL, 1.80 mmol, 1.20 eq.) was added at -78 °C and the mixture was stirred for 5 h at -78 °C. A solution of $ZnCl_2$ (6.00 mL, 6.00 mmol, 4.00 eq., 1M in THF) was then added to the reaction dropwise over 15 min at -78 °C and the temperature was let to raise to rt. During this time a premixed solution of $Pd(dba)_2$ (21.6 mg, 0.04 mmol, 2.5 mol%), tri(2-furyl)phosphine (34.8 mg, 0.15 mmol, 10 mol%) and 1-bromo-2-iodobenzene (0.28 mL, 2.25 mmol, 1.50 eq.) in THF (7.0 mL) was prepared and stirred for 15 min. This solution was added to the reaction and the mixture was refluxed overnight. The reaction was diluted with CH_2Cl_2 (20 mL) and poured onto NH_4Cl (15 mL). This then was extracted with CH_2Cl_2 (2 × 15 mL), washed with $NaHCO_3$ (1 × 15 mL), brine (1 × 15 mL), dried ($MgSO_4$), concentrated in *vacuo* and purified by flash column chromatography (PE/EtOAc/Et_3N, 95/2.5/2.5) to give 2-(*α*-bromo-phenyl)-5-trimethylsilyl-1',2',3',4',5'-pentamethylazaferrocene (328 mg, 45%) as an orange solid (m.p. 134-136 °C). Rf 0.67 (^{n}hexane/EtAOc, 9/1); IR υ_{max} 2965 (CH), 2900 (CH), 1483, 1409, 1373, 1244, 1014 cm^{-1}; ^{1}H NMR (600 MHz) δ 0.37 (9H, s, Si(C<u>H</u>$_3$)$_3$), 1.67 (15H, s, C<u>H</u>$_3$-Cp*), 4.27 (1H, d, *J* = 2.7 Hz, C<u>H</u>-Pyrrole), 5.55 (1H, d, *J* = 2.6 Hz, C<u>H</u>-

Pyrrole), 7.08 (1H, t, *J* = 7.3 Hz, C<u>H</u>^{5}-Ar), 7.35 (1H, t, *J* = 7.6 Hz, C<u>H</u>^{4}-Ar), 7.62 (1H, d, *J* = 7.8 Hz, C<u>H</u>^{6}-Ar), 8.35 (1H, d, *J* = 7.4 Hz, C<u>H</u>^{3}-Ar); ^{13}C NMR (150 MHz) -0.6 ((H$_3$<u>C</u>)$_3$-Si), 10.6 (<u>C</u>H$_3$-Cp*), 76.2 (<u>C</u>H-Pyrrole), 80.6 (H$_3$C-<u>C</u>-Cp*), 81.7 (<u>C</u>H-Pyrrole), 98.4 ((H$_3$C)$_3$Si-<u>C</u>-Pyrrole), 104.1 (Ar-<u>C</u>-Pyrrole), 120.5 (<u>C</u>^{1}-Ar), 127.0 (H<u>C</u>^{4}-Ar), 127.3 (H<u>C</u>^{5}-Ar), 131.5 (H<u>C</u>^{3}-Ar), 134.3 (H<u>C</u>^{6}-Ar), 136.4 (<u>C</u>^{2}-Ar); m/z (EI) 486 (18%, M(^{81}Br)+H), 485 (53%, M(^{81}Br)), 484 (22%, M(^{79}Br)+H), 483 (55%, M(^{79}Br)); HRMS $C_{23}H_{30}FeBrNSi$ calcd. 483.06747, found 483.06828.

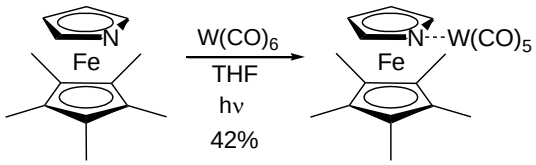


(+/-)-466b **(+/-)-477**

2-(*α*-trimethylsylil-phenyl)-1',2',3',4',5'-pentamethylazaferrocene ((+/-)-477).

To a solution of 2-(*α*-bromo-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (150 mg, 0.36 mmol) in THF (2.0 mL) ^{n}BuLi (0.16 mL, 0.40 mmol, 1.10 eq.) was added at -90 °C and the mixture was stirred at -90 °C for 1.5 h. At this point TMSCl (55 μL, 0.43 mmol, 1.20 eq.) was added and the temperature was let to raise to r.t. The reaction was stirred at r.t. for 1.5 h. The solvent was removed under reduced pressure and the crude material was purified by flash column chromatography (^{n}hexane→^{n}hexane/EtOAc, 99/1) to give -(*α*-trimethylsylil-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (75 mg, 52%), as a brown oil. Rf 0.25 (^{n}hexane/EtOAc, 98/2); IR υ_{max} 2950 (CH), 2901 (CH), 1589, 1380 cm^{-1}; ^{1}H NMR (600 MHz) δ 0.23 (9H, s, Si(C<u>H</u>$_3$)$_3$), 1.73 (15H, s, C<u>H</u>$_3$-Cp*), 4.30 (1H, s, C<u>H</u>-Pyrrole), 4.62 (1H, s, C<u>H</u>-Pyrrole), 5.00 (1H, s, C<u>H</u>-Pyrrole),

7.23 (1H, t, *J* = 7.3 Hz, C<u>H</u>^{5}-Ar), 7.43 (1H, t, *J* = 7.2 Hz, C<u>H</u>^{4}-Ar), 7.61 (1H, d, *J* = 7.4 Hz, C<u>H</u>^{5}-Ar), 7.83 (1H, d, *J* = 7.7 Hz, C<u>H</u>^{3}-Ar); ^{13}C NMR (150 MHz) 2.26 ((H_3<u>C</u>)$_3$-Si), 10.7 (<u>C</u>H_3-Cp*), 72.4 (<u>C</u>H-Pyrrole), 76.2 (<u>C</u>H-Pyrrole), 81.0 (H_3C-<u>C</u>-Cp*), 91.3 (<u>C</u>H-Pyrrole), 105.7 (Ar-<u>C</u>-Pyrrole), 125.5 (H<u>C</u>^{5}-Ar), 128.1 (H<u>C</u>^{3}-Ar), 128.2 (H<u>C</u>^{4}-Ar), 135.9 (H<u>C</u>^{6}-Ar), 138.2 (<u>C</u>^{1}-Ar), 142.0 (<u>C</u>^{2}-Ar); m/z (EI) 405 (7%, M), 390 (12%, M-CH_3); HRMS $C_{23}H_{31}FeNSi$ calcd. 405.15695, found 405.15740.

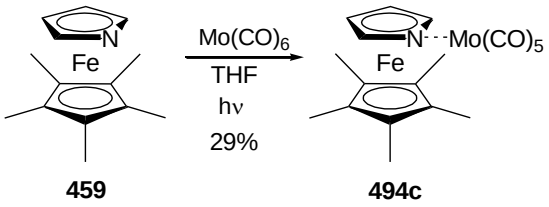


459 **494d**

(1',2',3',4',5'-Pentamethylazaferrocene)tungsten pentacarbonyl (**494d**).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (100 mg, 0.39 mmol) in (7.0 mL) $W(CO)_6$ (137 mg, 0.39 mmol, 1.00 eq.) was added and the reaction was stirred in THF (5.0 mL) at r.t. under irradiation (254 nm) for 3 days. The mixture was concentrated under *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 9/1) to give (1',2',3',4',5'-pentamethylazaferrocene)tungsten pentacarbonyl (96 mg, 42%) as an orange solid (m.p. 150 °C, decomp.). Rf 0.75 (^{n}hexane/EtAOc, 7/3); IR υ_{max} 2913, 2068, 1854, 1380, 1015 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.92 (15H, s, C<u>H</u>$_3$-Cp*), 4.26 (2H, s, C<u>H</u>-Pyrrole), 5.03 (2H, s, C<u>H</u>-Pyrrole); ^{13}C NMR (150 MHz) 10.9 (<u>C</u>H_3-Cp*), 76.2 (<u>C</u>H-Pyrrole), 82.8 (H_3C-<u>C</u>-Cp*), 97.0 (<u>C</u>H-Pyrrole), 198.6 (<u>C</u>O); m/z (EI) 582 (15%, M+H), 581 (55%, M), 441 (52%, M-5 × CO), 257 (100%, M-W(CO)$_5$); HRMS $C_{19}H_{19}FeNO_5W$ calcd. 581.01166, found 581.01132;

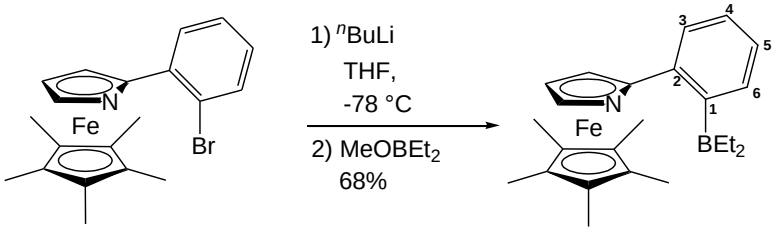
Anal. Calcd. for $C_{19}H_{19}FeNO_5W$: C, 39.27; H, 3.30; N, 2.41. Found C, 39.82; H, 3.63; N, 2.26%.



459 **494c**

(1',2',3',4',5'-Pentamethylazaferrocene)molibdenum pentacarbonyl (494c).

To a solution of 1',2',3',4',5'-pentamethylazaferrocene (100 mg, 0.39 mmol) in (7.0 mL) $Mo(CO)_6$ (103 mg, 0.39 mmol, 1.00 eq.) was added and the reaction was stirred in THF (5.0 mL) at r.t. under irradiation (254 nm) for 3 days. The mixture was concentrated under *vacuo* and purified by flash column chromatography (^{n}hexane/EtOAc, 9/1) to give (1',2',3',4',5'-pentamethylazaferrocene)molibdenum pentacarbonyl (56 mg, 29%) as an orange-brown solid (m.p. 115 °C, decomp.). Rf 0.78 (^{n}hexane/EtAOc, 7/3); IR υ_{max} 2914, 2071, 1866, 1380, 1117, 1014 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.93 (15H, s, C<u>H</u>$_3$-Cp*), 4.26 (2H, s, C<u>H</u>-Pyrrole), 4.88 (2H, s, C<u>H</u>-Pyrrole); ^{13}C NMR (150 MHz) 11.0 (<u>C</u>H$_3$-Cp*), 75.7 (<u>C</u>H-Pyrrole), 82.4 (H$_3$C-<u>C</u>-Cp*), 95.7 (<u>C</u>H-Pyrrole), 204.6 (<u>C</u>O); m/z (EI) 494 (4%, M), 411 (3%, M-3 × CO), 355 (12%, M-5 × CO), 257 (100%, M-$Mo(CO)_5$); HRMS $C_{19}H_{19}FeNO_5Mo$ calcd. 494.96611, found 494.96574; Anal. Calcd. for $C_{19}H_{19}FeNO_5Mo$: C, 46.28; H, 3.88; N, 2.84. Found C, 46.28; H, 4.09; N, 2.72%.



(+/-)-466b **(+/-)-486**

2-(*α*-Diethylboryl-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (**(+/-)-486**).

To a solution of (300 mg, 0.73 mmol) in THF (5.0 mL) ^{n}BuLi (0.32 mL, 0.80 mmol, 1.10 eq.) was added at -78 °C and the solution was stirred at -78 °C for 2 h. $MeOBEt_2$ (1.46 mL, 1.46 mmol, 2.00 eq.) was then added and the solution was stirred at r.t. for 2 hours. The solvent was removed under reduced pressure and the resulting red oil was purified by column chromatography (^{n}hexane/EtOAc, 9/1) to give 2-(*α*-Diethylboryl-phenyl)-1',2',3',4',5'-pentamethylazaferrocene (200 mg, 68%) as a red oil which solidifies upon standing (m.p. 67-69 °C). Rf 0.64 (^{n}hexane/EtOAc, 9/1); IR υ_{max} 2898 (CH), 2858 (CH), 1453, 1375, 1257, 1154 cm^{-1}; ^{1}H NMR (600 MHz) δ 1.93 (15H, s, C<u>H</u>$_3$-Cp*), 4.26 (2H, s, C<u>H</u>-Pyrrole), 4.88 (2H, s, C<u>H</u>-Pyrrole); ^{13}C NMR (150 MHz) 11.0 (<u>C</u>H$_3$-Cp*), 75.7 (<u>C</u>H-Pyrrole), 82.4 (H$_3$C-<u>C</u>-Cp*), 95.7 (<u>C</u>H-Pyrrole), 204.6 (<u>C</u>O); ^{11}B NMR (160 MHz) δ -1.66; m/z (CI) 402 (4%, M+H), 373 (25%, M-C_2H_5), 372 (100%, M-C_2H_6), 344 (10%, M-C_4H_{11}); HRMS $C_{24}H_{33}FeBN$ (M+H) calcd. 483.06747, found 483.06828; Anal. Calcd. for $C_{24}H_{32}FeBN$: C, 71.85; H, 8.04; N, 3.49. Found C, 70.87; H, 7.90; N, 3.32%.

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