Synthesis of Functionalised Cobalt Sandwich Complexes for Application in Asymmetric Catalysis

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Doyle Joseph Cassar

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School of Chemistry
University of East Anglia, Norwich
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Supervised by Dr Christopher J Richards

Statement of Original Work

The research described in this thesis has been conducted by the author, Mr Doyle Cassar, and is, to the best of his knowledge, original. Where other people's work has been referred to, this has been cited by corresponding references.

Doyle Cassar

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Abstract

The reaction of cobalt sandwich complex (η^5-(*N*,*N*-dimethylaminomethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt with sodium tetrachloropalladate and *N*-acetyl-*D*-phenylalanine gave planar chiral palladacycle di-μ-chloridebis[(η^5-(S_p)-2-(*N*,*N*-dimethylaminomethyl)cyclopentadienyl,1-*C*,3′-*N*)(η^4-tetraphenylcyclobutadiene)cobalt]dipalladium in 92% *ee*, 64% yield. The enantioselective palladation methodology was subsequently applied to corresponding *N*,*N*-diethyl (82% *ee*, 39% yield) and pyrrolidinyl (>98% *ee*, 43% yield) cobalt sandwich complexes. The complex derived from the pyrrolidinyl ligand was tested as a catalyst in the allylic imidate rearrangement (up to 99 % *ee*), showcasing comparable reactivity and selectivity to that seen in literature examples.

The diastereoselective palladation of a range of (η^5-oxazolinylcyclopentadienyl-(η^4-tetraphenylcyclobutadiene)cobalt complexes was tested by reaction with palladium acetate. Acetate dimer di-μ-acetatobis[(η^5-(*S*)-(S_p)-2-(2'-4'-methylcyclohexyl)oxazolinyl)cyclopentadienyl, 1-*C*, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) precipitated as a single diasteroisomer from the reaction media and was tested as a catalyst in the allylic imidate rearrangement (80% *ee*).

In addition, access to modified sandwich complexes was realised using the Friedel-Crafts reaction. Complex (η^4-tetraphenylcyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt underwent reaction with acid chlorides/aluminum chloride to give exclusively *para*-acylation. Reaction of unsymmetrical *bis*-aryl alkynes [PhCC(*o*-RC_6H_4), R = Me, $_i$Pr] with Na($C_5H_4CO_2Me$) and $CoCl(PPh_3)_3$ gave predominantly (η^4-1,3-diaryl-2,4-diphenylcyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt metallocenes (1,3-[*trans*] vs 1,2-[*cis*] selectivity up to 6:1). Friedel-Crafts reaction on the major isomers gave exclusively the *para*-acylation of the unsubstituted phenyl groups.

Acknowledgements

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Finally, I would like to thank my family, especially my parents, Saviour and Karen, my brother Lewis and sister Maria for their support throughout this long process. Without their backing and encouragement, I would not have completed all that I have.

List of Abbreviations

acac	acetylacetonate
AIBN	2,2'-azoisobutyronitrile
Ar	aromatic
Bn	benzyl
Bu	butyl
C	Celsius
CAP	cobalt amino palladacycle
Cat.	Catalyst
CBz	carbobenzyloxy
CD	circular dichroism
CIP	Cahn, Ingold, Prelog
COD	cyclooctadiene
conv.	conversion
COP	cobalt oxazoline palladacycle
Cp	cyclopentadienyl
Cy	cyclohexyl
d	doublet
de.	diastereomeric excess
dba	dibenzylideneacetone
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCC	dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
dd	doublet of doublets
DHQD	dihydroquinidine
DMAP	dimethylaminopyridine
DME	dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
DPEN	1,2-diphenyl-1,2-ethylenediamine
dr	diastereomeric ratio
dt	doublet of triplets
DuPhos	Dupont's phospholane
ee.	enantiomeric excess
ES	electrospray
Et	ethyl
FBIP	ferrocene bis-oxazoline palladacycle
FIP	ferrocene imidazole palladacycle
FOP	ferrocene oxazoline palladacycle
h	hours
hfacac	hexafluoroacetylacetonate
HMBC	heteronuclear multiple-bond correlation
HPLC	high-performance liquid chromatography
Hz	Hertz
i	*iso*

IPA	*iso*-propyl alcohol
L	ligand
L_n	a number of ligands
m	multiplet
MALDI	matrix-assisted laser desorption/ionization
Me	methyl
Mes	mesityl
mol	mole
Mp	melting point
Ms	mesylate
MS	mass spectrometry
MTPA	α-methoxy-α-trifluoromethylphenylacetic acid
NBS	*N*-bromosuccinimide
NMO	*N*-methylmorpholine-*N*-Oxide
NMR	nuclear magnetic resonance
NOe	nuclear Overhauser effect
OAc	acetate
OTf	triflate
OTs	tosylate
PDMS	polydimethylsiloxane
Ph	phenyl
Phe	phenylalanine
PS	polystyrene
psi	pounds per square inch
PMP	*para*-methoxyphenyl
ppm	parts per million
Pr	propyl
PTSA	*p*-toluenesulfonic acid
q	quartet
quant.	quantitatively
rac	racemic
rt	room temperature
s	singlet
sat.	saturated
STAB	sodium triacetoxyborohydride
t	tertiary
t	triplet
tert	tertiary
TFA	trifluoroacetic acid
THF	tetrahydrofuran
Tipp	2,4,6-tri(*iso*-propyl)benzene sulfonic acid
TLC	thin layer chromatography
TPAP	tetrapropylammonium perruthenate
TMS	trimethylsilyl
Tol	tolyl

Chapter 1 - Introduction

1.1 General Introduction

This thesis is primarily concerned with the scalemic synthesis and applications to catalysis of planar chiral palladacycle complexes, whose ligands are based upon a cobalt sandwich complex motif. The selective modification of the cobalt metallocenes will also be described and their subsequent use in catalysis explored.

Throughout the literature, most planar chiral metallocenes are modelled upon a ferrocene core and indeed there are many reviews associated with the synthesis of ferrocenyl ligands and their subsequent use in asymmetric catalysis.[1–10] Most of the work on planar chiral metallocycles based upon a cobalt metallocene core has been carried out by Richards and Overman, with Overman having particular success utilising a diastereomerically pure cobalt-oxazoline palladacycle (COP) in the catalysis of the allylic imidate rearrangement and other related reactions.[11–18]

Unlike most palladium catalysis, palladacycle chemistry utilises a palladium atom in which the oxidation state is fixed, (at +2), which is much less common. The palladacycles are therefore Lewis Acidic in nature and their subsequent chemistry is dictated by this.[19–21]

This chapter serves to give a literature survey of the synthesis and applications of planar chiral palladacycles. Following this review, subsequent chapters will be concerned with the scalemic synthesis of planar chiral palladacycles and their application to asymmetric synthesis.

Each of these chapters will be preceded by a short introduction which will refer back to the main review in this chapter and highlight the most recent and relevant literature associated with it. Detailed experimental procedures, appendices and references follow the main discussion.

1.2 Palladacycles

1.2.1 Definition and Discovery

An organopalladium compound can be simply described as a compound containing at least one palladium-carbon bond. A palladacycle can be generally defined as any palladium compound containing a palladium-carbon bond intramolecularly stabilised by at least one donor atom Y (typically N, P or O) to give, most commonly, a stabilised five or six-membered chelate ring (Figure 1).

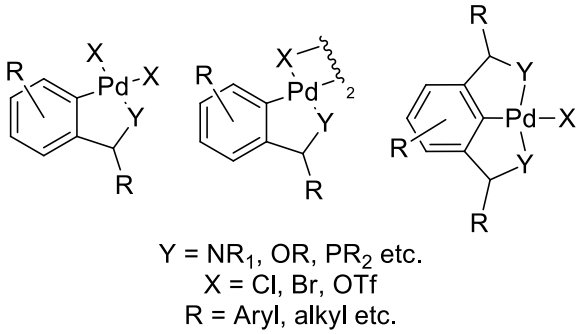
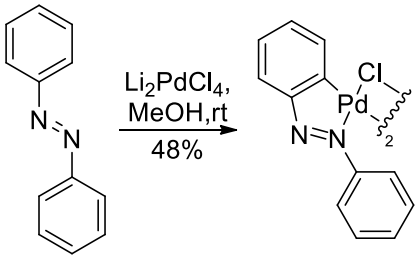


Figure 1

Palladacycles were first discovered by Cope and Siekman in the mid-1960s where they were initially isolated from the carbopalladation of azobenzene **1** with palladium(II) chloride, to give palladacycle **2**, (Scheme 1).[22,23] Since then, due to their thermal stability in the solid state, palladacycles have become an extensively studied branch of organometallic chemistry that have been successfully employed as precatalysts and intermediates in Heck[24] and Suzuki couplings;[25] Buchwald-Hartwig aminations;[26,27] Stille reactions[28] and other palladium-mediated reactions.[29]

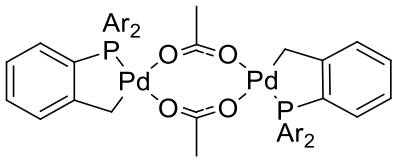
The use of palladacycles as catalyst precursors is a relatively recent development, with the first applications reported in the mid-1980s with the hydrogenation of C=C bonds using a cyclopalladated triphenylphosphite complex.[30] This was followed by the use of cyclopalladated azobenzenes, hydrazobenzenes, or *N*,*N*-dimethylbenzylamine complexes in



1 **2**

Scheme 1

the selective reduction of nitro-aromatics, nitro-alkenes, nitriles, alkynes, alkenes and aromatic carbonyl compounds.[31,32] Probably the most important example of palladacycles as precatalysts was showcased in 1995 when Herrmann *et al.* synthesised a cyclopalladated tri-*o*-tolyl-phosphine complex **3**, (Figure 2),[24] which was used as a catalyst for Heck cross-coupling reactions. These new substrates could activate more economic substrates than those applied thus far, such as aryl chlorides, allowing for the industrial application of cross-coupling reactions. Since then palladacycles have been used as catalysts for a variety of transformations.[33–35]



3
Ar = *o*-tolyl

Figure 2

1.2.2 Classification of Palladacycles

Palladacycles can be formally assigned to two different classes, based on the organic fragment: anionic four-electron, CY-type, or six-electron donor, YCY-type, complexes. The CY-type palladacycles usually exist as halogen or acetate bridged dimers as two geometric isomers coined *cisoid* and *transoid*, depending on the position of the Y ligands with respect to each other, (Figure 3). Additionally, CY complexes can be found as neutral **4**,[36] cationic **5**[37] and anionic **6**[38] species, depending on the nature of other ligands.

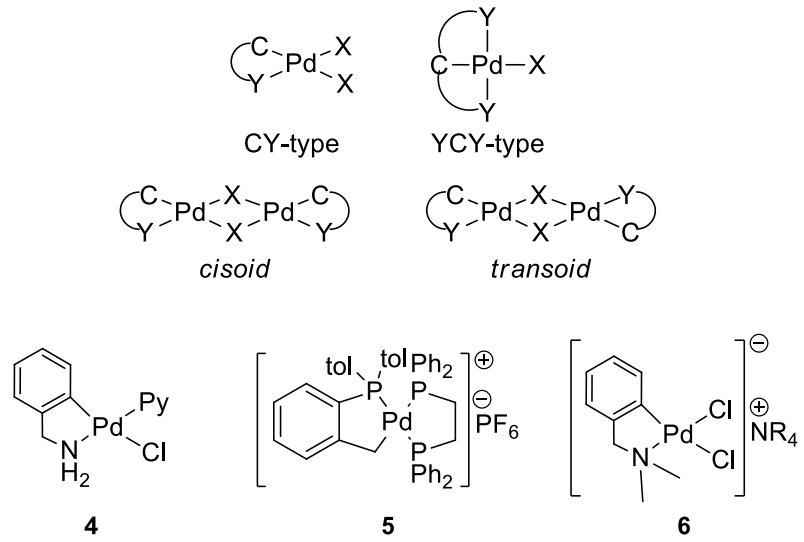


Figure 3

There are a wide variety of donor functionalities found in palladacycles, examples of which include amines, imines, pyridines, thioketones, amides, amidines and oxazolines.[17,39–44] The most common types of palladacycles are derived from tertiary amines or imines, and complexes from primary amine derivatives are rare.[45] The metallated carbon atom is usually sp^2 hybridised as in examples **4–6**, but complexes with sp^3, (benzylic **7**[46]), or sp^2 vinylic carbons **8**[47] are known. The size of the metalated ring can range from 3–11 atoms, with the most common palladacycles having five- or six-membered rings (Figure 4).[48–52]

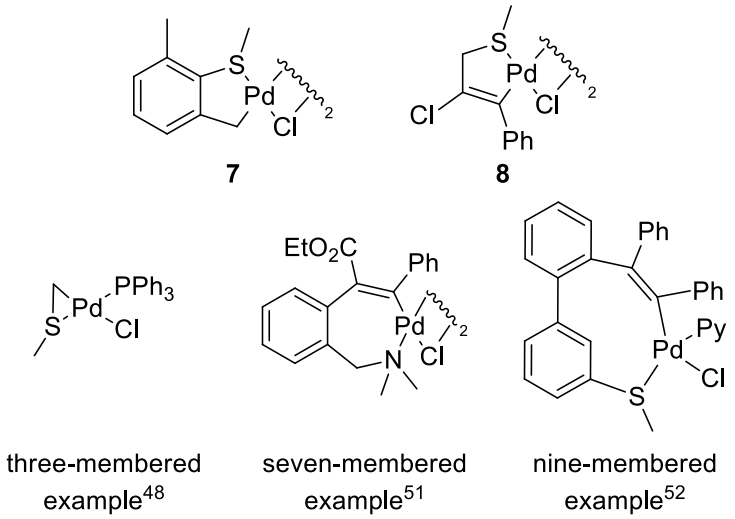
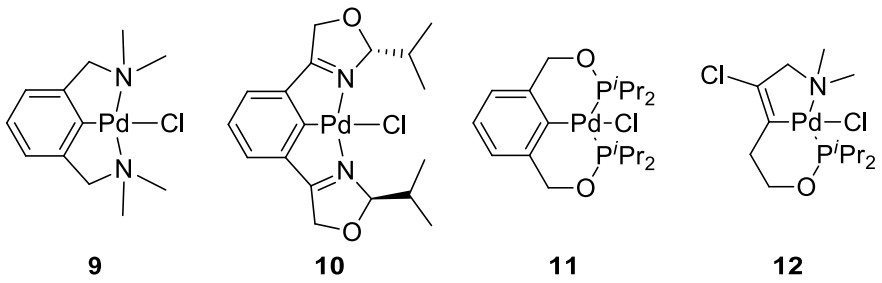


Figure 4

The YCY variety of complexes, commonly termed pincer complexes, usually contain two symmetrical five or six-membered rings (Figure 5, **9, 10** and **11**).[53,54] Recently, unsymmetrical YCY complexes such as **12** have also been found and characterised.[55,56]



9 **10** **11** **12**

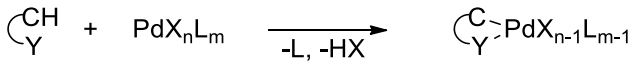
Figure 5

1.3 Palladacycle Synthesis

There are a variety of methods for generating the required palladacycles – the most common being C-H bond activation, oxidative addition or transmetalation. All methods generally produce a five or six-membered chelate, driven by the formation of a stable Pd-C bond. The next few sections will give a general overview of the use of these methods in the synthesis of palladacycles.

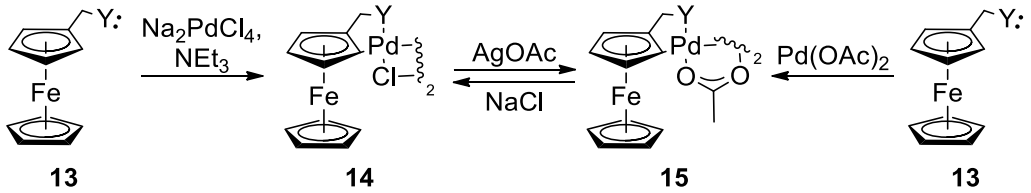
1.3.1 C–H Activation

The direct chelation-assisted palladation of a C–H bond is the most simple and common of all techniques used to generate the required palladium complex, also coined *ortho*-palladation. The process is directly comparable to directed *ortho*-metallation, but in this instance a palladacycle is formed if the palladium-heteroatom bond is thermodynamically stable (Scheme 2). The successful application of this method relies heavily on the ability of the intramolecular heteroatom lone-pairs to bind, (reversibly), to the metal centre, facilitating metalation and, in turn, dictating the regioselectivity of the reaction.



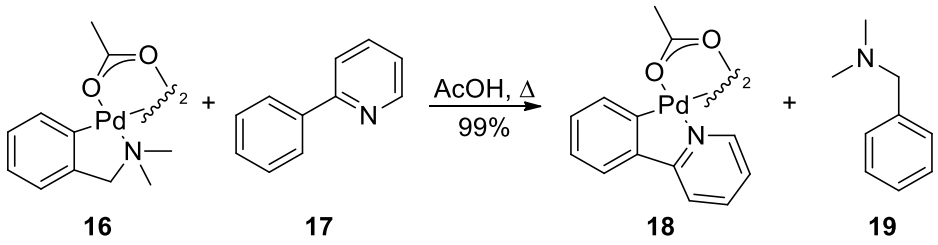
Scheme 2

Common reagents for palladation include tetrachloropalladate salts together with a base,[57] or palladium acetate in acetic acid, dichloromethane, benzene or toluene, (Scheme 3). For example, treatment of generalised ferrocenyl ligand **13** with either palladium acetate or sodium tetrachloropalladate leads to the formation of cyclometalated complexes **14** and **15** respectively. The chloride and acetate bridged dimers can be readily interconverted *via* reaction with a suitable salt.

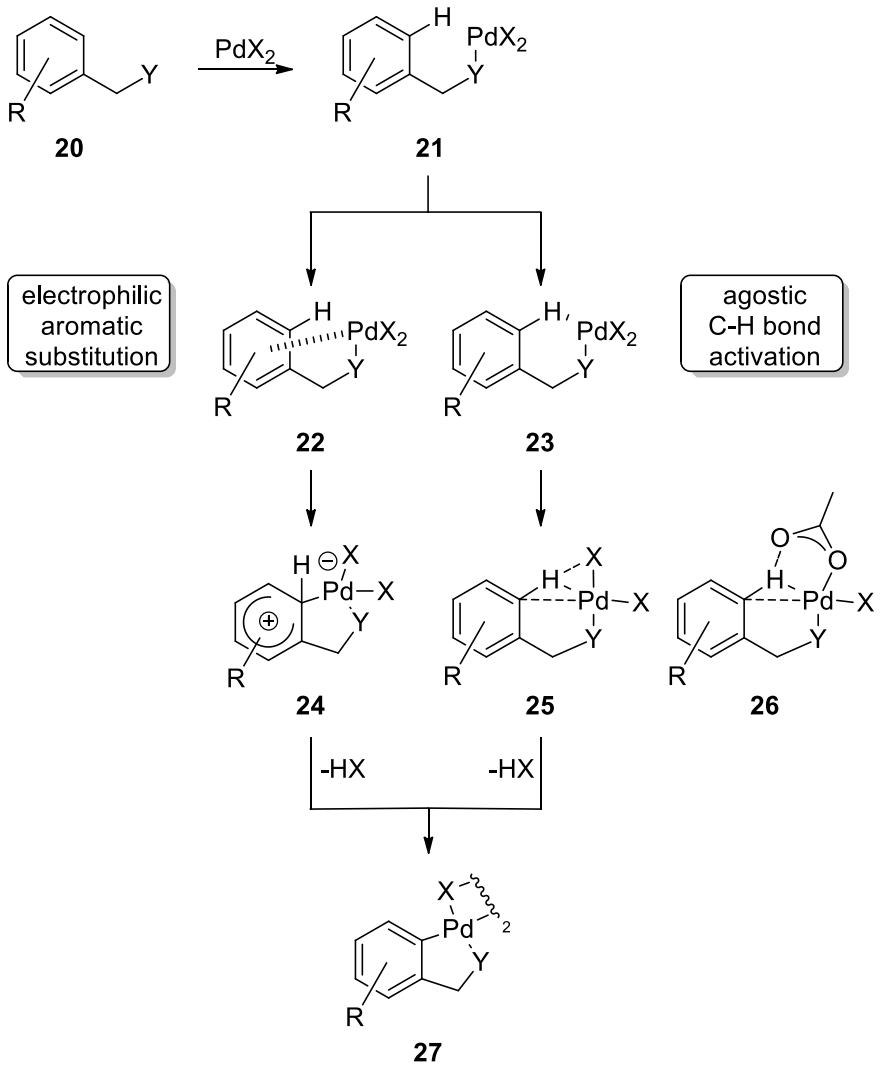


Scheme 3

Alternatively, a ligand exchange process using another palladacycle can be used (Scheme 4), whereby reaction between complex **16** and ligand **17** results in the formation of new palladacycle **18** and regeneration of amine **19**.[58] This process is known as transcyclopalladation (or transcyclometalation), and is usually carried out in acidic media. The reaction is thought to follow a dissociative pathway *via* protonolysis of starting palladacycle **16**, forming an inorganic Pd(II)-salt, which is followed by cyclometalation with the more reactive second ligand **17**.[59]



Scheme 4



Scheme 5

The cyclometalation of aryl C–H bonds has been extensively studied and details of the mechanism are largely understood.[60] Early investigations showed that reaction rates were correlated with the electron donating ability of the substituents of the arene. Thus a mechanism for the palladation was postulated to proceed *via* an electrophilic aromatic substitution pathway (Scheme 5).[61,62] The process proceeds initially with heteroatom coordination to give complex **21**, which then forms π-coordinated aryl complex **22**. Subsequent rearrangement to arenium intermediate **24** and proton abstraction gives the cyclopalladated product **27**. Neither the sigma or π-intermediate complexes have been isolated, but related platinum(II) complexes have been successfully isolated and characterised, and much comparison has been drawn between the two metals.[63]

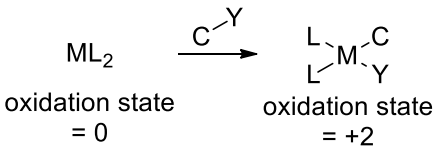
More recently, it was shown using DFT calculations that the cyclopalladation of dimethylbenzylamine proceeds *via* intermediate **23** (Scheme 5) where there is a six-membered ring with a palladium-hydrogen agostic interaction.[64] This interaction was found to instigate the C–H activation process, proceeding *via* intermediate **25** (X = OAc, **26**), which is stabilised by the $AcO^{\cdots}H–C_{aryl}$ H–bonding. Formation of the σ-bond was calculated to proceed with minimal energy of activation (0.1 $kcalmol^{-1}$), to give product palladacycle **27**.

The acetate ligand fulfils the requirement of a ligand, as well as acting as an intramolecular base for the process. Palladium-carbon bond forming and deprotonation occur simultaneously; as such this process has been termed as a concerted metallation deprotonation or CMD pathway.

Alternative pathways have been proposed, including a four-membered transition state or an oxidative addition sequence. These were found to be less probable due to a less favoured arrangement of the acetate ligands around the metal center. The activation barriers have also been calculated for these pathways and were found to be twice and thrice as high respectively.[65]

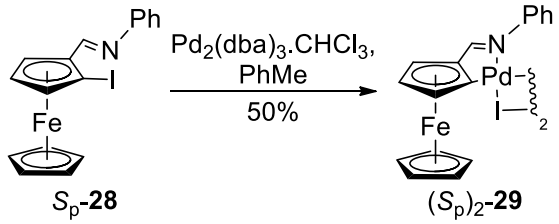
1.3.2 Oxidative Addition

Oxidative addition of aryl halides or alkyl halides containing a two-electron donor is a common method used when the required palladacycle cannot be prepared using C-H activation. The reaction requires a two-electron process where metal, M, is inserted into a covalent bond C–Y to give the resultant oxidised complex, with ligand C and Y *cis* to one another (Scheme 6). In this process the coordination number and formal oxidation state of the metal both increase by two units.

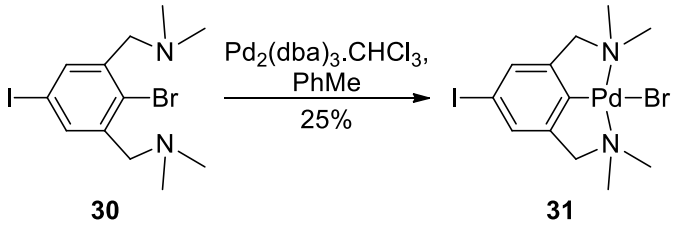


Scheme 6

For the formation of palladacycles, the most common sources of Pd(0) used are $Pd(PPh_3)_4$, $Pd(dba)_2$ and $Pd_2(dba)_3$ which generate dimeric halogen-bridged palladacycles, neutral pincer complexes or monomeric triphenylphosphine ligated complexes, depending on the ligand and conditions employed. For example, reaction of iodo-ferrocene derivative S_p-**28** with $Pd_2(dba)_3$ in toluene gives iodo-bridge palladacyle $(S_p)_2$-**29** (Scheme 7).[66]



Scheme 7



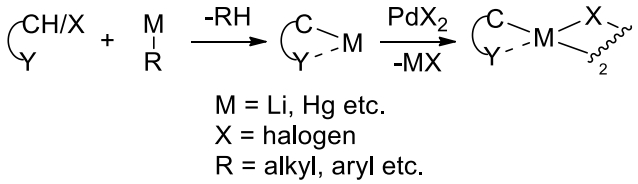
Scheme 8

Moreover, oxidative addition can be used to cyclometalate ligands, such as **30**, that contain reactive functionalities, to give pincer complex **31**, that can be subsequently derivatised (Scheme 8).[67] The drawback to the oxidative addition process is that the required aryl or alkyl halogen may require a multi-step synthesis.

1.3.3 Transmetalation

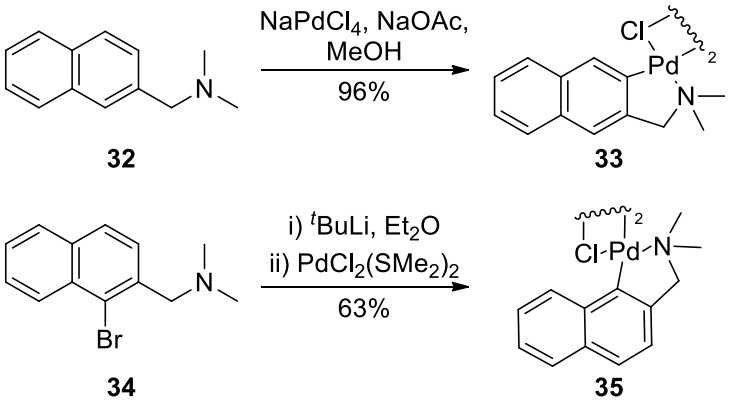
A further alternative to C–H activation for the synthesis of metallacycles is the use of transmetalation to introduce the required metal into the ligand framework. The metal used in

the process must be more electropositive than palladium; as such organolithium or organomercurial reagents are commonly used. Usually ligands are treated with the metalating agent allowing for the formation of a metallated intermediate *via* selective metalation by deprotonation or by metal/halogen exchange. Subsequent treatment with a Pd(II) source facilitates the formation of the palladacycle by transmetalation (Scheme 9).



Scheme 9

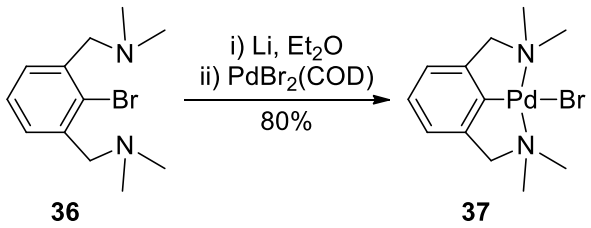
Transmetalation allows for the selective synthesis of palladacycles. Van Koten *et al* reported the synthesis of napthyl complexes in the 1- or 3-position under controlled conditions. Direct palladation of ligand **32** resulted in metallation at the 3-position to give palladacycle **33**. Employing 1-bromo-napthyl derivative **34**, the Van Koten group could gain access to the 1-



Scheme 10

palladated complex **35** *via* transmetalation (Scheme 10).[68]

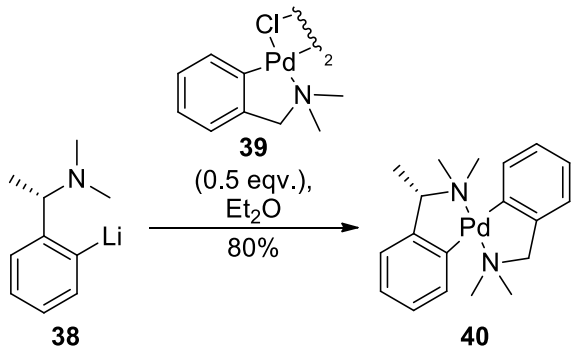
Transmetalation can also be extended to pincer complexes. Lithiation of bis-amino ligand **36** with lithium metal gives the organolithium intermediate which was quenched with $PdBr_2COD$ to give complex **37** (Scheme 11).[53]



36 **37**

Scheme 11

Additionally, there are examples of bis-cyclopalladated compounds synthesised using transmetalation. Complex **40** could be easily formed by transmetalation *via* treatment of lithiated ligand **38** with palladacycle **39** to give the unsymmetrical monomer (Scheme 12).[69] Similar cyclometalated compounds containing N- or O-donor atoms could also be accessed using organomercurial reagents.[70]



38 **40**

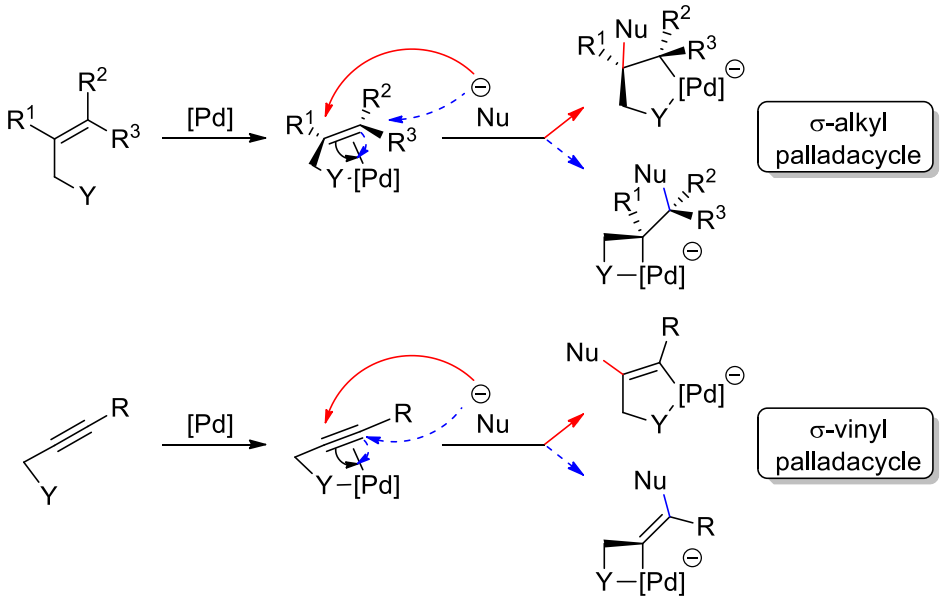
Scheme 12

1.3.4 Other Synthetic Methods

There are a few methods used in the generation of palladacycles which do not involve the popular methods described previously. These methods allow for a ligand framework to be built *in situ* with the formation of the palladacycle.

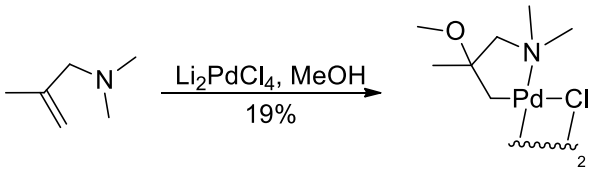
An increasingly used methodology is that based on nucleophile-palladation reactions of unsaturated organic substrates, which contain electron-donor heteroatoms as part of their framework (Scheme 13). The reaction proceeds first by the binding of an alkene, or alkyne, *via* the electron donor group of the unsaturated species, at palladium. This is followed by a regioselective nucleophilic attack at one of the unsaturated carbon atoms, leading to a σ-

alkyl or σ-vinyl palladium complex.[65] The pathway in which a four-membered ring palladacycle is formed, (blue path), is generally less favoured due to ring-strain and other steric effects.



Scheme 13

The first example seen for this method of palladacycle synthesis was observed by Cope and co-workers in the 1960s whilst using alcohols as the solvent in their palladation reactions (Scheme 14).[71] Tertiary allylic amine **41** underwent alkoxypalladation in the presence of lithium tetrachloropalladate and methanol to give chloride-bridged dimer **42**.

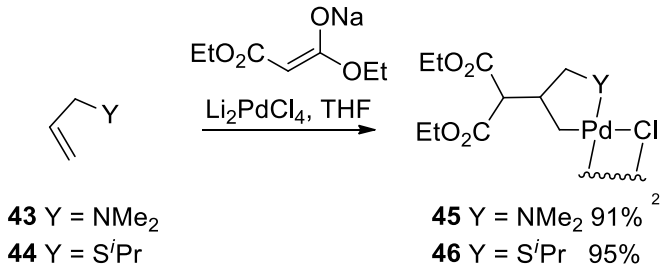


41 **42**

Scheme 14

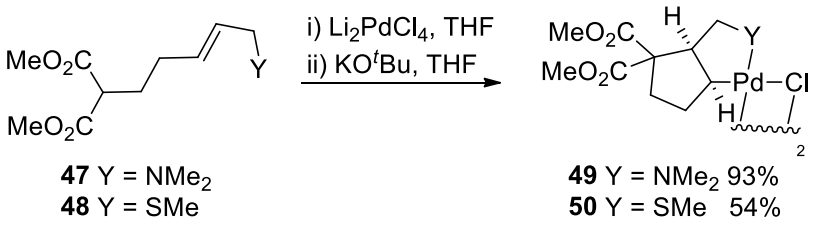
Extension of this methodology allowed for the generation of new palladacycles formed by addition of carbon nucleophiles derived from diethyl malonate (carbopalladation, Scheme 15).[72] Reaction of either amine **43** or thioether **44** with lithium tetrachloropalladate generates an intermediate palladium complex which, upon addition of the sodium enolate, undergoes

cyclisation to form palladacycles **45** and **46**. This methodology was repeated using a number of enolates all of which gave palladacycles in good yield.



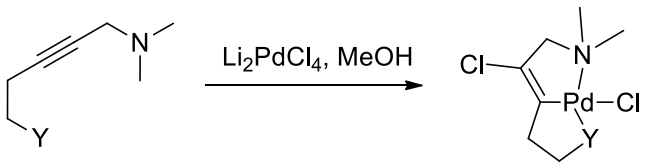
Scheme 15

Interestingly, this methodology can also be used to generate new palladacycles *via* an intramolecular reaction (Scheme 16).[73] Amines and thioethers of type **47** and **48** with an in-built malonate moiety can be exploited in this type of process by first reacting with lithium tetrachloropalladate. Treatment of the intermediate complex with potassium *tert*-butoxide forms the enolate, which subsequently undergoes intramolecular ring closure to yield chloride-bridged dimers **49** and **50**.



Scheme 16

The reaction of propargylamines, thioethers or phosphines **51–53** under the same conditions used in the alkoxy- and carbopalladation reactions leads to the formation of a palladacycle containing a Pd-vinyl bond. However, the resultant palladacycle product results from the nucleophilic addition of a chloride anion present in the reaction mixture rather than other nucleophiles available. This so-called halopalladation has been used to good effect, particularly in the generation of a variety of unsymmetrical pincer-type palladcycles **54–56** (Scheme 17).[56]



51 Y = NMe_2
52 Y = S^tBu
53 Y = PPh_2

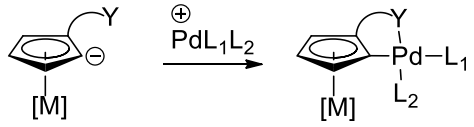
54 Y = NMe_2 60%
55 Y = S^tBu 72%
56 Y = PPh_2 56%

Scheme 17

1.4 Structural Aspects of Palladacycles

The palladium-carbon bond distance in palladacycles usually falls between 1.9 and 2.3 Å depending upon the structural and electronic features of the complex; such as the type of palladated carbon or the nature of the donor group *etc*.[74,75] Acetate dimer palladacycles usually exist as the *transoid* isomer, whereas the halogen dimer metallocycles usually adopt both *cisoid* and *transoid* isomeric forms, although it is usually the *trans* isomer that crystallises.[19]

Palladacycles with ancillary ligands L_1 and L_2 (Scheme 18, **58**), are distinguished by the larger *trans* influence of the anionic carbon ligand compared to the neutral heteroatom (Y) ligand component. This is revealed as the palladium bond located *trans* to the Pd–C (Pd–L_1) is longer than the one located in the *cis* position (Pd–L_2) where L_1=L_2, and also by analysis of the kinetic and thermodynamic products arising from ligand substitution.[76] Common ligand systems where L_1=L_2, for example acetylacetonate (acac), are usually introduced using a ligand substitution reaction following initial palladation.

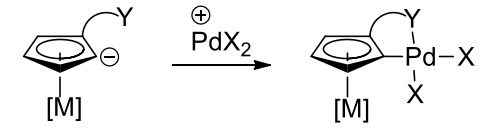


57 **58**

Scheme 18

1.5 Metallocene-based Palladacycles

A sub-category of palladacycles (such as **59**) are those that contain a ligand motif comprised of a metallocene, (**57**, most commonly ferrocene, Scheme 19). A significant feature of these palladacycles is that the complexed palladium becomes a direct component of the element of planar chirality displayed by the compound. This contrasts to most bidentate ligands, where the complexed palladium is more removed from the center of chirality, (if present), as such there is great interest in the asymmetric synthesis and use of such complexes. The next few sections explores planar chirality, scalemic synthesis and use of planar chiral metallocene-based palladacycles.



57 **59**

[M] = Fe-C_5H_5, Fe-$(CPh)_5$, Co-$(CPh)_4$ etc.
X = Cl, Br, Oac, PPh3 etc.
Y = N, O, P, S etc.

Scheme 19

1.5.1 Central and Planar Chirality in Metallocenes

A chiral molecule can be defined as a molecule that has a non-superimposable mirror image. Metallocenes can display chirality in derivatives with at least two or more different substituents on the same ring to give a structure which cannot be superimposed on its mirror image. The Cahn-Ingold-Prelog (CIP) rules[77] are used to assign the non-superimposable molecules (enantiomers), with either *R* or *S* configuration. For molecules displaying planar chirality the observer regards the molecule from the side of the ring to be assigned. The substituents are then analysed for priority according to the CIP rules (ranked by atomic number). If the shortest path from the substituent with the highest priority to that following in hierarchy is clockwise, the chirality descriptor is *R*, if anti-clockwise it is *S* (Figure 6).[78] If the metallocene bears rings both containing two or more different substituents, the process is

started on the ring with the highest priority substituent and assigned. The molecule is then inverted and the process is repeated on the other ring. To show that the chirality descriptor for the metallocene belongs to its planar element, it is written as R_p or S_p respectively. If the metallocene under consideration has an element of central chirality as well as planar chirality, the descriptor for central chirality is by convention, written first. So, (*S*, *R*) or (*S*, R_p) should mean that the compound contains an element of central chirality with *S* configuration and an element of planar chirality with *R* configuration.

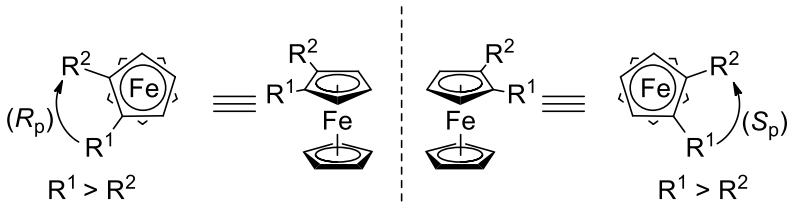


Figure 6

These rules for determining the configuration of chirality in metallocenes are well established, with the majority of authors using this method to assign chirality in their compounds. However, in their paper on stereochemical nomenclature, Cahn, Ingold and Prelog stated that for metallocenes, the element of planar chirality can be "reduced" to central chirality, by considering single bonds between ring carbon atoms and the central metal ion (Figure 7).[78] This means that every ring carbon can be considered as a distorted tetrahedron to which the rules for central chirality apply. The carbon atom bearing the substituent with the highest priority then becomes the chirality descriptor for the whole molecule.

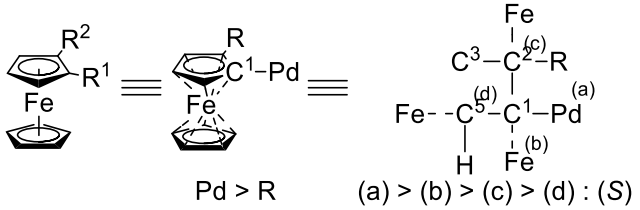


Figure 7

A variety of methods have been used to confirm the absolute configuration of planar chiral metallocycles. Earlier studies used chemical correlation and/or circular dichroism (CD), whereas most now use X-ray crystallography. The dominance of the planar chiral element on the chiroptical properties of molecules has led to a 'rule of thumb' method to emerge as a means for temporarily assigning the stereochemistry of these palladacycles. Generally, a positive value for specific rotation, (usually determined at 598 nm), is indicative of a palladacycle with R_p configuration – with a negative value characteristic for the S_p complexes.[79] A definitive assignment of absolute configuration can be made using X-ray crystallography, either where the metallocene ligand contains a stereocenter of known configuration, or by determination of the absolute structure (Flack) parameter.

1.6 Asymmetric Synthesis of Planar Chiral Metallocene-Based Palladacycles

The first examples of the asymmetric synthesis of planar chiral metallocycles date from the late 1970s with the pioneering work of Viatschaelav Sokolov.[80,81] However, it is only since the millennium that they have found widespread application, primarily as catalysts for the allylic imidate rearrangement as showcased by Larry Overman.[11,82]

Scalemic planar chiral palladacycles are generally synthesised using C–H activation or *ortho*-metalation reactions (as discussed previously). The resultant palladacycle can be obtained as an enriched enantiomer using a variety of methods that will be discussed in the next few sections, which include: resolution; diastereotopic C–H activation, controlled by one or more stereogenic centers contained on the metallocene ligand; and enantioselective palladation using an external enantiopure metalating reagent. Alternatively, transmetalation may be used, or oxidative addition of an enriched planar chiral aryl halide ligand.

As with previous examples of palladacycles, planar chiral metallocycles can exist as *cis* or *trans* isomers with respect to the orientation of the C–Y ligand about the $Pd_2(\mu\text{–}X)_2$ core. As

a consequence, when palladated, there are six possible stereoisomers for generalised ferrocenyl palladacycle **60** (Figure 8).

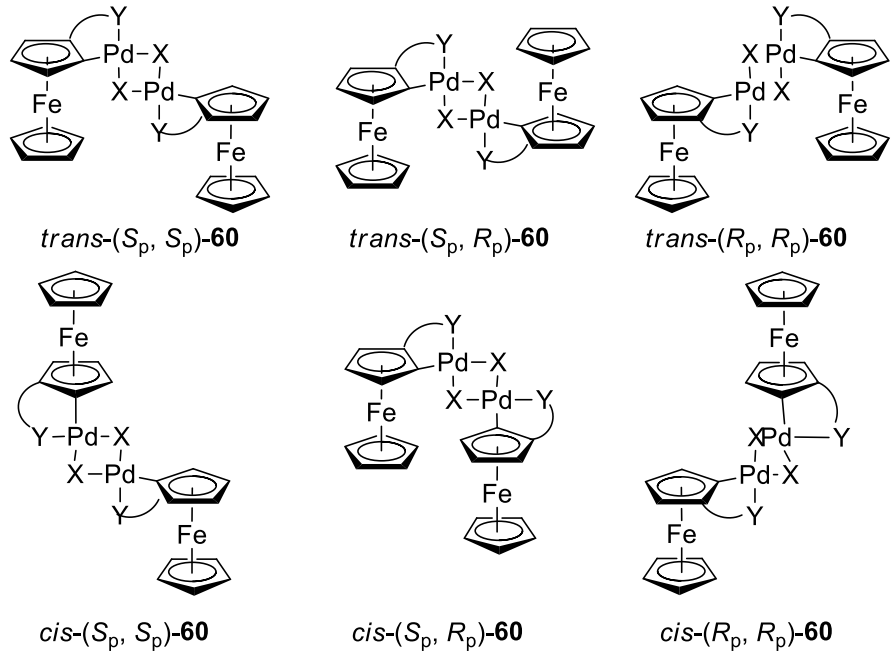


Figure 8

Although uncommon, there are examples of the *cis* isomers. Lopez *et al*[83] reported the X-ray crystal structure of *cis*-(S_p,S_p)-**61** in 1996 and in 1999 Mak[84] showed that the formation of *cis*-(S_p,R_p)-**62** was possible, albeit as the minor product to the respective *cis*-(S_p,S_p) isomer (Figure 9). To date, neither the *cis*-(S_p,R_p) nor *cis*-(R_p,R_p) isomers have been isolated as a single compound.

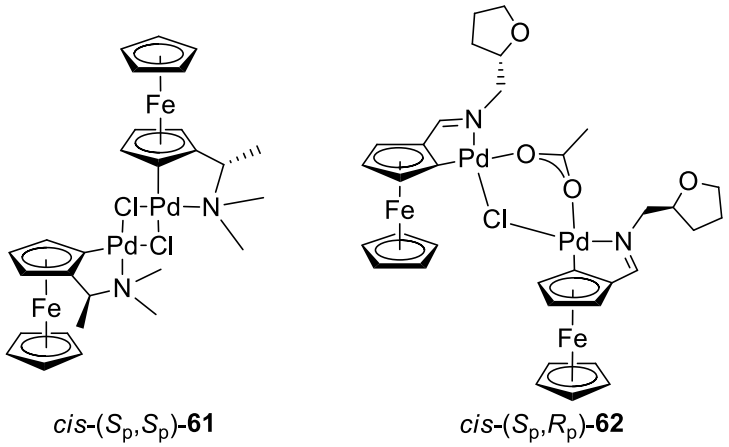
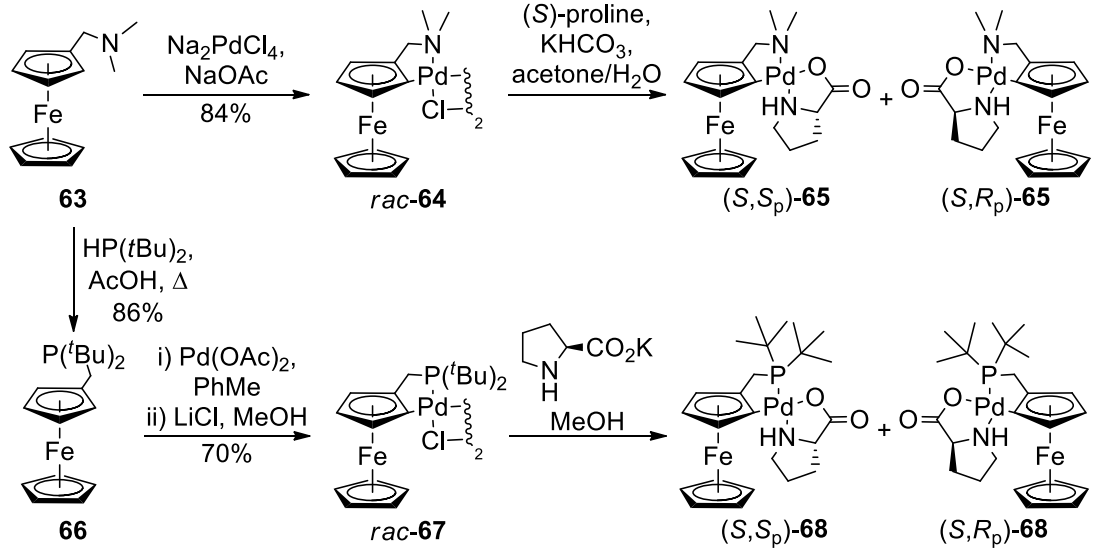


Figure 9

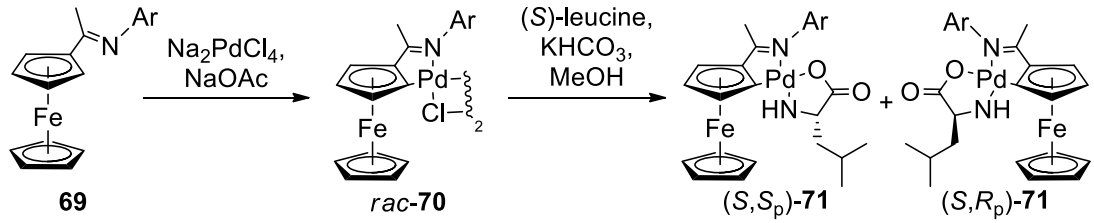
1.6.1 Resolution of Racemic or Diastereomeric Mixtures

There are few examples showcasing the separation of enantiomers from a racemic mixture of planar-chiral palladacycles. The resolution is usually achieved by reaction of the palladacycle with an enantiopure amino acid, and then separation of the resulting diastereoisomers. The first reported method came in 1981 when Nonoyama presented the resolution of palladacycle *rac*-**64** (Scheme 21).[85] Reaction of the racemic palladacycle with (*S*)-proline in the presence of potassium hydrogencarbonate gave two diastereoisomers (S,S_p)-**65** and (S,R_p)-**65** which could be separated by fractional crystallisation. Similarly, *rac*-**72** could be separated utilising the same method to give phosphopalladacycles (S,S_p)-**68** and (S,R_p)-**68**.[86] After separation, the proline adducts could be returned to chloride-bridged dimers by reaction with dilute hydrochloric acid in dichloromethane.



Scheme 21

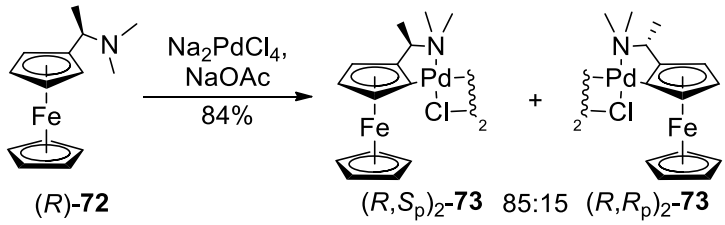
Wu *et al*[87] demonstrated the resolution of ketimine-derived palladacycle *rac*-**70** with (*S*)-leucine, where the resultant diastereoisomers (S,S_p)-**71** and (S,R_p)-**71** were separated using preparative thin-layer chromatography (Scheme 22).[88,89] The diastereomeric adducts could be returned to the chloride-bridged dimers by reaction with LiCl in AcOH.



Scheme 22

1.6.2 Diastereotopic C–H Activation

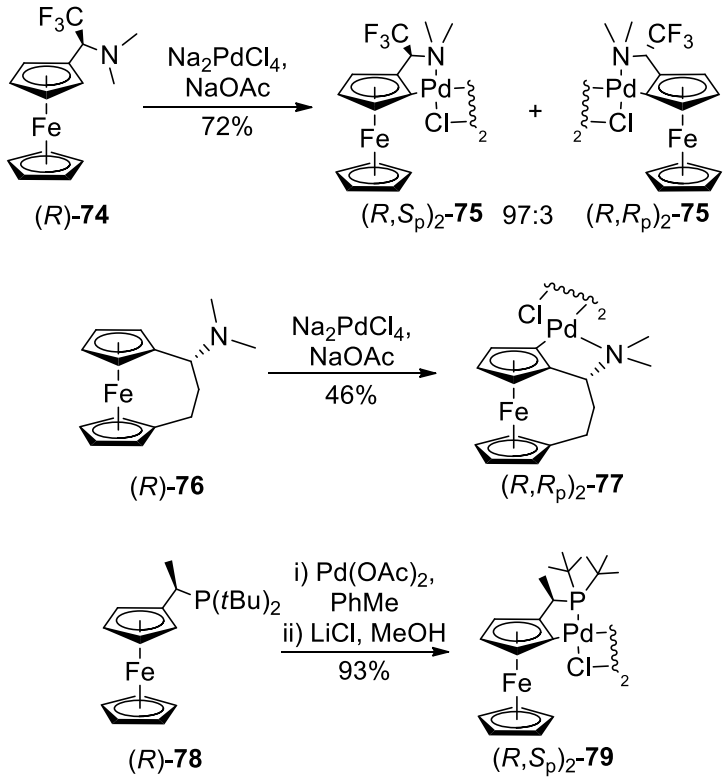
The majority of planar chiral palladacycles seen in the literature are synthesised using a diastereotopic C–H activation protocol, whereby the chirality of the ligand controls the selectivity of the subsequent palladation. One of the most versatile and well-known metallocene-based chiral ligands is *N*,*N*-dimethyl-1-ferrocenylamine (*R*)-**72**, also known as Ugi's amine, named after its discoverer.[90] Readily available as both enantiomers,[91,92] it has been successfully used as a starting material for the synthesis of a number of 1,2-disubstituted planar chiral ferrocene derivatives due to the high diastereoselectivity of lithiation (dr = 96:4).[9,10,93] In 1977 Sokolov reported the palladation of (*R*)-**72** showing that the reaction proceeds with similar diastereoselectivity, such that the palladation yields (R,S_p)$_2$-**73** and (R,R_p)$_2$-**73** with a dr of 85:15 (Scheme 23).[94] This was confirmed subsequently by Overman and co-workers[95] and it was also shown that the major diastereoisomer (R,S_p)$_2$-**73** could be isolated as a single isomer *via* precipitation from the reaction media.[83]



Scheme 23

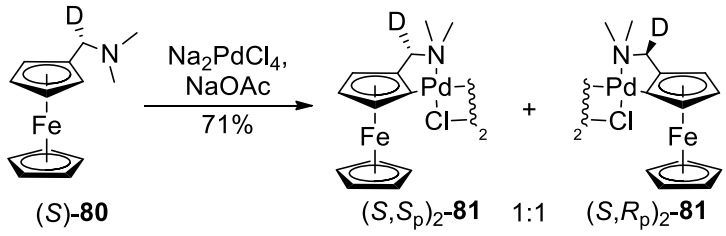
Related trifluoromethyl analogue (*R*)-**74** provided palladacycles (R,S_p)$_2$-**75** and (R,R_p)$_2$-**75** under the same conditions with an improved dr of 97:3 (Scheme 24).[96] Constraining the

conformational freedom of the dimethylamino group by use of ligand (*R*)-**76** also improves the diastereoselectivity of palladation, with only (R,R_p)$_2$-**77** reportedly isolated.[97] Di-*tert*-butylphosphino analogue of Ugi's amine (*R*)-**78** also shows high diastereoselectivity when palladated, similarly with only one diastereoisomer (R,R_p)$_2$-**79** formed.[98]



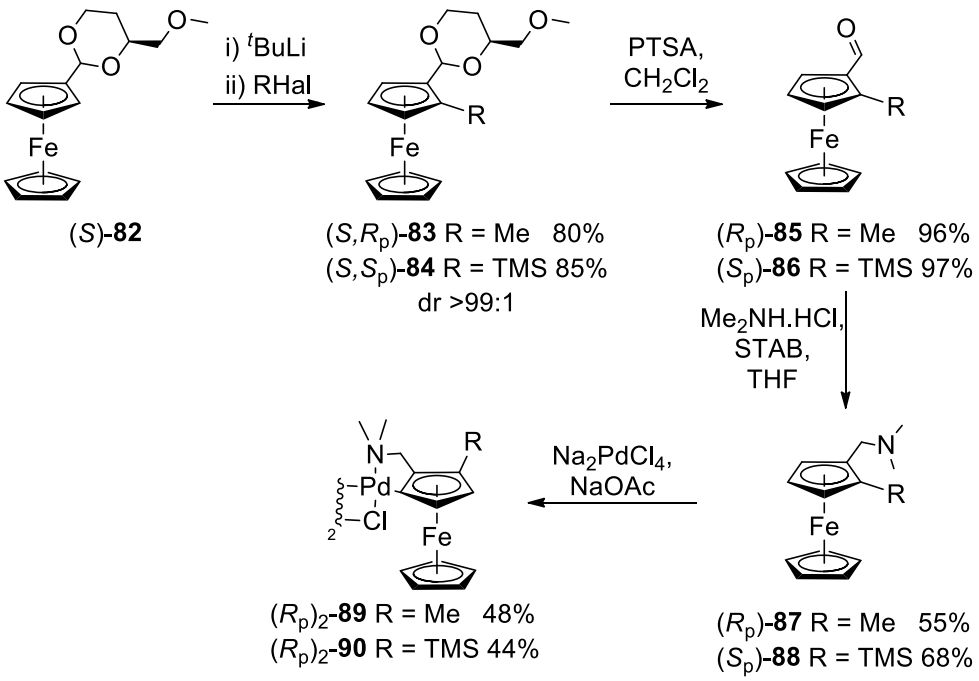
Scheme 24

The importance of the conformational control over diastereoselectivity was investigated using scalemic deuterated ligand (*S*)-**80** (Scheme 25). Palladation resulted in palladacycles (S,S_p)$_2$-**81** and (S,R_p)$_2$-**81** with little stereoinduction (<1%).[99]



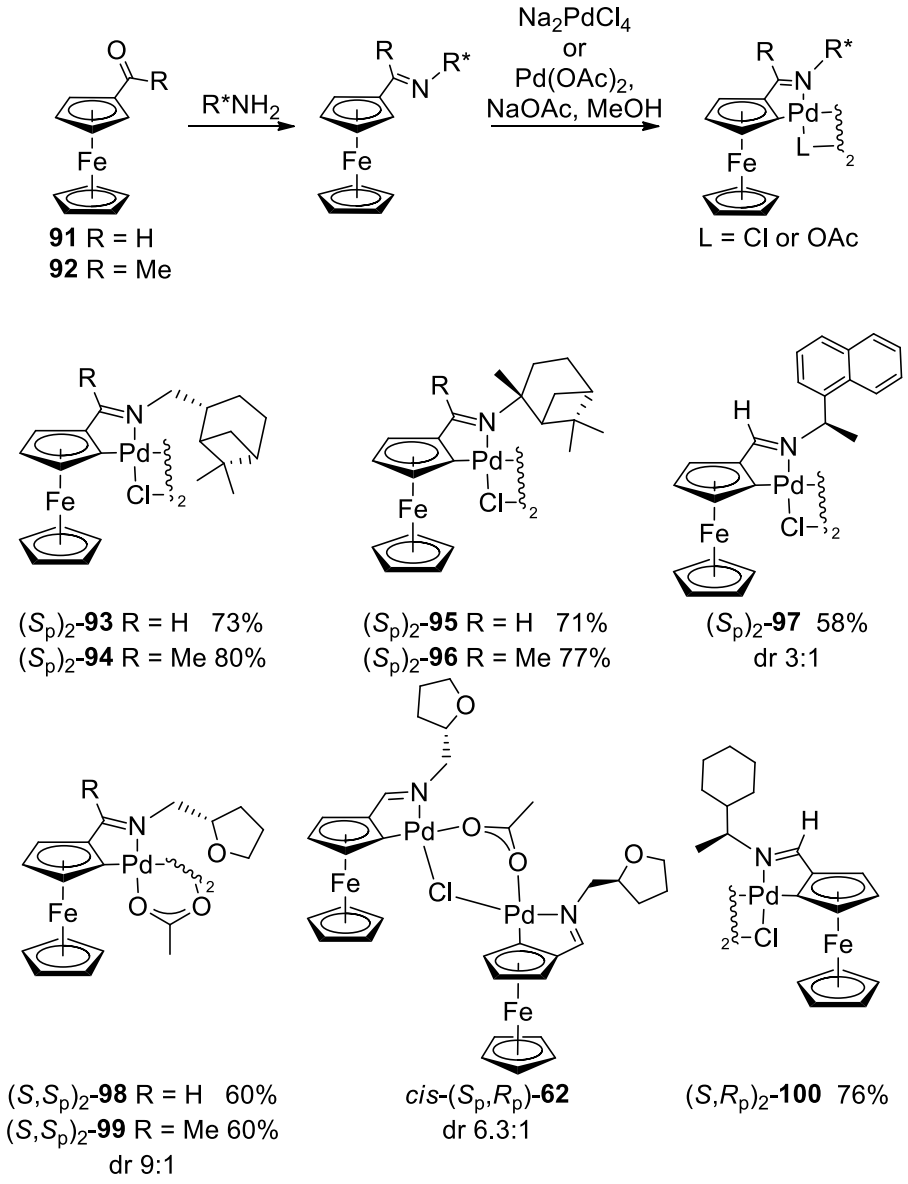
Scheme 25

An alternative procedure illustrated by Overman utilised a blocking group in the α-position of the metallocene precursor to palladation. Employing a procedure for highly diastereoselective metalation, originally showcased by Kagan,[100,101] Overman showed that acetal **82** underwent selective lithiation as the first step in the synthesis of enantiopure aldehydes **85** and **86**. Following reductive amination, reaction with sodium tetrachloropalladate gave palladacycles $(R_p)_2$-**89** and $(R_p)_2$-**90** due to the presence of the blocking group (Scheme 26).[66]



Scheme 26

Due to the ease of their synthesis, there are numerous examples of the diastereoselective palladation of ferrocenylimines. Synthesised either from ferrocenecarboxaldehyde **91** or acetylferrocene **92** *via* condensation with enantiopure primary amines R*NH_2 (Scheme 27), they offer a quick route to highly enantioenriched palladacycles.

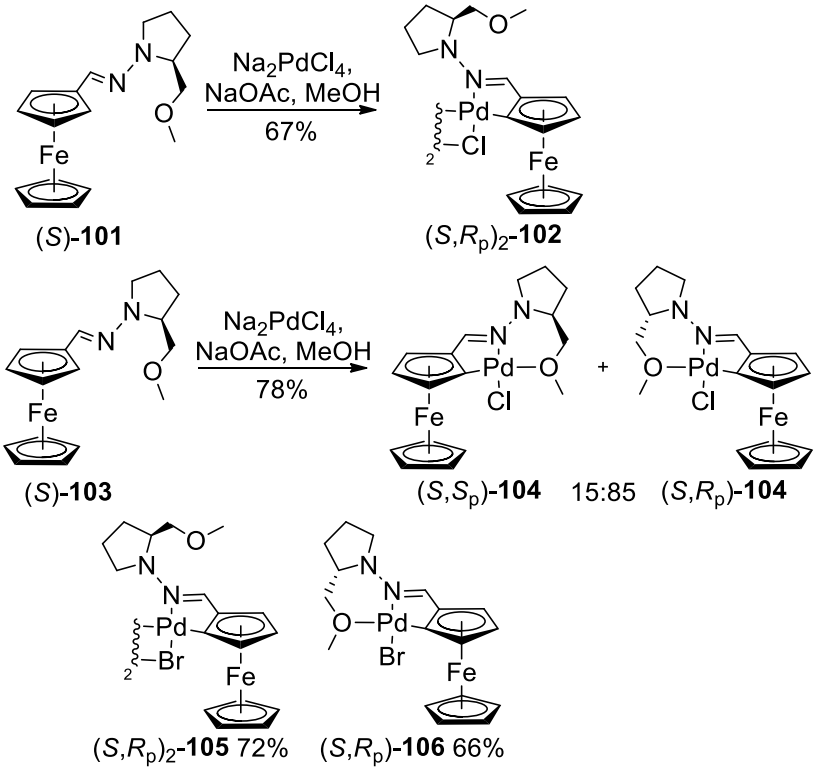


Scheme 27

The first example of this chemistry was described in 1997 utilising (–)-*cis*-myrtanylamine as the chiral amine leading to $(S_p)_2$-**93** and $(S_p)_2$-**94** as single diastereoisomers. Similarly, $(S_p)_2$-**95** and $(S_p)_2$-**96** could be synthesised utilising a related chiral amine.[102] The use of (*R*)-1-napthylethylamine resulted in the modest preference for compound $(R,S_p)_2$-**97** displaying the same sense of diastereoselectivity.[103] The aldimine and ketimine derived from (*S*)-tetrahydrofurylamine gave a ratio of 9:1 of acetate-bridged dimers $(S,S_p)_2$-**98** and $(S,S_p)_2$-**99**, respectively, when reacted with palladium acetate.[84] Reaction of the aldimine ligand with sodium tetrachloropalladate and palladium acetate resulted in the formation of $(S,S_p)_2$-

chloride bridge dimer and mixed acetate dimer *cis*-(S_p,R_p)-**62** in a 6.3:1 ratio. Finally, utilising a (*S*)-1-cyclohexylamine derived chiral imine, resulted in the formation of (S,R_p)$_2$-**100** as a single diastereoisomer.[104]

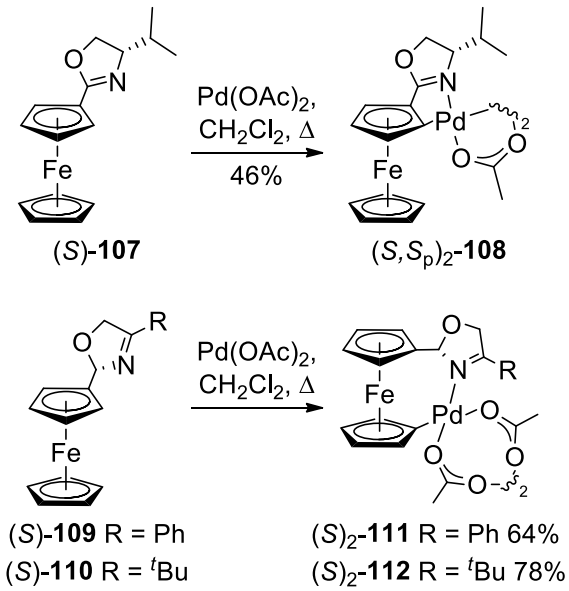
Related to the above examples are chiral ligands derived from hydrazine (*S*)-1-amino-2-(methoxymethyl)pyrrolidine. Reaction of the hydrazine with acetylferrocene gave hydrazone (*S*)-**101**, which underwent palladation to give (S,R_p)$_2$-**102** as the major isomer (Scheme 28).[105] Palladation of hydrazone (*S*)-**103** derived similarly from ferrocenecarboxaldehyde resulted in the synthesis of ether coordinated monomers (S,R_p)-**104** and (S,S_p)-**104**, with a 85:15 ratio of diastereoisomers.[106] Lastly, use of palladium acetate in place of sodium tetrachloropalladate with similar hydrazone ligands, followed by addition of lithium bromide yielded bromide-bridged dimer (S,R_p)$_2$-**105** and monomer (S,R_p)-**106**, which showcased higher diastereoselectivity than for the previous examples (9:1 for (S,R_p)$_2$-**105**: (S,S_p)$_2$-**105** and 100:0 for (S,R_p)-**106**:(S,S_p)-**106** respectively).[107]



Scheme 28

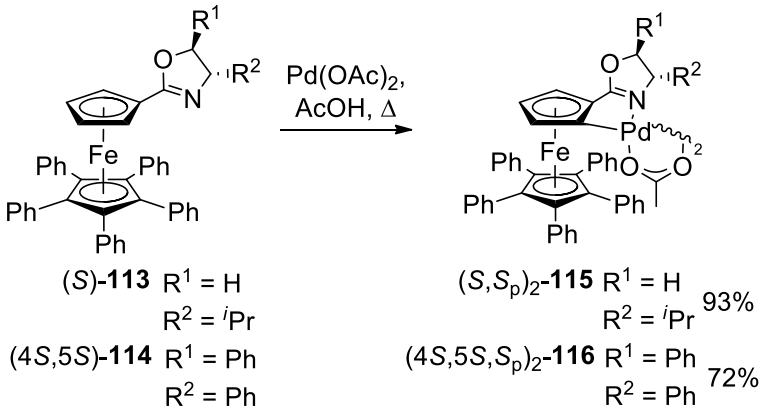
Another class of metallocene-based chiral ligands that undergo highly diastereoselective metalation are motifs containing oxazolines; commonly derived from enantiopure amino alcohols[17,108,109] or by a lesser known azridine-carboxylic ester ring expansion method.[110]

Ferrocenyl oxazoline (*S*)-**107**, like Ugi's amine, was shown to undergo highly diastereoselective lithiation,[108,111,112] and direct palladation yielded $(S,S_p)_2$-**108** exclusively in 46% yield (Scheme 29).[113] Again, the diastereoselection matched that of the lithiation reaction, i.e. the kinetic product was formed in both cases. In contrast, related 4-ferrocenyl-1,3-oxazolines (*S*)-**109** and (*S*)-**110** when palladated resulted in no formation of a new planar chiral center. Instead, interannular palladation gave the trinuclear complexes $(S)_2$-**111** and $(S)_2$-**112**, provided that the R group did not contain a C–H bond in the α-position.[114]



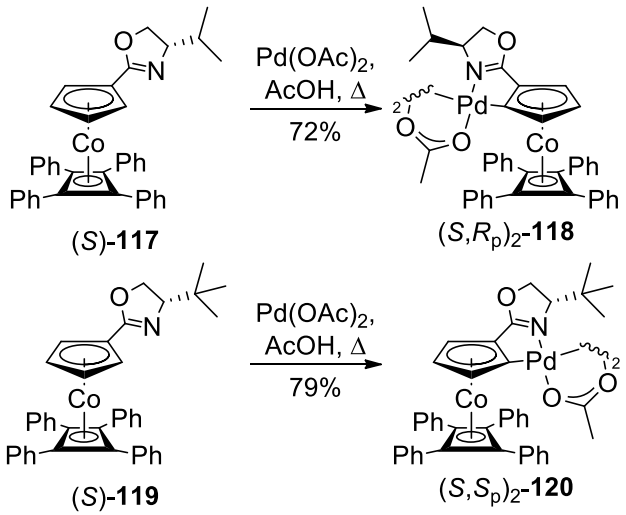
Scheme 29

In the same manner, related pentaphenylferrocene-derived oxazolines (*S*)-**113** and (4*S*,5*S*)-**114** were shown to undergo cyclometalation to give palladacycles $(S,S_p)_2$-**115** and $(4S,5S,S_p)_2$-**116**, respectively, in good yield, as single diastereoisomers (Scheme 30).[115]



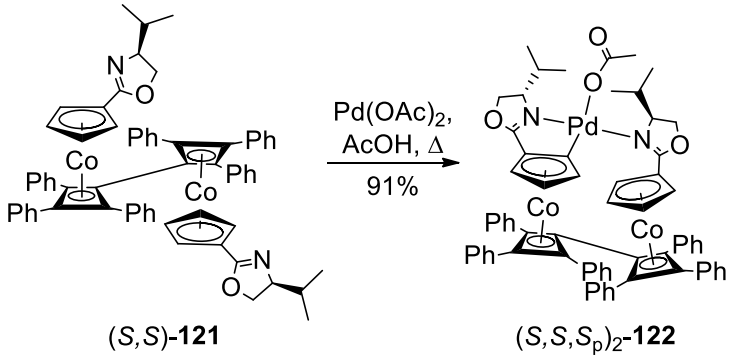
Scheme 30

In 1999, Richards showed that structurally related cobalt-oxazoline ligand (*S*)-**117** also readily underwent palladation to give cobalt-oxazoline palladacycle (COP-OAc), $(S,R_p)_2$-**118** again as a single diastereoisomer (Scheme 31).[17] The opposite configuration for the element of planar chirality, when compared to previous ferrocenyl examples, was rationalised to be due to steric repulsion between the oxazoline moiety and the lower (η^4-tetraphenylcyclobutadienyl)-ring. It was later found that this configuration was in fact the thermodynamic product of the reaction, by using ^{1}H-NMR studies of the palladation reaction: where initial formation of the kinetic $(S,S_p)_2$-**118** diastereoisomer was seen before switching to the resultant major isomer.[116] A related oxazoline, derived from (*S*)-*tert*-leuinol, (*S*)-**119**, was shown to give the kinetic product for palladation, (as in the ferrocenyl oxazoline series), by treatment with palladium acetate in acetic acid, yielding palladacycle (*S*, $S_p)_2$-**120** as a single diastereoisomer.[117]



Scheme 31

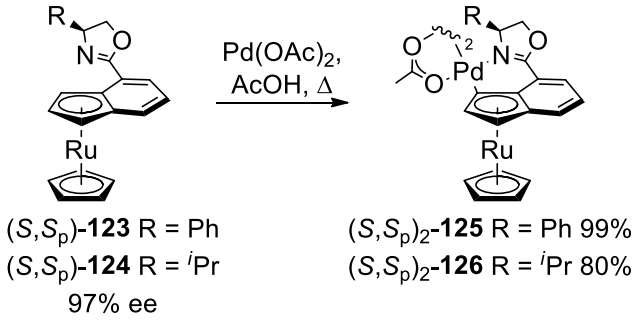
Recently, it was shown that a new pincer-type ligand based on the COP system could be synthesised from bisoxazoline ligand (*S*,*S*)-**127**. Reaction of the ligand under analogous conditions as described above gave bisoxazoline palladacycle (S,S,S_p)-**128** as a single isomer (Scheme 32).[118]



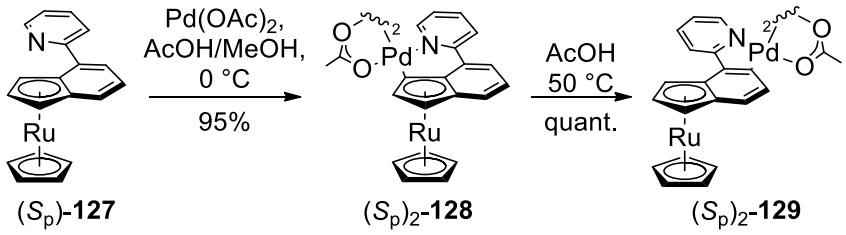
Scheme 32

Oxazoline ligands bearing ruthenium-based metallocenes have also shown high diastereoselectivity upon palladation. Enriched planar chiral ligands (S,S_p)-**123** and (S,S_p)-**124**, when palladated, yielded exclusively the *peri*-palladation products (S,S_p)$_2$-**125** and (S,S_p)$_2$-**126** as a single diastereoisomer (Scheme 33).[119] In other examples, using a similar motif but instead with a pyrrolindyl donating group at the 2-position, (S_p)-**127**, revealed that at low temperatures, the major product was the *peri*-palladation product (S_p)$_2$-**128**; but upon heating, only the *ortho*-palladation product (S_p)$_2$-**129** was isolated as a single isomer

(Scheme 34). This demonstrated that the initial *peri*-palladation is a consequence of the kinetic selectivity of the reaction, and the *ortho*-palladation complex is the thermodynamic product.

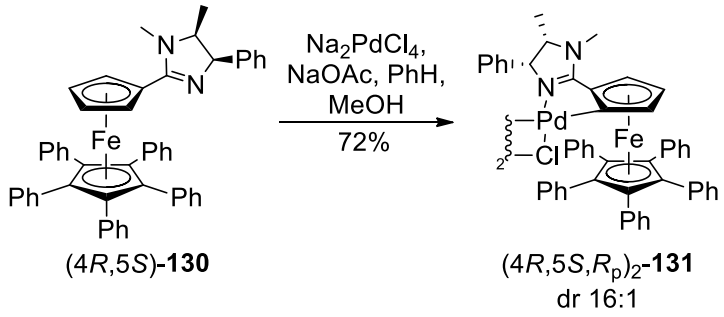


Scheme 33

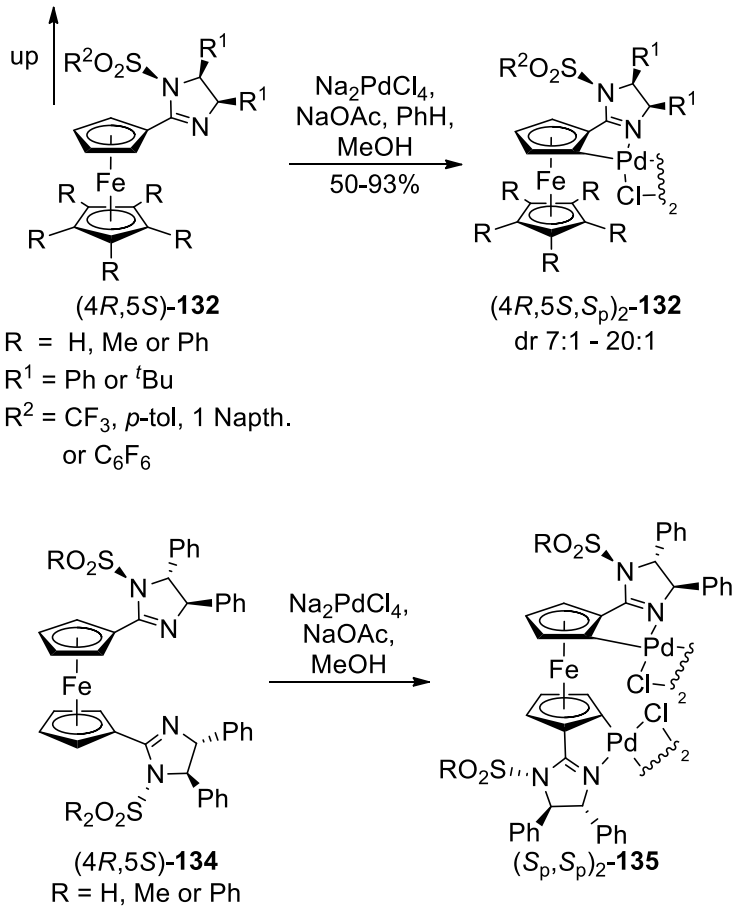


Scheme 34

Related pentaphenylferrocene-derived imidazoline complex (4*R*,5*S*)-**130** undergoes cyclopalladation to give predominantly (4*R*,5*S*,R_p)$_2$-**131** where, similar to above, the kinetic product is formed, in which the phenyl group is *endo* to the lower C_5Ph_5 ligand (Scheme 35).[120]



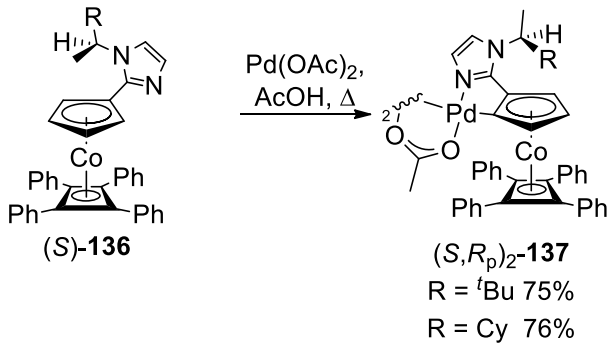
Scheme 35



Scheme 36

The origin of diastereoselection with the similar *N*-sulfonyl-substituted imidozolines (4*R*,5*R*)-**132** is attributed to the operation of a relay controlling the chirality of the sulfonated nitrogen: the conformation where the sulfonyl group points away from the ferrocenyl floor is favoured, in turn, dictating the site of palladation. Good diastereoselectivities have been reported for palladation reactions leading to ferrocenyl, pentamethylferrocenyl and pentaphenylferrocenyl derivatives (4*R*,5*S*,S_p)$_2$-**133**, and in each case the best selectivities gained (20:1) was seen where R^2 = *para*-tolyl (Scheme 36).[121] This approach was repeated to produce the first bispalladacycle, (S_p,S_p)$_2$-**135**, obtained through direct palladation, which could be isolated as a single diastereoisomer using chromatography.[122,123]

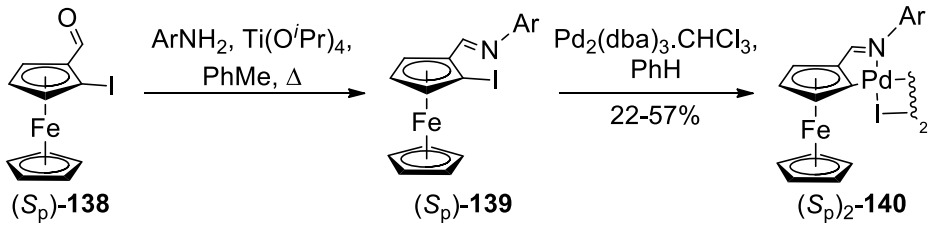
Finally, imidazole complexes, derived from chiral amines, of type (*S*)-**136** have also been shown to undergo diastereoselective palladation. Reaction of the ligand in acetic acid with palladium acetate gave (*S*,R_p)$_2$-**137** as a single diastereoisomer (Scheme 37).[124]



Scheme 37

1.6.3 Oxidative Addition

The strategy employed in the generation of scalemic palladacycles, when using oxidative addition protocols, relies heavily upon the generation of an enantiopure precursor. 2-Iodoferrocenecarboxaldehyde (S_p)-**138**, generated using the Kagan methodology outlined in Scheme 26, was condensed with a series of aromatic amines. The resultant imines were reacted with a source of palladium(0) to give palladacycles (S_p)$_2$-**140** (Scheme 38). [66]

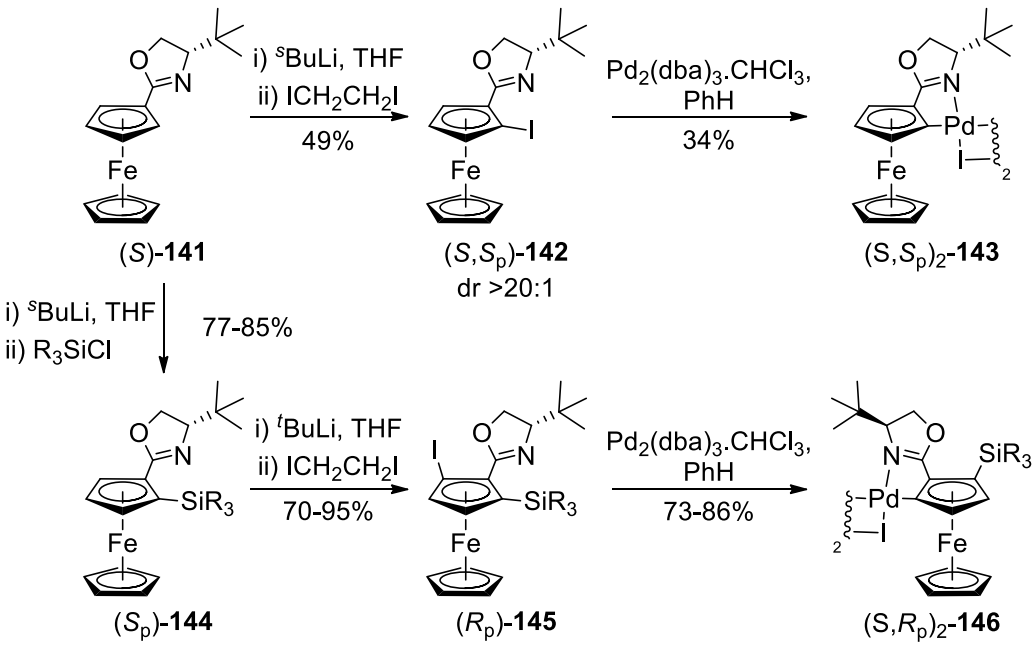


Scheme 38

An alternative approach to the Kagan method, is the use of ferrocenyl oxazolines as the oxazoline itself can be used as the ligand component.[125] Overman showed that starting with the (*S*)-*tert*-leucinol-derived oxazoline (*S*)-**141**, both (S_p)$_2$ and (R_p)$_2$ palladacycles could be accessed in a few steps (Scheme 39).[12,126] The former was synthesised by lithiation and subsequent iodine quench to form (*S*,S_p)-**142**, followed by Pd(0) insertion to form (*S*,S_p)$_2$-**143**.

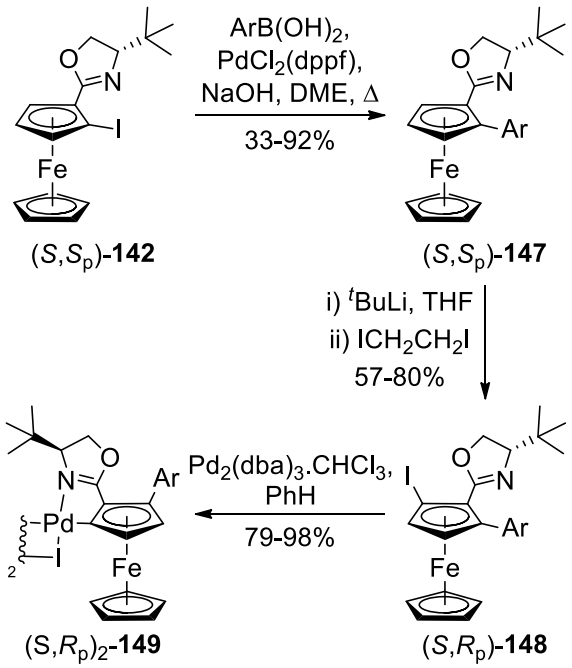
Several examples of the (*S*,R_p)$_2$ palladacycles were constructed by lithiation of (*S*)-**141**, followed by a silyl quench to introduce a bulky tri-alkyl group giving metallocene S_p-**144**.

Iodination to give (R_p)-**145** and subsequent oxidative insertion with a palladium(0) source lead to the generation of palladacycles of type (S,R_p)$_2$-**146**.



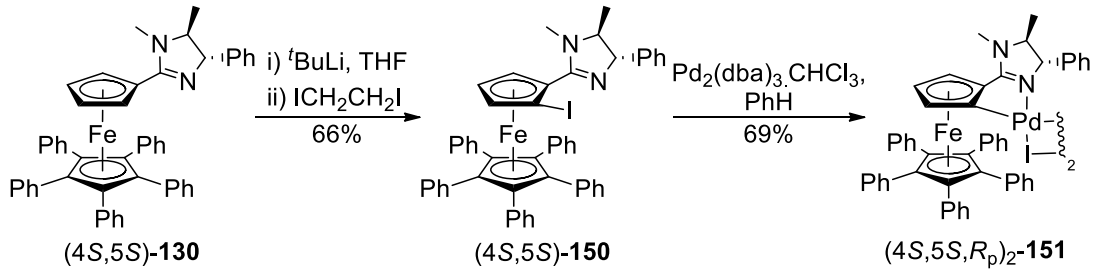
Scheme 39

Alternatively, the group demonstrated that using a Suzuki coupling reaction on iodo compound (S,S_p)-**142** to introduce aryl blocking groups, they could use a similar procedure of lithiation, incorporation of iodine and Pd(0) insertion, to yield palladacycles (S,R_p)$_2$-**149** (Scheme 40).



Scheme 40

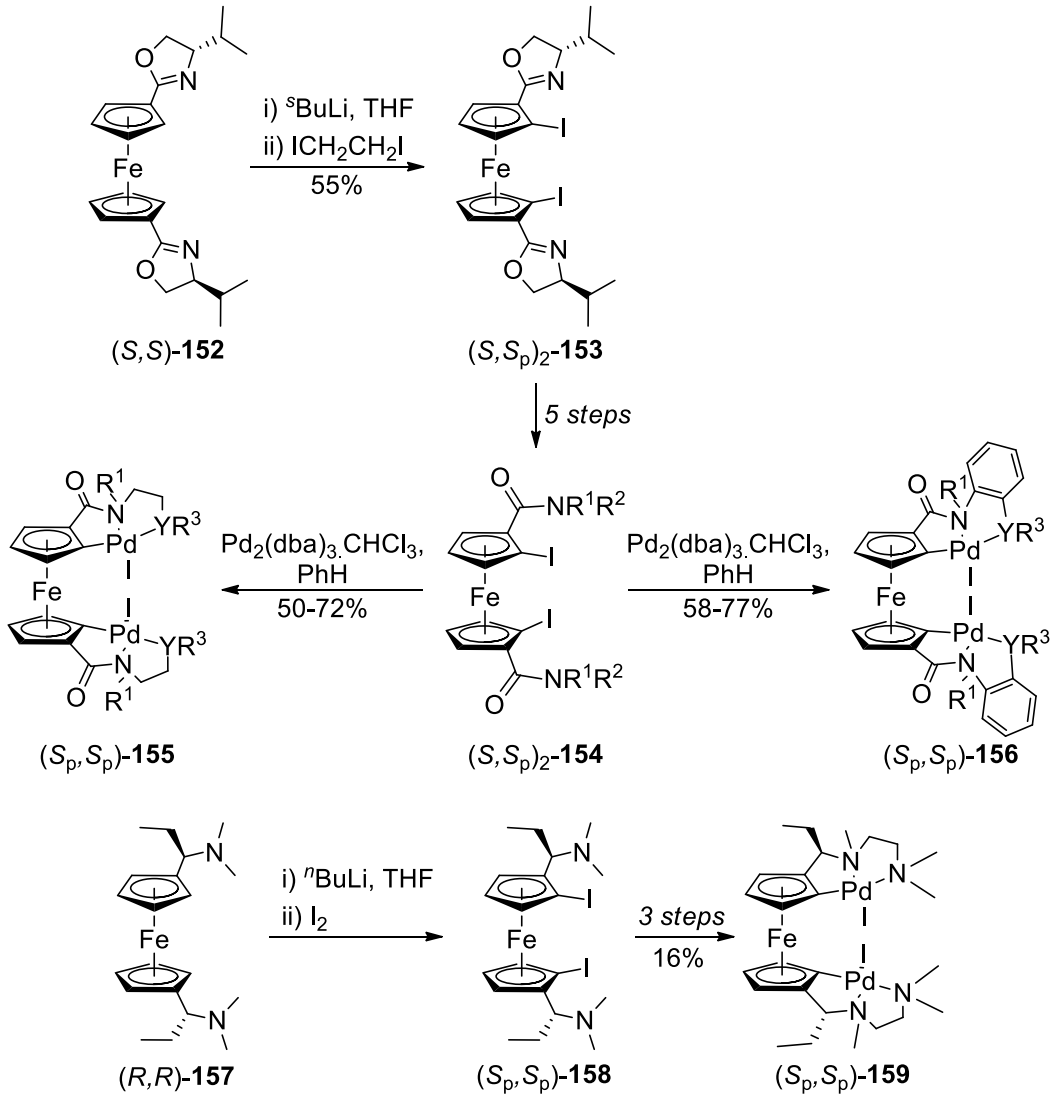
A similar approach to above utilised pentaphenylferrocene derivative (4S, 5*S*)-**130** and iodo compound (4S, 5*S*, S_p)-**150** to generate palladacycle (4*S*, 5*S*, S_p)$_2$-**151** *via* a highly selective lithiation step (16:1 dr, Scheme 41).[120]



Scheme 41

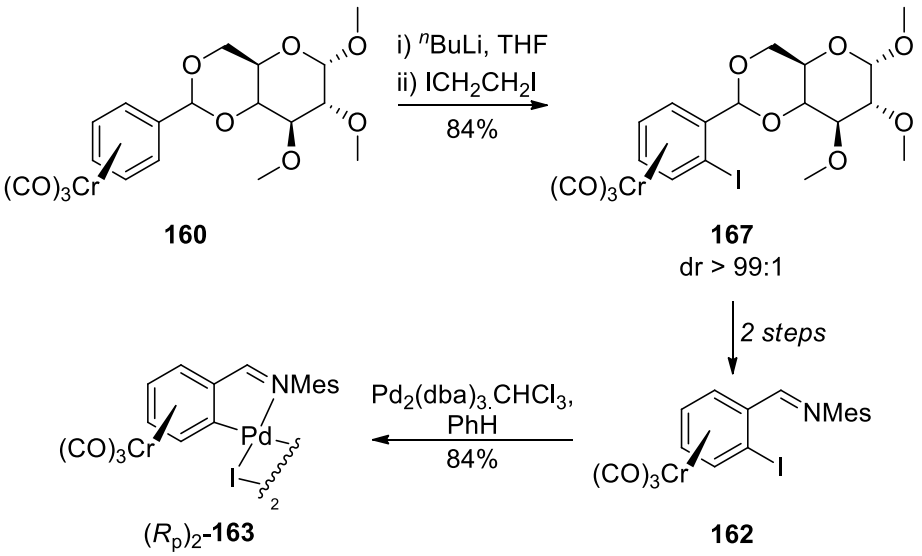
Ferrocenyl bis-palladacycles have also been synthesised in a similar manner from bis-oxazoline (*S*,*S*)-**152**. Lithiation and subsequent quench with ethylene diiodide gave the bis-iodide ligand (S,S_p)$_2$-**153** with a dr of 10:1.[127] Purification of (S,S_p)$_2$-**153** by column chromatography yielded an almost diastereomerically pure sample and manipulation of the oxazoline to give bis-amides (S_p,S_p)-**154** provided a suitable precursor for palladation. The palladacycles (S_p,S_p)-**155** and (S_p,S_p)-**156** were generated using a standard oxidative addition

protocol (Scheme 42).[128] Similarly, the highly diastereoselective lithiation of diamine (*R*,*R*)-**157** was used as a prerequisite for the synthesis of (S_p,S_p)-**159**.[128]



Scheme 42

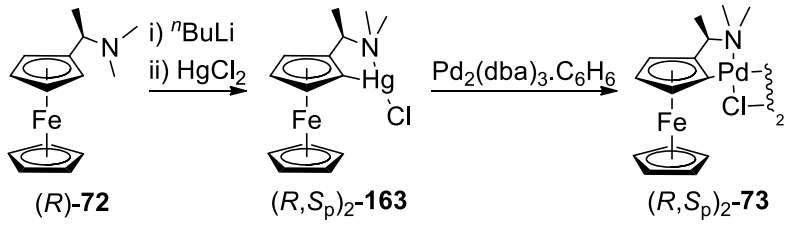
Zipp and Overman described the multi-step preparation of enantiopure cyclopalladated (η^6-arene)tricarbonylchromium complex (R_p)$_2$-**163** (Scheme 43). Treatment of scalemic sugar derivative **160** with butyllithium, followed by a quench with ethylene diiodide gave *ortho*-iodo substrate **161**[129] with high diastereoselectivity (dr = >99:1). Further manipulation to imine **162** and treatment with Pd(0), under normal conditions gave the palladacycle in good yield.[21]



Scheme 43

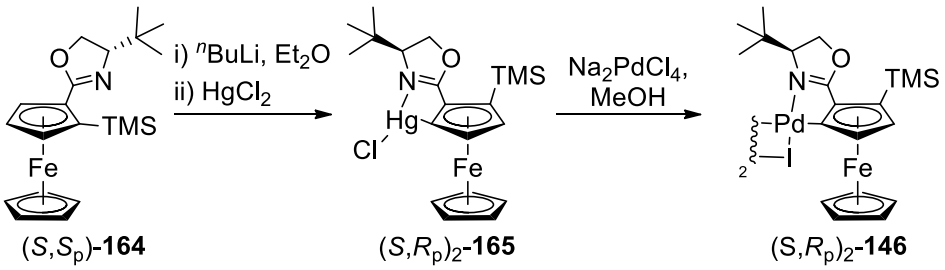
1.6.4 Transmetalation

Another alternative to direct C–H activation for the synthesis of palladacycles is the use of transmetalation to introduce the required palladium into the metallocene framework. However, there are few examples reported using this approach. An alternative method for the generation of palladacycle $(R,S_p)_2$-**73** was used to confirm the identity of the major diastereoisomer for the palladation of Ugi's amine (*R*)-**72**. Although no yields are quoted, the group first exploited the highly diastereotopic lithiation of amine (*R*)-**72** followed by two sequential transmetalations; first using mercuric chloride to give $(R,S_p)_2$-**163**, then upon treatment with a source of Pd(0), resulting in the isolation of palladacycle $(R,S_p)_2$-**73** (Scheme 44).[94]



Scheme 44

Using a similar approach, Overman showed that transmetalation could be used to give palladacycle $(S,R_p)_2$-**166** as a single diastereoisomer, albeit in low yield (Scheme 45).[12]

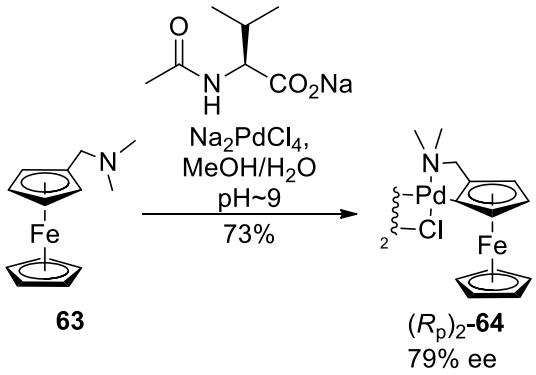


Scheme 45

1.6.5 Enantioselective Palladation

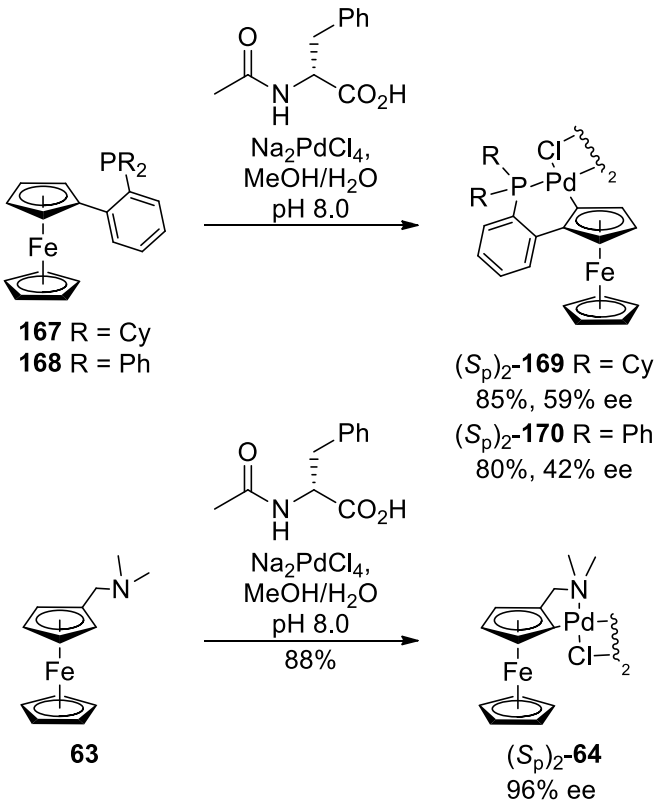
Most of the methods described thus far have utilised a ligand-bound chiral auxiliary to control the diastereoselective metalation. An attractive alternative to this approach involves the use of a stoichiometric chiral reagent to effect the enantioselective synthesis of the planar chiral palladacycle.

The first example of this process was demonstrated by Sokolov in 1978, where ligand **63** was treated with sodium tetrachloropalladate in the presence of stoichiometric sodium salt of (*S*)-*N*-acetylvaline (Scheme 46).[80,130] This resulted in partial enantioselective formation of palladacycle $(R_p)_2$-**64**, with the yield and *ee* of the product dependent on pH. Under basic conditions (pH ~9), a maximum *ee* of 79% could be gained. A slight modification to this procedure, using (*S*)- and (*R*)-*N*-acetylleucine gave $(R_p)_2$-**64** and $(S_p)_2$-**64**, respectively, with an *ee* of 81%.[131]



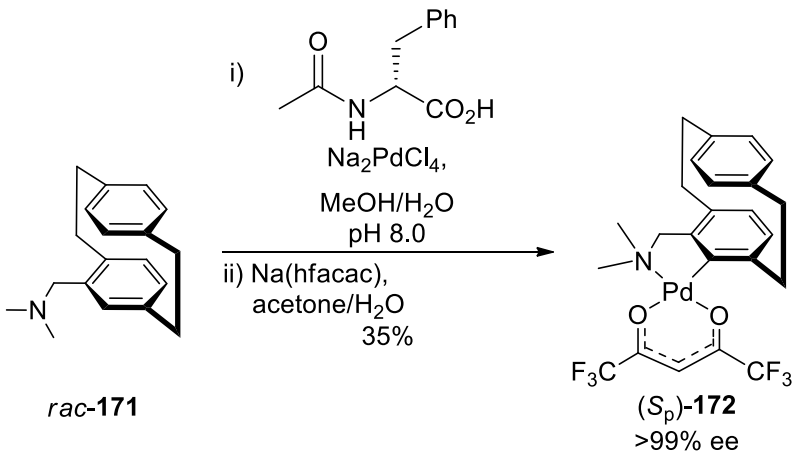
Scheme 46

In 2009, Richards showcased an updated methodology of the Sokolov approach, using (*R*)-*N*-acetylphenylalanine as the stoichiometric chiral reagent at pH 8.[132] The group were able to palladate phosphinophenylferrocenyl ligands **167** and **168** to give palladacycles $(S_p)_2$-**169** and $(S_p)_2$-**170** in good yield, with moderate enatioselectivities, (59 and 42% *ee* respectively, Scheme 47). Additionally, they reported that amine ligand **63** could be palladated using their improved conditions to give palladacycle $(S_p)_2$-**64**, in great yield and a higher enantioselectivity than reported previously (88% and 96% respectively).



Scheme 47

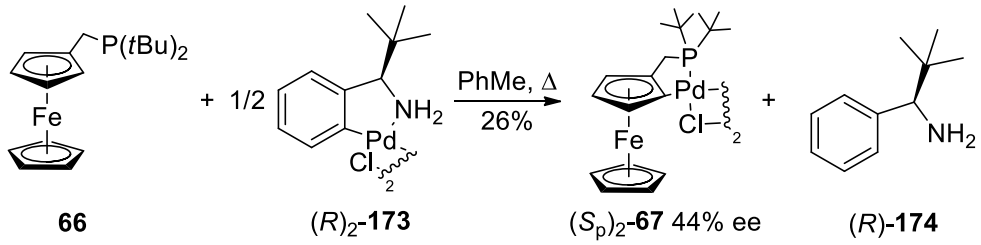
This method has been recently extended to the kinetic resolution of [2,2]-paracyclophane *rac*-**171** to give the product palladacycle (S_p)-**172** in more than 99% *ee* (where a selectivity factor of 205 was obtained, Scheme 48).[133]



Scheme 48

1.6.6 Transcyclopalladation

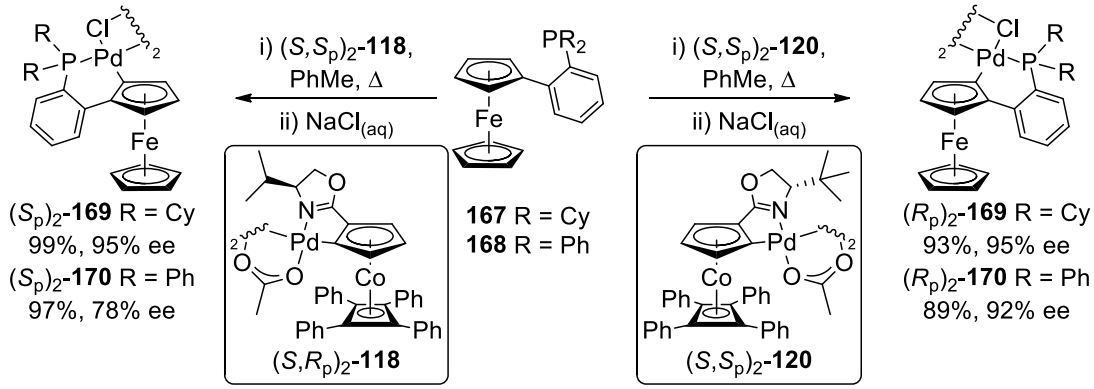
Palladacycles may be formed by the exchange of cyclometalated ligands,[58,59] which typically involves the transfer of palladium from a C,N-chelate to a C,P-chelate, driven by the greater strength of the phosphorus-palladium bond in the latter. Transcyclopalladation defines a subcategory of this process, in which the reaction proceeds without formation of dissociated metal salts. Asymmetric transcyclopalladation is possible; the first example was showcased in 2003 with the palladation of prochiral phosphine **66**. Heating the ligand with half an equivalent of the C,N-palladacycle $(R)_2$-**173** gave complex $(S_p)_2$-**67** in moderate *ee*, together with recovered amine (*R*)-**174** (Scheme 49).[134]



Scheme 49

In 2005, Richards illustrated that higher enantioselectivities could be achieved utilising palladacycles $(S,R_p)_2$-**118** and $(S,S_p)_2$-**120** (Scheme 50).[135] Heating prochiral dicyclohexylphosphine **167** with $(S,R_p)_2$-**118**, followed by a brine wash, yielded phosphopalladacycle $(S_p)_2$-**169** in high *ee* and yield. Use of the opposite diastereoisomer

$(S,S_p)_2$-**120** resulted in a switch in the configuration seen for the resultant palladacycle $(R_p)_2$-**169**, which was also recovered in high *ee*. Use of diphenylphosphine analogue **168** with $(S,R_p)_2$-**118** and $(S,S_p)_2$-**120** gave the corresponding $(S_p)_2$-**170** and $(R_p)_2$-**170** palladacycles in 78 and 92% *ee* respectively.



Scheme 50

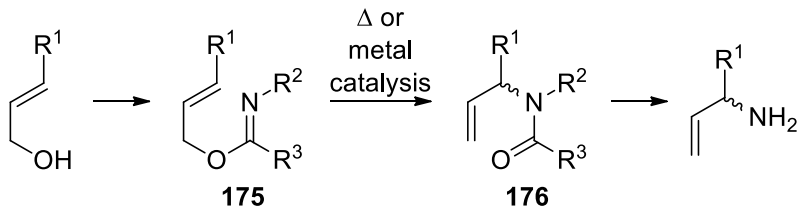
1.7 Use of Planar Chiral Metallocene-Based Palladacycles in Asymmetric Synthesis

1.7.1 The Allylic Imidate Rearrangement

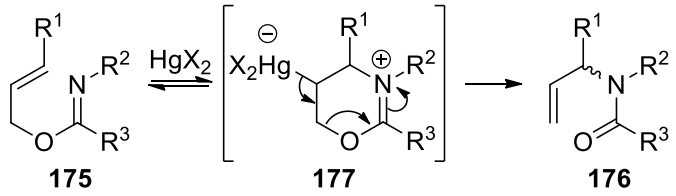
The allylic imidate rearrangement, (or Overman rearrangement), was first developed by Overman in the mid-1970s as a key step in the conversion of allylic alcohols into allylic amines (Scheme 51).[136–138] This [3,3]-sigmatropic rearrangement can be undertaken by heating imidate **175** to high temperatures (typically >140 °C), the reaction proceeding with a concerted rearrangement to give the more stable amide **176**. Alternatively, addition of mercury(II) salts leads to an increased rate of reaction (up to 10^{12}) at lower temperatures, with the reaction proceeding *via* a two-step iminomercuration-deoxymercuration mechanism (Scheme 52).

In this process, the electrophilic mercuric halide ligates the carbon-carbon double bond, promoting nucleophilic attack by the imino nitrogen at the C-3 position to form intermediate **177**. The dihydrooxarine can then undergo cleavage of the carbon-nitrogen bond to reform

the starting material or of the carbon-oxygen bond to form the rearranged amide – the latter is favoured due to the thermodynamic driving force.



Scheme 51

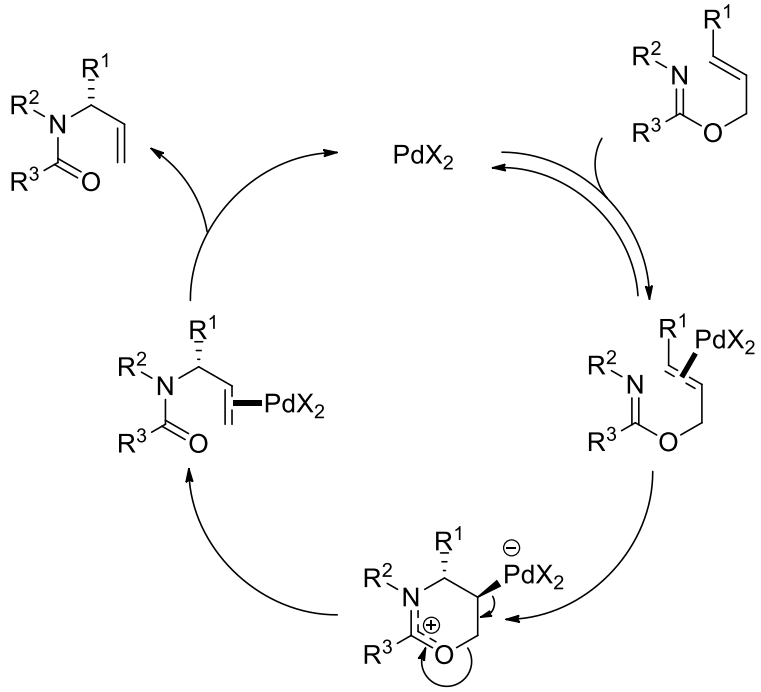


Scheme 52

With the discovery of the mercury catalysed rearrangement, further investigations into alternative methods of reaction acceleration were undertaken. Electrophilic reagents such as HCl, $TiCl_4$, $AlMe_3$ and $(ArO)_2AlMe$ were used and the reaction was shown to be promoted at 111 °C.[139] Although rate enhancement was seen, the product yields were poor due to the formation of numerous side products, often with a loss of stereocontrol. It was reasoned that for these reagents, the reaction proceeds *via* an intermediate carbonium ion, which would result in the side products observed. It was later discovered that palladium(II) complexes were superior catalysts for the rearrangement.[138,140–145] In contrast, the zero-valent complex $Pd(Ph_3)_4$ was shown to be a poor catalyst, giving either [3,3] or [1,3] rearranged products due to the formation of Pd-π-allyl complexes.[141] These discoveries lead to the generation of new chiral complexes aimed at investigating the asymmetric allylic imidate rearrangement.[12,66,82,95,114,120,121,126,128,145–148]

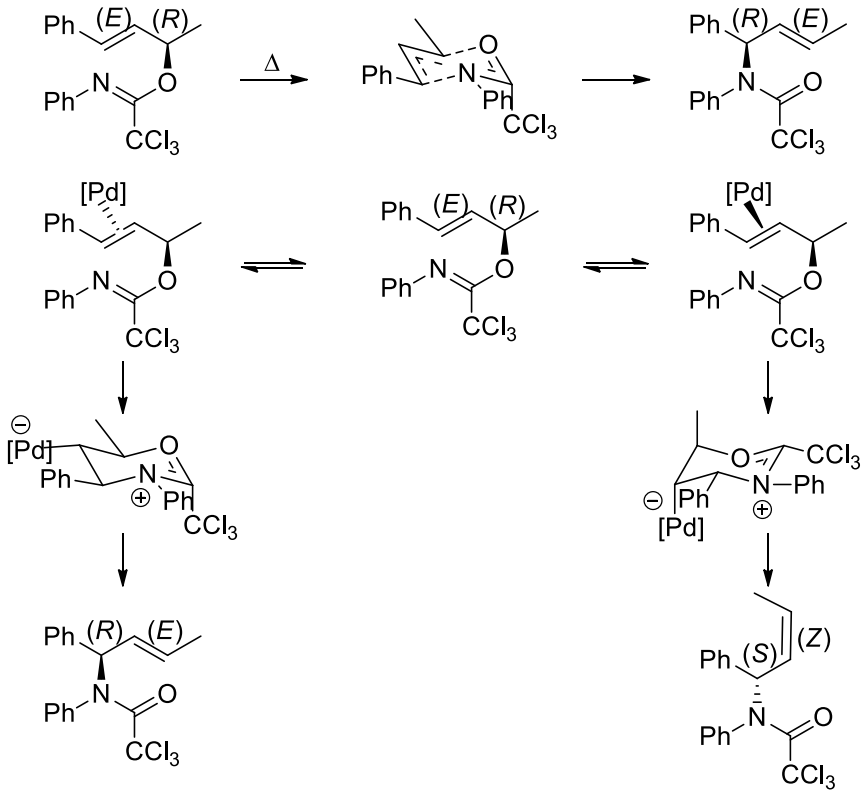
The catalytic cycle for the rearrangement process is thought to proceed by a cyclisation-induced rearrangement, (CIR), in which the palladium(II) coordinates to the olefin moiety to bring about an intramolecular nucleophilic attack by the imidate nitrogen (Scheme

53).[136,141,149] Collapse of the six-membered intermediate and dissociation of the Pd(II)-catalyst gives the rearranged product. This mechanism is closely related to the mechanism originally proposed by Henry for the Pd(II)-catalysed allylic acetate rearrangements[150] and subsequently by Overman for the $PdCl_2$-catalysed Cope rearrangements.[151]



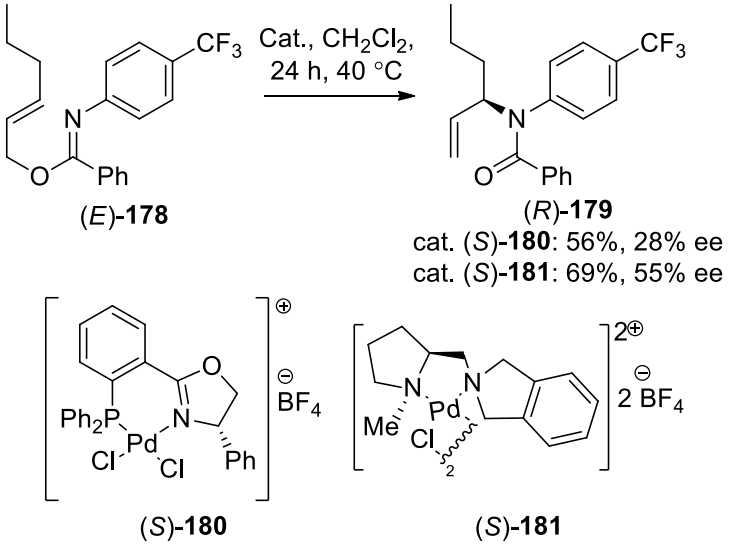
Scheme 53

The proposed mechanism contrasts to the concerted thermal rearrangement pathway, which proceeds *via* a chair-like transition state resulting in the efficient transfer of stereochemical information (as with the Cope rearrangement, Scheme 54). For the palladium-catalysed reaction, where the substrate contains a stereogenic center, the alkene faces are diastereotopic, therefore coordination to which dictates the stereochemical outcome.[141]



Scheme 54

Excellent results for the rearrangement have been achieved using achiral Pd(II) sources, regularly employing 4–8 mol % of catalyst in aprotic solvents, at room temperature. This led to the synthesis of cationic palladium(II) complexes containing chiral N,N- and N,P-ligands (Scheme 55). Reactions involving these complexes were slow, resulted in moderate enantioselectivities and were compromised by the formation of by-products arising from competing ionization of the imidate.[152] In contrast it was observed that $PdCl_2(NCMe)_2$ resulted in the near quantitative rearrangement of imidate (*E*)-**178** to (*R*)-**179** within minutes at room temperature.[95] It was reasoned that if olefin coordination is the enantioselective step, planar chiral ligands that project chirality perpendicular to the Pd square plane might enhance the discrimination of prochiral faces of the alkene double bond. This resulted in the examination of neutral palladium(II) species containing two anionic ligands, a requirement met by palladacycle complexes.



Scheme 55

1.7.1.1 Rearrangement of Allylic N-Arylbenzimidates

In 1997 Overman and Hollis presented the first use of planar chiral palladacycles in enantioselective catalysis for the allylic imidate rearrangement, by using cyclopalladated ferrocenyl amines (Figure 10).[95] Catalyst $(R,S_p)_2$-**73** was shown to be a moderate catalyst for the rearrangement of imidate (*E*)-**178**, giving 67% *ee*, without any by-products arising from imidate ionization.[95] To improve on the low yield obtained from the reaction (35% after 7 days at room temperature) other bridging ligands were tested, the most effective being trifluoroacetate complex $(R,S_p)_2$-**182**, which gave (*R*)-**179** in 98% yield and 61% *ee*.

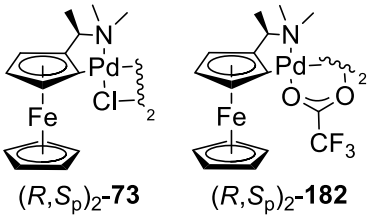
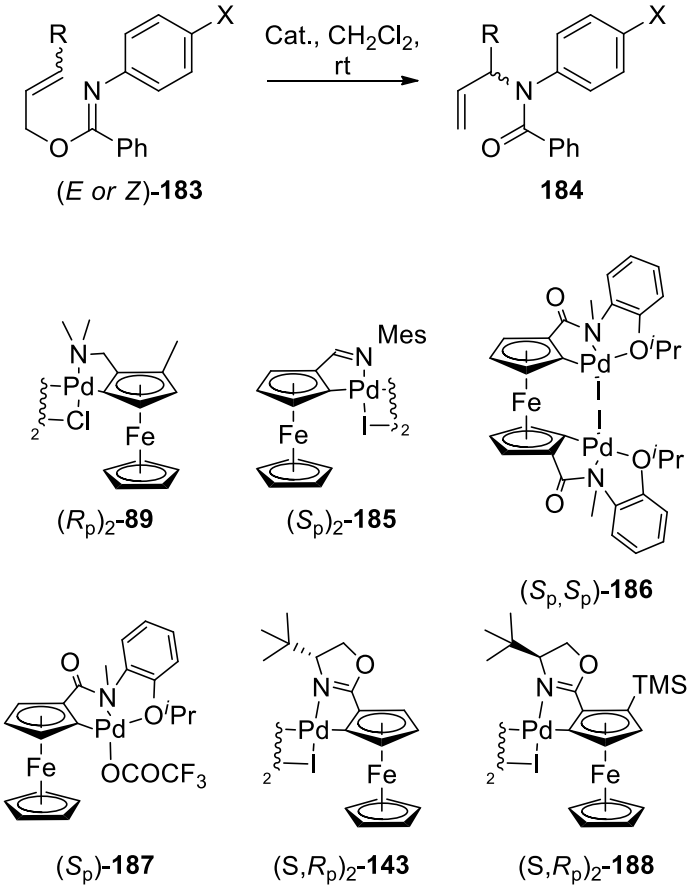


Figure 10

Since this development, other planar chiral palladacycles have been shown to be good catalysts for the rearrangement of arylbenzimidates of type (*E*)-**183**, (Scheme 56, Table 1). Overman employed chloride $(R_p)_2$-**89** which was shown to be a poor catalyst for the rearrangement (34% yield after 48 hours at 40 °C, 49% *ee*). Addition of silver

trifluoroacetate resulted in decomposition of the catalyst, so instead thallium trifluoroacetate was used. This improved the yield of the reaction, but the enantioselectivity remained low (entry 1).[66] Imine derived palladacycle $(S_p)_2$-**185** was shown to have similar selectivity and yield after activation with thallium triflate (entry 2). Substrates (*Z*)-**183** resulted in allylic benzamide products of opposite absolute configuration in slightly higher *ee* (entry 3).[66]

Later, Kang *et al* utilised bis-palladacycle (S_p,S_p)-**186** for the rearrangement. After activation, using excess silver trifluoroacetate, good yields and enantioselectivities were seen with both (*E*)-**183** and (*Z*)-**183** (entries 4 and 5).[128] The group also showed that tridentate-palladacycle (S_p)-**187** was a poor catalyst for the rearrangement (entry 6). The group saw decomposition of the catalyst under the conditions used, and reasoned that this was hindering catalysis.



Scheme 56

Entry	Cat. Precursor	Cat. Loading [mol %]	Additive (mol %)	Config. of **184**	X	R	Yield [%]	*ee* [%] (config.)
1[66]	$(R_p)_2$-**89**	10	TlTFA (22)	*E*	CF_3	Pr	73	40 (*S*)
2[66]	$(S_p)_2$-**185**	11	TlOTf (35)	*E*	CF_3	Pr	80	46 (*R*)
3[66]	$(S_p)_2$-**185**	11	TlOTf (35)	*Z*	CF_3	Pr	45	66 (*S*)
					OMe	Pr	78	73 (*S*)
4[128]	(S_p,S_p)-**186**	5	AgTFA (excess)	*E*	OMe	Pr	91	92 (*R*)
					OMe	Ph	90	87 (*S*)
5[128]	(S_p,S_p)-**186**	5	AgTFA (excess)	*Z*	OMe	Pr	85	90 (*S*)
					OMe	^{i}Bu	70	86 (*S*)
6[128]	(S_p)-**187**	3.5	none	*E*	OMe	Pr	32	30 (*R*)
7[12,126]	$(S\ S_p)_2$-**143**	5	AgTFA (20)	*E*	CF_3	Pr	86	8 (*S*)
8[12,126]	$(S,R_p)_2$-**143**	5	AgTFA (20)	*E*	CF_3	Pr	77	69 (*S*)
9[12,126]	$(S,R_p)_2$-**188**	5	AgTFA (20)	*E*	CF_3	Pr	57	79 (*S*)
					OMe	Pr	93	83 (*S*)
10[12,126]	$(S,R_p)_2$-**188**	5	AgTFA (20)	*Z*	CF_3	Pr	67	91 (*R*)
					OMe	Pr	83	91 (*R*)

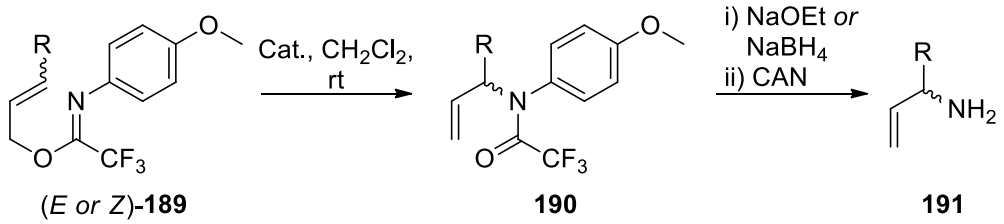
Table 1 – Enantioselective rearrangement of allylic *N*-arylbenzimidates (*E*)- and (*Z*)-**183**, catalysed by planar chiral palladacycles (Scheme 56)[18]

Overman has also utilised ferrocenyl-oxazoline palladacycles (FOP) for the rearrangement. Application of both diastereoisomers $(S,S_p)_2$-**143** and $(S,R_p)_2$-**143** resulted in a significantly higher enantioselectivity with the (S,R_p) complex (entries 7 and 8). It was reasoned that in the matched (S,R_p) case, the ferrocene and *tert*-butyl groups are oriented above and below the palladium(II) square plane. This is in contrast with the mismatched (S,S_p) diastereoisomer, where they are on the same side.[12,126]

Palladacycle $(S_p,R_p)_2$-**188** showed improved enantioselectivities for the rearrangement of both (*E*)-**183** and (*Z*)-**183** arylbenzimidates (entries 9 and 10).[12,126] The increased selectivity is due to the resultant active catalyst (after silver salt addition) being much more stable than in similar systems.

1.7.1.2 Rearrangement of Allylic N-(4-methoxyphenyl)trifluoroacetimidates

Products from the rearrangement of *N*-arylbenzimidates proved to be of limited use in synthesis due to difficulty in removing the two nitrogen substituents, namely a benzoyl and a 4-methoxyphenyl (PMP) group. More useful substrates were found to be related *N*-(4-methoxyphenyl)trifluoroacetimidates (*E* or *Z*)-**189**, as the product amides **190** can be easily deprotected over two steps to give free amine **191** (Scheme 57). Firstly, the trifluoroacetyl group can be removed with a sodium ethoxide solution or with sodium borohydride. This can be followed by oxidative de-arylation with cerium ammonium nitrate (CAN) with yields ranging from 62–74% over the two steps.[12]



Scheme 57

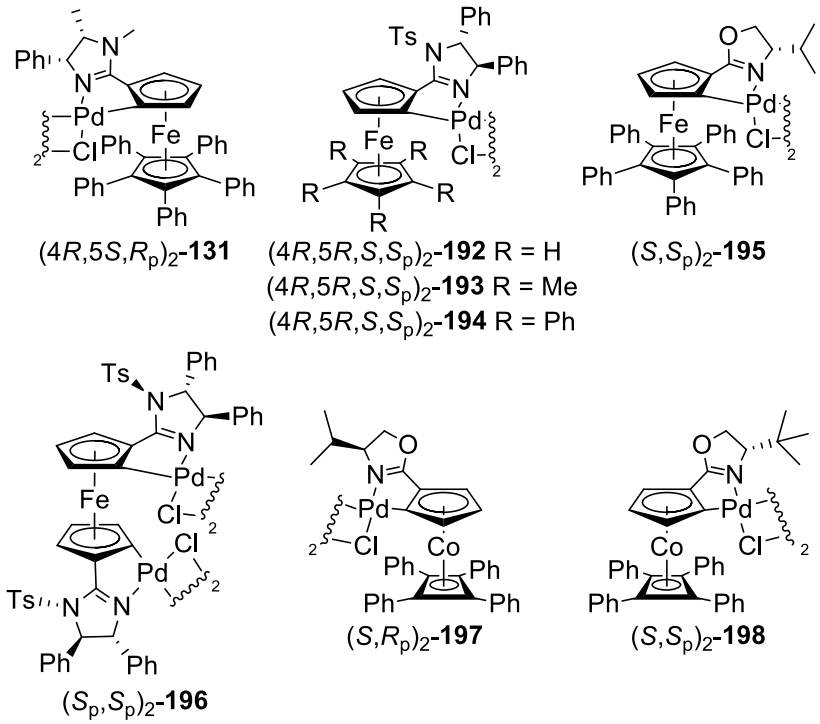


Figure 11

Entry	Cat. Precursor	Cat. Loading [mol %]	Additive (mol %)	Config. of **189**	R	Yield [%]	*ee* [%] (config.)
1[12]	$(S,R_p)_2$-**188**[b]	7.5	AgTFA (30)	*E*	Pr	88	76 (*S*)
					^{i}Bu	73	84 (*S*)
					Ph	46	46 (*R*)
2[12]	$(S,R_p)_2$-**188**[b]	7.5	AgTFA (30)	Z	Pr	21	87 (*R*)
					^{i}Bu	21	90 (*R*)
3[120]	$(4R,5R,R_p)_2$-**131**[c]	5	$AgNO_3$ (30)	*E*	Pr	96	88 (*S*)
					Me	93	88 (*S*)
4[121]	$(4R,5R,S,S_p)_2$-**192**[c]	5	AgOTf (20)	*Z*	Pr	75	89 (*S*)
					^{i}Bu	69	96 (*S*)
5[121]	$(4R,5R,S,S_p)_2$-**193**[a][c]	5	AgTFA (20)	*Z*	Pr	72	93 (*S*)
					^{i}Bu	82	96 (*S*)
6[121]	$(4R,5R,S,S_p)_2$-**194**[a][d]	0.05	AgTFA (0.2)	*E*	Pr	95	95 (*R*)
					Me	98	92 (*R*)
7[115]	$(S,S_p)_2$-**195**[a][d]	0.05	$AgNO_3$ (0.19)	*E*	Pr	99	97 (*R*)
8[115]	$(S,S_p)_2$-**195**[d]	0.5	$AgNO_3$ (0.19)	*E*	^{i}Pr	76	99 (*R*)
					Cy	99	99 (*R*)
9[122,123]	$(S_p,S_p)_2$-**196**[e]	0.1	AgOTs (0.6)	*Z*	Pr	97	97 (*S*)
					Me	97	94 (*S*)
					^{i}Bu	93	99 (*S*)
10[153]	$(S,R_p)_2$-**197**	5	none	*E*	Pr	92	92 (*S*)
					Me	85	82 (*S*)
					^{i}Bu	88	94 (*S*)
11[153]	$(S,R_p)_2$-**197**	5	none	*Z*	Pr	78	89 (*R*)
					Me	87	86 (*R*)
					^{i}Bu	58	90 (*R*)
12	$(S,S_p)_2$-**198**[b]	5	AgTFA (20)	*E*	Pr	64	41 (*R*)
13	$(S,S_p)_2$-**198**[b]	5	AgTFA (20)	*Z*	Pr	24	58 (*S*)

Table 2 - Enantioselective rearrangement of allylic *N*-(4-methoxyphenyl)trifluoroacetimidates (*E*)- and (*Z*)-**189**, catalysed by planar chiral palladacycles (Scheme 57, Figure 11).[18] [a] Performed at 40 °C. [b] With 20 mol % of 1,8-bis(dimethylamino)naphthalene. [c] With 10 mol % of 1,8-bis(dimethylamino)naphthalene. [d] With 0.1 mol % of 1,8-bis(dimethylamino)naphthalene. [e] Performed in $CHCl_3$ at 55 °C.

A range of planar chiral ferrocenyl derived palladacycles have been shown to be efficient in the catalysis of the trifluoroimidate rearrangement, the most successful are highlighted in Figure 11 and Table 2.[18] Good activity was shown for the rearrangement of both (*E*)-**189** and (*Z*)-**189** using the catalyst derived from $(S,R_p)_2$-**188** (entries 1 and 2). Upon activation with four equivalents of silver trifluoroacetate, good enantioselectivities were seen for the rearrangement of the (*Z*)-isomer, albeit with lower yield when compared with the results gained for the (*E*)-isomer. Both isomers required the inclusion of 20 mol % of 1,8-bis(dimethylamino)naphthalene as an acid scavenger to prevent decomposition of the substrate.[12]

The Peters group has had particular success in the area utilising palladacycles with a ligand system based around chiral imidazoline motifs (FIPs). The first of such systems used was palladacycle $(4R,5R,R_p)_2$-**131**, which was shown to be efficient in the catalysis of (*E*)-trifluoroimidates, resulting in good yield and enantioselectivities, (entry 3).[120] This promising result prompted the group to develop similar systems that were more electron-deficient. Soon thereafter the generation and use of imidazoline-derived palladacycles containing an electron withdrawing *N*-sulfonyl moiety was reported.[121] As with previous ferrocene systems, silver salt activation was necessary, but excellent enantioselectivities were obtained for the rearrangement of (*Z*)-imidates when using catalysts $(4R,5R,S,S_p)_2$-**192** and $(4R,5R,S,S_p)_2$-**193** (entries 4 and 5). Poorer results were gained when using the (*E*)-isomer. The bulkier pentaphenylferrocene derived catalyst $(4R,5R,S,S_p)_2$-**194** proved to be the most efficient catalyst for the rearrangement of (*E*)-trifluoroimidates, but conversely was poor for catalysis of the (*Z*)-isomer. High enantioselectivity and yield could be achieved and maintained whilst using a low catalyst loading, in the catalysis of (*Z*)-trifluoroimidates (0.1 mol % of palladium, entry 6). The group also showed that varying the sulfonyl moiety did not significantly alter enantioselectivities, but did prolong reaction time under the same conditions.

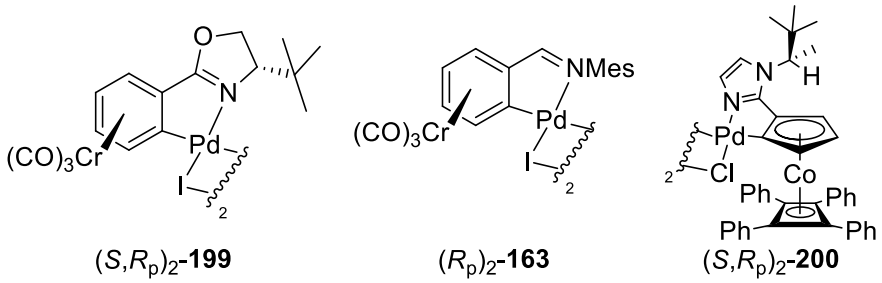
Structurally related oxazoline-based palladacycles (FOPs) were shown to be excellent catalysts for the rearrangement. In particular palladacycle $(S,S_p)_2$-**195**, upon silver salt activation, was shown to be a superior catalyst to the imidazoline systems, such that good selectivities and yields were obtained for the majority of cases, including the more demanding substrates (where R = ^{i}Pr or Cy, entries 7 and 8).[115] As with the previous example, only the rearrangement of the (*E*)-imidates provided good results.

Peters overcame this issue by showing that bis-imidazoline derived palladacycles could be effective catalysts for the rearrangement of (*Z*)-imidate substrates. Chloride-dimer $(S_p,S_p)_2$-**196** was initially shown to be inactive as a catalyst for the rearrangement of (*Z*)-**189**, but after the screening of a number of silver salts, silver tosylate provided some promising results. The use of 0.1 mol % of catalyst $(S_p,S_p)_2$-**196** in chloroform at 55 °C, with silver salt activation, resulted in excellent yields and enantioselectivities seen for a number of (*Z*)-substrates (entry 9).[123] The catalyst and updated methodology has since been used on a wide range of imidates with ester, ketone, ether, silyl ether, acetal, and protected amine functionalities as the R substituent, all showcasing good yield and selectivity.[122]

Non-ferrocene based palladacycles have also been shown to be effective in this rearrangement. In 2003, Overman showed that chloride-bridged dimer $(S,R_p)_2$-**197** (COP-Cl) was an efficient catalyst for the rearrangement of both (*E*)-**189** and (*Z*)-**189** without the need of silver salt activation (entries 10 and 11).[153] Structurally related cobalt oxazoline $(S,S_p)_2$-**198** was also shown to catalyse the rearrangement of both (*E*)- and (*Z*)-**189** (R= Pr), with the best results obtained following activation with silver trifluoroacetate (entries 12 and 13).[117] These enantioselectivities, significantly lower than the results obtained with COP-Cl revealed the S,R_p combination to be the matched pairing of central and planar chiralities.[18]

Other non-ferrocene based palladacycles have been used in the trifluoroimidate rearrangement, albeit not with the success of the FIP, FOP or COP catalysts. Moderate results were gained using (η^6-arene)tricarbonylchromium(0) complexes $(S,R_p)_2$-**199** and

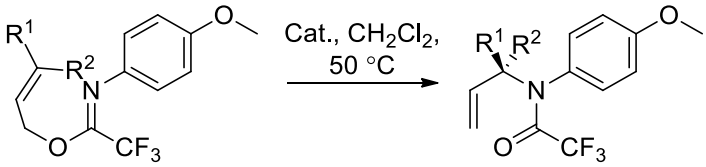
$(R_p)_2$-**163** (Figure 12).[153] Upon activation with thallium triflate reasonable yields and enantioselectivities were gained for the rearrangement of (*E*)- and (*Z*)-**189** (R = Pr, 13–66% yield, 42–82% *ee*). Another system based on a cobalt metallocene motif was also shown to have promise in the rearrangement. Following activation with silver trifluoroacetate, the imidazole-derived palladacycle complex $(S,R_p)_2$-**200** gave good enantioselectivities for the rearrangement of (*E*)- and (*Z*)-imidates (R = Pr, 86% and 88% *ee* for the *S* and *R* amides respectively).[124] The activity demonstrated by this system was significantly lower than that of the similar oxazoline analogue.



$(S,R_p)_2$-**199** $(R_p)_2$-**163** $(S,R_p)_2$-**200**

Figure 12

The use of the trifluoroacetimidate rearrangement has also been extended to the formation of quaternary centers utilising both FIP and FOP catalysts $(4R,5R,S,S_p)_2$-**194** and $(S,S_p)_2$-**193** (Scheme 58 and Table 3).[115,154] Substrates **201** where substituent R^1 or R^2 are a methyl group proceed to amide **202** with good yields and excellent enantioselectivities at 50 °C. For some substrates the catalyst loading can be lowered to 0.05–1 mol % whilst maintaining high selectivity (entries 3, 4 and 8). For substrates containing groups larger than a methyl group, higher catalyst loadings were used to push the reaction to completion (entries 5,6 and 12). Although the isolated yields eroded, the selectivity of the reaction remained good. In all reactions, the acid-catalysed elimination of the trifluoacetamide was a competitive reaction pathway. This was suppressed by the addition of a proton sponge, (3–4 equivalents of 1,8-bis(dimethylamino)naphthalene), as an acid scavenger. This methodology was shown to be tolerant with a wide range of R^1 and R^2 groups and was subsequently used in the synthesis of α, α-disubstituted α- and β-amino acids.



201 **202**

Scheme 58

Entry	Cat. Precursor	Cat. Loading [mol %]	Additive (mol %)	R^1	R^2	*t* [h]	Yield [%]	*ee* [%] (config.)
1[115]	$(S,S_p)_2$-**195**[a]	2	$AgNO_3$ (7.4)	$(CH_2)_2Ph$	Me	24	71	98 (*R*)
2[115]	$(S,S_p)_2$-**195**[a]	2	$AgNO_3$ (7.4)	$(CH_2)_2Ph$	Me	72	90	99 (*R*)
3[115]	$(S,S_p)_2$-**195**[a]	1	$AgNO_3$ (3.7)	Me	CH_2OBn	24	98	97 (*R*)
4[115]	$(S,S_p)_2$-**195**[a]	0.5	$AgNO_3$ (1.85)	Me	CH_2OBn	24	74	96 (*R*)
5[115]	$(S,S_p)_2$-**195**[a]	4	$AgNO_3$ (14.8)	$(CH_2)_3OTIPS$	CH_2OBn	48	95	97 (*R*)
6[115]	$(S,S_p)_2$-**195**[a]	2	$AgNO_3$ (7.4)	$(CH_2)_3OTIPS$	CH_2OBn	72	95	97 (*R*)
7[154]	$(4R,5R,S,S_p)_2$-**194**[b]	2	AgTFA (7.5)	$(CH_2)_2Ph$	Me	60	94	99.6 (*R*)
8[154]	$(4R,5R,S,S_p)_2$-**194**[b]	0.5	AgTFA (1.86)	$(CH_2)_2Ph$	Me	60	79	97 (*R*)
9[154]	$(4R,5R,S,S_p)_2$-**194**[b]	2	AgTFA (7.5)	$(CH_2)_2OTIPS$	Me	60	73	96 (*R*)
10[154]	$(4R,5R,S,S_p)_2$-**194**[b]	2	AgTFA (7.5)	$(CH_2)_2NBnBoc$	Me	60	64	93 (*R*)
11[154]	$(4R,5R,S,S_p)_2$-**194**[b]	2	AgTFA (7.5)	Me	CH_2OBn	60	84	99 (*R*)
12[154]	$(4R,5R,S,S_p)_2$-**194**[b]	4	AgTFA (15)	$(CH_2)_3OTIPS$	CH_2OBn	84	51	97 (*R*)

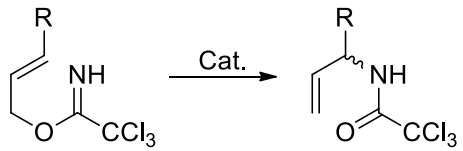
Table 3 – Palladacycle-catalysed enantioselective rearrangement of allylic trifluoroacetimidate **201**, for the synthesis of quaternary centers (Scheme 58, Figure 11). [a] With 4 equivalents (per cat.) of 1,8-bis(dimethylamino)naphthalene. [b] With 3 equivalents (per cat.) of 1,8-bis(dimethylamino)naphthalene.

1.7.1.3 Rearrangement of Allylic Trichloroacetimidates

The trichloroacetimidate substrate **203** was proposed to be an ideal candidate for the asymmetric allylic imidate rearrangement due to its ease of formation (reaction of an allylic

alcohol and trichloroacetonitrile under basic conditions), relative ease of product amide deprotection and its diverse use in synthesis. However, the number of reports on the asymmetric rearrangement of trichloroimidates is relatively few compared with the trifluoro-analogue.

The first attempts to develop this reaction were hindered by slow reaction rates, poor yields, and low enantioselectivities.[82] In 2003, Overman and co-workers made a breakthrough when they showed that $(S,R_p)_2$-**197** (COP-Cl) catalyses the rearrangement of (*E*)-**203** in excellent yield and enantioselectivity with no need for pre-activation with silver salts (Scheme 59).[155]



(*E*)-**203** **204**

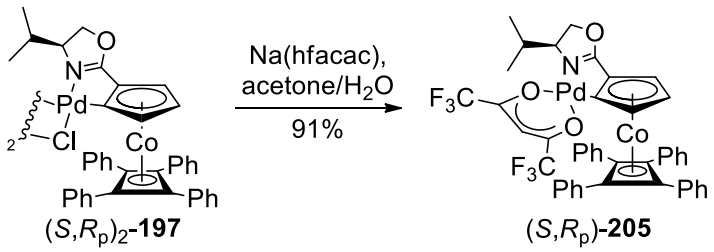
Scheme 59

Using a catalyst loading of 5 mol %, COP-Cl could catalyse the rearrangement at room temperature in 18 hours giving good yields and enantioselectivities over a number of substrates (Table 4, entry 1). An increased overall yield could be obtained by reaction at 38 °C, with little change in enantioselectivity (entry 2). Catalyst loading could also be decreased to 1 mol % by increasing the substrate concentration from 0.6M to 1.2M (entry 3). The catalyst was shown to be tolerant of a range of Lewis basic functionalities, giving excellent yields and selectivity (entry 4).[155]

Chloride-bridged dimer $(S,R_p)_2$-**197** has limited solubility in many solvents notwithstanding dichloromethane. This prompted the synthesis of the monomeric hexafluoroacetylacetonate (hfacac) complex (S,R_p)-**205**, by a simple ligand substitution reaction (Scheme 60).[156] The rearrangement could be now carried out in a number of solvents including THF and MeCN, with no significant drop in yield or enantioselectivity (entries 5 and 6).

Entry	Cat. Precursor	Cat. Loading [mol %]	T [°C]	Solvent	*t* [h]	R	Yield [%]	*ee* [%] (config.)
1[155]	$(S,R_p)_2$-**197** [a]	5	rt	CH_2Cl_2	18	Pr	80	94 (*S*)
						Me	85	92 (*S*)
						$(CH_2)_2Ph$	83	96 (*S*)
2[155]	$(S,R_p)_2$-**197** [a]	5	38	CH_2Cl_2	18	Pr	99	95 (*S*)
						^{i}Bu	95	96 (*S*)
						Cy	82	96 (*S*)
3[155]	$(S,R_p)_2$-**197** [b]	1	38	CH_2Cl_2	18	^{i}Bu	92	98 (*S*)
4[155]	$(S,R_p)_2$-**197** [a]	5	38	CH_2Cl_2	18	$(CH_2)_3OAc$	97	92 (*S*)
						$(CH_2)_2COMe$	98	95 (*S*)
						$CH_2OTBDMS$	98	96 (*R*)
						$(CH_2)_3NBn(Boc)$	96	95 (*S*)
5[156]	(S,R_p)-**205**[c]	5	50	THF	5	Pr	93	91 (*S*)
					8	Me	94	91 (*S*)
					8	^{i}Bu	99	98 (*S*)
6[156]	(S,R_p)-**205**[c]	1	50	MeCN	20	Pr	82	92 (*S*)
					22	Me	91	91 (*S*)
					29	^{i}Bu	95	95 (*S*)
7[157]	$(S,R_p)_2$-**197**[c]	0.25	70	MeCN	48	Pr	88	92 (*S*)
						Me	82	89 (*S*)
						Bn	68	92 (*S*)
8[115]	$(S,S_p)_2$-**195**[d]	0.25	60	CH_2Cl_2	24	$(CH_2)_2Ph$	99	95 (*R*)

Table 4 - Enantioselective rearrangement of allylic trichloroacetimidate (*E*)-**203**, catalysed by planar chiral palladacycles (Scheme 59). [a] Substrate concentration of 0.6 M. [b] Substrate concentration of 1.2 M. [c] Substrate concentration of 2.6 M. [d] With 3.7 equivalents of $AgNO_3$ and 1 mol % of 1,8-bis(dimethylamino)naphthalene.



Scheme 60

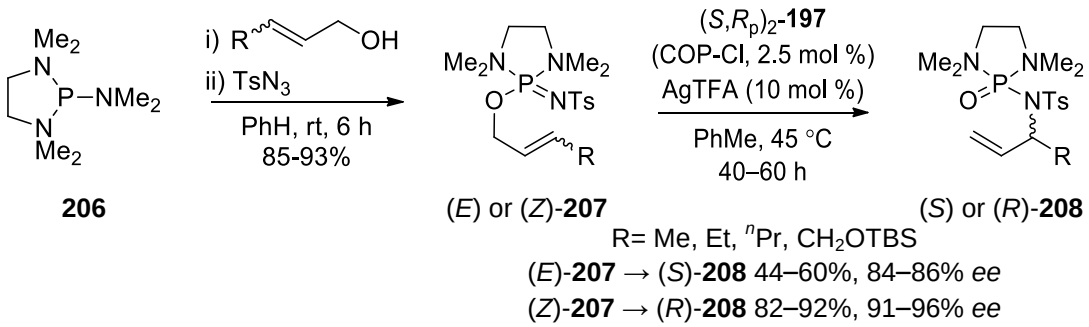
It has also been shown that COP-Cl reactions can be carried out in MeCN, wherein catalyst loading can be significantly reduced to 0.25 mol % (entry 7).[157] Under these conditions reaction time and temperature were increased to 48 hours and 70 °C respectively to compensate for the low catalyst loading, but there was no major loss in yield or selectivity. Lastly, a FOP catalyst was shown to be active for the rearrangement, although it has only been demonstrated on one substrate (entry 8).[115] Activation of FOP $(S,S_p)_2$-**195** with 3.7 equivalents of silver nitrate gave a catalyst with comparable activity to that seen in the COP systems.

1.7.2 Related [3,3]-Sigmatropic Rearrangements Catalysed by Planar Chiral Palladacycles

An analogous reaction to the allylic imidate rearrangement is the [3,3]-aza-phospha-oxa-Cope rearrangement of imino-diazaphospholidines **207** into phosphoramides **208** (Scheme 61). The reaction is driven by the increased stability of the P=O over the P=N bond, with DFT studies of the transformation revealing an energy change for the process of −24.4 kcal mol^{-1}.[158] The process has been shown to proceed at room temperature when catalysed by $PdCl_2(MeCN)_2$,[159] and as such it was an ideal candidate for catalysis by planar chiral palladacycles.

Initial studies proved unsuccessful, with a number of palladium(II) complexes giving little/no selectivity or yield for the process. The most promising result was gained using catalyst $(S,R_p)_2$-**197** (COP-Cl), where reaction with (*E*)-**207** (R = Et), gave (*S*)-**208** in 30% yield (70% *ee*) at 100 °C in toluene, but a byproduct arising from the formal [1,3]-rearrangement was also seen. It was found that the addition of silver salts, most notably

silver trifluoroacetate, significantly increased the yield and selectivity of the reaction, whilst diminishing the formation of the [1,3]-rearrangement product. Under optimized conditions, using a substrate concentration of 0.8–2.0 M, a series of imino-diazaphospholidines were successfully rearranged to give the corresponding phosphoramides.[158]



206 (*E*) or (*Z*)-**207** (*S*) or (*R*)-**208**

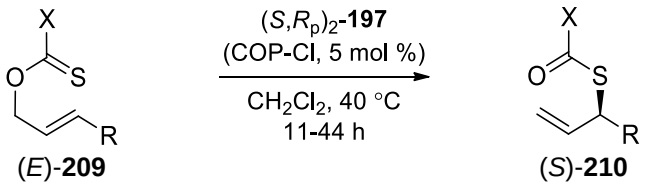
R= Me, Et, ^{n}Pr, CH_2OTBS

(*E*)-**207** → (*S*)-**208** 44–60%, 84–86% *ee*

(*Z*)-**207** → (*R*)-**208** 82–92%, 91–96% *ee*

Scheme 61

Related [3,3]-sigmatropic rearrangements of prochiral *O*-allyl carbamothioates have also been shown to be successfully catalysed by COP-Cl, to form chiral *S*-allyl carbamothioates (Scheme 62).[14] A series of carbamothioates (*E*)-**209** were rearranged into (*S*)-**210** using 5 mol% of $(S,R_p)_2$-**197** in good yields, albeit that the enantioselectivities obtained were lower than that seen in the allylic imidate rearrangement.



(*E*)-**209** (*S*)-**210**

X= NMe_2, $N(CH_2)_3$

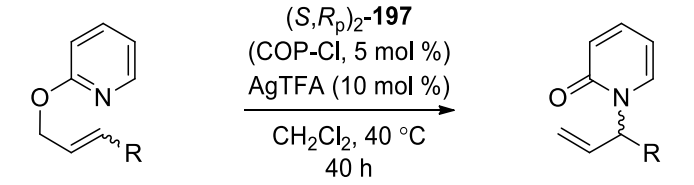
R= ^{n}Pr, $CH_2OTBDMS$, CH_2OH, $CH_2NPh(Boc)$

55–99% yield, 61–87% *ee*

Scheme 62

Another related [3,3]-rearrangement is that used in the formation of chiral 2-pyridones **211** from 2-alkoxypyridines **212** (Scheme 63).[160] Under optimized conditions, catalyst $(S,R_p)_2$-**197** (COP-Cl), with the addition of 10 mol % of silver trifluoroacetate, can facilitate the rearrangement in moderate to good yields and enantioselectivities over a number of substrates. The methodology could also be extended to form substituted heterocycles

containing an α-stereogenic center by using substrates containing quinoline, isoquinoline and benzothiazole heterocycles.



(*E*) or (*Z*)-**211** (*S*) or (*R*)-**212**

R= Et, ^{n}Pr, Ph, $CH_2OTBDMS$

(*E*)-**211** → (*S*)-**212** 33–91% yield, 47–86% *ee*

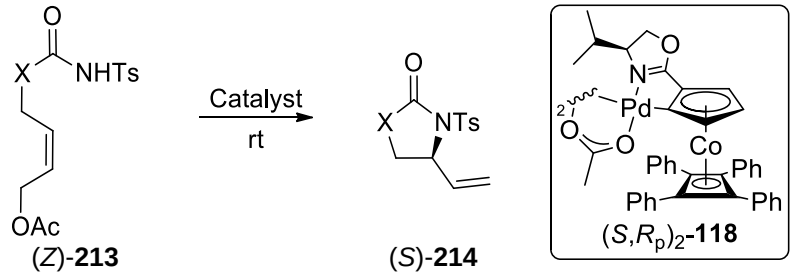
(*Z*)-**211** → (*R*)-**212** 61–93% yield, 83–96% *ee*

Scheme 63

1.7.3 Miscellaneous Reactions Catalysed by Planar Chiral Palladacycles

1.7.3.1 Intramolecular Aminopalladation

In 2002, Overman an co-workers published the enantioselective synthesis of vinyl-substituted 2-oxazolidinones **213** from (*Z*)-allylic acetates **214** using FOP catalyst $(S,R_p)_2$-**188** (Scheme 64, Table 5).[161]



(*Z*)-**213** (*S*)-**214** $(S,R_p)_2$-**118**

Scheme 64

Utilising 5 mol % of catalyst loading and 4 equivalents of silver trifluoroacetate, the reaction went to completion giving excellent yield and good enantioselectivity (entry 1). The catalyst loadings could also be significantly reduced, with only a slight reduction in yields, although selectivities remained consistent, (entries 2 and 3). Enantioenriched 2-pyrrolidinones and 2-imidazolidinones (from (*Z*)-**213** where X = CH_2 and NH respectively) could also be prepared in similar fashion, with comparable yields and enantioselectivities (entries 4 and 5). It

should be noted that the *Z* configuration of the starting allylic *N*-arylsulfonylcarbamate was shown to be essential for the process, as the *E* stereoisomer of **213** underwent the transformation slowly at room temperature giving poor selectivity (22% yield after 4 days, 65% *ee*).

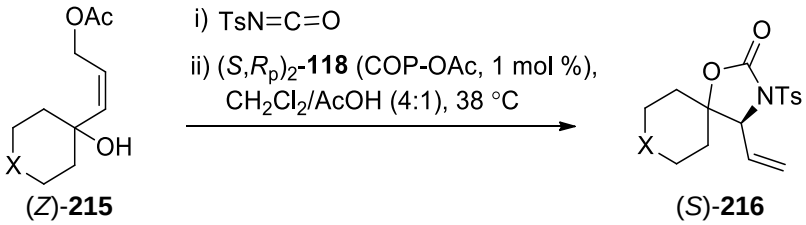
Entry	Cat. Precursor	Cat. Loading [mol %]	Additive (mol %)	X	Solvent (ratio)	*t* [h]	Yield [%]	*ee* [%] (config.)
1[161]	$(S,R_p)_2$-**188**[a]	5	AgTFA (20)	O	CH_2Cl_2/$MeNO_2$ (1:1)	48	96	91 (*S*)
2[161]	$(S,R_p)_2$-**188**[a]	1	AgTFA (4)	O	CH_2Cl_2/$MeNO_2$ (1:1)	48	91	90 (*S*)
3[161]	$(S,R_p)_2$-**188**[a]	0.5	AgTFA (2)	O	CH_2Cl_2/$MeNO_2$ (1:1)	48	86	91 (*S*)
4[161]	$(S,R_p)_2$-**188**[a]	5	AgTFA (20)	NH	CH_2Cl_2/$MeNO_2$ (1:1)	48	96	90 (*S*)
5[161]	$(S,R_p)_2$-**188**[a]	5	AgTFA (20)	CH_2	CH_2Cl_2/$MeNO_2$ (1:1)	48	95	90 (*S*)
6[162]	$(S,R_p)_2$-**118**[b]	1	None	O	CH_2Cl_2	6	>99	71 (*S*)
7[162]	$(S,R_p)_2$-**118**[b]	5	None	O	CH_2Cl_2/AcOH (19:1)	4.5	>99	90 (*S*)
8[162]	$(S,R_p)_2$-**118**[b]	1	None	O	CH_2Cl_2/AcOH (4:1)	10	94	92 (*S*)
9[162]	$(S,R_p)_2$-**118**[b]	1	None	O	AcOH	16	75	90 (*S*)

Table 5 – Palladacycle-catalysed asymmetric formation of heterocycles *via* intramolecular aminopalladation (Scheme 64). [a] Substrate concentration of 1.0 M [b] Substrate concentration of 1.5 M.

It was later discovered, (in 2005), that $(S,R_p)_2$-**118** (COP-OAc) was a superior catalyst for the transformation and did not require prior activation with silver salts.[162] Reaction of (*Z*)-**213** (where X = O) with 1 mol % of COP-OAc was sufficient for the reaction to reach completion, albeit with low selectivity (entry 6). Increasing the catalyst loading and using acetic acid as co-solvent improved the reaction time, yield and selectivity for the reaction (entry 7). A compromise of yields and selectivities was found using a 4:1 mixture of dichloromethane and acetic acid, giving (*S*)-**214** in 94% yield and 92% *ee* after 10 hours

(entry 8). Performing the reaction in only acetic acid caused erosion in yield and an elongated reaction time (entry 9).

The formation of spirocyclic 4-vinyloxazolidin-2-ones **216** was also shown to be possible using a modified procedure (Scheme 65). Crude allylic *N*-tosylcarbamates prepared *in situ* from the reaction of allylic alcohol (*Z*)-**215** with *N*-sulfonylisocyanate gave an intermediate carbamate, which upon subjection to the catalytic conditions used previously, gave spirocycles (*S*)-**216** in good yield and selectivity.

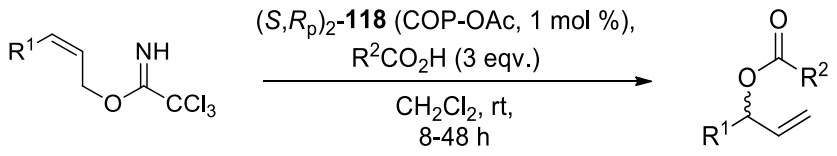


Scheme 65

1.7.3.2 Allylic Ester and Ether Synthesis

During investigations into the formation of the aforementioned 4-vinyloxazolidin-2-ones, Overman and his group noticed that whilst using an acetoxybutenyl trichloroacetimidate as a starting reagent, they isolated a ~1:1 mixture of desired 4-vinyloxazolidine and an allylic ester. The result suggested that S_N2' displacement of the imidate by acetic acid was occurring competitively with intramolecular cyclisation of the imidate nitrogen.[15]

Subsequent experiments revealed that using an excess of acetic acid (or other carboxylic acids) and 1 mol % of the acetate-bridge dimer $(S,R_p)_2$-**118** (COP-OAc), (*Z*)-**203** could be converted enantioselectively into allylic esters **217** (Scheme 66).[15,163] This esterification reaction has been adapted to give an iterative approach to the synthesis of 1,3-polyols.[164]



(*Z*)-**203** **217**

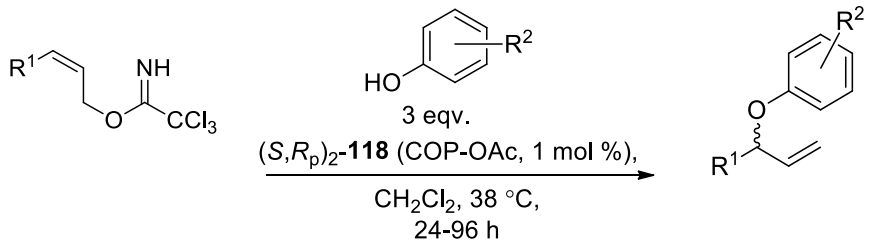
R^1= ^{n}Pr, ^{i}Bu, Cy, CH_2OPMB, CH_2OH, CH_2OAc, $(CH_2)_2Ph$

R^2 = Me, Ph

45–98% yield, 93–99% *ee*

Scheme 66

This type of process could be exploited further by exchanging the nucleophile used in the transformation. Allylic aryl ethers **218** could be formed from (*Z*)-**203** using similar conditions used in the formation of the allylic esters, by utilising substituted phenols as the external nucleophiles instead of carboxylic acids (Scheme 67).[16] A wide range of imidate substrates were subjected to 1 mol % of $(S,R_p)_2$-**118** (COP-OAc) and 3 equivalents of a variety of phenols to give an assortment of allylic ethers in good yield and high selectivity. The process was not as facile as in the ester formation, and reaction times were significantly longer with the transformations having to be carried out at 38 °C.



(*Z*)-**203** **218**

R^1= ^{n}Pr, $CH_2OTBDPS$, CH_2OTBS

R^2 = 4-Me, 4-OMe, 4-Cl, 2-Br, 4-OAc, 2-OAc, 3-CHO, 2,6-F, 1-napthyl

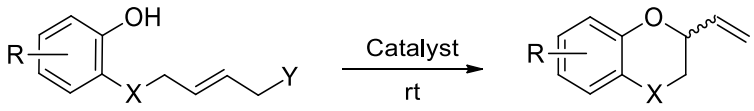
61–97% yield, 90–98% *ee*

Scheme 67

A further extension of this work was presented in 2012, reporting the formation of 2-vinyl oxygen heterocycles *via* an intramolecular displacement reaction (Scheme 68, Table 6).[165] Using the trichloroimidate moiety as a leaving group, reaction of substituted phenol (*E*)-**219** with catalyst *ent*-$(S,R_p)_2$-**118** [*ie*. $(R,S_p)_2$-**118**] gave vinyl-1,4-benzodioxane **220** (where X = O) in 92% yield and 92% *ee* (entry 1). Enantioselectivity could be increased and reaction time shortened by increasing the catalyst loading (entry 2). The transformation could also be

used to form benzoxazines (X = NTs) with excellent yield and enantioselectivity seen (entry 3).

Substitution of the leaving group to acetate allowed for access to 2-vinylchromanes (X = CH_2), and the reaction of such starting alkenes was found to be enhanced by the addition of heterogeneous bases, in particular potassium fluoride. Optimized conditions allowed for 2 mol % of $(S,R_p)_2$-**118** (COP-OAc) to be employed leading to the formation of substituted chromanes **220** (X = CH_2) in good yield and enantioselectivity (entries 4–7).



(*E*)-**219** **220**

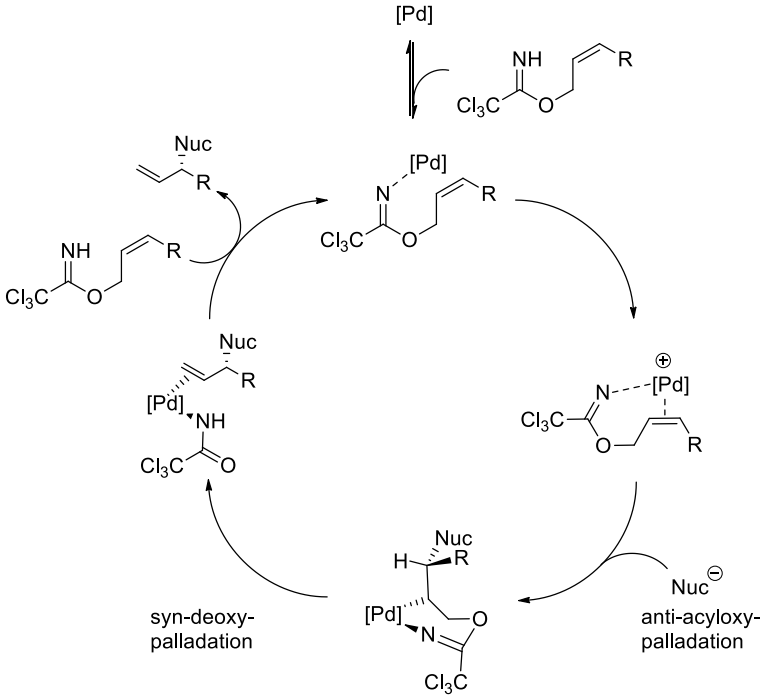
Scheme 68

Entry	Catalyst	Cat. Loading [mol %]	Additive (equiv.)	X	Y	R	Solvent	*t* [h]	Yield [%]	*ee* [%] (config.)
1	*ent*-$(S,R_p)_2$-**118** [a]	0.5	None	O	$OC(=NH)CCl_3$	H	CH_2Cl_2	72	92	92 (*S*)
2	*ent*-$(S,R_p)_2$-**118**[a]	2	None	O	$OC(=NH)CCl_3$	H	CH_2Cl_2	18	90	94 (*S*)
3	*ent*- $(S,R_p)_2$-**118**[a]	2	None	NTs	$OC(=NH)CCl_3$	H	CH_2Cl_2	15	98	98 (*S*)
4	$(S,R_p)_2$-**118**[b]	2	KF (1)	CH_2	OAc	H	CH_2Cl_2	24	89	94
5	$(S,R_p)_2$-**118**[b]	2	KF (1)	CH_2	OAc	4-Br	CH_2Cl_2	6	82	88
6	$(S,R_p)_2$-**118**[b]	2	KF (1)	CH_2	OAc	4-Br	$CHCl_3$	10	92	90
7	$(S,R_p)_2$-**118**[b]	2	KF (1)	CH_2	OAc	4-OMe	CH_2Cl_2	36	95	95

Table 6 - Palladacycle-catalysed asymmetric formation of heterocycle **220** (Scheme 68). [a] Substrate concentration of 0.2 M [b] Substrate concentration of 1.0 M.

The mechanism for the COP-OAc catalysed allylic ester and ether processes has been postulated based on DFT calculations and system modelling, and has been extended to the intramolecular formation of vinyl oxygen heterocycles.[166] Deuterium labelling studies

revealed that the reaction of trichloroacetimidates with carboxylic acids proceeded in an overall antarafacial fashion, requiring that the steric courses of the oxypalladation and deoxypalladation steps be different.[167] DFT calculations suggested that the most likely mechanism was where palladium-imidate coordination occurs first, followed by alkene coordination to form a chelated-cationic palladium intermediate (Scheme 69). *Anti*-acyloxypalladation by external nucleophilic attack at the C3 position of the palladium-imidate complex generates an intermediate with a palladium-carbon bond. Subsequent *syn*-deoxypalladation forms an alkene trichloroacetate complex which undergoes substitution with the substrate allylic trichloroimidate, liberating the chiral allylic product and regenerating the palladium-imidate intermediate.[167] The DFT calculations support the proposal that chelation of the allylic trichloroacetimidate substrate generates a cationic palladium(II)-alkene complex, which thereafter significantly lowers the activation energy for oxypalladation, (by up to 19.2 kcalmol^{-1}).[167]

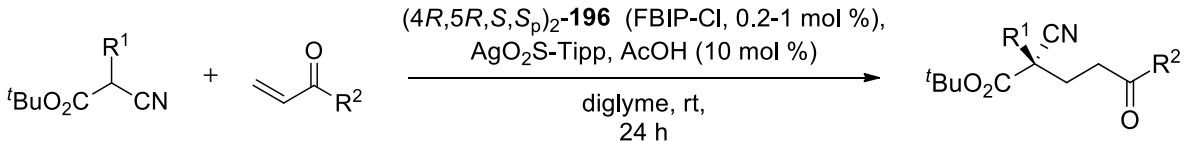


Scheme 69

1.7.3.3 Michael Additions Catalysed by Planar Chiral Palladacycles

Peters has had particular success in utlising ferrocene bis-imidazole and oxazoline derived palladacycles (FBIP and FOP), in particular $(4R,5R,S,S_p)_2$-**196** (FBIP-Cl) and $(S,S_p)_2$-**195** (FOP-Cl), in a number of transformations that do not involve a [3,3]-rearrangement. An area in which good results have been gained is in forming new carbon-carbon bonds *via* conjugate addition reactions.

In 2008 Peters and co-workers published work using $(4R,5R,S,S_p)_2$-**196** (FBIP-Cl) to generate quaternary stereocenters by reaction of cyano esters **221** with vinyl ketone analogues **222** (Scheme 70).[168] Under optimized conditions, catalyst loadings could be reduced to as low as 0.2 mol % with Michael-adduct products **223** isolated in excellent yields and good enantioselectivities. During the optimization studies, a silver salt derived from 2,4,6-tri(iso-propyl)benzenesulfonic acid, (AgO_2S-Tipp), was shown to give the best enantioselectivities, and it was reasoned that this was due to the large sulfonate counterion formed upon activation of the catalyst. This process has also been repeated using cyclohex-2-enone as the Michael acceptor.[169]



221 **222** **223**

R^1 = Ph, 4-BrC_6H_4,4-FC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4
R^2 = Me, Et, ^{n}Pr, Ph
90–99% yield, >98:2 dr, 77–95% *ee*

Scheme 70

In 2010, Peters published work on a domino aza-lactone formation-Michael addition reaction of benzoylated racemic amino acids **224** with β-substituted enones **225** catalysed by FBIP-Cl (Scheme 71).[170] Under optimized conditions, FBIP-Cl was shown to efficiently

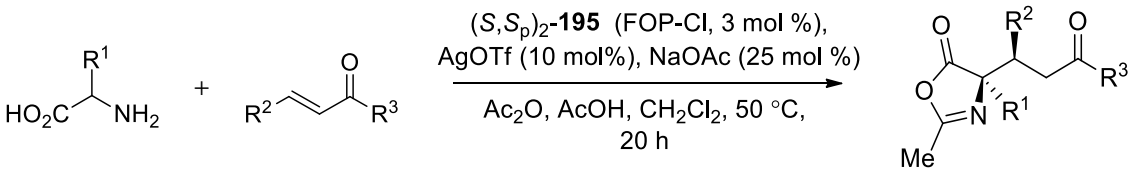
catalyse Michael addition of a range of substrates, after activation with silver triflate, to give azalactones **226** in good yield and enantioselectivity.

224 **225** **226**

R^1= Me, Et, ^{n}Pr, Bn
R^2 = Ph, ^{i}Pr, 3,4-$(OMe)_2C_5H_3$, 4-Br C_6H_4,4-$OMeC_6H_4$, 4-ClC_6H_4, 4-$O_2NC_6H_4$
R^3 = Me, Et, Ph
64–95% yield, >98:2 dr, 76–99% *ee*

Scheme 71

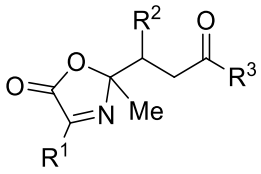
The method was later updated, (in 2012), to a one-pot strategy using unprotected amino acids **227** and acid anhydrides. Although the reaction was successful and selectivities were excellent, the *in situ* formation of the required benzoyl protected amines caused issues when trying to isolate the product aza-lactones, due to the use of a large excess of benzoyl anhydride.[171,172] Instead, acetic anhydride was used in conjunction with $(S,S_p)_2$-**195** (FOP-Cl), to give aza-lactones **228** in moderate yield and excellent selectivities (Scheme 72).[173] After screening, FOP-Cl was chosen as catalyst, as FBIP-Cl gave a mixture of product and unwanted C2 addition adduct **229** (6:1, Figure 13) under identical conditions.



227 **225** **228**

R^1= Me, Et, ^{n}Pr, ^{n}Bu, ^{i}Bu
R^2 = Me, Ph, ^{i}Pr, 3,4-$(OMe)_2C_5H_3$, 4-Br C_6H_4,4-$OMeC_6H_4$, 4-ClC_6H_4, 4-$O_2NC_6H_4$
R^3 = Me, Et
26–72% yield, >99:1 dr, 62–99% *ee*

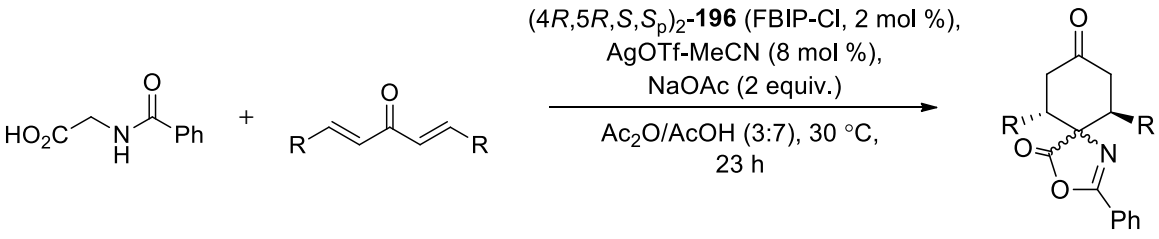
Scheme 72



229

Figure 13

Peters has also published an extension of the methodology to the synthesis of spirocyclic azlactones by a double Michael addition.[174] By taking a benzoyl protected amino acid **230** and reacting in the presence of (4*R*,5*R*,*S*,S_p)$_2$-**196** (FBIP-Cl) with dienones **231**, it was possible to access the *trans* spirocyclic aza-lactones *trans*-**232** in moderate yields and good enantioselectivities (Scheme 72). Interestingly, the group found that the active catalyst in this process, after treatment of FBIP-Cl with silver triflate and acetonitrile, was (4*R*,5*R*,*S*,S_p)-**233** (figure 14).

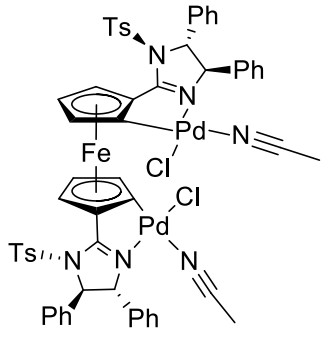


230 **231** *trans*-**232**

R = Ph, 4-Br C_6H_4,4-OMeC_6H_4, 4-ClC_6H_4, 4-MeC_6H_4

43–89% yield, 63–96% *ee*

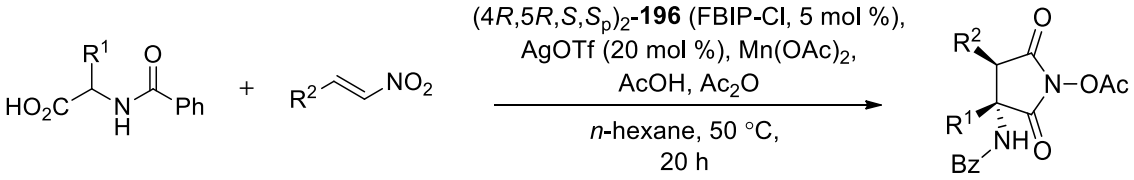
Scheme 72



(4*R*,5*R*, S_p,S_p)-**233**

Figure 14

In 2013, this reaction was extended further by changing the Michael acceptor to a nitroolefin **234**. Using a similar protocol to the previous reactions, but adding a stoichiometric oxidant [$Mn(OAc)_2$], Peters was able to synthesise quaternary amino succinimides *via* a Nef-type reaction from benzyl-protected amino acids **235** (Scheme 73).[175]



R^1= Me, Et, ^{n}Pr, ^{n}Bu,
R^2 = Ph, 4-Br C_6H_4,4-$OMeC_6H_4$, 4-ClC_6H_4, 4-MeC_6H_4
78–95% yield, 78–94% *ee*

Scheme 73

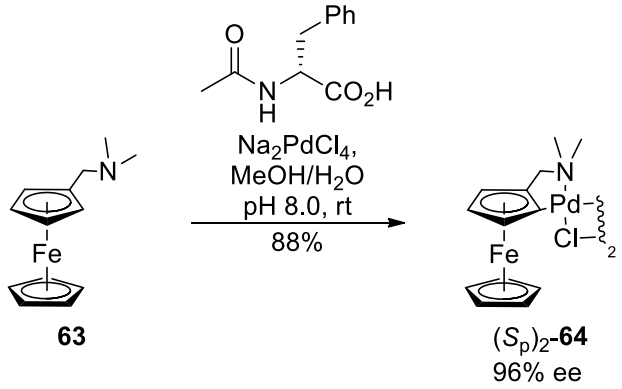
Under optimized conditions, 5 mol % of $(4R,5R,S,S_p)_2$-**196** (FBIP-Cl) could catalyse the reaction to give succinimides **235** in excellent yields and enantioselectivities over a number of substrates.

Chapter 2 – Results & Discussion 1

2.1 Introduction

There are numerous examples in the literature of chiral palladacycle-catalysed asymmetric transformations,[14–16,82,115,153,165,175,176] as a consequence new methods for generating the aforementioned palladacycles stereoselectively are in great demand. Many examples of these palladacycles involve an auxiliary-mediated diastereoselective C–H activation protocol as the basis for forming the palladium-carbon bond.[17,98,102,115,117,123,177–179] There are far fewer examples of planar chiral palladacycles derived from enantioselective C–H activation of an achiral ligand.

In 1979 Sokolov reported the *N*-acetyl amino acid mediated enantioselective palladation of *N,N*-dimethylaminoferrocene **63**,[80] and more recently Richards reported updated conditions allowing for the generation of palladacycle $(S_p)_2$-**64** in 96% *ee* using *N*-acetyl-*D*-phenylalanine (Scheme 74).[132]

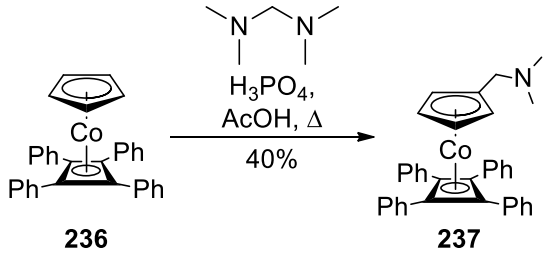


Scheme 74

Cobalt sandwich complexes have been shown to be versatile ligands in the synthesis of planar chiral palladium complexes.[17,117,180] As such, this chapter serves to showcase the use of prochiral cobalt sandwich complex ligands, towards the development of new cobalt amino palladacycles (CAP). These were derived using the enantioselective palladation protocol and their application in asymmetric synthesis was tested subsequently.

2.2 Synthesis of Amine Ligands

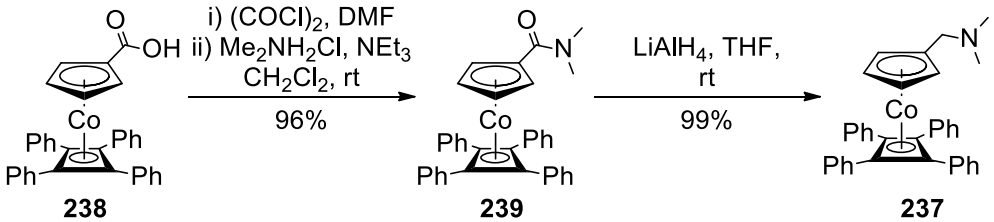
A range of amine substrates were first synthesised for testing in asymmetric palladation reactions. Amine **237** was synthesised using a literature Mannich-type procedure, where complex **236** was reacted with *N,N,N',N'*-tetramethyldiaminomethane under acidic conditions to yield the amine in modest yield (Scheme 75).[181] Due to the low yield achieved, relatively harsh conditions and laborious work-up an alternative path to **237** was sought.



236 **237**

Scheme 75

A relatively facile route to amine **237** was realised by reaction of acid **238** (Chapter 4)[182] under Vilsmeier conditions with oxalyl chloride and catalytic DMF to form an acid chloride, which was subsequently treated with dimethylamine hydrochloride to give amide **239** (Scheme 76). Formation of the amide was confirmed by the appearance of two broad methyl singlets in the ^{1}H-NMR spectrum of **239**; the lines broadened due to hindered rotation about the C–N bond. Reduction with lithium aluminium hydride gave amine **237** in 95% yield over the 2 steps.

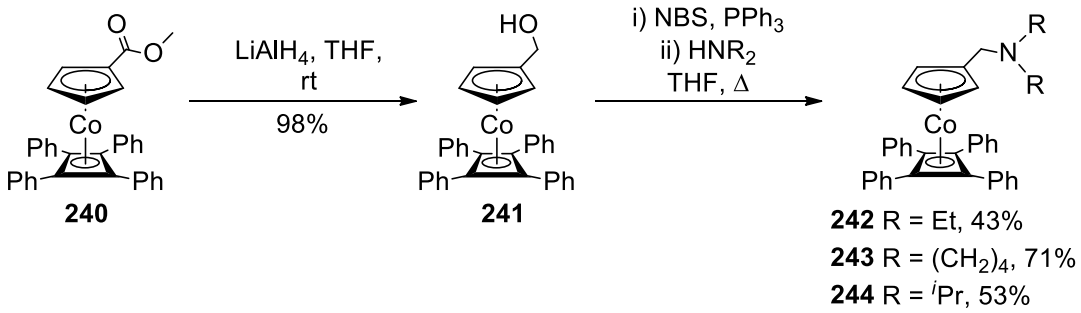


238 **239** **237**

Scheme 76

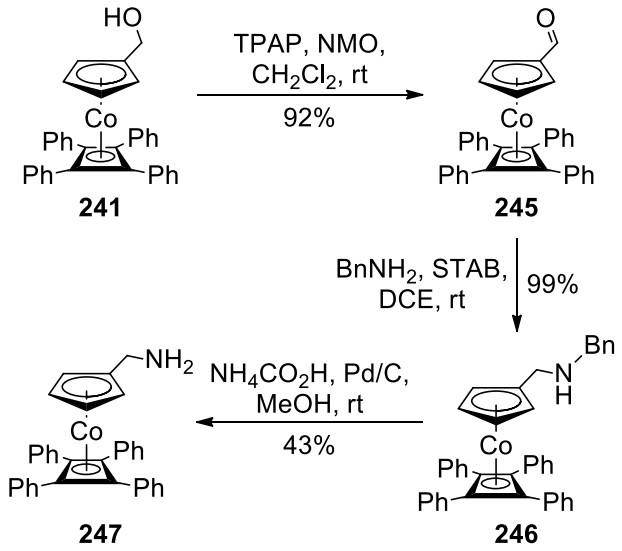
A different strategy was employed for the synthesis of amines **242–244** (Scheme 77). Reduction of ester **240**[183] with LAH gave primary alcohol **241** in good yield. A Mitsunobu-

type reaction of alcohol **241** with PPh_3 and NBS gives an intermediary bromomethyl metallocene, which can be quenched with a variety of secondary amines to give **242–244**, in a range of yields. Differentially substituted amines can also be synthesised using a similar method, where R groups associated with the amine are no longer equivalent.[184] These complexes are potentially interesting because when palladated diastereoisomers are formed, the resultant complexes would be chiral at nitrogen, as well as planar chiral.



Scheme 77

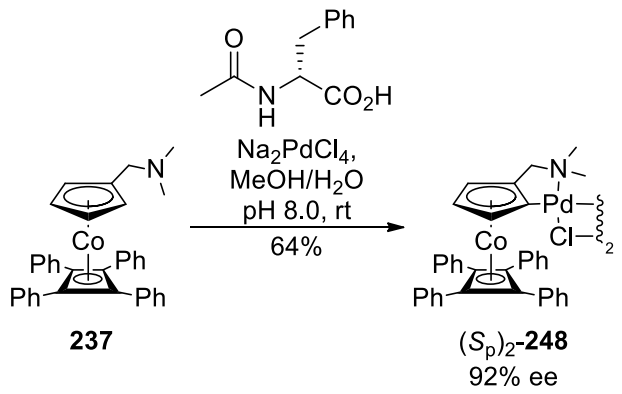
Other amines could be accessed *via* oxidation of primary alcohol **241** with TPAP/NMO to give aldehyde **245**, which readily underwent reductive amination with benzylamine to give secondary amine **246** in near quantitative yield (Scheme 78). Subsequent hydrogenolysis gave the debenzylated primary amine **247** and not (η^5-methylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene) cobalt, an alternative reduction product which would have resulted from hydrogenolysis of the nitrogen-carbon (α-metallocene) bond. Further differentially substituted amines have been formed previously by installation of a Cbz-group and subsequent reduction.[184]



Scheme 78

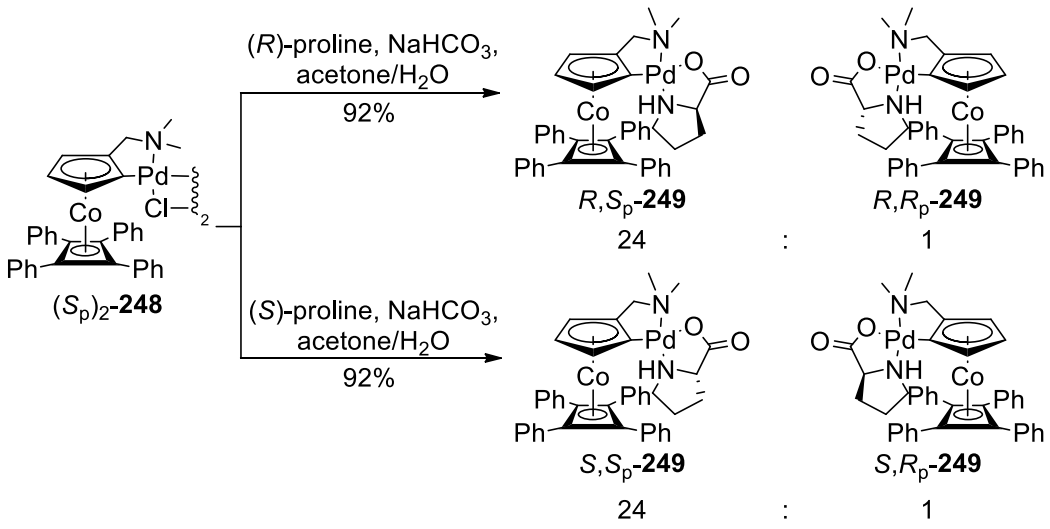
2.3 Amino Acid Mediated Enantioselective Palladation

Amine **237** was first to be tested for the chiral carboxylate mediated asymmetric palladation, as it is the cobalt analogue of ferrocene **63**, which is known to be a good substrate for similar reactions.[185] Also the palladation of amine **237** has been reported previously using a mixture of lithium tetrachloropalladate and sodium acetate in methanol.[180] Treatment of the achiral tertiary amine with sodium tetrachloropalladate and *N*-acetyl-*D*-phenylalanine under basic conditions at room temperature gave new chloride-bridged cobalt amine palladacycle or CAP-Cl $(S_p)_2$-**248** in 64% yield as a 1:1 mixture of *cis*:*trans* isomers (Scheme 79).



Scheme 79

The enantiomeric excess of palladacycle $(S_p)_2$-**248** was calculated to be 92% following reaction with (*R*)-proline (Scheme 80) and subsequent comparison of the resultant diastereomeric ^{1}H-NMR signals for adducts *R*,S_p-**249** and *R*,R_p-**249**. In particular, comparison of the signals for cyclopentadienyl protons for *R*,S_p-**249** at 4.43 ppm (t, 1H) and for *R*,R_p-**249** at 4.36 ppm (brs, 2H) proved useful due to baseline separation of signals (Figure 15 [a]). The chemical shifts were confirmed to be indeed signals relating to stereoisomers and not *cis*/*trans* regioisomers, by reaction of palladacycle $(S_p)_2$-**248** with (*S*)-proline to form related adducts *S*,S_p-**249** and *S*,R_p-**249** (Figure 15 [b]). Comparison of spectra reveals that the cyclopentadienyl signals for *S*,S_p-**249** are indeed present in the spectra for *R*,S_p-**249**. This could be further confirmed by palladation of amine **237** by heating with palladium(II) acetate in toluene for 2 hours to afford racemic acetate dimer *rac*-**250** (Scheme 81). Treatment with (*S*)-proline, gave the expected 1:1 mixture of *S*,S_p-**249** and *S*,R_p-**249**, and the chemical shifts for each respective diastereoisomer match that seen previously (Figure 15 [c]). The asymmetric palladation was also performed at 0 ^{o}C and for a longer reaction time, both of which yielded no significant change in enantioselectivity or reaction yield.



Scheme 80

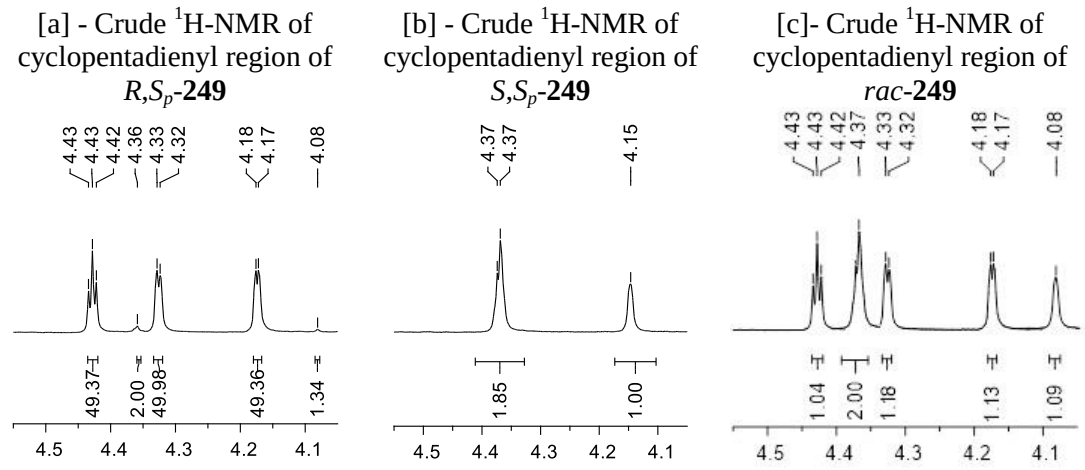
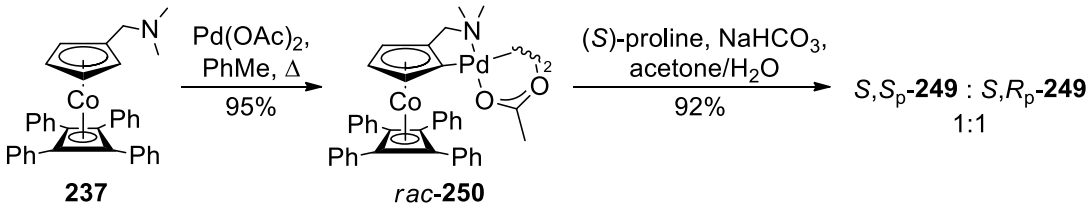


Figure 15



Scheme 81

The absolute configuration of $(S_p)_2$-**248** was established by recrystallisation of the proline adduct S,S_p-**249** from CH_2Cl_2/hexane. A small quantity of the major diastereoisomer was obtained pure and the element of planar chirality was confirmed to be S_p by X-ray crystallography (Figure 16).

The pyrrolidine ring is disordered, with alternative sites for one methylene group at C(24a) and C(24b). The other four members of the ring are co-planar, so that the five-membered ring adopts an envelope shape with the flap either up or down, with respect to the plane. Also, compound S,S_p-**249** was insoluble in a variety of solvents, both polar and apolar. This is due to the nature of this pyrrolidine ring, where the hydrogen of C(22) and nitrogen N(21) are pointing up with respect to the pyrrolidine ring, allowing for hydrogen bonding between molecules. This is the opposite for R,S_p-**249**, and as such it is soluble in most solvents.

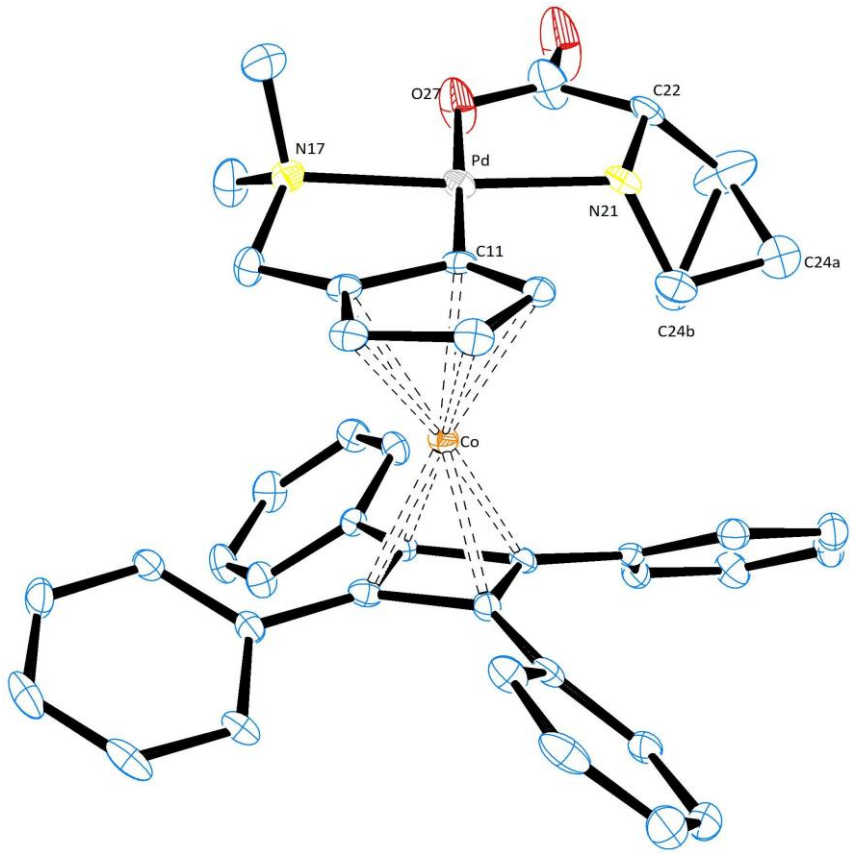
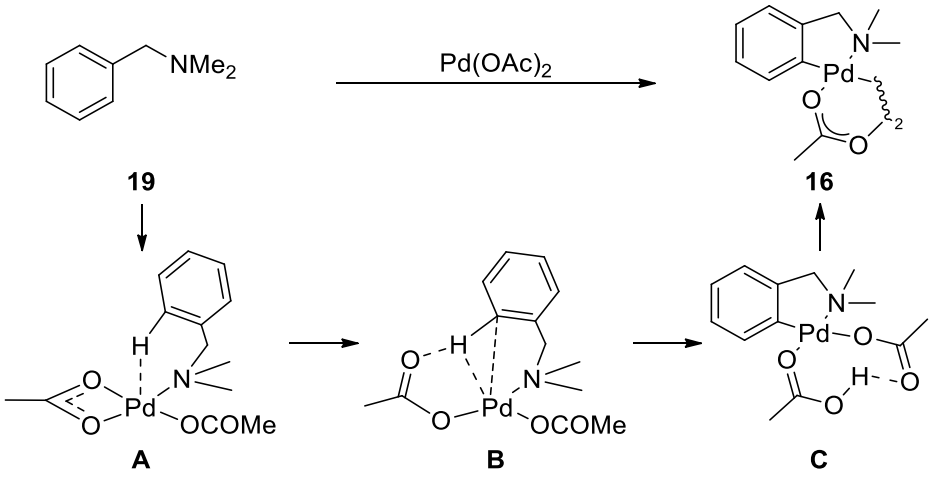


Figure 16 – X-Ray representation of *S*,S_p-**249**. Principal bond lengths [Å] include: Pd–C(11) 1.973(4), Pd–N(17) 2.092(4), Pd–N(21) 2.023(4), Pd–O(27) 2.082(4); mean Co–C(C4-ring) 1.991(5), mean Co–C(cp) 2.07(2). Principal angles [°] include: C(11) –Pd-N(17) 82.68(18), N(21) –Pd–O(27) 82.509(16).

2.4 Origins of Enantioselectivity and Mechanism

The high enantioselectivity showed by the palladation suggests that the reaction must proceed with a chiral palladium intermediate, induced by coordination of a carboxylate ligand derived from the deprotonation of *N*-acetyl-*D*-phenylalanine.[186] Palladation reactions in which palladium acetate and/or palladium-carboxylate species are present have been shown to proceed *via* a concerted metallation deprotonation (CMD) pathway, as discussed in the previous chapter (Scheme 82), whereby the carbon-palladium bond is formed as the carbon-hydrogen bond is broken.[187] It was shown that the cyclopalladation of dimethylbenzylamine **19** to palladacycle **16** proceeds *via* an intermediate where η^1- and η^2-

acetate ligands are associated (A). Dissociation of an oxygen of the η^2-acetate ligand *via* transistion state 1 (TS1, Figure 17) results in an agostic and H-bonded intermediate (B) which is set up for hydrogen transfer. This occurs with minimal energy activation *via* TS2 to give (C).[64,186]



Scheme 82

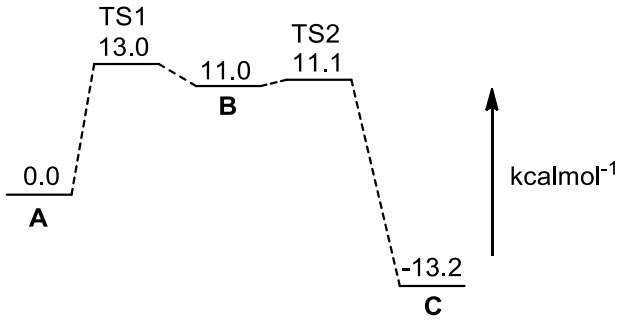
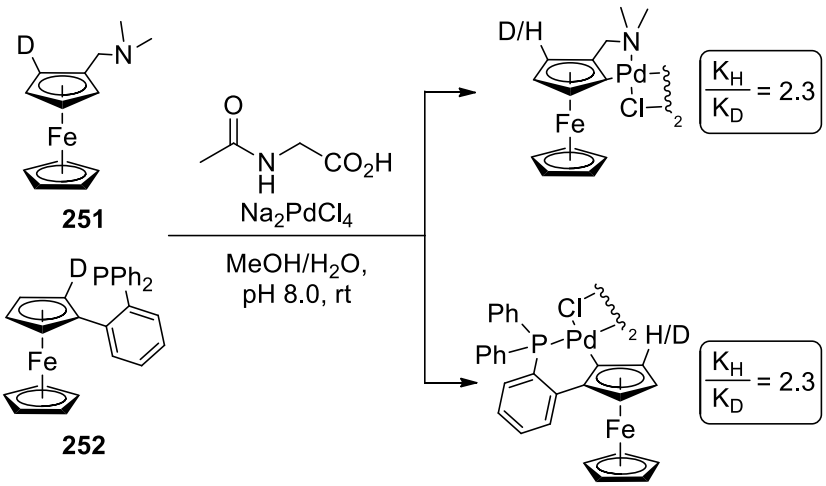


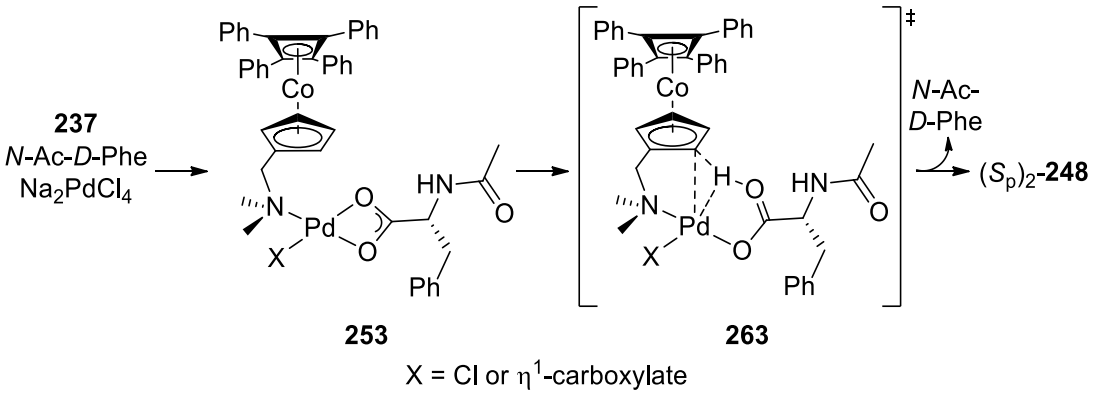
Figure 17

A mechanism consistent with carboxylate accelerated cyclopalladation has an intramolecular isotope effect of >1.[188–193] It has been shown that a value of 2.5 is seen for the palladation of *N*,*N*-dimethyl- derivative **237**,[184] which is very similar to a value of 2.3 determined for the palladation of ferrocene analogues (**251** and **252**) under the same conditions (Scheme 83).[132] The consistent nature of these results demonstrates that the amino acid mediated palladation is following the predicted CMD pathway resulting in the preferential formation of the S_p palladacycle.



Scheme 83

A proposed mechanism for the process based on DFT calculations of the cyclometallation of dimethylbenzylamine **19** by palladium(II) acetate,[64] and an extension of this process to the *N*-acetyl-*D*-phenylalanine mediated palladation of phosphinoferrocenes, is postulated in Scheme 84.[64,186] In this process amine **237**, amino acid and sodium tetrachloropalladate initially form a chiral amine-η^2-carboxylate ligated complex **253**. This leads to transition state **254** in which the carbonyl oxygen of the η^1-carboxylate ligand participates in the deprotonation, (assisted by an agostic interaction), with simultaneous formation of the carbon-palladium bond in the vacant coordination site. Replacement of ligand X with the nitrogen of the amino acid to form a chelate would possibly be geometrically incompatible with the carbonyl groups participation as a base.



Scheme 84

To probe this reaction further a non-linear experiment was undertaken, by varying the *ee* of the *N*-acetyl-*D*-phenylalanine used in the cyclometallation (Table 7, Figure 18). Conditions used were analogous to those for the previous palladation reactions, and the enantiomeric excesses were calculated by conversion of the respective chloride dimers to the R,S_p-**249** proline adducts. A small positive non-linear effect was seen with respect to the *ee* of metallocene $(S_p)_2$-**248**. This result is consistent with an active species monomer where neither the (*S*/*S*) nor (*R*/*R*) dimeric resting state is thermodynamically favored and therefore the (*S*/*R*) is.[194] It could also be possible that the deprotonation may be facilitated by a second η^1-carboxylate ligand, *i.e.* where ligand X (Scheme 84) is a carboxylate. The reaction would therefore be slower with the (*S*/*R*) intermediate monomer.

ee of *N*-Acetyl-*D*-Phenylalanine	Major Integral	Minor Integral	*ee* of $(S_p)_2$-**248**
0	1.00	1.00	0
27	1.13	0.92	42
50	1.15	0.48	65
75	1.03	0.26	78
100	1.00	0.06	94

Table 7 – Non-linear effect study of the enantioselective palladation of amine **237**

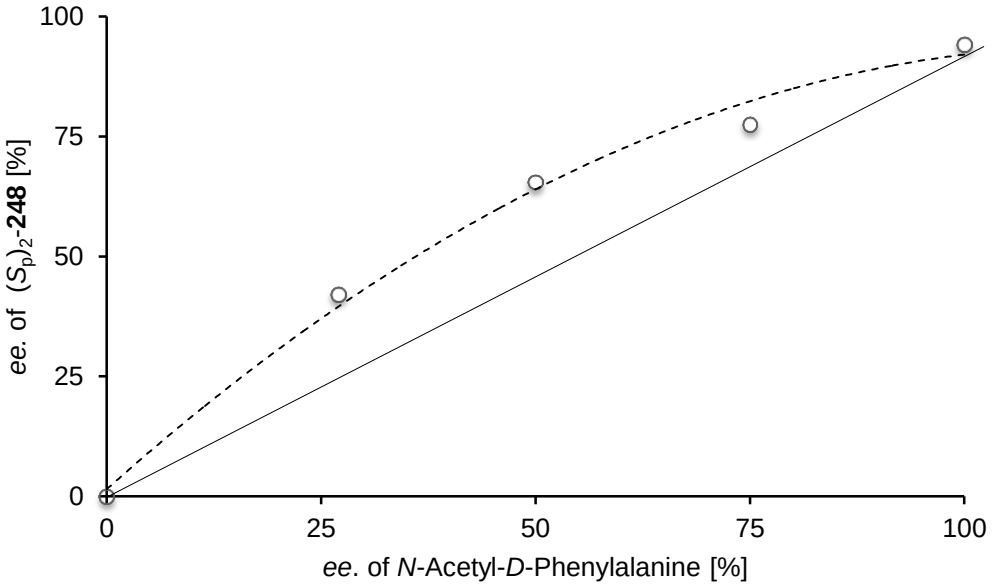


Figure 18 – Non-linear effect study of the enantioselective palladation of amine **237**

The transition state proposed for the CMD pathway may also give insight into the origins of the enantioselectivity for the palladation by making a comparison of the coordinated carboxylate ligand to torsions (designated ψ and φ, Figure 19) in peptide conformational analysis of similar examples such as Ac-ala-NHMe.[195] The extended β-conformation ($\psi \approx 120$, $\varphi \approx -120$) is the most stable in water.[196] In this transition state (**255**), the η^1-carboxylate ligand is orientated in such a way that the methine hydrogen of the stereogenic center is pointed towards the amine substituent.[185] Conversely, drawing the transition state for the minor product under the same conditions (**256**), it can be seen that the benzyl group at the stereogenic center would now be projecting towards the amine ligand. The pathway in which there is the least steric repulsion between the carboxylate and ligand would consequently be the more favorable, leading to the major stereoisomer seen.

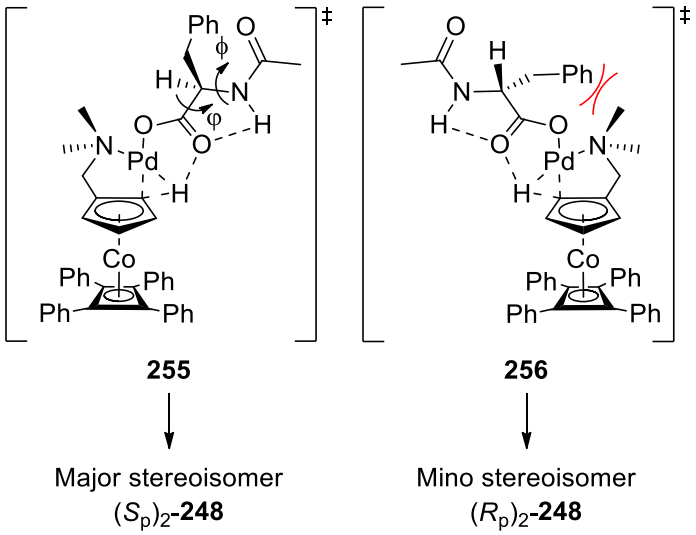


Figure 19

2.5 Resolution of Enantiomers & Ligand Substitution

The majority of palladacycles used as catalysts in the literature have chloride, acetate or acetylacetonate ligands; therefore a method for obtaining a diastereomerically pure variety of these types was needed. Fortunately proline adducts *R*,S_p-**249** and *S*,R_p-**249** could be readily separated *via* column chromatography as the major diastereoisomer *R*,S_p-**249** has a higher R_f value (0.24) than that of the minor *S*,R_p-**249** (0.16) in 2.5% MeOH/CH_2Cl_2. If

necessary, further purification by recrystallisation was accomplished from CH_2Cl_2/hexane, to give a diastereomerically pure sample, an example of which was analysed using X-ray crystallography (Figure 20). An absolute configuration parameter of 0.12(3) shows that the crystal is not racemic and provides further evidence for the element of planar chirality being S_p.

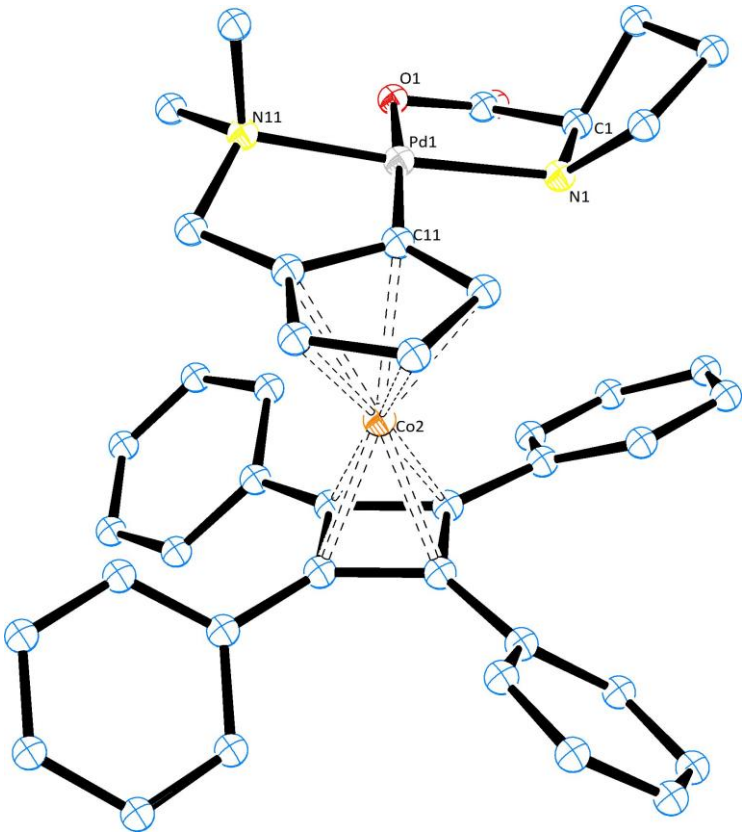
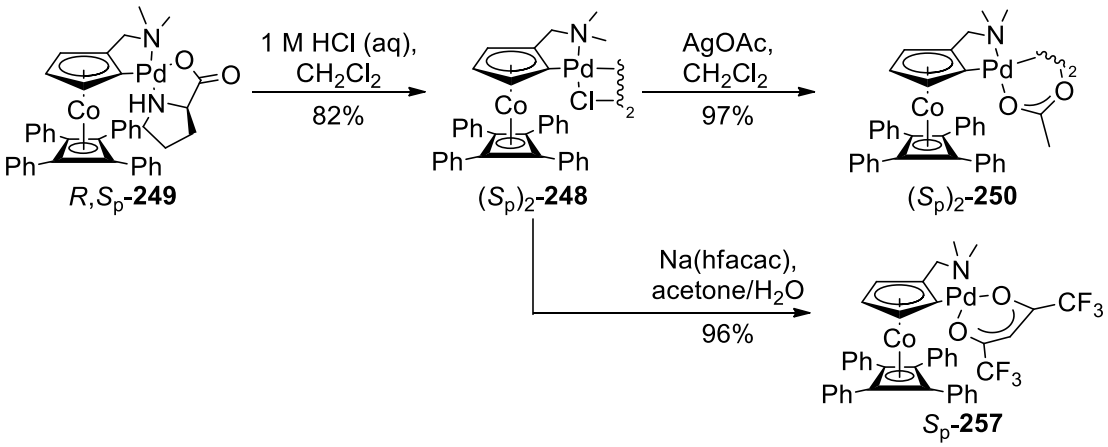


Figure 20 – X-Ray crystal structure of *R*,S_p-**249**. Principal bond lengths [Å] include: Pd–C(11) 1.981(2), Pd–N(1) 2.038(19), Pd–N(11) 1.978(4), Pd–O(1) 2.128(16); mean Co–C(C4-ring) 1.983(2), mean Co–C(cp) 2.068(2). Principal angles [°] include: C(11) –Pd–N(11) 82.02(9), N(1) –Pd–O(1) 82.509(16).

The previous example *S*,S_p-**249** showcased low solubility due to hydrogen bonding, as the pyrrolidine ring projects down towards the phenyl substituents. For *R*,S_p-**249** it can be seen that the pyrrolidinyl ring is projected up away from the phenyl substituents

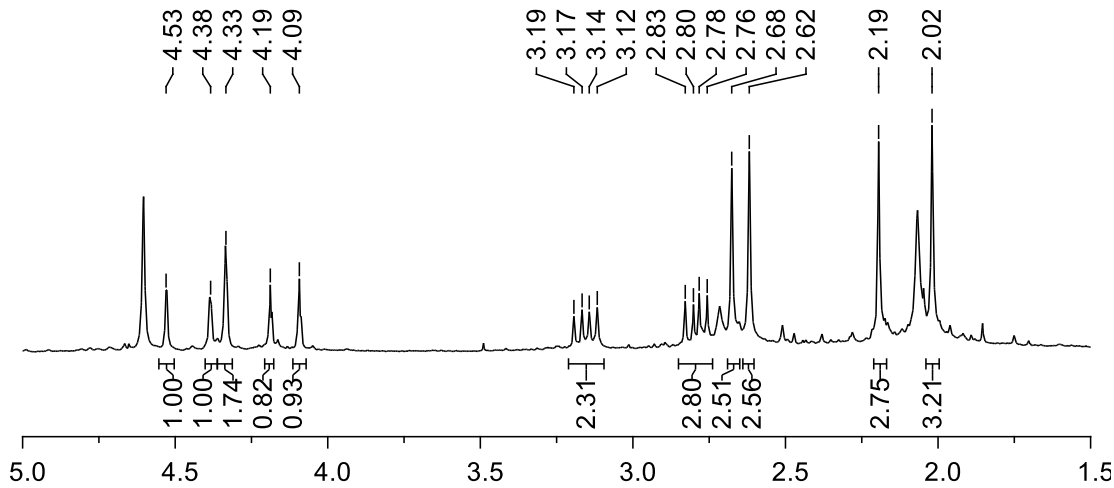
[C(4)–N(1)–Pd(1) 117.7°(13)] which disrupts hydrogen bonding and in turn increases solubility.

With a diastereomerically pure sample, conversion to the chloride-bridged dimer could be accomplished by reaction of *R*,S_p-**249** in CH_2Cl_2 as a biphasic mixture with aqueous 1 M HCl overnight to give enantiomerically pure chloride ligated palladacycle $(S_p)_2$-**248** (Scheme 85). The overall effect of this process can be seen in Figure 21 where the ^{1}H-NMR spectra for the crude materials for palladacycle $(S_p)_2$-**248** before and after the resolution are shown. The chloride dimer can be readily converted to the acetate-bridged dimer $(S_p)_2$-**250** by reaction with silver acetate in near quantitative yield. Complex $(S_p)_2$-**248** can also be reacted with Na(hfacac) in acetone/water to give monomer S_p-**257**. All attempts to form $(S_p)_2$-**250** and S_p-**257** directly from adduct *R*,S_p-**249** were unsuccessful.



Scheme 85

(S_p)$_2$-**248** before resolution:



(S_p)$_2$-**248** after resolution:

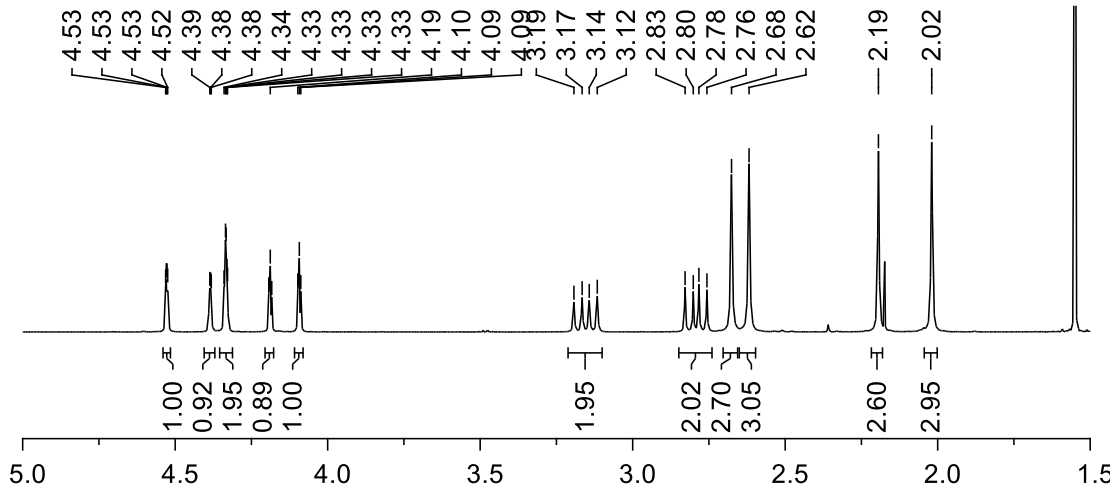


Figure 21

A racemic sample of complex **257** was synthesised using a method described previously in the chapter (Scheme 81), by reaction of the parent amine **237** with palladium acetate and subsequent ligand exchange with Na(hfacac). The structure of *rac*-**257** could be elucidated by recrystallisation from CH_2Cl_2/hexane and subsequent analysis using X-ray crystallography (Figure 22). Interestingly for this example, there is torsion of the palladium square-plane with respect to the cyclopentadienyl ring, pushing the co-ordination site *trans* to N(1) down towards the phenyl rings. This subsequently may have a positive or negative effect on catalytic activity and/or selectivity. Complex *rac*-**257** shows good agreement with the *trans*-influence associated with such square planar systems. This is a thermodynamic effect concerning the ability of a ligand to weaken the bond *trans* to it in preference to those

that are *cis*.[197] Studies on similar Pd(II) systems show that carbanion groups exert a superior *trans*-influence over other ligands such as amines. As such the bond *trans* to the carbanion ligand is weakened and in turn lengthened.[198] An analogous result can be seen with *rac*-**257**, where a carbanion-metal bond has a bond length of 1.955 Å, which is shorter than that of the bonds *cis* [Pd–N(1) 2.085 Å, Pd–O(1) 2.046 Å] and therefore a stronger bond. In turn the bond *trans* to C(5) [Pd–O(2)] is weakened and is lengthened to 2.119 Å.

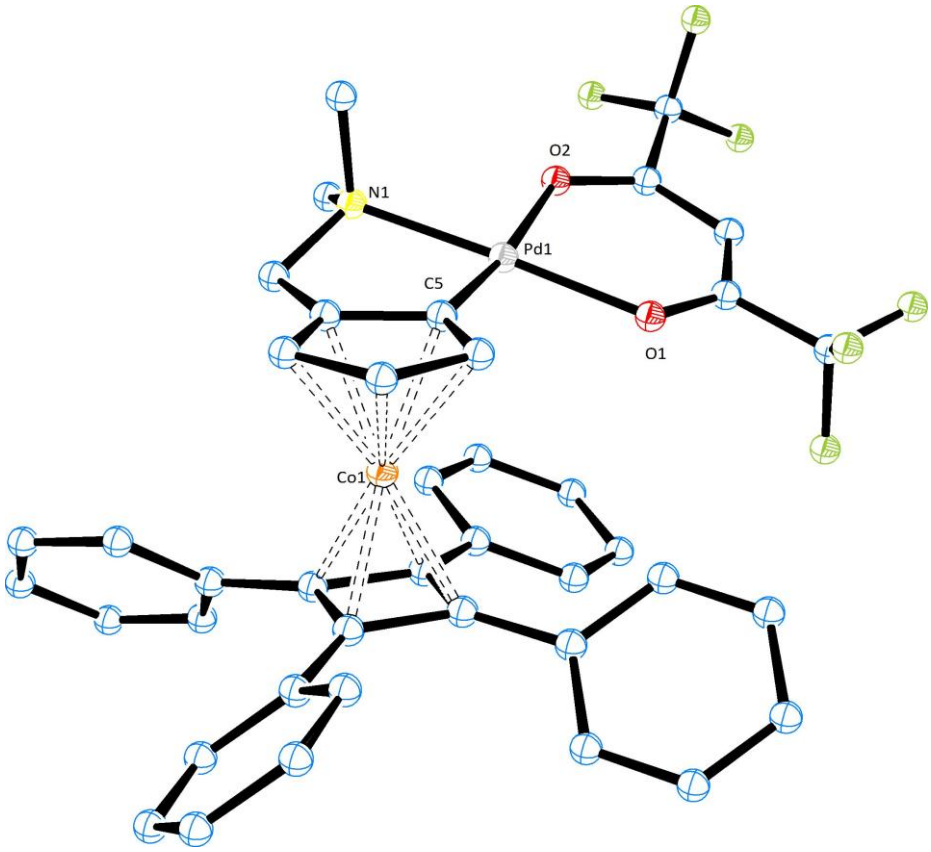
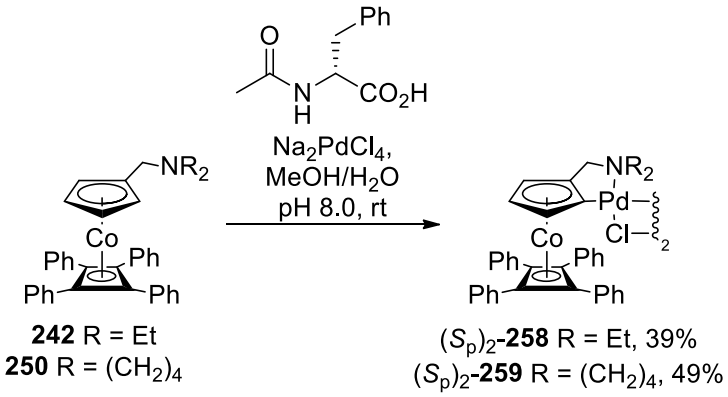


Figure 22 – X-Ray crystal structure of *rac*-**257**. Principal bond lengths [Å] include: Pd-C(5) 1.955(3), Pd-N(1) 2.085(3), Pd-O(1) 2.046(2), Pd-O(2) 2.119(2); mean Co-C(C4-ring) 1.979(3), mean Co-C(cp) 2.058(3). Principal angles [°] include: C(5)-Pd-N(1) 81.87(12), O(1)-Pd-O(2) 91.33(9).

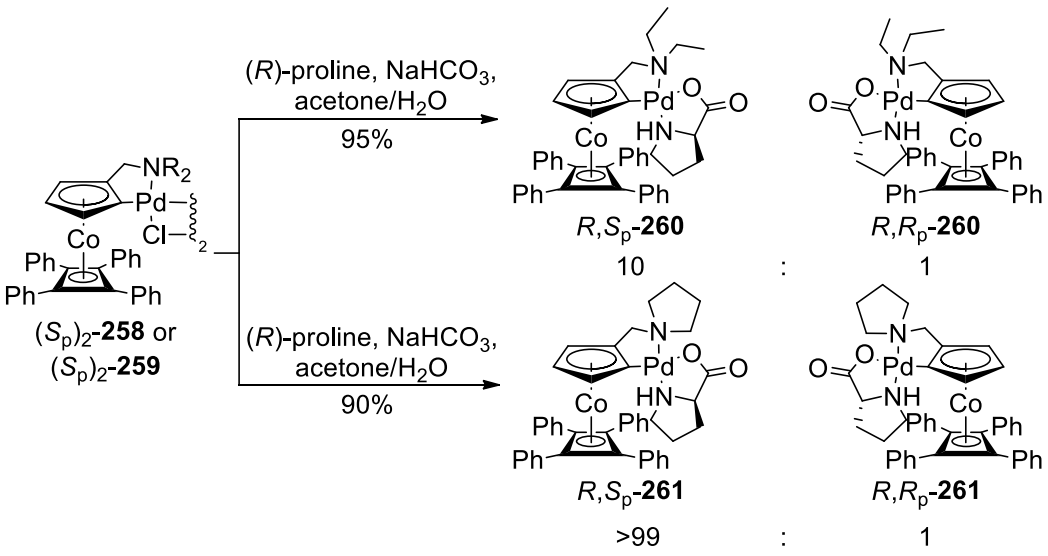
2.6 Extension of the Methodology

Amines **242**, **243**, **244**, **246** and **247** were also subjected to the same amino acid mediated palladation protocol as *N*,*N*-dimethyl analogue **237** yielding only two new palladacycles. Complexes $(S_p)_2$-**258** and $(S_p)_2$-**259** derived from *N*,*N*-diethyl- and pyrrolidinyl- complexes **242** and **243** respectively revealed the latter amines to be suitable for the reaction (Scheme 86). A decreased yield for the asymmetric palladation, when compared with $(S_p)_2$-**248**, for these amines suggests that these are limiting reagents for this process. Asymmetric palladation has also previously been carried out on differentially substituted amines (where R≠R), all with no success, inferring that such systems seem to have the wrong balance, in terms of electronics and sterics, to facilitate the cyclopalladation.[184]



Scheme 86

Utilising the same method for determining *ee* as for the *N*,*N*-dimethyl derivative, reaction of the palladacycles with (*R*)-proline revealed the *ee* of $(S_p)_2$-**258** to be 87% and for $(S_p)_2$-**259** to be 98% (Scheme 87, Figure 23 [a] and[b]). In the former case, the *ee* calculations were based on signals for cyclopentadienyl protons at 4.43 (major) and 4.38 ppm (minor). In the latter case, the *ee* determination could not be made directly from the ^{1}H-NMR of adduct *R*,S_p-**261** as the minor diastereoisomer could not be seen. Instead a ratio of diastereoisomers of >99:1 was assigned by reaction of complex $(S_p)_2$-**259** with (*S*)-proline to give *S*,S_p-**261** and spiking of the original *R*,S_p-**261** ^{1}H-NMR sample with *S*,S_p-**261**.



Scheme 87

[a] - ^{1}H-NMR spectrum of cyclopentadienyl region for the crude reaction mixture of R,S_p-**260**

[b] - ^{1}H-NMR spectrum of cyclopentadienyl region for the crude reaction mixture of R,S_p-**261**

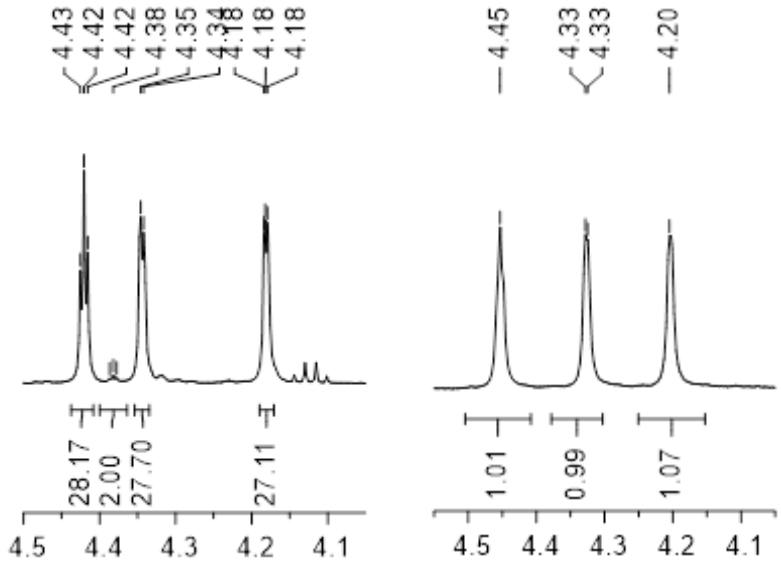


Figure 23

The absolute configuration of palladacycles $(S_p)_2$-**258** and $(S_p)_2$-**259** were initially assigned to be S_p by their respective values for specific rotation, where a positive value is R_p and negative is S_p (by comparison to known examples).[79] This was confirmed by the correspondence of the CD-spectra of these two additional palladacycles with the CD spectrum for $(S_p)_2$-**248** (Figure 24, in particular negative bands at 230 and 330 nm).

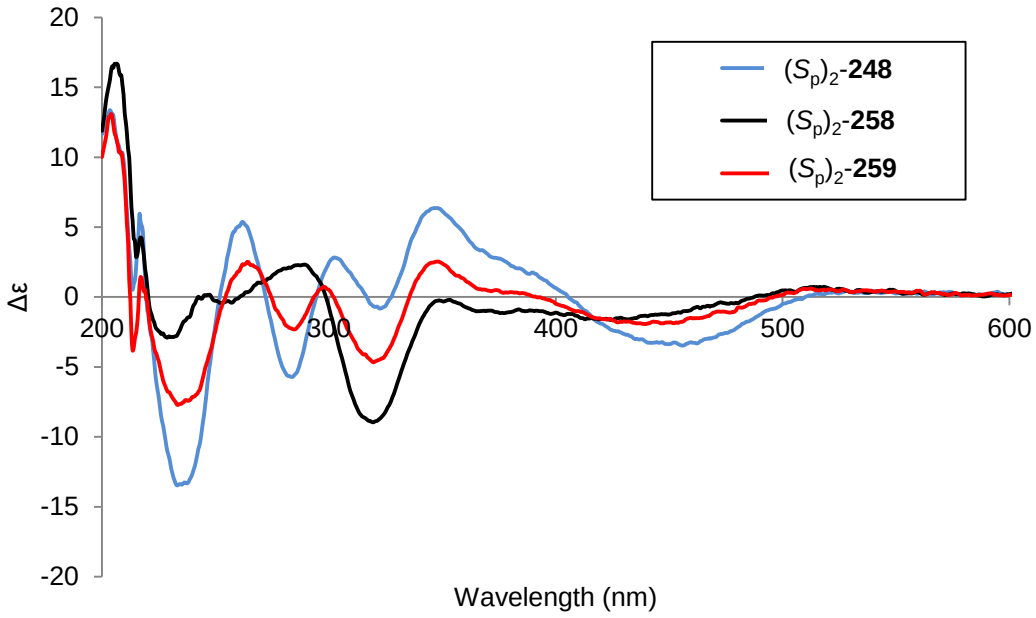


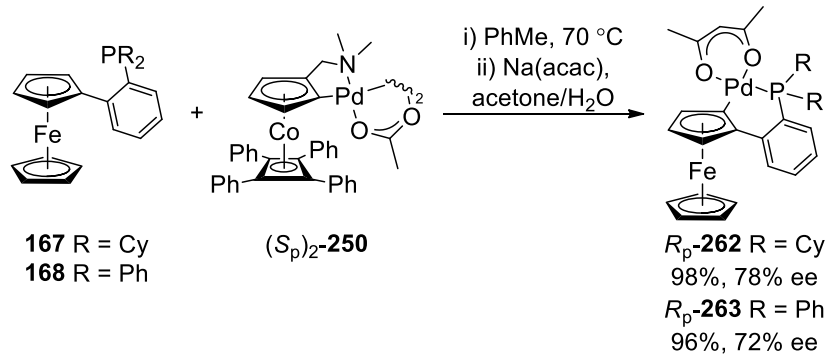
Figure 24 – CD spectra of palladacycles $(S_p)_2$-**248**, $(S_p)_2$-**258** and $(S_p)_2$-**259**.

2.7 Application in Asymmetric Synthesis

2.7.1 Transcyclopalladation

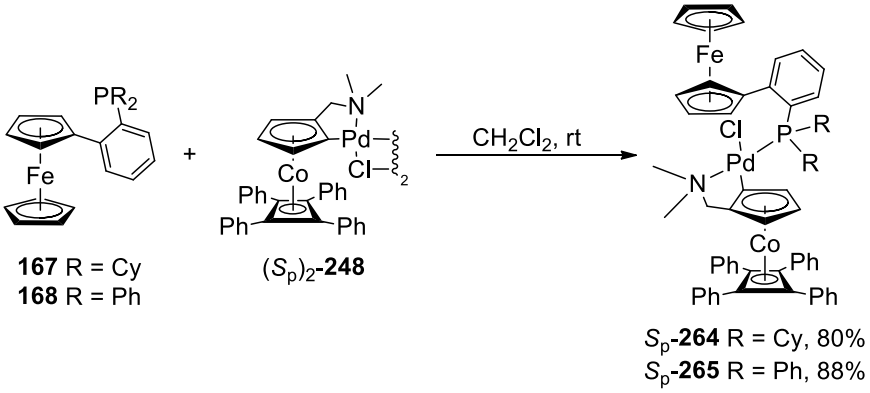
Investigation into the use of these new CAP complexes in asymmetric synthesis started with their application in transcyclopalladation reactions, a term coined to describe the transfer of cyclometalated ligands without the formation of dissociated metal salts.[199,200] As shown in the previous chapter, asymmetric transcyclopalladation has been carried out successfully using palladacycles derived from (*R*)-3-amino-3-phenyl-2,2-dimethylpropane with moderate selectivity,[134] and it has been reported that reaction of COP-OAc, (S,R_p)-**118**, with prochiral phosphines **167** and **168** gives phosphopalladacycles S_p-**262** and S_p-**263** in up to 95% *ee* (R = Cy).[135] Extension of this method to the complex derived from the *N*,*N*-dimethylamino derivative obtained following proline resolution proved successful (Scheme 88). Combination of $(S_p)_2$-**250** with phosphine **168** (R = Ph) followed by heating at 70 °C in toluene for 24 h initially gave an acetate bridged dimer phosphopalladacycle. Conversion to the monomeric acac derivative by treatment with sodium acetylacetonate gave R_p-**263** which was determined to have an enantiomeric excess of 72% by chiral HPLC analysis. In the

same way phosphine **167** (R = Cy) gave an *ee* of 78% for complex R_p-**262** following transcyclopalladation. The absolute configuration of the resultant phosphopalladacycles was confirmed by comparison of the values for specific rotation obtained to those in the literature.[135]



Scheme 88

Reaction of ligands **167** and **168** with chloride bridged palladacycle $(S_p)_2$-**248** resulted in the formation of monomeric adducts S_p-**264** and S_p-**265** (Scheme 89). Recrystallisation of S_p-**265** from CH_2Cl_2/hexane afforded crystals suitable for analysis by X-ray crystallography (Figure 25). In common with most other nitrogen ligand based palladacycles, the added phosphine is incorporated *trans* to the nitrogen, the thermodynamic ligand substitution product.[76]



Scheme 89

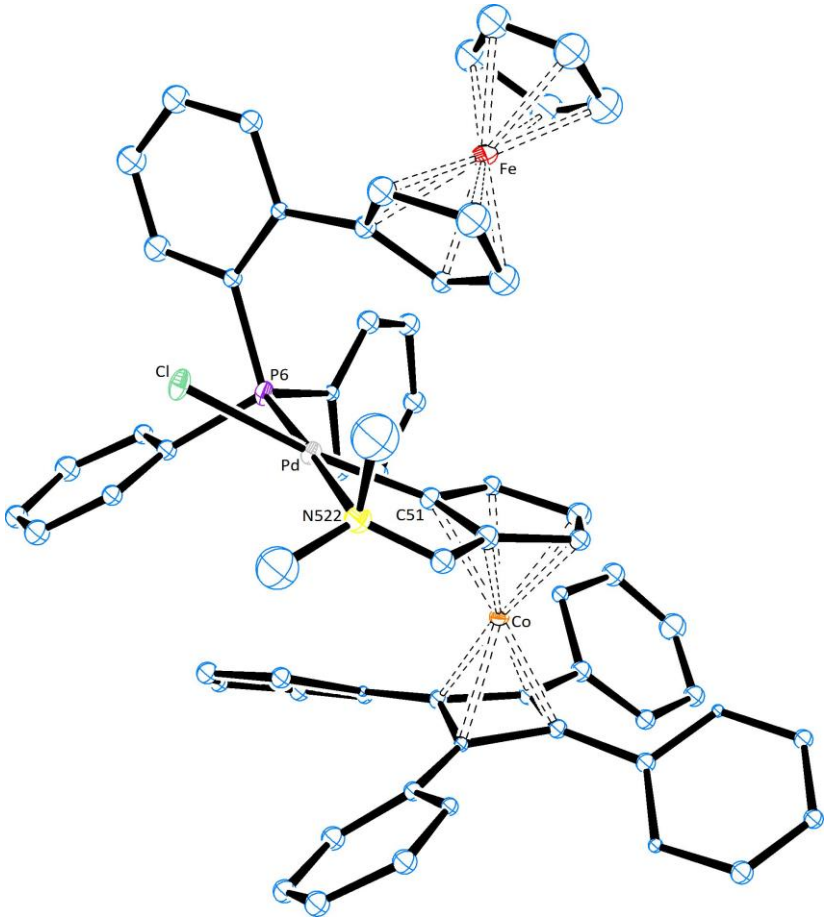
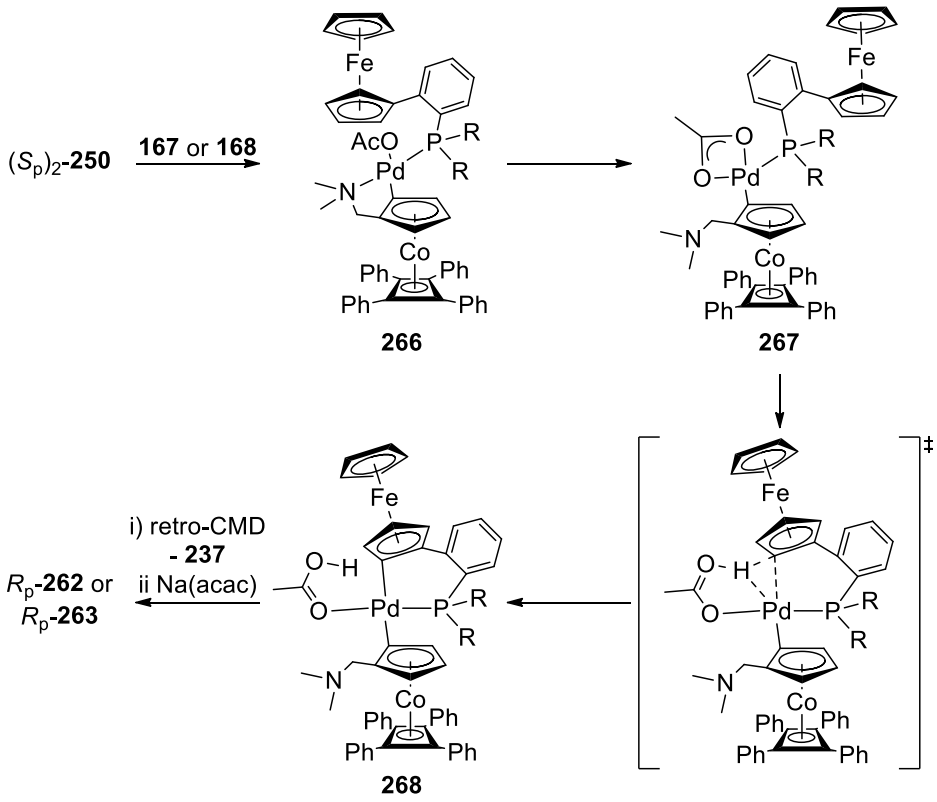


Figure 25 – X-Ray crystal structure of S_p-**265**. Principal bond lengths [Å] include: Pd–Cl 2.383(4), Pd–C(51) 2.004(16), Pd–N(522) 2.193(10), Pd–P(6) 2.271(4); mean Co–C(C4-ring) 1.97(4), mean Co–C(cp) 2.05(7), mean Fe–C(subs.-cp) 2.00(4), mean Fe–C(cp) 2.03(4). Principal angles [°] include: C(51) –Pd–N(522) 80.9(6), P(6) –Pd–Cl 87.8(2).[184]

The X-ray crystal structure of S_p-**265** provides understanding into the stereocontrol displayed by the transcyclopalladation process. The ferrocenyl group is pushed above the palladium square-plane, as beneath is blocked by the phenyl groups of the lower η^4-cyclobutadienyl moiety. This, coupled with the *trans*-to-nitrogen co-ordination geometry are instrumental in controlling the enantioselectivity of palladium transfer. A pathway for this process can be postulated (Scheme 90), based again on the cyclometallation of dimethylbenzylamine by palladium(II) acetate and related studies.[64,186] The process starts with formation of monomeric acetate compound **266** followed by dissociation of the amine ligand to form a η^2-

acetate bridged complex **267**. Acetate assisted concerted-metalation-deprotonation (CMD) gives intermediate complex **268**. Subsequent protonolysis of the cobalt complex carbon-palladium bond by retro-CMD releases amine **237** and gives an acetate ligated phosphopalladacycle, which dimerises to give an acetate dimer. Reaction with sodium acetylacetonate relinquishes the palladacycle products R_p-**262** and R_p-**263**.[135] Although rotation is possible about the carbon-palladium bond in monomeric acetate **267**, the conformer where the coordinated phosphine is orientated away from the dimethylaminomethyl moiety is favoured. As such the planar chirality displayed by this monodentate species is also a factor in controlling the enantioselectivity of the process.



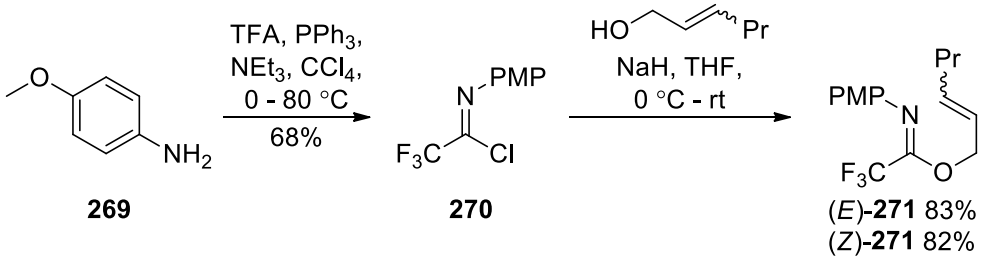
Scheme 90

2.7.2 Catalysis of the Allylic Imidate Rearrangement

It has been shown though kinetic and modeling studies, that in the COP-Cl catalysed allylic imidate rearrangement, the planar chirality is the key factor in controlling the facial selectivity of nitrogen addition to the alkene moiety.[167] This is bound *trans* to the oxazoline

nitrogen in the rate and enantioselectivity determining anti-imino palladation step.[13] It was therefore anticipated that the new CAP-Cl complexes would themselves be suitable candidates as catalysts for the allylic imidate rearrangement.

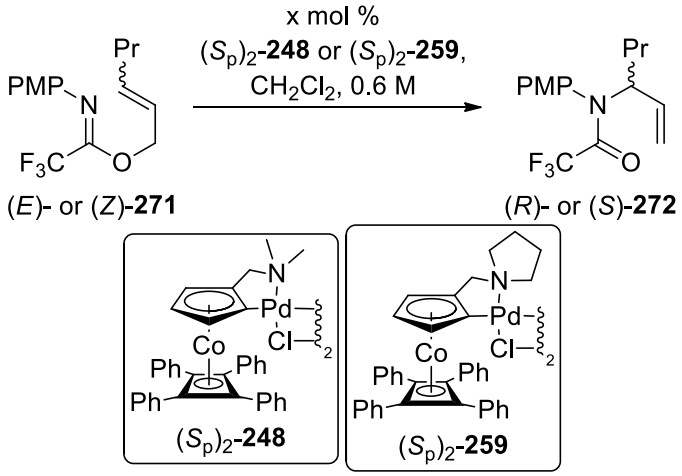
Substrates for catalysis could be synthesised following literature methods.[11,201] Reaction of *p*-anisidine **269** with TFA and triphenylphosphine in carbon tetrachloride gave imidoyl chloride **270** in 68% yield after distillation. Imidates (*E*)- or (*Z*)-**271** could then be readily accessed by reaction of the imidoyl chloride with corresponding (*E*)- or (*Z*)-allylic alcohol after deprotonation with sodium hydride (Scheme 91).



269 **270** (*E*)-**271** 83% (*Z*)-**271** 82%

Scheme 91

Catalysis was first investigated with the representative (*E*)- and (*Z*)-*N*-(*para*-methoxyphenyl)trifluoroacetimidate substrates **271** (Scheme 92, Table 8). Reactions were first carried out to check catalytic activity using 5 mol % of (S_p)-**248** and 0.6 M solution of substrate at room temperature for 60 h. These conditions gave modest conversion for the formation of (*R*)-**272** (75% *ee*) and (*S*)-**272** (20% *ee*) from the corresponding *E* and *Z* substrates respectively, (entries 1 and 2). These conditions were repeated using palladacycle (S_p)$_2$-**259**, providing a similar result for the *E* substrate, but showcasing an increased selectivity when using the *Z* substrate, albeit with lower conversion, (entries 3 and 4). It has been shown for similar systems that catalytic activity and/or selectivity can be increased by the use of a proton sponge, (PS, 1,8-bis(dimethylamino)naphthalene). As such the addition of this was tested.[202]



Scheme 92

Entry	Catalyst	x [mol %]	Time [h]	Temp [°C]	**271** config.	Conversion [%][b] (yield [%])	*ee* **272** [% (config.)][c]
1	(S_p)-**248**[a]	5	60	rt	*E*	50	75 (*R*)
2	(S_p)$_2$-**248**[a]	5	60	rt	*Z*	54	20 (*S*)
3	(S_p)$_2$-**259**	5	60	rt	*E*	48	75 (*R*)
4	(S_p)$_2$-**259**	5	60	rt	*Z*	26	43 (*S*)
5	(S_p)$_2$-**259**[d]	5	24	38	*E*	43	86 (*R*)
6	(S_p)$_2$-**259**[e]	5	24	38	*E*	> 99 (82)	81 (*R*)
7	(S_p)$_2$-**259**[d,e]	5	24	38	*E*	>99 (84)	83 (*R*)
8	(S_p)$_2$-**259**[d,e]	0.5	24	38	*E*	33	65 (*R*)

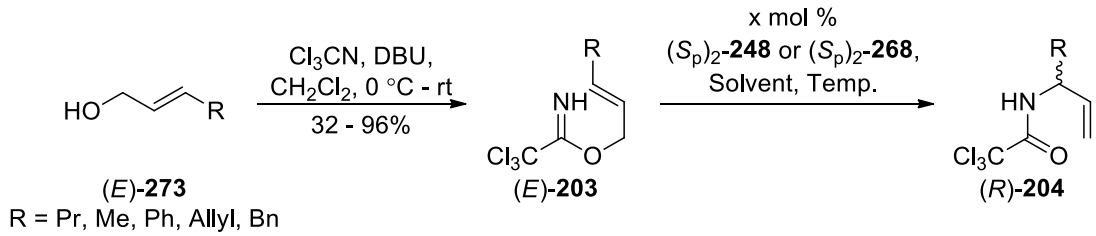
Table 8 – Palladacycle catalysed rearrangement of trifluoroacetimidates using CAP catalysts (Scheme 92). [a] Catalyst *ee* greater than 98%. [b] Determined by ^{1}H-NMR spectroscopy. [c] Determined by chiral HPLC analysis after removal of trifluoroacetate group. [d] With 20 mol % of 1,8-bis(dimethylamino)naphthalene. [e] With 19 mol % of $AgNO_3$.

Focusing on (S_p)$_2$-**259** and substrate (*E*)-**271**, due to best selectivity, the temperature was also increased to 38 °C and with the addition of PS, the selectivity increased to 86% *ee* but the conversion was still modest (entry 5). Under similar conditions using 5 mol % of (S,R_p)-COP-Cl resulted in the complete conversion and up to 92% *ee*.[11]

Assuming a correlation between conversion and the rate of catalysis, the reduced activity seen with these CAP catalysts can be attributed to the increased basicity of the amine ligand

and increased electron density on the palladium centre, causing a slower rate of substrate binding and reaction. Related chloride-bridged ferrocene imidazole derived palladacycles also show poor activity as catalysts for the allylic imidate rearrangement due to the electron donating properties of the ferrocenyl moiety.[121,122,154] For these systems activity could be increased by the addition of silver salts, where it has been shown that the activated catalyst is a Pd(III) species resulting from chloride ligand extraction and subsequent metal oxidation.[202] As such these conditions were tested, and with the addition of 3.8 equivalents with respect to $(S_p)_2$-**259** of silver nitrate, resulted in complete conversion of substrate (*E*)-**271** to (*R*)-**272** in 81% *ee* (entry 6). Essentially the same result was achieved with the addition of a PS (entry 7). Under analogous conditions but with a lower catalyst loading of 0.5 mol % gave an erosion of enantioselectivity and conversion (entry 8).

Encouraged by these results, the next substrates investigated were the more challenging (*E*)-trichloroacetimidates (Scheme 93, Table 9). Synthesis of the substrates could be achieved in one-step, unlike the previous trifluoroimidate examples. Reaction of a range of allylic alcohols (*E*)-**273** with trichloroacetonitrile, in the presence of DBU at 0 °C, afforded the desired range of trichloroacetimidates (*E*)-**203** (Scheme 93).[203]



(*E*)-**273**
R = Pr, Me, Ph, Allyl, Bn

(*E*)-**203**

(*R*)-**204**

Scheme 93

As with the previous example, the *N*,*N*-dimethylamino derived palladacycle $(S_p)_2$-**248** from the proline resolution was tested first. A catalyst loading of 5 mol % with a concentration of 0.6 M of (*E*)-**203** in CH_2Cl_2 at elevated temperature gave (*R*)-**204** with good conversion but modest selectivity (55% *ee*, Table 9, entry 1). Lowering the catalyst loading systematically, resulted in reduced conversion but the selectivity was maintained (entries 2–4). The reduced conversion seen may be due to competitive processes occurring at the lower loadings.

Entry	Catalyst	x [mol %]	R	Solvent	Time [h]	Temp [°C]	Imidate Conc. [M]	Conv. [%][b] (yield [%])	*ee* of **204** [%, (config.)][c]
1	(S_p)-**248**[a]	5	^{n}Pr	CH_2Cl_2	39	38	0.6	89 (65)	55 (*R*)
2	(S_p)-**248**[a]	2.5	^{n}Pr	CH_2Cl_2	39	38	0.6	45	57 (*R*)
3	(S_p)-**248**[a]	1	^{n}Pr	CH_2Cl_2	39	38	0.6	33	62 (*R*)
4	(S_p)-**248**[a]	0.5	^{n}Pr	CH_2Cl_2	39	38	0.6	22	68 (*R*)
5	(S_p)$_2$-**259**	5	^{n}Pr	CH_2Cl_2	39	38	0.6	51	86 (*R*)
6	(S_p)$_2$-**259**	2.5	^{n}Pr	CH_2Cl_2	39	38	0.6	61	25 (*R*)
7	(S_p)$_2$-**259**	1	^{n}Pr	CH_2Cl_2	39	38	0.6	30	23 (*R*)
8	(S_p)$_2$-**259**	0.5	^{n}Pr	CH_2Cl_2	39	38	0.6	29	27 (*R*)
9	(S_p)$_2$-**259**[d]	5	^{n}Pr	CH_2Cl_2	39	38	0.6	30	71 (*R*)
10	(S_p)$_2$-**259**[e]	5	^{n}Pr	CH_2Cl_2	39	38	0.6	>99 (77)	73 (*R*)
11	(S_p)$_2$-**259**[d,e]	5	^{n}Pr	CH_2Cl_2	39	38	0.6	>99 (78)	99 (*R*)
12	(S_p)$_2$-**259**[d,e]	2	^{n}Pr	CH_2Cl_2	39	38	0.6	34	76 (*R*)
13	(S_p)$_2$-**259**[d,e]	1	^{n}Pr	CH_2Cl_2	39	38	0.6	8	64 (*R*)
14	(S_p)$_2$-**259**[d,e]	0.5	^{n}Pr	CH_2Cl_2	39	38	0.6	7	64 (*R*)
15	(S_p)$_2$-**259**	5	^{n}Pr	CH_3CN	48	70	2.6	95 (81)	82 (*R*)
16	(S_p)$_2$-**259**	2	^{n}Pr	CH_3CN	48	70	2.6	68	78 (*R*)
17	(S_p)$_2$-**259**	0.5	^{n}Pr	CH_3CN	48	70	2.6	32	55 (*R*)
18	(S_p)$_2$-**259**[d,e]	5	^{n}Pr	CH_3CN	48	70	2.6	84 (58)	80 (*R*)
19	(S_p)$_2$-**259**[d,e]	2	^{n}Pr	CH_3CN	48	70	2.6	79 (60)	88 (*R*)
20	(S_p)$_2$-**259**[d,e]	0.5	^{n}Pr	CH_3CN	48	70	2.6	25	32 (*R*)
21	(S_p)$_2$-**259**[d,e]	5	Ph	CH_2Cl_2	39	38	0.6	65	5 (*R*)
22	(S_p)$_2$-**259**[d,e]	5	Allyl	CH_2Cl_2	39	38	0.6	58 (55)	71 (*R*)
23	(S_p)$_2$-**259**[d,e]	5	Me	CH_2Cl_2	39	38	0.6	66 (66)	91 (*R*)
24	(S_p)$_2$-**259**[d,e]	5	Bn	CH_2Cl_2	39	38	0.6	>99 (70)	87 (*R*)

Table 9 - Palladacycle catalysed rearrangement of trichloroacetimidates using CAP catalysts (Scheme 92). [a] Catalyst *ee* greater than 98%. [b] Determined by ^{1}H-NMR spectroscopy. [c] Determined by chiral HPLC analysis. [d] With 4 x mol % of 1,8-bis(dimethylamino)naphthalene. [e] With 3.8 x mol % of $AgNO_3$.

Using analogous conditions to the *N*,*N*-dimethylamino derivative, (S_p)$_2$-**259** was tested for catalytic activity (entries 5–8). Modest conversions were seen over the range of catalyst loadings, but good selectivity for (*R*)-**204** (86% *ee*) was seen at 5 mol % loading. At lower

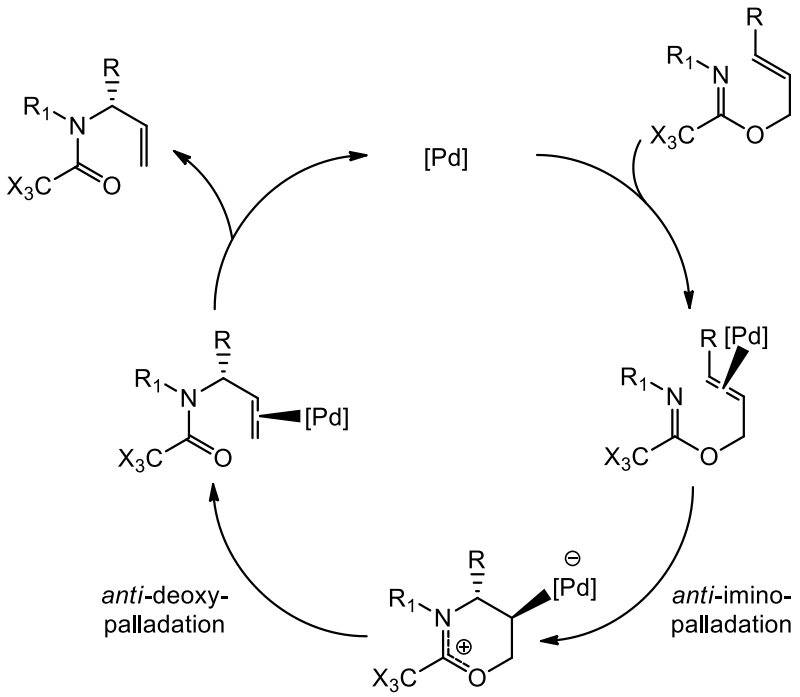
loadings there was erosion of enantioselectivity, akin to with the trifluoroacetimidate substrate. Using the optimum catalyst loading of 5 mol % the PS was added resulting in a reduced conversion and selectivity (entry 9). Conversion was increased to 99% upon addition of silver nitrate (entry 10) although enantioselectivity for (*R*)-**204** (73% *ee*) remained modest. However, upon use of silver nitrate and PS, conversion and enantioselectivity could be increased to >99% and 99% *ee* respectively (entry 11). Unfortunately, when lowering catalyst loading, conversion and enantioselectivity decreased (entries 12–14).

Previous studies showed that for COP-Cl the catalyst loading could be significantly decreased, whilst retaining enantioselectivity and conversion, by using CH_3CN as the solvent, with an increased concentration, reaction time and temperature (2.6 M, 48 h and 70 °C respectively).[157] As such these conditions were tested. Without silver salt activation and using a catalyst loading of 5 mol %, conversion could be increased to 95% (over the previous analogous example, entry 5), but enantioselectivity of (*R*)-**204** decreased to 82% *ee* (entry 15). Upon lowering the catalyst loadings, a decrease in conversion and selectivity was seen (entries 16 & 17), albeit with better results than under previous conditions. The use of silver salt activation and addition of PS resulted in similar conversion, but increased enantioselectivity at lower loadings (entries 18–20).

The most promising conditions were still using silver salt activation and PS at 5 mol % catalyst loadings. A small range of substrates were examined using these conditions (entries 21–24). Phenyl containing substrate (*E*)-**203** (R = Ph) is a known limiting substrate for this process due to blocking of nucleophilic attack at the alkene. As such this was not expected to proceed but surprisingly the reaction progressed with mild conversion but little stereoinduction (entry 21). The allyl containing trichloroacetimidate (*E*)-**203** (R = allyl) is also a known challenging substrate, as the additional alkene functionality is capable of competitive co-ordination. Reaction under analogous conditions resulted in (*R*)-**204** in 71%

ee (entry 22). In contrast, methyl and benzyl containing derivatives are good substrates and reacted smoothly to give (*R*)-**204** (R = Bn and Me) in 91 and 87% *ee* respectively (entries 23 & 24). These results are comparable to the COP-Cl catalysed rearrangement of trichloroacetimidates.[157]

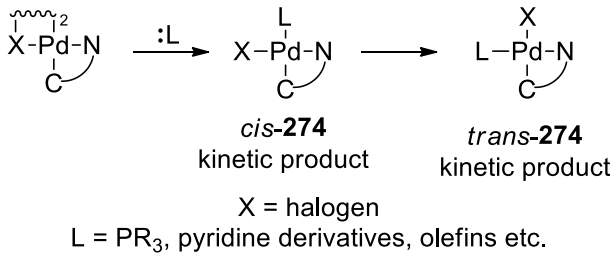
The palladium catalysed rearrangement of allylic imidates has been proposed to proceed *via* a step-wise cyclisation-induced rearrangement (Scheme 94).[150,204] This process is initiated by activation of the olefin moiety towards intramolecular nucleophilic attack by co-ordination to the palladium. Subsequent palladium-carbon bond formation *via* an *anti*-imino-palladation step generates a palladium alkyl species which undergoes *anti*-deoxy-palladation to give a η^2-olefin coordinated species. Subsequent dissociation of the new alkene relinquishes the rearranged product and catalyst.



Scheme 94

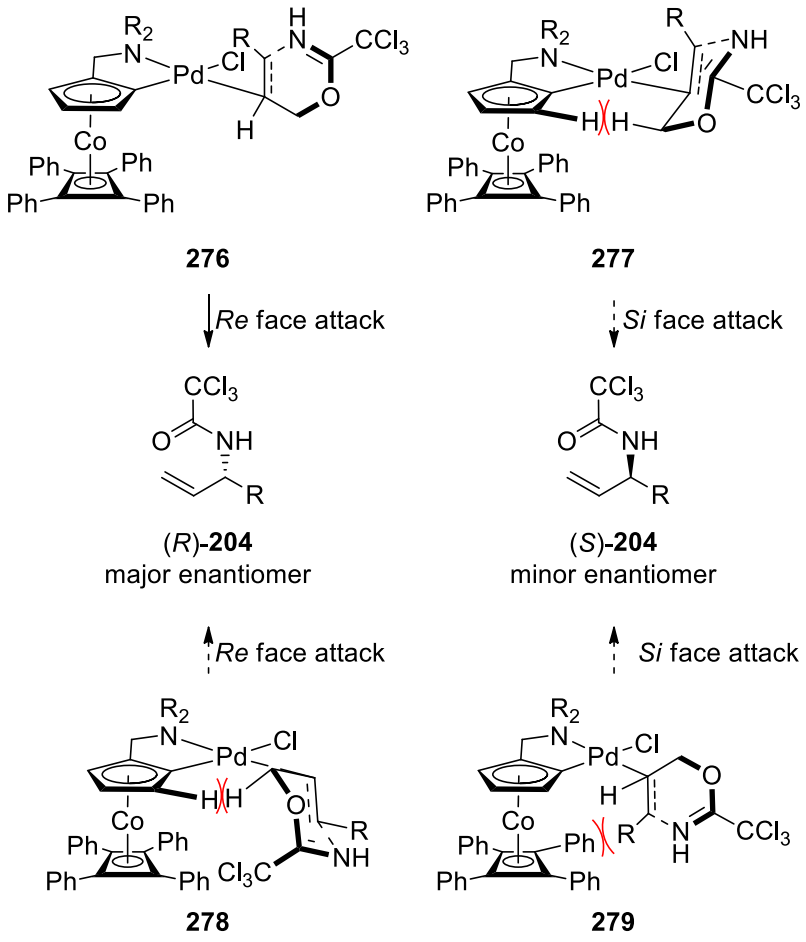
A model for stereoinduction has been postulated previously for the COP-Cl catalysed rearrangement of trichloroacetimidates, using 2-(2-furyl)-2-oxazoline as an electronic model for the chiral oxazoline ligand in COP-Cl.[13] It was shown that an olefin favoured coordination *trans* to the oxazoline to give intermediate *trans*-**274** over the corresponding *cis*

isomer, *cis*-**274**, by nearly 7 kcal mol^{-1} (Scheme 95). This is in agreement with the established order of the kinetic *trans* effect,[205] where in transition complex *trans*-**274** the π-accepting chloride ligand is *trans* to the strongest π-donor, the carbanion ligand. It was stated that this *trans* configuration projects the imidate substituent away from the oxazoline moiety in COP-Cl, as such the changing of the oxazoline fragment should have little effect on the enantioselectivity of the rearrangement,[13] thus the planar chirality of the COP ligand is largely responsible for the selectivity shown. This allows for the valid extension of the model for enantioselectivity of the COP-Cl catalysed allylic imidate rearrangement to the new CAP systems. This is further confirmed by the relationship between planar chirality and product chirality (S_p palladacycle gives *R* product) being the same in the COP and CAP systems.



Scheme 95

From the *trans* coordinated olefin it is possible to draw four transition states containing a coordinated alkene substrate (Scheme 96), where the imidate fragment is in an envelope conformation, with the R group and palladium in the pseudoequatorial positions. Minimisation of steric interactions in the transition state between the imidate fragment and cyclopentadienyl ring or lower cyclobutadienyl ring is a key factor in influencing their stability.



Scheme 96

Transition states where there is interaction between Cp-H and a methylene proton of the imidate (**277** and **278**) are disfavoured. Likewise, for arrangement **279** where there is steric interaction between the R group and lower phenyl group. For the corresponding COP-Cl system, it was shown that arrangement **276** had the lowest energy transition state, (up to 3.4 kcal mol^{-1} less), leading to the major product.

2.8 Conclusion

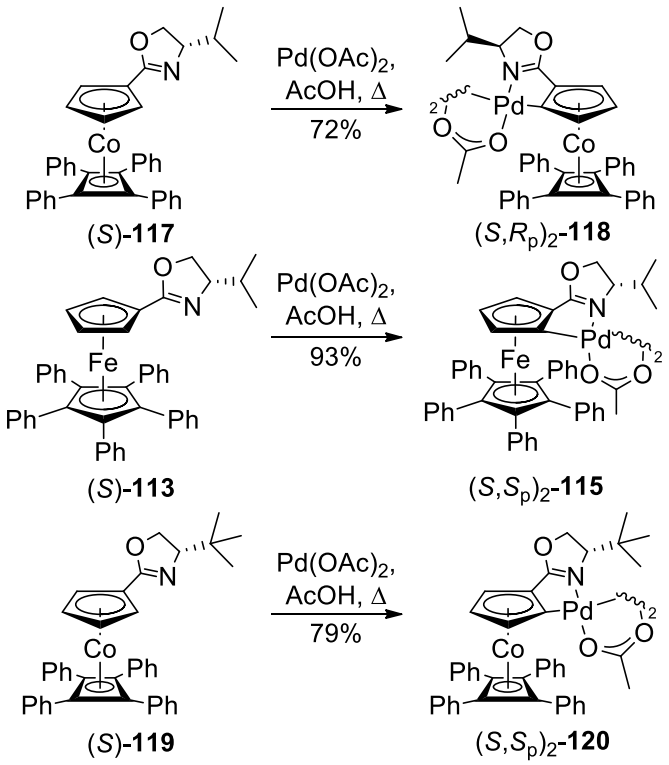
In conclusion, the enantioselective palladation of (η^5-(dimethylaminomethyl)cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) **237** with sodium tetrachloropalladate mediated by *N*-acetyl-*D*-phenylalanine under basic conditions gave the chloride-bridged dimer palladacycle $(S_p)_2$-**248** in 92% *ee*. It has been postulated that this process proceeds *via* a concerted metallation-deprotonation pathway mediated by a

chiral η^1-carboxylate ligand, which is consistent with an intramolecular isotope effect >1, (experimentally determined to be 2.5 for this process). The enantiopurity of $(S_p)_2$-**248** can be increased to >98% *ee* by reaction with (*R*)-proline, separation of the resultant diastereoisomers by column chromatography and subsequent reaction with dilute aqueous hydrochloric acid. A catalogue of related aminomethyl-substituted cobalt complexes were synthesised, but the enantioselective palladation protocol was limited to *N*,*N*-diethyl- (82% *ee*) and pyrrolidinyl- (>98% *ee*) substituents. Application of these new CAP complexes to the asymmetric synthesis of ferrocene-based phosphopalladacycles, using transcyclopalladation, allowed for the synthesis of the aforementioned palladacycles in up to 78% *ee*. The catalytic activity and enantioselectivity of *N*,*N*-dimethyl- and pyrrolidinyl-derived chloride bridge palladacycles was tested, showing that the addition of 3.8 equivalents of silver nitrate and 4 equivalents of a proton sponge greatly improved results. The catalyst generated from pyrrolidinyl-derived palladacycle $(S_p)_2$-**259** resulted in the rearrangement of (*E*)-trichloroacetimidates with high enantioselectivity (up to 99% *ee*). The enantioselectivity shown by these systems can be rationalised by comparison to the COP-Cl catalysed allylic imidate rearrangement of trichloroimidates.

Chapter 3 – Results and Discussion 2

3.1 Introduction

The importance of cobalt oxazoline palladacycles (COP) and related ferrocene-based palladacycles in asymmetric synthesis has been highlighted in the previous chapters. Central to the success of these metallocenes is the high diastereoselectivity of C–H activation/palladium-carbon bond formation, as controlled by a heterocyclic chiral auxiliary. A notable feature of these reactions is the formation of opposite elements of planar chirality between similar ligand substrates under the same reaction conditions, (Scheme 97).[17,115,117]

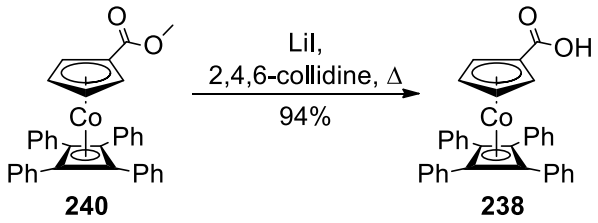


Scheme 97

There is little known about the relevance of matched or mismatched pairing of central and planar chirality in these complexes for the control of enantioselectivity in asymmetric catalysis. As such, this chapter serves to examine and highlight the factors influencing the diastereoselectivity of COP synthesis and the consequential effect on catalysis.

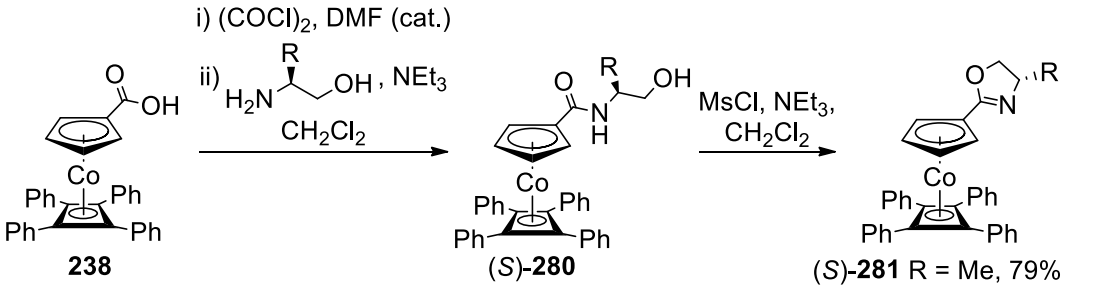
3.2 Synthesis of Ligands

A range of cobalt oxazoline ligands could be readily synthesised from cobalt sandwich complex ester **240** in a few steps using literature procedures (Chapter 4).[182] Firstly, formation of acid **238** could be achieved by saponification of the ester by using stoichiometric lithium iodide and heating in 2,4,6-collidine (Scheme 98). Disappearance of the characteristic methyl signal at 3.19 ppm for methyl ester **240** in the ^{1}H-NMR spectra of **238** could be used to confirm that the reaction had indeed been realised.



Scheme 98

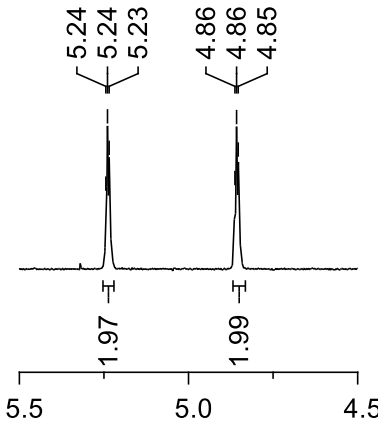
Formation of the oxazoline ligands could be carried out as a one-pot procedure.[182] Treatment of acid **238** with oxalyl chloride and catalytic DMF generated an acid chloride, which could be directly treated with a range of (*S*)-amino alcohols, providing intermediate hydroxylamides (*S*)-**280** that readily ring-close upon treatment with mesyl chloride to form the required oxazolines (Scheme 99).



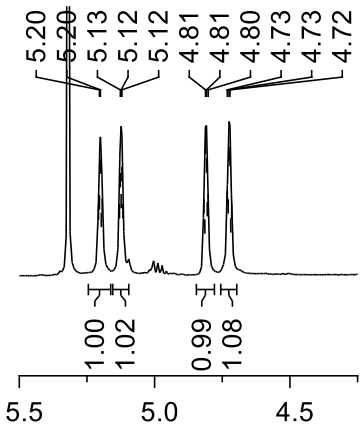
Scheme 99

Comparison of signals seen for cyclopentadienyl protons in the ^{1}H-NMR spectra of complexes **238** and (*S*)-**117** illustrates the formation of the required oxazoline. The signals for the Cp-H of acid **238** appear as two signals each integrating for 2 protons due to chemical equivalence (Figure 26 [a]). For oxazoline (*S*)-**117** the shifts for the Cp-H are now diastereotopic and magnetically inequivalent so they are seen as four separate signals (Figure 26 [b]). The formation of the intermediate amide (*S*)-**280** could be seen as a minor product if the reaction had not reached completion by appearance of a signal at 5.24 ppm corresponding to the amide NH (Figure 26 [c]). Fortunately, the R_f values for amide and oxazoline are significantly different and as such each complex could be isolated by column chromatography without contamination. The intermediate amide could then be resubjected to mesyl chloride and triethylamine to give the desired oxazoline (Scheme 99).

[a] - ^{1}H-NMR of cyclopentadienyl region of **238**



[b] - ^{1}H-NMR of cyclopentadienyl region of (*S*)-**117**



[c] - ^{1}H-NMR of cyclopentadienyl region of (*S*)-**280**

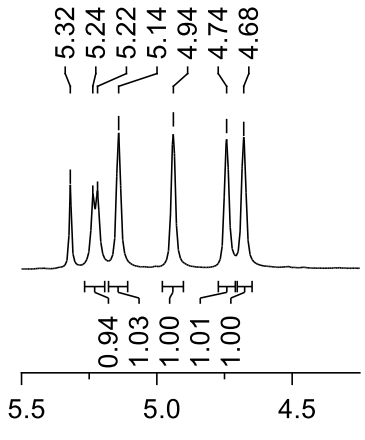
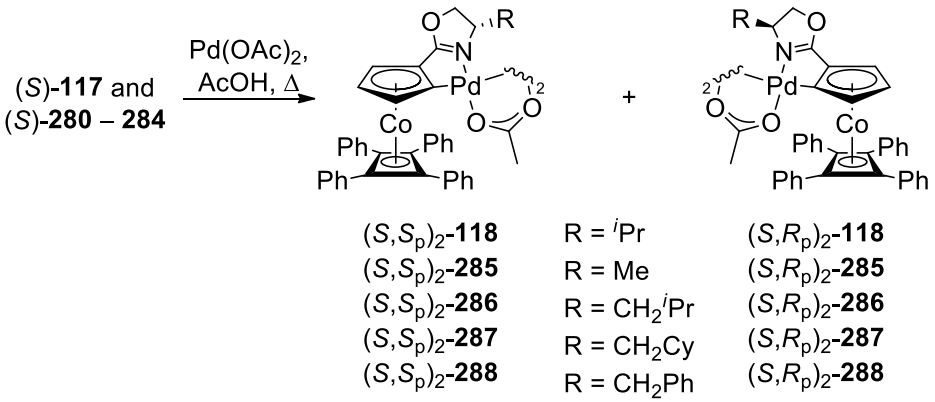


Figure 26

3.3 Diastereoselective Palladation Studies

The literature procedure for diastereoselective palladation of (*S*)-**117** involves heating the oxazoline with $Pd(OAc)_2$ in acetic acid at 95 °C for 30 minutes, resulting in the precipitation of palladacycle $(S,R_p)_2$-**118** as a single diastereoisomer (Scheme 100, Table 10, Entry 1).[17] This procedure has also been used previously to generate $(S,S_p)_2$-**120** from the precursor

oxazoline (*S*)-**119**.[117] Subjection of new oxazolines to the same conditions resulted in the desired precipitation of complexes from the reaction media, but only one palladacycle was formed; that derived from the oxazoline where R = CH_2Cy (*S*)-**283** (Entry 4).



Scheme 100

Entry	Oxazoline (substituent)	Solvent[a]	Major product	Diastereomeric Ratio (dr) [b]	Yield [%][c]
1	(*S*)-**117** (^{i}Pr)	AcOH	(S,R_p)$_2$-**118**	>100:1	72
2	(*S*)-**281** (Me)	AcOH	**289**	n/a	26
3	(*S*)-**282** ($CH_2{}^i$Pr)	AcOH	**290**	n/a	97
4	(*S*)-**283** (CH_2Cy)	AcOH	(S,S_p)$_2$-**287**	>100:1	70
5	(*S*)-**284** (CH_2Ph)	AcOH	**291**	n/a	89

Table 10 – Diastereoselective palladation of cobalt oxazoline ligands (Scheme 100). [a] At 95 ^{o}C, 30 min. in AcOH. [b] Determined by ^{1}H NMR spectroscopy. [c] For both diastereoisomers where applicable.

The formation of a palladacycle containing complex can be confirmed by inspection of the ^{1}H-NMR spectra of the complexes and comparison to the parent oxazoline. For palladacycle complexes there are three distinct signals relating to the cyclopentadienyl protons, whereas there are two sets of two diastereotopic cyclopentadienyl hydrogen signals observed in the spectrum of the starting oxazoline. The identity of an oxazoline coordinated palladium as the new cyclopentadienyl ring substituent was confirmed by the reduction in wavenumber of ν(C=N) to 1578 cm^{-1} from the value of 1656 cm^{-1} measured for (*S*)-**283**, and by the single

methyl singlet at 1.99 ppm in the ^{1}H-NMR spectrum arising from the bridging acetate ligands.

The configuration of the new element of planar chirality was determined to be S_p and thus the identity of the palladacycle as $(S,S_p)_2$-**287** by comparison of known values for specific rotation of $(S,R_p)_2$-**118** (+942)[17] and $(S,S_p)_2$-**120** (−903),[117] where a negative sign of rotation is indicative of S_p configuration, ($(S,S_p)_2$-**287**, −407). This was also confirmed by comparison of the CD-spectra of $(S,S_p)_2$-**287**, $(S,S_p)_2$-**286** (*vide infra*) and $(S,R_p)_2$-**118** (R = CH_2Cy, $CH_2{}^{i}Pr$ and ^{i}Pr respectively, Figure 27). Correspondence in the profiles for similarly configured palladacycles $(S,S_p)_2$-**287** and $(S,S_p)_2$-**286** was observed, with the parent and oppositely configured palladacycle $(S,R_p)_2$-**118** giving specifically different bands of absorption at 450 and 250 nm. The configuration of the planar chirality in $(S,S_p)_2$-**287** (R = CH_2Cy) was later conclusively confirmed to be S_p by X-ray crystallography analysis of similar palladacycle $(S,S_p)_2$-**286** (R = $CH_2{}^{i}Pr$) (*vide infra*).

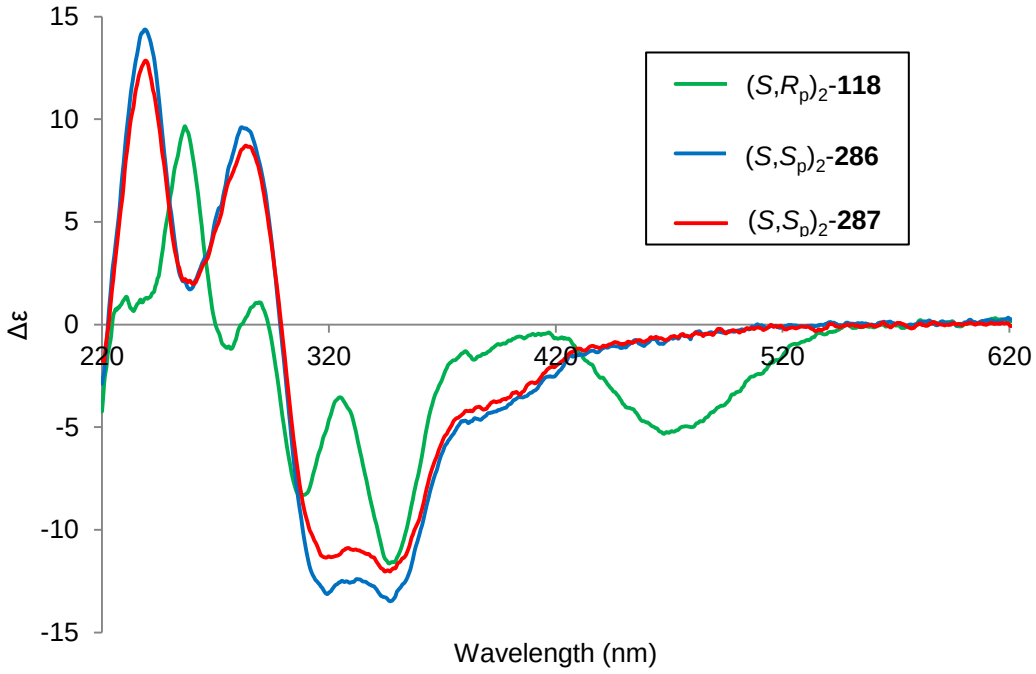
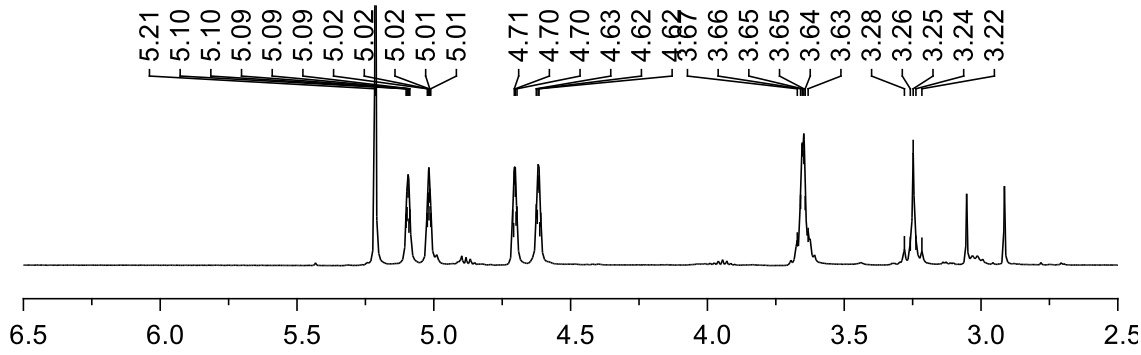
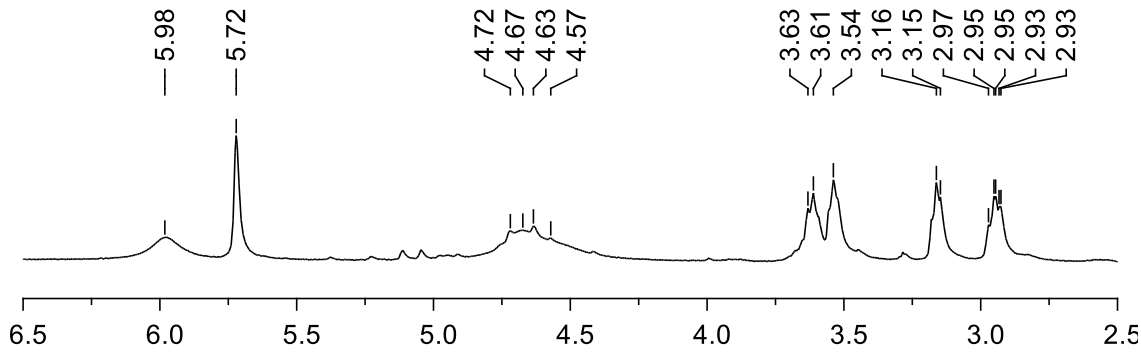


Figure 27– CD spectra of palladacycles $(S,R_p)_2$-**118**, $(S,S_p)_2$-**286** and $(S,S_p)_2$-**287**.

[a] - ^{1}H-NMR of cyclopentadienyl region of oxazoline (*S*)-**282**:



[b] - ^{1}H-NMR of cyclopentadienyl region of intermediate **290**:



[c] - ^{1}H-NMR of cyclopentadienyl region of palladacycle $(S,S_p)_2$-**286**:

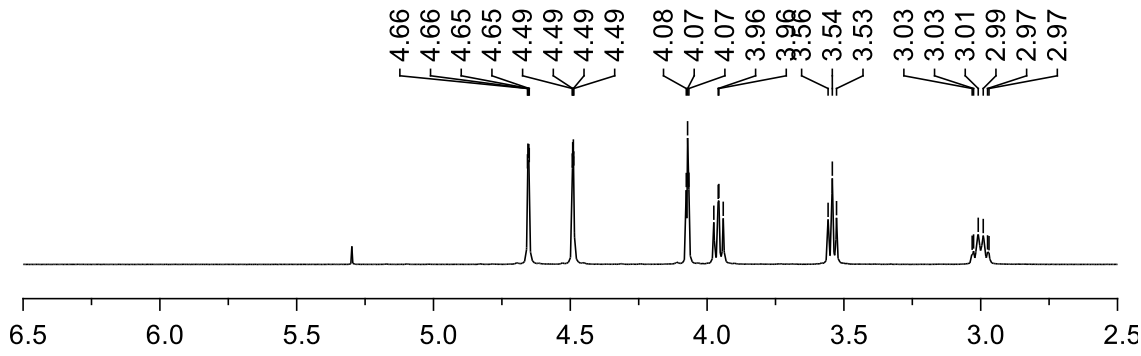
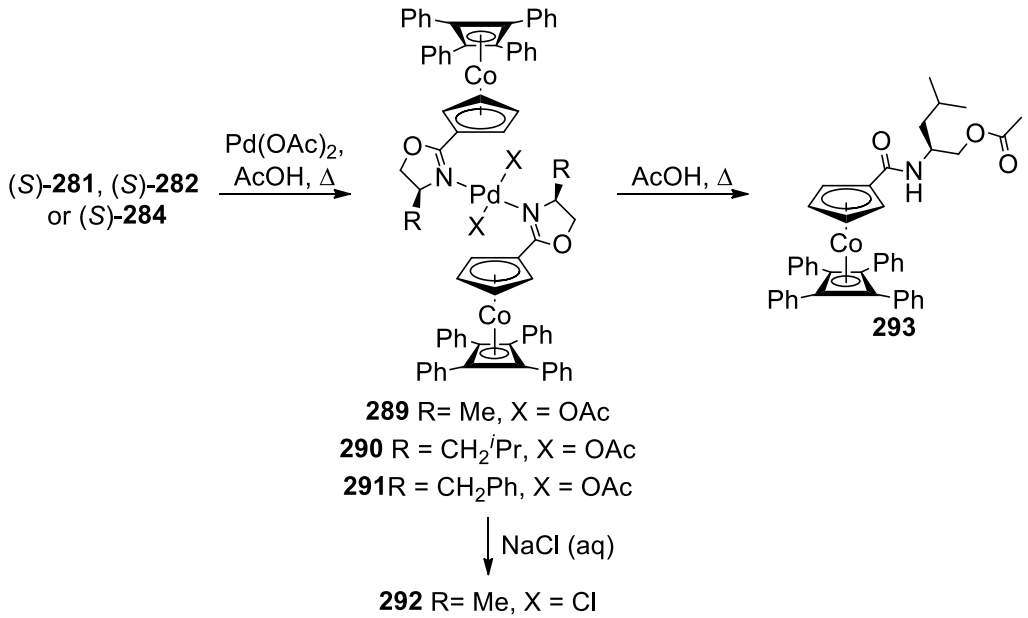


Figure 28

By comparison of the cyclopentadienyl region of the ^{1}H-NMR spectra for oxazoline ligand (*S*)-**282** (R = $CH_2{}^{i}Pr$), the precipitated intermediate **290** and palladacycle $(S,S_p)_2$-**286**, (Figure 28), it was possible to see that the intermediary complex was indeed neither starting oxazoline nor palladacycle. This is due to the lack of either four Cp–H signals relating to the parent oxazoline (Figure 28 [a]) or three Cp–H signals relating to a palladacycle (Figure 28

[c]). Other techniques were unhelpful in identifying the intermediate, including LC-MS, as both the intermediate and palladacycle fragment gave a molecular ion equal to that of the starting ligand. Instead, the precipitates obtained from the reaction of oxazolines (*S*)-**281**, (*S*)-**282** or (*S*)-**284** with $Pd(OAc)_2$ (Table 10, entries 2, 3 & 5) were identified as palladium acetate adducts **289-291** (Scheme 101) by the similarity of the four cyclopentadienyl proton signals arising in the ^{1}H-NMR spectrum to those observed previously for the analogous *trans*-chloride adduct **292**.[117] The *trans*-geometry was assigned by comparison with other complexes of general structure $Pd(OAc)_2L_2$.[206,207] Two of the four diastereotopic cyclopentadienyl proton signals in all of these *trans*-adducts are observed at a significantly higher chemical shift compared to the starting oxaxoline ligands (Figure 28 [b], *e.g.* 5.98 and 5.72 for intermediate **290**). This may be due to the proximity of cyclopentadienyl α-hydrogens to the palladium environment perpendicular to the square-plane and the resultant deshielding effect. This was deduced by looking at the published X-ray structure for the analogous *trans*-chloride adduct **292**.[117]

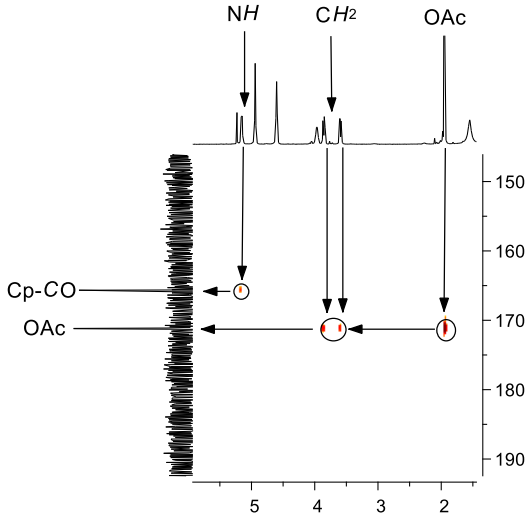


Scheme 101

An attempt to convert adduct **290** (R = $CH_2{}^iPr$) into a palladacycle was carried out by re-heating the intermediate in acetic acid at 95 ^oC for 30 minutes. This resulted only in

oxazoline ring opening and isolation of **293** (Scheme 101). This was confirmed to be the correct product from the two amide possibilities from the ring opening of oxazoline (*S*)-**282** by looking at the HMBC and NOe spectra (Figure 29). From the HMBC it can be seen that there is correlation between the hydrogen of the NH and the carbonyl carbon α-to the cyclopentadienyl ring, as such they must be bonded. Also in the NOe, a correlation between NH and cyclopentadienyl protons can be seen, which is only possible in isomer **293**.

HMBC spectra of **293**:



NOeSY spectra of **293**:

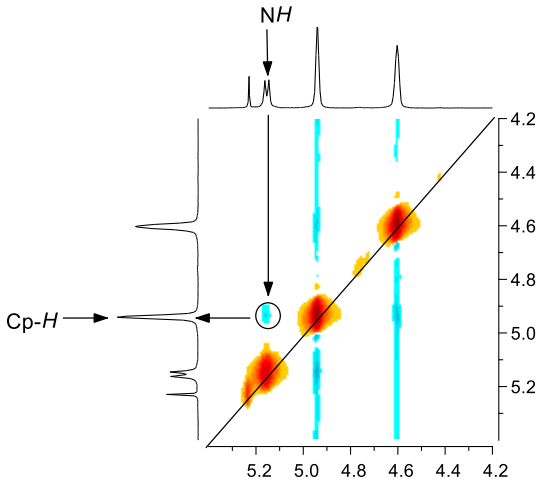
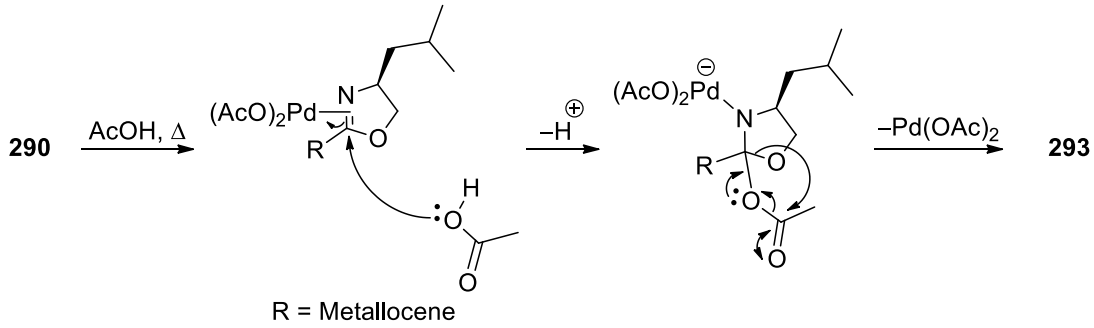


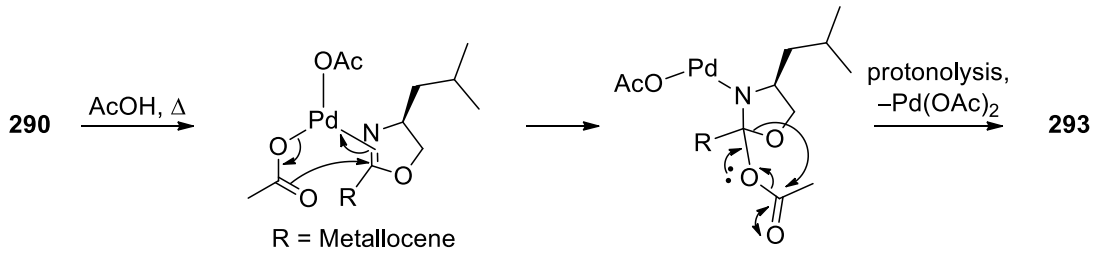
Figure 29

This outcome is consistent with the known Pd(II) promoted ring-opening of an oxazoline by acetate to form an acetate substituted amide.[208] In this process it is postulated that the palladium dissociates under acidic conditions, and then subsequently promotes nucleophilic attack upon the imine carbon of the oxazoline. This is followed by COMe transfer to give amide **293** (Scheme 102, Pathway A). Another plausible route involves an intramolecular transfer of acetate from palladium to the oxazoline (Pathway B). This is followed by a similar transfer of COMe, and then subsequent protonolysis of the resultant palladium ligated compound relinquishes amide **293**.

Pathway A:

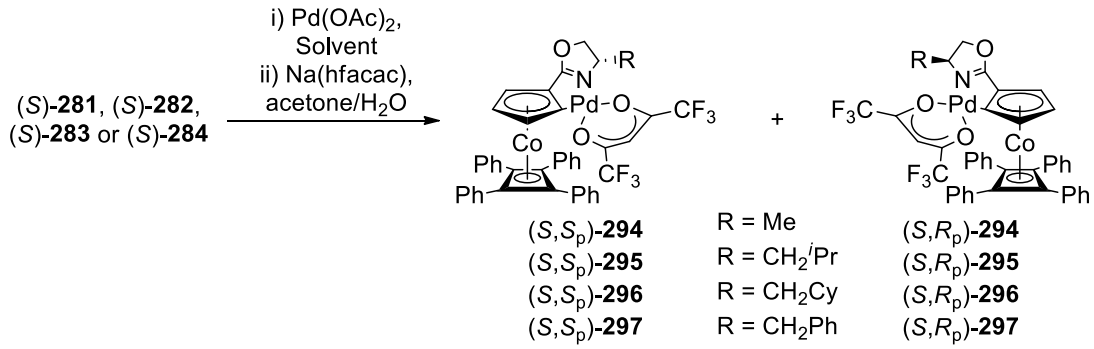


Pathway B:



Scheme 102

To avoid the precipitation of intermediate complexes, the palladation reaction was screened using solvents in which the intermediate was soluble (Table 11). The diastereoselectivity of palladacycle $(S,S_p)_2$-**118** could be determined directly using ^{1}H-NMR spectroscopy, by comparison of signals arising for the methyl protons to literature chemical shifts for the respective configurations.[116] For the other ligands the acetate dimers provided no such resolved signals, but reaction of the crude acetate dimers with Na(hfacac) in acetone/water (Scheme 103), provided diastereomeric monomers **294–297** that could be seen cleanly in the ^{1}H-NMR spectra; in particular peaks for the Cp-protons and the CH of the hfacac ligand were most useful.



Scheme 103

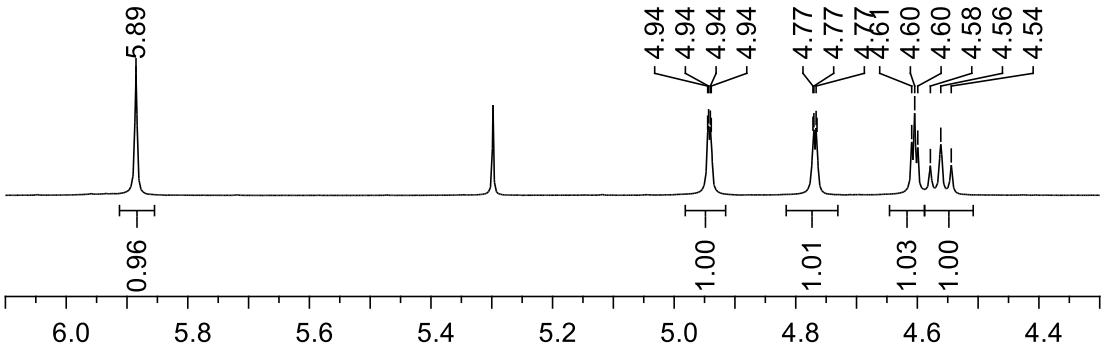
Entry	Oxazoline (substituent)	Solvent[a]	Major product	Diastereomeric Ratio (dr) [b]
1	(*S*)-**117** (^{i}Pr)	CH_2Cl_2	(S,S_p)$_2$-**118**	2:1
2	(*S*)-**281** (Me**)**	CH_2Cl_2	(S,S_p)-**294**	2.5:1[c]
3	(*S*)-**282** ($CH_2{}^i$Pr)	CH_2Cl_2	(S,S_p)-**295**	13:1[c][d]
4	(*S*)-**283** (CH_2Cy)	CH_2Cl_2	(S,S_p)-**296**	1.5:1[c]
5	(*S*)-**284** (CH_2Ph)	CH_2Cl_2	n/a	1:1[c][e]
6	(*S*)-**282** ($CH_2{}^i$Pr)	PhMe	n/a	1:1[c]
7	(*S*)-**283** (CH_2Cy)	PhMe	n/a	1:1[c]
8	(*S*)-**284** (CH_2Ph)	PhMe	(S,R_p)-**297**	1.4:1[c][f]

Table 11 – [a] At R.T., 16 h. in CH_2Cl_2 or at 95 °C, 1 h. in PhMe [b] Determined by ^{1}H-NMR spectroscopy. [c] Determined following conversion to monomeric hfacac complexes. [d] Diastereomeric purity (>100:1) achieved by recrystallisation from CH_2Cl_2/hexane. [e] Contaminated with the product of *exo*-palladation (1.4:1 *exo:endo*). [f] Contaminated with the product of *exo*-palladation (1:1.1 *exo:endo*)

To confirm which signals corresponded to the two possible palladacycle configurations, comparison of the diastereomerically pure hfacac complex (S,S_p)-**296** from palladation in acetic acid and the complex resulting from palladation in CH_2Cl_2 was undertaken (Figure 30). From this it can be seen that the signal for the methine CH at 5.89 ppm corresponds to the S_p configuration of palladacycle, therefore the signal downfield at 5.92 ppm must accord to the palladacycle with the R_p planar element. This rationale can also be applied to the Cp–H signals. Further confirmation can be sought, as the specific rotation for the 1.5:1 mixture

of (S,S_p)-**296**/(S,R_p)-**296** is negative (−91.6), with the sign of rotation matching that of the pure diastereoisomer (−532). Using this example, where the signal for the methine proton of the palladacycle with the R_p configuration appears downfield, allowed for the selectivities of all palladation reactions to be calculated, (all assignments were also confirmed by measurement of specific rotation of mixtures).

^{1}H-NMR of cyclopentadienyl region of diastereomerically pure (S,S_p)-**296:**



^{1}H-NMR of cyclopentadienyl region of the 1.5:1 mixture of (S,S_p)-**305**/(S,R_p)-**296**:

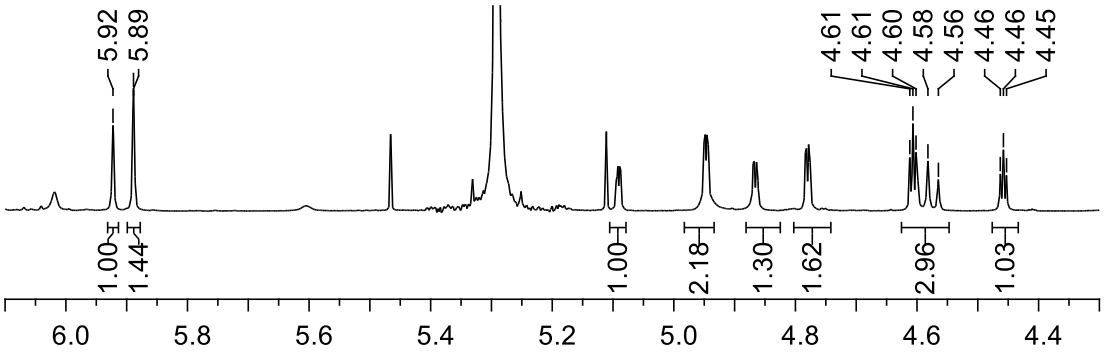
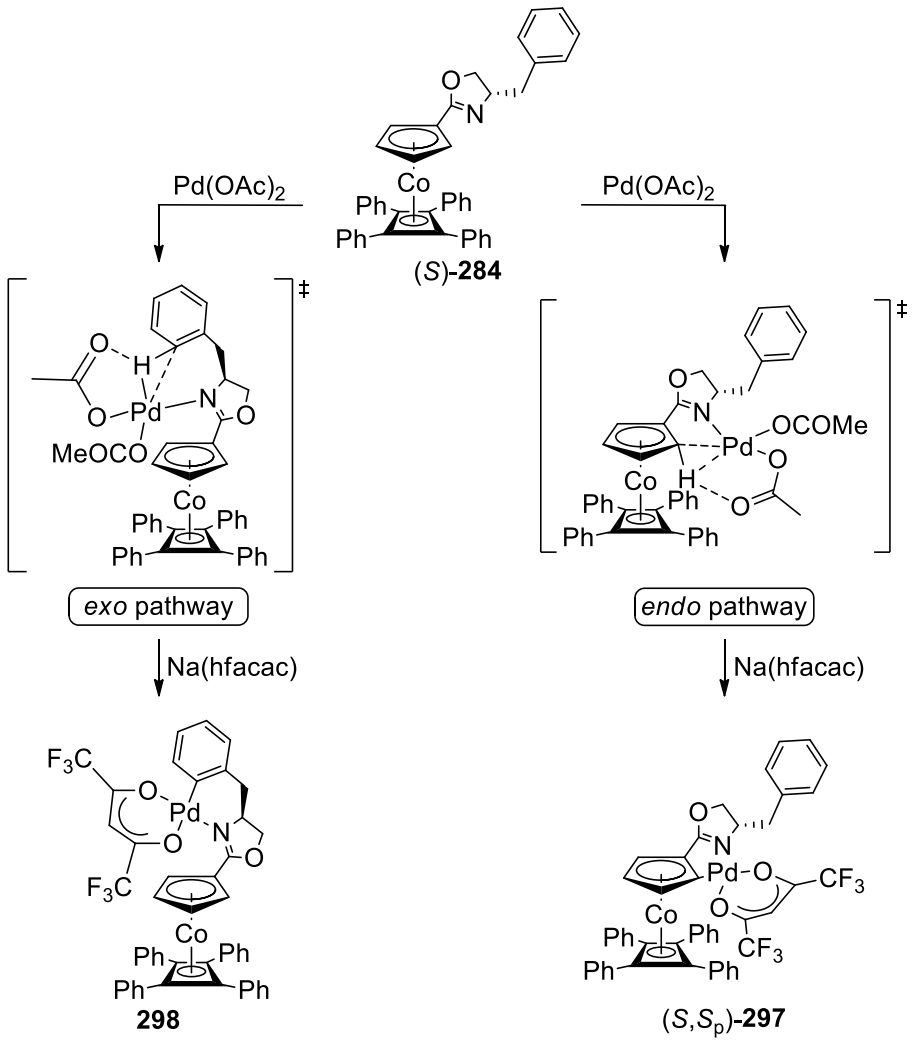


Figure 30

Moderate selectivities were observed for the palladation of ligands (*S*)-**281**, (*S*)-**282** and (*S*)-**283** in CH_2Cl_2 (where R = Me, $CH_2{}^iPr$ and CH_2Cy respectively, entries 1, 2 & 4), with the best selectivity resulting from the palladation of ligand (*S*)-**282** (13:1, S_p:R_p, entry 3). Interestingly, the major product for the palladation of (*S*)-**117** (R = ^{i}Pr) was the (S,S_p)-diastereoisomer, which is the opposite to that seen in the palladation carried out in acetic acid. As such, more studies were carried out on this process (*vide infra*). Reaction of oxazoline ligands where R = $CH_2{}^iPr$, CH_2Cy and CH_2Ph in toluene resulted in little/no selectivity (entries 6, 7 & 8).

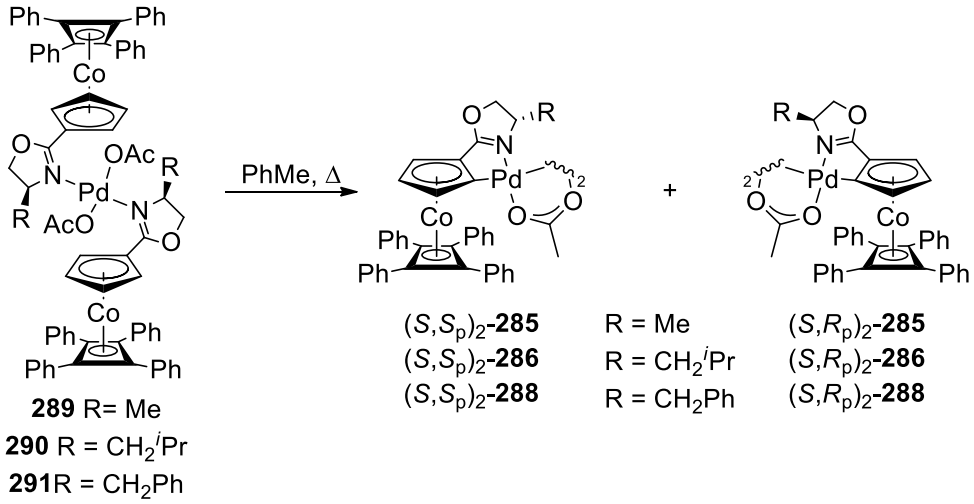


Scheme 104

The palladation of the oxazoline (*S*)-**284** (R = CH_2Ph) resulted in the formation of *exo* palladation product **298**, in which there is a palladacycle containing an *ortho*-carbon/palladium bond on the oxazoline benzyl substituent. This process proceeds *via* the concerted metallation deprotonation (CMD) pathway seen in previous chapters, but instead of abstraction of a proton of the cyclopentadienyl ring to form a 5-membered ring *via* the *endo* pathway, there is a competitive process whereby a 6-membered ring is formed by removal of a proton from the *ortho*-carbon of the benzyl substituent (Scheme 104). There was little selectivity for the *endo* or *exo* product when the palladation was carried out in either toluene or CH_2Cl_2, (entries 5 & 8), and there seems to be little discrimination as a function of the size of ring formed.[209] The formation of the *exo*-palladation product **298** could be confirmed by the retention of four signals for the cyclopentadienyl protons in the

^{1}H-NMR spectrum, and the appearance of signals corresponding to the benzyl-group phenyl protons integrating for 1, 2 and 1 at 7.05, 6.94 and 6.72 ppm respectively.

The conversion of palladium acetate adducts **289–291** into palladacycles was achieved by heating in toluene at reflux for 2h, (Scheme 105, Table 12). Complexes containing the methyl and benzyl substituent resulted in poor selectivity (entries 1 & 3) for the S_p palladacycle, but unlike previous examples for complex (*S*)-**284**, the *exo* palladation product was not observed. This could be due to the fact the *exo*-cyclic product is considered to be the kinetic product of these reactions, since in some cases the *exo*-cyclic complex has been shown to isomerise to the thermodynamic *endo*-complex at elevated temperatures.[210]



Scheme 105

Entry	Complex (substituent)	Solvent[a]	Major product	Diastereomeric Ratio (dr) [b]
1	**289** (Me)	PhMe	$(S,S_p)_2$-**285**	1.7:1[c]
2	**290** ($CH_2{}^iPr$)	PhMe	$(S,S_p)_2$-**286**	8.1:1[c][d]
3	**291** (CH_2Ph)	PhMe	$(S,S_p)_2$-**288**	1.8:1[c]

Table 12 – [a] At reflux. 2 h. in PhMe [b] Determined by ^{1}H-NMR spectroscopy. [c] Determined following conversion to monomeric hfacac complexes. [d] Diastereomeric purity (>100:1) achieved by recrystallisation from CH_2Cl_2/hexane.

Good selectivity (8:1) was observed for the $CH_2{}^iPr$ substituted oxazoline to give the S_p palladacycle as the major product (entry 2). The palladacycle could be recrystallised from CH_2Cl_2/hexane to afford a diastereomerically pure sample which was then analysed by X-ray crystallography to confirm the formation of a S_p palladacycle (Figure 31). An absolute structure parameter of 0.000(7) confirmed that the crystal was indeed not racemic.

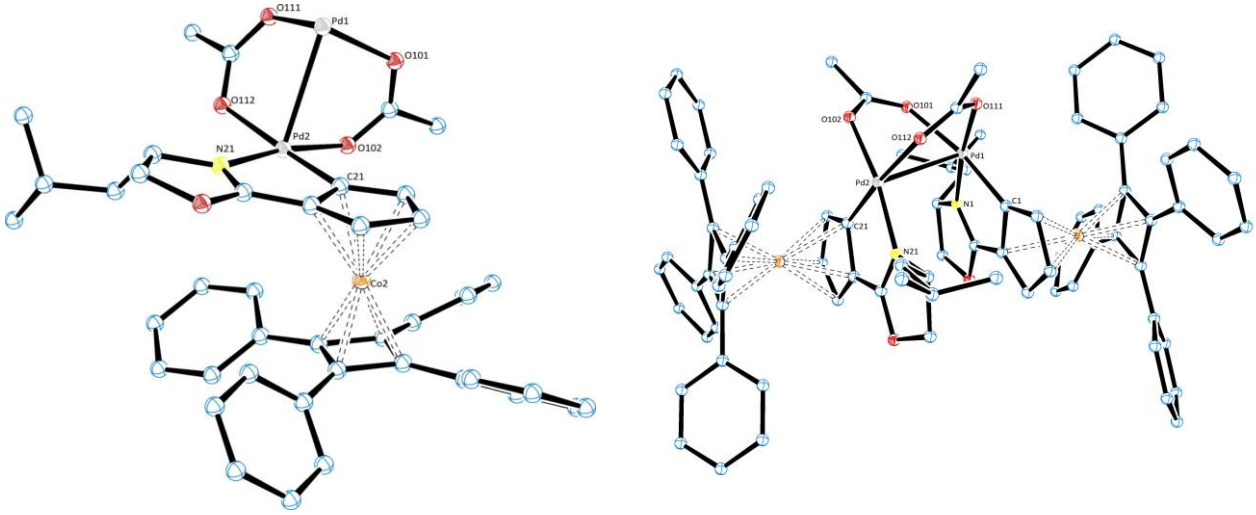


Figure 31 – X-Ray crystal structure of $(S, S_p)_2$-**286**. Principal bond lengths [Å] include: Pd(1) –Pd(2) 2.836(2), Pd(2) –C(21) 1.957(3), Pd(2) –N(21) 2.029(3), Pd(2) –O(102) 2.033(2), Pd(2) –O(112) 2.120(2); mean Co–C(C4-ring) 1.986(5), mean Co–C(cp) 2.071(3). Principal angles [°] include: C(21) –Pd–N(21) 81.24(11), O(102) –Pd–O(112) 91.44(9).

The $Pd_2(\mu\text{-OAc})_2$ unit of $(S,S_p)_2$-**286** has a Pd–Pd distance of 2.836(2) Å indicative of weak metal-metal bonding,[211] and the 'open-book' or 'clam' shape resulting from the bridging ligands is a structural feature found in all acetate-bridged palladacycles. Similar to other dimeric μ^2-acetate bridged palladacycles, complex $(S,S_p)_2$-**286** forms only the *trans*-acetate dimer. For a racemic planar chiral palladacycle containing a μ^2-bridging ligand up to six dimeric structures are possible: *trans*-S_p,S_p, *trans*-R_p,R_p, *trans*-S_p,R_p, *cis*-S_p,S_p, *cis*-R_p,R_p and *cis*-S_p,R_p. Coupled with the *trans* geometry, a planar chiral acetate-bridged palladacycle is only feasible with matched S_p,S_p or R_p,R_p configurations, a mixed S_p,R_p configuration results in a severe steric clash between the bulky ligands (Figure 32). In addition to $(S,S_p)_2$-**286**, the

majority of reported X-ray crystal stuctures of planar-chiral acetate-bridged palladacycles are all *trans*-S_pS_p or *trans*-R_p,R_p.[84,115,119,212] By minimising the number of dimeric acetate-bridged palladacycles formed on palladation, it is likely that self-recognition is important in the selective precipitation of diastereomerically pure (S,S_p)$_2$-**286** and (S,S_p)$_2$-**287** (R = CH_2Cy) from acetic acid.

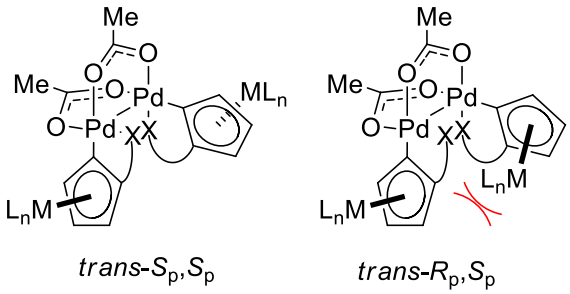
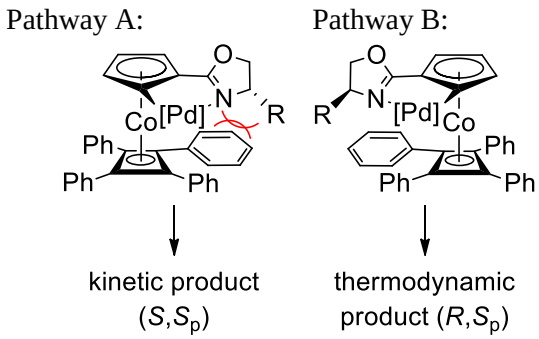


Figure 32

3.4 Origins of Diastereoselectivity

Previously, the origins of diastereoselectivity in similar palladation reactions have been likened to the highly selective lithiation of related ferrocenyl oxazoline complexes.[111,112,120,129] In these processes it is reasoned that the substituent on the ligand is important in controlling the site of metallation (Scheme 106).[17,116,117] Due to blocking by the lower cyclobutadienyl moiety of the ligand, the metallating agent (in this case palladium acetate) must approach from above the cyclopentadienyl ring. The most favourable conformation for approach is represented in pathway A where the bulky group R is pointed away from the metallating agent and hence it has no interaction with the oxazolinyl moiety. This leads to the kinetic product being the major diastereoisomer formed, in this instance the S,S_p-palladacycle. Conversely, in the formation of the R_p palladacycle, the metallating reagent is blocked by the R-group of the oxazolinyl ligand leading to the S,R_p-thermodynamic product, in which there is no interaction between the R-substituent and the tetraphenylcyclobutadiene moiety (pathway B).



Scheme 106

A previous study on the palladation of the ^{i}Pr substituted oxazoline (*S*)-**117** in acetic acid at 95 °C revealed that initially the ratio of $(S,R_p)_2$-**118**:$(S,S_p)_2$-**118** was 1:2 (after 5 minutes), as determined by ^{1}H-NMR spectroscopy. This ratio changed to >20:1 in favour of the (S,R_p)-palladacycle after 30 minutes, which then exclusively precipitates from solution as the major thermodynamic diastereoisomer.[116] A similar study was conducted on the palladation of CH_2Cy oxazoline (*S*)-**283**, which revealed that the ratio of $(S,S_p)_2$-**287**:$(S,R_p)_2$-**287** (>30:1) did not change appreciably prior to precipitation of the major kinetic product $(S,S_p)_2$-**287**, as a single diastereoisomer.

Further examination of the palladation of the ^{i}Pr substituted oxazoline (*S*)-**117** in CH_2Cl_2 at room temperature again revealed a change in diastereoselectivity over time, with the initial preference for $(S,S_p)_2$-**118** seen and then switching to the (S,R_p)-palladacycle after prolonged stirring, (after 18 hr, Figure 33). The introduction of an additional 0.1 equivalents of diastereomerically pure $(S,R_p)_2$-**118** into the reaction mixture after 2 hours resulted in the same ratio (1.4:1, R_p:S_p) of diastereoisomers on equilibration. It should be noted that the amount of starting oxazoline ligand and coordination complex had disappeared from the ^{1}H-NMR spectra after 5 minutes, showing that the selectivities seen are indeed a consequence of a reverse in configuration, rather than a product arising from palladation.

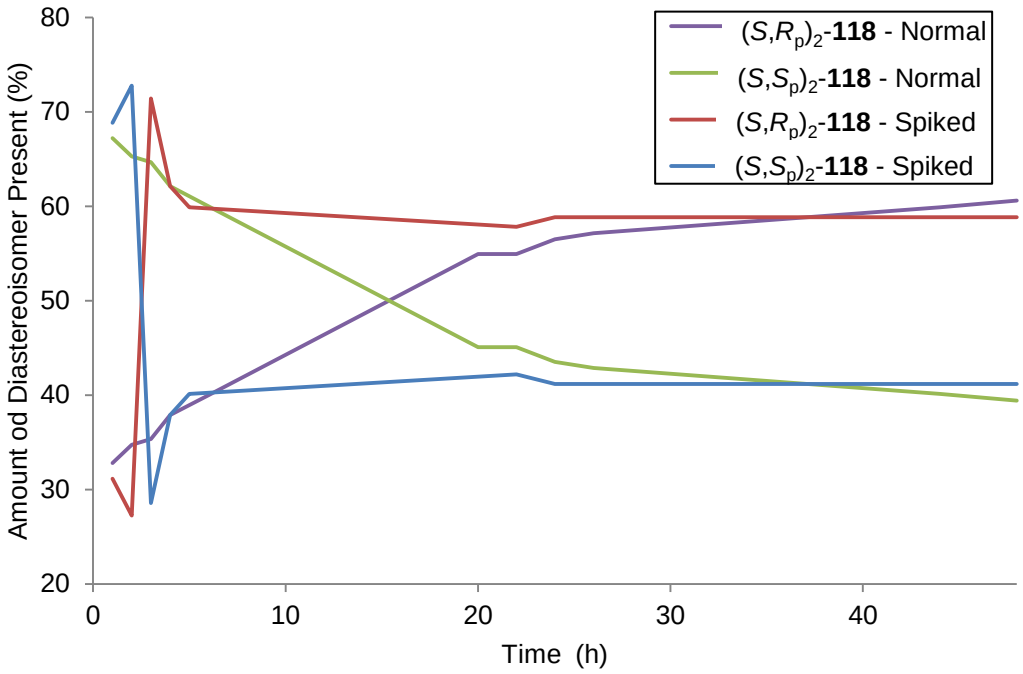


Figure 33

Examination of the palladation of the CH_2Cy oxazoline under analogous conditions revealed an initial ratio of $(S,R_p)_2$-**287**:$(S,S_p)_2$-**287** of 1:3, which decreased slightly to 1:2 with stirring. Similarly, palladation of the $CH_2{}^{i}Pr$ oxazoline established that initial selectivity peaked at a ratio of 1:23 of diastereoisomers $(S,R_p)_2$-**286**:$(S,S_p)_2$-**286** which again decreased over time to a final selectivity of 1:13 (R_p:S_p).

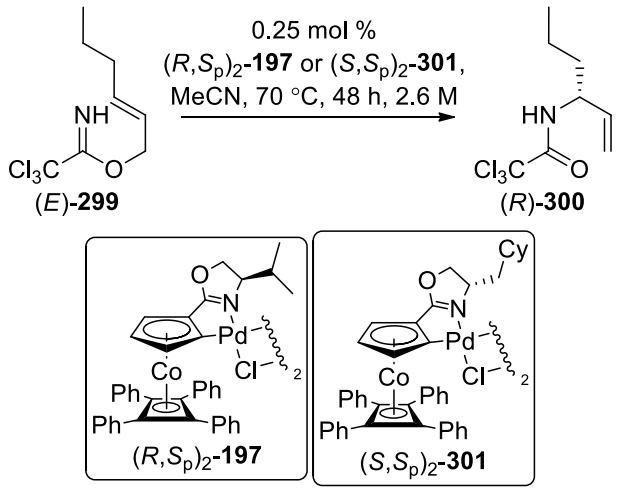
From these examples it is apparent that the palladation process in both AcOH and CH_2Cl_2 is a reversible process due to the possibility a retro-CMD pathway in the palladation step, allowing for equilibrium in all cases. Common to all these oxazolines is the kinetic preference for the formation of the (S,S_p)-palladacycle diastereoisomer, which conforms to the selectivity seen in other examples.[115,117] The relative rate of epimerisation for (S,R_p)-**118**/(S,S_p)-**118** seems to be faster than that seen for the CH_2Cy and $CH_2{}^{i}Pr$ examples. This may be due to the increased flexibility associated with the oxazoline substituent, (for CH_2Cy and $CH_2{}^{i}Pr$ examples), as such equilibrium to the thermodynamic (S,R_p)-palladacycle can occur slower resulting in the (S,S_p)-palladacycle being the major product seen. The selectivity seen in the reactions shown in AcOH is enhanced by the preferential precipitation

of the insoluble major diastereoisomer produced, whereas in CH_2Cl_2 the resultant palladacycles are soluble and can reach equilibrium. Thus although the kinetic selectivity is always the same for all examples, the outcome of these palladation reactions is governed by the subtle balance between possible epimerisation and palladacycle solubility.

3.5 Use in Asymmetric Synthesis

3.5.1 Catalysis of the Allylic Imidate Rearrangement

Preliminary catalytic studies in the trichloroimidate rearrangement were undertaken using chloride-bridged analogues of complexes $(R,S_p)_2$-**118** and $(S,S_p)_2$-**287**.[213] The chloride-bridged dimers could be readily synthesised through reaction of the acetate dimers with 2M NaCl in acetone.[11] Reaction of imidate (*E*)-**299** with 0.25 mol % of $(R,S_p)_2$-**197** in acetonitrile at 70 °C gave (*R*)-**300** in 93% yield and 93% *e.e.* (Scheme 107), which is comparable to that reported previously.[214] Using the same catalyst loading and conditions, it was shown that complex $(S,S_p)_2$-**301** was a slightly less active catalyst, giving (*R*)-**300** in 74% yield and 80% *ee*. Further catalytic studies will need to be investigated in the future.



Scheme 107

3.6 Conclusion

In conclusion, the diastereoselective palladation of a range of chiral oxazoline cobalt sandwich complex ligands was investigated. Formation of the chiral ligands could be achieved by reaction of (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) **238** with a range of chiral amino alcohols and subsequent cyclisation. Palladation of the oxazoline ligands with palladium (II) acetate in acetic acid led to the formation of new planar chiral palladacycle complexes, in which di-μ-acetatobis[(η^5-(*S*)-(S_p)-2-(2'-4'-methylcyclohexyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (S,S_p)$_2$-**287** precipitated as a single diastereoisomer. Related oxazoline ligands, using the same conditions, precipitated from the reaction media as an intermediate bis-oxaoline complex, which could undergo a CMD process in toluene at elevated temperatures to form the desired cyclometalated complexes. Alternatively, palladation reactions could be carried out in dichloromethane to give a catalogue of chiral palladacycles in a range of selectivities (1:1 – 13:1). All examples gave the opposite stereochemistry, with regards to the planar chiral element, for palladation when compared with literature example di-μ-acetatobis[(η^5-(*S*)-(R_p)-2-(2'-4'-methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (S,R_p)$_2$-**118** (COP-OAc). Studies on the palladation reaction, by monitoring diastereoselectivity over time, showed that the examples (S,S_p)$_2$-**286** and (S,S_p)$_2$-**287** selectively form the kinetic product for the reaction, whereas (S,R_p)$_2$-**118** initially forms the S_p palladacycle, but subsequently equilibrates to give the thermodynamic R_p palladacycle. Finally, preliminary catalyst screening in the trichloroimidate rearrangement showed that chloride-bridged dimer (S,S_p)$_2$-**301** could catalyse the reaction with low catalyst loading (0.25 mol %, 74% yield, 80% *ee*.).

Chapter 4 – Results and Discussion 3

4.1 Introduction

As discussed in previous chapters, COP systems can be readily synthesised as single diastereoisomers in minimal steps using relatively cheap, commercial reagents; it is also a highly selective catalyst for many reactions. Although these complexes exhibit a range of benefits, the industrial use of catalysts similar to and including COP are relatively sparse, with most chiral synthons still being produced from natural chiral building blocks or *via* resolution of racemic mixtures. One reason for this oversight is that the catalysts must be recovered and re-used to become a viable option.

Overcoming this issue has been a hot topic in recent years. The most successful method being the immobilisation of an asymmetric catalyst on a non-soluble support, creating a chiral heterogeneous catalyst that can be freely recovered from the reaction mixture. Unfortunately 'heterogenisation' proves to be a major challenge because when the catalyst is fixed it invariably loses a proportion of its activity, (compared with its homogeneous counterpart).

Even with this drawback, the idea of heterogenisation is an attractive one and could potentially lead to highly selective, reusable catalysts, as such this chapter serves to give a brief introduction to the field and subsequently highlight efforts towards the modification of COP-systems to allow for immobilization onto a solid support.

4.1.1 Immobilisation of Homogeneous Catalysts

Immobilisation of homogeneous catalysts occurs by the covalent or non-covalent attachment of the chiral ligand, metal, or preassembled complex to a support. Four different methodologies have been developed for the heterogenisation of homogeneous catalysts:

Adsorption, Encapsulation/Entrapment, Electrostatic Interaction or Covalent Linking/Tethering (Figure 34).[215]

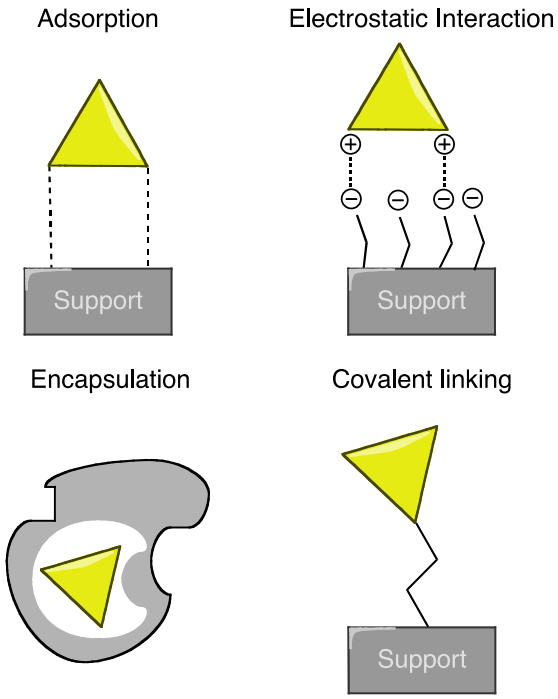


Figure 34[215]

4.1.1.1 Adsorption

Catalysts immoblised by the adsorption method rely on van der Waals interactions between the catalyst and the support. This is an attractive approach, as it renders the synthetic modification of the chiral ligand unnecessary. However, as this is only a weak interaction, the catalyst will readily leach into the solution, as an equilibrium is found between the catalyst in solution and catalyst adsorbed.[215] The stability of a supported catalyst can be improved greatly by modification of the chiral metal-ligand complex to give hydrogen bonding with a polar solid support.[216]

Chiral rhodium phosphine catalysts have been immobilised utilising this method whereby the phosphine ligand was modified to incorporate a sulfonic acid group. This allowed for the attachment of the catalyst to a solid support *via* hydrogen bonding with silanols on the

surface of silica (Figure 35).[217] The immobilised catalyst could subsequently be used as an asymmetric catalyst for the hydrogenation of olefins.

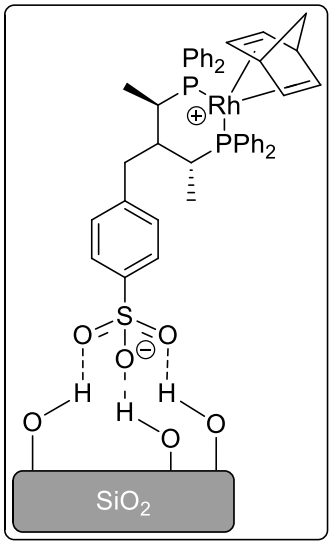
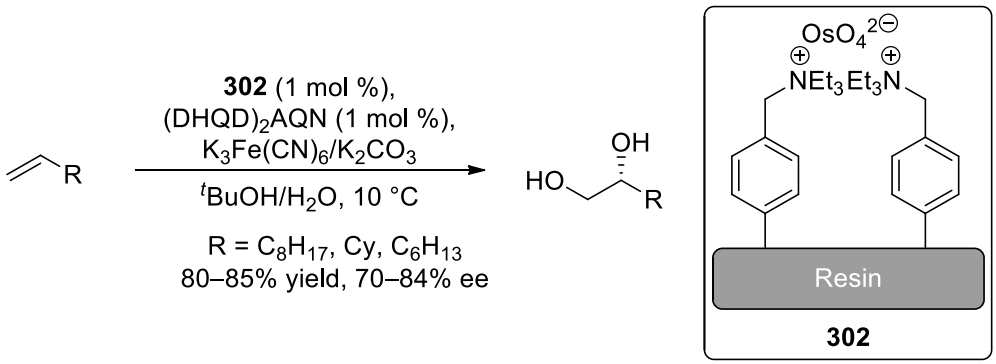


Figure 35

4.1.1.2 Electrostatic Interaction

Many porous solids, including zeolites, zeotypes and mesoporous silicates can act as ion exchangers. This provides an excellent method for the immobilisation of metal cations and complexes through electrostatic interactions.[218] This has been the method of choice for developing heterogeneous catalysts for a number of synthetic transformations.[219–221] This process also provides direct immobilisation of the metal itself, allowing for the recycling of expensive or toxic metals.

A good example of this is in the immobilisation of the OsO_4^{2-} ion onto quartenary ammonium groups supported on styrene-based polymers, such as derivitised Merrifield's resin **302** (Scheme 108). The catalyst was shown to be an excellent catalyst in the dihydroxylation of a number of olefins, exhibiting good yields and selectivity.[222]



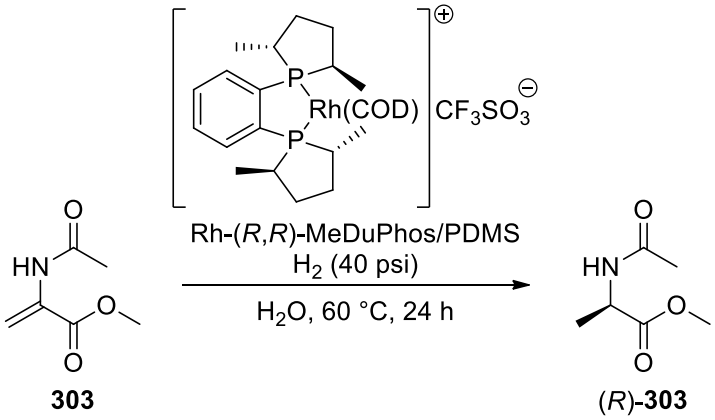
Scheme 108

4.1.1.3 Encapsulation

Encapsulation is the only catalyst immobilisation technique that does not require any favourable interaction between the catalyst and the support and because of this, it is the only method that attempts to mimic the homogeneous catalysed reaction process. In general, the complexes can either be successively assembled within the pores of a mesoporous material,[223] or the presynthesised catalyst can be entrapped by building the solid support around the catalyst using polymerisation techniques. In both cases, the diameter of the pores must be small enough (or conversely the catalyst must be large enough) such that the catalyst cannot leach into the surrounding reaction media. As a consequence, the accessibility of the active catalyst is restricted and can lead to longer reaction times.[224]

An example of this type of approach was illustrated in 1999 by the first immobilisation of Rh–MeDuPHOS by occlusion in a polydimethylsiloxane (PDMS) film (Scheme 109).[225] Initial results in the asymmetric hydrogenation of methyl-acetamidoacrylate **303** were promising, but the reaction conditions caused leaching of the catalyst into the reaction media. Subesequent studies revealed that using water as the solvent, catalyst leaching could be significantly reduced (<5% over 100 hours in solution).[226] Under the optimized conditions, asymmetric hydrogenation could be carried out to give acetyl-protected amino ester (*R*)-**304** in comparible selectivities to that of the homogeneous system albeit with a longer reaction time (24 h, 97% *ee* heterogeneous, 2 h, 99% *ee* homogeneous). The loss in

selectivity was accounted for by a small presence of Pt present in the PDMS film, which is a byproduct of the initial polymerisation step.



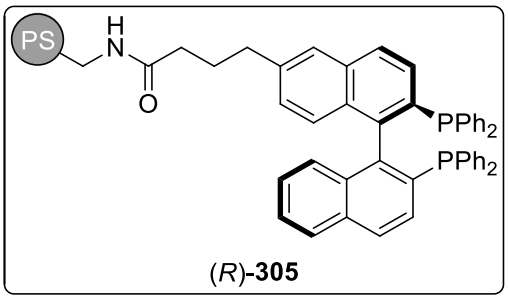
Scheme 109

4.1.1.4 Covalent Linking

A more classical approach to the heterogenisation of catalysts is to immobilise a ligand or its metal complex *via* a covalent linkage to a suitable support. There are three main approaches to this type of immobilisation, the first is by covalently linking the catalyst to a functionalised polymer resin, such as Merrifields resin. Secondly, co-polymerisation can be used by selecting suitable monomers, and lastly catalysts can be immobilised on inorganic supports such a silicon oxides.

To achieve minimal interactions between the catalyst and the solid support, the anchoring point in the ligand structure is usually as far removed from the active site as possible. Furthermore, a long and flexible linker between the catalyst and a highly swellable polymer are usually chosen to aid reactivity.[215]

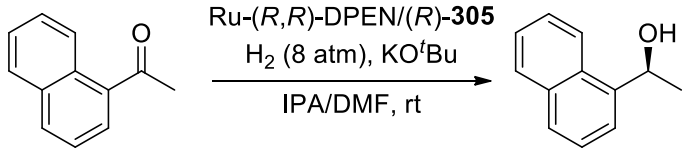
There are many examples of covalent linking between chiral ligands and polymer resins. Bayston and co-workers successfully immobilised (*R*)-BINAP on a polystyrene (PS) ligand through an alkyl amide at its 6-position (Figure 36). High enantioselectivities were gained for the ruthenium-catalysed hydrogenation of β-ketoesters (up to 99% yield and 97 % *ee*).[227]



(*R*)-**305**

Figure 36

In 2001 Noyori took immobilised catalyst (*R*)-**305** and showed that it was possible to obtain high turnover numbers (TON) in the ruthenium-(*R*,*R*)-DPEN-catalysed hydrogenation of ketones (Scheme 110). The hydrogenation of acetonapthone **306** worked particularly well with a TON of 33000 reported in a total of 14 consecutive experiments, whilst utilising the same batch of catalyst.[228]



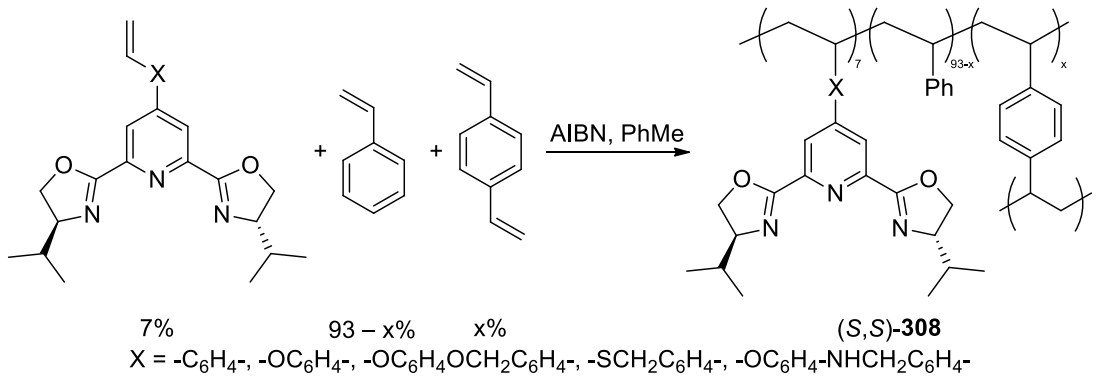
306 (*S*)-**307**

Run 1: reaction time = 26 h, conversion 99%, 98% ee
Run 14: reaction time = 86 h, conversion 93%, 97% ee

Scheme 110

Co-polymerisation of suitable monomers, allows for the integration of the ligand into the backbone of the polymer support. Radical polymerisation is the most commonly used method, with the polymerisation of vinyl- modified ligands with styrene and divinylbenzene[229] (Scheme 111) or polymerisation of amines with isocyanates to form polyurethanes[230] the methodologies of choice.

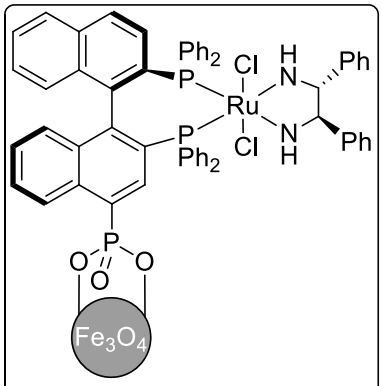
Polymer (*S*,*S*)-**308** has been used as a ligand in the stereoselective cyclopropanation of styrene, with results gained comparible with those seen for the homogeneous counterpart (yields over 60%, with up to 90% *ee* can be obtained in four successive reactions).[229]



Scheme 111

The heterogenisation of catalysts using inorganic materials as the solid support is a method wherein the derivitised catalyst is covalently bound to materials such as silica, alumina oxide or zeolites. This method offers a number of advantages over other applications: their rigid structure does not alow for aggregation of the catalyst, they offer increased thermal stability over other examples, and they are insoluble in organic solvents.[231]

An interesting example of this type of heterogenisation was demonstrated by Lin *et al.*, where they used super-paramagnetic magnetite nanoparticles (Fe_3O_4) as a support for the [Ru-(binap)(dpen)] complex, (*R*,*R*,*R*)-**309** (Figure 37). The group successfully demonstrated that the catalyst was slightly more active in the asymmetric hydrogenation of ketones compared with its homogeneous counterpart. Also, the magnetite nanoparticles can readily be magnetised by an external magnet, and as such the nanoparticles and therefore the catalyst can be removed from the reaction media by use of an external magent. The catalyst was recycled using this method up to 14 times without a decrease in the conversion or enantioselectivity (100% conversion, 97–98% *ee*).

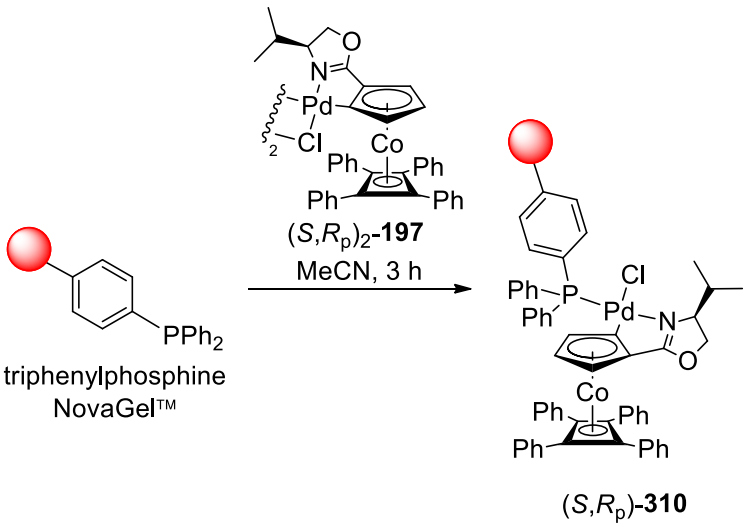


(*R*,*R*,*R*)-**309**

Figure 37

4.1.2 Strategy for Immobilisation

Richards has previously shown that immobilisation of COP-systems is possible. Reaction of COP-Cl $(S,R_p)_2$-**197** with tripheylphosphine NovaGel gave coordinated heterogeneous complex (S,R_p)-**310** (Scheme 112).[214] This complex was shown to catalyse the rearrangement of propyl-trichloroimidates with good yield and selectivity (91% yield and 94% *ee* of rearranged product). However, subsequent isolation by filtration and re-use of the catalyst resulted in good selectivities seen (93% and 89% *ee* seen for runs 2 and 3 resepectively) but also a sharp decrease in yield (27% and 17% seen for runs 2 and 3 respectively). It was suggested that the erosion in yields was due to leaching of the catalyst because of the weak bonding mode used for immobilisation. The active catalyst was a homogeneous catalyst resulting from phosphine dissociation.[214]



Scheme 112

With this in mind, it was rationalised that the most attractive strategy for the immobilisation of COP catalysts would involve finding a method where derivitisation is simple and will not effect the catalytic activity of the system. The ideal system therefore would be a covalently linked metallocene, in which the tethered part of the molecule is as far removed from the catalyst active site as possible. In this case it was envisioned that the binding would be ideally situated on the aryl groups of the lower cyclobutadiene moeity of the metallocene, with the catalyst in a monomeric state, to avoid leaching (Figure 38).

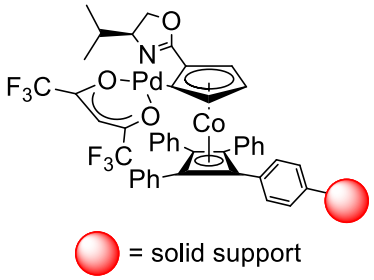
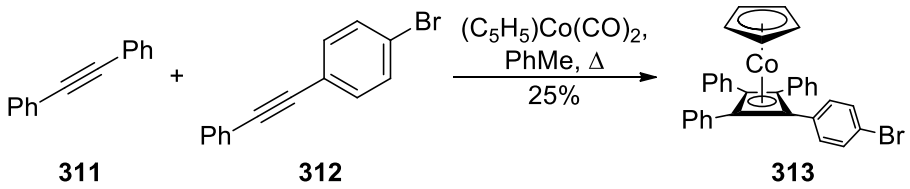


Figure 38

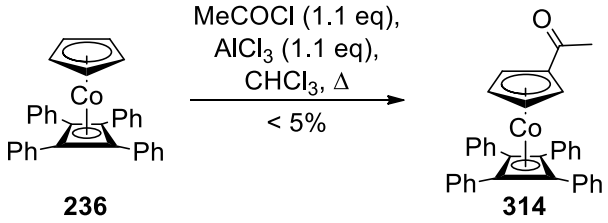
In the literature, examples of aryl-substituted metallocenes are sparse, with differentially substituted aryl derivatives proving a significant challenge. For example, reaction of diphenylacetylene **311**, 4-bromodiphenylacetylene **312** and (η^5-cyclopentadienyl)cobaltdicarbonyl (Scheme 113) results in an essentially statistical mixture of the four expected metallocenes, and thus a low yield of the product required, in this

instance (η^4-4-bromophenyltriphenylcyclobutadiene)(η^5cyclopentadienyl)cobalt **313** (25%).[232] A better method for aryl-modification was therefore required to give the desired handle for immobilisation and Friedel-Crafts acylation was suggested for use.



Scheme 113

In contrast to ferrocene, cobalt metallocene **236** is a very poor substrate for Friedel-Crafts substitution, and attempts to perform this reaction have been reported to result in only trace amounts of cyclopentadienyl ring acylated product **314** (Scheme 114).[181]



Scheme 114

It was reasoned that substitution at the cyclopentadienyl ring might be reduced/prevented by utilisation of COP precursor **240**, where deactivation of the cyclopentadienyl component of the metallocene by the introduction of an ester moiety would result in selective Friedel-Crafts substitution of one of the phenyl groups of the lower cyclobutadienyl ring (Figure 39).

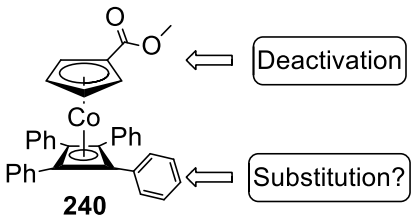
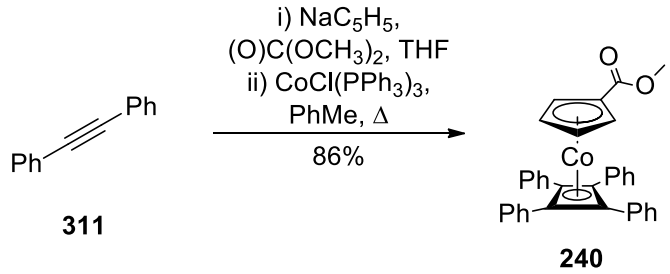


Figure 39

4.2 Regioselective Synthesis of Derivatised Metallocenes

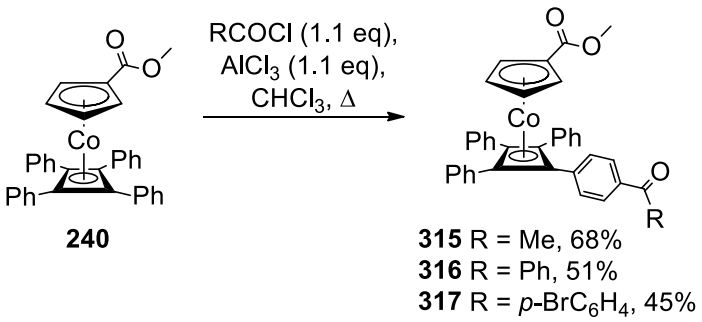
Cobalt metallocene complexes can be synthesised by a variety of methods.[17,181] The most facile route was to take $CoCl(PPh_3)_3$ and react with suitable ligands with heating. Reaction of cobalt(II) chloride hexahydrate with triphenylphosphine under anhydrous conditions, and subsequent reduction with sodium borohydride gave the required cobalt complex precursor, $CoCl(PPh_3)_3$, in 94% yield. Reaction of $CoCl(PPh_3)_3$ with 2 equivalents of diphenylacetylene **311** and 1 equivalent of $NaC_5H_4COOCH_3$, which was generated *in situ* by reaction of sodium cyclopentadienide and dimethyl carbonate, gave metallocene **240** in good yield (Scheme 115).[17]



Scheme 115

Friedel-Crafts reaction of cobalt metallocene with 1.1 equivalents of acetyl chloride/aluminium chloride resulted in a 1:4.6:1 ratio of unsubstituted, mono and diacylated products respectively (Scheme 116). The major *para*-substituted product **315** was isolated in 68% yield *via* chromatography as exclusively the *trans* regioisomer. The appearance of a characteristic IR carbonyl stretch at 1685 cm^{-1} and an acetyl methyl singlet peak at 2.57 ppm in the ^{1}H-NMR spectrum of **315** integrating for 3 protons confirmed that the acylation had been sucessful, with a single peak confirming *para*-only substitution. There is also a doublet shifted downfield at 7.77 ppm integrating for 2 protons, which is consistant with mono-substitution of the electron withdrawing functional group. The disubstituted compound arising from this reaction can either be *cis* or *trans* with respect to which phenyl groups the substitution occurs. This was found to occur with no selectivity (1:2 ratio of *trans*:*cis* isomers) inferring that the first acylation does not effect the latter. This methodology was

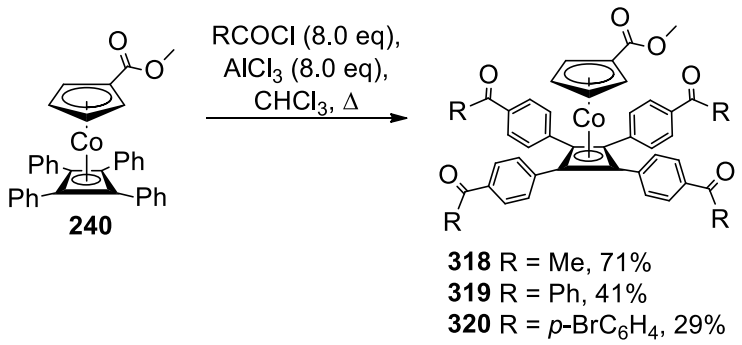
extended to generate other monosubstituted metallocenes **316** and **317** by variation of the acid chloride used. Mass spectrometry was used to confirm that monosubstitution had taken place due to complexity in the aromatic region of the ^{1}H-NMR spectra.



Scheme 116

The relative ease of substitution can be rationalised as similar ferrocenyl systems exert a strong activating effect with a σ_p* of –0.65 calculated, which is comparible to that of a methoxy group (σ_p* = –0.78).[233] As such cobalt metallocenes are comparible and would activate the conjugated phenyl substituent towards electrophilic aromatic substitution. *Para*-substitution is preferred to *ortho*-substitution due to steric hindrance at the *ortho* postions.

With an established methodology in hand, the protocol was extended to form tetraacylated metallocenes (Scheme 117). Reaction of metallocene **240** with 8 equivalents of acetyl chloride and aluminium chloride, with a prolonged reaction time of 16 hours, afforded the tertaacyclated compound **318**, with little or no by-products. As before, acylation was confirmed by ^{1}H-NMR spectroscopy, with the appearance of a single methyl singlet peak at 2.57 ppm, in this instance, integrating for 12 protons. Also, the aromatic region of the spectrum becomes simplified to just two signals integrating for 8 protons each, confirming tetra-substitution as the derivatised cyclobutadiene ring becomes symmetrical – if di-, tri- or *ortho*-substitution had taken place, the expected ^{1}H-NMR spectrum in the aromatic region would be more complex.



Scheme 117

Use of benzoyl chloride and 4-bromobenzoyl chloride gave tetrasubstituted metallocenes **319** and **320**, the latter requiring a longer reaction time of 48 hours. The formation of **319** could be confirmed *via* ^{1}H-NMR spectroscopy (Figure 40). Protons H^{b} and H^{c} downfield at 7.85 and 7.75 ppm respectively, both integrating for 8 protons, confirms that tetra-substitution has taken place. Also, protons *para* to the ketone moiety (H^{e}) are also present. Compound **320** was decidely more difficult to comfirm that tera-substituion had occurred, due to the relative complexity shown in the aromatic region of the ^{1}H-NMR spectrum. Instead, comparison of the theoretical and observed isotope patterns of the LCMS for compound **320** confirmed that indeed tetra-substitution had indeed taken place.

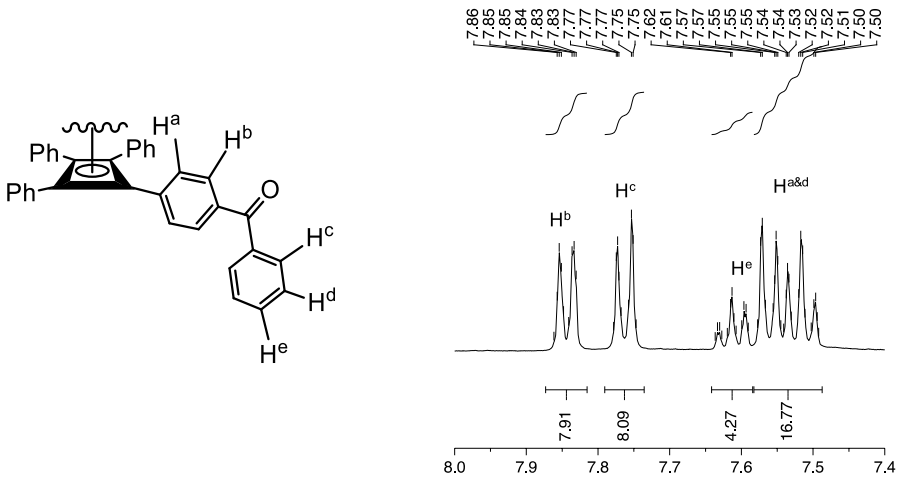


Figure 40 – ^{1}H-NMR of the aromatic region of substituted complex **319**

The structure of **319** was elucidated by crystallographic analysis (Figure 41) providing absolute confirmation of the *trans*-selectivity in these reactions. Interestingly, the benzoyl groups are all orientated such that they are pointing away from each other. With the *trans*-carbonyl oxygens O(1) and O(3) pointing up and down perpendicular to the plane with respect to the metallocene and oxygens O(2) and O(4) pointing left and right parallel to the plane of the metallocene. This would be the arrangement in which there is the least steric repulsion between the substituted phenyl rings leading to a propeller orientation of the aromatic rings.

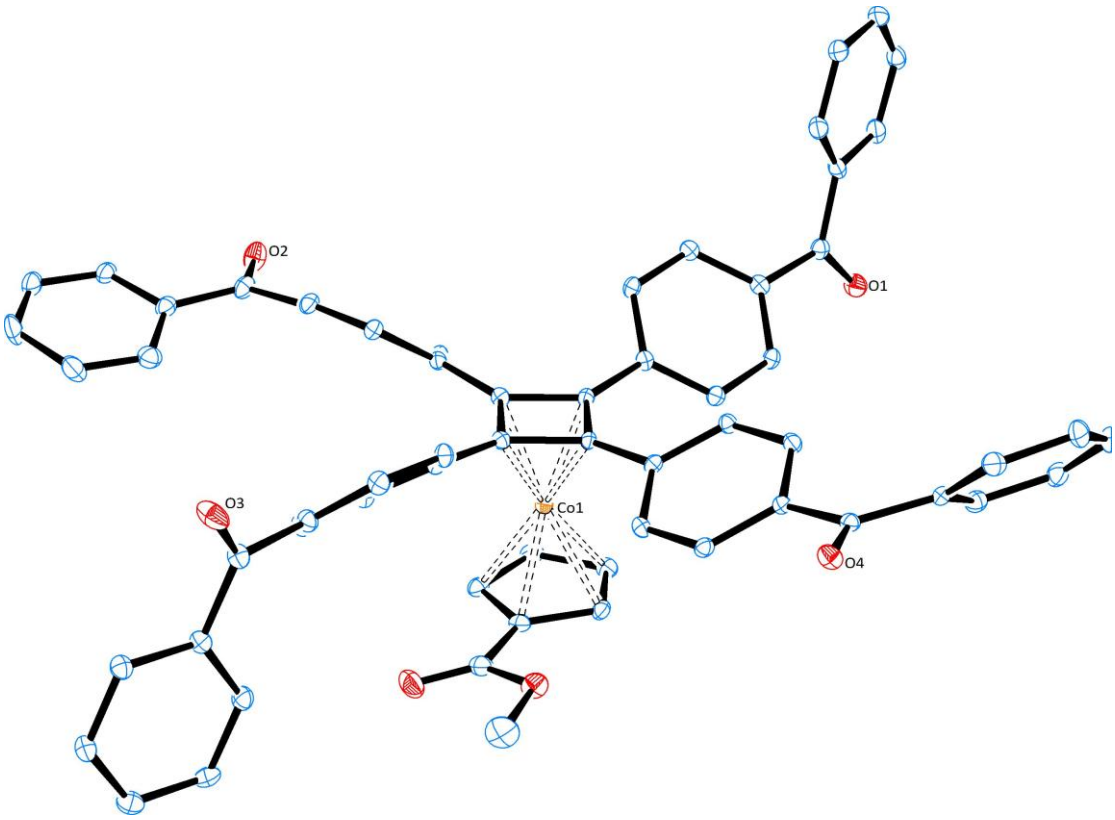
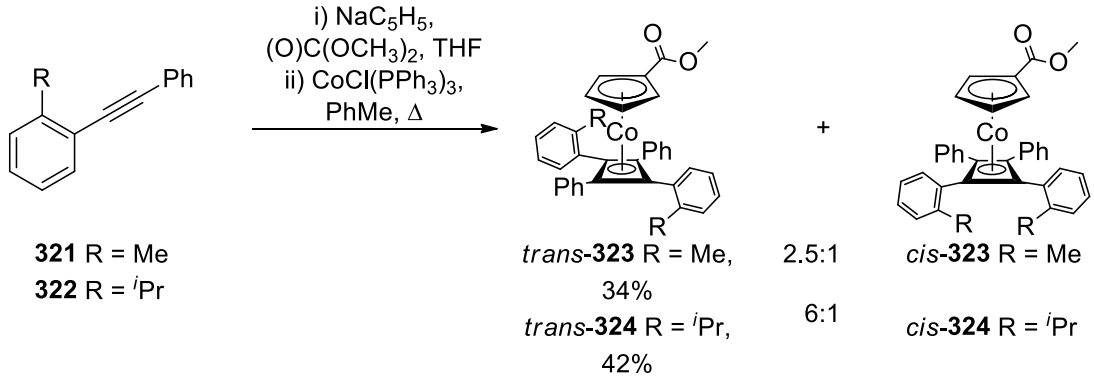


Figure 41 – X-Ray crystal structure of **319**. Principal bond lengths [Å] include: mean Co–C(C4-ring) 1.989(3), mean Co–C(cp) 2.071(3).

4.3 Regioselective Synthesis of Metallocenes and Extension of Friedel-Crafts Methodology

An alternative strategy to direct substitution was employed to generate new disubstituted aryl cobalt complexes stereoselectively from two possible *trans* or *cis* isomers. Previous attempts to synthesise an anologue of **240** from di(*ortho*-tolyl)-acetylene were unsuccessful, suggesting the unfavourable arrangement in these metallocenes of contigious *ortho*-substituted aryl groups. Instead, reaction of (*ortho*-tolyl)-phenylacetylene **321** under reaction conditions previously used for cobalt metallocene formation[17] resulted in a 2.5:1 ratio of stereoisomers of metallocene **323** (Scheme 118), which was determined from the ^{1}H-NMR spectrum of the crude reaction mixture. Purification of the major isomer *trans*-**323** was achieved *via* two recrytallisations from CH_2Cl_2/hexane and the expected *trans* regiochemistry was confirmed by X-ray crystallography (Figure 42).



Scheme 118

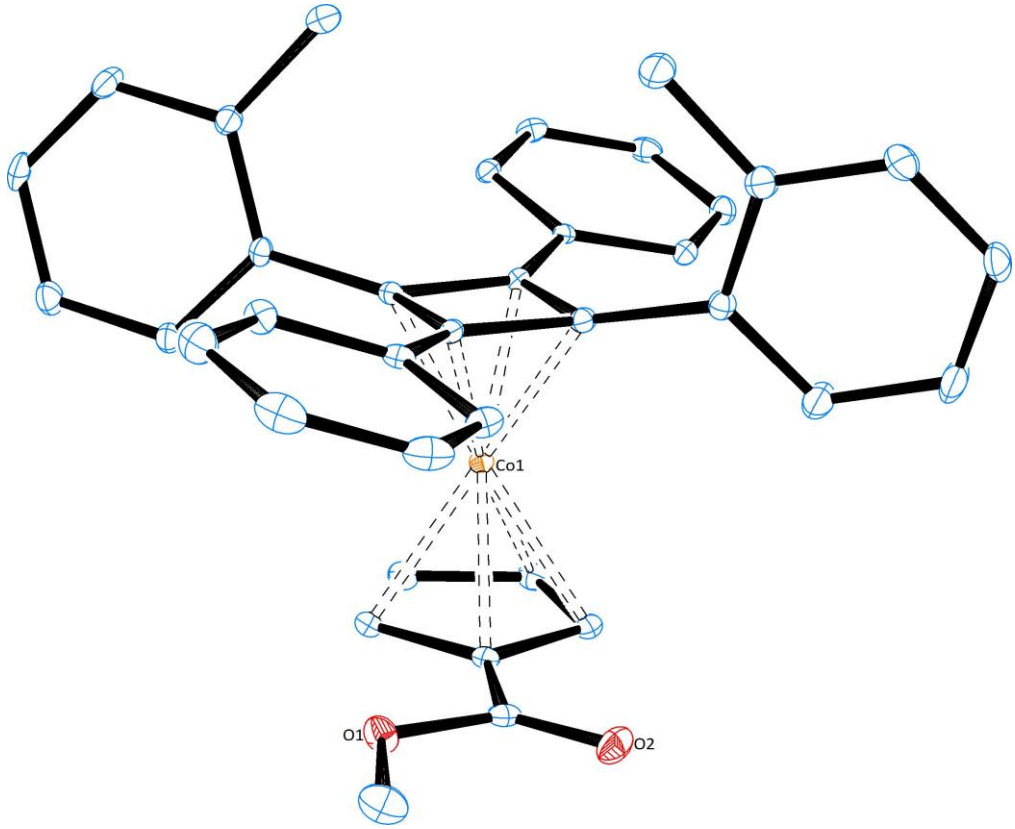


Figure 42 – X-Ray crystal structure of *trans*-**323**. Principal bond lengths [Å] include: mean Co–C(C4-ring) 1.992(2), mean Co–C(cp) 2.081(2).

It was reasoned that an *ortho*-substituent with a larger steric bulk would allow for better selectivity on steric grounds. Extension of the methodology, using (*ortho*-*iso*-propylphenyl)-phenylacetylene **322** resulted in a higher selectivity, with a *trans/cis* isomer ratio of 6:1. Recrystallisation from CH_2Cl_2/hexane afforded metallocene *trans*-**324** exclusively, which was confirmed by X-ray crystallography (Figure 43). The distance between the two isopropyl methine carbons is only 3.952 Å revealing that accommodation of the additional methyl groups of *tert*-butyl *ortho*-substituents would require a significant distortion in the cyclobutadienyl ring. With this in mind, a synthesis was not attempted.

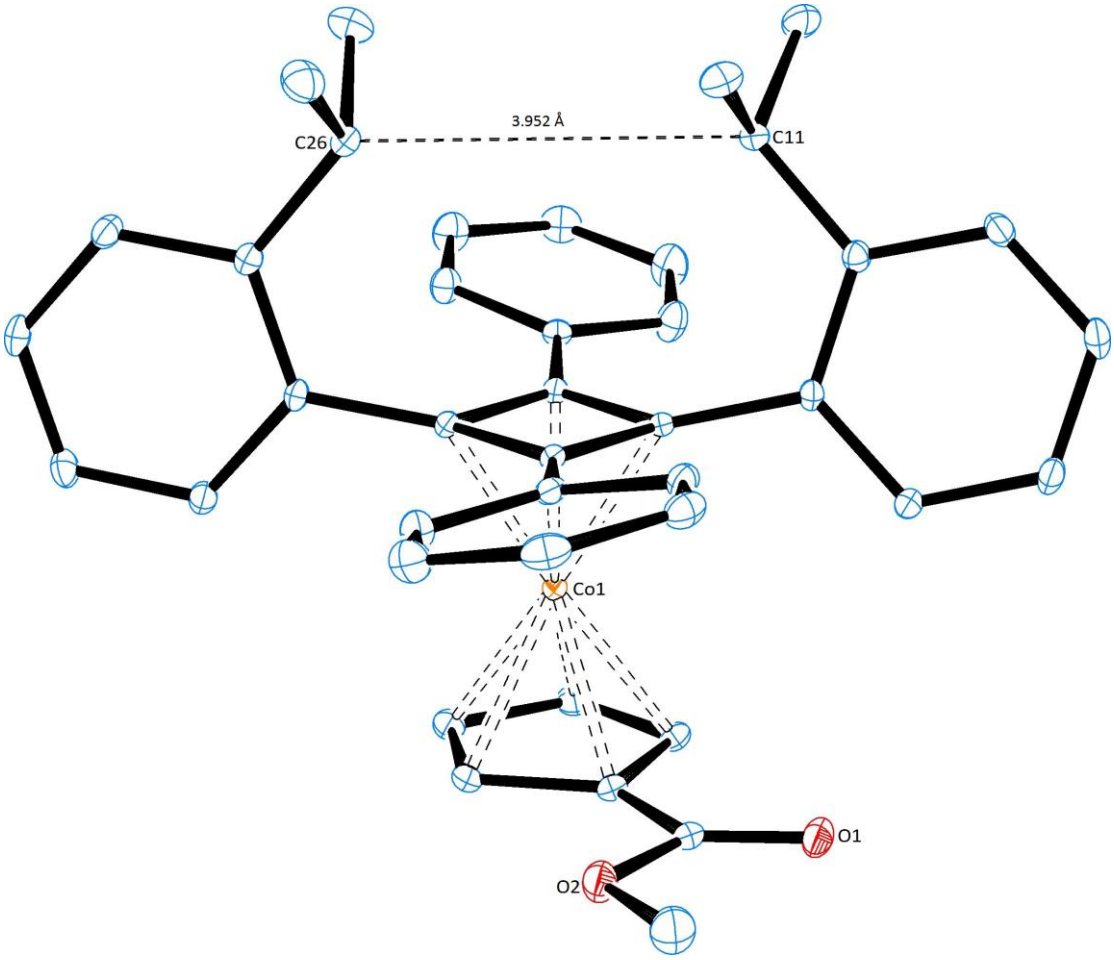
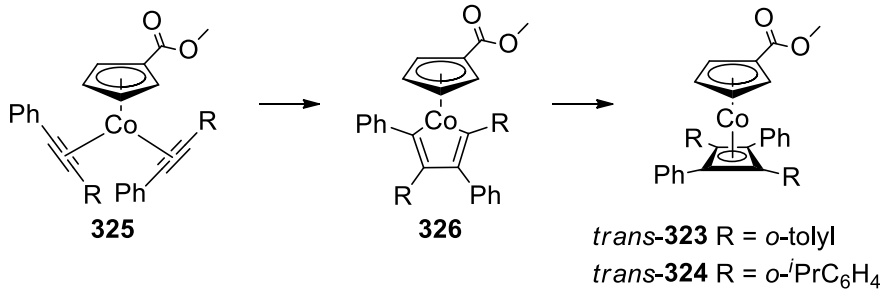


Figure 43 – X-Ray crystal structure of *trans*-**324.** Principal bond lengths [Å] include: C(11)–C(26) 3.952; mean Co–C(C4-ring) 1.989(15), mean Co–C(cp) 2.075(15).

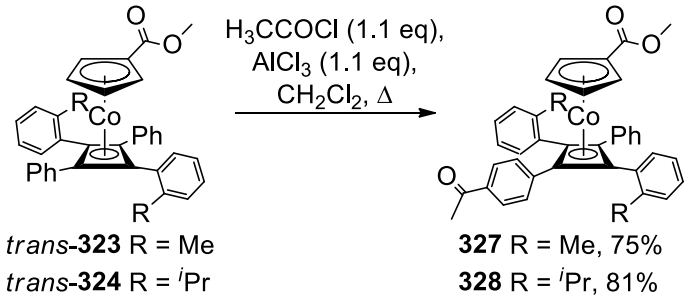
The regiochemistry of the major isomers of *trans*-**323** and *trans*-**324** is in agreement with a study on the use of mixed disubstituted acetylenes for the synthesis of η^5-cyclopentadienyl-(triphenylphosphine)cobaltacyclopentadiene complexes.[234] In these reactions the *trans*-regiochemistry of the major isomer is controlled by the steric requirement of the acetylene substituents. Related coordinatively unsaturated cobaltacyclopentadiene complexes are therefore intermediates in the synthesis of tetraphenylmetallocenes *trans*-**323** and *trans*-**324**.[183] The formation of the metallocenes occurs *via* oxidative cyclisation of a *bis*-(η^2-alkyne) complex **325** with the larger substituted-aryl groups in the more favourable *trans* orientation. This then proceeds through a cobaltcyclopentadienyl complex **326**, which is

followed by reductive elimination/η^4-coordination to give the metallocenes *trans*-**323** and *trans*-**324** (Scheme 119).



Scheme 119

The X-ray structures of *trans*-**323**/**324** give insight into the orientation of the substituted and unsubstituted aryl groups, the former being essentially perpendicular to the cyclobutadienyl ring. The unsubstituted phenyl groups are therefore 'pushed' to lie almost coplanar with the cyclobutadienyl ring, as such it was anticipated that orbital overlap between the phenyl substituents and η^4-cyclobutadiene/cobalt moiety would significantly increase the susceptibility of the unsubstituted phenyl groups for Friedel-Crafts acylation. Reaction of *trans*-**323**/**324** with 1.1 equivalents of acetyl chloride/aluminium chloride resulted in the generation of exclusively *para*-substituted metallocenes **327** and **328** (Scheme 120) in a shorter reaction time and greater yield, when compared with the unsubstituted systems. The formation of cobalt metallocene **328** showed enhanced yield over methyl-substituted derivative **327**, which is due to the greater 'flattening' of the phenyl rings. The *iso*-propyl substituents causes more distortion than in the corresponding methyl-substituted complex, thus is has increased susceptibility to substitution, hence the enhanced rate and yield seen.



Scheme 120

Confirmation of the mono-*trans* substitution can be seen in the ^{1}H-NMR spectra of **327**/**328** with the appearance of a characteristic methyl singlet for an acetyl group at 2.45 ppm. Furthermore, aromatic substitution of the unsubstituted phenyl rings can be confirmed by comparison of the aromatic region of the ^{1}H-NMR spectra for *trans*-**324** and **328** (Figure 44). For complex *trans*-**324** signals arising from protons H^{a}, H^{b} and H^{c} come at 6.80, 6.90 and 6.95 ppm respectively. For acylated product **328**, signals for H^{c} are no longer present and the signals for H^{b} are shifted downfield to 7.56 ppm, consistent with the addition of an electron withdrawing group. The conclusion that substitution occurred on the unsubstituted aromatic rings is valid because the shifts corresponding to protons H^{d-g} remain unchanged throughout. Due to the conformational rigidity of these complexes, proton H^{g} pushed into the proximity of the metal. As such the chemical shift seen is further downfield than the other aromatic protons. This same rationale can be applied to complexes *trans*-**323** and **327**.

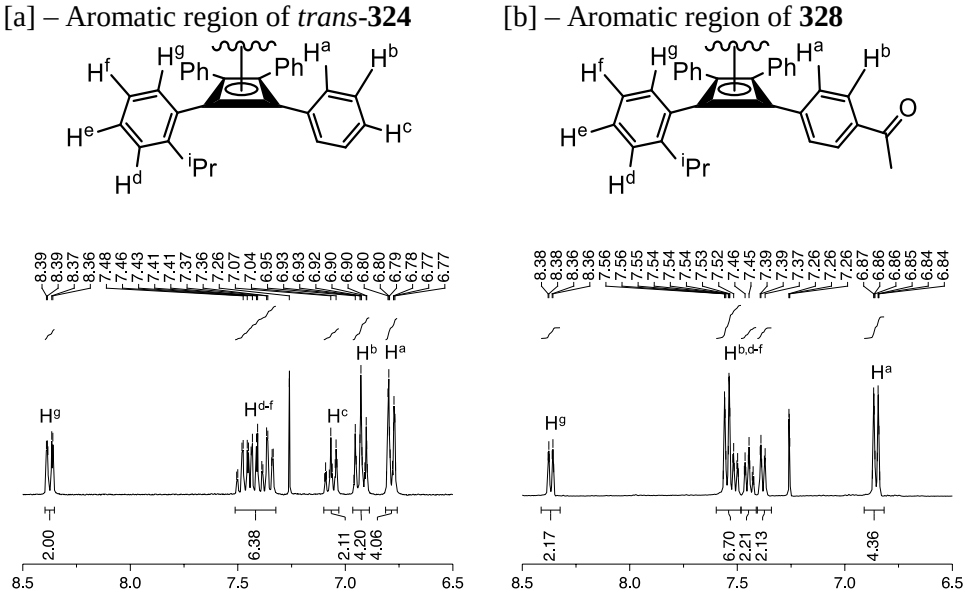
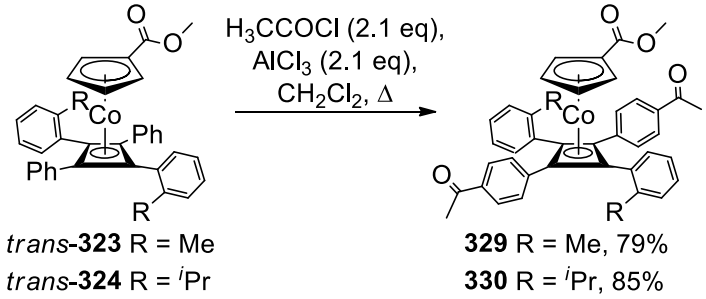


Figure 44

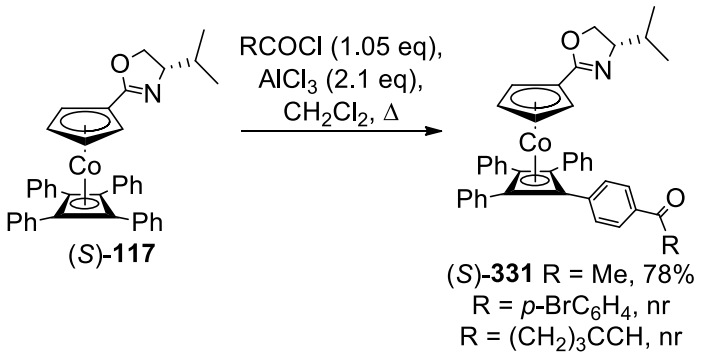
Extension of this methodology, using 2.1 equivalents of acetyl chloride/aluminium chloride resulted in the formation of diacylated metallocenes **329** and **330** with complete conformational control (Scheme 121). Substitution again can be confirmed by the ^{1}H-NMR spectra, with the appearance of a methyl peak at 2.45 ppm integrating for 6 protons as a single signal, inferring *trans*-only substitution.



Scheme 121

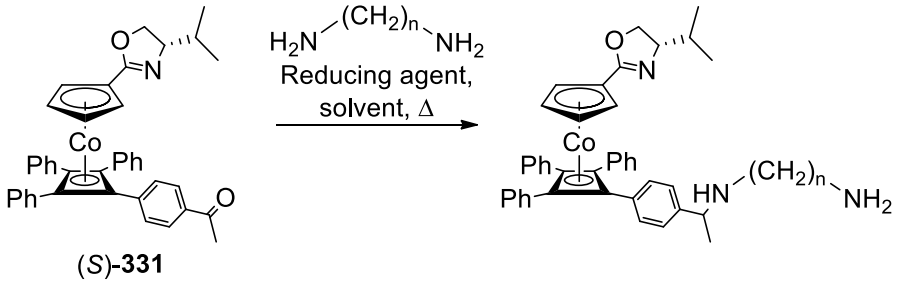
4.4 Synthesis of Derivatised COP Systems

With an established methodology found, the viability of the reaction in forming derivatives of cobalt oxazoline ligands with a handle for immobilisation was tested. Direct synthesis of the functionalised oxazoline (*S*)-**331** from metallocene **315** could be realised using the standard oxazoline formation protocol seen in previous chapters.[182] A simpler and higher yielding route to the target could be realised by reaction of ligand (*S*)-**117** with 1.05 equivalents of acetyl chloride and 2.1 equivalents of aluminium chloride to yield mono-acylated metallocene (*S*)-**331** in good yield (Scheme 122). Acid chlorides that could be useful for later immobilisation were tested under the same conditions. Unfortunately all attempts to synthesis these further derived analogues proved unsuccessful and only starting materials were recovered from the reaction mixture(s). This may be due to the enhanced deactivation of the system by the oxazoline substituent.



Scheme 122

A method for attachment of ligand (*S*)-**331** to a solid support was required and it was postulated that reductive amination may be a valid approach, as there are many methods in the literature for the binding of ligands to a support using amine linkers. A model study using a variety of diamines and reducing agents was undertaken (Scheme 123, Table 13). All reactions attempted were unsuccessful and only starting ketone (*S*)-**331** was isolated.



(*S*)-**331**

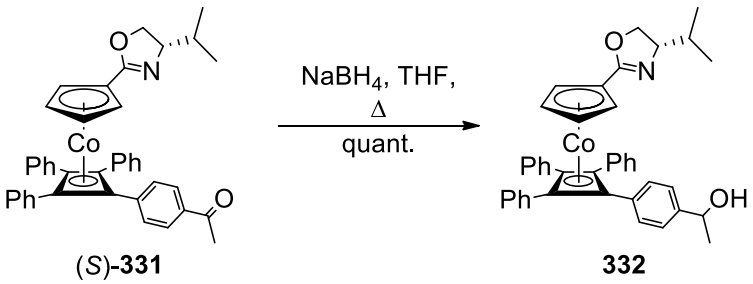
Scheme 123

Entry	n	Reducing Agent	Solvent	Yield [%]
1	3	$NaCNBH_3$	DCE	nr
2	3	$Na(OAc)_3BH$	MeOH	nr
3	3	$NaCNBH_3$	DCE	nr
4	6	$Na(OAc)_3BH$	MeOH	nr
5	12	$NaCNBH_3$	DCE	nr
6	12	$Na(OAc)_3BH$	MeOH	nr
7	12	$NaBH_4$	CH_2Cl_2	nr

Table 13

As it is the imine formation that is the rate determining step for the reaction, it was thought that the imine intermediate was not being formed. As such, imine formation was attempted using acid catalysis and Dean-Stark apparatus, followed by introduction of the reducing agent, but this was also ineffective. This lack of reactivity is due to the positive inductive effect shown by these metallocenes, increasing the electron density at the carbonyl center. Due to this inherent lack of activity, a different method was sought.

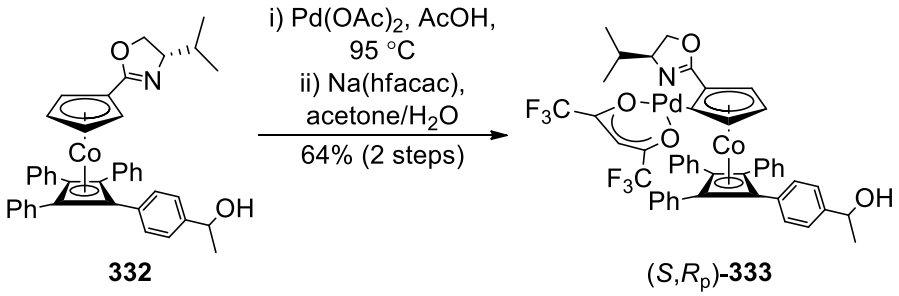
Transformation of the unreactive carbonyl to a functional group with increased reactivity was needed; as such secondary alcohol **332** could be readily accessed by reaction of complex (*S*)-**331** with sodium borohydride in THF at reflux (Scheme 124). The reaction proceeded with essentially quantitative conversion and the resultant alcohol could be confirmed from the ^{1}H-NMR spectrum by the transformation of a singlet for the acetyl group into a doublet shifted upfield at 1.54 ppm for the resultant alcohol methyl group.



(*S*)-**331** **332**

Scheme 124

To test the viability of alcohol **332** in the diastereoselective palladation reaction, the complex was treated with $Pd(OAc)_2$ under the standard palladation conditions of the parent oxazoline ligand (Scheme 125). Unlike the parent COP system, precipitation of a complex did not occur, but upon ligand exchange with sodium hexafluoroacetonate, the monomer complex (S,R_p)-**333** was isolated after column chromatography. A value for specific rotation of +589 for (S,R_p)-**333** indicates that the palladation proceeds, as with the unsubstituted example, to give the planar *R* configuration.

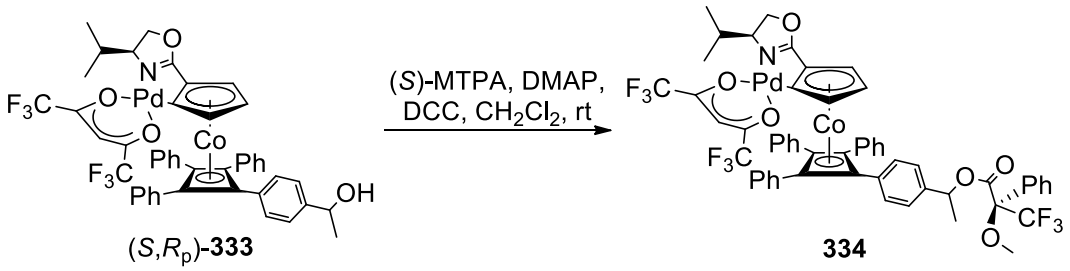


332 (S,R_p)-**333**

Scheme 125

To test for stereoinduction in the reduction step, the complex (S,R_p)-**333** was investigated using Mosher's analysis. Complex (S,R_p)-**333** was treated with (*S*)-Mosher's acid, ((*S*)-MTPA), in the presence of DMAP and DCC to form Mosher's ester **334** (Scheme 126). Similar analysis on an analogous system using (±)-1-phenylethanol showed that the signals in the ^{1}H-NMR spectra arising from the diastereotopic methoxy methyl groups came at 3.54 and 3.46 ppm respectively.[235] By looking at the ^{1}H-NMR spectra of ester **334** (Figure 45) it can be seen that two singlet signals arising for methoxy methyls are observed with a similar Δδ of 0.07 ppm. A ratio for peaks of 1:1 shows that there is no stereoinduction in the

reduction step. Further studies on the effect of this new stereocenter on palladation and eventual catalytic activity need to be undertaken.



Scheme 126

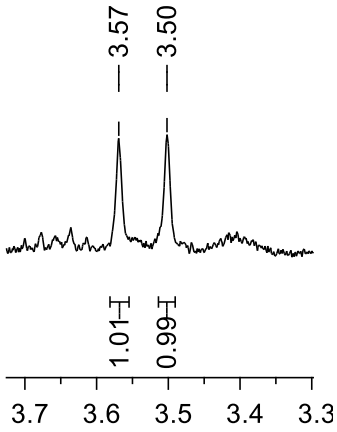
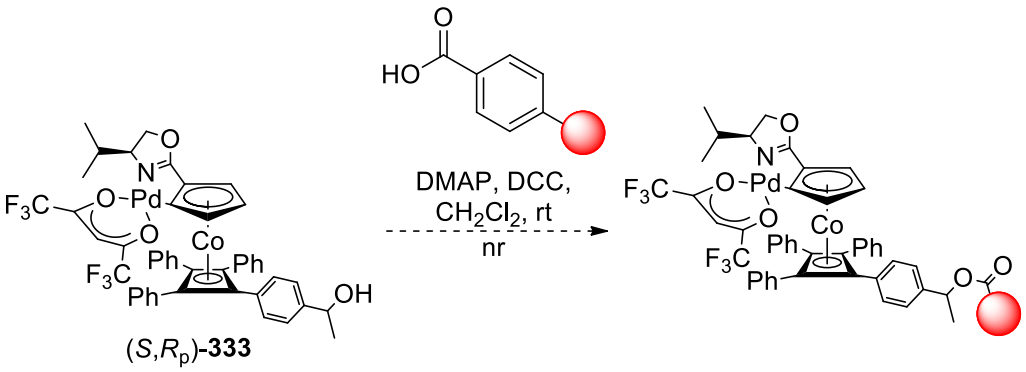


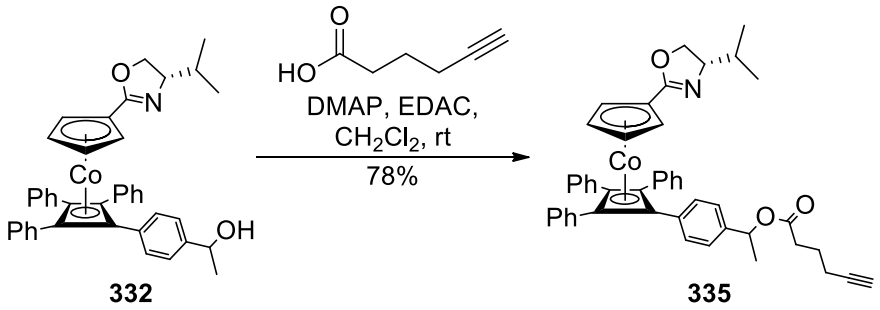
Figure 45 – ^{1}H-NMR of methoxy signals present in palladacycle **334**

Although the effect of the new stereogenic center on catalytic activity was not known, attempts to attach the modified catalyst to a solid support were carried out. Esterification between a functionalised Merrifield's resin and alcohol (S,R_p)-**333** was attempted, using the same protocol to that used to form the Mosher's ester (Scheme 127). Unfortunately, all attempts to link the catalyst to polymer failed. It was reasoned that this could be due to the bulky nature of the catalyst and consequential restriction of access required site of reaction on the polymer. It was hypothesised that the introduction of a linker would allow for immobilisation.



Scheme 127

Click chemistry was considered as an alternative method. This could be realised by reaction of alcohol **332** with modified esterification conditions, utilising EDAC, catalytic DMAP and 5-hexynoic acid to give ester **335** (Scheme 128). This new complex has the required linker, but also has a terminal alkyne group that could later be utilised for attachment of the catalyst to the solid support. Confirmation of the formation of complex **335** was accomplished using MALDI-MS, as the ^{1}H-NMR spectrum was complex. Also, this was fortified by the disappearance of an alcohol stretch in the respective IR spectrum for the complex and the addition of a band for an ester moiety at 1732 cm^{-1}.



Scheme 128

Studies towards the palladation of this functionalised oxazoline ligand, subsequent immobilisation and catalytic testing will need to be carried out in the future.

4.5 Conclusion

In conclusion, the Friedel-Crafts reaction of (η^4-tetraphenylcyclobutadiene)(η^5-

carbomethoxycyclopentadienyl)-cobalt **240** results in the exclusive *para*-substitution of the phenyl groups allowing for the efficient synthesis of mono- and tetra-substituted cobalt metallocenes.

The synthesis of related cobalt metallocenes by the cyclodimerisation of *ortho*-phenyl substituted phenylacetylenes results in the selective formation *trans*-metallocenes (with a selectivity of up to 6:1 *trans*:*cis*). Extension of the Friedel-Crafts methodology to the major isomers of these complexes resulted in conformationally controlled mono- or di-*para*-phenyl substitution.

The Friedel-Crafts methodology was used in the derivatisation of cobalt oxazoline ligand (*S*)-**117**, allowing for the stereoselective formation of functionalised ligand **332** as a precursor to an immobilised COP catalyst.

The conformational selectivity as well as regio- and stereoselectivity illustrated in this work, coupled with the extension to oxazoline ligands, will permit access to a variety of substituted cobalt metallocenes for application in catalyst and materials synthesis.

Chapter 5 - Conclusion

Firstly this body of work showcased the development of new planar chiral palladacycles from achiral ligands using an enantioselective palladation methodology. The palladation of (η^5-(dimethylaminomethyl)cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) **237** with sodium tetrachloropalladate mediated by *N*-acetyl-*D*-phenylalanine under basic conditions resulted in chloride-bridged dimer palladacycle $(S_p)_2$-**248** in 92% *ee*. The enantiopurity of the palladacycle was increased to >98% *ee* by reaction with (*R*)-proline and separation of the resultant diastereoisomers. Extension of the palladation methodology to other amines gave new palladacycles with *N*,*N*-diethyl- (82% *ee*) and pyrrolidinyl- (>98% *ee*) substituents.

The new CAP complexes were shown to be active catalysts (uon silver salt activation) for the rearrangement of (*E*)-trichloroacetimidates giving chiral amines with high enantioselectivity (up to 99% *ee*). The enantioselectivity shown by these systems can be rationalised by comparison to the COP-Cl catalysed allylic imidate rearrangement of trichloroimidates. Also, application of these new CAP complexes to the asymmetric synthesis of ferrocene-based phosphopalladacycles, using transcyclopalladation, allowed for the synthesis of the aforementioned palladacycles in up to 78% *ee*.

Secondly, diastereoselective palladation of a range of chiral oxazoline cobalt sandwich complexes was investigated, as previous literature examples gave seemingly unrational outcomes. The chiral ligands were shown to be readily accessible by reaction of (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) **238** with a range of chiral amino alcohols and subsequent cyclisation. Palladation of the oxazoline ligands with palladium (II) acetate in acetic acid led to the formation of new planar chiral palladacycle complexes, in which di-μ-acetatobis[(η^5-(*S*)-(S_p)-2-(2'-4'-methylcyclohexyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) $(S,S_p)_2$-**287** precipitated as a single

diastereoisomer. Related oxazoline ligands, using the same conditions, precipitated from the reaction media as an intermediate bis-oxaoline complex, which could undergo a CMD process in toluene at elevated temperatures to form the desired cyclometalated complexes.

All examples were shown to give the opposite stereochemistry, with regards to the planar chiral element, for palladation when compared with literature example di-μ-acetatobis[(η^5-(*S*)-(R_p)-2-(2'-4'-methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) ($S,R_p)_2$-**118** (COP-OAc). Studies on the palladation reaction, by monitoring diastereoselectivity over time, showed that the examples ($S,S_p)_2$-**286** and ($S,S_p)_2$-**287** selectively form the kinetic product for the reaction, whereas ($S,R_p)_2$-**118** initially forms the S_p palladacycle, but subsequently equilibrates to give the thermodynamic R_p palladacycle. Finally, preliminary catalyst screening in the trichloroimidate rearrangement showed that chloride-bridged dimer ($S,S_p)_2$-**301** could catalyse the reaction with low catalyst loading (0.25 mol %, 74% yield, 80% *ee*.).

Lastly, an investigation into the immobilisation of COP-acac was undertaken. The Friedel-Crafts reaction was chosen to modify the lower cyclobutadienyl moiety of the catalyst framework, so that catalytic activity would not be affected.

Friedel-Crafts reaction of catalyst precursor (η^4-tetraphenylcyclobutadiene)(η^5-carbomethoxycyclopentadienyl)-cobalt **240** resulted in the exclusive *para*-substitution of the phenyl groups allowing for the efficient synthesis of mono- and tetra-substituted cobalt metallocenes. The synthesis of related cobalt metallocenes by the cyclodimerisation of *ortho*-phenyl substituted phenylacetylenes resulted in the selective formation of *trans*-metallocenes (with a selectivity of up to 6:1 *trans*:*cis*). Extension of the Friedel-Crafts methodology to the major isomers of these complexes resulted in conformationally controlled mono- or di-*para*-phenyl substitution.

The Friedel-Crafts methodology was used in the derivatisation of cobalt oxazoline ligand

(*S*)-**117**, allowing for the stereoselective formation of functionalised ligand **332** as a precursor to an immobilised COP catalyst. All attempts to couple the functionalised catalyst to a solid support were unsuccessful.

Chapter 6 - Experimental Section

General Methods

Thin layer chromatography (TLC) was performed on Merck Silica Gel 60 F254 and was visualized with UV light, iodine or potassium permanganate stain. Column Chromatography was performed on SiO_2 (40 – 63 μm). NMR spectra were recorded on Varian NMR 300 MHz, 400 MHz or Bruker 400 MHz, 500 MHz instruments. The residual solvent protons (^1H) or the solvent carbons (^{13}C) were used as internal standards for chemical shift determinations. IR spectra were recorded on a Fourier transform interferometer; only diagnostic and/or intense peaks are reported. Melting points were measured in a melting point apparatus and are uncorrected. HPLC data was recorded using Hitachi Elite LaChrom software fitted with a L2400 UV detector, L2300 column oven, L2200 autosampler, L2130 pump and a DICEL CHIRAL CEL OD–H column, (φ = 4.6 mm, length = 250 mm), fitted with pre-column (φ = 4.6 mm, length = 20 mm). All reagents and solvents were purchased from commercial sources and were purified using standard methods where required. Specifically acetyl chloride was distilled from quinolidine and aluminium chloride was purified by sublimation prior to use. Toluene THF were dried over sodium and THF were dried over sodium and benzophenone ketal. Dichloromethane was dried over CaH_2. Chloroform and methanol were dried over 4 Å molecular sieves and stored under nitrogen. The petroleum ether used refers to that fraction boiling in the range of 40 – 60 °C.

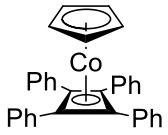
Tris(triphenylphosphine)cobalt(I) chloride[181]

$$CoCl(PPh_3)_3$$

A suspension of cobalt(II) chloride hexahydrate (9.62 g, 0.04 mol) and triphenylphosphine (32.2 g, 0.12 mol) in ethanol (600 mL) was degassed with argon over a 30-minute period with stirring. The solution was heated to 80 °C for 1 h and then left to cool to room temperature. $NaBH_4$ (2.00 g, 0.05 mol) was added over a 10-minute period. On completion

the solution was filtered. Ethanol was used to wash the precipitate (2 × 50 mL) proceeded by washings with water to remove excess $NaBH_4$ (2 × 10 mL). Finally the precipitate was washed with hexane and then collected and dried *in vacuo* to give the product (32.9 g, 0.04 mol, 93%), as a brown powder. m.p. 135–139 °C (dec).

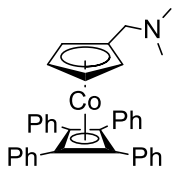
(η^5-cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[181]



236

A solution of sodium cyclopentadienide (2.80 mL of a 2 M solution in THF, 5.60 mmol) was added to a suspension of tris(triphenylphosphine)cobalt(I) chloride (5.00 g, 5.68 mmol) and diphenylacetylene (2.22 g, 12.5 mmol) in toluene (50 mL). The mixture was heated to reflux for 16 h and then cooled to room temperature. The solvent was removed *in vacuo* and the residue was triturated with petroleum ether until copious amounts of precipitate was formed. The precipitate was collected *via* filtration, washed with petroleum ether and then redissolved in hot ethyl acetate and filtered to remove any insoluble material. The solvent was removed *in vacuo* to give the product as an orange solid (1.56 g, 3.19 mmol, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.18 ppm (m, 20H, Ar–*H*), 4.59 ppm (s, 5H, Cp–*H*). Spectral data matched that previously reported.

(η^5-(dimethylaminomethyl)cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[181]

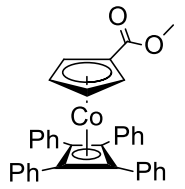


237

Phosphoric acid (2.00 mL, 38.5 mmol) was added to a hot suspension of (η^5-cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene) cobalt (1.00 g, 2.08 mmol) in acetic acid

(100 mL). *N,N,N',N'*-tetramethyldiaminomethane (5.00 mL, 36.7 mmol) was added and the mixture was heated to reflux for 16 h. On completion the mixture was cooled and poured onto water (400 mL). The solution was washed with ethyl acetate (3 × 100 mL) and the organic extracts were collected and combined and then washed with $NaHCO_3$ (100 mL portions) until effervescence stopped. The organic phases were collected and dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* to give the crude product. Purification *via* column chromatography (SiO_2, 15:4:1 hexanes/ethyl acetate/triethylamine) gave the product as a yellow solid (651 mg, 1.21 mmol, 58%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.40 (m, 8H, Ar–*H*), 7.33–7.21 (m, 12H, Ar–*H*), 4.73 (t, *J* = 2.0 Hz, 2H, Cp–*H*), 4.68 (d, *J* = 2.1 Hz, 2H, Cp–*H*), 2.90 (s, 2H, CH_2), 2.24 ppm (s, 6H, 2 × CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.42, 128.95, 128.10, 126.30, 93.84, 84.21, 83.66, 74.89, 56.53, 44.95 ppm. Spectral data matched that previously reported.

(η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[182]

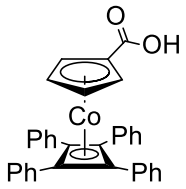


240

A flask was charged with sodium cyclopentadienide (3.40 mL of a 2 M solution in THF, 6.80 mmol) in THF (20 mL). Dimethyl carbonate (1.7 mL, 20 mmol) was added and the solution was heated to reflux for 4 h. The solution was cooled to room temperature and a solution of tris(triphenylphosphine)cobalt (I) chloride (5.00 g, 5.68 mmol) and diphenylacetylene (2.40 g, 13.5 mmol) in toluene was added *via* cannulae. The resulting mixture was brought to reflux for 5 h. On completion, the solution was concentrated under reduced pressure. The residue was suspended in hexane (100 mL), filtered and the resulting solid was washed with hexane (500 mL). The filter-cake was dissolved with dichloromethane and the resulting organic solution was collected. The solution was

concentrated *in vacuo* to give product as a mustard coloured solid (2.71 g, 4.88 mmol, 86%). (If not pure, product was filtered through silica eluting with CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.36 (m, 8H, Ar–*H*), 7.29–7.15 (m, 12H, Ar–*H*), 5.19–5.13 (m, 2H, Cp–*H*), 4.77–4.71 (m, 2H, Cp–*H*), 3.19 ppm (s, 3H, C(O)OC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.61, 135.35, 129.01, 128.18, 126.94, 86.76, 86.55, 84.71, 76.54, 51.39 ppm. Spectral data matched that previously reported.

(η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[182]

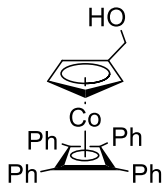


238

238

(η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (1.00 g, 1.72 mmol) and lithium iodide (495 mg, 3.70 mmol) were refluxed in 2,4,6-collidine (20 mL) for 16 h. On completion, the solution was cooled to room temperature and diluted with CH_2Cl_2 (20 mL). The solution was washed with 2 M HCl solution (20 mL) and the aqueous layer was extracted with CH_2Cl_2 (20 mL). The organic layers were combined, washed with 2 M HCl solution (4 × 20 mL) and then dried over $MgSO_4$. The solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography (SiO_2, 7:3 hexanes/ethyl acetate) gave the product as an orange solid (921 mg, 1.62 mmol, 94%). m.p. 246–248 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.36 (m, 8H, Ar–*H*), 7.29–7.15 (m, 12H, Ar–*H*), 5.19–5.13 (m, 2H, Cp–*H*), 4.77–4.71 ppm (m, 2H, Cp-*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.12, 135.01, 129.02, 128.78, 127.71, 92.89, 89.34, 89.12, 77.21 ppm. Spectral data matched that previously reported.

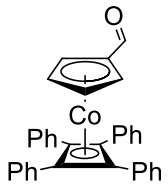
(η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[236]



241

To a solution of (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (500 mg, 0.95 mmol) in THF (25 mL) was added $LiAlH_4$ (163 mg, 4.29 mmol) and the mixture was stirred at room temperature for 16 h. On completion the reaction was quenched with H_2O (50 mL) and the aqeous layer was extracted with EtOAc (2 × 50 mL). The organic layer was collected, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 97:3 CH_2Cl_2/MeOH) gave the product as an orange solid (482 mg, 0.94 mmol, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.45 (m, 8H, Ar–*H*), 7.28–7.19 (m, 12H, Ar–*H*), 4.72 (t, *J* = 2.0 Hz, 2H, Cp–*H*), 4.61 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 4.09 ppm (s, 2H, C*H*$_2$OH); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.52, 135.18, 129.14, 128.57, 84.12, 81.95, 75.31, 59.81 ppm. Spectral data matched that previously reported.

(η^5-formylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) [236]

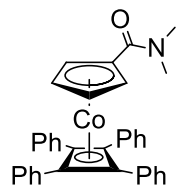


245

To a solution of (η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (542 mg, 1.07 mmol) dissolved in CH_2Cl_2 (2 mL) was added ground 4Å molecular sieves (500 mg) and *N*-methylmorpholine *N*-oxide (217 mg, 1.61 mmol). The solution was stirred for 5 minutes and tetrapropylammonium perruthenate

(18 mg, 0.05 mmol) was added in one portion. The solution was stirred for 1 h at room temperature. On completion the mixture was filtered through a short pad of Celite and the solution was subsequently washed with sodium sulfite solution (5 mL), brine (5 mL) and saturated $CuSO_4$ solution (10 mL). The solution was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude product was redissolved in a minimum volume of CH_2Cl_2 and an orange solid precipitated on the addition of petroleum ether. Filtration yielded the product as an orange solid (430 mg, 0.85 mmol, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.34 (s, 1H, C*H*O), 7.50–7.45 (m, 8H, Ar–*H*), 7.34–7.24 (m, 12H, Ar–*H*), 5.26 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 4.92 ppm (t, *J* = 2.1 Hz, 2H, Cp–*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 191.48, 135.23, 129.19, 128.59, 127.46, 92.78, 89.18, 83.53, 77.52 ppm. Spectral data matched that previously reported.

(η^5-(N-N-dimethylcarboxamide)-cyclopentadienyl)-(η^4-tetrapheynylcyclobutadiene)cobalt(I)

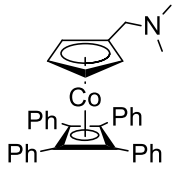


239

A flask was charged with (η^5-carboxycyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) (1.00 g, 1.91 mmol) and dissolved in CH_2Cl_2 (20 mL). Oxalyl chloride (0.33 mL, 3.85 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution is concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride as a red/brown solid. To a solution of dimethylamine hydrochloride (0.311 g, 3.81 mmol) and triethylamine (2.30 mL, 16.5 mmol) in CH_2Cl_2 (20 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (30 mL) *via* cannula. The resulting solution was stirred at room temperature. After 16 h the solution was washed with water (50 mL) and brine (50 mL). The organic layer was dried

over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was dissolved in a minimum volume of CH_2Cl_2 and purified by column chromatography (SiO_2, 7:3 hexanes/ethyl acetate) to give the product as an orange solid (1.01 g, 1.83 mmol, 96%). m.p. 249 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.44 (m, 8H, Ar–*H*), 7.32–7.18 (m, 12H, Ar–*H*), 5.16 (brs, 2H, Cp–*H*), 4.75 (brs, 2H, Cp–*H*), 2.79 (brs, 3H, C*H*$_3$), 2.64 (brs, 3H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): 135.64, 129.04, 128.12, 126.64, 85.46, 84.89, 77.36, 76.26 (C=O and 2 × CH3 not observed) ppm; IR (neat): ν = 3052, 2923, 1967, 1609, 1596, 1496, 1388, 1267, 1162, 1027 cm^{-1}; HRMS (ESI^+): *m/z* calcd for $C_{36}H_{31}CoNO$: 552.1732 $[M+H]^+$; found 552.1726.

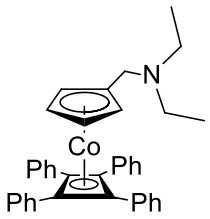
(η^5-(dimethylaminomethyl)cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)-cobalt(I)[181]



237

A flask was charged with (η^5-(N-N-dimethylcarboxamide)-cyclopentadienyl)-(η^4-tetrapheynylcyclobutadiene)cobalt(I) (986 mg, 1.78 mmol) and dissolved in THF (20 mL). The flask was cooled in an ice-water bath and lithium aluminium hydride (214 mg, 5.34 mmol) was added in two portions. The reaction was left to stir for 16 h. On completion, water (20 mL) was added and the aqueous layer was extracted with CH_2Cl_2 (3 × 20mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the product as an orange solid (959 mg, 1.77 mmol, 99%). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.40 (m, 8H, Ar–*H*), 7.33–7.21 (m, 12H, Ar–*H*), 4.73 (t, *J* = 2.0 Hz, 2H, Cp–*H*), 4.68 (d, *J* = 2.1 Hz, 2H, Cp–*H*), 2.90 (s, 2H, C*H*$_2$), 2.24 ppm (s, 6H, 2 × C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.42, 128.95, 128.10, 126.30, 93.84, 84.21, 83.66, 74.89, 56.53, 44.95 ppm. Spectral data matched that previously reported.

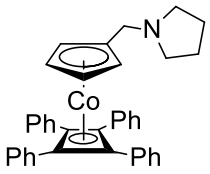
(η^5-(N,N-diethylaminomethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt



242

A solution of (η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (100 mg, 0.20 mmol) and PPh_3 (51 mg, 0.20 mmol) in THF (3 mL) was cooled to -20 ^oC and NBS (35 mg, 0.30 mmol) was added in one portion. The mixture was stirred for 10–15 minutes and Et_2NH (20 μL, 0.20 mmol) was added in one portion. The reaction was then allowed to warm to r.t. and then heated at reflux for 1 h. The reaction mixture was cooled to r.t. and diluted with CH_2Cl_2 (15 mL). The mixture was washed with 10% HCl (10 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 19:1 CH_2Cl_2/MeOH) gave the product as a yellow solid (45 mg, 0.08 mmol, 41%). m.p. 140–142 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.40 (m, 8H, Ar–*H*), 7.31–7.18 (m, 12H, Ar–*H*), 4.57 (s, 4H, Cp–*H*), 2.92 (s, 2H, C*H*$_2$NEt$_2$), 2.25 (q, *J* = 7.2 Hz, 4H, C*H*$_2$CH$_3$), 0.88 ppm (t, *J* = 7.2 Hz, 6H, CH$_2$C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.34, 128.82, 127.98, 126.19, 84.14, 83.67, 74.74, 49.07, 11.84 ppm; IR (neat): ν = 3057, 2966, 2921, 1597, 1499, 1446, 1068, 1020, 814, 780, 743, 698, 589, 564 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{38}H_{36}CoN$: 565.2180 $[M]^+$; found 565.2170.

(η^5-(1-pyrrolidinylmethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I)

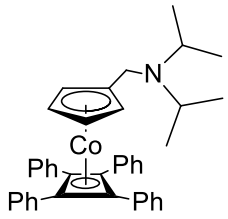


243

A solution of (η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (1.00 g, 2.00 mmol) and PPh_3 (524 mg, 2.00 mmol) in THF (30 mL) was cooled to 0 ^oC in a

ice/brine bath and NBS (356 mg, 2.00 mmol) was added in one portion. The mixture was stirred for 10–15 minutes and pyrrolidine (0.18 mL, 2.20 mmol) was added in one portion. The reaction was then allowed to warm up to r.t. and refluxed for 1 h. The reaction mixture was cooled to r.t. and diluted with CH_2Cl_2 (30 mL). The mixture was washed with 10% HCl (50 mL), dried over $MgSO_4$ and concentrated in vacuo. Purification by column chromatography (SiO_2, 19:1 CH_2Cl_2/MeOH) gave the product as a yellow/brown solid (1.03 g, 1.84 mmol, 92%). m.p. 180–182 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.52–7.40 (m, 8H, Ar–*H*), 7.31–7.18 (m, 12H, Ar–*H*), 4.75–4.70 (m, 2H, Cp–*H*), 4.62–4.58 (m, 2H, Cp–*H*), 2.84 (s, 2H, C*H*$_2$NMe$_2$), 2.34–2.26 (m, 4H, N(C*H*$_2$CH$_2$)$_2$), 1.70–1.64 ppm (m, 4H, N(CH$_2$*CH*$_2$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.35, 128.92, 128.08, 126.31, 84.06, 83.75, 74.93, 53.68, 52.60, 23.41 ppm; IR (neat): ν = 2924, 1596, 1497, 1446, 1261, 1023, 816, 781, 746, 701, 589, 564 cm^{-1}; HRMS (ESI): m/z calcd for $C_{38}H_{35}CoN$: 564.2096 $[M+H]^+$; found 564.2094.

(η^5-(N,N-diisopropylaminomethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I)

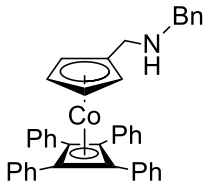


244

A solution of (η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.01 mmol) and PPh_3 (3 mg, 0.01 mmol) in THF (3 mL) was cooled to 0 ^oC in a ice/brine bath and NBS (2 mg, 0.01 mmol) was added in one portion. The mixture was stirred for 10–15 minutes and diisopropylamine (1.40 µL, 0.011 mmol) was added in one portion. The reaction was then allowed to warm up to r.t. and refluxed for 1 h. The reaction mixture was cooled to r.t. and diluted with CH_2Cl_2 (3 mL). The mixture was washed with 10% HCl (5 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column

chromatography (SiO_2, 19:1 CH_2Cl_2/MeOH) gave the product as a yellow solid (31 mg, 0.005 mmol, 53%). m.p. 157-160 ^oC; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (8H, m, Ar–*H*), 7.15 (12H, m, Ar–*H*), 4.53 (2H, brs, Cp–*H*), 4.46 (2H, brs, Cp-*H*), 2.80 (2H, m, 2 × C*H*$(CH_3)_2$, 2.75 (2H, s, CpCH_2N), 0.72 ppm (12H, d, *J* = 6.6, 4 x CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.59, 132.14, 128.55, 126.14, 84.27, 82.85, 74.61, 46.26, 20.58, 11.44 ppm; HRMS (ESI): *m/z* calcd for $C_{40}H_{41}CoN$: 594.2566 $[M+H]^+$, found: 594.2562.

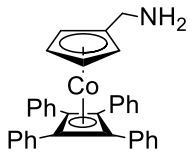
(η^5-N-benzylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I)



246

To a mixture of (η^5-formylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (2.61 g, 5.13 mmol) and benzylamine (0.55 g, 5.13 mmol) dissolved in 1,2-dichloroethane (35 mL) was added sodium triacetoxyborohydride (1.72 g, 8.12 mmol) in one portion. The mixture was stirred at room temperature for 1.5 h. On completion, the reaction mixture was quenched by adding saturated aqueous $NaHCO_3$ solution (50 mL) and the product was extracted with EtOAc (2 × 40 mL). The organic extracts were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* to give the crude product. Purification by column chromatography (SiO_2, 19:1 CH_2Cl_2/EtOAc) to give product as a yellow solid (3.00 g, 4.45 mmol, 97%). m.p. 145–147 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.43 (dd, *J* = 8.0, 1.4 Hz, 8H, Ar–*H*),), 7.33–7.11 (m, 17H, Ar–*H*),), 4.66 (t, *J* = 1.8 Hz, 2H, Cp–*H*), 4.57 (t, *J* = 1.9 Hz, 2H, Cp–*H*), 3.52 (s, 2H, CH_2Ph), 3.13 ppm (s, 2H, CH_2NH); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.33, 135.43, 129.01, 128.88, 128.14, 128.10, 126.62, 83.68, 82.56, 74.89, 53.56, 45.38 ppm; IR (neat): *v* = 3080, 3059, 3028, 2924, 2823, 2246, 1597, 1499, 1449, 1379, 909, 733, 697cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{41}H_{35}NCo$: 600.2102 $[M+H]^+$; found: 600.2093.

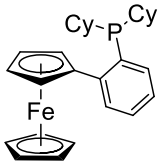
(η^5-aminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)-cobalt(I)



247

To a stirred suspension of (η^5-*N*-benzylaminomethylcyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) (3.00 g, 5.00 mmol) and an equal weight of 10% Pd/C in methanol (20 mL), anhydrous ammonium formate (1.80 g, 28.5 mmol) was added in a single portion. The resulting reaction mixture was stirred at reflux for 2 h. On completion, the solution was filtered through a pad of celite and then washed with chloroform (20 mL). The combined organic filtrate was evaporated *in vacuo* and purified by column chromatography (SiO_2, 3:2 CH_2Cl_2/EtOAc) to give the product as a yellow solid (1.09 g, 2.05 mmol, 43%). m.p. 116 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.42 (m, 8H, Ar–*H*), 7.25–7.18 (m, 12H, Ar–*H*), 4.63 (t, *J* = 2.0 Hz, 2H, Cp–*H*), 4.57 (t, *J* = 2.0 Hz, 2H, Cp–*H*), 3.27 ppm (brs, 2H, C*H*$_2$NH$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ =136.22, 128.75, 128.09, 126.37, 83.57, 81.84 , 74.85, 53.54 ppm; IR (neat): ν = 3052, 2923, 2162, 1610, 1596, 1573, 1453, 1497, 1453, 1387, 1267, 1231, 1106, 1054 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{34}H_{28}NCoNa$: 532.1451 $[M+Na]^+$; found: 532.1438.

2-(dicyclohexylphosphino)phenylferrocene[135]

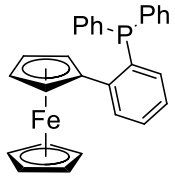


167

A solution of 2-bromophenylferrocene (500 mg, 1.47 mmol) dissolved in THF (10 mL) was cooled to approximately –78 ^oC in an acetone/CO_2 bath. To this ^{n}Bu-Li (0.64 mL of a 2.5 M solution in hexane, 1.61 mmol) was added and the solution was stirred at –78 ^oC for 1 h. Chlorodicyclohexylphosphine (0.45 mL, 2.06 mmol) was then added and the solution was

brought to r.t. and stirred for 2 h. On completion the reaction was quenched with H_2O (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification with column chromatography (SiO_2, 19:1 hexanes/EtOAc) yielded the product as a red crystalline solid (626 mg, 1.31 mmol, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (ddd, *J* = 7.8, 3.7, 1.3 Hz, 1H, Ar–*H*), 7.41 (dt, *J* = 7.7, 1.7 Hz, 1H, Ar–*H*), 7.35–7.30 (m, 1H, Ar–*H*), 7.21 (td, *J* = 7.5, 1.4 Hz, 1H, Ar–*H*), 4.57 (dd, *J* = 3.3, 1.7 Hz, 2H, Cp–*H*), 4.28 (t, *J* = 1.8 Hz, 2H, Cp–*H*), 4.15 (s, 5H, Cp–*H*), 1.85–1.47 (m, 11H, Cy–*H*), 1.31–0.92 ppm (m, 11H, Cy–*H*); ^{31}P NMR (202 MHz, $CDCl_3$): δ = –12.35 ppm. Spectral data matched that previously reported.

2-(diphenylphosphino)phenylferrocene[135]

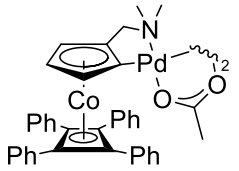


168

A solution of 2-bromophenylferrocene (500 mg, 1.47 mmol) dissolved in THF (10 mL) was cooled to approximately –78 ^{o}C in an acetone/CO_2 bath. To this ^{n}Bu-Li (0.64 mL of a 2.5 M solution in hexane, 1.61 mmol) was added and the solution was stirred at –78 ^{o}C for 1 h. Chlorodiphenylphosphine (0.37 mL, 2.06 mmol) was then added and the solution was brought to r.t. and stirred for 2 h. On completion the reaction was quenched with H_2O (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification with column chromatography (SiO_2, 19:1 hexanes/EtOAc) yielded the product as a red crystalline solid (570 mg, 1.19 mmol, 81%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.94 (ddd, *J* = 7.8, 3.7, 1.3 Hz, 1H, Ar–*H*), 7.37–7.17 (m, 11H, Ar–*H*), 7.11 (td, *J* = 7.5, 1.4 Hz, 1H, Ar–*H*), 6.83 (ddd, *J* = 7.2, 3.8, 1.3 Hz, 1H, Ar–*H*), 4.42 (brs, 2H, Cp–*H*), 4.18

(brs, 2H, Cp–*H*), 4.07 ppm (s, 5H, Cp–*H*); ^{31}P NMR (202 MHz, $CDCl_3$): δ = –12.15 ppm. Spectral data matched that previously reported.

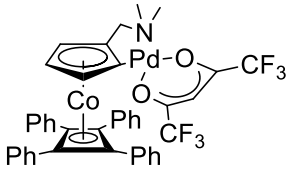
rac-di-aceto-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)[180]



***rac*-250**

A solution of $Pd(OAc)_2$ (20 mg, 0.09 mmol) and (η^5-(dimethylaminomethyl)cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.09 mmol) in toluene (10 mL) was heated to 70 °C for 2 h. On completion the solvent was removed *in vacuo* to give the product as an orange solid (74 mg, 0.10 mmol, 58%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68–7.62 (m, 16H, Ar–*H*), 7.24–7.15 (m, 24H, Ar–*H*), 4.22 (s, 2H, Cp–*H*), 4.06 (s, 2H, Cp–*H*), 4.02 (s, 2H, Cp–*H*), 3.09–3.01 (d, *J* = 13.9 Hz, 2H, C*H*H), 2.80–2.73 (d, *J* = 13.8 Hz, 2H, CH*H*), 2.30 (s, 6H, $N(CH_3)_2$), 2.14 (s, 6H, O_2CCH_3), 1.72 ppm (s, 6H, $N(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.74, 137.88, 137.01, 136.27, 129.25, 129.20, 129.05, 128.82, 128.24, 127.98, 127.89, 127.82, 126.18, 125.65, 125.31, 103.12, 101.43, 84.10, 83.55, 80.17, 77.60, 77.23, 75.14, 74.78, 74.50, 65.15, 53.99, 51.82, 24.15, 21.48 ppm.

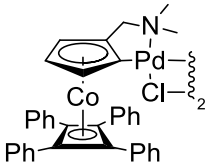
rac-hexafluoroacetylacetonate{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-palladium(II)



***rac*-257**

To a solution of *rac*-di-μ-acetato-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II) (50mg, 0.04 mmol) in acetone (0.66 mL) was added sodium hexafluoroacetylacetonate (82 mg, 0.40 mmol) followed by water (0.33 mL). The reaction was stirred vigorously overnight. On completion the precipitate was filtered to give the product as an orange solid (17 mg, 0.02 mmol, 99%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). m.p. 225 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.71–7.47 (m, 8H, Ar–*H*), 7.34–7.08 (m, 12H, Ar–*H*), 5.87 (s, 1H, C*H*CO), 4.62 (dd, *J* = 2.3, 1.0 Hz, 1H, Cp–*H*), 4.50 (d, *J* = 1.5 Hz, 1H, Cp–*H*), 4.37 (t, *J* = 2.4 Hz, 1H, Cp–*H*), 3.41 (d, *J* = 13.9 Hz, 1H, C*H*HNMe$_2$), 2.92 (d, *J* = 13.9 Hz, 1H, CH*H*NMe$_2$), 2.76 (s, 3H, NCH_3), 2.48 ppm (s, 3H, NCH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.40 (q, $J_{C\text{-}F}$ = 8.0 Hz), 174.12 (q, $J_{C\text{-}F}$ = 7.4 Hz), 136.77, 129.14, 127.92, 126.15, 118.95 (q, $J_{C\text{-}F}$ = 38.9 Hz), 116.68 (q, $J_{C\text{-}F}$ = 38.6 Hz), 102.94, 101.83, 90.23, 84.49, 79.55, 75.44, 74.87, 65.71, 53.53, 51.12 ppm.

S_p-di-μ-chloro-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II) [180]

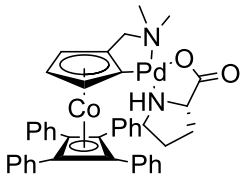


$(S_p)_2$-**248**
92% *ee*

A solution of (*R*)-*N*-acetylphenylalanine (740 mg, 3.57 mmol) and NaOH (66 mg, 1.65 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (439 mg, 1.49 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous 50% NaOH or conc. HCl as required and the mixture was allowed to stir for 20 minutes. A solution of *(*η^5-(dimethylaminomethyl)cyclopentadienyl)(*η^4*-tetraphenylcyclobutadiene)cobalt(I) (800 mg, 1.49 mmol) in MeOH/CH_2Cl_2 (75/15 mL) was then added in portions over 5 minutes. The solution was allowed to stir for 16 h at r.t. On completion, the reaction mixture was

diluted with CH_2Cl_2 (150 mL) and washed with brine (2 × 100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product as an orange solid (650 mg, 0.48 mmol, 64%), *ee* = 92% as determined by formation of the proline adducts. m.p. 143–145 °C; $[\alpha]_D^{21}$ = –289 (c = 1.1 mg/mL in CH_2Cl_2). Further characterisation data below.

S_p-(π-(dimethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(L)-Proline

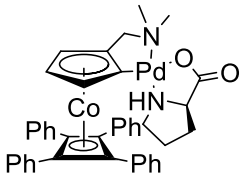


$(S,S_p)_2$-**249**
24:1 dr

A solution of S_p-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (50 mg, 0.04 mmol) in acetone (1 mL) was added to a solution of $NaHCO_3$ (31 mg, 0.37 mmol) and (*S*)-proline (43 mg, 0.37 mmol) in water (0.5 mL). During the addition a copious amount of precipitate was formed. The reaction was vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (50 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2 × 25 mL). The organic phases were combined, dried over $MgSO_4$, filtered and solvent was removed *in vacuo* yielding the product as an orange solid (50 mg, 0.07 mmol, 90%). Ratio of (S,S_p)-**256**: (S,R_p)-**256** = 24:1. Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). m.p. 190–192 °C; $[\alpha]_D^{20}$ = –99 (*c* = 1.29 mg/mL in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.56 (m, 8H, Ar–*H*), 7.26–7.22 (m, 12H, Ar–*H*), 4.36 (brs, 2H, Cp–*H*), 4.15 (t, *J* = 2 Hz, 1H, Cp–*H*), 3.93 (app. q, *J* = 7.6 Hz, 1H, NHC*H*), 3.20 (d and brs, *J* = 13.2 Hz, 2H, C*H*HNMe$_2$ and N*H*), 2.87 (d, *J* = 13.2 Hz, 1H, CH*H*NMe$_2$), 2.65 (s, 3H, CH_3), 2.50–2.40 (m, 1H, NHC*H*H), 2.38 (s, 3H, CH_3), 2.20–2.00 (m, 3H, 3 × C*H*), 1.60–1.50 (m, 1H, C*H*H),

1.24–1.18 ppm (m, 1H, CH*H*); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.72, 129.05, 128.23, 126.25, 103.75, 101.58, 84.33, 82.67, 77.85, 74.01, 64.28, 52.60, 51.70, 51.17, 29.89, 26.10 ppm (*C*=O not observed); IR (neat): ν = 2450, 2919, 1597, 1496, 1443, 1379, 1366, 1259, 1152, 1066, 1018, 845, 803, 740, 697 cm^{-1}; HRMS (EI): *m/z* calculated for $C_{41}H_{40}CoN_2O_2Pd$: 757.1466 $[M+H]^+$; found 757.1468.

S_p-(π-(Dimethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(D)-Proline

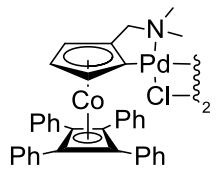


(R,S_p)$_2$-**249**
33:1 dr

A solution of S_p-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (50 mg, 0.04 mmol) in acetone (10 mL) was added to a solution of $NaHCO_3$ (88 mg, 1.04 mmol) and (*R*)-Proline (85 mg, 0.74 mmol) in water (5 mL). During the addition a copious amount of precipitate was formed. The reaction was vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (50 mL). The phases were separated and the aqueous was washed with further portions of CH_2Cl_2 (2 × 25 mL). The organic phases were combined, dried over $MgSO_4$, filtered and solvent was removed *in vacuo* yielding the crude product. Ratio of (R,R_p)-**256**: (R,S_p)-**256** = 1:33. Purification by column chromatography eluting with (SiO_2, 97:3 CH_2Cl_2/MeOH) gave the diastereomerically pure product as an orange/red solid (45 mg, 0.06 mmol, 81%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). $[\alpha]_D^{21}$ = +26 (*c* = 0.5 mg/mL in CH_2Cl_2); m.p. 236 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.78–7.38 (m, 8H, Ar–*H*), 7.35–6.99 (m, 12H, Ar–*H*), 4.37 (t, *J* = 2.4 Hz, 1H, Cp–*H*), 4.26 (d, *J* = 1.9 Hz, 1H, Cp–*H*), 4.11 (brs, 1H, Cp–*H*), 3.27 (dd, *J* = 13.7, 8.6 Hz, 1H, NHC*H*), 3.10 (d, *J* = 13.2 Hz, 1H, C*H*HNMe$_2$), 3.06–2.94 (m, 1H,

NHC*H*H), 2.90–2.78 (m, 1H, NHCH*H*), 2.74 (d, *J* = 13.2 Hz, 1H, CH*H*NMe_2), 2.53 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.15–1.96 (m, 2H, C*H*H and N*H*), 1.85 (ddt, *J* = 13.3, 8.9, 4.7 Hz, 1H, CH*H*), 1.79–1.69 (m, 1H, C*H*H), 1.43–1.28 ppm (m, 1H, CH*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.42, 136.85, 128.96, 128.39, 126.26, 104.29, 97.65, 84.79, 84.03, 79.69, 73.86, 66.28, 63.57, 53.07, 51.43, 50.79, 29.74, 25.53 ppm; IR (neat): *v* = 3056, 2917, 2849, 2160, 1972, 1655, 1596, 1498, 1446, 1373, 1263, 1113, 1067, 1017, 823, 778, 694 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{41}H_{40}O_2N_2PdCo$: 757.1466 $[M+H]^+$; found: 757.1467.

S_p-di-μ-chloro-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)

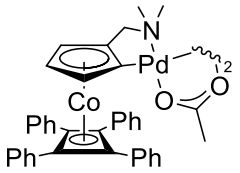


(S_p)$_2$-**248**
>98% *ee*
1:0.9 mixture of isomers

Dilute hydrochloric acid (0.64 mL of a 0.5 M solution) was added to a solution of S_p-(π-(dimethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(*D*)-Proline (100 mg, 0.13 mmol) in CH_2Cl_2 (2 mL) and the mixture stirred vigorously for 16 h. The solution was diluted with CH_2Cl_2 (5 mL) and washed with brine (3 × 5 mL). The organic layer was collected, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product as an orange solid (73 mg, 0.05 mmol, 82%). m.p. 191 ^{o}C (decomp.); $[\alpha]_D^{21}$ = –310 (*c* = 0.5 mg/mL in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$), 1:0.9 mixture of isomers: δ = 7.77–7.53 (m, 32H, Ar–*H*), 7.37–7.09 (m, 48H, Ar–*H*), 4.53 (d, *J* = 1.2 Hz, 2H, Cp–*H*), 4.38 (d, *J* = 1.5 Hz, 2H, Cp–*H*), 4.33 (brs, 4H, Cp–*H*), 4.19 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 4.09 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 3.18 (d, *J* = 13.4 Hz, 2H, C*H*HNMe_2), 3.13 (d, *J* = 13.3 Hz, 2H, C*H*HNMe_2), 2.81 (d, *J* = 13.4 Hz, 2H, CH*H*NMe_2), 2.77 (d, *J* = 13.2 Hz, 2H, CH*H*NMe_2), 2.67 (s, 6H,

C*H*$_3$), 2.62 (s, 6H, C*H*$_3$), 2.19 (s, 6H, C*H*$_3$), 2.02 ppm (s, 6H, C*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.83, 136.78, 129.42, 129.36, 128.09, 128.06, 125.95, 125.87, 103.09, 102.71, 102.31, 101.91, 85.03, 83.46, 81.07, 80.36, 77.73, 74.84, 74.81, 64.64, 64.55, 53.57, 52.21, 51.87, 51.52 ppm; IR (neat): ν = 3056, 2886, 1659, 1597, 1498, 1446, 1389, 1352, 1266, 1155, 1067, 1024, 984, 957, 910, 842, 809, 780, 739, 697, 563 cm^{-1}; Elemental analysis calcd. (%) for $C_{72}H_{62}Cl_2Co_2N_2Pd_2$: C 63.73, H 4.61, N 2.07; found C 63.75, H 4.55, N 2.16.

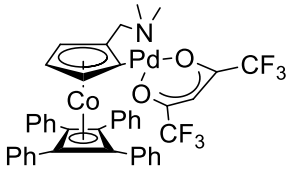
S_p-di-aceto-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)



(S_p)$_2$-250
>98% *ee*

To a solution of S_p-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt)-dipalladium(II) (20 mg, 0.02 mmol) in acetone (1 mL) was added silver acetate (5 mg, 0.03 mmol). The solution was stirred vigorously overnight and then the solution filtered through a short pad of celite, eluting with CH_2Cl_2. The solvent was then removed *in vacuo* to give the product as an orange solid (20 mg, 0.01 mmol, 97%). $[\alpha]_D^{18}$ = −155 (*c* = 2.6 mg/mL, in CH_2Cl_2); m.p. 162–164 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.71–7.60 (m, 16H, Ar−*H*), 7.25–7.14 (m, 24H, Ar-*H*), 4.22 (d, *J* = 1.3 Hz, 2H, Cp−*H*), 4.06 (t, *J* = 2.2 Hz, 2H, Cp−*H*), 4.02 (br s, 2H, Cp−*H*), 3.05 (d, *J* = 13.9 Hz, 2H, C*H*HNMe$_2$), 2.76 (d, *J* = 13.9 Hz, 2H, CH*H*NMe$_2$), 2.30 (s, 6H, NC*H*$_3$), 2.15 (s, 6H, 2 × O_2CC*H*$_3$), 1.71 ppm (s, 6H, NC*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 179.70, 135.96, 128.15, 126.78, 124.60, 102.08, 100.39, 83.06, 79.13, 74.10, 73.46, 64.11, 52.95, 50.78 24.14 ppm; IR (neat): ν = 3055, 2920, 1577, 1498, 1412, 1261, 1176, 1023, 957, 740, 692, 617 cm^{-1}; Elemental analysis calcd. (%) for $C_{76}H_{68}Co_2N_2O_4Pd_2$: C 65.01, H 4.88, N 2.00; found C 65.18, H 4.96, N 2.04.

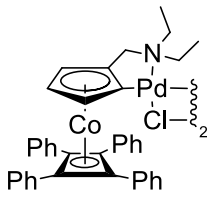
S_p-hexafluoroacetylacetonate{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-palladium(II)



S_p-**257**
>98% *ee*

To a solution of S_p-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt)-dipalladium(II) (20 mg, 0.02 mmol) in acetone/water (2:1 mL) was added sodium hexafluoroactylacetonate (7 mg, 0.03 mmol). The solution was stirred vigorously for 16 h. On completion, the solution was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL). The organic layer was collected, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the product as an orange solid (12 mg, 0.01 mmol, 96%). Crystals for X-ray analysis were obtained by slow diffusion of hexane into CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). $[\alpha]_D^{19} = -160$ (*c* = 1.0 mg/mL in CH_2Cl_2); m.p. 219 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.71–7.47 (m, 8H, Ar–*H*), 7.34–7.08 (m, 12H, Ar–*H*), 5.87 (s, 1H, C*H*CO), 4.62 (dd, *J* = 2.3, 1.0 Hz, 1H, Cp–*H*), 4.50 (d, *J* = 1.5 Hz, 1H, Cp–*H*), 4.37 (t, *J* = 2.4 Hz, 1H, Cp–*H*), 3.41 (d, *J* = 13.9 Hz, 1H, C*H*HNMe$_2$), 2.92 (d, *J* = 13.9 Hz, 1H, CH*H*NMe$_2$), 2.76 (s, 3H, NC*H*$_3$), 2.48 ppm (s, 3H, NC*H*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.40 (q, $J_{C\text{-}F}$ = 8.0 Hz), 174.12 (q, $J_{C\text{-}F}$ = 7.4 Hz), 136.77, 129.14, 127.92, 126.15, 118.95 (q, $J_{C\text{-}F}$ = 38.9 Hz), 116.68 (q, $J_{C\text{-}F}$ = 38.6 Hz), 102.94, 101.83, 90.23, 84.49, 79.55, 75.44, 74.87, 65.71, 53.53, 51.12 ppm; IR (neat): ν = 3056, 2928, 2160, 1623, 1597, 1545, 1498, 1481, 1458, 1253, 1195, 1144, 1024, 950, 779, 695 cm^{-1}; Elemental analysis calcd. (%) for $C_{41}H_{32}CoF_6NO_2Pd.2H_2O$: C 55.58, H 4.10, N 1.58; found C 55.54, H 3.90, N 1.80.

S_p-di-μ-chloro-bis{[π-1-(diethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)

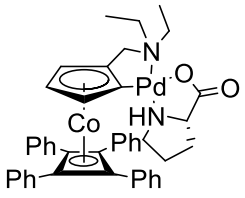


$(S_p)_2$-**258**
82% *ee*
1:0.6 mixture of isomers

A solution of (*R*)-*N*-acetylphenylalanine (250 mg, 1.21 mmol) and NaOH (39 mg, 0.98 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (263 mg, 0.89 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous NaOH or HCl as required and the mixture was allowed to stir for 20 minutes. A solution of (η^5-(*N*-*N*-diethylaminomethyl)cyclopentadienyl)-(η^4-tetrapheynylcyclobutadiene)cobalt(I) (500 mg, 0.88 mmol) in 5:1 MeOH/CH_2Cl_2 (90 mL) was then added in portions over 5 minutes. The solution was allowed to stir for 16 h at r.t. On completion, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with brine (2 × 100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product as an orange solid (244 mg, 0.17 mmol, 39%), *ee* = 82% as determined by formation of the proline adducts. m.p. >200 ^oC (decomp); $[\alpha]_D^{24}$ = –618 (*c* = 0.5 mg/mL in CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) 1:0.6 mixture of isomers: δ = 7.70–7.60 (m, 32H, Ar–*H*), 7.29–7.15 (m, 48H, Ar–*H*), 4.47 (dd, *J* = 2.3, 1.1 Hz, 2H, Cp–*H*), 4.32 (t, *J* = 2.2 Hz, 4H, Cp–*H*), 4.30–4.27 (m, 2H, Cp–*H*), 4.24 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 4.17 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 3.29 (d, *J* = 13.9 Hz, 2H, C*H*HNEt$_2$), 3.22 (d, *J* = 13.9 Hz, 2H, C*H*HNEt$_2$), 2.75 (d, *J* = 13.9 Hz, 4H, CH*H*NEt$_2$), 2.68–2.43 (m, 16H, CH_2CH$_3$), 1.52 (t, *J* = 7.1, Hz, 6H, CH$_2$CH_3), 1.52 (t, *J* = 7.1, Hz, 6H, CH$_2$CH_3), 0.92–0.84 ppm (m, 12H, CH$_2$CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.74, 136.68, 129.32, 129.26, 127.95, 127.92, 129.79, 125.76, 84.27, 82.65, 79.50, 79.44, 77.24, 76.45, 75.55, 60.41, 57.44, 57.28, 55.39, 55.33, 54.32, 53.22, 14.53, 14.22, 10.01, 9.80 ppm; IR (neat): ν

= 3056, 2971, 2929, 1596, 1498, 1444, 1387, 909, 734, 695 cm^{-1}; Elemental analysis calcd. (%) for $C_{76}H_{70}Cl_2Co_2N_2Pd_2$: C 64.60, H 4.99, N 1.98; found C 64.70, H 4.89, N 2.04.

S_p-(π-(diethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(L)-Proline

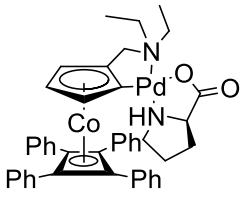


S,S_p-**260**
10:1 dr

A solution of S_p-di-μ-chloro-bis([π-1-(diethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (20 mg, 0.01 mmol) in acetone (1 mL) was added to a solution of $NaHCO_3$ (3 mg, 0.04 mmol) and (*S*)-proline (3 mg, 0.03 mmol) in water (0.5 mL). During the addition a copious amount of precipitate was formed. The reaction was then vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2 × 2 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* yielding the product as an orange solid (21 mg, 0.03 mmol, 95%). Ratio of *S*,R_p-**269**: *S*,S_p-**269** = 1:10. $[\alpha]_D^{21}$ = −104 (*c* = 0.7 mg/mL in CH_2Cl_2); m.p. 206–208 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55 (dd, *J* = 6.6, 3.0 Hz, 8H, Ar–*H*), 7.25–7.21 (m, 12H, Ar–*H*), 4.40 (t, *J* = 2.4 Hz, 1H, Cp–*H*), 4.34 (d, *J* = 1.6 Hz, 1H, Cp–*H*), 4.13 (d, *J* = 1.5 Hz, 1H, Cp–*H*), 3.92 (dd, *J* = 15.2, 7.6 Hz, 1H, NC*H*), 3.29 (d, *J* = 13.9 Hz, 2H, 2 x C*H*H), 2.88 (d, *J* = 13.7 Hz, 2H, 2 x C*H*H), 2.78–2.55 (m, 3H, 3 x C*H*H), 2.49–2.27 (m, 2H, 2 x C*H*H), 2.17–2.06 (m, 4H, N*H* & C*H*H), 1.40–1.31 (m, 3H, CH_2CH_3), 0.94 ppm (t, *J* = 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.08, 136.79, 129.01, 128.20, 126.21, 84.38 84.0, 81.39, 79.62 74.82, 73.96, 66.17, 58.09, 54.23, 53.31, 52.52, 29.97, 26.07, 13.52, 9.84 ppm; IR (neat): *v* = 3453, 2929, 2852, 1725, 1594, 1492, 1446, 1381,

1255, 1179, 1156, 1122, 1071, 1021, 804, 778, 740, 699 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{43}H_{44}CoN_2O_2Pd$: 785.1780 $[M+H]^+$; found: 785.1773.

S_p-(π-(Diethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(D)-Proline

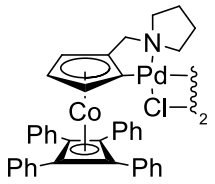


R,S_p-**260**
14:1 dr

A solution of S_p-di-μ-chloro-bis([π-1-(diethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (20 mg, 0.01 mmol) in acetone (1 mL) was added to a solution of $NaHCO_3$ (3 mg, 0.04 mmol) and (*R*)-proline (3 mg, 0.03 mmol) in water (0.5 mL). During the addition a copious amount of precipitate was formed. The reaction was then vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2 × 2 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* yielding the product as an orange solid (21 mg, 0.03 mmol, 97%). Ratio of *R*,R_p-**269**: *R*,S_p-**269** = 1:14. $[\alpha]_D^{21}$ = +79 (*c* = 0.6 mg/mL in CH_2Cl_2); m.p. 215 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67 (dd, *J* = 7.6, 1.8 Hz, 8H, Ar–*H*), 7.32–7.23 (m, 12H, Ar–*H*), 4.44 (t, *J* = 2.4 Hz, 1H, Cp–*H*), 4.38–4.36 (m, 1H, Cp–*H*), 4.22–4.19 (m, 1H, Cp–*H*), 3.35 (ddd, *J* = 9.1, 7.8, 5.6 Hz, 1H, NC*H*), 3.28–3.15 (m, 2H, C*H*H), 3.18–3.03 (m, 1H, C*H*H), 3.04–2.93 (m, 2H, 2 x C*H*H), 2.77 (dt, *J* = 14.6, 7.3 Hz, 1H, C*H*H), 2.73–2.62 (m, 1H, C*H*H), 2.44 (dq, *J* = 13.8, 6.9 Hz, 1H, C*H*H), 2.24–2.11 (m, 2H, CH_2CH_3), 2.00–1.89 (m, 1H), 1.89–1.78 (m, 2H, N*H* & C*H*H), 1.48 (t, *J* = 7.1 Hz, 3H, CH_2CH_3), 0.80 ppm (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.29, 136.88, 128.92, 128.34, 126.18, 104.97, 98.15, 84.21, 83.24, 79.55, 73.84, 66.06, 58.78, 53.02, 51.41, 50.71, 29.64, 29.38, 25.43, 14.08, 6.79 ppm; IR (neat): *v* = 3453, 2929, 2852, 1725, 1594, 1492,

1446, 1381, 1255, 1179, 1156, 1122, 1071, 1021, 804, 778, 740, 699 cm^{-1}; HRMS (ESI): *m/z* calculated for $C_{43}H_{44}CoN_2O_2Pd$: 785.1782 $[M+H]^+$; found: 785.1784.

S_p-di-μ-chloro-bis{[π-1-(Pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)

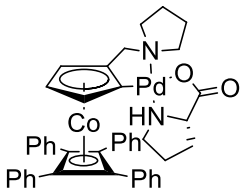


$(S_p)_2$-**259**
>98% *ee*
1:1 mixture of isomers

To a solution of (*R*)-*N*-acetylphenylalanine (251 mg, 1.21 mmol) and NaOH (39 mg, 0.98 mmol) in water (15 mL) was added to a solution of $Na_2Pd_2Cl_4$ (263 mg, 0.89 mmol) in MeOH (50 mL). The pH of the mixture was adjusted to 8.0 using either aqueous NaOH or HCl as required and the mixture was allowed to stir for 20 minutes. A solution of (η^5-(pyrrolindinylmethyl)cyclopentadienyl)-(η^4-(tetrapheynylcyclobutadiene)cobalt(I) (500 mg, 0.89 mmol) in 5:1 MeOH/CH_2Cl_2 (90 mL) was then added in portions over 5 minutes. The solution was allowed to stir for 16 h at r.t. On completion, the reaction mixture was diluted with CH_2Cl_2 (150 mL) and washed with brine (2 × 100 mL). The organic phase was dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, 4:1 hexanes/EtOAc) gave the product as an orange solid (270 mg, 0.19 mmol, 43%), *ee* >98% as determined by formation of the proline adducts. m.p. >200 °C (decomp); $[\alpha]_D^{24}$ = −266 (*c* = 0.5 mg/mL in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) 1:1 mixture of isomers: δ = 7.72–7.63 (m, 32H, Ar−*H*), 7.28–7.16 (m, 48H, Ar−*H*), 4.53–4.50 (m, 2H, Cp−*H*), 4.38–4.35 (m, 2H, Cp−*H*), 4.31 (d, *J* = 1.5 Hz, 2H, Cp−*H*), 4.26 (d, *J* = 1.5 Hz, 2H, Cp−*H*), 4.23 (t, *J* = 2.4 Hz, 2H, Cp−*H*), 4.15–4.09 (m, 2H, Cp−*H*), 3.44–3.32 (m, 4H, CpC*H*HN), 3.08–2.81 (m, 16H, CpCH*H*N & NCH_2), 2.32–2.23 (m, 2H, NCH_2), 2.08–2.03 (m, 2H, NCH_2), 1.81 (ddd, *J* = 9.3, 6.2, 3.5 Hz, 4H, NCH_2CH_2), 1.76–1.60 (m, 8H,

NCH_2CH_2), 1.53–1.45 ppm (m, 4H, NCH_2CH_2); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.75, 136.68, 129.34, 129.28, 127.94, 125.79, 125.72, 103.20, 102.85, 102.75, 102.31, 84.84, 82.99, 80.55, 79.96, 77.60, 76.71, 75.25, 74.68, 74.66, 60.46, 60.38, 60.28, 60.22, 59.67, 30.95, 22.00, 21.65, 21.55, 21.30 ppm; IR (neat): ν = 3056, 2966, 1596, 1498, 1443, 909, 734, 695 cm^{-1}; Elemental analysis calcd. (%) for $C_{76}H_{66}Cl_2Co_2N_2Pd_2$: C 64.79, H 4.72, N 1.98; found C 64.81, H 4.60, N 2.07.

S_p-(π-(Pyrrolidinylmethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(L)-Proline

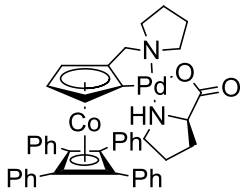


S,S_p-**261**
>99:1 dr

A solution of S_p-di-μ-chloro-bis([π-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (20 mg, 0.01 mmol) in acetone (2 mL) was added to a solution of $NaHCO_3$ (3 mg, 0.04 mmol) and (*S*)-proline (3 mg, 0.03 mmol) in water (1 mL). During the addition a copious amounts of precipitate was formed. The reaction was then vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH_2Cl_2 (2 × 2 mL). The organic phases were combined, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* yielding the product as an orange solid (20 mg, 0.03 mmol, 90%). Ratio of *S*,R_p-**270**: *S*,S_p-**270** = 1:99. $[\alpha]_D^{21}$ = −37 (*c* = 1.1 mg/mL in CH_2Cl_2); m.p. 206–208 °C; ^{1}H NMR (500 MHz, d_6-DMSO): δ = 7.52–7.46 (m, 8H, Ar–*H*), 7.28–7.20 (m, 12H, Ar–*H*), 5.52–5.44 (m, 1H, N*H*), 4.36 (s, 2H, Cp–*H*), 4.25 (s, 1H, Cp–*H*), 3.60–3.52 (q, *J* = 7.9 Hz, 1H, NHC*H*), 3.19–3.01 (m, 2H, NHC*H*H & CpCH*H*N), 3.01–2.94 (m, 1H, NHC*H*H), 2.92–2.84 (m, 1H, NCH_2), 2.79 (d, *J* = 14.5 Hz, 1H, CpC*H*HN), 2.35–2.21 (m, 2H, CH_2), 2.14–2.04 (m, 1H, C*H*H), 1.82–1.61 (m, 5H, CH_2), 1.44–1.33 (m, 1H, CH*H*),

1.24–1.16 ppm (m, 2H, *CH*$_2$); ^{13}C NMR – not obtained due to poor solubility in $CDCl_3$ and d_6-DMSO; IR (neat): ν = 3444, 2925, 2855, 1733, 1623, 1590, 1497, 1459, 1378, 1259, 1170, 1070, 1023, 926, 782, 745, 702 cm^{-1}; HRMS (ESI): *m*/*z* calculated for $C_{43}H_{42}CoN_2O_2Pd$: 783.1623 $[M+H]^+$; found: 783.1615.

S$_p$*-(π-(Pyrrolidinylmethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-)palladium(II)(D)-Proline*

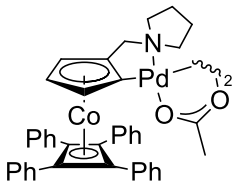


R,*S*$_p$-**260**
>99:1 dr

A solution of *S*$_p$-di-*μ*-chloro-bis([*π*-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (20 mg, 0.014 mmol) in acetone (2 mL) was added to a solution of $NaHCO_3$ (3 mg, 0.034 mmol) and *D*-Proline (3 mg, 0.028 mmol) in water (1 mL). During the addition copious amounts of precipitate was formed. The reaction was then vigorously stirred for 16 h at r.t. and then diluted with CH_2Cl_2 (5 mL). The phases were separated and the aqueous was washed with further portions of CH_2Cl_2 (2 × 2 mL). The organic phases were combined, dried over $MgSO_4$ and solvent was removed *in vacuo* yielding the product as an orange solid (0.011 g, 50%). Ratio of *R*,*R*$_p$-**270**: *R*,*S*$_p$-**270 =** 1:99. $[\alpha]_D^{23}$ = +72 (*c* = 0.5 mg/mL in CH_2Cl_2); m.p. 206–208 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 6.4 Hz, 8H, Ar–*H*), 7.29–7.26 (m, 12H, Ar–*H*), 4.45 (t, *J* = 2.3 Hz, 1H, Cp–*H*), 4.33 (d, *J* = 2.6 Hz, 1H, Cp–*H*), 4.20 (d, *J* = 2.5 Hz, 1H, Cp–*H*), 3.44 (dt, *J* = 11.5, 7.6 Hz, 1H, NHC*H*), 3.34 (ddt, *J* = 13.5, 9.1, 4.9 Hz, 2H, 2 x NHC*H*H), 3.13–2.91 (m, 4H, *CH*$_2$), 2.71–2.61 (m, 1H, C*H*H), 2.47-2.35 (m, 1H, C*H*H), 2.18–2.10 (m, 1H, C*H*H), 2.05–1.95 (m, 2H, C*H*$_2$.), 1.94–1.89 (m, 2H, C*H*$_2$), 1.88–1.79 (m, 1H, C*H*H), 1.78–1.72 (m, 1H, C*H*H), 1.64 (brs, 1H, N*H*), 1.51–1.38 (m, 1H, C*H*H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.32, 136.76, 128.87, 128.26, 126.09, 104.56, 97.53, 84.31, 83.78, 79.33, 73.73, 66.13,

59.97, 59.65, 59.13, 52.98, 29.60, 25.44, 22.06, 21.95 ppm; IR (neat): ν = 3444, 2925, 2855, 1733, 1623, 1590, 1497, 1459, 1378, 1259, 1170, 1070, 1023, 926, 782, 745, 702 cm^{-1}; HRMS (ESI): *m*/*z* calculated for $C_{43}H_{42}CoN_2O_2Pd$: 783.1623 $[M+H]^+$; found: 783.1614.

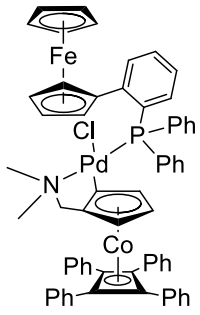
S_p-di-aceto-bis{[π-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt(I)}-dipalladium(II)



>98% *ee*

To a solution of S_p-di-μ-chloro-bis([π-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (100 mg, 0.07 mmol) in acetone (1 mL) was added silver acetate (28 mg, 0.17 mmol). The solution was stirred vigorously overnight and then the solution filtered through a short pad of celite, eluting with CH_2Cl_2. The solvent was then removed *in vacuo* to give the product as an orange solid (88 mg, 0.06 mmol, 88%). $[\alpha]_D^{23}$ = −146 (*c* = 1.0 mg/mL, in CH_2Cl_2); m.p. 162–164 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (dd, *J* = 7.9, 1.5 Hz, 16H, Ar−*H*), 7.23–7.16 (m, 24H, Ar−*H*), 4.17–4.15 (m, 2H, Cp−*H*), 4.07 (t, *J* = 2.3 Hz, 2H, Cp−*H*), 3.97–3.95 (m, 2H, Cp−*H*), 3.31–3.19 (m, 2H, C*H*HN), 3.00–2.88 (m, 2H, CH*H*N), 2.44–2.35 (m, 2H, C*H*H), 2.34–2.25 (m, 2H, C*H*H), 1.76 (s, 6H, O_2CCH_3), 1.56 (s, 6H, CH*H*), 1.35–1.22 ppm (m, 6H, CH*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 179.70, 136.76, 128.87, 128.26, 126.09, 102.08, 100.39, 83.06, 79.13, 74.10, 73.46, 64.11, 29.60, 25.44, 22.06, 21.95 ppm; IR (neat): ν = 3058, 2910, 1575, 1501, 1412, 1268, 1175, 1023, 957, 740, 698 cm^{-1}; Elemental analysis calcd. (%) for $C_{80}H_{72}Co_2N_2O_4Pd_2$: C 65.98, H 4.99, N 1.92; found C 65.75, H 4.96, N 1.95.

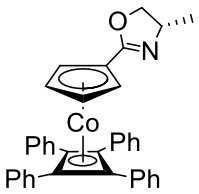
Chloro[(η^5-(S_p)-N,N-dimethylaminomethylcyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]2-(diphenylphosphino)phenylferrocene-palladium(II)



S_p-**265**

To a solution of $_pS$-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrapheynylcyclobutadienecobalt) dipalladium(II) (10 mg, 0.02 mmol) in CH_2Cl_2 (1 mL) was added 2-(diphenylphosphino)phenylferrocene (7 mg, 0.01 mmol) and the solution was stirred for 16 h. The solvent was removed *in vacuo* and the product was purified by column chromatography (SiO_2, 49:1 CH_2Cl_2/MeOH) to give the product as a red/orange solid (15 mg, 0.01 mmol, 88%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). $[\alpha]_D^{21}$ = +26 (c = 0.5 mg/mL in CH_2Cl_2); m.p. 171 ^oC; 1H NMR (500 MHz, $CDCl_3$): δ = 7.90–7.80 (m, 2H, Ar–*H*), 7.48–7.10 (m, 28H, Ar–*H*), 7.00 (t, *J* = 7.6 Hz, 1H, Ar-*H*), 6.90 (t, *J* = 6.8 Hz, 2H, Ar–*H*), 6.76 (dd, *J* = 11.1, 7.5 Hz, 1H, Ar–*H*), 4.48 (brs, 1H, Cp–*H*), 4.36 (brs, 1H, Cp–*H*), 4.12 (s, 1H, Cp–*H*), 4.07 (s, 1H, Cp–*H*), 4.00 (s, 1H, Cp–*H*), 3.93 (s, 5H, Cp–*H*), 3.84 (s, 1H, Cp–*H*), 3.22 (s, 1H, Cp–*H*), 3.03 (d, *J* = 14.1 Hz, 1H, C*H*HNMe$_2$), 2.92 (dd, *J* = 14.0, 2.5 Hz, 1H, CH*H*NMe$_2$), 2.65 (s, 3H, *CH*$_3$), 2.38 ppm (d, *J* = 2.4 Hz, 3H, *CH*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 136.66, 135.99, 132.84, 130.20, 129.42, 129.06, 128.05, 127.99, 127.95, 127.91, 127.52, 127.44, 125.89, 120.35, 80.82, 77.60, 77.29, 77.03, 76.78, 76.24, 73.82, 69.68, 61.90, 52.06 ppm; ^{31}P NMR (202 MHz, $CDCl_3$): δ = 32.22 ppm; IR (neat): ν = 3056, 2923, 1732, 1596, 1497, 1436, 1194, 911, 732, 695, 559 cm^{-1}; Elemental analysis calcd. (%) for $C_{64}H_{54}ClCoFeNPPd$: C 68.34, H 4.85, N 1.25; found C 66.35, H 5.05, N 1.46.

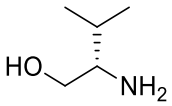
η^5-(S)-2-(4-methyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[117]



(*S*)-**281**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (200 mg, 0.38 mmol) and dissolved in CH_2Cl_2 (5 mL). Oxalyl chloride (0.07 mL, 0.76 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-alaninol (0.04 mL, 0.53 mmol) and triethylamine (0.32 mL, 2.28 mmol) in CH_2Cl_2 (8 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (20 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.07 mL, 0.95 mmol) was then added in one portion and the resulting solution was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as a yellow solid (169 mg, 0.30 mmol, 79%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.43 (m, 8H, Ar–*H*), 7.32–7.19 (m, 12H, Ar–*H*), 5.18 (dt, *J* = 2.7, 1.4 Hz, 1H, Cp–*H*), 5.11 (dt, *J* = 2.8, 1.4 Hz, 1H, Cp–*H*), 4.82–4.78 (m, 1H, Cp–*H*), 4.74 (td, *J* = 2.6, 1.6 Hz, 1H, Cp–*H*), 3.87-3.72 (m, 1H, oxazoline–*H*), 3.66 (dd, *J* = 9.4, 7.6 Hz, 1H, oxazoline–*H*), 3.35 (t, *J* = 7.7 Hz, 1H, oxazoline–*H*), 1.10 (d, *J* = 6.6 Hz, 3H, *CH*$_3$). Spectral data matched that previously reported.

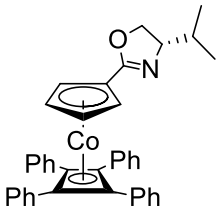
(S)-Valinol[237]



To a flask charged with $NaBH_4$ (7.75 g, 85.36 mmol) suspended in THF (200 mL) was added (*S*)-valine (10.0 g, 205 mmol) in one portion. The suspension was cooled to 0 ^oC and a solution of iodine (21.5 g, 85.36 mmol) in THF (50 mL) was added dropwise whilst maintaining a temperature below 5 ^oC. On addition, the solution was heated to reflux for 16h. On completion, the solution was cooled and MeOH (100 mL) was added and the solvent was removed *in vacuo*. The resultant residue was redissolved in aqueous 50% potassium hydroxide solution and stirred for 4 h. The aqueous layer was extracted with CH_2Cl_2 (4 × 100 mL) and the organic layers were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by Kugelrohr distillation gave the product as a colourless oil (8.20 g, 79.61 mmol, 94%). bp: 110 ^oC (5 mbar); ^1H NMR (400 MHz, $CDCl_3$): δ = 3.63 (dd, *J* = 10.5, 4.0 Hz, 1H, C*H*HOH), 3.27 (dd, *J* = 10.4, 8.8 Hz, 1H, CH*H*OH), 2.54 (ddd, *J* = 8.8, 6.4, 4.0 Hz, 1H, NC*H*), 1.79 (br s, 2H, H_2N), 1.64–1.49 (m, 1H, C*H*$(CH_3)_2$), 0.91 ppm (2 x d, *J* = 5.5 Hz, 6H, CH(C$H_3)_2$). Spectral data matched that previously reported.

(*S*)-Valinol was converted to the corresponding hydrochloride salt by treatement of the free-base with aqueous 2 M HCl solution in ether.

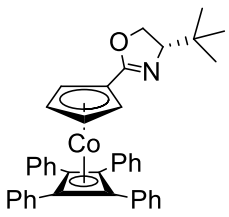
η^5-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[17]



(*S*)-**117**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (4.00 g, 7.63 mmol) and dissolved in CH_2Cl_2 (120 mL). Oxalyl chloride (1.31 mL, 15.3 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-valinol.HCl (1.50 g, 10.7 mmol) and triethylamine (6.33 mL, 45.8 mmol) in CH_2Cl_2 (80 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (100 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (1.48 mL, 19.1 mmol) was then added in one portion and the resulting solution was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (150 mL) and brine (150 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as a yellow solid (3.39 g, 5.72 mmol, 75%). m.p. = 160–162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.44 (m, 8H, Ar–*H*), 7.27–7.17 (m, 12H, Ar–*H*), 5.20 (brs, 1H, Cp–*H*), 5.09 (brs, 1H, Cp–*H*), 4.80 (brs, 1H, Cp–*H*), 4.62 (brs, 1H, Cp–*H*), 3.56–3.41 (m, 3H, oxazoline–*H*), 1.40 (oct, *J* = 6.7 Hz, 1H, C*H*(CH_3)$_2$), 0.97 (d, *J* = 6.7 Hz, 3H CH(C*H*$_3$)$_2$), 0.77 ppm (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)$_2$). Spectral data matched that previously reported.

η^5-(S)-2-(4-tertbutyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)[117]

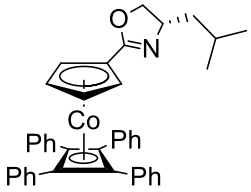


(*S*)-**119**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (0.96 g, 1.83 mmol) and dissolved in CH_2Cl_2 (10 mL). Oxalyl chloride (0.31 mL, 3.66 mmol) and dimethylformamide (3 drops) were added

sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-*tert*-leucinol (0.30 g, 2.56 mmol) and triethylamine (1.50 mL, 11.0 mmol) in CH_2Cl_2 (10 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (20 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.36 mL, 4.58 mmol) was then added in one portion and the resulting solution was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (15 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as a yellow solid (0.62 g, 1.04 mmol, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47–7.42 (m, 8H, Ar–*H*), 7.20 (t, *J* = 7.4 Hz, 12H, Ar–*H*), 5.22 (s, 1H, Cp–*H*), 5.00 (s, 1H, Cp–*H*), 4.77 (s, 1H, Cp–*H*), 4.72 (s, 1H, Cp–*H*), 3.69 (t, *J* = 7.7 Hz, 1H, oxazoline–*H*), 3.41–3.27 (m, 1H, oxazoline–*H*), 3.32–3.21 (m, 1H, oxazoline–*H*), 0.79 ppm (s, 9H, $C(CH_3)_3$). Spectral data matched that previously reported.

η^5-(S)-2-(4-isobutyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)

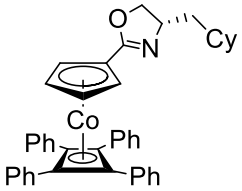


(*S*)-**282**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (2.65 g, 5.05 mmol) and dissolved in CH_2Cl_2 (50 mL). Oxalyl chloride (0.87 mL, 10.1 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-leucinol (0.90 mL, 7.07 mmol) and triethylamine (4.20 mL, 30.3 mmol) in CH_2Cl_2 (20 mL) was

added a solution of the crude acid chloride in CH_2Cl_2 (30 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.98 mL, 12.6 mmol) was then added in one portion and the resulting solution was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as a golden solid (2.43 g, 3.99 mmol, 79%). $[\alpha]_D^{23} = -114$ (c = 1.4 mg/mL in CH_2Cl_2); m.p. 116 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.32 (m, 8H, Ar–*H*), 7.21–7.07 (m, 12H, Ar–*H*), 5.09 (dt, *J* = 2.7, 1.4 Hz, 1H, Cp–*H*), 5.02 (dt, *J* = 2.6, 1.4 Hz, 1H, Cp–*H*), 4.70 (td, *J* = 2.4, 1.4 Hz, 1H, Cp–*H*), 4.62 (td, *J* = 2.5, 1.4 Hz, 1H, Cp–*H*), 3.70–3.60 (m, 2H, oxazoline–*H*), 3.30–3.20 (m, 1H, oxazoline–*H*), 1.58 (tt, *J* = 13.3, 6.7 Hz, 1H, *CH*HCH$(CH_3)_2$), 1.30 (dt, *J* = 13.2, 6.4 Hz, 2H, *CH*H*CH*$(CH_3)_2$), 0.92 (dt, *J* = 13.7, 6.9 Hz, 1H, CH_2*CH*$(CH_3)_2$), 0.82 ppm (t, *J* = 6.3 Hz, 6H, CH_2*CH*$(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$): δ = 135.37, 128.93, 127.94, 126.43, 86.37, 84.98, 84.62, 84.50, 82.13, 75.97, 72.13, 64.63, 45.32, 25.45, 22.82, 22.66 ppm, (C=N not observed)**;** IR (neat): *v* = 2918, 2850, 2161, 1972, 1655, 1596, 1498, 1446, 1113, 742, 694 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{40}H_{37}CoNO$: 606.2202 $[M+H]^+$; found: 606.2197.

η^5-(S)-2-(4-methylcyclohexyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)

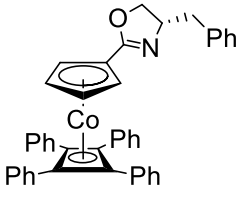


(*S*)-**283**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (965 mg, 1.84 mmol) and dissolved in CH_2Cl_2 (25 mL).

Oxalyl chloride (0.32 mL, 3.69 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-cyclohexylalaninol (500 mg, 2.58 mmol) and triethylamine (1.50 mL, 11.1 mmol) in CH_2Cl_2 (10 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (20 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.36 mL, 4.60 mmol) was then added in one portion and the resulting mixture was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as an orange solid (868 mg, 1.34 mmol, 73%). $[\alpha]_D^{21} = -33$ (c = 0.6 mg/mL in CH_2Cl_2); m.p. 175 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.32 (m, 8H, Ar–*H*), 7.17–7.05 (m, 12H, Ar–*H*), 5.09–5.04 (m, 1H, Cp–*H*), 4.99 (dd, *J* = 4.1, 1.4 Hz, 1H, Cp–*H*), 4.68–4.64 (m, 1H, Cp–*H*), 4.58 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 3.72–3.64 (m, 1H, oxazoline–*H*), 3.64–3.58 (m, 1H, oxazoline–*H*), 3.21 (t, *J* = 7.5 Hz, 1H, oxazoline–*H*), 1.66–1.52 (m, 4H, Cy–*H*), 1.30–1.02 (m, 7H, Cy–*H*), 0.83–0.72 ppm (m, 2H, Cy–*H*); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 159.44, 134.32, 127.88, 126.88, 125.38, 85.35, 83.92, 83.62, 83.40, 81.04, 74.90, 71.15, 63.01, 43.03, 33.80, 32.40, 32.35, 25.88, 25.55, 25.22 ppm; IR (neat): *v* = 2917, 2850, 2161, 1972, 1656, 1596, 1498, 1446, 1116, 742, 694 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{43}H_{41}CoNO$: 646.2515 $[M+H]^+$; found: 646.2506.

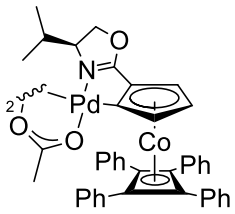
η^5-(S)-2-(4-benzyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I)



(*S*)-**284**

A flask was charged with crude (η^5-carboxycyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (1.01 g, 1.93 mmol) and dissolved in CH_2Cl_2 (25 mL). Oxalyl chloride (0.33 mL, 3.85 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated *in vacuo* redissolved in CH_2Cl_2 and re-concentrated *in vacuo* to give the crude acid chloride. To a solution of (*S*)-phenylalaninol (409 mg, 2.70 mmol) and triethylamine (1.60 mL, 11.6 mmol) in CH_2Cl_2 (10 mL) was added a solution of the crude acid chloride in CH_2Cl_2 (20 mL) *via* cannula. The resulting solution was maintained at room temperature and after 2 h the solution was cooled to 0 °C in an ice bath. Methanesulfonyl chloride (0.37 mL, 4.83 mmol) was then added in one portion and the resulting solution was allowed to warm to room temperature. After 16 h the solution was washed with saturated aqueous sodium bicarbonate (20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification with column chromatography (SiO_2, 9:1 hexanes/EtOAc) yielded the product as a yellow solid (1.16 g, 1.81 mmol, 94%). $[\alpha]_D^{19} = -66$ (c = 1.0 mg/mL in CH_2Cl_2); m.p. 131 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.49–7.41 (m, 8H, Ar–*H*), 7.33–7.17 (m, 15H, Ar–*H*), 7.17–7.12 (d, *J* = 7.1 Hz, 2H, Ar–*H*), 5.24–5.16 (m, 1H, Cp–*H*), 5.15–5.06 (m, 1H, Cp–*H*), 4.79 (dd, *J* = 4.0, 2.5 Hz, 1H, Cp–*H*), 4.72 (dd, *J* = 4.0, 2.5 Hz, 1H, Cp–*H*), 4.07–3.92 (m, 1H, oxazoline–*H*), 3.62–3.42 (m, 2H, oxaoline–*H*), 3.00 (dd, *J* = 13.7, 4.9 Hz, 1H, C*H*HPh), 2.31–2.18 ppm (dd, *J* = 13.7, 9.5 Hz, 1H, CH*H*Ph); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 161.38, 138.66, 135.43, 129.14, 129.05, 128.63, 128.11, 126.62, 126.44, 86.57, 84.81, 82.17 76.13, 71.28, 67.84, 41.82 ppm**;** IR (neat): *v* = 2918, 2850, 2160, 1972, 1655, 1596, 1498, 1446, 1113, 742, 694 cm^{-1}; HRMS (ASAP) *m/z* calculated for $C_{43}H_{35}CoNO$: 640.2045 $[M+H]^+$; found: 640.2043.

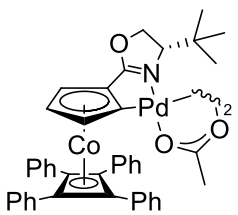
di-μ-acetatobis[(η^5-(S)-(R_p)-2-(2'-4'-methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)[17]



(S,R_p)$_2$-**118**

A flask was charged with η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.08 mmol) and then dissolved in glacial acetic acid (0.5 mL). Palladium(II) acetate (19 mg, 0.08 mmol) was added in one portion. The solution was then heated at 95 °C and formation of an orange precipitate is observed. After 30 minutes, the solution was cooled to room temperature and filtered to provide an orange solid. This solid was washed with cooled glacial acetic acid (2 mL) and dried under vacuum to provide the product as a mustard coloured solid (44 mg, 0.03 mmol, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.62 (dd, *J* = 7.8, 1.9 Hz, 16H, Ar–*H*), 7.30–7.19 (m, 24H, Ar–*H*), 4.69 (d, *J* = 2.7 Hz, 2H, Cp–*H*), 4.64 (d, *J* = 2.4 Hz, 2H, Cp–*H*), 4.25 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 4.09 (dd, *J* = 8.5, 4.0 Hz, 2H, oxazoline–*H*), 3.36 (t, *J* = 9.1 Hz, 2H, oxazoline–*H*), 3.05–2.95 (m, 2H, oxazoline–*H*), 1.97 (s, 6H, O_2CCH_3), 1.77 (m, 6H, $CH(CH_3)_2$), 0.46 (d, *J* = 7.1 Hz, 2H, $CH(CH_3)_2$), –0.06 ppm (d, *J* = 6.7 Hz, 6H, $CH(CH_3)_2$). Spectral data matched that previously reported.

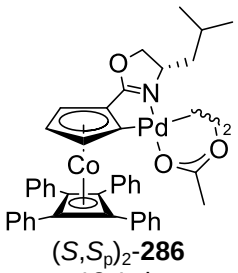
di-μ-acetatobis[(η^5-(S)-(S_p)-2-(4'-tertbutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)[117]



(S,S_p)$_2$-**120**

A flask was charged with η^5-(*S*)-2-(4-*tert*-butyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.08 mmol) and then dissolved in glacial acetic acid (0.5 mL). Palladium(II) acetate (19 mg, 0.08 mmol) was added in one portion. The solution was then heated at 95 °C and formation of an orange precipitate is observed. After 30 minutes, the solution was cooled to room temperature and filtered to provide an orange solid. This solid was washed with glacial acetic acid (2 mL) and dried under vacuum to provide the product as a mustard coloured solid (65 mg, 0.04 mmol, 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (dd, *J* = 6.5, 3.0 Hz, 16H, Ar–*H*), 7.20 (dd, *J* = 6.4, 3.7 Hz, 24H, Ar–*H*), 4.58 (d, *J* = 1.7 Hz, 2H, Cp–*H*), 4.40 (d, *J* = 1.3 Hz, 2H, Cp–*H*), 4.11 (dd, *J* = 8.6, 3.8 Hz, 2H, Cp–*H*), 3.89 (t, *J* = 2.4 Hz, 2H, oxazoline–*H*), 3.74 (t, *J* = 9.1 Hz, 2H, oxazoline–*H*), 2.58 (dd, *J* = 9.6, 3.8 Hz, 2H, oxazoline–*H*), 2.02 (s, 6H, C*H*$_3$), 0.39 ppm (s, 18H, C(C*H*$_3$)$_3$). Spectral data matched that previously reported.

di-μ-acetatobis[(η^5-(S)-(S_p)-2-(2'-4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)

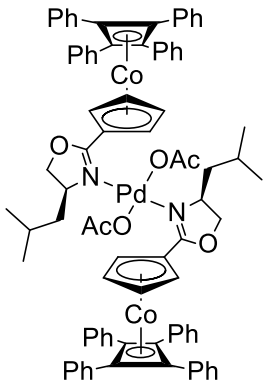


(S,S_p)$_2$-**286**
13:1 dr

A flask was charged with η^5-(*S*)-2-(4-*iso*-butyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.08 mmol) and palladium(II) acetate (19 mg, 0.08 mmol) in CH_2Cl_2 (0.5 mL). The solution was then stirred at room temperature for 16 h. The solvent was removed *in vacuo* to yield the product as an orange solid (44 mg, 0.03 mmol, 73%). Crystals suitable for X-ray crystallography were obtained by slow diffusion of hexane into a CH_2Cl_2 solution (~50:1 hexane: CH_2Cl_2). $[\alpha]_D^{19}$ = –721 (c = 1.2 mg/mL in CH_2Cl_2); m.p. 266 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.67–7.60 (m, 16H, Ar–*H*), 7.24–

7.19 (m, 24H, Ar–*H*), 4.68–4.63 (m, 2H, Cp–*H*), 4.52–4.46 (m, 2H, Cp–*H*), 4.07 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 4.00–3.92 (m, 2H, oxazoline–*H*), 3.54 (t, *J* = 7.7 Hz, 2H, oxazoline–*H*), 3.05–2.95 (m, 2H, oxazoline–*H*), 2.00 (s, 6H, O_2CCH_3), 1.41–1.31 (m, 2H, C*H*H^{i}Pr), 1.15–1.04 (m, 2H, C*H*$(CH_3)_2$), 0.71 (d, *J* = 6.6 Hz, 6H, CH$(CH_3)_2$), 0.67 (d, *J* = 6.6 Hz, 6H, CH$(CH_3)_2$), 0.19 ppm (ddd, *J* = 13.6, 11.3, 4.7 Hz, 2H, CH*H*^{i}Pr); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.91, 172.12, 135.91, 129.23, 127.99, 126.35, 97.70, 86.86, 85.66, 83.33, 76.90, 76.52, 59.68, 42.76, 25.41, 23.97, 23.35, 21.77 ppm (Cp-C not seen); IR (neat): *v* = 3058, 2956, 1605, 1575, 1505, 694 cm^{-1}; Elemental analysis calcd. (%) for $C_{84}H_{76}Co_2N_2O_6Pd_2$: C 65.50, H 4.98, N 1.82; found C 65.59, H 5.04, N 1.91.

Formation of trans-bis(oxazoline) coordination complex

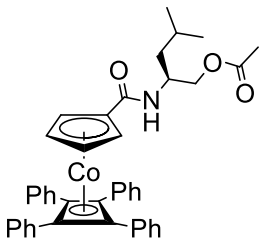


290

A flask was charged with η^5-(*S*)-2-(4-*iso*-butyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (500 mg, 0.83 mmol) and then dissolved in glacial acetic acid (1 mL). Palladium(II) acetate (185 mg, 0.83 mmol) was added in one portion. The solution was then heated at 95 °C and formation of an orange precipitate is observed. After 30 min, the solution was cooled to room temperature and filtered to provide an orange solid. This solid was washed with glacial acetic acid (2 mL) and dried under vacuum to provide the product as an orange solid (573 mg, 0.40 mmol, 97%). $[\alpha]_D^{24}$ = +151 (c = 2.0 mg/mL in CH_2Cl_2); m.p. 188-190 ^oC; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.33 (m, 16H, Ar–*H*), 7.24–7.12 (m, 24H, Ar–*H*), 6.05 (brs, 2H, Cp–*H*), 5.79 (s, 2H, Cp–*H*), 4.90–4.57 (m,

4H, Cp–*H*), 3.75–3.64 (m, 2H, oxazoline–*H*), 3.63–3.56 (m, 2H, oxazoline–*H*), 3.27–3.18 (m, 2H, oxazoline–*H*), 3.08–2.96 (m, 2H, C*H*(CH_3)$_2$), 2.06 (app d, *J* = 3.6 Hz, 6H, O_2CCH_3), 1.58–1.42 (m, 2H), 1.02–0.86 ppm (m, 12H, CH(C*H*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ =175.64, 165.53, 135.46, 128.99, 128.23, 126.63, 86.17, 85.43, 84.10, 76.36, 72.43, 43.21, 25.95, 23.86, 22.42, 21.74, 21.03 ppm; IR (neat): ν = 3059, 2957, 1717, 1634, 1614, 1575, 1417, 1384, 1154, 696 cm^{-1}; Elemental analysis calcd. (%) for $C_{84}H_{78}Co_2N_2O_6Pd$: C 70.26, H 5.59, N 1.95; found C 70.08, H 5.35, N 1.85.

(η^5-(S)-N-2-(1-Aceto-3-methylpentyl)carboxamide- cyclopentadienyl)(η^4-tetraphenylcyclobutadiene)cobalt(I)

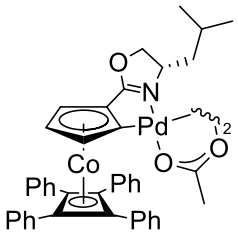


293

A flask charged with intermediate **290** (80 mg, 0.06 mmol) dissolved in AcOH (5 mL) and was heated to 90 °C for 4 h. On completion, the solvent was removed in vacuo. The crude residue was redissolved in CH_2Cl_2 (5 mL) and washed with aqueous sodium hydrocarbonate solution (5 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by column chromatography on silca eluting with CH_2Cl_2/EtOAc (9:1) gave the product as an orange oil (16 mg, 0.02 mmol, 86%). $[\alpha]_D^{26}$ = +24.4 (c = 1.6 mg/mL in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.3 Hz, 8H, Ar–*H*), 7.32–7.19 (m, 12H, Ar–*H*), 5.22 (brd, *J* = 8.4 Hz, 1H, N*H*), 5.01 (s, 2H, Cp–*H*), 4.72–4.63 (m, 2H, Cp–*H*), 4.09–3.99 (m, 1H, CH_2CHN), 3.92 (dd, *J* = 11.2, 5.6 Hz, 1H, NHCH*H*CH), 3.67 (dd, *J* = 11.2, 4.7 Hz, 1H, NHC*H*HCH), 2.01 (s, 3H, C*H*$_3$), 1.49–1.38 (m, 1H, C*H*(C*H*$_3$)$_2$), 1.11–1.02 (m, 1H, C*H*H^{i}Pr), 0.99–0.91 ppm (m, 1H, C*H*H^{i}Pr), 0.86 ppm (t, *J* = 5.9 Hz, 6H, CH(C*H*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 171.32, 165.80, 135.44,

128.93, 128.32, 126.94, 90.82, 86.92, 86.62, 82.25, 81.98, 76.31, 65.97, 47.00, 40.53, 24.83, 22.86, 22.69, 21.11 ppm; IR (neat): ν = 3332, 3059, 2957, 1739, 1644, 1520, 1499, 1240, 1026, 910, 733, 697 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{42}H_{41}CoNO_3$: 666.2413 $[M+H]^+$; found:666.2413.

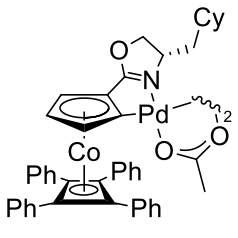
Conversion of trans-bis(oxazoline) coordination complex to di-μ-acetatobis[(η⁵-(S)-(S$_p$)-2-(2'-4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η⁴-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)



$(S,S_p)_2$-**286**
13:1 dr

A flask was charged with the intermediate complex (500 mg, 0.35 mmol) dissolved in toluene (2 mL). The solution was brought to reflux and stirred for 2 h. On completion, the solution was cooled and the solvent was removed *in vacuo* to yield the product as an orange solid (504 mg, 0.32 mmol, 94%). Spectral data matched that reported above.

di-μ-acetatobis[(η⁵-(S)-(S$_p$)-2-(2'-4'-methylcyclohexyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η⁴-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)

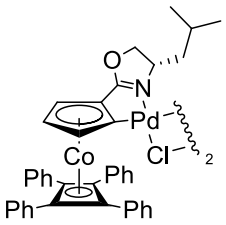


$(S,S_p)_2$-**287**

A flask was charged with η^5-(*S*)-2-(4-methylcyclohexyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (419 mg, 0.65 mmol) and then dissolved in glacial acetic acid (0.5 mL). Palladium(II) acetate (146 mg, 0.65 mmol) was added in one portion.

The solution was then heated at 95 °C and formation of an orange precipitate is observed. After 30 minutes, the solution was cooled to room temperature and filtered to provide an orange solid. This solid was washed with cooled glacial acetic acid (2 mL) and dried under vacuum to provide the product as a mustard coloured solid (370 mg, 0.23 mmol, 70%). $[\alpha]_D^{19}$ = –407 (c = 1.0 mg/mL in CH_2Cl_2); m.p. 248 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.63–7.46 (m, 16H, Ar–*H*), 7.23–7.02 (m, 24H, Ar–*H*), 4.55 (s, 2H, Cp–*H*), 4.39 (s, 2H, Cp–*H*), 4.01–3.93 (m, 2H, Cp–*H*), 3.88 (t, *J* = 8.5 Hz, 2H, oxazoline–*H*), 3.47 (t, *J* = 7.5 Hz, 2H, oxazoline–*H*), 3.02–2.86 (m, 2H, oxazoline–*H*), 1.92 (s, 6H, O_2CCH_3), 1.72–1.17 (m, 30H, C*H*HCy + Cy–*H*), 1.15–0.90 (m, 8H, Cy–*H*), 0.84–0.49 (m, 8H, Cy–*H*), 0.05 ppm (t, *J* = 12.4 Hz, 2H, CH*H*Cy); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 180.93, 172.11, 135.92, 129.24, 127.98, 126.34, 86.67, 85.68, 83.26, 77.25, 77.07, 76.49, 59.24, 41.20, 34.78, 33.76, 32.21, 31.00, 26.37, 26.06, 25.93, 23.98 ppm; IR (neat): ν = 3057, 2921, 2849, 1606, 1577, 1499, 1414, 694 cm^{-1}; Elemental analysis calcd. (%) for $C_{90}H_{84}Co_2N_2O_6Pd_2$: C 66.71, H 5.24, N 1.73; found C 62.77, H 5.04, N 1.91.

di-μ-chlorobis[(η^5-(S)-(S$_p$)-2-(2'-4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)

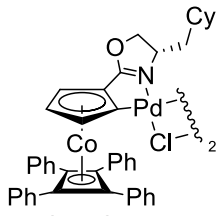


1:1.3 mixture of isomers

A flask was charged with di-μ-acetatobis[(η^5-(*S*)-(*S$_p$*)-2-(2'-4'-*iso*-butyl)oxazolinyl)cyclopentadienyl, 1-*C*, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (20 mg, 0.01 mmol) dissolved in acetone (0.5 mL). To this solution was added a 2 M NaCl solution (0.06 mL, 0.13 mmol) and the solution was vigorously stirred at r.t. for 4 h, in which time a precipitate was formed.

The precipitate was collected by filtration, washed with water and acetone and dried under *vacuum* to yield the product as a yellow solid (7 mg, 0.01 mmol, 99%). $[\alpha]_D^{25}$ = −1222 (c = 1.9 mg/mL in CH_2Cl_2); m.p. 183−185 °C; ^{1}H NMR (500 MHz, $CDCl_3$), 1:1.3 mixture of isomers: δ = 7.72–7.65 (m, 16H, Ar−*H*), 7.64–7.57 (m, 16H, Ar−*H*), 7.31–7.16 (m, 48H, Ar−*H*), 4.77 (dd, *J* = 2.5, 1.1 Hz, 2H, Cp−*H*), 4.71 (dd, *J* = 2.8, 1.0 Hz, 2H, Cp−*H*), 4.70–4.66 (m, 4H, Cp−*H*), 4.58 (t, *J* = 7.8 Hz, 2H, oxazoline−*H*), 4.52 (t, *J* = 8.7 Hz, 2H, oxazoline−*H*), 4.46 (t, *J* = 2.5 Hz, 2H, Cp−*H*), 4.32 (t, *J* = 2.5 Hz, 1H, Cp−*H*), 3.93 (dd, *J* = 8.3, 6.4 Hz, 2H, oxazoline−*H*), 3.89–3.72 (m, 6H, oxazoline−*H*), 1.81 (ddd, *J* = 12.9, 10.1, 2.3 Hz, 2H, C*H*H^{i}Pr), 1.55–1.48 (m, 2H, C*H*H^{i}Pr), 1.37–1.24 (m, 4H, C*H*$(CH_3)_2$), 0.94–0.77 (m, 24H, CH$(CH_3)_2$), 0.38 (4 x d, *J* = 4.2 Hz, 4H, CH*H*^{i}Pr) ppm; ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.84, 173.73, 135.82, 135.79, 129.45, 129.36, 128.15, 128.10, 126.59, 126.47, 100.12, 99.92, 89.00, 88.80, 83.21, 81.95, 77.73, 77.23, 77.07, 77.00, 76.65, 76.45, 76.32, 60.76, 60.62, 43.58, 43.27, 31.09, 25.65, 25.58, 23.79, 23.67, 21.51, 21.39 ppm; IR (neat): ν = 3058, 2957, 1601, 1506, 1469, 1371, 742, 696 cm^{-1}; Elemental analysis calcd. (%) for $C_{80}H_{70}Co_2N_2O_2Cl_2Pd_2$: C 64.35, H 4.74, N 1.88; found C 62.81, H 5.15, N 1.76.

di-μ-chlorobis[(η^5-(S)-(S$_p$)-2-(2'-4'-cyclohexyl)oxazolinylmethyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)

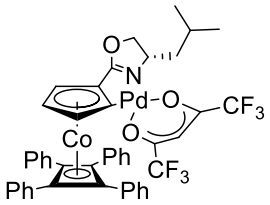


(S,S_p)$_2$-**301**
1:1.4 mixture of isomers

A flask was charged with di-μ-acetatobis[(η^5-(*S*)-(*$_p$S*)-2-(2'-4'-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-*C*, 3'-*N*)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (50 mg, 0.03 mmol) dissolved in acetone (1 mL). To this solution was added a 2 M NaCl solution (0.2 mL, 0.31 mmol) and

the solution was vigorously stirred at rt for 4 h, in which time a precipitate was formed. The precipitate was collected by filtration, washed with water and acetone and dried under *vacuum* to yield the product as a yellow solid (24 mg, 0.02 mmol, 99%). $[\alpha]_D^{25} = -1113$ (c = 3.4 mg/mL in CH_2Cl_2); m.p. 203 °C; ^{1}H NMR (500 MHz, $CDCl_3$), 1:1.4 mixture of isomers: δ = 7.71–7.65 (m, 16H, Ar–*H*), 7.64–7.58 (m, 16H, Ar–*H*), 7.28–7.16 (m, 48H, Ar–*H*), 4.76 (dd, *J* = 2.3, 1.1 Hz, 2H, Cp–*H*), 4.71 (dd, *J* = 2.8, 1.0 Hz, 2H, Cp–*H*), 4.71–4.65 (m, 4H, Cp–*H*), 4.63–4.55 (m, 2H, oxazoline–*H*), 4.52 (t, *J* = 8.7 Hz, 2H, oxazoline–*H*), 4.46 (t, *J* = 2.5 Hz, 2H, Cp–*H*), 4.34 (t, *J* = 2.6 Hz, 2H, Cp–*H*), 3.93 (dd, *J* = 8.3, 6.4 Hz, 2H, oxazoline–*H*), 3.89–3.74 (m, 6H, oxazoline–*H*), 1.95–1.85 (m, 2H, C*H*HCy), 1.83–1.44 (m, 24H, C*H*HCy + Cy–*H*), 1.35–0.78 (m, 22H, Cy–*H*), 0.44–0.25 ppm (m, 4H, CH*H*Cy); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.81, 173.72, 135.83, 135.79, 129.45, 129.35, 128.15, 128.10, 126.57, 126.46, 99.93, 99.35, 89.22, 89.05, 85.92, 85.35, 83.30, 82.08, 77.37, 77.29, 76.41, 76.30, 60.36, 60.18, 42.25, 41.91, 35.11, 34.17, 32.17, 31.08, 26.73, 26.66, 26.56, 26.49, 26.39, 26.21 ppm; IR (neat): ν = 3056, 2923 2851, 1601, 1506, 1446, 1183, 741, 696 cm^{-1}; Elemental analysis calcd. (%) for $C_{86}H_{78}Co_2N_2O_2Cl_2Pd_2$: C 65.66, H 5.01, N 1.78; found C 65.53, H 5.01, N 1.83.

hexafluoroacetylacetonate[(η^5-(S)-(S_p)-2-(2'-(4'- isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)

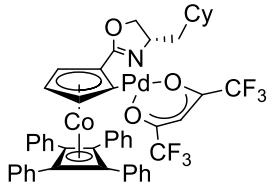


(S,S_p)-**295**

A flask was charged with di-μ-acetatobis[(η^5-(S)-($_p$S)-2-(2'-4'-*iso*-butyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (10 mg, 0.01 mmol) and sodium hexafluroacetylacetonate (14 mg, 0.06 mmol) in acetone/water (2:1 solution, 2 mL). The

solution was stirred vigorously for 16 h in which time a precipitate had formed. The solution was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to yield the product as an orange solid (10 mg, 0.01 mmol, >99%). $[\alpha]_D^{25}$ = **–**919 (c = 1.6 mg/mL in CH_2Cl_2); m.p. 253 ^oC; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.63–7.57 (m, 8H, Ar**–***H*), 7.27–7.22 (m, 4H, Ar**–***H*), 7.21–7.15 (m, 8H, Ar**–***H*), 5.92 (s, 1H, C**–***H* hfacac), 4.97 (dd, *J* = 2.3, 0.9 Hz, 1H, Cp**–***H*), 4.80 (dd, *J* = 2.6, 0.8 Hz, 1H, Cp**–***H*), 4.64 (t, *J* = 2.5 Hz, 1H, Cp**–***H*), 4.59 (t, *J* = 8.3 Hz, 1H, oxazoline**–***H*), 3.91–3.75 (m, 2H, oxazoline**–***H*), 1.85–1.72 (m, 1H, C*H*H^{i}Pr), 1.40–1.30 (m, 1H, C*H*$(CH_3)_2$), 0.87 (2 x d, *J* = 2.4 Hz, 6H, CH$(CH_3)_2$), 0.57–0.46 ppm (m, 1H, CH*H*^{i}Pr); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.77, 174.07 (d, $J_{C\text{-}F}$ = 4.7 Hz), 173.80 (d, $J_{C\text{-}F}$ = 4.8 Hz), 135.78, 129.22, 127.92, 126.59, 118.93 (d, $J_{C\text{-}F}$ = 55.7 Hz), 116.66 (d, $J_{C\text{-}F}$ = 55.1 Hz). 100.00, 90.24, 88.43, 86.60, 81.71, 77.21, 76.51, 60.29, 43.76, 25.42, 23.63, 21.25 ppm; ^{19}F NMR (471 MHz, $CDCl_3$): δ = **–**74.69, **–**75.63 ppm; IR (neat): *v* = 3060, 2960, 1627, 1600, 1512, 1480, 1259, 1209, 1151, 704 cm^{-1}; Elemental analysis calcd. (%) for $C_{45}H_{36}CoNO_3F_6Pd$: C 58.87, H 3.96, N 1.53; found C 58.71, H 4.05, N 1.68.

hexafluoroacetylacetonate[(η^5-(S)-(S_p)-2-(2'-(4'-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo-butadiene)cobalt(I)]palladium(II)



(S,S_p)-**296**

A flask was charged with di-μ-acetatobis[(η^5-(S)-($_p$S)-2-(2'-4'-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (30 mg, 0.02 mmol) and sodium hexafluroacetylacetonate (43 mg, 0.19 mmol) in acetone/water (2:1 solution, 2 mL). The

solution was stirred vigorously for 16 h in which time a precipitate had formed. The solution was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to yield the product as an orange solid (31 mg, 0.02 mmol, 99%). $[\alpha]_D^{25}$ = −532 (c = 5.2 mg/mL in CH_2Cl_2); m.p. 204 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62–7.54 (m, 8H, Ar−*H*), 7.25–7.20 (m, 4H, Ar−*H*), 7.19–7.13 (m, 8H, Ar−*H*), 5.88 (s, 1H, C−*H* hfacac), 4.94 (dd, *J* = 2.3, 1.0 Hz, 1H, Cp−*H*), 4.77 (dd, *J* = 2.6, 1.0 Hz, 1H, Cp−*H*), 4.60 (t, *J* = 2.6 Hz, 1H, Cp−*H*), 4.60–4.53 (m, 1H, oxazoline−*H*), 3.91–3.81 (m, 1H, oxazoline−*H*), 3.80–3.73 (m, 1H, oxazoline−*H*), 1.90–1.80 (m, 1H, C*H*HCy), 1.76–1.57 (m, 3H, Cy−*H*), 1.52–1.44 (m, 1H, Cy−*H*), 1.37–0.78 (m, 7H, Cy−*H*), 0.51–0.40 ppm (m, 1H, CH*H*Cy); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 174.66, 174.02 (d, $J_{C\text{-}F}$ = 10.0 Hz), 173.75 (d, $J_{C\text{-}F}$ = 10.6 Hz), 135.77, 129.20, 127.90, 126.57, 118.92 (d, $J_{C\text{-}F}$ = 54.9 Hz), 116.66 (d, $J_{C\text{-}F}$ = 53.9 Hz), 99.98, 90.22, 88.44, 86.61, 81.68, 77.30, 77.04, 76.48, 59.90, 34.89, 34.17, 31.99, 31.07, 26.48, 26.00 ppm; ^{19}F NMR (471 MHz, $CDCl_3$): δ = −74.69, −75.56 ppm; IR (neat): *v* = 3060, 2926, 2854, 1634, 1601, 1574, 1258, 1209, 1150, 704 cm^{-1}; Elemental analysis calcd. (%) for $C_{48}H_{40}CoNO_3F_6Pd$: C 60.16, H 4.22, N 1.46; found C 57.25, H 4.36, N 1.81.

General Methods for Palladation and ^{1}H-NMR/^{19}F NMR Data for Diastereoisomers

General Method for Palladation of Oxazoline Ligands

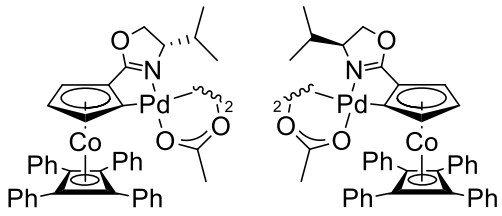
A flask was charged with the oxazoline ligand (1 eq.) and dissolved in the required solvent (5 mL/mmol). To this solution palladium(II) acetate (1 eq.) was added in one portion. The flask was sealed and the solution was stirred at the required temperature for the allotted time. The products were isolated either by filtration or by removal of the solvent *in vacuo*.

General Method for Conversion to hfacac Monomers

A flask was charged with crude acetate-bridged palladacycle (1 eq.) and sodium hexafluroacetylacetonate (10 eq.) in acetone/water (2:1 solution, generally 2 mL). The solution was stirred vigorously for 16 h in which time a precipitate forms. The solution was diluted with CH_2Cl_2 (5 mL) and washed with water (5 mL). The organic layer was collected and dried over $MgSO_4$. The products were isolated by removal of the solvent *in vacuo*.

All diastereoselectivities are based on ^{1}H-NMR signals of crude acetate dimers or hfacac monomers.

di-μ-acetatobis[(η^5-(S)-2-(2'-4'-methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)

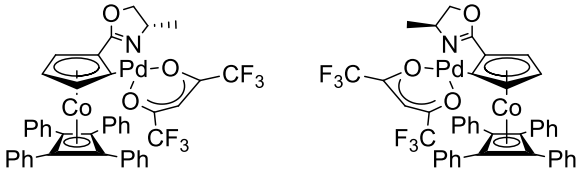


$(S,S_p)_2$-**118** $(S,R_p)_2$-**118**

$(S,R_p)_2$: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.62 (dd, *J* = 7.8, 1.9 Hz, 16H, Ar–*H*), 7.30–7.19 (m, 24H, Ar–*H*), 4.69 (d, *J* = 2.7 Hz, 2H, Cp–*H*), 4.64 (d, *J* = 2.4 Hz, 2H, Cp–*H*), 4.25 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 4.09 (dd, *J* = 8.5, 4.0 Hz, 2H, oxazoline–*H*), 3.36 (t, *J* = 9.1 Hz, 2H, oxazoline–*H*), 3.05-2.95 (m, 2H, oxazoline–*H*), 1.97 (s, 6H, C*H*$_3$), 1.77 (m, 2H, C*H*$(CH_3)_2$), 0.46 (m, 6H, CH$(CH_3)_2$), –0.06 ppm (d, *J* = 6.7 Hz, 6H, CH$(CH_3)_2$).

$(S,S_p)_2$: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.70–7.61 (m, 16H, Ar–*H*), 7.27–7.16 (m, 24H, Ar–*H*), 4.62–4.57 (m, 2H, Cp–*H*), 4.36 (dd, *J* = 2.1, 0.9 Hz, 2H, Cp–*H*), 4.08 (t, *J* = 2.4 Hz, 2H, Cp–*H*), 3.93–3.85 (m, 2H, oxazoline–*H*), 3.83–3.74 (m, 2H, oxazoline–*H*), 2.88–2.79 (m, 2H, oxazoline–*H*), 1.98 (s, 6H, C*H*$_3$), 1.46–1.34 (m, 2H, C*H*$(CH_3)_2$), 0.55 (d, *J* = 7.0 Hz, 6H, CH$(CH_3)_2$), 0.12 ppm (d, *J* = 6.8 Hz, 6H, CH$(CH_3)_2$).

hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'-methyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)

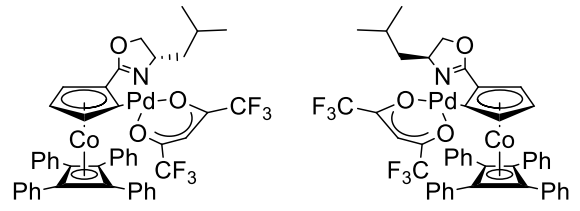


(S,S_p)-**294** (S,R_p)-**294**

(S,R_p): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 8H, Ar–*H*), 7.21–7.13 (m, 12H, Ar–*H*), 5.94 (s, 1H, C–*H* hfacac), 5.11 (dd, *J* = 2.4, 1.0 Hz, 1H, Cp–*H*), 4.88 (dd, *J* = 2.7, 1.0 Hz, 1H, Cp–*H*), 4.49 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 4.07 – 3.95 (m, 3H, oxazoline–*H*), 1.19 ppm (d, *J* = 6.5 Hz, 3H, C*H*$_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.29, –75.70 ppm.

(S,S_p): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62–7.56 (m, 8H, Ar–*H*), 7.29–7.20 (m, 12H, Ar–*H*), 5.91 (s, 1H, C–*H* hfacac), 4.97 (dd, *J* = 2.4, 1.0 Hz, 1H, Cp–*H*), 4.82 (dd, *J* = 2.7, 1.0 Hz, 1H, Cp–*H*), 4.62 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 3.65 (t, *J* = 8.1 Hz, 1H, oxazoline–*H*), 3.55–3.45 (m, 2H, oxazoline–*H*), 1.00 ppm (d, *J* = 6.5 Hz, 3H, C*H*$_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.70, –75.67 ppm.

hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'- isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



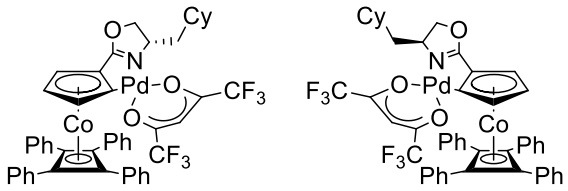
(S,S_p)-**295** (S,R_p)-**295**

(S,R_p): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.55–7.49 (m, 8H, Ar–*H*), 7.30–7.13 (m, 12H, Ar–*H*), 5.94 (s, 1H, C–*H* hfacac), 5.12 (dd, *J* = 2.3, 1.0 Hz, 1H, Cp–*H*), 4.88 (dd, *J* = 2.7, 1.0 Hz, 1H, Cp–*H*), 4.47 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 4.17–4.10 (m, 1H, oxazoline–*H*), 4.00–3.92 (m,

1H, oxazoline–*H*), 3.40–3.31 (m, 1H, oxazoline–*H*), 1.82–1.68 (m, 1H, C*H*H^{i}Pr), 1.53–1.41 (m, 1H, C*H*(CH$_3$)$_2$), 1.24–1.14 (m, 1H, CH*H*^{i}Pr), 0.85 ppm (2 × d, *J* = 2.4 Hz, 6H, CH(C*H*$_3$)$_2$); ^{19}F NMR (471 MHz, CDCl$_3$): δ = –74.23, –75.55 ppm.

(*S*,*S*$_p$): ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.61–7.55 (m, 8H, Ar–*H*), 7.25–7.20 (m, 4H, Ar–*H*), 7.19–7.13 (m, 8H, Ar–*H*), 5.90 (s, 1H, C–*H* hfacac), 4.95 (dd, *J* = 2.3, 0.9 Hz, 1H, Cp-*H*), 4.78 (dd, *J* = 2.6, 0.8 Hz, 1H, Cp–*H*), 4.62 (t, *J* = 2.5 Hz, 1H, Cp–*H*), 4.57 (t, *J* = 8.3 Hz, 1H, oxazoline–*H*), 3.89–3.73 (m, 2H, oxazoline–*H*), 1.83–1.70 (m, 1H, C*H*H^{i}Pr), 1.38–1.28 (m, 1H, C*H*(CH$_3$)$_2$), 0.85 (2 x d, *J* = 2.4 Hz, 6H, CH(C*H*$_3$)$_2$), 0.55–0.44 ppm (m, 1H, CH*H*^{i}Pr); ^{19}F NMR (471 MHz, CDCl$_3$): δ = –74.69, –75.63 ppm

hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'- cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



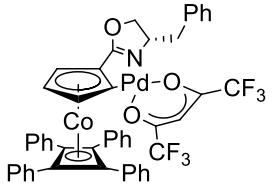
(*S*,*S*$_p$)-**296** (*S*,*R*$_p$)-**296**

(*S*,*R*$_p$): ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.54–7.49 (m, 8H, Ar–*H*), 7.21–7.13 (m, 12H, Ar–*H*), 5.93 (s, 1H, C–*H* hfacac), 5.10 (dd, *J* = 2.5, 1.0 Hz, 1H, Cp–*H*), 4.88 (dd, *J* = 2.7, 1.0 Hz, 1H, Cp–*H*), 4.47 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 4.17–4.10 (m, 1H, oxazoline–*H*), 4.00–3.92 (m, 1H, oxazoline–*H*), 3.46–3.36 (m, 1H, oxaozline–*H*), 1.81–1.45 (m, 8H, CH*H*Cy + Cy–*H*), 1.23–1.09 (m, 2H), 0.98–0.77 ppm (m, 3H, CH*H*Cy + Cy–*H*); ^{19}F NMR (471 MHz, CDCl$_3$): δ = –74.25, –75.52 ppm.

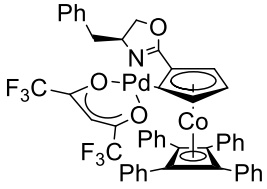
(*S*,*S*$_p$): ^{1}H NMR (500 MHz, CDCl$_3$): δ = 7.62–7.54 (m, 8H, Ar–*H*), 7.25–7.20 (m, 4H, Ar–*H*), 7.19–7.13 (m, 8H, Ar–*H*), 5.88 (s, 1H, C–*H* hfacac), 4.94 (dd, *J* = 2.3, 1.0 Hz, 1H, Cp–*H*), 4.77 (dd, *J* = 2.6, 1.0 Hz, 1H, Cp–*H*), 4.60 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 4.60–4.53 (m, 1H,

oxazoline–*H*), 3.91–3.81 (m, 1H, oxazoline–*H*), 3.80–3.73 (m, 1H, oxazoline–*H*), 1.90–1.80 (m, 1H, C*H*HCy), 1.76–1.57 (m, 3H, Cy–*H*), 1.52–1.44 (m, 1H, Cy–*H*), 1.37–0.78 (m, 7H, Cy–*H*), 0.51–0.40 ppm (m, 1H, CH*H*Cy); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.69, –75.56 ppm.

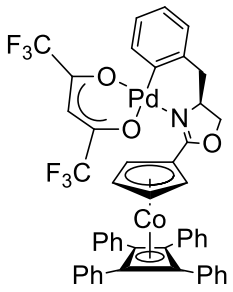
hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'-benzyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



(S,S_p)-**297**



(S,R_p)-**297**



298

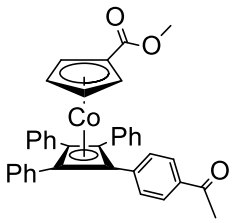
(*S,R*$_p$): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (dd, *J* = 8.3, 1.4 Hz, 8H, Ar–*H*), 7.37–7.14 (m, 8H, Ar–*H*), 7.06 (dd, *J* = 8.0, 1.3 Hz, 4H, Ar–*H*), 5.98 (s, 1H, C–*H* hfacac), 5.14 (dd, *J* = 2.4, 1.0 Hz, 1H, Cp–*H*), 4.88 (dd, *J* = 2.7, 1.0 Hz, 1H, Cp–*H*), 4.50 (t, *J* = 2.6 Hz, 1H, Cp–*H*), 4.27 (dd, *J* = 8.5, 5.5 Hz, 1H, oxazoline–*H*), 3.74 (t, *J* = 8.9 Hz, 1H, oxazoline–*H*), 3.70–3.60 (m, 1H, oxazoline–*H*), 3.12 (dd, *J* = 13.6, 3.3 Hz, 1H, C*H*HPh), 2.55 ppm (dd, *J* = 13.6, 9.4 Hz, 1H, CH*H*Ph); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.22, –76.51 ppm.

(*S,S*$_p$): ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66–7.59 (m, 8H, Ar–*H*), 7.37–7.14 (m, 10H, Ar–*H*), 5.94 (s, 1H, C–*H* hfacac), 5.01 (dd, *J* = 2.3, 1.1 Hz, 1H, Cp–*H*), 4.81 (dd, *J* = 2.6, 1.1 Hz, 1H, Cp–*H*), 4.66 (t, *J* = 2.5 Hz, 1H, Cp–*H*), 4.36 (t, *J* = 8.3 Hz, 1H, oxazoline–*H*), 4.07–3.93 (m, 2H, oxazoline–*H*), 3.34 (dd, *J* = 12.8, 2.8 Hz, 1H, C*H*HPh), 1.57 ppm (dd, *J* = 12.9, 11.1 Hz, 1H, CH*H*Ph); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.64, –76.50 ppm.

Exo palladation product: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.38 (m, 7H, Ar–*H*), 7.30–7.27 (m, 2H, Ar–*H*), 7.14 (t, *J* = 7.7 Hz, 7H, Ar–*H*), 7.06 (dd, *J* = 7.6, 1.2 Hz, 1H, Ph–*H*),

6.98–6.88 (m, 2H, Ph–*H*), 6.73 (dd, *J* = 7.1, 1.6 Hz, 1H, Ph–*H*), 5.99 (s, 1H, C–*H* hfacac), 5.73–5.63 (m, 1H, Cp–*H*), 5.43 (s, 1H, Cp–*H*), 5.03–4.91 (m, 1H, Cp–*H*), 4.77–4.63 (m, 1H, Cp–*H*), 4.11–4.01 (m, 1H, oxazoline–*H*), 3.73 (d, *J* = 8.6 Hz, 1H, oxazoline–*H*), 3.64–3.50 (m, 2H, oxazoline–*H* + C*H*HPh), 2.49 ppm (d, *J* = 14.5 Hz, 1H, CH*H*Ph); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –74.85, –76.05 ppm.

(η^4-1-(4'-Acetylphenyl)-2,3,4-triphenylcyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I)

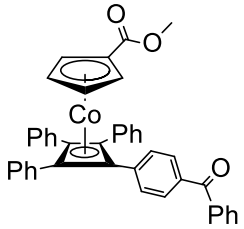


315

Acetyl chloride (70 μL, 1.02 mmol) and aluminium chloride (136 mg, 1.02 mmol) were stirred at room temperature in chloroform (20 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (500 mg, 0.93 mmol) was added in one portion and the mixture was then heated at 50 °C for 2 h. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange-brown solid (369 mg, 0.64 mmol, 68%); m.p. 82 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 7.9 Hz, 2H, Ar–*H*), 7.44 (dd, *J* = 12.4, 8.1 Hz, 6H, Ar–*H*), 7.37 (d, *J* = 7.5 Hz, 2H, Ar–*H*), 7.33–7.14 (m, 9H, Ar–*H*), 5.17 (s, 2H, Cp–*H*), 4.76 (s, 2H, Cp–*H*), 3.19 (s, 3H, C(O)O*CH*$_3$), 2.57 ppm (s, 3H, Ar–C(O)*CH*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.49, 166.45, 141.38, 137.78, 135.53, 134.65,

134.56, 132.38, 130.13, 129.97, 129.15, 128.71, 128.36, 128.29, 128.20, 127.13, 126.98, 86.64, 86.49, 84.63, 73.94, 51.23 ppm (^{13}C for Me not observed); IR (neat): ν = 3056, 2923, 1708, 1677, 1597, 1280, 1264, 1140 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{37}H_{30}CoO_3$ $[M+H]^+$: 581.1521; found: 581.1522.

(η^4-1-(4'-Benzoylphenyl)-2,3,4-triphenylcyclobutadiene)(η^5-carbo-methoxycyclopentadienyl)cobalt(I)

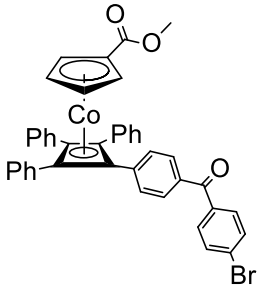


316

Benzoyl chloride (110 μL, 1.02 mmol) and aluminium chloride (136 mg, 1.02 mmol) were stirred at room temperature in chloroform (20 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (500 mg, 0.93 mmol) was added in one portion and the mixture was then heated at 50 °C for 4 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange-brown solid (302 mg, 0.47 mmol, 51%); m.p. 58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10 (dd, *J* = 8.2, 1.0 Hz, 2H, Ar–*H*), 7.80 (dd, *J* = 8.1, 1.0 Hz, 2H, Ar–*H*), 7.66 (d, *J* = 8.1 Hz, 2H, Ar–*H*), 7.62–7.52 (m, 2H, Ar–*H*), 7.51–7.41 (m, 9H, Ar–*H*), 7.37 (dd, *J* = 7.1, 1.7 Hz, 2H, Ar–*H*), 7.32 –7.16 (m, 5H, Ar–*H*), 5.19 (dd, *J* = 3.1, 1.2 Hz, 2H, Cp–*H*), 4.80–4.75 (m, 2H, Cp–*H*), 3.21 ppm (s, 3H, C(O)O*CH*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.53, 166.49, 141.40, 137.78, 135.53,

134.66, 134.57, 133.90, 132.37, 130.17, 130.00, 129.25, 129.08, 128.82, 128.61, 128.32, 128.21, 128.20, 128.12, 127.05, 86.68, 86.34, 84.84, 84.47, 76.71, 73.95, 51.39 ppm; IR (neat): ν = 3060, 2920, 2850, 1704, 1685, 1653, 1597, 1277 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{42}H_{32}CoO_3$ $[M+H]^+$: 643.1678; found: 643.1676.

(η^4-1-(4'-(4''-Bromobenzoyl)phenyl)-2,3,4-triphenylcyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt(I)

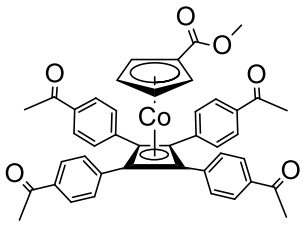


317

4-Bromobenzoyl chloride (43.9 mg, 0.20 mmol) and aluminium chloride (27.2 mg, 0.20 mmol) were stirred at room temperature in chloroform (2 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (100 mg, 0.19 mmol) was added in one portion and the mixture was then heated at 50 °C for 12 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (5 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (5 mL), saturated sodium hydrogen carbonate solution (5 mL), and finally brine (5 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange-brown solid (61 mg, 0.08 mmol, 45%); m.p. 245 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 8.6 Hz, 2H, Ar–*H*), 7.67–7.60 (m, 4H, Ar–-*H*), 7.48 (dd, *J* = 11.4, 5.1 Hz, 6H, Ar–*H*), 7.39 (d, *J* = 6.5 Hz, 2H, Ar–*H*), 7.33–7.18 (m, 9H, Ar–*H*), 5.21 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 4.80 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 3.24 ppm (s, 3H, C(O)O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.29, 166.36, 141.90,

136.61, 134.98, 134.69, 134.61, 131.81, 131.62, 130.10, 129.27, 128.81, 128.42, 128.34, 127.53, 127.28, 127.13, 86.91, 86.65, 84.83, 73.91, 51.49 ppm; IR (neat) ν = 3050, 1717, 1651, 1595, 1583, 1279, 1144, 721 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{42}H_{31}CoO_3Br$ $[M+H]^+$: 721.0783; found: 721.0785.

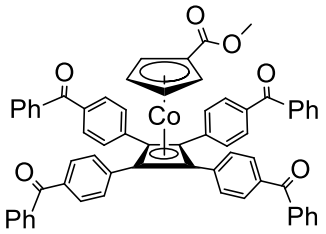
(η^4-1,2,3,4-(4'-Acetylphenyl)(cyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I)



318

Acetyl chloride (1.06 mL, 14.9 mmol) and aluminium chloride (1.98 g, 14.9 mmol) were stirred at room temperature in chloroform (40 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (1.00 g, 1.86 mmol) was added in one portion and the mixture was then heated at 50 °C for 48 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (60 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (60 mL), saturated sodium hydrogen carbonate solution (60 mL), and finally brine (60 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (1:1) gave the product as an orange-brown solid (946 mg, 1.31 mmol, 71%); m.p. 91 °C; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.81 (m, 8H, Ar–*H*), 7.51–7.43 (m, 8H, Ar–*H*), 5.23–5.19 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 4.83 - 4.79 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 3.22 (s, 3H, C(O)O*CH*$_3$), 2.61 ppm (s, 12H, Ar-C(O)*CH*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.41, 165.70, 139.79, 135.79, 128.73, 128.37, 86.98, 86.79, 84.79, 76.01, 51.23, 26.41 ppm; IR (neat): ν = 2923, 1710, 1676, 1598, 1261, 956, 829 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{43}H_{39}CoNO_6$ $[M+NH_4]^+$: 724.2104; found: 724.2082.

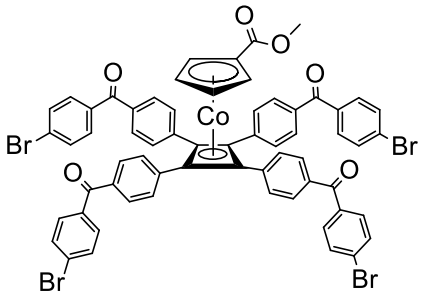
(η^4-1,2,3,4-(4'-Benzoylphenyl)(cyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I)



319

Benzoyl chloride (860 μL, 7.43 mmol) and aluminium chloride (0.99 g, 7.43 mmol) were stirred at room temperature in anhydrous chloroform (20 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (500 mg, 0.93 mmol) was added in one portion and the mixture was then heated at 50 °C for 48 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (1:1) gave the product as an orange-brown solid (369 mg, 0.39 mmol, 41%). Slow evaporation from CH_2Cl_2:petroleum ether (1:50) yielded crystals eligible for x-ray analysis; m.p. 168 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.75 (dt, *J* = 8.2, 1.1 Hz, 8H, Ar–*H*), 7.72–7.67 (m, 8H, Ar–*H*), 7.57–7.52 (m, 4H, Ar–*H*), 7.51–7.42 (m, 16H, Ar–*H*), 5.26–5.17 (dq, *J* = 2.1, 0.9 Hz, 2H, Cp–*H*), 4.87–4.77 (td, *J* = 2.2, 1.0 Hz, 2H, Cp–*H*), 3.30–3.18 ppm (d, *J* = 0.8 Hz, 3H, C(O)O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.95, 138.27, 136.35, 135.13, 131.52, 129.26, 128.90, 127.48, 127.48, 85.78, 83.93, 75.17, 74.21, 50.50 ppm; IR (neat): ν = 3059, 2919, 2850, 1711, 1652, 1596, 1584, 1271, 925 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{63}H_{44}CoO_6$ $[M+H]^+$: 955.2464; found: 955.2459.

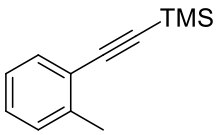
(η^4-1,2,3,4-(4'-(4''-Bromobenzoyl)phenyl)(cyclobutadiene)(η^5-carbo-methoxycyclopentadienyl)cobalt(I)



320

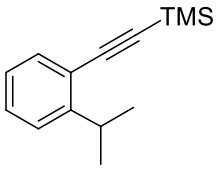
4-Bromobenzoyl chloride (333 mg, 1.52 mmol) and aluminium chloride (203 mg, 1.52 mmol) were stirred at room temperature in anhydrous chloroform (4 mL) for 30 minutes. (η^5-carbomethoxycyclopentadienyl)-(η^4-tetraphenyl-cyclobutadiene)cobalt(I) (100 mg, 0.19 mmol) was added in one portion and the mixture was then heated at 50 °C for 48 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (10 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (10 mL), saturated sodium hydrogen carbonate solution (10 mL), and finally brine (10 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the hexanes/EtOAc (4:1) gave the product as a brown solid (69 mg, 0.05 mmol, 29%); m.p. 206 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70 (dt, J = 17.0, 5.3 Hz, 24H, Ar–*H*), 7.54 (d, J = 8.5 Hz, 8H, Ar–*H*), 5.29 (s, 2H, Cp–*H*), 4.89 (s, 2H, Cp–*H*), 3.30 ppm, (s, 3H, C(O)O*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.22, 139.69, 136.23, 136.01, 131.96, 131.62, 130.39, 128.76, 127.91, 87.25, 87.02, 85.18, 76.31, 69.04, 51.74 ppm; IR (neat): v = 3051, 1713, 1652, 1595, 1583, 1278, 924, 758 cm^{-1}; LCMS (ESI$^+$) *m/z* calculated for $C_{63}H_{39}CoO_6Br_4$ $[M]^+$: 1271.9; found: 1271.9. Molecular formulae confirmed *via* theoretical isotope pattern.

Trimethyl(o-tolylethynyl)silane[238]



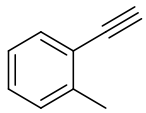
To a stirred mixture of 2-iodotoluene (4.26 mL, 22.9 mmol), $PdCl_2(PPh_3)_2$ (782 mg, 1.11 mmol) and CuI (436 mg, 2.29 mmol) in NEt_3 (20 mL, 0.14 mol), trimethylsilylacetylene (3.59 mL, 25.2 mmol) was added dropwise at 0 ºC. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography using hexane as eluent afforded the product as a yellow oil (4.02 g, 21.30 mmol, 93%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.52 (m, 1H, Ar–*H*), 7.19–7.05 (m, 3H, Ar–*H*), 2.45 (s, 3H, Ar–CH_3), 0.27 ppm (s, 9H, Si(CH_3)$_3$). Spectral data matched that previously reported.

Trimethyl(2-(isopropylphenyl)ethynyl]silane[239]



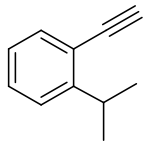
To a stirred mixture of 1-iodo-2-isopropylbenzene (3.25 mL, 20.3 mmol), $PdCl_2(PPh_3)_2$ (712 mg, 1.02 mmol) and CuI (387 mg, 2.03 mmol) in NEt_3 (20 mL, 0.14 mol), trimethylsilylacetylene (3.18 mL, 22.3 mmol) was added dropwise at 0 ºC. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography on silica gel using hexane as eluent afforded the product as a yellow oil (4.05 g, 18.68 mmol, 92%); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 6.9 Hz, 1H, Ar–*H*), 7.32–7.22 (m, 2H, Ar–*H*), 7.14–7.07 (m, 1H, Ar–*H*), 3.48 (hept, *J* = 6.8 Hz, 1H, C*H*(CH_3)$_2$), 1.28 (d, *J* = 6.9 Hz, 6H, CH(CH_3)$_2$), 0.28 ppm (s, 9H). Spectral data matched that previously reported.

1-Ethynyl-2-methylbenzene[240]



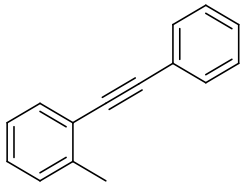
To a stirred solution of trimethyl(*o*-tolylethynyl)silane (4.00 g, 21.2 mmol) in MeOH (10 mL) at room temperature was added K_2CO_3 (1.46 g, 10.6 mmol). The reaction was left to react overnight. Upon completion, the reaction was quenched with water (50 mL) and extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was then purified by flash chromatography on silica gel using hexanes/EtOAc (10:1) as eluent to afford the product as a colourless oil (1.97 g, 16.96 mmol**,** 80%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 7.9 Hz, 1H, Ar–*H*), 7.26–7.19 (m, 2H, Ar–*H*), 7.16 (t, *J* = 7.9 Hz, 1H, Ar–*H*), 2.53 (s, 1H, C≡C*H*), 2.50 ppm (s, 3H, Ar–CH_3). Spectral data matched that previously reported.

1-Ethynyl-2-isopropylbenzene[239]



To a stirred solution of trimethyl(2-(isopropylphenyl)ethynyl]silane (4.05 g, 18.7 mmol) in MeOH (10 mL) at room temperature was added K_2CO_3 (1.29 g, 9.36 mmol). The reaction was left to react overnight. Upon completion, the reaction was quenched with water (50 mL) and extracted with Et_2O (2 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo*. The crude residue was then purified by flash chromatography eluting with hexanes/EtOAc (10:1) to afford the product as a colourless oil (2.11 g, 14.59 mmol, 78%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 7.7 Hz, 1H, Ar–*H*), 7.4 –7.30 (m, 2H, Ar–*H*), 7.26–7.13 (m, 1H, Ar–*H*), 3.57 (hept, *J* = 6.8 Hz, 1H, C*H*$(CH_3)_2$), 3.30 (s, 1H, CC*H*), 1.33 ppm (d, *J* = 6.9 Hz, 6H, CH($CH_3)_2$). Spectral data matched that previously reported.

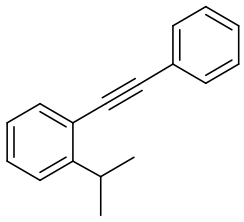
2-(Phenylethynyl)toluene[241]



321

To a stirred mixture of iodobenzene (1.87 mL, 16.8 mmol), $PdCl_2(PPh_3)_2$ (590 mg, 0.84 mmol) and CuI (320 mg, 1.68 mmol) in Et_3N (20 mL, 0.14 mol), 1-ethynyl-2-methylbenzene (1.95 g, 16.8 mmol) was added dropwise at 0 ºC. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography using hexane as eluent afforded the product as an oil (3.07 g, 15.96 mmol, 95%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56–7.49 (m, 3H, Ar–*H*), 7.39–7.33 (m, 3H, Ar–*H*), 7.24–7.14 (m, 3H, Ar–*H*), 2.40 ppm (s, 3H, Ar–CH_3). Spectral data matched that previously reported.

(2-Isopropylphenyl-ethynyl)benzene[242]

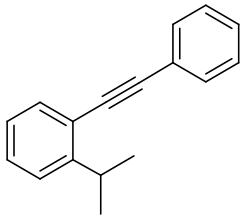


322

To a stirred mixture of iodobenzene (1.63 mL, 14.6 mmol), $PdCl_2(PPh_3)_2$ (512 mg, 0.73 mmol) and CuI (279 mg, 1.46 mmol) in Et_3N (20 mL, 0.14 mol), 1-ethynyl-2-isopropylbenzene (2.11 g, 14.6 mmol) was added dropwise at 0 ºC. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography using hexane as eluent afforded the product as an oil (2.91 g, 13.29 mmol,

91%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.51 (m, 3H, Ar–*H*), 7.42–7.31 (m, 5H, Ar–*H*), 7.24–7.15 (m, 1H, Ar–*H*), 3.58 (hept, *J* = 6.9 Hz, 1H, C*H*(CH_3)$_2$), 1.34 ppm (d, *J* = 6.9 Hz, 6H, CH(*C*H_3)$_2$). Spectral data matched that previously reported.

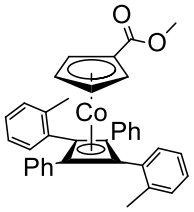
Alternative Synthesis of (2-Isopropylphenyl-ethynyl)benzene[242]



322

To a stirred mixture of 1-iodo-2-isopropylbenzene (1.95 mL, 12.2 mmol), $PdCl_2(PPh_3)_2$ (421 mg, 0.61 mmol) and CuI (233 mg, 1.22 mmol) in Et_3N (20 mL, 0.14 mol), phenylacetylene (xx g, xx mmol) was added dropwise at 0 ºC. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated *in vacuo*. Purification of the residue by flash chromatography using hexane as eluent afforded the product as an oil (2.68 g, 12.1 mmol, 99%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.51 (m, 3H, Ar–*H*), 7.42–7.31 (m, 5H, Ar–*H*), 7.24–7.15 (m, 1H, Ar–*H*), 3.58 (hept, *J* = 6.9 Hz, 1H, C*H*(CH_3)$_2$), 1.34 ppm (d, *J* = 6.9 Hz, 6H, CH(*C*H_3)$_2$). Spectral data matched that previously reported.

(η^4-1,3-o-Tolyl-2,4-phenylcyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (trans-major)



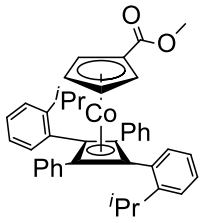
323
cis:*trans*, 1:2.5

Dimethyl carbonate (2.98 mL, 35.4 mmol) was added to a solution of sodium cyclopentadienide (6.05 mL of a 2M solution in THF, 12.1 mmol) in THF (20 mL) with stirring and the solution was heated at reflux for 4 hours. Once the solution had cooled to room temperature it was added *via* cannulae to a solution of tris(triphenylphosphine)cobalt(I) chloride (8.84 g, 10.1 mmol) and 2-(Phenylethynyl)toluene (4.46 g, 23.2 mmol) in toluene. The resulting mixture was heated at reflux for 5 hours. On completion the solution was concentrated under reduced pressure. The residue was purified by column chromatography eluting with CH_2Cl_2/petroleum ether (1:1) yielding the crude product as a dark yellow-orange solid. Ratio of crude yield: *cis*:*trans*, 1:2.5, (determined by ^{1}H NMR). Crude mixture was recrystallised twice from CH_2Cl_2:hexane, (1:50), to give dark yellow crystals (1.95 g, 3.44 mmol, 34%); m.p. 221 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.25 (dd, *J* = 7.4, 1.6 Hz, 2H, Ar–*H*), 7.43–7.30 (m, 4H, Ar–*H*), 7.22–7.17 (m, 2H, Ar–*H*), 7.09–7.02 (m, 2H, Ar-–*H*), 6.95–6.88 (m, 4H, Ar–*H*), 6.80–6.75 (m, 4H, Ar–*H*), 5.70–5.67 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 4.80–4.76 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 3.10 (s, 3H, C(O)O*CH*$_3$), 2.18 ppm (s, 6H, Ar-*CH*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.61, 138.19, 137.57, 133.51, 133.37, 129.78, 128.42, 128.10, 126.19, 126.13, 124.98, 85.88, 85.64, 84.12, 79.79, 51.06, 20.95 ppm; IR (neat): ν = 3686, 3217, 1707, 1603, 1501 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{37}H_{31}CoO_2$ $[M]^+$: 567.1734; found: 567.1728.

(η^4-1,2-o-Tolyl-3,4-phenylcyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (cis-minor)

^{1}H NMR *cis* (minor) stereoisomer: (400 MHz, $CDCl_3$): δ = 7.64–7.56 (dd, *J* = 7.74, 1.35, 2H, Ar–*H*),7.43–7.30 (m, 4H, Ar–*H*), 7.22–7.17 (m, 2H, Ar–*H*), 7.09–7.02 (m, 2H, Ar–*H*), 6.95–6.88 (m, 4H, Ar–*H*), 6.80–6.75 (m, 4H, Ar–*H*), 5.40–5.35 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 4.99–4.95 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 3.31 (s, 3H, C(O)O*CH*$_3$), 2.42 (s, 3H), 2.31 ppm (s, 3H, Ar–*CH*$_3$).

(η^4-1,3-(2-isopropylphenyl)-2,4-phenylcyclobutadiene) (η^5-carbomethoxy-cyclopentadienyl)cobalt (I) (trans-major)



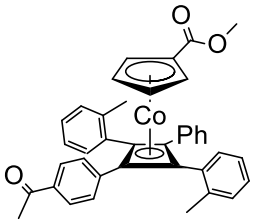
324
cis:*trans*, 1:6

Dimethyl carbonate (1.7 mL, 20 mmol) was added to a solution of sodium cyclopentadienide (3.4 mL of a 2M solution in THF, 6.8 mmol) in THF (20 mL) with stirring and the solution was heated at reflux for 4 hours. Once the solution had cooled to room temperature it was added *via* cannulae to a solution of tris(triphenylphosphine)cobalt(I) chloride (5.00 g, 5.7 mmol) and (2-Isopropylphenyl-ethynyl)benzene (2.93 g, 13.3 mmol) in toluene. The resulting mixture was heated at reflux for 5 hours. On completion the solution was concentrated under reduced pressure. The residue was purified by column chromatography eluting with CH_2Cl_2:petroleum ether 1:1 yielding the crude product as a dark yellow-orange solid. Ratio of crude yield: *cis*:*trans*, 1:6, (determined by ^{1}H NMR). Crude mixture was recrystallised from CH_2Cl_2:hexane, (1:50), to give dark yellow crystals (1.15 g, 1.85 mmol, 42%); m.p. 236 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39–8.35 (m, 2H, Ar–*H*), 7.51–7.32 (m, 6H, Ar–*H*), 7.10–7.03 (m, 2H, Ar–*H*), 6.96–6.89 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 4H, Ar–*H*), 6.81–6.76 (m, 4H, Ar–*H*), 5.74–5.68 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 4.84–4.78 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 3.38–3.22 (dt, *J* = 13.6, 6.8 Hz, 2H, C*H*(CH_3)$_2$), 3.11 (s, 3H, C(O)O*CH*$_3$), 0.94–0.89 ppm (d, *J* = 6.9 Hz, 12H, CH(*CH*$_3$)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.19, 148.82, 136.97, 134.06, 133.80, 131.92, 128.34, 128.06, 126.01, 125.55, 125.25, 85.83, 85.46, 84.33, 84.21, 79.64, 76.57, 51.20, 50.93, 30.69, 30.46, 23.72, 23.48 ppm; IR (neat): *v* = 3059, 2961, 1703, 1466, 1283, 1143 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{41}H_{40}CoO_2$ $[M+H]^+$: 623.2355; found: 623.2356.

(η^4-1,2-(2-isopropylphenyl)-3,4-phenylcyclobutadiene) (η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (cis-minor)

^{1}H NMR *cis* (minor) stereoisomer: (400 MHz, $CDCl_3$): δ = 7.64–7.56 (dd, *J* = 7.74, 1.35, 2H, Ar–*H*), 7.51–7.32 (m, 6H, Ar–*H*), 7.10–7.03 (m, 2H, Ar–*H*), 6.96–6.89 (ddd, *J* = 8.2, 6.9, 1.1 Hz, 4H, Ar–*H*), 6.81–6.76 (m, 4H, Ar–*H*), 5.29–5.23 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 5.06–5.01 (t, *J* = 2.2 Hz, 2H, Cp–*H*), 3.80–3.64 (dt, *J* = 13.6, 6.8 Hz, 2H, C*H*$(CH_3)_2$), 3.24 (s, 3H, C(O)O*CH*$_3$), 0.77–0.70 (d, *J* = 6.8 Hz, 3H, CH(*CH*$_3$)$_2$), 0.64–0.58 ppm (d, *J* = 6.8 Hz, 3H, CH(*CH*$_3$)$_2$).

(η^4-1-(4'-acetylphenyl)-3-phenyl-2,4-(o-tolyl)cyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt(I)

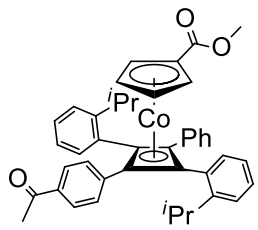


327

Acetyl chloride (0.07 mL, 0.97 mmol) and aluminium chloride (129 mg, 0.97 mmol) were stirred at room temperature in CH_2Cl_2 (20 mL) for 30 minutes. (η^4-1,3-*o*-Tolyl-2,4-phenylcyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (500 mg, 0.88 mmol) was added in one portion and the mixture was then heated at reflux for 2 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange-brown solid (397 mg, 0.63 mmol, 75%); m.p. 203 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32–8.26 (dd, *J* = 7.4, 1.7 Hz, 2H,

Ar–*H*), 7.56–7.49 (m, 2H, Ar–*H*), 7.44–7.32 (m, 4H, Ar–*H*), 7.22–7.18 (m, 2H, Ar–*H*), 7.11–7.04 (m, 1H, Ar–*H*), 6.98–6.90 (m, 2H, Ar–*H*), 6.86–6.76 (m, 4H, Ar–*H*), 5.73-5.67 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 4.81–4.76 (t, *J* = 2.1 Hz, 2H, Cp–*H*), 3.12–3.08 (d, *J* = 1.1 Hz, 3H, C(O)O*CH*$_3$), 2.45–2.40 (d, *J* = 1.0 Hz, 3H, C(O)*CH*$_3$), 2.20–2.14 ppm (s, 6H, Ar–*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.63, 166.13, 144.35, 138.20, 136.97, 134.57, 133.59, 132.97, 130.09, 128.74, 128.65, 128.55, 126.72, 126.45, 125.21, 124.75, 85.89, 84.51, 80.55, 74.75, 51.41, 29.91, 26.63, 22.91, 21.28, 14.35 ppm; IR (neat): *v* = 3065, 2923, 1704, 1598, 1463, 1280 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{39}H_{37}CoNO_3$ $[M+NH_4]^+$: 626.2100; found: 626.2086.

(η^4-1-(4'-acetylphenyl)-3-phenyl- 2,4-(o-isopropylphenyl)cyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt(I)

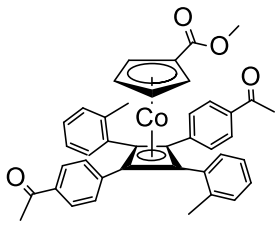


328

Acetyl chloride (0.06 mL, 0.88 mmol) and aluminium chloride (117 mg, 0.88 mmol) were stirred at room temperature in CH_2Cl_2 (20 mL) for 30 minutes. (η^4-1,3-(2-isopropylphenyl)-2,4-phenylcyclobutadiene) (η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (500 mg, 0.80 mmol) was added in one portion and the mixture was then heated at reflux for 2 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as a dark orange solid (432 mg, 0.65 mmol,

81%); m.p. 245 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34–8.27 (dt, *J* = 7.4, 1.5 Hz, 2H, Ar–*H*), 7.51–7.39 (m, 4H, Ar–*H*), 7.39–7.33 (m, 2H, Ar–*H*), 7.32–7.26 (m, 1H, Ar–*H*), 7.06–6.98 (m, 1H, Ar–*H*), 6.90–6.83 (td, *J* = 7.8, 1.6 Hz, 2H, Ar–*H*), 6.81-6.69 (ddt, *J* = 18.5, 8.4, 1.4 Hz, 4H, Ar–*H*), 5.69–5.65 (q, *J* = 1.8 Hz, 2H, Cp–*H*), 4.77–4.73 (q, *J* = 1.8 Hz, 2H, Cp–*H*), 3.25–3.14 (hept, *J* = 6.9 Hz, 2H, C*H*$(CH_3)_2$), 3.05–3.01 (d, *J* = 1.3 Hz, 3H, C(O)O*CH*$_3$), 2.39–2.35 (d, *J* = 1.3 Hz, 3H, C(O)*CH*$_3$), 0.88–0.82 ppm (dt, *J* = 6.8, 1.4 Hz, 12H, CH(*CH*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.70, 166.08, 148.86, 143.86, 136.39, 134.52, 134.01, 131.49, 129.08, 128.51, 128.47, 126.71, 126.27, 125.59, 125.54, 125.13, 85.98, 85.90, 84.70, 80.45, 79.59, 76.90, 75.69, 51.40, 30.96, 29.92, 26.64, 23.95, 23.92 ppm; IR (neat): ν = 2960, 2924, 1712, 1678, 1597, 1465, 1268 cm^{-1}; HRMS (ESI^{+}) *m/z* calculated for $C_{43}H_{42}CoO_3$ $[M+H]^{+}$: 665.2460; found: 665.2456.

(η^4-1,3-(4'-acetylphenyl)-2,4-(o-tolyl)cyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I)

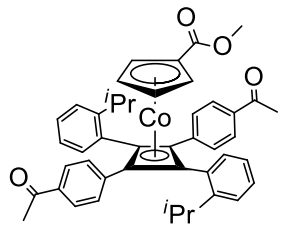


329

Acetyl chloride (0.13 mL, 1.85 mmol) and aluminium chloride (247 mg, 1.85 mmol) were stirred at room temperature in CH_2Cl_2 (20 mL) for 30 minutes. (η^4-1,3-*o*-Tolyl-2,4-phenylcyclobutadiene)(η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (500 mg, 0.88 mmol) was added in one portion and the mixture was then heated at reflux for 4 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to

give the crude product as a brown residue. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as a dark orange solid (453 mg, 0.70 mmol, 79%); m.p. 226 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31−8.26 (dd, *J* = 7.1, 1.9 Hz, 2H, Ar−*H*), 7.56−7.50 (m, 4H, Ar−*H*), 7.46−7.35 (m, 4H, Ar−*H*), 6.87−6.81 (m, 4H, Ar−*H*), 5.74−5.66 (t, *J* = 2.2 Hz, 2H, Cp−*H*), 4.82−4.76 (t, *J* = 2.1 Hz, 2H, Cp−*H*), 3.12−3.03 (s, 3H, C(O)O*CH*$_3$), 2.44−2.38 (s, 6H, C(O)*CH*$_3$), 2.18−2.12 ppm (s, 6H, Ar−*CH*$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.57, 166.12 143.47, 138.09, 134.88, 133.54, 130.25, 128.85, 128.78, 126.61, 124.89, 85.93, 84.73, 76.91, 51.44, 29.90, 26.65, 21.25 ppm; IR (neat): *v* = 2918, 2850, 1707, 1674, 1596, 1265 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{41}H_{36}CoO_4$ $[M+H]^+$: 651.940; found: 651.1937.

(η^4-1,3-(4'-acetylphenyl)-2,4-(o-isopropylphenyl)cyclobutadiene)(η^5-carbomethoxycyclopentadienyl)cobalt(I)

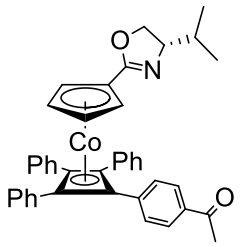


330

Acetyl chloride (0.12 mL, 1.68 mmol) and aluminium chloride (224 mg, 1.68 mmol) were stirred at room temperature in CH_2Cl_2 (20 mL) for 30 minutes. (η^4-1,3-(2-isopropylphenyl)-2,4-phenylcyclobutadiene) (η^5-carbomethoxy-cyclopentadienyl)cobalt(I) (500 mg, 0.80 mmol) was added in one portion and the mixture was then heated at reflux for 4 hours. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (30 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (30 mL), saturated sodium hydrogen carbonate solution (30 mL), and finally brine (30 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting

with hexanes/EtOAc (5:1) gave the product as a dark orange solid (482 mg, 0.68 mmol, 85%); m.p. 260 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35−8.26 (dt, *J* = 8.1, 1.3 Hz, 2H, Ar−*H*), 7.53−7.42 (m, 6H, Ar−*H*), 7.42−7.35 (m, 2H, Ar−*H*), 7.34−7.28 (m, 2H, Ar−*H*), 6.85−6.75 (m, 4H, Ar−*H*), 5.71−5.66 (m, 2H, Cp−*H*), 4.78−4.74 (m, 2H, Cp−*H*), 3.21−3.13 (p, *J* = 6.8 Hz, 2H, C*H*(CH_3)$_2$), 3.03 (s, 3H, C(O)O*CH*$_3$), 2.40−2.36 (m, 6H, C(O)*CH*$_3$), 0.89−0.84 ppm (dd, *J* = 6.9, 1.2 Hz, 12H, CH(*CH*$_3$)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.64, 165.89, 148.80, 142.99, 134.83, 133.96, 130.96, 129.38, 128.62, 126.44, 125.69, 125.24, 86.00, 85.94, 84.89, 81.05, 77.08, 76.91, 51.43, 31.03, 29.91, 26.65, 23.96 ppm; IR (neat): *v* = 2958, 2924, 2864, 1711, 1679, 1597, 1265 cm^{-1}; HRMS (ESI^{+}) *m/z* calculated for $C_{45}H_{44}CoO_4$ [M+H]$^{+}$: 707.2566; found: 707.2566.

η^5-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-acetylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)

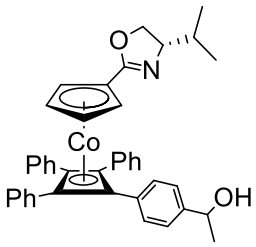


(*S*)-**331**

Acetyl chloride (60 μL, 0.89 mmol) and aluminium chloride (234 mg, 1.78 mmol) were stirred at room temperature in CH_2Cl_2 (10 mL) for 30 minutes. η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (500 mg, 0.85 mmol) was added in one portion and the mixture was then heated at reflux for 16 h. On completion the solution was left to cool then poured onto an iced 2 M HCl solution (5 mL) and the mixture stirred for 15 minutes. The organic layer was separated, washed with water (5 mL), saturated sodium hydrogen carbonate solution (5 mL), and finally brine (5 mL). The organic layer was collected, dried over $MgSO_4$ and the solvent was removed *in vacuo* to give the crude product as a brown residue. Purification by column chromatography eluting

with hexanes/EtOAc (5:1) gave the product as an orange-brown residue (421 mg, 0.66 mmol, 78%). $[\alpha]_D^{24} = -23$ (c = 4.2 mg/mL in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80–7.76 (m, 2H, Ar–*H*), 7.52–7.44 (m, 6H, Ar–*H*), 7.44–7.38 (m, 2H, Ar–*H*), 7.33–7.17 (m, 9H, Ar–*H*), 5.22 (brs, 1H, Cp–*H*), 5.10 (brs, 1H, Cp–*H*), 4.80 (s, 1H, Cp–*H*), 4.71 (s, 1H, Cp–*H*), 3.59–3.48 (m, 2H, oxazoline–*H*), 3.46–3.37 (m, 1H, oxaozline–*H*), 2.59 (s, 3H, CO*CH*$_3$), 1.43–1.34 (m, 1H, C*H*(CH_3)$_2$), 0.96 (d, *J* = 6.7 Hz, 3H, CH(*CH*$_3$)$_2$), 0.74 ppm (d, *J* = 6.7 Hz, 3H, CH(*CH*$_3$)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 197.77, 142.26, 134.94, 129.26, 128.23, 126.94, 86.58, 85.07, 84.74, 82.35, 76.59, 73.69, 72.74, 69.73, 33.05, 26.68, 19.61, 18.42 ppm; IR (neat): *v* = 3059, 2958, 1682, 1652, 1599, 1499, 1267, 1115, 733, 705 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{41}H_{36}CoNO_2$ $[M]^+$: 634.2157; found: 634.2139.

η^5-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)

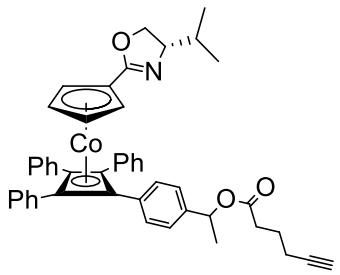


332

To a flask charged with η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-acetylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I) (66 mg, 0.10 mmol) dissolved in THF (2 mL) was added $NaBH_4$ in one portion. The solution was then heated to reflux for 16 h. On completion, the solution was cooled to r.t. and water (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the organic phases were combined, washed with brine (5 mL) and dried over $MgSO_4$. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as a yellow residue (66 mg, 0.10 mmol, 99%). $[\alpha]_D^{25} = +46$ (c = 9.4 mg/mL in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.39 (m, 8H, Ar–*H*), 7.31–7.16 (m, 12H, Ar–*H*), 5.21–5.16 (m, 1H, Cp–*H*), 5.07 (dd, *J* = 2.5, 1.1 Hz, 1H, Cp–

H), 4.87 (qd, *J* = 6.4, 2.0 Hz, 1H, C*H*OH), 4.80–4.76 (m, 1H, Cp–*H*), 4.70 (td, *J* = 2.6, 1.6 Hz, 1H, Cp–*H*), 3.54–3.37 (m, 3H, oxazloline–*H*), 1.54 (dd, *J* = 6.5, 1.0 Hz, 3H, CH_3), 1.47–1.36 (m, 1H, C*H*(CH_3)$_2$), 0.95 (d, *J* = 6.7 Hz, 3H, CH(*C*H_3)$_2$), 0.74 ppm (d, *J* = 6.7 Hz, 3H, CH(*C*H_3)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 197.77, 142.26, 134.94, 129.26, 128.23, 126.94, 86.58, 85.07, 84.74, 82.35, 76.59, 73.69, 72.74, 69.73, 33.05, 26.68, 19.61, 18.42 ppm; IR (neat): *v* = 3390, 3059, 2964, 2246, 1651, 1599, 1499, 909, 733, 705 cm^{-1}; HRMS (ESI$^+$) *m/z* calculated for $C_{41}H_{39}CoNO_2$ $[M+H]^+$: 636.2307; found: 636.2296.

η^5-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-1-phenylethylhex-5-ynoate)-2,3,4-triphenylcyclobutadiene)cobalt(I)

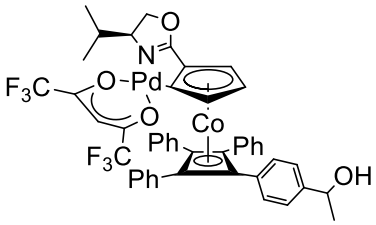


335

To a flask charged with 5-hexynoic acid (42 µl, 0.38 mmol) dissolved in CH_2Cl_2 (5 mL) was added EDAC (60 mg, 0.38 mmol) and DMAP (3 mg, 0.03 mmol). The solution was then stirred for 10 minutes. η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I) (200 mg, 0.32 mmol) was added in one portion and the solution was stirred at r.t. for 16 h. On completion, water (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the organic phases were combined, washed with brine (5 mL) and dried over $MgSO_4$. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange residue (182 mg, 0.25 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75–7.69 (m, 8H, Ar–*H*), 7.66–7.61 (m, 8H, Ar–*H*), 7.34–7.14 (m, 24H, Ar–*H*), 4.81–4.78 (m, 1H, Cp–*H*), 4.75–4.72 (m, 1H, Cp–*H*), 4.72–4.70 (m, 2H, Cp–*H*), 4.61 (t, *J* = 7.9 Hz, 1H, ArC*H*O), 4.55 (t, *J*

= 8.7 Hz, 1H, ArC*H*CH_3), 4.49 (t, *J* = 2.5 Hz, 1H, Cp−*H*), 4.35 (t, *J* = 2.5 Hz, 1H, Cp−*H*), 3.96 (dd, *J* = 8.1, 6.5 Hz, 1H, oxazoline−*H*), 3.91–3.75 (m, 3H, oxazoline−*H*), 2.20 (s, 1H, C≡C*H*), 1.90–1.79 (m, 1H,OCC$H_2(CH_2)_2$), 1.61–1.50 (m, 1H, OC$(CH_2)_2$CH_2), 1.40–1.26 (m, 2H, OCCH_2CH_2CH_2), 0.93 (d, *J* = 6.6 Hz, 3H, CH_3), 0.90–0.78 (m, 12H, 2 x CH(C$H_3)_2$), 0.50–0.32 ppm (m, 2H, 2 x C*H*$(CH_3)_2$); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.81, 173.70, 135.81, 135.77, 129.43, 129.34, 128.15, 128.10, 126.58, 126.46, 99.92, 99.35, 89.11, 88.92, 85.90, 85.32, 83.34, 82.05, 77.73, 77.37, 76.84, 76.63, 76.40, 76.27, 60.72, 60.59, 53.58, 43.55, 43.24, 31.09, 25.61, 25.55, 23.79, 23.66, 21.49, 21.37 ppm; IR (neat): *v* = 3297, 3059, 2961, 1732, 1712, 1599, 1158, 1244, 708, 639 cm^{-1}; HRMS (ESI^+) *m/z* calculated for $C_{47}H_{45}CoNO_3$ $[M+H]^+$: 731.2759; found: 731.2751.

hexafluoroacetylacetonate[(η^5-(S)-(R_p)-2-(2'-(4'- methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N) (η^4-1-(4'-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)]palladium(II)

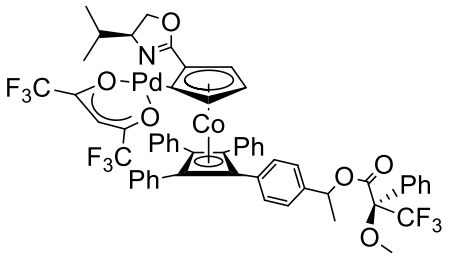


(*S*,R_p)-**333**

A flask was charged with η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I) (910 mg, 1.34 mmol) and then dissolved in glacial acetic acid (2 mL). Palladium(II) acetate (298 mg, 1.34 mmol) was added in one portion. The solution was then heated at 95 °C for 30 minutes. On completion, the solvent was removed *in vacuo* to give a crude orange solid. The crude product was redissolved in acetone (2 mL) and sodium hexafluroacetylacetonate (975 mg, 4.24 mmol) was added with water (1 mL). The mixture was vigorously stirred for 16 h. On completion, water (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the

organic phases were combined, washed with brine (5 mL) and dried over $MgSO_4$. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange/red solid (410 mg, 0.43 mmol, 64%). $[\alpha]_D^{20.7}$ = +589 (c = 8.9 mg/mL in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.48 (m, 8H, Ar–*H*), 7.25–7.21 (m, 2H, Ar–*H*), 7.22–7.12 (m, 9H, Ar–*H*), 5.92 (s, 1H, C*H*), 5.17–5.06 (m, 1H, Cp–*H*), 4.92–4.83 (m, 2H, C*H*OH & Cp–*H*), 4.53–4.45 (m, 1H, Cp–*H*), 4.29 (dd, *J* = 8.3, 5.1 Hz, 1H, oxazoline–*H*), 3.69 (td, *J* = 9.6, 2.5 Hz, 1H, oxazoline–*H*), 3.47–3.35 (m, 1H, oxazoline–*H*), 2.08–1.97 (m, 1H, C*H*$(CH_3)_2$), 1.53 (d, *J* = 6.4 Hz, 3H, CH_3), 0.80 (d, *J* = 7.0 Hz, 3H, CH(CH_3)$_2$), 0.76 ppm (d, *J* = 6.9 Hz, 3H, CH(CH_3)$_2$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = −74.21, −75.72 ppm.

Mosher's Ester Method[235]



334

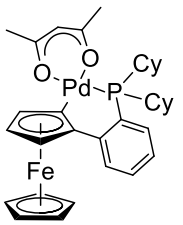
To a flask charged with (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid (3 mg, 0.01 mmol) dissolved in CH_2Cl_2 (5 mL) was added DCC (2 mg, 0.01 mmol) and DMAP (1 mg, 0.001 mmol). The solution was then stirred for 10 minutes. η^5-(*S*)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(η^4-1-(4'-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I) (10 mg, 0.01 mmol) was added in one portion and the solution was stirred at r.t. for 16 h. On completion, water (5 mL) was added. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL) and the organic phases were combined, washed with brine (5 mL) and dried over $MgSO_4$. A crude ^{1}H-NMR was used to determine diastereoselectivity, using peaks seen for methoxy methyls at 3.57 and 3.50 ppm.

Transcyclopalladation and Catalysis

General Procedure for Transcyclopalladation[135]

A mixture of palladacycle (0.02 mmol) and either *2*-(diphenylphosphino)phenylferrocene (20 mg, 0.04 mmol) or 2-(dicyclohexylphosphino)phenylferrocene (20 mg, 0.04 mmol) were heated in toluene (0.5 mL) for 24 h. After cooling the solvent was removed *in vacuo* and to the residue was redissolved in 2:1 acetone/water (2 mL) and to this added sodium acetylacetonate (0.005 g, 0.04 mmol). After stirring at room temperature for 16 h. the mixture was diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$), filtered and the solvent removed *in vacuo*. Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the products as orange/red solids.

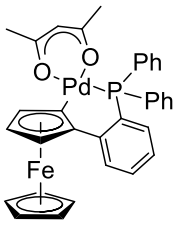
acetylacetonate[R_p-2-(2-dicyclohexylphosphino)phenylferroene-C1,P)]palladium(II)[135]



R_p-**262**

Isolated as an orange/red solid (26 mg, 0.04 mmol, 98%), chiral HPLC analysis was used to determine the absolute configuration and enantiomeric excess (Chiracel OD-H, 99.7:0.3 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.62 (brs, 1H, Ar–*H*), 7.39 (t, *J* = 7.5 Hz, 1H, Ar–*H*), 7.33 (t, *J* = 7.5 Hz, 1H, Ar–*H*), 7.13 (t, *J* = 7.5 Hz, 1H, Ar–*H*), 5.33 (s, 1H, C*H*), 4.86 (brs, 1H, Cp–*H*), 4.69 (brs, 1H, Cp–*H*), 4.44 (brs, 1H, Cp–*H*), 4.06 (s, 5H, Cp–*H*), 2.07 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.44–0.80 ppm (m, 22H, Cy–*H*); ^{31}P NMR (202 MHz, $CDCl_3$): δ = 36.17 ppm. Spectral data matched that previously reported.

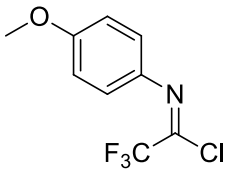
acetylacetonate[R_p-2-(2-diphenylphosphino)phenylferroene-C1,P)]palladium(II)[135]



R_p-**263**

Isolated as an orange/red solid (25 mg, 0.04 mmol, 96%), chiral HPLC analysis was used to determine the absolute configuration and enantiomeric excess (Chiracel OD-H, 99.7:0.3 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (brs, 1H, Ar–*H*), 7.61 (dd, *J* = 8.1, 1.5 Hz, 1H, Ar–*H*), 7.59–7.45 (m, 3H, Ar–*H*), 7.45–7.31 (m, 3H, Ar–*H*), 7.31–7.25 (m, 2H, Ar–*H*), 7.23–7.13 (m, 2H, Ar–*H*), 7.10–7.03 (m, 1H, Ar–*H*), 6.93–6.85 (m, 1H, Ar–*H*), 5.29 (s, 1H, C*H*), 4.88 (brs, 1H, Cp–*H*), 4.72 (brs, 1H, Cp–*H*), 4.37 (brs, 1H, Cp–*H*), 3.99 (s, 5H, Cp–*H*), 2.08 (s, 3H, C*H*$_3$), 1.61 ppm (s, 3H, C*H*$_3$); ^{31}P NMR (202 MHz, $CDCl_3$): δ = 30.78 ppm. Spectral data matched that previously reported.

N-(p-Anisyl)-2,2,2-trifluoroacetimidoyl chloride[153,201]

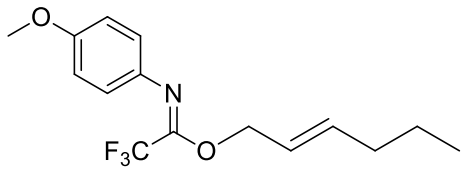


270

To a flask charged with PPh_3 (34.5 g, 132 mmol) suspended in CCl_4 (21.1 mL) was added NEt_3 (7.3 mL, 53 mmol). The flask was cooled in an ice-bath and trifluoroacetic acid (3.4 mL, 44 mmol) was added slowly and the solution was stirred for 10 minutes. After the time had elapsed, a solution of *p*-anisidine (6.48 g, 53 mmol) in CCl_4 (21.1 mL) was added *via* cannula and the solution was heated to reflux for 3 hr. On completion the mixture was cooled to r.t. and diluted with petroleum ether (50 mL), filtered and the resultant residual solid was washed with petrol. The organic filtrate was collected and the solvent was

removed *in vacuo*. Purification *via* bulb-to-bulb distillation afforded the product as a pale yellow oil (7.09 g, 29.92 mmol, 68%). Bp: 89 °C (5 mbar); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.29 (m, 2H, Ar–*H*), 7.00–6.93 (m, 2H, Ar–*H*), 3.85 ppm (s, 3H, O*CH*$_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –71.29 ppm. Spectral data matched that previously reported.

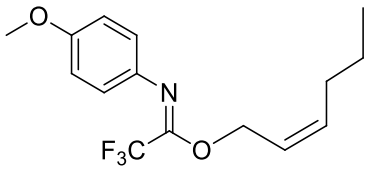
(E)-2,2,2-Trifluoroacetimidic acid hex-2-enyl ester[11]



(*E*)-**271**

A suspension of sodium hydride (0.203 g, 5.06 mmol) in THF (4 mL) was cooled in an ice-brine bath to 0 °C and (*E*)-hex-2-en-1-ol (0.60 mL, 5.06 mmol) was added dropwise. Upon completion, the solution was stirred at 0 °C for 30 minutes and then was warmed to r.t. and stirred for 90 minutes. A solution of *N*-(*p*-Anisyl)-2,2,2-trifluoroacetimidoyl chloride (1.00 g, 4.22 mmol) in THF (4 mL) was added to the reaction mixture *via* cannula and the solution was stirred at r.t. for 16 h. On completion the solvent was removed *in vacuo* and the residue was dissolved in hexane (20 mL) and filtered through a pad of Celite. The solvent was concentrated *in vacuo* and purification with column chromatography (SiO_2, 98.5/1.5 hexanes/EtOAc) gave the product as a pale yellow oil (1.06 g, 3.50 mmol, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.85 (d, *J* = 8.5 Hz, 2H, Ar–*H*), 6.81–6.72 (m, 2H, Ar–*H*), 5.93–5.81 (m, 1H, *H*C=CH), 5.74–5.63 (m, 1H, HC=C*H*), 4.70 (brs, 1H, O*CH*$_2$), 3.79 (s, 3H, O*CH*$_3$), 2.08 (q, *J* = 7.0 Hz, 2H, *CH*$_2$CH$_2$CH$_3$), 1.45 (sext, *J* = 7.1 Hz, 2H, CH$_2$*CH*$_2$CH$_3$), 0.93 ppm (t, *J* = 7.3 Hz, 3H, CH$_2$CH$_2$*CH*$_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –65.23 ppm. Spectral data matched that previously reported.

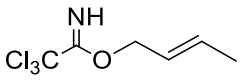
(Z)-2,2,2-Trifluoroacetimidic acid hex-2-enyl ester[11]



(*Z*)-**271**

A suspension of sodium hydride (0.203 g, 5.06 mmol) in THF (4 mL) was cooled in an ice-brine bath to 0 °C and (*Z*)-hex-2-en-1-ol (0.60 mL, 5.06 mmol) was added dropwise. Upon completion, the solution was stirred at 0 °C for 30 minutes and then was warmed to r.t. and stirred for 90 minutes. A solution of *N*-(*p*-Anisyl)-2,2,2-trifluoroacetimidoyl chloride (1.00 g, 4.22 mmol) in THF (4 mL) was added to the reaction mixture *via* cannula and the solution was stirred at r.t. for 16 h. On completion the solvent was removed *in vacuo* and the residue was dissolved in hexane (20 mL) and filtered through a pad of Celite. The solvent was concentrated *in vacuo* and purification with column chromatography (SiO_2, 98.5/1.5 hexanes/EtOAc) gave the product as a pale yellow oil (1.04 g, 3.46 mmol, 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.85 (d, J = 8.7 Hz, 2H, Ar–*H*), 6.81-6.72 (m, 2H, Ar–*H*), 5.80–5.64 (m, 2H, *H*C=C*H*), 4.82 (brs, 1H, O*CH*$_2$), 3.79 (s, 3H, O*CH*$_3$), 2.19–2.06 (m, 2H, *CH*$_2$CH$_2$CH$_3$), 1.43 (sext, J = 7.3 Hz, 2H, CH$_2$*CH*$_2$CH$_3$), 0.94 ppm (t, J = 7.3 Hz, 3H, CH$_2$CH$_2$*CH*$_3$); ^{19}F NMR (471 MHz, $CDCl_3$): δ = –65.23 ppm. Spectral data matched that previously reported.

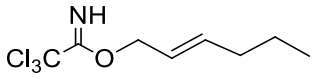
(E)-2,2,2-Trichloroacetimidic acid but-2-enyl ester[203]



A solution of crotyl alcohol (2.35 mL, 27.74 mmol) and DBU (0.83 mL, 5.55 mmol) in CH_2Cl_2 (139 mL) was cooled to 0 °C. Trichloroacetonitrile (4.17 mL, 41.61 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in vacuo* and

the crude residue was purified *via* column chromatography (SiO_2, 97:3 hexanes/EtOAc) to give the product as a colourless oil (3.82 g, 17.48 mmol, 63%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (s, 1H, N*H*), 5.94–5.83 (m, 1H, *H*C=CH), 5.74–5.65 (m, 1H, HC=C*H*), 4.72 (d, *J* = 6.3 Hz, 2H, CH_2), 1.75 ppm (d, *J* = 6.5 Hz, 3H, CH_3). Spectral data matched that previously reported.

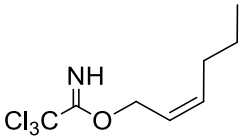
(E)-2,2,2-Trichloroacetimidic acid hex-2-enyl ester[203]



(*E*)-**299**

A solution of (*E*)-hex-2-en-1-ol (3.27 mL, 27.8 mmol) and DBU (0.84 mL, 5.6 mmol) in CH_2Cl_2 (170 mL) was cooled to 0 °C. Trichloroacetonitrile (4.17 mL, 41.7 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant orange solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in vacuo* and the crude residue was purified *via* column chromatography (SiO_2, 99:1 hexanes/EtOAc) to give the product as a colourless oil (6.49 g, 26.69 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (s, 1H, N*H*), 5.90–5.80 (m, 1H, *H*C=CH), 5.72–5.62 (m, 1H, HC=C*H*), 4.73 (d, *J* = 6.3 Hz, 2H, OCH_2CH=CH), 2.05 (q, *J* = 7.1 Hz, 2H, $CH_2CH_2CH_3$), 1.42 (sext., *J* = 7.4 Hz, 2H, $CH_2CH_2CH_3$), 0.90 ppm (t, *J* = 7.4 Hz, 3H, $CH_2CH_2CH_3$). Spectral data matched that previously reported.

(Z)-2,2,2-Trichloroacetimidic acid hex-2-enyl ester[203]

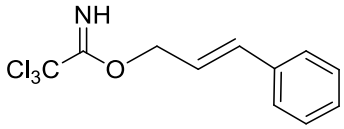


(*Z*)-**299**

A solution of (*Z*)-hex-2-en-1-ol (2.00 mL, 23.7 mmol) and DBU (0.71 mL, 4.75 mmol) in CH_2Cl_2 (150 mL) was cooled to 0 °C. Trichloroacetonitrile (3.58 mL, 35.6 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant

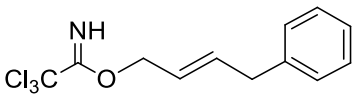
orange solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in vacuo* and the crude residue was purified *via* column chromatography (SiO_2, 49:1 hexanes/EtOAc) to give the product as a colourless oil (5.30 g, 22.8 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.28 (s, 1H, N*H*), 5.76–5.63 (m, 2H, *H*C=C*H*), 4.84 (d, *J* = 6.1 Hz, 2H, O*CH*$_2$), 2.12 (q, *J* = 7.1 Hz, 2H, *CH*$_2$CH$_2$CH$_3$), 1.42 (sext, *J* = 7.3 Hz, 2H, CH$_2$*CH*$_2$CH$_3$), 0.91 ppm (t, *J* = 7.4 Hz, 3H, CH$_2$CH$_2$*CH*$_3$). Spectral data matched that previously reported.

(E)-2,2,2-Trichloroacetimidic acid 3-phenylprop-2-enyl ester[203]



A solution of cinnamyl alcohol (2.00 g, 14.91 mmol) and DBU (0.45 mL, 2.98 mmol) in CH_2Cl_2 (75 mL) was cooled to 0 °C. Trichloroacetonitrile (2.24 mL, 22.36 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in vacuo* and the crude residue was purified *via* column chromatography (SiO_2, 97:3 hexanes/EtOAc) to give the product as a yellow oil (2.75 g, 9.84 mmol, 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.28 (s, 1H, N*H*), 7.36–7.31 (m, 2H, Ar–*H*), 7.27–7.22 (m, 2H, Ar–*H*), 7.20–7.15 (m, 1H, Ar–*H*), 6.72-6.63 (m, 1H, PhC*H*=CH), 6.39–6.24 (m, 1H, PhCH=C*H*), 4.88 ppm (dt, *J* = 6.1, 1.3 Hz, 2H, *CH*$_2$). Spectral data matched that previously reported.

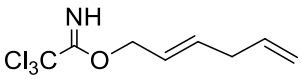
(E)-2,2,2-Trichloroacetimidic acid 4-phenylbut-2-enyl ester[203]



A solution of (*E*)-4-phenylbut-2-en-1-ol (0.20 g, 1.35 mmol) and DBU (0.04 mL, 0.27 mmol) in CH_2Cl_2 (7.5 mL) was cooled to 0 °C. Trichloroacetonitrile (0.20 mL, 2.03 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in*

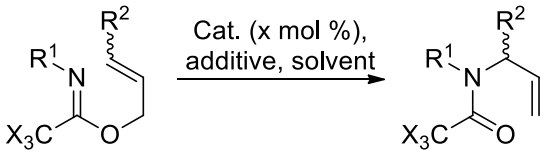
vacuo and the crude residue was purified *via* column chromatography (SiO_2, 97:3 hexanes/EtOAc) to give the product as a yellow oil (0.181 g, 0.62 mmol, 46%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.32 (s, 1H, N*H*), 7.32 (t, *J* = 7.0 Hz, 2H, Ar−*H*), 7.25–7.17 (m, 3H, Ar−*H*), 6.12–6.00 (m, 1H, *H*C=CH), 5.85–5.72 (m, 1H, HC=C*H*), 4.83–4.76 (m, 2H, O*CH*$_2$), 3.45 ppm (d, *J* = 6.7 Hz, 2H, *CH*$_2$Ph). Spectral data matched that previously reported.

(E)-2,2,2-Trichloroacetimidic acid hex-2,5-dienyl ester[243]



A solution of (*E*)-hex-2,5-dien-1-ol (0.90 g, 10.70 mmol) and DBU (0.32 mL, 2.14 mmol) in CH_2Cl_2 (75 mL) was cooled to 0 °C. Trichloroacetonitrile (1.61 mL, 16.05 mmol) was added dropwise whilst maintaining the temperature of the solution below 5 °C. The resultant solution was stirred for 1 hour at 0 °C. On completion the solvent was removed *in vacuo* and the crude residue was purified *via* column chromatography (SiO_2, 97:3 hexanes/EtOAc) to give the product as a yellow oil (0.787 g, 3.42 mmol, 32%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.28 (s, 1H, N*H*), 5.98–5.63 (m, 3H, 3 x C=C*H*), 5.09–5.01 (m, 2H, C=*CH*$_2$), 4.76 (d, *J* = 6.1 Hz, 2H, O*CH*$_2$), 2.84 ppm (t, *J* = 6.4 Hz, 2H, *CH*$_2$). Spectral data matched that previously reported.

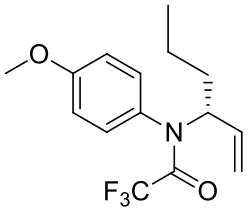
General Procedure for Catalysis of the Allylic Imidate Rearrangement[203]



To a flask charged with catalyst was added the required amount of imidate stock solution. If silver salts and/or proton sponge was used this was subsequently added. The solution was protected from light then heated to the desired temperature for the allotted time. On completion, the solution was passed through a short pad of Celite and the solvent was removed *in vacuo*. Purification *via* column chromatography (SiO_2, 24:1 hexanes/EtOAc)

yielded the product amides as oils.

2,2,2-trifluoro-N-(4-methoxyphenyl-N-(1-propylallyl)acetamide[11]



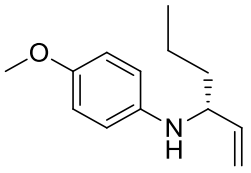
(*R*)-**272**

Isolated as pale yellow oil, enantiomeric excess was determined after removal of the trifluoroacetyl group. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.75 (d, *J* = 8.9 Hz, 2H, Ar-*H*), 6.57 (d, *J* = 8.9 Hz, 2H, Ar–*H*), 5.72 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H, *H*C=CH_2), 5.18 (dt, *J* = 17.2, 1.3 Hz, 1H, HC=C*H*H-*trans*), 5.10 (dt, *J* = 10.3, 1.2 Hz, 1H, HC=CH*H-cis*), 5.02 (q, *J* = 7.6 Hz, 1H, N*CH*), 3.73 (s, 3H, OCH_3), 1.63–1.50 (m, 2H, $CH_2CH_2CH_3$), 1.49–1.40 (m, 2H, $CH_2CH_2CH_3$), 0.94 ppm (t, *J* = 7.3 Hz, 3H, $CH_2CH_2CH_3$). Spectral data matched that previously reported.

General Procedure for Deprotection of Trifluoroacetyl Group[121]

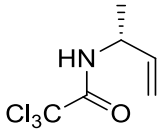
The allylic amide was dissolved in an isopropanol/water mixture (10:1, 1 mL). Sodium borohydride (6 equiv.) was added in one portion at rt. The solution was stirred overnight. Water was subsequently added and the mixture extracted three times with CH_2Cl_2. The organic phases are combined and dried over $MgSO_4$ and the solvent is removed *in vacuo*. Purification of the residue by flash chromatography (SiO2, 19:1 hexanes/EtOAc) gave the products as oils.

N-(4-Methoxyphenyl)-3-amino-1-hexene[11]



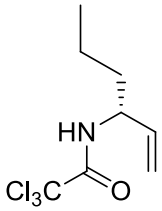
Isolated as a pale yellow oil, chiral HPLC analysis was used to determine enantiomeric excess (Chiracel OD-H, 99.8:0.2 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.76 (td, *J* = 8.9, 2.9 Hz, 2H, Ar–*H*), 6.57 (td, *J* = 8.9, 2.9 Hz, 2H, Ar–*H*), 5.72 (ddd, *J* = 16.9, 10.3, 6.4 Hz, 1H, *H*C=CH_2), 5.19 (td, *J* = 17.2, 1.3 Hz, 1H, HC=C*H*H-*trans*), 5.11 (td, *J* = 10.3, 1.1 Hz, 1H, HC=CH*H*-*cis*), 3.71–3.76 (m, 1H, NC*H*), 3.74 (s, 3H, OCH_3), 3.37 (broad s, 1H, N*H*), 1.48–1.63 (m, 2H, $CH_2CH_2CH_3$), 1.40–1.48 (m, 2H, $CH_2CH_2CH_3$), 0.95 ppm (t, J = 7.3 Hz, 3H, $CH_2CH_2CH_3$). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(but-3-en-2-yl)acetamide[203]



Isolated as a pale yellow oil, chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.56 (brs, 1H, N*H*), 5.87 (ddd, *J* = 17.2, 10.5, 5.1 Hz, 1H, *H*C=CH_2), 5.29–5.22 (m, 1H, HC=C*H*H), 5.22-5.15 (m, 1H, HC=CH*H*), 4.54 (dddt, *J* = 8.4, 6.8, 5.0, 1.6 Hz, 1H, NC*H*), 1.35 ppm (d, *J* = 6.9 Hz, 3H, CH_3). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(1-hexen-3-yl)acetamide[203]

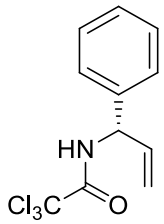


(*R*)-**300**

Isolated as a pale yellow oil, chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.49 (brs, 1H, N*H*), 5.78 (ddd, *J* = 16.0, 9.8, 5.6 Hz, 1H, *H*C=CH_2), 5.22 (dd, 1H, *J* = 15.8, 0.9 Hz, HC=CH*H*-*trans*), 5.17 (dd, *J* = 9.8, 0.9 Hz, 1H, HC=C*H*H-*cis*), 4.47–4.43 (m,

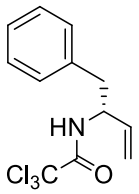
1H, NC*H*), 1.67 (q, *J* = 7.1 Hz, 2H, *CH*$_2$CH$_2$CH$_3$), 1.40 (sext., *J* = 7.4 Hz, 2H, CH$_2$*CH*$_2$CH$_3$), 0.94 ppm (t, *J* = 7.4 Hz, 3H, CH$_2$CH$_2$*CH*$_3$). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(1-phenylallyl)acetamide[203]



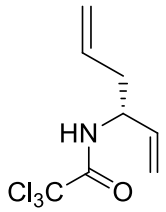
Isolated as a pale yellow oil, chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 0.8 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.25 (m, 5H, Ar–*H*), 6.95, (brs, 1H, N*H*), 6.05 (ddd, *J* = 16.0, 10.3, 5.42 Hz, 1H, *H*C=CH$_2$), 5.59–5.51 (m, 1H, NC*H*),), 5.36 (d, *J* = 10.3 Hz, 1H, HC=C*H*H-*cis*), 5.30 ppm (dd, *J* = 16.8 Hz, 1H, HC=CH*H-trans*). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(1-benzylallyl)acetamide[214]



Isolated as a pale yellow oil, chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 1.0 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.33–7.17 (m, 5H, Ar–*H*), 6.56 (brs, 1H, N*H*), 5.85 (ddd, *J* = 16.5, 10.8, 5.4 Hz, 1H, *H*C=CH$_2$), 5.19 (dd, *J* = 10.3, 1.2 Hz, 1H, HC=C*H*H-*cis*), 5.18 (dd, *J* = 17.7, 1.2 Hz, 1H, HC=CH*H-trans*), 4.76–4.67 (m, 1 H, NC*H*), 3.01 (dd, *J* = 13.8, 6.6 Hz, 1H, *CH*HPh), 2.92 ppm (dd, 1H, *J* =13.6, 6.6 Hz, *C*H*H*Ph). Spectral data matched that previously reported.

2,2,2-Trichloro-N-[1-(2-propenyl)allyl]acetamide[214]

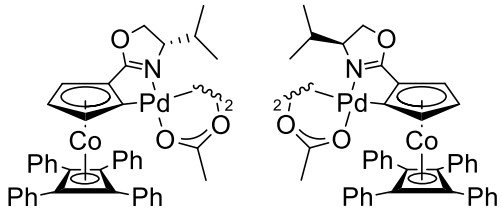


Isolated as a pale yellow oil, chiral HPLC analysis was used to determine the enantiomeric excess (Chiracel OD-H, 99.5:0.5 *n*-hexane/IPA, 1.0 mL/min). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.63 (brs, 1H, N*H*), 5.89–5.74 (m, 2H, 2 x *H*C=CH_2), 5.74–5.62 (m, 1H, C=C*H*H), 5.28–5.13 (m, 1H, HC=C*H*H), 5.12–5.01 (m, 2H, 2 x HC=CH*H*), 4.81 (d, *J* = 6.5 Hz, 6H), 4.54 (p, *J* = 7.1 Hz, 1H, NC*H*), 2.52–2.35 ppm (m, 2H, CH_2). Spectral data matched that previously reported.

Chapter 7 - Appendix

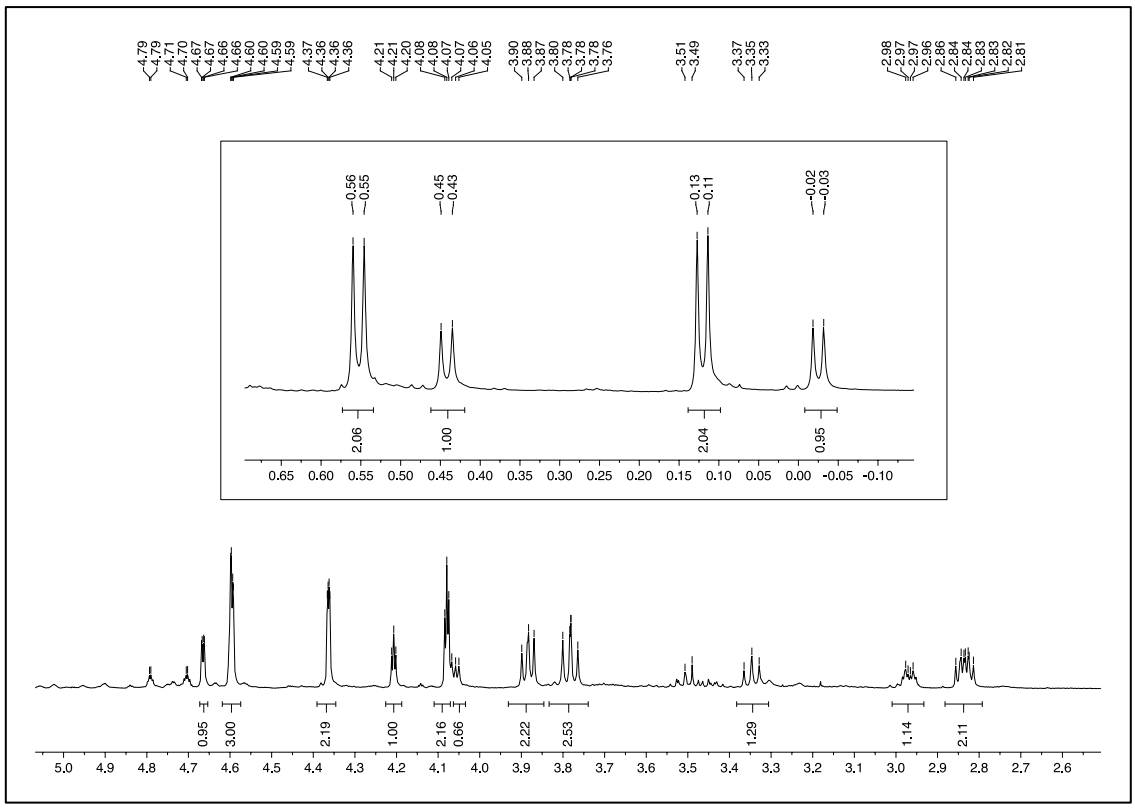
NMR Spectra used to calculate diastereoselectivity of palladation reactions

di-μ-acetatobis[(η^5-(S)-2-(2'-4'-methylethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II)



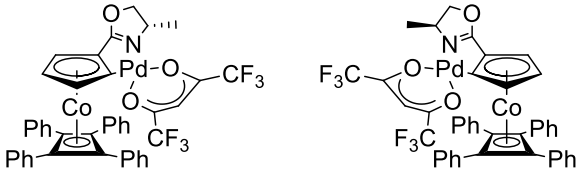
(S,S_p)$_2$-**118** (S,R_p)$_2$-**118**

Crude ^{1}H-NMR of mixture of acetate dimers (*solvent = CH_2Cl_2, temp = rt, time = 16h, ratio ca. 2:1* [S_p:R_p]):



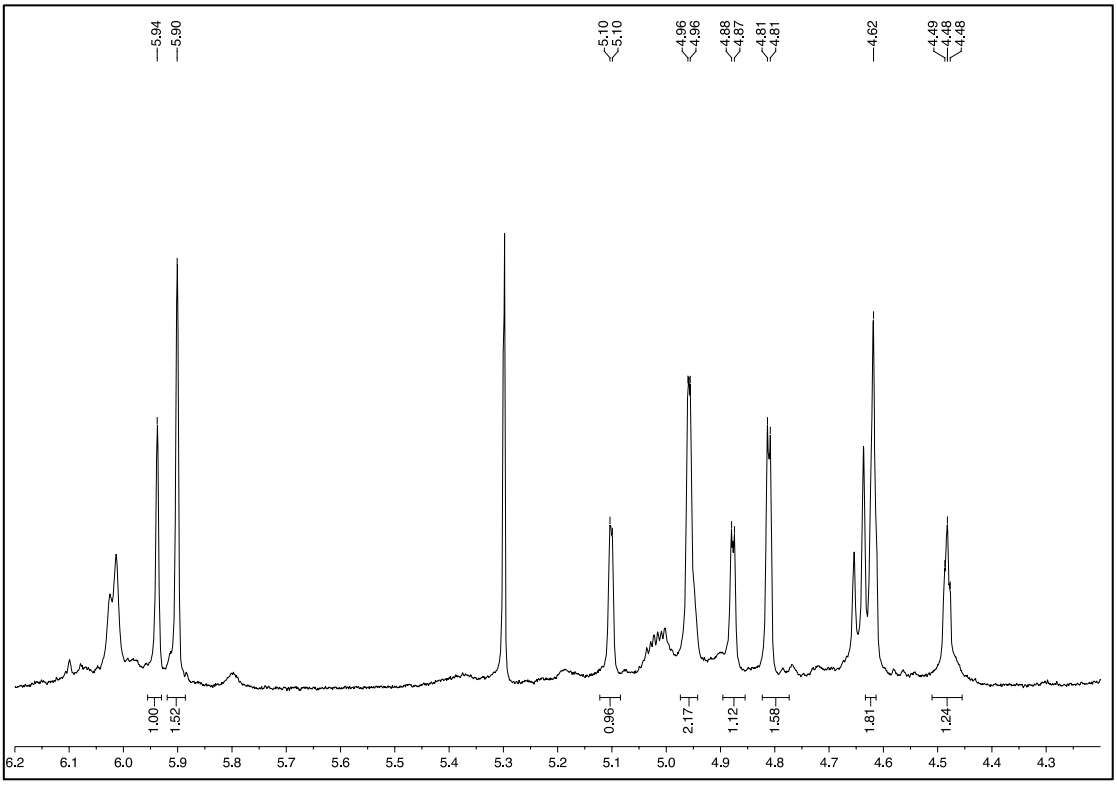
$[\alpha]_D^{26}$ = –600 (c = 0.3 mg/mL in CH_2Cl_2).

hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'-methyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



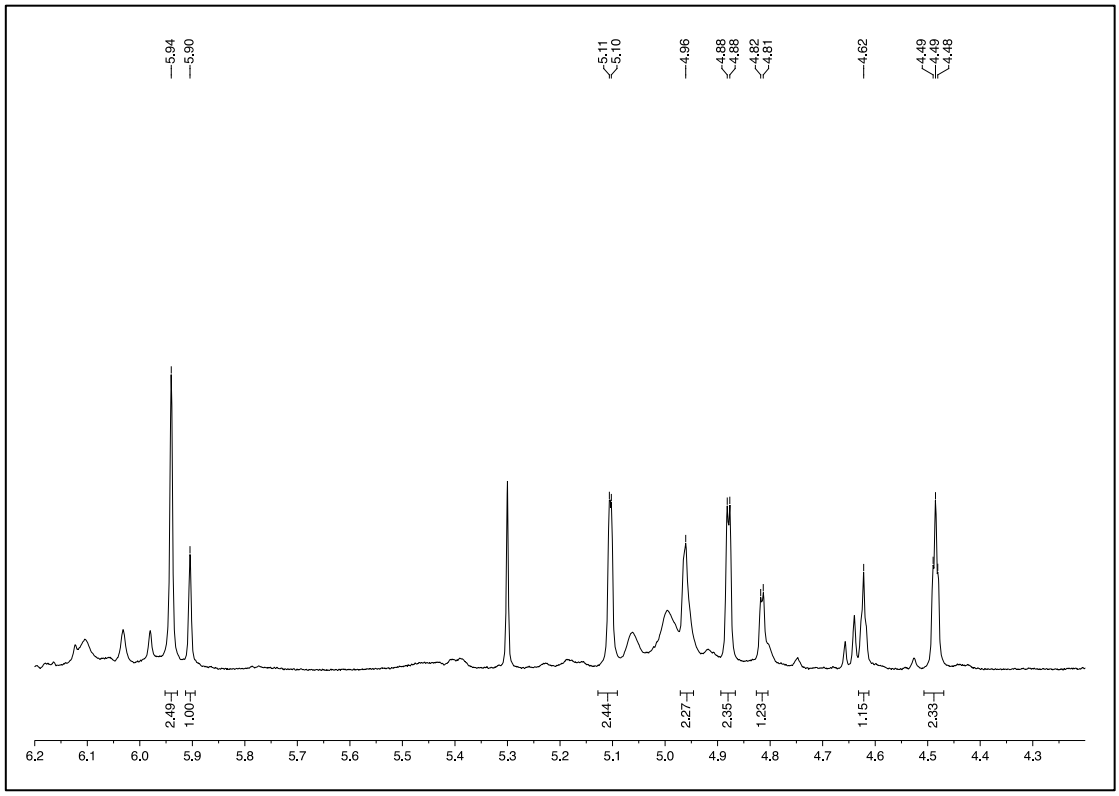
(S,S_p)-**294** (S,R_p)-**294**

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = AcOH, temp = 95 °C, time = 30 min, ratio ca. 1.5:1* [S_p:R_p]):



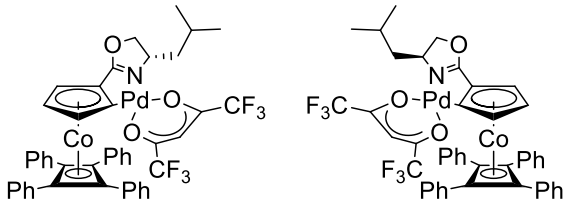
$[\alpha]_D^{24}$ = –443 (c = 0.7 mg/mL in CH_2Cl_2).

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = CH_2Cl_2, temp = rt, time = 16h, ratio ca. 1:2.5* [S_p:R_p]):



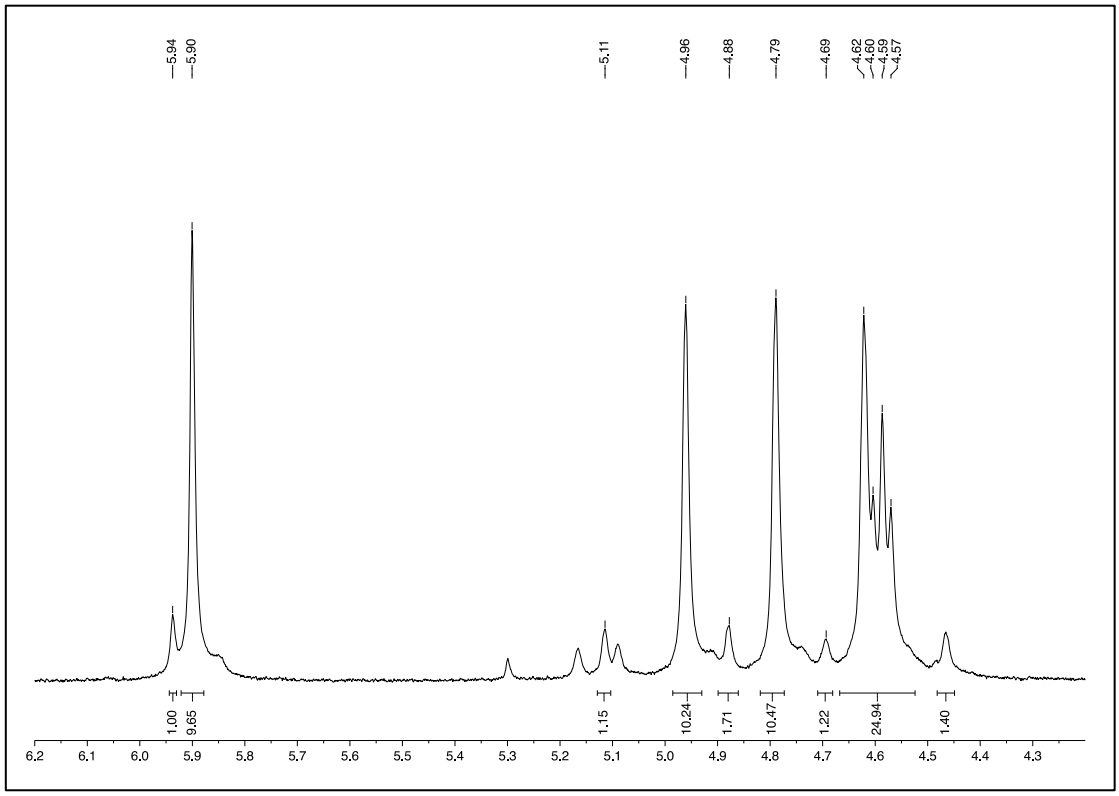
$[\alpha]_D^{24}$ = +467 (c = 0.6 mg/mL in CH_2Cl_2).

hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'- isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



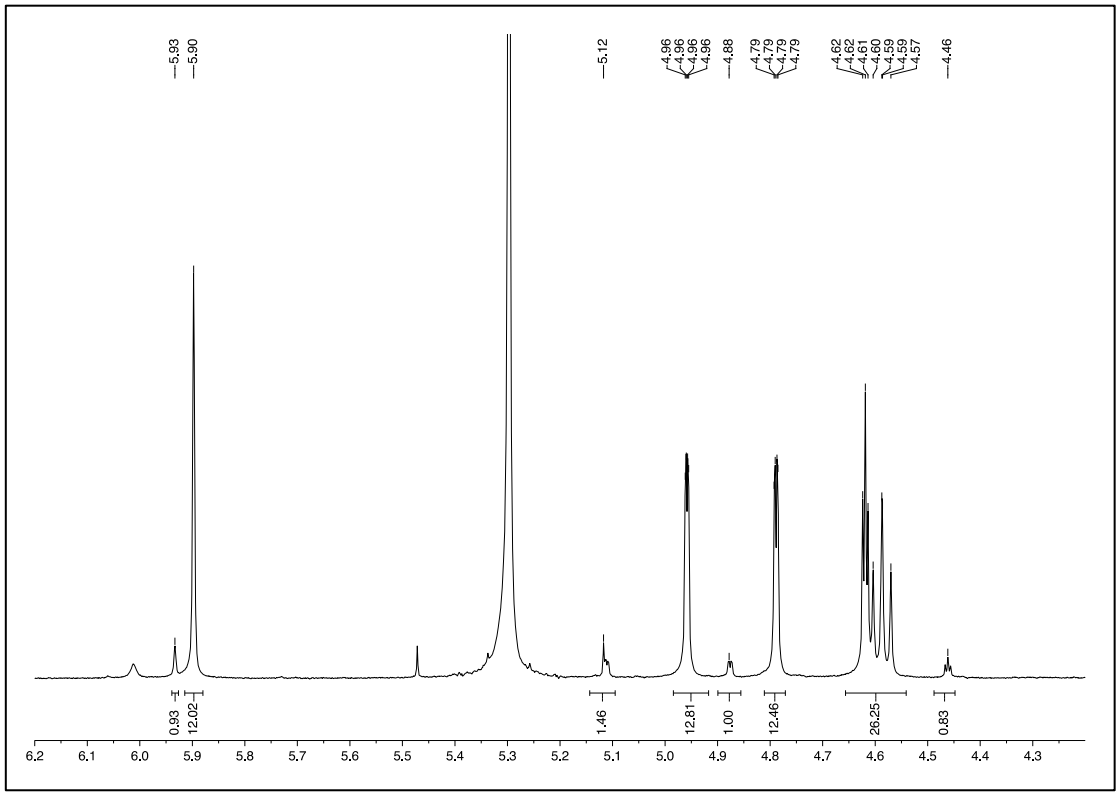
(S,S_p)-**295** (S,R_p)-**295**

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = AcOH, temp = 95 °C, time = 30min, ratio ca. 10:1* [S_p:R_p]):



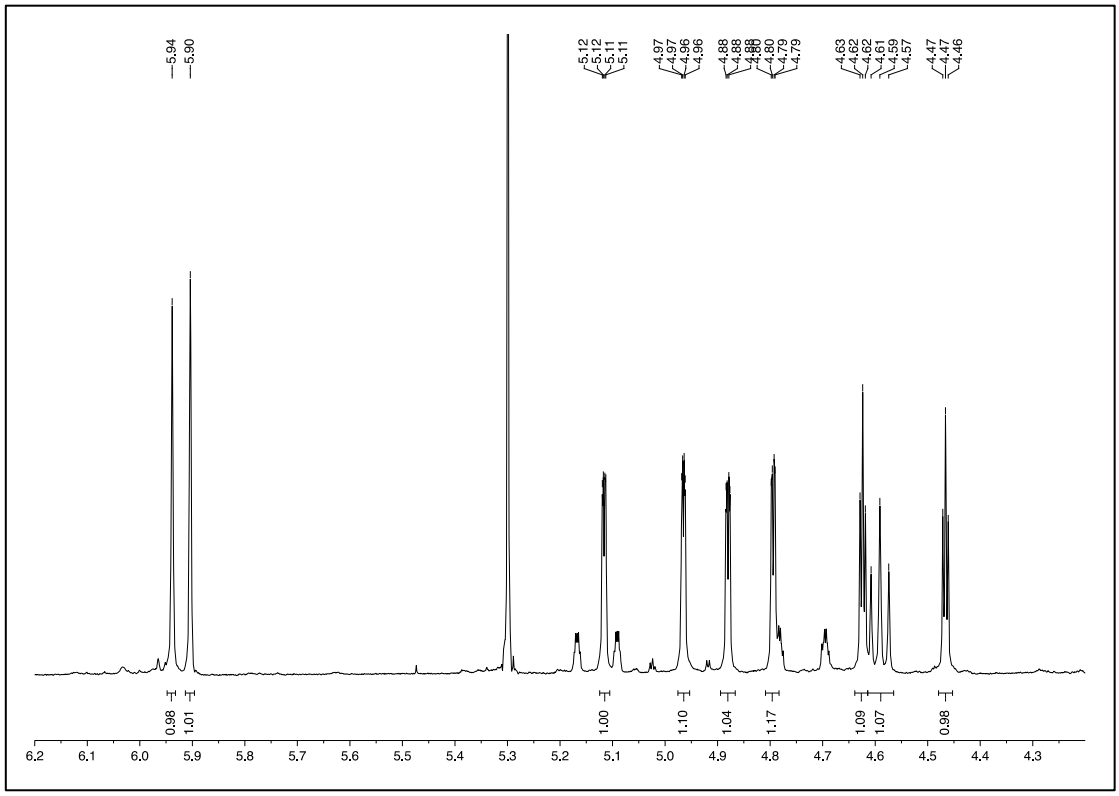
$[\alpha]_D^{26}$ = −545 (c = 1.5 mg/mL in CH_2Cl_2).

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = CH_2Cl_2, temp = rt, time = 16h, ratio ca. 13:1* [S_p:R_p]):

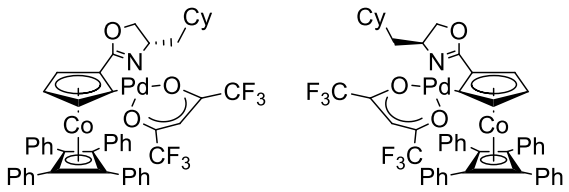


$[\alpha]_D^{26}$ = −586 (c = 2.2 mg/mL in CH_2Cl_2).

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = PhMe, temp = 95 °C, time = 1h, ratio ca. 1:1* [S_p:R_p]):

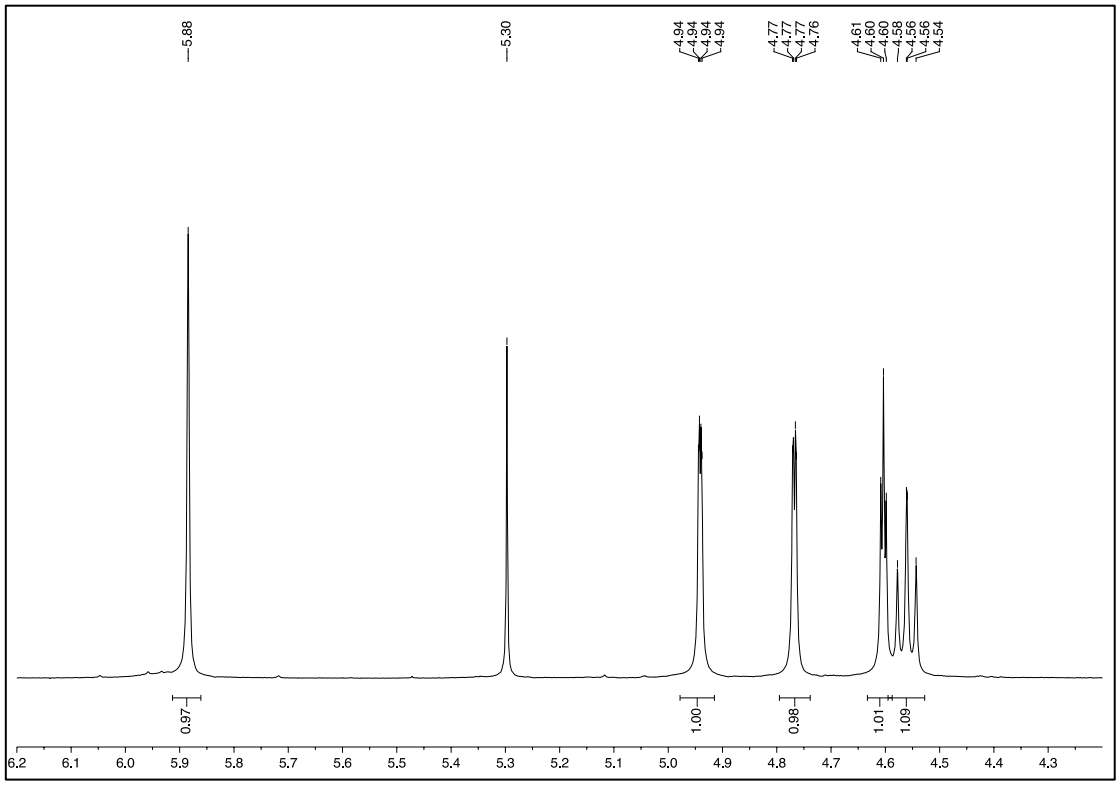


hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'- cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



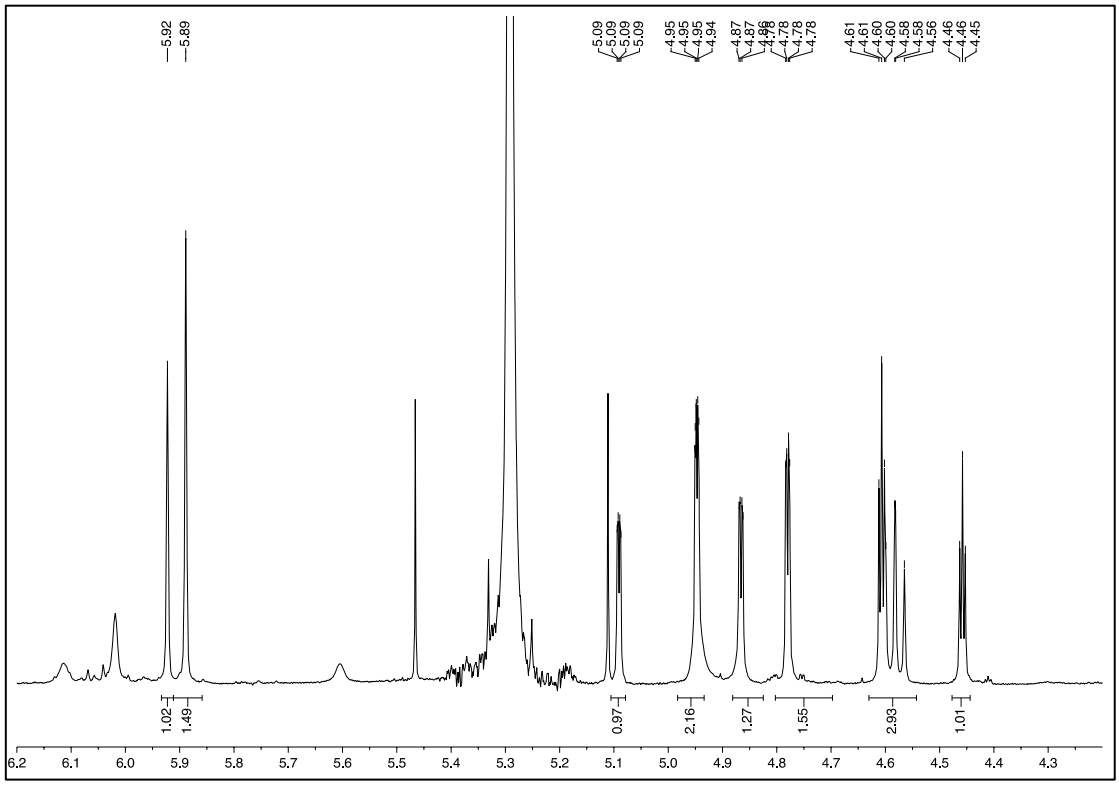
(S,S_p)-**296** (S,R_p)-**296**

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = AcOH, temp = 95 °C,time = 30 min, ratio ca. >100:1* [S_p:R_p]):



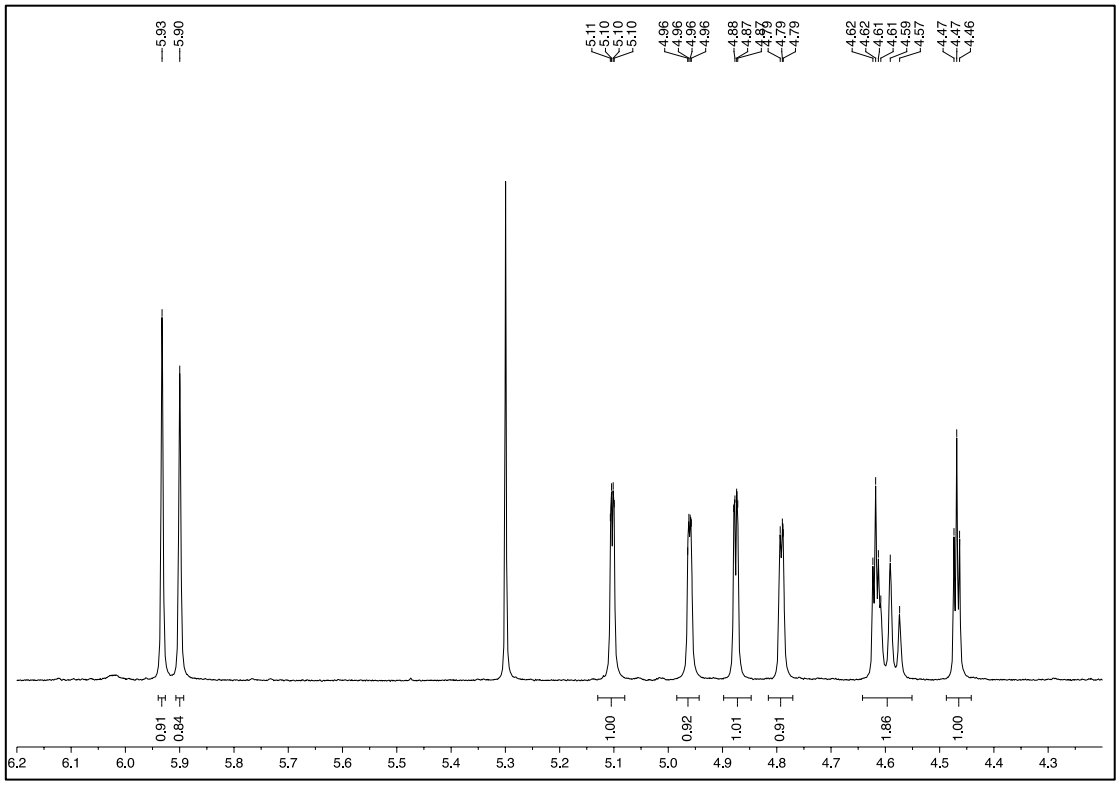
$[\alpha]_D^{25}$ = −532 (c = 5.2 mg/mL in CH_2Cl_2).

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = CH_2Cl_2, temp = rt, time = 16h, ratio ca. 2:1* [S_p:R_p]):

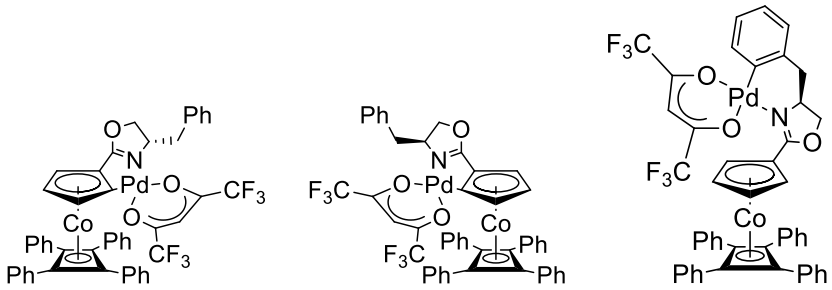


$[\alpha]_D^{26}$ = –91.6 (c = 1.2 mg/mL in CH_2Cl_2).

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = PhMe, temp = 95 °C,time = 1h, ratio ca. 1:1* [S_p:R_p]):

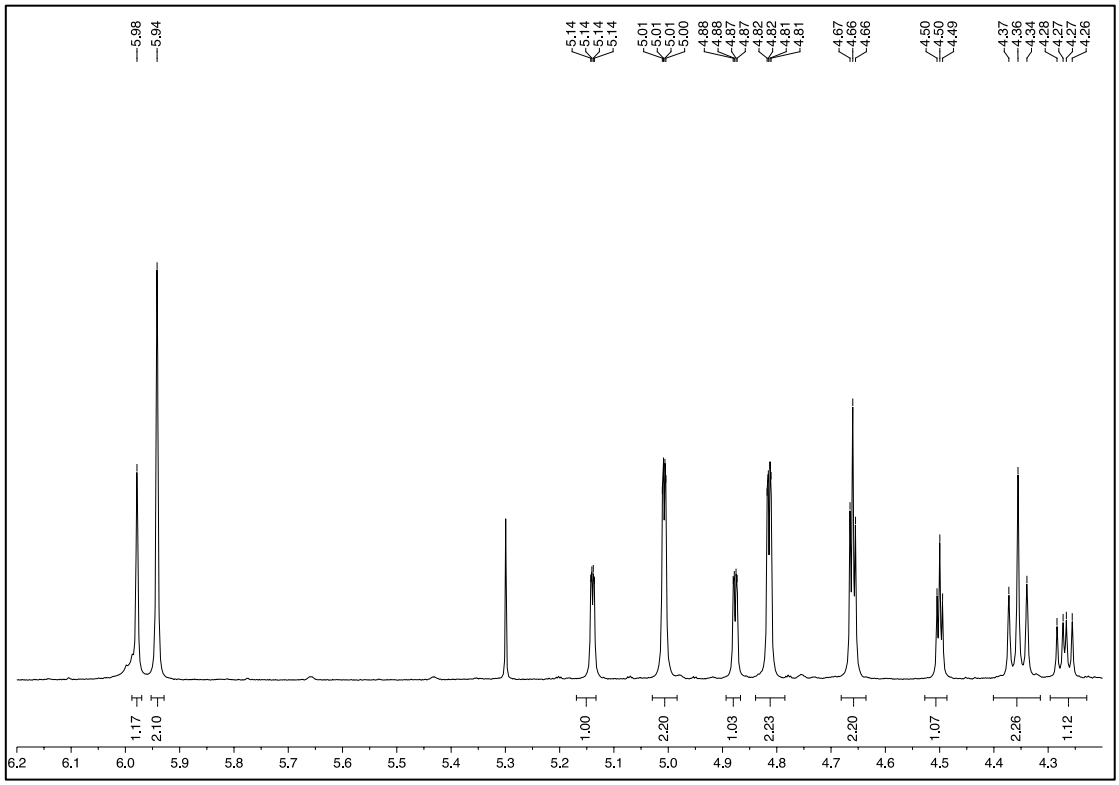


hexafluoroacetylacetonate[(η^5-(S)-2-(2'-(4'-benzyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N)(η^4-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)



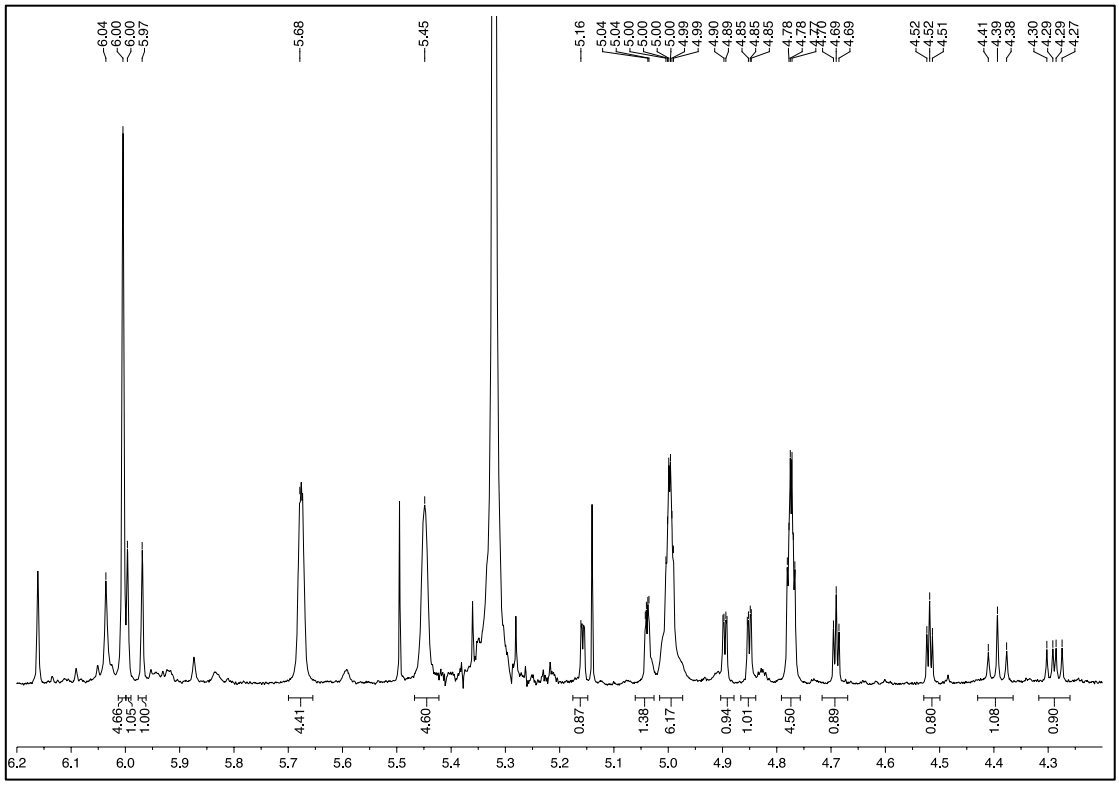
(S,S_p)-**297** (S,R_p)-**297** **298**

Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = AcOH, temp = 95 °C,time = 30 min, ratio ca. 2:1* [S_p:R_p]):

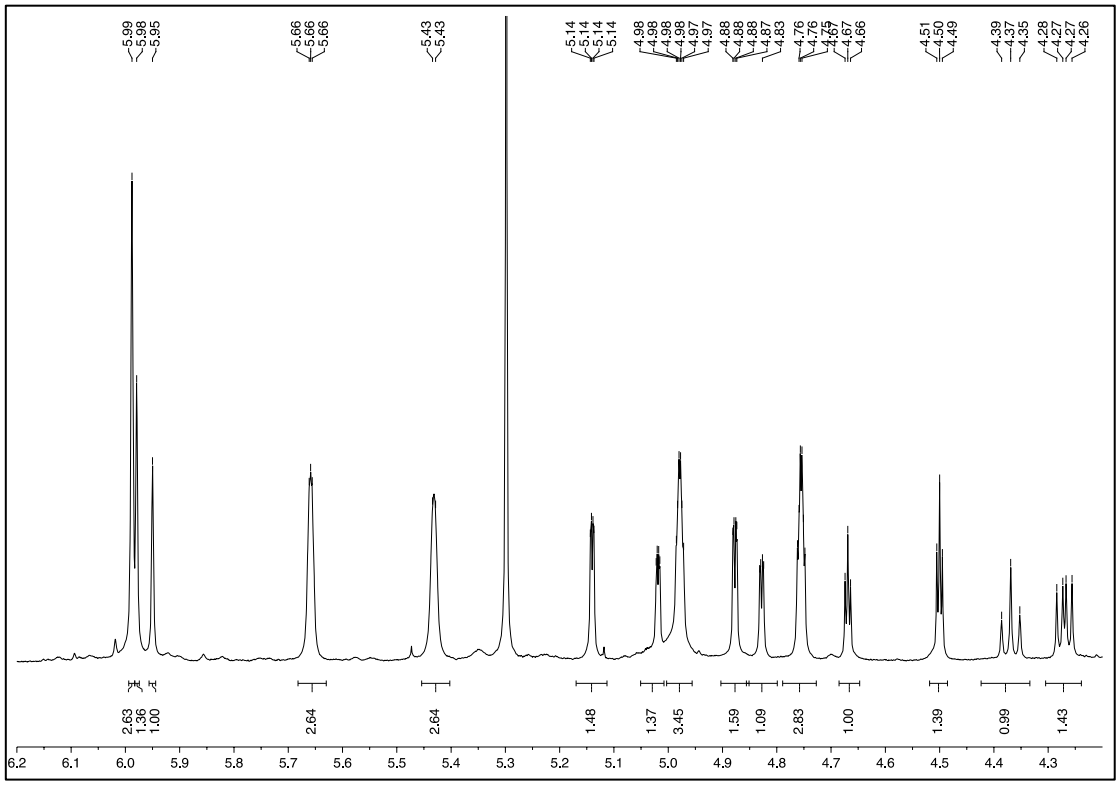


$[\alpha]_D^{25}$ = −215 (c = 2.7 mg/mL in CH_2Cl_2).

Crude ^{1}*H-NMR of mixture of hfacac monomers* (*solvent =* CH_2Cl_2*, temp = rt, time = 16h, ratio ca. 4.5:1:1* [*exo:*R_p*:*S_p]):



Crude ^{1}H-NMR of mixture of hfacac monomers (*solvent = PhMe, temp = 95 °C, ratio ca. 2.6:1.4:1* [*exo*:R_p:S_p])*:*



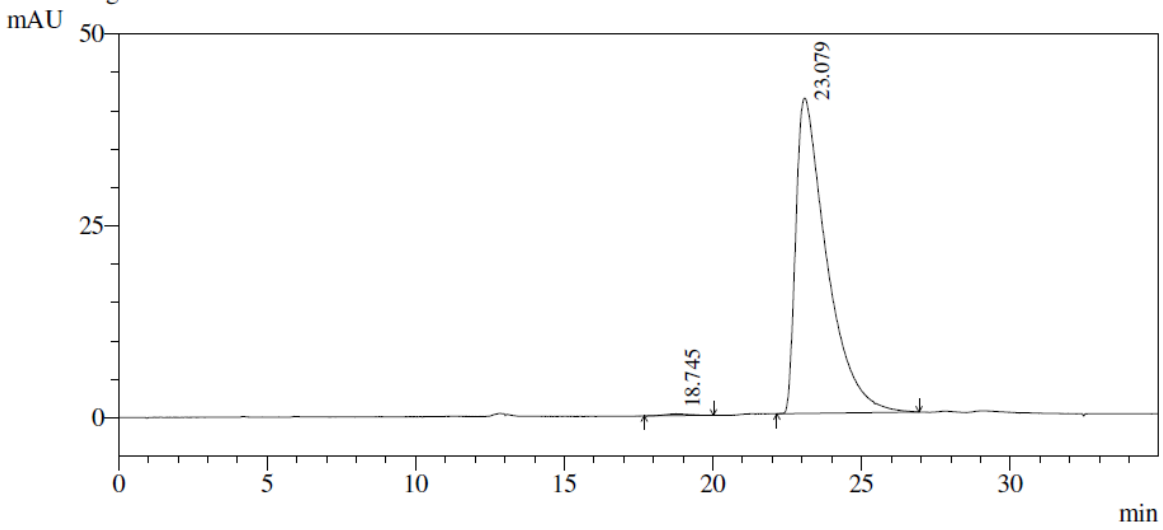
HPLC Data for enantioselective catalysis

==== Shimadzu LCsolution Analysis Report ====

Information:

Acquired by	: Admin
Sample Name	: DJC-528
Tray#	: 1
Vial #	: 7
Injection Volume	: 5 uL
Data File Name	: DJC-528(run2).lcd
Method File Name	: IPA 0.5$0.8flow.lcm
Temperature	: 21 degrees

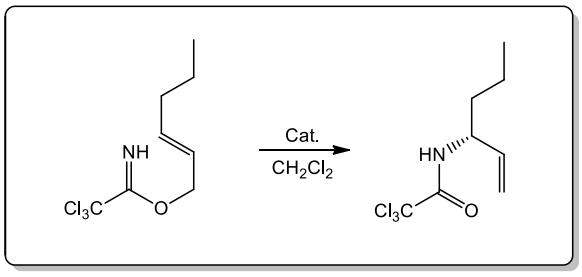
Chromatogram:



Quantitative Results:

PDA

ID#	Name	Ret. Time	Area	Height	Area %
1	RT18.745	18.745	11603	219	0.389
2	RT23.079	23.079	2970777	41115	99.611

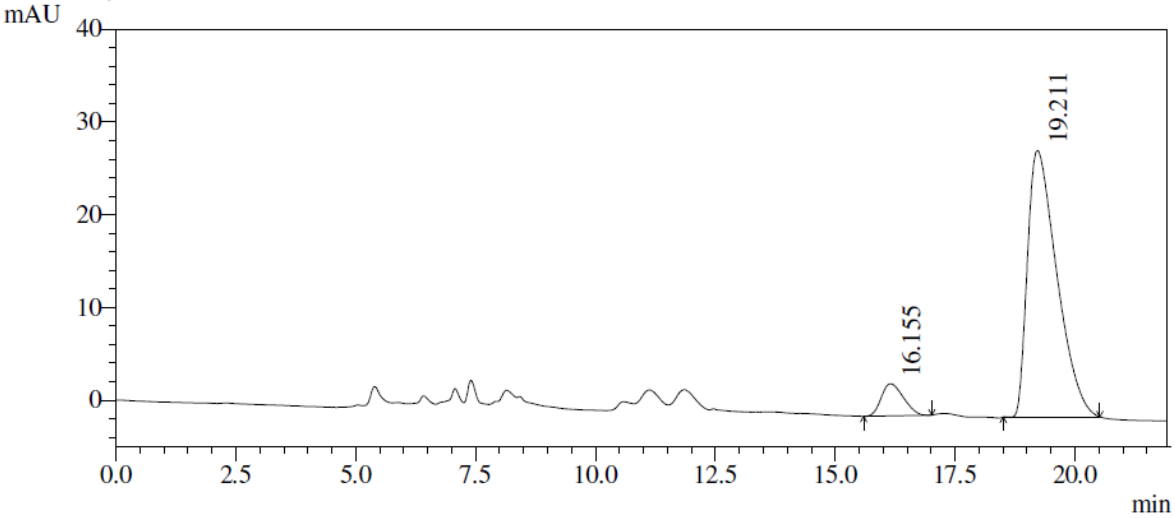


==== Shimadzu LCsolution Analysis Report ====

C:\Documents and Settings\Andy\Desktop\DJC\DJC-521(run 2).lcd

Sample Name	: DJC-521
Tray#	: 1
Vial #	: 38
Injection Volume	: 10 uL
Data File Name	: DJC-521(run 2).lcd
Method File Name	: IPA 0.5$0.8flow.lcm
Batch File Name	:
Data Acquired	: 5/25/2013 12:32:08 PM
Data Processed	: 5/25/2013 12:55:38 PM
Temperature	: 21 degrees

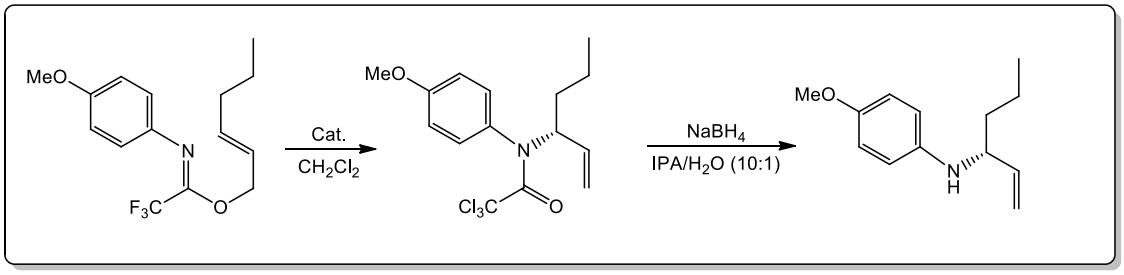
Chromatogram:



Quantitative Results:

PDA

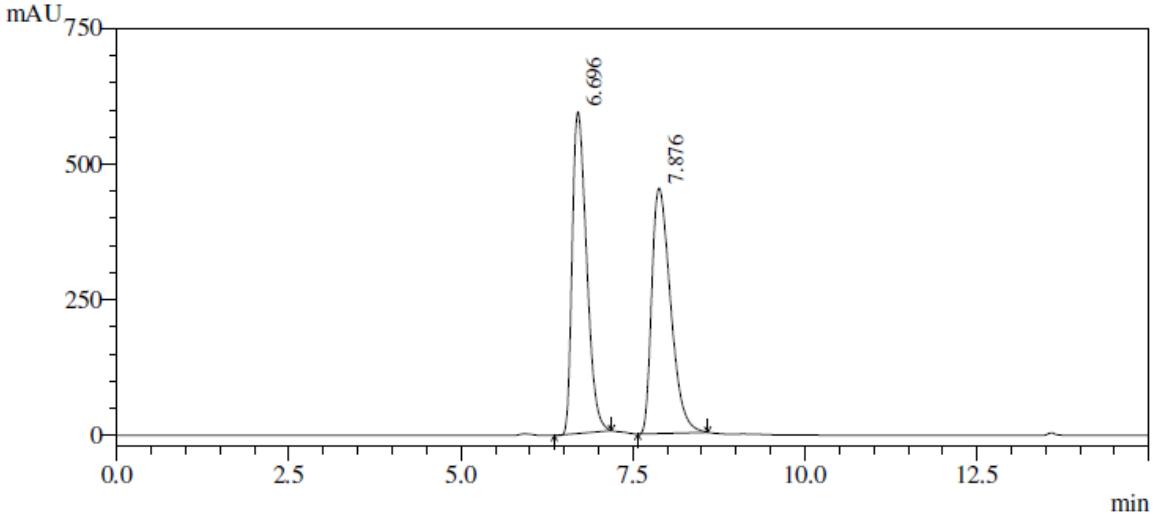
ID#	Name	Ret. Time	Area	Height	Area %
1	RT16.155	16.155	110344	3450	8.258
2	RT19.211	19.211	1225841	28711	91.742



==== Shimadzu LCsolution Analysis Report ====

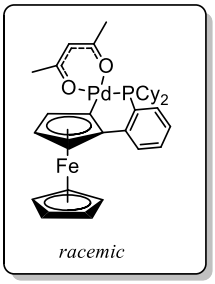
Information:
Acquired by : Admin
Sample Name : DJC-PCy2acac (racemic)
Tray# : 1
Vial # : 5
Injection Volume : 10 uL
Data File Name : DJC-PCy2acac (racemic).lcd
Method File Name : 99.7hex0.3IPA0.8mlmin.lcm
Temperature : 21 degrees

Chromatogram:



Quantitative Results:
PDA

ID#	Name	Ret. Time	Area	Height	Area %
1	RT6.696	6.696	8604621	593285	49.994
2	RT7.876	7.876	8606662	452618	50.006



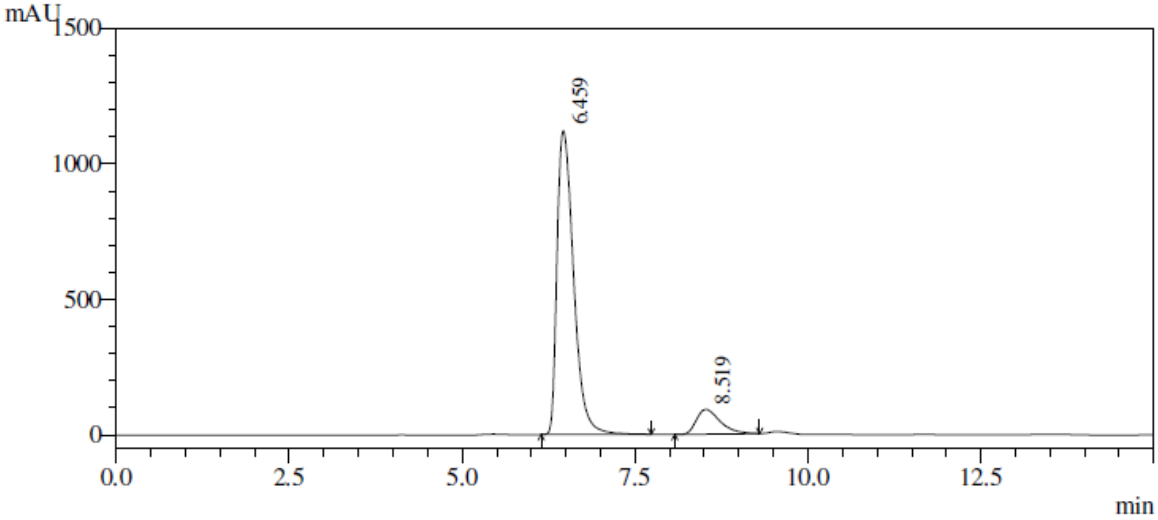
racemic

==== Shimadzu LCsolution Analysis Report ====

Information:

Acquired by	: Admin
Sample Name	: DJC-567
Tray#	: 1
Vial #	: 7
Injection Volume	: 5 uL
Data File Name	: DJC-567.lcd
Method File Name	: 99.7hex0.3IPA0.8mlmin.lcm
Temperature	: 21 degrees

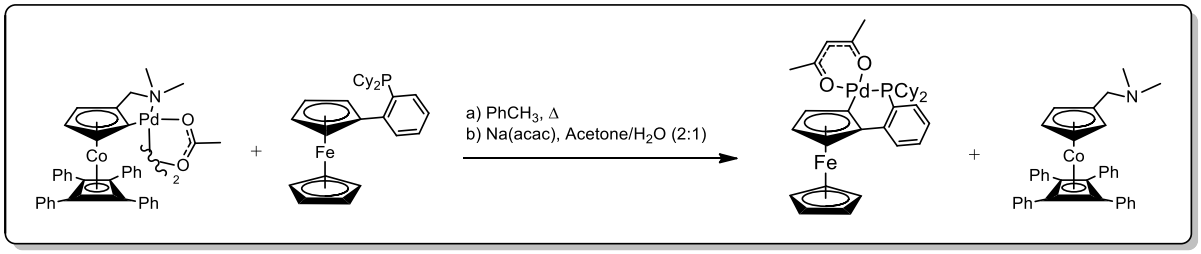
Chromatogram:



Quantitative Results:

PDA

ID#	Name	Ret. Time	Area	Height	Area %
1	RT6.459	6.459	18700412	1121239	89.452
2	RT8.519	8.519	2205018	91497	10.548

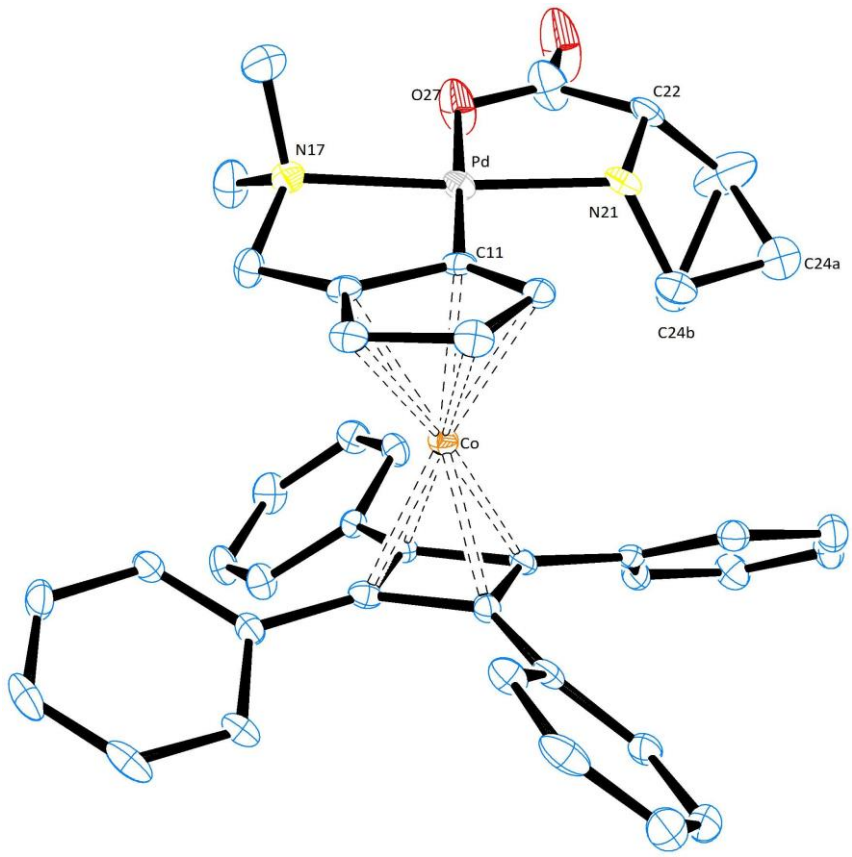


X-Ray data

All X-ray data within this thesis has been previously published in journals, as such all supplementary data is available online, or has been submitted to the Cambridge Crystallographic Data Centre and is available free of charge *via* www.ccdc.cam.ac.uk/data_request/cif. Data that is available online but does not have a CCDC number is given herein.

*X-Ray representation for R,S_p-**249**:*

CCDC-931363



*X-Ray representation and data for R,R_p-**249**:*

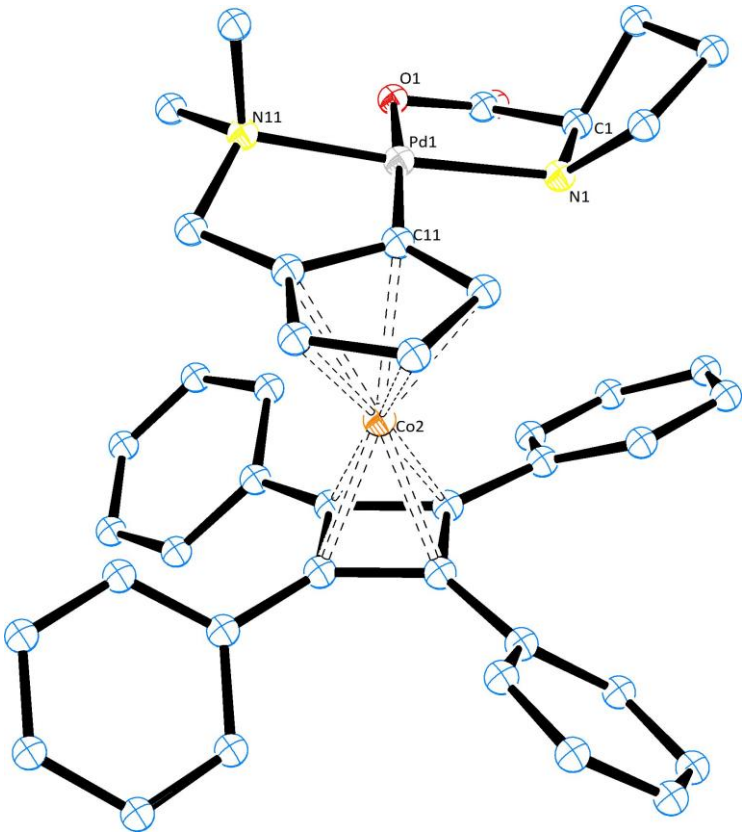


Table 14. Crystal data and structure refinement.

Identification code	**2013ncs0001/ DJC-387**
Empirical formula	C41H43CoN2O4Pd
Formula weight	793.10
Temperature	100(2) K
Wavelength	0.71075 Å
Crystal system	Orthorhombic

Space group	*P*212121	
Unit cell dimensions	a = 28.653(2) Å	a = 90°
	b = 8.5350(7) Å	b = 90°
	c = 14.5829(11) Å	g = 90°
Volume	3566.3(5) $Å^3$	
Z	4	
Density (calculated)	1.477 Mg / m^3	
Absorption coefficient	1.014 mm^{-1}	
F(000)	1632	
Crystal Blade;	orange	
Crystal size	0.160 × 0.050 × 0.010 mm^3	
Θ range for data collection	3.110 − 27.482°	
Index ranges	$-30 \le h \le 33, -11 \le k \le 10, -18 \le l \le 10$	
Reflections collected	14604	
Independent reflections	7438 [*Rint* = 0.0963]	
Completeness to Θ = 25.242°	96.3 %	
Absorption correction	Semi−empirical from equivalents	
Max. and min. transmission	1.000 and 0.426	

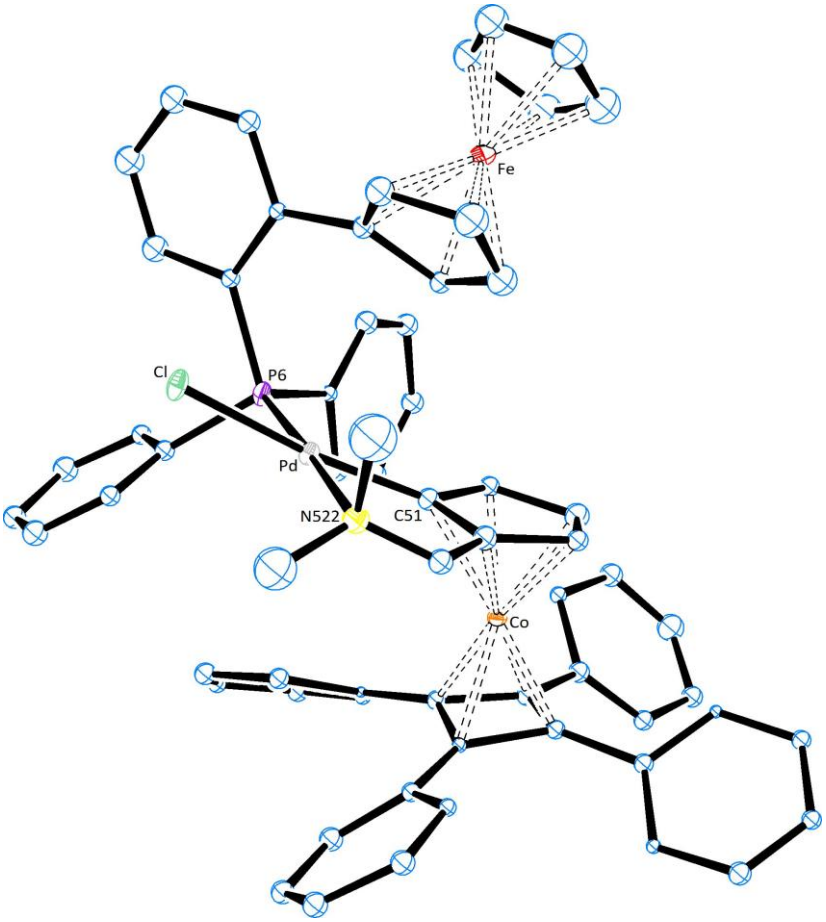
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7438 / 489 / 444
Goodness-of-fit on F^2	1.110
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.1196, $wR2$ = 0.2973
R indices (all data)	$R1$ = 0.1782, $wR2$ = 0.3314
Absolute structure parameter	0.12(3)
Extinction coefficient	n/a
Largest diff. peak and hole	2.845 and −1.789 e Å^{-3}

Diffractometer: *Rigaku AFC12* goniometer equipped with an enhanced sensitivity (HG) *Saturn724+* detector mounted at the window of an *FR-E+ SuperBright* molybdenum rotating anode generator with HF *Varimax* optics (100μm focus). **Cell determination and data collection**: *CrystalClear-SM Expert 3.1 b25* (Rigaku, 2012). **Data reduction, cell refinement and absorption correction**: *CrystalClear-SM Expert 3.1 b25* (Rigaku, 2012). **Structure solution**: *SUPERFLIP* (Palatinus, L. & Chapuis, G. (2007). J. Appl. Cryst. 40, 786-790.) **Structure refinement**: *SHELXL-2012* (Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122). **Graphics:** *ORTEP3 for Windows* (L. J. Farrugia, J. Appl. Crystallogr. 1997, 30, 565.

Special details: There are 2 water molecules in the asymmtreic unit, for which it was not possible to locate their hydrogen atoms, but they are included in the given formula. The data quality is not great, resulting in the use of global ADP restraints (SIMU and DELU).

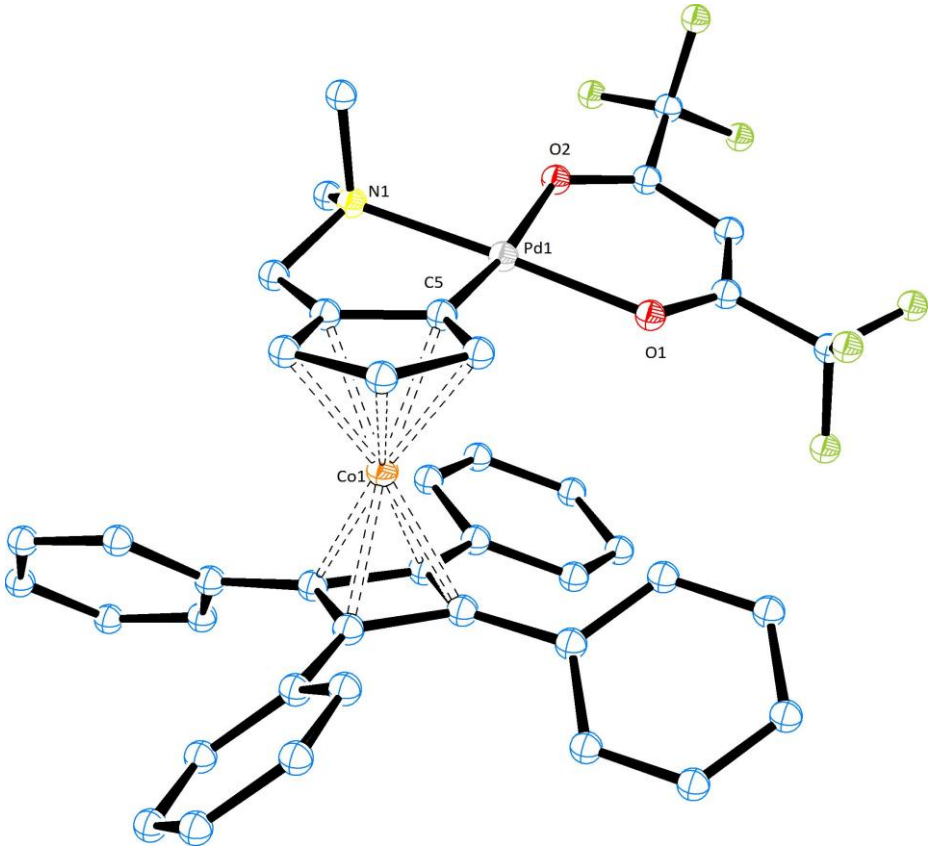
*X-Ray representation for S_p-**265**:*

CCDC-931365



*X-Ray representation for rac-**257**:*

CCDC-931364



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