Synthesis of Functionalised Cobalt Sandwich Complexes for Application in Asymmetric Catalysis

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Supervised by Dr Christopher J Richards

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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 \((\eta^5-(N,N\text{-dimethylaminomethyl})\text{cyclopentadienyl})(\eta^4\text{-tetr phenylcyclobutadiene})\text{cobalt}\) with sodium tetrachloropalladate and \(N\text{-acetyl-D-phenylalanine}\) gave planar chiral palladacycle \(\mu\text{-chloridebis}[\eta^5-(S_p)-2-(N,N\text{-dimethylaminomethyl})\text{cyclopentadienyl},1-C,3'-N](\eta^4\text{-tetrapheny lcy clobutadiene})\text{cobalt}\) dipalladium in 92\% ee, 64\% yield. The enantioselective palladation methodology was subsequently applied to corresponding \(N\text{-diethyl (82\% ee, 39\% yield) and pyrrolidinyl (98\% ee, 43\% yield) cobalt sandw ich complexes. The complex derived from the pyrrolidinyl ligand was tested as a catalyst in the allylic imidate rearrangement (up to 99\% ee), showcasing comparable reactivity and selectivity to that seen in literature examples.\)

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

In addition, access to modified sandwich complexes was realised using the Friedel-Crafts reaction. Complex \((\eta^4\text{-tetr phenylcyclobutadiene})(\eta^5\text{-carbomethoxy)cyclopentadienyl})\text{cobalt}\) underwent reaction with acid chlorides/aluminum chloride to give exclusively \(\text{para}-\text{acylation}.\) Reaction of unsymmetrical \(\text{bis-ary l alkynes [PhCC}(o\text{-RC_6H_4}), R = \text{Me, } \text{iPr}\) with \(\text{Na(C_6H_4CO_2Me) and CoCl(PPh_3)_3}\) gave predominantly \((\eta^4\text{-1,3-diaryl-2,4-diphenylcyclobutadiene})(\eta^5\text{-carbomethoxy)cyclopentadienyl})\text{cobalt metallocenes (1,3-[trans] vs 1,2-[cis] selectivity up to 6:1). Friedel-Crafts reaction on the major isomers gave exclusively the \(\text{para}-\text{acylation of the unsubstituted phenyl groups.}\)
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<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tr>
<td>acac</td>
<td>acetylacetonate</td>
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<tr>
<td>AIBN</td>
<td>2,2’-azoisobutyronitrile</td>
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<tr>
<td>Ar</td>
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<td>Bn</td>
<td>benzyl</td>
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<td>Bu</td>
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</tr>
<tr>
<td>C</td>
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<td>CAP</td>
<td>cobalt amino palladacycle</td>
</tr>
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<td>Cat.</td>
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<td>CIP</td>
<td>Cahn, Ingold, Prelog</td>
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<tr>
<td>IPA</td>
<td>iso-propyl alcohol</td>
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<tr>
<td>L</td>
<td>ligand</td>
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<tr>
<td>$L_n$</td>
<td>a number of ligands</td>
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<tr>
<td>m</td>
<td>multiplet</td>
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<tr>
<td>MALDI</td>
<td>matrix-assisted laser desorption/ionization</td>
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<tr>
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<tr>
<td>psi</td>
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<td>parts per million</td>
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<td>propyl</td>
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<td>PTSA</td>
<td>$p$-toluenesulfonic acid</td>
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<td>q</td>
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<td>STAB</td>
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<td>triplet</td>
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<td>tertiary</td>
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<td>THF</td>
<td>tetrahydrofuran</td>
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<td>Tipp</td>
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<td>TLC</td>
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<tr>
<td>TPAP</td>
<td>tetrapropylammonium perruthenate</td>
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<td>TMS</td>
<td>trimethylsilyl</td>
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<td>Tol</td>
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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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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).

![Image of palladacycle structure]

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). 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 and Suzuki couplings; Buchwald-Hartwig aminations; Stille reactions and other palladium-mediated reactions.

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. This was followed by the use of cyclopalladated azobenzenes, hydrazobenzenes, or N,N-dimethylbenzylamine complexes in
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

![Scheme 1](image)

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 537 and anionic 638 species, depending on the nature of other ligands.
There are a wide variety of donor functionalities found in palladacycles, examples of which include amines, imines, pyridines, thioketones, amides, amidines and oxazolines.\textsuperscript{17,39–44} The most common types of palladacycles are derived from tertiary amines or imines, and complexes from primary amine derivatives are rare.\textsuperscript{45} The metallated carbon atom is usually \( sp^2 \) hybridised as in examples \textbf{4}–\textbf{6}, but complexes with \( sp^3 \), (benzylic \textbf{7}), or \( sp^2 \) vinylic carbons \textbf{8}\textsuperscript{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 \textbf{4}).\textsuperscript{48–52}
The YCY variety of complexes, commonly termed pincer complexes, usually contain two symmetrical five or six-membered rings (Figure 5, 9, 10 and 11). Recently, unsymmetrical YCY complexes such as 12 have also been found and characterised.

![Figure 5](image)

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 metatation and, in turn, dictating the regioselectivity of the reaction.
Common reagents for palladation include tetrachloropalladate salts together with a base,\textsuperscript{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.

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.\textsuperscript{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.\textsuperscript{59}
The cyclometalation of aryl C–H bonds has been extensively studied and details of the mechanism are largely understood. 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). 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.
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.\textsuperscript{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⁻···H–Caryl 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.\textsuperscript{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.
For the formation of palladacycles, the most common sources of Pd(0) used are Pd(PPh$_3$)$_4$, Pd(dba)$_2$ and Pd$_5$(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 $S_p$-$\text{28}$ with Pd$_2$(dba)$_3$ in toluene gives iodo-bridge palladacycle ($S_p$)$_2$-$\text{29}$ (Scheme 7).\textsuperscript{66}

Moreover, oxidative addition can be used to cyclometalate ligands, such as $\text{30}$, that contain reactive functionalities, to give pincer complex $\text{31}$, that can be subsequently derivatised (Scheme 8).\textsuperscript{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).

\[
\begin{align*}
\text{CH}/X + \text{M} & \quad \text{M} + \text{RH} \quad \text{PdX}_2 \\
\text{Y} & \quad \text{M} \quad \text{MX} \\
\text{R} & \quad \text{X} \quad \text{PdX}_2 \\
\end{align*}
\]

M = Li, Hg etc.
X = halogen
R = alkyl, aryl etc.

**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]

**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 PdBr₂COD to give complex 37 (Scheme 11).53
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). Similar cyclometalated compounds containing N- or O-donor atoms could also be accessed using organomercurial reagents.

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 $\sigma$-vinyl palladium complex.\textsuperscript{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.

\begin{align*}
\text{Scheme 13}
\end{align*}

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).\textsuperscript{71} Tertiary allylic amine 41 underwent alkoxy palladation in the presence of lithium tetrachloropalladate and methanol to give chloride-bridged dimer 42.

\begin{align*}
\text{Scheme 14}
\end{align*}

Extension of this methodology allowed for the generation of new palladacycles formed by addition of carbon nucleophiles derived from diethyl malonate (carbopalladation, Scheme 15).\textsuperscript{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.

Interestingly, this methodology can also be used to generate new palladacycles via an intramolecular reaction (Scheme 16). 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.

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 palladacycles 54–56 (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.\textsuperscript{74,75} Acetate dimer palladacycles usually exist as the \textit{transoid} isomer, whereas the halogen dimer metallocycles usually adopt both \textit{cisoid} and \textit{transoid} isomeric forms, although it is usually the \textit{trans} isomer that crystallises.\textsuperscript{19}

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

A sub-category of palladacycles (such as 59) are those that contain a ligand motif comprised of a metalloocene, (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 metalloocene-based palladacycles.

Scheme 19

1.5.1 Central and Planar Chirality in Metalloccenes

A chiral molecule can be defined as a molecule that has a non-superimposable mirror image. Metalloccenes 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 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). If the metalloocene 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). 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 Metalloocene-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 \textit{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 metalloocene 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 \textit{cis} or \textit{trans} isomers with respect to the orientation of the C–Y ligand about the Pd\(_2(\mu-X)_2\) 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.\textsuperscript{83} reported the X-ray crystal structure of cis-\((S_p,S_p)\)-61 in 1996 and in 1999 Mak\textsuperscript{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). Reaction of the racemic palladacycle with (S)-proline in the presence of potassium hydrogen carbonate gave two diastereoisomers (S,S<sub>p</sub>)-65 and (S,R<sub>p</sub>)-65 which could be separated by fractional crystallisation. Similarly, rac-72 could be separated utilising the same method to give phosphopalladacycles (S,S<sub>p</sub>)-68 and (S,R<sub>p</sub>)-68. After separation, the proline adducts could be returned to chloride-bridged dimers by reaction with dilute hydrochloric acid in dichloromethane.

![Scheme 21](attachment:image)

Wu et al.<sup>87</sup> demonstrated the resolution of ketimine-derived palladacycle rac-70 with (S)-leucine, where the resultant diastereoisomers (S,S<sub>p</sub>)-71 and (S,R<sub>p</sub>)-71 were separated using preparative thin-layer chromatography (Scheme 22).<sup>88,89</sup> The diastereomeric adducts could be returned to the chloride-bridged dimers by reaction with LiCl in AcOH.
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 metalloocene-based chiral ligands is \(N,N\)-dimethyl-1-ferrocenylamine (\(R\))-72, also known as Ugi’s amine, named after its discoverer.\(^9\) 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 (\(R\),\(S\))\(_{\text{sp}}\)-73 and (\(R\),\(R\))\(_{\text{sp}}\)-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 (\(R\),\(S\))\(_{\text{sp}}\)-73 could be isolated as a single isomer via precipitation from the reaction media.\(^83\)

**Scheme 22**

**1.6.2 Diastereotopic C–H Activation**

Related trifluoromethyl analogue (\(R\))-74 provided palladacycles (\(R\),\(S\))\(_{\text{sp}}\)-75 and (\(R\),\(R\))\(_{\text{sp}}\)-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)p2-77 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)p2-79 formed.98

The importance of the conformational control over diastereoselectivity was investigated using scalemic deuterated ligand (S)-80 (Scheme 25). Palladation resulted in palladacycles (S,S)p2-81 and (S,R)p2-81 with little stereoinduction (<1%).99
An alternative procedure illustrated by Overman utilised a blocking group in the $\alpha$-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 ferrocencarboxaldehyde 91 or acetylferrocene 92 via condensation with enantiopure primary amines $R^*\text{NH}_2$ (Scheme 27), they offer a quick route to highly enantioenriched palladacycles.
The first example of this chemistry was described in 1997 utilising \((-\text{cis})\)-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. The use of \((R)\)-1-napthylethylamine resulted in the modest preference for compound \((R,S_p)_2\)-97 displaying the same sense of diastereoselectivity. 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. 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)-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)-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)-105 and monomer (S,R_p)-106, which showcased higher diastereoselectivity than for the previous examples (9:1 for (S,R_p)-105: (S,S_p)-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\textsuperscript{17,108,109} or by a lesser known azridine-carboxylic ester ring expansion method.\textsuperscript{110}

Ferrocenyl oxazoline (S)-107, like Ugi’s amine, was shown to undergo highly diastereoselective lithiation,\textsuperscript{108,111,112} and direct palladation yielded (S,S\textsubscript{p})\textsubscript{2}-108 exclusively in 46\% yield (Scheme 29).\textsuperscript{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)\textsubscript{2}-111 and (S)\textsubscript{2}-112, provided that the R group did not contain a C–H bond in the α-position.\textsuperscript{114}

![Scheme 29](image-url)

In the same manner, related pentaphenylferrocene-derived oxazolines (S)-113 and (4S,5S)-114 were shown to undergo cyclometalation to give palladacycles (S,S\textsubscript{p})\textsubscript{2}-115 and (4S,5S,S\textsubscript{p})\textsubscript{2}-116, respectively, in good yield, as single diastereoisomers (Scheme 30).\textsuperscript{115}
In 1999, Richards showed that structurally related cobalt-oxazoline ligand (S)-\textbf{117} also readily underwent palladation to give cobalt-oxazoline palladacycle (COP-OAc), (S,\textit{R}$_p$)$_2$-\textbf{118} again as a single diastereoisomer (Scheme 31).\textsuperscript{17} The opposite configuration for the element of planar chirality, when compared to previous ferroceny1 examples, was rationalised to be due to steric repulsion between the oxazoline moiety and the lower (\textit{\eta}$_4$-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,\textit{S}$_{p}$)$_2$-\textbf{118} diastereoisomer was seen before switching to the resultant major isomer.\textsuperscript{116} A related oxazoline, derived from (S)-\textit{tert}-leuino1, (S)-\textbf{119}, was shown to give the kinetic product for palladation, (as in the ferroceny1 oxazoline series), by treatment with palladium acetate in acetic acid, yielding palladacycle (S, \textit{S}$_{p}$)$_2$-\textbf{120} as a single diastereoisomer.\textsuperscript{117}
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,p)-128 as a single isomer (Scheme 32).  

Oxazoline ligands bearing ruthenium-based metallocenes have also shown high diastereoselectivity upon palladation. Enriched planar chiral ligands (S,p)-123 and (S,p)-124, when palladated, yielded exclusively the peri-palladation products (S,p),2-125 and (S,p),2-126 as a single diastereoisomer (Scheme 33).  

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.

Related pentaphenylferrocene-derived imidazoline complex \( (4R,5S)\)-130 undergoes cyclopalladation to give predominantly \( (4R,5S,R_p)_2\)-131 where, similar to above, the kinetic product is formed, in which the phenyl group is \textit{endo} to the lower \( C_5Ph_5 \) ligand (Scheme 35).\(^{120}\)
The origin of diastereoselection with the similar $N$-sulfonyl-substituted imidozolines (4R,5R)-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 (4R,5S,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
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

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 \((S)\)-\textit{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)\textsubscript{2}146.

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)\textsubscript{2}149 (Scheme 40).
A similar approach to above utilised pentaphenylferrocene derivative (4S, 5S)-130 and iodo compound (4S, 5S, S_p)-150 to generate palladacycle (4S, 5S, S_p)\textsubscript{2}-151 via a highly selective lithiation step (16:1 dr, Scheme 41).\textsuperscript{120}

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)\textsubscript{2}-153 with a dr of 10:1.\textsuperscript{127} Purification of (S,S)\textsubscript{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).\textsuperscript{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.\textsuperscript{128}

Zipp and Overman described the multi-step preparation of enantiopure cyclopalladated \((\eta^6\)-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 \(161\textsuperscript{129}\) with high diastereoselectivity \((\text{dr} = >99:1)\). Further manipulation to imine \(162\) and treatment with Pd(0), under normal conditions gave the palladacycle in good yield.\textsuperscript{21}
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).

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).
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).\textsuperscript{80,130} This resulted in partial enantioselective formation of palladacycle ($R_p)_2\textsuperscript{-64}$, 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 ($R_p)_2\textsuperscript{-64}$ and ($S_p)_2\textsuperscript{-64}$, respectively, with an ee of 81%.\textsuperscript{131}
In 2009, Richards showcased an updated methodology of the Sokolov approach, using \((R)\)-N-acetylphenylalanine as the stoichiometric chiral reagent at pH 8.\textsuperscript{132} The group were able to palladate phosphinophenylferrocenyl ligands \textbf{167} and \textbf{168} to give palladacycles \((S_p)_2\textbf{169}\) and \((S_p)_2\textbf{170}\) in good yield, with moderate enantioselectivities, (59 and 42\% \textit{ee} respectively, Scheme 47). Additionally, they reported that amine ligand \textbf{63} could be palladated using their improved conditions to give palladacycle \((S_p)_2\textbf{64}\), in great yield and a higher enantioselectivity than reported previously (88\% and 96\% respectively).

![Scheme 47](image)

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

Palladacycles may be formed by the exchange of cyclometalated ligands, 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)$_2$-67 in moderate ee, together with recovered amine (R)-174 (Scheme 49).^134

In 2005, Richards illustrated that higher enantioselectivities could be achieved utilising palladacycles (S,R)$_2$-118 and (S,S)$_2$-120 (Scheme 50).^135 Heating prochiral dicyclohexylphosphine 167 with (S,R)$_2$-118, followed by a brine wash, yielded phosphopalladacycle (S)$_2$-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**

With the discovery of the mercury catalysed rearrangement, further investigations into alternative methods of reaction acceleration were undertaken. Electrophilic reagents such as HCl, TiCl₄, AlMe₃ and (ArO)₂AlMe were used and the reaction was shown to be promoted at 111 °C. 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. In contrast, the zero-valent complex Pd(Ph₃)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. These discoveries lead to the generation of new chiral complexes aimed at investigating the asymmetric allylic imidate rearrangement.

**Scheme 52**

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
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\textsuperscript{150} and subsequently by Overman for the PdCl\textsubscript{2}-catalysed Cope rearrangements.\textsuperscript{151}

The proposed mechanism contrasts to the concerted thermal rearrangement pathway, which proceeds \textit{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.\textsuperscript{141}
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. In contrast it was observed that PdCl₂(NCMe)_2 resulted in the near quantitative rearrangement of imidate (E)-178 to (R)-179 within minutes at room temperature. 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.
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). Catalyst $(R,S)_p$-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. 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 $(R,S)_p$-182, which gave $(R)$-179 in 98% yield and 61% ee.

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 $(R)_p$-89 which was shown to be a poor catalyst for the rearrangement (34% yield after 48 hours at 40 °C, 49% ee). Addtion 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). 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).

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). 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.

\[
\begin{align*}
\text{(E or Z)-183} & \quad \xrightarrow{\text{Cat., CH}_2\text{Cl}_2, \ \text{rt}} \quad \text{184} \\
(R_p)_2\text{89} & \quad (S_p)_2\text{185} \\
(S_p)\text{187} & \quad (S,R_p)_2\text{143} \\
(S_p,S_p)\text{186} & \quad (S,R_p)_2\text{188}
\end{align*}
\]

Scheme 56
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<th>Additive (mol %)</th>
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<th>R</th>
<th>Yield [%]</th>
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**Table 1** – Enantioselective rearrangement of allylic N-arylbenzimidates (E)- and (Z)-183, catalysed by planar chiral palladacycles (Scheme 56)<sup>18</sup>

Overman has also utilised ferrocenyl-oxazoline palladacycles (FOP) for the rearrangement. Application of both diastereoisomers (S<sub>S</sub>,S<sub>p</sub>)-143 and (S<sub>R</sub>,R<sub>p</sub>)-143 resulted in a significantly higher enantioselectivity with the (S<sub>R</sub>,R<sub>p</sub>) complex (entries 7 and 8). It was reasoned that in the matched (S<sub>R</sub>,R<sub>p</sub>) 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<sub>S</sub>,S<sub>p</sub>) diastereoisomer, where they are on the same side.<sup>12,126</sup>

Palladacycle (S<sub>p</sub>,R<sub>p</sub>)-188 showed improved enantioselectivities for the rearrangement of both (E)-183 and (Z)-183 arylbenzimidates (entries 9 and 10).<sup>12,126</sup> 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](image-url)

\((E\) or \(Z\))-189 → 190 → 191

\((4R,5S,R_p)_2\)-131 \(\rightarrow\) \((4R,5S,S_p)_2\)-192 \(\text{R} = \text{H}\)

\((4R,5R,S,S_p)_2\)-193 \(\text{R} = \text{Me}\)

\((4R,5R,S,S_p)_2\)-194 \(\text{R} = \text{Ph}\)

\((S,R_p)_2\)-197

\((S,S_p)_2\)-198

Figure 11
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Table 2 - Enantioselective rearrangement of allylic N-(4-methoxyphenyl)trifluoroacetimidates (E)- and (Z)-189, catalysed by planar chiral palladacycles (Scheme 57, Figure 11).  

[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 CHCl₃ 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.\textsuperscript{18} Good activity was shown for the rearrangement of both (\textit{E}-189 and (\textit{Z}-189 using the catalyst derived from (\textit{S,R}_p)\textsubscript{2}-188 (entries 1 and 2). Upon activation with four equivalents of silver trifluoroacetate, good enantioselectivities were seen for the rearrangement of the (\textit{Z})-isomer, albeit with lower yield when compared with the results gained for the (\textit{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.\textsuperscript{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 (4\textit{R,R,R}_p)\textsubscript{2}-131, which was shown to be efficient in the catalysis of (\textit{E})-trifluoroimidates, resulting in good yield and enantioselectivities, (entry 3).\textsuperscript{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 \textit{N}-sulfonyl moiety was reported.\textsuperscript{121} As with previous ferrocene systems, silver salt activation was necessary, but excellent enantioselectivities were obtained for the rearrangement of (\textit{Z})-imidates when using catalysts (4\textit{R,S,R}_p)\textsubscript{2}-192 and (4\textit{R,S,R}_p)\textsubscript{2}-193 (entries 4 and 5). Poorer results were gained when using the (\textit{E})-isomer. The bulkier pentaphenylferrocene derived catalyst (4\textit{R,S,S}_p)\textsubscript{2}-194 proved to be the most efficient catalyst for the rearrangement of (\textit{E})-trifluoroimidates, but conversely was poor for catalysis of the (\textit{Z})-isomer. High enantioselectivity and yield could be achieved and maintained whilst using a low catalyst loading, in the catalysis of (\textit{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 \((SSp)_2\) 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 \(R=\text{Pr or Cy, entries 7 and 8}\)).\(^{115}\) 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 \((Sp,Sp)_2\) 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 \((Sp,Sp)_2\) 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 \((S,Rp)_2\) (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 \((Sp,Sp)_2\) was also shown to catalyse the rearrangement of both \((E)\) and \((Z)-189\) (\(R=\text{Pr}\)), 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 \(S,Rp\) 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 \((\eta^6\text{-arene})\text{tricarbonylchromium}(0)\) complexes \((S,Rp)_2\) and

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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,Rp)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). The activity demonstrated by this system was significantly lower than that of the similar oxazoline analogue.

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,Sp)2-194 and (S,Sp)2-193 (Scheme 58 and Table 3). Substrates 201 where substituent R1 or R2 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 trifluoroacetamide was a competitive reaction pathway. This was suppressed by the addition of a proton sponge, (3–4 equivalents of 1,8-bis(dimehtylamino)naphthalene), as an acid scavenger. This methodology was shown to be tolerant with a wide range of R1 and R2 groups and was subsequently used in the synthesis of α, α-disubstituted α- and β-amino acids.
Scheme 58

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. Precursor</th>
<th>Cat. Loading [mol %]</th>
<th>Additive (mol %)</th>
<th>R¹</th>
<th>R²</th>
<th>t [h]</th>
<th>Yield [%]</th>
<th>ee [%] (config.)</th>
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</thead>
<tbody>
<tr>
<td>1¹¹⁵</td>
<td>(S,S)p₂-195ᵃ</td>
<td>2</td>
<td>AgNO₃ (7.4)</td>
<td>(CH₂)₂Ph</td>
<td>Me</td>
<td>24</td>
<td>71</td>
<td>98 (R)</td>
</tr>
<tr>
<td>2¹¹⁵</td>
<td>(S,S)p₂-195ᵃ</td>
<td>2</td>
<td>AgNO₃ (7.4)</td>
<td>(CH₂)₂Ph</td>
<td>Me</td>
<td>72</td>
<td>90</td>
<td>99 (R)</td>
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<td>AgNO₃ (3.7)</td>
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<td>CH₂OBn</td>
<td>24</td>
<td>98</td>
<td>97 (R)</td>
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<tr>
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<td>AgNO₃ (1.85)</td>
<td>Me</td>
<td>CH₂OBn</td>
<td>24</td>
<td>74</td>
<td>96 (R)</td>
</tr>
<tr>
<td>5¹¹⁵</td>
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<td>4</td>
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<td>CH₂OBn</td>
<td>48</td>
<td>95</td>
<td>97 (R)</td>
</tr>
<tr>
<td>6¹¹⁵</td>
<td>(S,S)p₂-195ᵃ</td>
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<td>AgNO₃ (7.4)</td>
<td>(CH₂)₃OTIPS</td>
<td>CH₂OBn</td>
<td>72</td>
<td>95</td>
<td>97 (R)</td>
</tr>
<tr>
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<td>(4R,5R,S,S)p₂-194ᵇ</td>
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<td>AgTFA (7.5)</td>
<td>(CH₂)₂Ph</td>
<td>Me</td>
<td>60</td>
<td>94</td>
<td>99.6 (R)</td>
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<tr>
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<td>73</td>
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<td>AgTFA (15)</td>
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<td>51</td>
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</tbody>
</table>

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. In 2003, Overman and co-workers made a breakthrough when they showed that \((S,R)p\)-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).

![Scheme 59](image)

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).

Chloride-bridged dimer \((S,R)p\)-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). 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).

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<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. Precursor</th>
<th>Cat. Loading [mol %]</th>
<th>T [°C]</th>
<th>Solvent</th>
<th>t [h]</th>
<th>R</th>
<th>Yield [%]</th>
<th>ee [%] (config.)</th>
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<td>rt</td>
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<td>Me</td>
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<td></td>
<td></td>
<td>(CH₂)₂Ph</td>
<td>83</td>
<td>96 (S)</td>
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<td>(S,R)p₂⁻197³⁵⁵</td>
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<td>38</td>
<td>CH₂Cl₂</td>
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<td>'Bu</td>
<td>99</td>
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<td>38</td>
<td>CH₂Cl₂</td>
<td>18</td>
<td>'Bu</td>
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<td>Me</td>
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<td>MeCN</td>
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<td>Me</td>
<td>91</td>
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<td>29 'Bu</td>
<td>95</td>
<td>95 (S)</td>
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<td>Me</td>
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<td>Bn</td>
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<td>92 (S)</td>
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<tr>
<td>8</td>
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<td>60</td>
<td>CH₂Cl₂</td>
<td>24</td>
<td>(CH₂)₂Ph</td>
<td>99</td>
<td>95 (R)</td>
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</table>

Table 4 - Enantioselective rearrangement of allylic trichloroacetimide (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 AgNO₃ and 1 mol % of 1,8-bis(dimethylamino)naphthalene.
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).\textsuperscript{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).\textsuperscript{115} Activation of FOP (S,S)p\textsubscript{2}-195 with 3.7 equivalents of silver nitrate gave a catalyst with comparable activity to that seen in the COP systems.

\textit{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 \textbf{207} into phosphoramides \textbf{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 \textasciitilde24.4 kcal mol\textsuperscript{1}.\textsuperscript{158} The process has been shown to proceed at room temperature when catalysed by PdCl\textsubscript{2}(MeCN)\textsubscript{2},\textsuperscript{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\textsubscript{2}-\textbf{197} (COP-Cl), where reaction with (E)-\textbf{207} (R = Et), gave (S)-\textbf{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.\(^{158}\)

![Scheme 61](image)

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.

![Scheme 62](image)

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.

\[
\text{(E) or (Z)-211} \quad \text{CH}_2\text{Cl}_2, 40 \degree \text{C} \quad 40 \text{h} \quad \text{(S) or (R)-212}
\]

\[
\begin{align*}
\text{R} & = \text{Et, } \text{"Pr, Ph, CH}_2\text{OTBDMS} \\
\text{(E)-211} & \rightarrow \text{(S)-212} \quad 33\text{-}91\% \text{ yield, 47\text{-}86\% ee} \\
\text{(Z)-211} & \rightarrow \text{(R)-212} \quad 61\text{-}93\% \text{ yield, 83\text{-}96\% ee}
\end{align*}
\]

Scheme 63

1.7.3 Miscellaneous Reactions Catalysed by Planar Chiral Palladacycles

1.7.3.1 Intramolecular Aminopalladation

In 2002, Overman and co-workers published the enantioselective synthesis of vinyl-substituted 2-oxazolidinones 213 from (Z)-allyl acetates 214 using FOP catalyst (S,R)p-188 (Scheme 64, Table 5).

\[
\begin{align*}
\text{OAc} & \quad \text{(Z)-213} \\
\text{X} & = \text{CH}_2 \quad \text{NH} \\
\text{NHTs} & \quad \text{Catalyst} \quad \text{rt} \\
\text{X} & \quad \text{NHTs} \quad \text{(S)-214}
\end{align*}
\]

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 = CH₂ 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% $ee$).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. Precursor</th>
<th>Cat. Loading [mol %]</th>
<th>Additive (mol %)</th>
<th>X</th>
<th>Solvent (ratio)</th>
<th>$t$ [h]</th>
<th>Yield [%]</th>
<th>$ee$ [%] (config.)</th>
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<tbody>
<tr>
<td>1$^{161}$</td>
<td>($S,R_p$)$_2$-188[a]</td>
<td>5</td>
<td>AgTFA (20)</td>
<td>O</td>
<td>CH$_2$Cl$_2$/MeNO$_2$ (1:1)</td>
<td>48</td>
<td>96</td>
<td>$91 (S)$</td>
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<tr>
<td>2$^{161}$</td>
<td>($S,R_p$)$_2$-188[a]</td>
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<td>AgTFA (4)</td>
<td>O</td>
<td>CH$_2$Cl$_2$/MeNO$_2$ (1:1)</td>
<td>48</td>
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<td>$90 (S)$</td>
</tr>
<tr>
<td>3$^{161}$</td>
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<td>AgTFA (2)</td>
<td>O</td>
<td>CH$_2$Cl$_2$/MeNO$_2$ (1:1)</td>
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</tr>
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<td>AgTFA (20)</td>
<td>NH</td>
<td>CH$_2$Cl$_2$/MeNO$_2$ (1:1)</td>
<td>48</td>
<td>96</td>
<td>$90 (S)$</td>
</tr>
<tr>
<td>5$^{161}$</td>
<td>($S,R_p$)$_2$-188[a]</td>
<td>5</td>
<td>AgTFA (20)</td>
<td>CH$_2$</td>
<td>CH$_2$Cl$_2$/MeNO$_2$ (1:1)</td>
<td>48</td>
<td>95</td>
<td>$90 (S)$</td>
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<tr>
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<td>O</td>
<td>CH$_2$Cl$_2$</td>
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<td>$&gt;99$</td>
<td>$71 (S)$</td>
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<tr>
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<td>94</td>
<td>$92 (S)$</td>
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<td>9$^{162}$</td>
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<td>AcOH</td>
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<td>75</td>
<td>$90 (S)$</td>
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**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.
Performing the reaction in only acetic acid caused erosion in yield and an elongated reaction time (entry 9).

The formation of spirocyclic 4-vinylazolidin-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.

\[
\text{Scheme 65}
\]

1.7.3.2 Allylic Ester and Ether Synthesis

During investigations into the formation of the aforementioned 4-vinylazolidin-2-ones, Overman and his group noticed that whilst using an acetoxybutenyl trichloroacetimidate as a starting reagent, they isolated a \(\sim 1:1\) mixture of desired 4-vinylazolidine and an allylic ester. The result suggested that \(S_n 2'\) displacement of the imidate by acetic acid was occurring competitively with intramolecular cyclisation of the imidate nitrogen.\(^\text{15}\)

Subsequent experiments revealed that using an excess of acetic acid (or other carboxylic acids) and 1 mol % of the acetate-bridge dimer \((S,R_p)_{218}\) (COP-OAc), (Z)-203 could be converted enantioselectively into allylic esters 217 (Scheme 66).\(^\text{15,163}\) This esterification reaction has been adapted to give an iterative approach to the synthesis of 1,3-polyols.\(^\text{164}\)
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). A wide range of imidate substrates were subjected to 1 mol % of (S,R)p-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.

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). Using the trichloroimidate moiety as a leaving group, reaction of substituted phenol (E)-219 with catalyst ent-(S,R)p-118 [ie. (R,S)p-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 benzoazines (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)$_2$-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).

![Scheme 68]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Cat. Loading [mol %]</th>
<th>Additive (equiv.)</th>
<th>X</th>
<th>Y</th>
<th>R</th>
<th>Solvent</th>
<th>t [h]</th>
<th>Yield [%]</th>
<th>ee [%] (config.)</th>
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<tr>
<td>1</td>
<td>ent-(S,R)$_2$-118$^a$</td>
<td>0.5</td>
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<td>CH$_2$Cl$_2$</td>
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<td>92 (S)</td>
</tr>
<tr>
<td>2</td>
<td>ent-(S,R)$_2$-118$^a$</td>
<td>2</td>
<td>None</td>
<td>O</td>
<td>OC(=NH)CCl$_3$</td>
<td>H</td>
<td>CH$_2$Cl$_2$</td>
<td>18</td>
<td>90</td>
<td>94 (S)</td>
</tr>
<tr>
<td>3</td>
<td>ent-(S,R)$_2$-118$^a$</td>
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<td>None</td>
<td>NTs</td>
<td>OC(=NH)CCl$_3$</td>
<td>H</td>
<td>CH$_2$Cl$_2$</td>
<td>15</td>
<td>98</td>
<td>98 (S)</td>
</tr>
<tr>
<td>4</td>
<td>(S,R)$_2$-118$^b$</td>
<td>2</td>
<td>KF (1)</td>
<td>CH$_2$</td>
<td>OAc</td>
<td>H</td>
<td>CH$_2$Cl$_2$</td>
<td>24</td>
<td>89</td>
<td>94</td>
</tr>
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<td>2</td>
<td>KF (1)</td>
<td>CH$_2$</td>
<td>OAc</td>
<td>4-Br</td>
<td>CH$_2$Cl$_2$</td>
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<td>82</td>
<td>88</td>
</tr>
<tr>
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<td>(S,R)$_2$-118$^b$</td>
<td>2</td>
<td>KF (1)</td>
<td>CH$_2$</td>
<td>OAc</td>
<td>4-Br</td>
<td>CHCl$_3$</td>
<td>10</td>
<td>92</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>(S,R)$_2$-118$^b$</td>
<td>2</td>
<td>KF (1)</td>
<td>CH$_2$</td>
<td>OAc</td>
<td>4-OMe</td>
<td>CH$_2$Cl$_2$</td>
<td>36</td>
<td>95</td>
<td>95</td>
</tr>
</tbody>
</table>

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. 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-acyloxy palladation 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. 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).

Scheme 69
Peters has had particular success in utilising 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). 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, \((\text{AgO}_2\text{S-Tipp})\), 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.

\[
\begin{align*}
\text{\text{Scheme 70}}
\end{align*}
\]

In 2010, Peters published work on a domino aza-lactone formation-Michael addition reaction of benzoylated racemic amino acids 224 with \(\beta\)-substituted enones 225 catalysed by FBIP-Cl (Scheme 71). 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.

\[
\begin{align*}
\text{HO}_2\text{C} = \text{NH} & \quad \text{Ph} \\
\text{+} & \\
\text{R}^1 & \quad \text{O} \quad \text{Ph} \\
\text{R}^2 \quad \text{O} \quad \text{R}^3 & \quad \text{O} \\
\text{R}^1 = \text{Me, Et, } \text{nPr, Bn} & \\
\text{R}^2 = \text{Ph, } \text{iPr, } 3,4\text{-}(\text{OMe})_2\text{C}_5\text{H}_3, 4\text{-Br C}_6\text{H}_4, 4\text{-OMeC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-O}_2\text{NC}_6\text{H}_4 & \\
\text{R}^3 = \text{Me, Et, Ph} & \\
\text{64–95% yield, } >98:2 \text{ dr, 76–99% ee} & \\
\end{align*}
\]

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 \textit{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.\textsuperscript{171,172} Instead, acetic anhydride was used in conjunction with (S,S\textsubscript{p})\textsubscript{2}195 (FOP-Cl), to give aza-lactones 228 in moderate yield and excellent selectivities (Scheme 72).\textsuperscript{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.

\[
\begin{align*}
\text{HO}_2\text{C} = \text{NH}_2 & \quad \text{Me} \\
\text{+} & \\
\text{R}^1 & \quad \text{O} \quad \text{Me} \\
\text{R}^2 \quad \text{O} \quad \text{R}^3 & \quad \text{O} \\
\text{R}^1 = \text{Me, Et, } \text{nPr, } \text{nBu, } \text{iBu} & \\
\text{R}^2 = \text{Me, Ph, } \text{iPr, } 3,4\text{-}(\text{OMe})_2\text{C}_5\text{H}_3, 4\text{-Br C}_6\text{H}_4, 4\text{-OMeC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-O}_2\text{NC}_6\text{H}_4 & \\
\text{R}^3 = \text{Me, Et} & \\
\text{26–72% yield, } >99:1 \text{ dr, 62–99% ee} & \\
\end{align*}
\]

Scheme 72
Peters has also published an extension of the methodology to the synthesis of spirocyclic azlactones by a double Michael addition. By taking a benzoyl protected amino acid and reacting in the presence of (4R,5R,S,S)p-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 (4R,5R,S,S)p-233 (figure 14).

Scheme 72

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).

\[
\text{HO}_2\text{C}\text{N}\text{HPh} + \text{R}^2\text{NO}_2 \xrightarrow{\text{(4R,5R,S,S)$_2$-196 (FBIP-Cl, 5 mol %), AgOTf (20 mol %), Mn(OAc)$_2$, AcOH, Ac$_2$O, n-hexane, 50 °C, 20 h}} \text{R}^1\text{NHOAc}
\]

\(\text{R}^1 = \text{Me, Et, }^{\text{n}}\text{Pr, }^{\text{n}}\text{Bu,}
\]
\(\text{R}^2 = \text{Ph, 4-Br C}_6\text{H}_4, 4\text{-OMeC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-MeC}_6\text{H}_4}
\]

78–95% yield, 78–94% ee

Scheme 73

Under optimized conditions, 5 mol % of (4R,5R,S,S)$_2$-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, 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. 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 and more recently Richards reported updated conditions allowing for the generation of palladacycle (S)p2-64 in 96% ee using N-acetyl-D-phenylalanine (Scheme 74).

Cobalt sandwich complexes have been shown to be versatile ligands in the synthesis of planar chiral palladium complexes. 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.

![Scheme 75](image)

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.

![Scheme 76](image)

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 \( \text{241} \) with \( \text{PPh}_3 \) and NBS gives an intermediary bromomethyl
metallocene, which can be quenched with a variety of secondary amines to give \( \text{242–244} \), in
a range of yields. Differentially substituted amines can also be synthesised using a similar
method, where \( \text{R} \) 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.

Other amines could be accessed \textit{via} oxidation of primary alcohol \( \text{241} \) with TPAP/NMO to
give aldehyde \( \text{245} \), which readily underwent reductive amination with benzylamine to give
secondary amine \( \text{246} \) in near quantitative yield (Scheme 78). Subsequent hydrogenolysis
gave the debenzyalted primary amine \( \text{247} \) and not \( \left( \eta^5\text{-methylcyclopentadienyl}\right) \left( \eta^4\text{-tetraphenylecyclobutadiene}\right) \) cobalt, an alternative reduction product which would have
resulted from hydrogenolysis of the nitrogen-carbon (\( \alpha \)-metallocene) bond. Further
differentially substituted amines have been formed previously by installation of a Cbz-group
and subsequent reduction.\(^{184}\)
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. Also the palladation of amine 237 has been reported previously using a mixture of lithium tetrachloropalladate and sodium acetate in methanol. 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).
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 \textit{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 \textit{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 °C and for a longer reaction time, both of which yielded no significant change in enantioselectivity or reaction yield.

\[
\begin{align*}
{(R)\text{-proline, NaHCO}_3,} & \quad \text{acetone/H}_2\text{O} \\
& \quad 92\% \\
\begin{array}{c}
\text{(S)proline, NaHCO}_3, \\
\text{acetone/H}_2\text{O}
\end{array} & \quad 92\%
\end{align*}
\]

Scheme 80
The absolute configuration of \((S_p)_2\text{-}248\) was established by recrystallisation of the proline adduct \(S,S_p\text{-}249\) from \(\text{CH}_2\text{Cl}_2/\text{hexane}\). 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 \(S,S_p\text{-}249\) 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 \(R,S_p\text{-}249\), 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 η¹- and η²-
acetate ligands are associated (A). Dissociation of an oxygen of the $\eta^2$-acetate ligand via transition 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).\textsuperscript{64,186}

![Scheme 82](image)

**Figure 17**

A mechanism consistent with carboxylate accelerated cyclopalladation has an intramolecular isotope effect of >1.\textsuperscript{188–193} It has been shown that a value of 2.5 is seen for the palladation of $N,N$-dimethyl- derivative\textsuperscript{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).\textsuperscript{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.
A proposed mechanism for the process based on DFT calculations of the cyclometallation of dimethylbenzylamine 19 by palladium(II) acetate, and an extension of this process to the N-acetyl-D-phenylalanine mediated palladation of phosphinoferrocenes, is postulated in Scheme 84. In this process amine 237, amino acid and sodium tetrachloropalladate initially form a chiral amine-η²-carboxylate ligated complex 253. This leads to transition state 254 in which the carbonyl oxygen of the η¹-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.
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 metalloocene $(S_p)_2$-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.\(^{104}\) It could also be possible that the deprotonation may be facilitated by a second $\eta^1$-carboxylate ligand, *i.e.* where ligand X (Scheme 84) is a carboxylate. The reaction would therefore be slower with the $(S/R)$ intermediate monomer.

<table>
<thead>
<tr>
<th>ee of N-Acetyl-D-Phenylalanine</th>
<th>Major Integral</th>
<th>Minor Integral</th>
<th>ee of $(S_p)_2$-248</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>1.00</td>
<td>1.00</td>
<td>0</td>
</tr>
<tr>
<td>27</td>
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<td>0.92</td>
<td>42</td>
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</tr>
<tr>
<td>100</td>
<td>1.00</td>
<td>0.06</td>
<td>94</td>
</tr>
</tbody>
</table>

*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 $\psi$ and $\phi$, Figure 19) in peptide conformational analysis of similar examples such as Ac-ala-NHMe. The extended $\beta$-conformation ($\psi \approx 120, \phi \approx -120$) is the most stable in water. In this transition state (255), the $\eta^1$-carboxylate ligand is orientated in such a way that the methine hydrogen of the stereogenic center is pointed towards the amine substituent. 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](image)

**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 diastereisomer $R,S_p$-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$_2$Cl$_2$. If
necessary, further purification by recrystallisation was accomplished from CH$_2$Cl$_2$/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$_2$Cl$_2$ 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](image-url)
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$_2$Cl$_2$/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. 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. 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 \(R \neq R\)), all with no success, inferring that such systems seem to have the wrong balance, in terms of electronics and steric demands, to facilitate the cyclopalladation.\(^{184}\)

![Scheme 86](image)

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 \(^1\text{H}-\text{NMR}\) 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 \(^1\text{H}-\text{NMR}\) sample with \(S,S_p\)-261.
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).
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. 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, and it has been reported that reaction of COP-OAc, (S,R)-118, with prochiral phosphines 167 and 168 gives phosphopalladacycles $S_p$-262 and $S_p$-263 in up to 95% ee ($R = \text{Cy}$). 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 ($R = \text{Ph}$) 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 \( R'_{262} \) 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.\(^{115}\)

Scheme 88

Reaction of ligands 167 and 168 with chloride bridged palladacycle \((S_p)_2\cdot248\) resulted in the formation of monomeric adducts \( S_p\cdot264 \) and \( S_p\cdot265 \) (Scheme 89). Recrystallisation of \( S_p\cdot265 \) from CH\(_2\)Cl\(_2\)/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 \( \text{trans} \) 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).\(^\text{184}\)

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 $\eta^1$-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.\(^\text{64,186}\) The process starts with formation of monomeric acetate compound 266 followed by dissociation of the amine ligand to form a $\eta^2$-
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.

\[
(S_p)_{2}^{250} \xrightarrow{167 \text{ or } 168} \xrightarrow{i) \text{ retro-CMD} - 237 \rightleftharpoons 267 \text{ or } R_p \text{-263} \xrightarrow{\text{Na(acac)}} \]

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.\textsuperscript{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.\textsuperscript{11,201} Reaction of \textit{p}-anisidine \textbf{269} with TFA and triphenylphosphine in carbon tetrachloride gave imidoyl chloride \textbf{270} in 68\% yield after distillation. Imidates (\textit{E})- or (\textit{Z})-\textbf{271} could then be readily accessed by reaction of the imidoyl chloride with corresponding (\textit{E})- or (\textit{Z})-allylic alcohol after deprotonation with sodium hydride (Scheme 91).

\begin{center}
\begin{tikzpicture}
\node at (0,0) [draw] (269) {\textbf{269}};
\node at (2,0) [draw] (270) {\textbf{270}};
\node at (6,0) [draw] (271) {\textbf{271}};
\draw[->] (269) -- node [midway, above] {TFA, PPh$_3$, NEt$_3$, CCl$_4$, 0 - 80 °C} (270);
\draw[->] (270) -- node [midway, above] {NaH, THF, 0 °C - rt} (271);
\end{tikzpicture}
\end{center}

\textbf{Scheme 91}

Catalysis was first investigated with the representative (\textit{E})- and (\textit{Z})-\textit{N}-\textit{(para}-methoxyphenyl)trifluoroacetimidate substrates \textbf{271} (Scheme 92, Table 8). Reactions were first carried out to check catalytic activity using 5 mol \% of (\textit{S}$_p$)-\textbf{248} and 0.6 M solution of substrate at room temperature for 60 h. These conditions gave modest conversion for the formation of (\textit{R})-\textbf{272} (75\% ee) and (\textit{S})-\textbf{272} (20\% ee) from the corresponding \textit{E} and \textit{Z} substrates respectively, (entries 1 and 2). These conditions were repeated using palladacycle (\textit{S}$_p$)$_2$-\textbf{259}, providing a similar result for the \textit{E} substrate, but showcasing an increased selectivity when using the \textit{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.\textsuperscript{202}
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.\textsuperscript{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.\textsuperscript{202} As such these conditions were tested, and with the addition of 3.8 equivalents with respect to (S)<sub>p</sub>-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).\textsuperscript{203}

![Scheme 93](image)

As with the previous example, the N,N-dimethylamino derived palladacycle (S)<sub>p</sub>-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<sub>2</sub>Cl<sub>2</sub> 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  | \(x\)  | R     | Solvent | Time | Temp | Imidate | Conv. [\(\%\)] | ee of 204 [%] |  
|-------|-----------|--------|-------|---------|------|------|---------|----------------|---------------|----------|  
| 1     | \((S_p)_2\text{-}248^{[d]}\) | 5      | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 89 (65)        | 55 (R)        |          |  
| 2     | \((S_p)_2\text{-}248^{[d]}\) | 2.5   | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 45 (R)         | 57 (R)        |          |  
| 3     | \((S_p)_2\text{-}248^{[d]}\) | 1     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 33 (R)         | 62 (R)        |          |  
| 4     | \((S_p)_2\text{-}248^{[d]}\) | 0.5   | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 22 (R)         | 68 (R)        |          |  
| 5     | \((S_p)_2\text{-}259\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 51 (R)         | 86 (R)        |          |  
| 6     | \((S_p)_2\text{-}259\) | 2.5   | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 61 (R)         | 25 (R)        |          |  
| 7     | \((S_p)_2\text{-}259\) | 1     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 30 (R)         | 23 (R)        |          |  
| 8     | \((S_p)_2\text{-}259\) | 0.5   | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 29 (R)         | 27 (R)        |          |  
| 9     | \((S_p)_2\text{-}259^{[d]}\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 30 (R)         | 71 (R)        |          |  
| 10    | \((S_p)_2\text{-}259^{[d]}\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | >99 (77)       | 73 (R)        |          |  
| 11    | \((S_p)_2\text{-}259^{[d]}\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | >99 (78)       | 99 (R)        |          |  
| 12    | \((S_p)_2\text{-}259^{[d]}\) | 2     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 34 (R)         | 76 (R)        |          |  
| 13    | \((S_p)_2\text{-}259^{[d]}\) | 1     | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 8 (R)          | 64 (R)        |          |  
| 14    | \((S_p)_2\text{-}259^{[d]}\) | 0.5   | \(^{1}\text{Pr}\) | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 7 (R)          | 64 (R)        |          |  
| 15    | \((S_p)_2\text{-}259\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 95 (81)        | 82 (R)        |          |  
| 16    | \((S_p)_2\text{-}259\) | 2     | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 68 (R)         | 78 (R)        |          |  
| 17    | \((S_p)_2\text{-}259\) | 0.5   | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 32 (R)         | 55 (R)        |          |  
| 18    | \((S_p)_2\text{-}259^{[d]}\) | 5     | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 84 (58)        | 80 (R)        |          |  
| 19    | \((S_p)_2\text{-}259^{[d]}\) | 2     | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 79 (60)        | 88 (R)        |          |  
| 20    | \((S_p)_2\text{-}259^{[d]}\) | 0.5   | \(^{1}\text{Pr}\) | CH\(_2\text{CN}\) | 48   | 70   | 2.6     | 25 (R)         | 32 (R)        |          |  
| 21    | \((S_p)_2\text{-}259^{[d]}\) | 5     | Ph    | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 65 (R)         | 5 (R)         |          |  
| 22    | \((S_p)_2\text{-}259^{[d]}\) | 5     | Allyl | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 58 (55)        | 71 (R)        |          |  
| 23    | \((S_p)_2\text{-}259^{[d]}\) | 5     | Me    | CH\(_2\text{Cl}_2\) | 39   | 38   | 0.6     | 66 (66)        | 91 (R)        |          |  
| 24    | \((S_p)_2\text{-}259^{[d]}\) | 5     | Bn    | CH\(_2\text{Cl}_2\) | 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 \(^1\text{H-}\text{NMR spectroscopy.}\) [c] Determined by chiral HPLC analysis. [d] With 4 \(x\) mol % of 1,8-bis(dimethylamino)naphtalene. [e] With 3.8 mol % of AgNO\(_3\).

Using analogous conditions to the \(N,N\)-dimethylamino derivative, \((S_p)_2\text{-}259\) was tested for catalytic activity (entries 5–8). Modest conversions were seen over the range of catalyst loadings, but good selectivity for \((R\text{-}204)\) (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 CH₃CN 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 \((R)-204\) \((R = \text{Bn and Me})\) 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 \(\eta^2\)-olefin coordinated species. Subsequent dissociation of the new alkene relinquishes the rearranged product and catalyst.

![Scheme 94](image)

A model for stereoinduction has been postulated previously for the COP-Cl catalysed rearrangement of trichloroacetimidates, using \(2-(2\text{-furyl})-2\text{-oxazoline}\) as an electronic model for the chiral oxazoline ligand in COP-Cl.\(^{13}\) It was shown that an olefin favoured coordination \(\text{trans}\) to the oxazoline to give intermediate \(\text{trans-274}\) over the corresponding \(\text{cis}\)
isomer, \textit{cis-274}, by nearly 7 kcal mol\textsuperscript{-1} (Scheme 95). This is in agreement with the established order of the kinetic trans effect\textsuperscript{205} where in transition complex \textit{trans-274} the π-accepting chloride ligand is trans to the strongest π-donor, the carbanion ligand. It was stated that this \textit{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\textsuperscript{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 (\textit{S}\textsubscript{p} palladacycle gives \textit{R} product) being the same in the COP and CAP systems.

\textbf{Scheme 95}

From the \textit{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.
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 \((\eta^5\text{-}(\text{dimethylaminomethyl})\text{cyclopentadienyl})\text{-}(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\) 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 \textit{via} a concerted metallation-deprotonation pathway mediated by a
chiral $\eta^1$-carboxylate ligand, which is consistent with an intramolecular isotope effect $>1$, (experimentally determined to be 2.5 for this process). The enantiopurity of $(S)_p$-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 $(S)_p$-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).

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](image)

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](image)
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 Rf 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).

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. 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 \( R = \text{CH}_2\text{Cy} \) (S)-283 (Entry 4).

The formation of a palladacycle containing complex can be confirmed by inspection of the \(^1\text{H}\)-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 \( \nu(\text{C}=\text{N}) \) to 1578 cm\(^{-1}\) from the value of 1656 cm\(^{-1}\) measured for (S)-283, and by the single

![Scheme 100](image)

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxazoline (substituent)</th>
<th>Solvent(^{[a]})</th>
<th>Major product</th>
<th>Diastereomeric Ratio (dr)(^{[b]})</th>
<th>Yield [%](^{[c]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(S)-117 (iPr)</td>
<td>AcOH</td>
<td>(S,R(^p))(_2)-118</td>
<td>&gt;100:1</td>
<td>72</td>
</tr>
<tr>
<td>2</td>
<td>(S)-281 (Me)</td>
<td>AcOH</td>
<td>289</td>
<td>n/a</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>(S)-282 (CH(_2)iPr)</td>
<td>AcOH</td>
<td>290</td>
<td>n/a</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>(S)-283 (CH(_2)Cy)</td>
<td>AcOH</td>
<td>(S,S(^p))(_2)-287</td>
<td>&gt;100:1</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td>(S)-284 (CH(_2)Ph)</td>
<td>AcOH</td>
<td>291</td>
<td>n/a</td>
<td>89</td>
</tr>
</tbody>
</table>
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 ($+942$)\textsuperscript{17} and $(S,S_p)_2$-120 ($-903$)\textsuperscript{17} 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 (\textit{vide infra}) and $(S,R_p)_2$-118 (R = CH$_2$Cy, CH$_2$Pr and iPr 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$_2$Cy) was later conclusively confirmed to be $S_p$ by X-ray crystallography analysis of similar palladacycle $(S,S_p)_2$-286 (R = CH$_2$Pr) (\textit{vide infra}).

![CD spectra of palladacycles](image)

\textbf{Figure 27}– CD spectra of palladacycles $(S,R_p)_2$-118, $(S,S_p)_2$-286 and $(S,S_p)_2$-287.
By comparison of the cyclopentadienyl region of the $^1$H-NMR spectra for oxazoline ligand (S)-282 (R = CH$_2$Pr), the precipitated intermediate 290 and palladacycle (S,S$_p$)-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 [b]).
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)\textsubscript{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 \textsuperscript{1}H-NMR spectrum to those observed previously for the analogous \textit{trans}-chloride adduct 292.\textsuperscript{117} The \textit{trans}-geometry was assigned by comparison with other complexes of general structure Pd(OAc)\textsubscript{2}L\textsubscript{2}.\textsuperscript{206,207} Two of the four diastereotopic cyclopentadienyl proton signals in all of these \textit{trans}-adducts are observed at a significantly higher chemical shift compared to the starting oxaxoline ligands (Figure 28 [b], \textit{e.g.} 5.98 and 5.72 for intermediate 290). This may be due to the proximity of cyclopentadienyl \textalpha-\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 \textit{trans}-chloride adduct 292.\textsuperscript{117}

\begin{center}
\includegraphics[width=\textwidth]{scheme101.png}
\end{center}

\textbf{Scheme 101}

An attempt to convert adduct 290 (R = CH\textsubscript{2}Pr) into a palladacycle was carried out by re-heating the intermediate in acetic acid at 95 °C for 30 minutes. This resulted only in

101
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.

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.

**Figure 29**

HMBC spectra of 293:  
NOeSY spectra of 293:
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 \(^1\text{H}-\text{NMR}\) 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 \(^1\text{H}-\text{NMR}\) spectra; in particular peaks for the Cp-protons and the CH of the hfacac ligand were most useful.
Table 11

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxazoline (substituent)</th>
<th>Solvent (^{[a]})</th>
<th>Major product</th>
<th>Diastereomeric Ratio (dr) (^{[b]})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(S)-117 ('Pr)</td>
<td>CH(_2)Cl(_2)</td>
<td>(S,S(_p))-118</td>
<td>2:1</td>
</tr>
<tr>
<td>2</td>
<td>(S)-281 (Me)</td>
<td>CH(_2)Cl(_2)</td>
<td>(S,S(_p))-294</td>
<td>2.5:1(^{[c]})</td>
</tr>
<tr>
<td>3</td>
<td>(S)-282 (CH(_2)Pr)</td>
<td>CH(_2)Cl(_2)</td>
<td>(S,S(_p))-295</td>
<td>13:1(^{[c][d]})</td>
</tr>
<tr>
<td>4</td>
<td>(S)-283 (CH(_2)Cy)</td>
<td>CH(_2)Cl(_2)</td>
<td>(S,S(_p))-296</td>
<td>1.5:1(^{[e]})</td>
</tr>
<tr>
<td>5</td>
<td>(S)-284 (CH(_2)Ph)</td>
<td>CH(_2)Cl(_2)</td>
<td>n/a</td>
<td>1:1(^{[f][g]})</td>
</tr>
<tr>
<td>6</td>
<td>(S)-282 (CH(_2)Pr)</td>
<td>PhMe</td>
<td>n/a</td>
<td>1:1(^{[e]})</td>
</tr>
<tr>
<td>7</td>
<td>(S)-283 (CH(_2)Cy)</td>
<td>PhMe</td>
<td>n/a</td>
<td>1:1(^{[e]})</td>
</tr>
<tr>
<td>8</td>
<td>(S)-284 (CH(_2)Ph)</td>
<td>PhMe</td>
<td>(S,R(_p))-297</td>
<td>1.4:1(^{[e][h]})</td>
</tr>
</tbody>
</table>

\(^{[a]}\) At R.T., 16 h. in CH\(_2\)Cl\(_2\) 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\(_2\)Cl\(_2\)/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\(_2\)Cl\(_2\) 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 \(\text{CH}_2\text{Cl}_2\) (where \(R = \text{Me}, \text{CH}_2\text{iPr}\) and \(\text{CH}_2\text{Cy}\) 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 \((S)-117\) \((R = \text{Pr})\) 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 \((\text{vide infra})\). Reaction of oxazoline ligands where \(R = \text{CH}_2\text{iPr}, \text{CH}_2\text{Cy}\) and \(\text{CH}_2\text{Ph}\) in toluene resulted in little/no selectivity (entries 6, 7 & 8).
The palladation of the oxazoline (S)-284 (R = CH\textsubscript{2}Ph) resulted in the formation of \textit{exo} palladation product 298, in which there is a palladacycle containing an \textit{ortho}-carbon/palladium bond on the oxazoline benzyl substituent. This process proceeds \textit{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 \textit{via} the \textit{endo} pathway, there is a competitive process whereby a 6-membered ring is formed by removal of a proton from the \textit{ortho}-carbon of the benzyl substituent (Scheme 104). There was little selectivity for the \textit{endo} or \textit{exo} product when the palladation was carried out in either toluene or CH\textsubscript{2}Cl\textsubscript{2}, (entries 5 & 8), and there seems to be little discrimination as a function of the size of ring formed.\textsuperscript{209} The formation of the \textit{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.\textsuperscript{210}

![Scheme 105](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Complex (substituent)</th>
<th>Solvent\textsuperscript{[a]}</th>
<th>Major product</th>
<th>Diastereomeric Ratio (dr)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>289 (Me)</td>
<td>PhMe</td>
<td>(S,S$_p$)$_2$-285</td>
<td>1.7:1\textsuperscript{[c]}</td>
</tr>
<tr>
<td>2</td>
<td>290 (CH$_2$Pr)</td>
<td>PhMe</td>
<td>(S,S$_p$)$_2$-286</td>
<td>8.1:1\textsuperscript{[e][d]}</td>
</tr>
<tr>
<td>3</td>
<td>291 (CH$_2$Ph)</td>
<td>PhMe</td>
<td>(S,S$_p$)$_2$-288</td>
<td>1.8:1\textsuperscript{[f]}</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]} At reflux. 2 h. in PhMe \textsuperscript{[b]} Determined by $^1$H-NMR spectroscopy. \textsuperscript{[c]} Determined following conversion to monomeric hfacac complexes. \textsuperscript{[d]} Diastereomeric purity ($>$100:1) achieved by recrystallisation from CH$_2$Cl$_2$/hexane.
Good selectivity (8:1) was observed for the CH$_2$Pr substituted oxazoline to give the $S_p$ palladacycle as the major product (entry 2). The palladacycle could be recrystallised from CH$_2$Cl$_2$/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$_2$(μ-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, 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 structures of planar-chiral acetate-bridged palladacycles are all trans-\(S_pS_p\) or trans-\(R_pR_p\).\(^{84,115,119,212}\) 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 \((S,S_p)_2-\textbf{286}\) and \((S,S_p)_2-\textbf{287}\) \((R = \text{CH}_2\text{Cy})\) 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).
A previous study on the palladation of the \( \text{Pr} \) 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 \(^1\text{H}-\text{NMR}\) 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 \( \text{CH}_2\text{Cy} \) 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 \( \text{Pr} \) substituted oxazoline \((S)-117\) in \( \text{CH}_2\text{Cl}_2 \) 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 \(^1\text{H}\)-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.
Examination of the palladation of the CH$_2$Cy oxazoline under analogous conditions revealed an initial ratio of (S,R)$_p$-287:(S,S)$_p$-287 of 1:3, which decreased slightly to 1:2 with stirring. Similarly, palladation of the CH$_2$iPr oxazoline established that initial selectivity peaked at a ratio of 1:23 of diastereoisomers (S,R)$_p$-286:(S,S)$_p$-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$_2$Cl$_2$ 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. The relative rate of epimerisation for (S,R)$_p$-118/(S,S)$_p$-118 seems to be faster than that seen for the CH$_2$Cy and CH$_2$iPr examples. This may be due to the increased flexibility associated with the oxazoline substituent, (for CH$_2$Cy and CH$_2$iPr 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$_2$Cl$_2$ 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 \((\eta^5\text{-carboxycyclopentadienyl})\)-(\(\eta^4\text{-tetraphenylcyclobutadiene})\)cobalt(I) \textbf{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-\(\mu\)-acetato\(\{(\eta^5\text{-}(S)-S_p)\text{-}(2'\text{-}4'\text{-methylcyclohexyl})\text{oxazolinyl})\text{cyclopentadienyl}, \text{1-C, 3'\text{-N})\}(\eta^4\text{-tetraphenylcyclobutadiene})\)cobalt(I)\]dipalladium(II) \((S,S_p)_2\) \textbf{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-\(\mu\)-acetato\(\{(\eta^5\text{-}(R)-R_p)\text{-}(2'\text{-}4'\text{-methylcyclohexyl})\text{oxazolinyl})\text{cyclopentadienyl}, \text{1-C, 3'\text{-N})\}(\eta^4\text{-tetraphenylcyclobutadiene})\)cobalt(I)\]dipalladium(II) \((S,R_p)_2\) \textbf{118} (COP-OAc). Studies on the palladation reaction, by monitoring diastereoselectivity over time, showed that the examples \((S,S_p)_2\) \textbf{286} and \((S,S_p)_2\) \textbf{287} selectively form the kinetic product for the reaction, whereas \((S,R_p)_2\) \textbf{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 \((S,S_p)_2\) \textbf{301} could catalyse the reaction with low catalyst loading (0.25 mol %, 74% yield, 80% \textit{ee}).
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).\textsuperscript{215}

\textbf{Figure 34}\textsuperscript{215}

\textit{4.1.1.1 Adsorption}

Catalysts immobilised 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.\textsuperscript{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.\textsuperscript{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 \textit{via} hydrogen bonding with silanols on the
surface of silica (Figure 35).\textsuperscript{217} The immobilised catalyst could subsequently be used as an asymmetric catalyst for the hydrogenation of olefins.

![Image of catalyst immobilised on silica]

**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.\textsuperscript{218} This has been the method of choice for developing heterogeneous catalysts for a number of synthetic transformations.\textsuperscript{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$_4$\textsuperscript{2-} ion onto quartenary ammonium groups supported on styrene-based polymers, such as derivitised Merrifield’s resin \textbf{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.\textsuperscript{222}
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, 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.

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). 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. Subsequent studies revealed that using water as the solvent, catalyst leaching could be significantly reduced (<5% over 100 hours in solution). Under the optimized conditions, asymmetric hydrogenation could be carried out to give acetyl-protected amino ester (R)-304 in comparable 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.

4.1.4 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 Merrifield's resin. Secondly, co-polymerisation can be used by selecting suitable monomers, and lastly catalysts can be immobilised on inorganic supports such as 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 \((R)-\text{BINAP}\) 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 \(\beta\)-ketoesters (up to 99\% yield and 97 \% ee).\(^{227}\)
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 acetonaphone 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

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 divinylbenzene229 (Scheme 111) or polymerisation of amines with isocyanates to form polyurethanes230 the methodologies of choice.

Polymer (S,S)-308 has been used as a ligand in the stereoselective cyclopropanation of styrene, with results gained comparable 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 allow 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 (Fe₃O₄) 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 magnet. The catalyst was recycled using this method up to 14 times without a decrease in the conversion or enantioselectivity (100% conversion, 97–98% ee).
4.1.2 Strategy for Immobilisation

Richards has previously shown that immobilisation of COP-systems is possible. Reaction of COP-Cl ($S_R$)$_2$-$197$ with triphenylphosphine NovaGel gave coordinated heterogeneous complex ($S_R$)-$310$ (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 respectively) 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.$^{214}$

![Figure 37](image.png)
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 moiety of the metallocene, with the catalyst in a monomeric state, to avoid leaching (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 (η⁵-cyclopentadienyl)cobalt dicarbonyl (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-bromophenyltriphenylcyclobutadiene)(η^5-cyclopentadienyl)cobalt (25%). 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).

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.\textsuperscript{17,181} The most facile route was to take CoCl\((\text{PPh}_3)_3\) 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\((\text{PPh}_3)_3\), in 94\% yield. Reaction of CoCl\((\text{PPh}_3)_3\) with 2 equivalents of diphenylacetylene \textbf{311} and 1 equivalent of NaC\textsubscript{5}H\textsubscript{4}COOCH\textsubscript{3}, which was generated \textit{in situ} by reaction of sodium cyclopentadienide and dimethyl carbonate, gave metallocene \textbf{240} in good yield (Scheme 115).\textsuperscript{17}

\begin{center}
\includegraphics[width=\textwidth]{scheme115.png}
\end{center}

\textbf{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 \textit{para}-substituted product \textbf{315} was isolated in 68\% yield \textit{via} chromatography as exclusively the \textit{trans} regioisomer. The appearance of a characteristic IR carbonyl stretch at 1685 cm\textsuperscript{-1} and an acetyl methyl singlet peak at 2.57 ppm in the \textsuperscript{1}H-NMR spectrum of \textbf{315} integrating for 3 protons confirmed that the acylation had been successful, with a single peak confirming \textit{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 \textit{cis} or \textit{trans} with respect to which phenyl groups the substitution occurs. This was found to occur with no selectivity (1:2 ratio of \textit{trans}:\textit{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 $\sigma_p^*$ of $-0.65$ calculated, which is comparable to that of a methoxy group ($\sigma_p^* = -0.78$). As such cobalt metallocenes are comparable 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 positions.

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.
Use of benzoyl chloride and 4-bromobenzoyl chloride gave tetrasubstituted metalloccenes 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 $H^e$ 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 ($H^f$) are also present. Compound 320 was decidedly more difficult to confirm that tera-substitution 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](image-url)

**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 Metallcocenes 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 analogue of 240 from di(ortho-tolyl)-acetylene were unsuccessful, suggesting the unfavourable arrangement in these metallocenes of contiguous 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 recrystallisations from CH\(_2\)Cl\(_2\)/hexane and the expected trans regiochemistry was confirmed by X-ray crystallography (Figure 42).

\[
\text{Scheme 118}
\]
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 CH₂Cl₂/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 η⁵-cyclopentadienyl-(triphenylphosphine)cobaltacyclopentadiene complexes. 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. The formation of the metallocenes occurs via oxidative cyclisation of a bis-(η²-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/$\eta^4$-coordination to give the metallocenes $trans$-$323$ and $trans$-$324$ (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 $\eta^4$-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.
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 $H^e$ 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.
Extension of this methodology, using 2.1 equivalents of acetyl chloride/aluminium chloride resulted in the formation of diacylated metalloccenes 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.
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. 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 monoacylated 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.

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.

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.
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.
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 hexafluoroacetionate, 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.

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 ($\pm$)-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. 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 $\Delta\delta$ 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](image)

**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.
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\(^{-1}\).

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 \((\eta^4\text{-tetraphenylcyclobutadiene})(\eta^5\text{-...}}\)
carbomethoxycyclopentadienyl)-cobalt 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 \((\eta^5\text{-}(\text{dimethylaminomethyl})\text{cyclopentadienyl})\text{-}(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\) with sodium tetrachloropalladate mediated by \(N\text{-acetyl}-D\text{-phenylalanine}\) under basic conditions resulted in chloride-bridged dimer palladacycle \((S_p)_2248\) in 92\% ee. The enantiopurity of the palladacycle was increased to >98\% ee by reaction with \((R)\text{-proline}\) and separation of the resultant diastereoisomers. Extension of the palladation methodology to other amines gave new palladacycles with \(N,N\text{-diethyl-}\) (82\% ee) and \(N\text{-pyrrolidinyl-}\) (>98\% ee) substituents.

The new CAP complexes were shown to be active catalysts (unon silver salt activation) for the rearrangement of \((E)\text{-trichloroacetimidates}\) 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 unratational outcomes. The chiral ligands were shown to be readily accessible by reaction of \((\eta^5\text{-carboxycyclopentadienyl})\text{-}(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\) 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 \(\text{di-\(\mu\text{-acetatobis}\[(\eta^5\text{-}(S)\text{-}\text{C})\text{-}(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\]dipalladium(II)}\) 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-$\mu$-acetatobis[$\eta^5$-($S$)-($R$)$_2$-2-(2’-4’-methylethyl)oxazolinyl]cyclopentadienyl, 1-C, 3’-N)]($\eta^4$-tetraphenylcyclobutadiene)cohabit(I)]dipalladium(II) ($S,R_p$)$_2$-$\mathbf{118}$ (COP-OAc). Studies on the palladation reaction, by monitoring diastereoselectivity over time, showed that the examples ($S,S_p$)$_2$-$\mathbf{286}$ and ($S,S_p$)$_2$-$\mathbf{287}$ selectively form the kinetic product for the reaction, whereas ($S,R_p$)$_2$-$\mathbf{118}$ 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 ($S,S_p$)$_2$-$\mathbf{301}$ 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 ($\eta^4$-tetraphenylcyclobutadiene)($\eta^5$-carbomethoxyxycyclopentadienyl)-cobalt $\mathbf{240}$ resulted in the exclusive $\text{para}$-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 $\text{ortho}$-phenyl substituted phenylacetylenes resulted in the selective formation of $\text{trans}$-metallocenes (with a selectivity of up to 6:1 $\text{trans}$:$\text{cis}$). Extension of the Friedel-Crafts methodology to the major isomers of these complexes resulted in conformationally controlled mono- or di-$\text{para}$-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 (\(^1\)H) 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, (\(\phi = 4.6\) mm, length = 250 mm), fitted with pre-column (\(\phi = 4.6\) 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\(^{181}\)

\[\text{CoCl}(\text{PPh}_3)_3\]

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 NaBH₄ (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).

\((\eta^5\text{-cyclopentadienyl} \cdot \eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\)^181

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 tritrated 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, CDCl₃): \(\delta = 7.58–7.18\) ppm (m, 20H, Ar–H), 4.59 ppm (s, 5H, Cp–H).

Spectral data matched that previously reported.

\((\eta^5\text{-dimeylaminomethyl)cyclopentadienyl} \cdot \eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\)^181

Phosphoric acid (2.00 mL, 38.5 mmol) was added to a hot suspension of \((\eta^5\text{-cyclopentadienyl}) \cdot (\eta^4\text{-tetraphenylcyclobutadiene})\) 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 \(\times\) 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 \textit{in vacuo} to give the crude product. Purification \textit{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\(_3\)): \(\delta = 7.51–7.40\) (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 \(\times\) CH\(_3\)); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta = 136.42, 128.95, 128.10, 126.30, 93.84, 84.21, 83.66, 74.89, 56.53, 44.95\) ppm. Spectral data matched that previously reported.

\(\eta^5\)-carbomethoxycyclopentadienyl)-(\(\eta^4\)-tetraphenylcyclobutadiene)cobalt(I)\(^{182}\)

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$_2$Cl$_2$). $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.44$–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$_3$H$_3$); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 166.61$, 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.

$^{\eta^5}$-carboxycyclopentadienyl-$^{\eta^4}$-tetraphenylcyclobutadiene)cobalt(I)$^{182}$

$^{\eta^5}$-carboxycyclopentadienyl-$^{\eta^4}$-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$_2$Cl$_2$ (20 mL). The solution was washed with 2 M HCl solution (20 mL) and the aqueous layer was extracted with CH$_2$Cl$_2$ (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 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.44$–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$_3$): $\delta = 191.12$, 135.01, 129.02, 128.78, 127.71, 92.89, 89.34, 89.12, 77.21 ppm. Spectral data matched that previously reported.
To a solution of \((\eta^5\text{-hydroxymethylcyclopentadienyl})\)-(\eta^4\text{-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\(_2\)O (50 mL) and the aqueous 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\(_2\)Cl\(_2\)/MeOH) gave the product as an orange solid (482 mg, 0.94 mmol, 99\%). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 7.50–7.45\) (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, CH\(_2\)OH); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta = 136.52, 135.18, 129.14, 128.57, 84.12, 81.95, 75.31, 59.81\) ppm. Spectral data matched that previously reported.

To a solution of \((\eta^5\text{-formylcyclopentadienyl})\)-(\eta^4\text{-tetraphenylcyclobutadiene})cobalt(I) (542 mg, 1.07 mmol) dissolved in CH\(_2\)Cl\(_2\) (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 CuSO₄ solution (10 mL). The solution was dried over MgSO₄, filtered and the solvent was removed in vacuo. The crude product was redissolved in a minimum volume of CH₂Cl₂ 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%). ¹H NMR (500 MHz, CDCl₃): δ = 9.34 (s, 1H, CHO), 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); ¹³C NMR (126 MHz, CDCl₃): 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.

\[(\eta^5-(N,N\text{-dimethylcarboxamide})\text{-cyclopentadienyl})-(\eta^4\text{-tetraphenylicyclobutadiene})\text{cobalt(I)}\]

![Diagram of the compound](image)

A flask was charged with \((\eta^5\text{-carboxycyclopentadienyl})(\eta^4\text{-tetraphenylicyclobutadiene})\text{cobalt(I)}\) (1.00 g, 1.91 mmol) and dissolved in CH₂Cl₂ (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 CH₂Cl₂ 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 CH₂Cl₂ (20 mL) was added a solution of the crude acid chloride in CH₂Cl₂ (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\textsubscript{4}, filtered, and concentrated \textit{in vacuo}. The residue was dissolved in a minimum volume of CH\textsubscript{2}Cl\textsubscript{2} and purified by column chromatography (SiO\textsubscript{2}, 7:3 hexanes/ethyl acetate) to give the product as an orange solid (1.01 g, 1.83 mmol, 96%). m.p. 249 °C; \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \( \delta = 7.55-7.44 \) (m, 8H, Ar–\( \text{H} \)), 7.32–7.18 (m, 12H, Ar–\( \text{H} \)), 5.16 (brs, 2H, Cp–\( \text{H} \)), 4.75 (brs, 2H, Cp–\( \text{H} \)), 2.79 (brs, 3H, CH\textsubscript{3}), 2.64 (brs, 3H, CH\textsubscript{3}); \textsuperscript{13}C NMR (126 MHz, CDCl\textsubscript{3}): 135.64, 129.04, 128.12, 126.64, 85.46, 84.89, 77.36, 76.26 (C=O and 2 × CH\textsubscript{3} not observed) ppm; IR (neat): \( \nu = 3052, 2923, 1967, 1609, 1596, 1496, 1388, 1267, 1162, 1027 \) cm\textsuperscript{–1}; HRMS (ESI\textsuperscript{+}): \( m/z \) calcd for C\textsubscript{36}H\textsubscript{31}CoNO: 552.1732 [M+H]\textsuperscript{+}; found 552.1726.

\((\eta^5\text{-(dimethylaminomethyl)cyclopentadienyl})-(\eta^4\text{-tetraphenylcyclobutadiene})\text{-cobalt(I)}\textsuperscript{181}

A flask was charged with \((\eta^5\text{(N-N-dimethylcarboxamide)-cyclopentadienyl})-(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\) (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\textsubscript{2}Cl\textsubscript{2} (3 × 20mL). The organic layer was dried over MgSO\textsubscript{4}, filtered and concentrated \textit{in vacuo} to give the product as an orange solid (959 mg, 1.77 mmol, 99%). \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \( \delta = 7.51–7.40 \) (m, 8H, Ar–\( \text{H} \)), 7.33–7.21 (m, 12H, Ar–\( \text{H} \)), 4.73 (t, \( J = 2.0 \) Hz, 2H, Cp–\( \text{H} \)), 4.68 (d, \( J = 2.1 \) Hz, 2H, Cp–\( \text{H} \)), 2.90 (s, 2H, CH\textsubscript{3}), 2.24 ppm (s, 6H, 2 × CH\textsubscript{3}); \textsuperscript{13}C NMR (126 MHz, CDCl\textsubscript{3}): \( \delta = 136.42, 128.95, 128.10, 126.30, 93.84, 84.21, 83.66, 74.89, 56.53, 44.95 \) ppm. Spectral data matched that previously reported.
A solution of (η^5-hydroxymethylcyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (100 mg, 0.20 mmol) and PPh₃ (51 mg, 0.20 mmol) in THF (3 mL) was cooled to -20 °C and NBS (35 mg, 0.30 mmol) was added in one portion. The mixture was stirred for 10–15 minutes and Et₂NH (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 CH₂Cl₂ (15 mL). The mixture was washed with 10% HCl (10 mL), dried over MgSO₄, filtered and concentrated in vacuo. Purification by column chromatography (SiO₂, 19:1 CH₂Cl₂/MeOH) gave the product as a yellow solid (45 mg, 0.08 mmol, 41%). m.p. 140–142 °C; ¹H NMR (300 MHz, CDCl₃): 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, CH₂NEt₂), 2.25 (q, J = 7.2 Hz, 4H, CH₂CH₃), 0.88 ppm (t, J = 7.2 Hz, 6H, CH₂CH₃); ¹³C NMR (126 MHz, CDCl₃): 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, 780, 743, 698, 589, 564 cm⁻¹; HRMS (ESI): m/z calculated for C₃₈H₃₆CoN: 565.2180 [M]+; found 565.2170.

A solution of (η^5-(1-pyrrolidinylmethyl)cyclopentadienyl)-(η^4-tetraphenylcyclobutadiene)cobalt(I) (1.00 g, 2.00 mmol) and PPh₃ (524 mg, 2.00 mmol) in THF (30 mL) was cooled to 0 °C 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 CH₂Cl₂ (30 mL). The mixture was washed with 10% HCl (50 mL), dried over MgSO₄ and concentrated in vacuo. Purification by column chromatography (SiO₂, 19:1 CH₂Cl₂/MeOH) gave the product as a yellow/brown solid (1.03 g, 1.84 mmol, 92%). m.p. 180–182 °C; ¹H NMR (400 MHz, CDCl₃): 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, CH₂NMe₂), 2.34–2.26 (m, 4H, N(CH₂CH₂)₂), 1.70–1.64 ppm (m, 4H, N(CH₂CH₂)₂); ¹³C NMR (126 MHz, CDCl₃): 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 C₃₈H₃₅CoN: 564.2096 [M+H]+; found 564.2094.

(η⁵-(N,N-diisopropylaminomethyl)cyclopentadienyl)(η⁴-
tetraphenylcyclobutadiene)cobalt(I)

A solution of (η⁵-hydroxymethylcyclopentadienyl)-(η⁴-
tetraphenylcyclobutadiene)cobalt(I) (50 mg, 0.01 mmol) and PPh₃ (3 mg, 0.01 mmol) in THF (3 mL) was cooled to 0 °C 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 CH₂Cl₂ (3 mL). The mixture was washed with 10% HCl (5 mL), dried over MgSO₄ and concentrated in vacuo. Purification by column
chromatography (SiO$_2$, 19:1 CH$_2$Cl$_2$/MeOH) gave the product as a yellow solid (31 mg, 0.005 mmol, 53%). m.p. 157-160 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 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 × CH(CH$_3$)$_2$, 2.75 (2H, s, CpCH$_2$N), 0.72 ppm (12H, d, J = 6.6, 4 × CH$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 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)

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$_2$Cl$_2$/EtOAc) to give product as a yellow solid (3.00 g, 4.45 mmol, 97%). m.p. 145–147 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 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$_2$Ph), 3.13 ppm (s, 2H, CH$_2$NH); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 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, 697 cm$^{-1}$; HRMS (ESI): m/z calculated for C$_{40}$H$_{33}$NCo: 600.2102 [M+H]$^+$; found: 600.2093.
To a stirred suspension of \((\eta^5\text{-N-benzylamino}-\text{cyclopentadienyl})(\eta^4\text{-tetraphenylcyclobutadiene})\text{-cobalt(I)}\) (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\(_2\)Cl\(_2\)/EtOAc) to give the product as a yellow solid (1.09 g, 2.05 mmol, 43\%). m.p. 116 \(^\circ\)C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.49\)–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, CH\(_2\)NH\(_2\)); \(^13\)C NMR (126 MHz, CDCl\(_3\)): \(\delta = 136.22, 128.75, 128.09, 126.37, 83.57, 81.84, 74.85, 53.54\) ppm; IR (neat): \(\nu = 3052, 2923, 2162, 1610, 1596, 1573, 1453, 1497, 1453, 1387, 1267, 1231, 1106, 1054\) cm\(^{-1}\); HRMS (ESI): \(m/z\) calculated for C\(_{34}\)H\(_{28}\)NCoNa: 532.1451 [M+Na]\(^+\); found: 532.1438.

2-(dicyclohexylphosphino)phenylferrocene\(^{135}\)

A solution of 2-bromophenylferrocene (500 mg, 1.47 mmol) dissolved in THF (10 mL) was cooled to approximately –78 \(^\circ\)C in an acetone/CO\(_2\) bath. To this \(^{6}\)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 \(^\circ\)C 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 H₂O (10 mL) and the aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried over MgSO₄ and the solvent was removed in vacuo. Purification with column chromatography (SiO₂, 19:1 hexanes/EtOAc) yielded the product as a red crystalline solid (626 mg, 1.31 mmol, 89%). ¹H NMR (500 MHz, CDCl₃): 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); ³¹P NMR (202 MHz, CDCl₃): δ = −12.35 ppm. Spectral data matched that previously reported.

2-(diphenylphosphino)phenylferrocene

A solution of 2-bromophenylferrocene (500 mg, 1.47 mmol) dissolved in THF (10 mL) was cooled to approximately −78 °C in an acetone/CO₂ bath. To this nBu-Li (0.64 mL of a 2.5 M solution in hexane, 1.61 mmol) was added and the solution was stirred at −78 °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 H₂O (10 mL) and the aqueous layer was extracted with CH₂Cl₂ (2 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried over MgSO₄ and the solvent was removed in vacuo. Purification with column chromatography (SiO₂, 19:1 hexanes/EtOAc) yielded the product as a red crystalline solid (570 mg, 1.19 mmol, 81%). ¹H NMR (500 MHz, CDCl₃): 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$_3$): $\delta = -12.15$ ppm.

Spectral data matched that previously reported.

**rac-di-aceto-bis[[\pi-1-(dimethylaminomethyl)cyclopentadieny1-2C,N]tetraphenylessocobalt(I)]-dipalladium(II)\textsuperscript{180}**

![rac-250]

A solution of Pd(OAc)$_2$ (20 mg, 0.09 mmol) and (\$^{5}$- (dimethylaminomethyl)cyclopentadienyl)(\$^{4}$-tetraphenylessocobalt(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$_3$): $\delta = 7.68–7.62$ (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, CH$_2$H), 2.80–2.73 (d, $J = 13.8$ Hz, 2H, CHH), 2.30 (s, 6H, N(CH$_3$)$_2$), 2.14 (s, 6H, O$_2$CCCH$_3$), 1.72 ppm (s, 6H, N(CH$_3$)$_2$); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta = 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-hexafiuoroacetylacetonate[[\pi-1-(dimethylaminomethyl)cyclopentadieny1-2C,N]tetraphenylessocobalt(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$_2$Cl$_2$ solution (~50:1 hexane: CH$_2$Cl$_2$). m.p. 225 °C; $^1$H 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, CHCO), 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, CHHNMMe$_2$), 2.92 (d, $J = 13.9$ Hz, 1H, CHHNMMe$_2$), 2.76 (s, 3H, NCH$_3$), 2.48 ppm (s, 3H, NCH$_3$). $^{13}$C NMR (126 MHz, CDCl$_3$): δ = 174.40 (q, $J_{C}$-$F$ = 8.0 Hz), 174.12 (q, $J_{C}$-$F$ = 7.4 Hz), 136.77, 129.14, 127.92, 126.15, 118.95 (q, $J_{C}$-$F$ = 38.9 Hz), 116.68 (q, $J_{C}$-$F$ = 38.6 Hz), 102.94, 101.83, 90.23, 84.49, 79.55, 75.44, 74.87, 65.71, 53.53, 51.12 ppm.

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

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$_2$Pd$_2$Cl$_4$ (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$_2$Cl$_2$ (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 CH₂Cl₂ (150 mL) and washed with brine (2 × 100 mL). The organic phase was
dried over MgSO₄, filtered and the solvent was removed in vacuo. Purification by column
chromatography (SiO₂, 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; [α]D₂¹ = −289 (c = 1.1 mg/mL in CH₂Cl₂). Further characterisation data below.

*S_p-(π-(dimethylaminomethyl)cyclopentadienyltetraphenylcyclobutadienecobalt-C,N-
palladium(II)(L)-Proline

![Chemical structure]

A solution of *S_p-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-
2C,N]tetrphenylcyclobutadienecobalt) dipalladium(II) (50 mg, 0.04 mmol) in acetone (1
mL) was added to a solution of NaHCO₃ (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 CH₂Cl₂ (50 mL).
The phases were separated and the aqueous phase was washed with further portions of
CH₂Cl₂ (2 × 25 mL). The organic phases were combined, dried over MgSO₄, filtered and
solvent was removed in vacuo yielding the product as an orange solid (50 mg, 0.07 mmol,
were obtained by slow diffusion of hexane into CH₂Cl₂ solution (~50:1 hexane: CH₂Cl₂).
m.p. 190–192 °C; [α]D₂⁰ = −99 (c = 1.29 mg/mL in CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃): 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, NHCH), 3.20 (d and brs, J = 13.2 Hz, 2H,
CHHNMe₂ and NH), 2.87 (d, J = 13.2 Hz, 1H, CHHNMe₂), 2.65 (s, 3H, CH₃), 2.50–2.40 (m,
1H, NHCHH), 2.38 (s, 3H, CH₃), 2.20–2.00 (m, 3H, 3 × CH), 1.60–1.50 (m, 1H, CHH),
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1.24–1.18 ppm (m, 1H, CHH); 13C NMR (100 MHz, CDCl3): 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 C₄₁H₄₀CoN₂O₂Pd: 757.1466 [M+H]+; found 757.1468.

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

A solution of Sₚ-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadienecobalt) dipalladium(II) (50 mg, 0.04 mmol) in acetone (10 mL) was added to a solution of NaHCO₃ (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 CH₂Cl₂ (50 mL). The phases were separated and the aqueous was washed with further portions of CH₂Cl₂ (2 × 25 mL). The organic phases were combined, dried over MgSO₄, filtered and solvent was removed in vacuo yielding the crude product. Ratio of (R,Rp)-256: (R,Sp)-256 = 1:33. Purification by column chromatography eluting with (SiO₂, 97:3 CH₂Cl₂/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 CH₂Cl₂ solution (~50:1 hexane: CH₂Cl₂). [α]D²¹ = +26 (c = 0.5 mg/mL in CH₂Cl₂); m.p. 236 °C; 1H NMR (500 MHz, CDCl₃): 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, NHCH), 3.10 (d, J = 13.2 Hz, 1H, CHHNMe₂), 3.06–2.94 (m, 1H,
NHCHH), 2.90–2.78 (m, 1H, NHCHH), 2.74 (d, J = 13.2 Hz, 1H, CHHNMe₂), 2.53 (s, 3H, CH₃), 2.36 (s, 3H, CH₃), 2.15–1.96 (m, 2H, CHH and NH), 1.85 (ddt, J = 13.3, 8.9, 4.7 Hz, 1H, CHH), 1.79–1.69 (m, 1H, CHH), 1.43–1.28 ppm (m, 1H, CH₃); ¹³C NMR (126 MHz, CDCl₃): 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): ν = 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 C₄₁H₄₀O₂N₂PdCo: 757.1466 [M+H]^+; found: 757.1467.

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

Dilute hydrochloric acid (0.64 mL of a 0.5 M solution) was added to a solution of Sₚ-(π-(dimethylaminomethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N- palladium(II)(D)-Proline (100 mg, 0.13 mmol) in CH₂Cl₂ (2 mL) and the mixture stirred vigorously for 16 h. The solution was diluted with CH₂Cl₂ (5 mL) and washed with brine (3 × 5 mL). The organic layer was collected, dried over MgSO₄, filtered and concentrated in vacuo. Purification by column chromatography (SiO₂, 4:1 hexanes/EtOAc) gave the product as an orange solid (73 mg, 0.05 mmol, 82%). m.p. 191 °C (decomp.); [α]D²¹ = −310 (c = 0.5 mg/mL in CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃), 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, CHHNMe₂), 3.13 (d, J = 13.3 Hz, 2H, CHHNMe₂), 2.81 (d, J = 13.4 Hz, 2H, CHHNMe₂), 2.77 (d, J = 13.2 Hz, 2H, CHHNMe₂), 2.67 (s, 6H,
CH$_3$, 2.62 (s, 6H, CH$_3$), 2.19 (s, 6H, CH$_3$), 2.02 ppm (s, 6H, CH$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 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): $\nu$ = 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$_2$Co$_2$N$_2$Pd$_2$: 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)

To a solution of $S_{p}$-di-μ-chloro-bis{[π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadiene cobalt}(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$_2$Cl$_2$. 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$_2$Cl$_2$); m.p. 162–164 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 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, CHHMe$_2$), 2.76 (d, $J$ = 13.9 Hz, 2H, CHHMe$_2$), 2.30 (s, 6H, NCH$_3$), 2.15 (s, 6H, 2 × O$_2$CCMe$_3$), 1.71 ppm (s, 6H, NCH$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 179.70, 135.96, 128.15, 126.78, 124.60, 102.08, 100.39, 83.06, 79.13, 74.10, 74.36, 64.11, 52.95, 50.78 ppm; IR (neat): $\nu$ = 3055, 2920, 1577, 1498, 1412, 1261, 1176, 1023, 957, 740, 692, 617 cm$^{-1}$; Elemental analysis calcd. (%) for C$_{76}$H$_{68}$Co$_2$N$_2$O$_4$Pd$_2$: C 65.01, H 4.88, N 2.00; found C 65.18, H 4.96, N 2.04.
To a solution of $S_p$-di-μ-chloro-bis([π-1-(dimethylaminomethyl)cyclopentadienyl-2C,N]tetrphenylcyclobutadienecobalt(II))-dipalladium(II) (20 mg, 0.02 mmol) in acetone/water (2:1 mL) was added sodium hexafluoroacetylacetonate (7 mg, 0.03 mmol). The solution was stirred vigorously for 16 h. On completion, the solution was diluted with CH$_2$Cl$_2$ (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$_2$Cl$_2$ solution (~50:1 hexane: CH$_2$Cl$_2$). [α]$_D^{19}$ = $–$160 (ε = 1.0 mg/mL in CH$_2$Cl$_2$); m.p. 219 °C; $^1$H 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, CHCO), 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, CHHNMe$_2$), 2.92 (d, $J = 13.9$ Hz, 1H, CHHNMe$_2$), 2.76 (s, 3H, NCH$_3$), 2.48 ppm (s, 3H, NCH$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$): δ = 174.40 (q, $J_{C,F} = 8.0$ Hz), 174.12 (q, $J_{C,F} = 7.4$ Hz), 136.77, 129.14, 127.92, 126.15, 118.95 (q, $J_{C,F} = 38.9$ Hz), 116.68 (q, $J_{C,F} = 38.6$ 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$_6$NO$_2$Pd.2H$_2$O: C 55.58, H 4.10, N 1.58; found C 55.54, H 3.90, N 1.80.
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 Na₂Pd₂Cl₄ (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 (η⁵-N,N-diethylaminomethyl)cyclopentadienyl)-(η⁴-tetraphenylcyclobutadiene)cobalt(I) (500 mg, 0.88 mmol) in 5:1 MeOH/CH₂Cl₂ (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 CH₂Cl₂ (100 mL) and washed with brine (2 × 100 mL). The organic phase was dried over MgSO₄, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO₂, 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 °C (decomp); [α]D²⁴ = −618 (c = 0.5 mg/mL in CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃): 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, CH₂NEt₂), 3.22 (d, J = 13.9 Hz, 2H, CH₂NEt₂), 2.75 (d, J = 13.9 Hz, 4H, CH₂NEt₂), 2.68–2.43 (m, 16H, CH₂CH₃), 1.52 (t, J = 7.1 Hz, 6H, CH₃CH₂), 1.52 (t, J = 7.1 Hz, 6H, CH₂CH₃), 0.92–0.84 ppm (m, 12H, CH₂CH₃); ¹³C NMR (126 MHz, CDCl₃): 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. (%): C₇₆H₇₀Cl₂N₂Pd₂: C 64.60, H 4.99, N 1.98; found C 64.70, H 4.89, N 2.04.

*S,p-(π-(diethylaminomethyl)cyclopentadienyl)tetraphenylocyclobutadienecobalt-C,N-palladium(II)(L)-Proline*

A solution of *S,p*-di-μ-chloro-bis([π-1-(diethylaminomethyl)cyclopentadienyl]-2C,N)tetraphenylocyclobutadienecobalt) dipalladium(II) (20 mg, 0.01 mmol) in acetone (1 mL) was added to a solution of NaHCO₃ (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 CH₂Cl₂ (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH₂Cl₂ (2 × 2 mL). The organic phases were combined, dried over MgSO₄, 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*₂₆₀: *S,S,p*₂₆₀ = 1:10. [α]D²¹ = −104 (c = 0.7 mg/mL in CH₂Cl₂); m.p. 206–208 °C; ¹H NMR (500 MHz, CDCl₃): 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, NCH), 3.29 (d, J = 13.9 Hz, 2H, 2 x CHH), 2.88 (d, J = 13.7 Hz, 2H, 2 x CHH), 2.78–2.55 (m, 3H, 3 x CHH), 2.49–2.27 (m, 2H, 2 x CHH), 2.17–2.06 (m, 4H, NH & CHH), 1.40–1.31 (m, 3H, CH₃CH₃), 0.94 ppm (t, J = 7.4 Hz, 3H, CH₃CH₃); ¹³C NMR (126 MHz, CDCl₃): 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): ν = 3453, 2929, 2852, 1725, 1594, 1494, 1446, 1381,
A solution of $S_p$-di-$\mu$-chloro-bis(1-$\pi$-(diethylaminomethyl)cyclopentadienyl-2C,N)tetrphenylcyclobutadienecobalt) 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$_2$Cl$_2$ (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH$_2$Cl$_2$ (2 x 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$_2$Cl$_2$); m.p. 215 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 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, NCH), 3.28–3.15 (m, 2H, CH$_2$CH$_3$), 2.77 (dt, $J$ = 14.6, 7.3 Hz, 1H, CHH), 2.73–2.62 (m, 1H, CHH), 2.44 (dq, $J$ = 13.8, 6.9 Hz, 1H, CHH), 2.24–2.11 (m, 2H, CH$_2$CH$_3$), 2.00–1.89 (m, 1H), 1.89–1.78 (m, 2H, NH & CHH), 1.48 (t, $J$ = 7.1 Hz, 3H, CH$_3$CH$_2$), 0.80 ppm (t, $J$ = 7.2 Hz, 3H, CH$_2$CH$_3$); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 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, 1368, 1289, 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;
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 Na₂PdCl₄ (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 (η⁵-(pyrrolidinylmethyl)cyclopentadienyl)-(η⁴-(tetraphenylcyclobutadiene)cobalt(I) (500 mg, 0.89 mmol) in 5:1 MeOH/CH₂Cl₂ (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 CH₂Cl₂ (150 mL) and washed with brine (2 × 100 mL). The organic phase was dried over MgSO₄, filtered and the solvent was removed in vacuo. Purification by column chromatography (SiO₂, 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); [α]₀²⁴ = −266 (c = 0.5 mg/mL in CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) 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, CpCHHN), 3.08–2.81 (m, 16H, CpCHHN & NCH₂), 2.32–2.23 (m, 2H, NCH₂), 2.08–2.03 (m, 2H, NCH₂), 1.81 (ddd, J = 9.3, 6.2, 3.5 Hz, 4H, NCH₂CH₂), 1.76–1.60 (m, 8H,
NCH₂CH₂), 1.53–1.45 ppm (m, 4H, NCH₂CH₂); ¹³C NMR (126 MHz, CDCl₃): 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 C₇₆H₆₆Cl₂Co₂N₂Pd₂: C 64.79, H 4.72, N 1.98; found C 64.81, H 4.60, N 2.07.

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

A solution of Sₐ₋-di-μ-chloro-bis([π-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadienecobalt) dipalladium(II) (20 mg, 0.01 mmol) in acetone (2 mL) was added to a solution of NaHCO₃ (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 CH₂Cl₂ (5 mL). The phases were separated and the aqueous phase was washed with further portions of CH₂Cl₂ (2 × 2 mL). The organic phases were combined, dried over MgSO₄, filtered and the solvent was removed in vacuo yielding the product as an orange solid (20 mg, 0.03 mmol, 90%). Ratio of Sₐ₋,Sₐ₋ 270: Sₐ₋,Sₐ₋ 270 = 1:99. [α]D²¹ = -37 (c = 1.1 mg/mL in CH₂Cl₂); m.p. 206–208 °C; ¹H NMR (500 MHz, d₆-DMSO): δ = 7.52–7.46 (m, 8H, Ar–H), 7.28–7.20 (m, 12H, Ar–H), 5.52–5.44 (m, 1H, NH), 4.36 (s, 2H, Cp–H), 4.25 (s, 1H, Cp–H), 3.60–3.52 (q, J = 7.9 Hz, 1H, NHCH), 3.19–3.01 (m, 2H, NHCHH & CpCHHN), 3.01–2.94 (m, 1H, NHCHH), 2.92–2.84 (m, 1H, NCH₂), 2.79 (d, J = 14.5 Hz, 1H, CpCHHN), 2.35–2.21 (m, 2H, CH₂), 2.14–2.04 (m, 1H, CHH), 1.82–1.61 (m, 5H, CH₂), 1.44–1.33 (m, 1H, CHH),
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): \( \nu = 3444, 2925, 2855, 1733, 1623, 1590, 1497, 1459, 1378, 1259, 1170, 1070, 1023, 926, 782, 745, 702 \text{ cm}^{-1} \); HRMS (ESI): \( m/z \) calculated for C\(_{43}\)H\(_{42}\)CoN\(_2\)O\(_2\)Pd: 783.1623 [M+H]\(^+\); found: 783.1615.

\( S_p^-\)-(\( \pi \)-Pyrrolidinylmethyl)cyclopentadienyl)tetraphenylcyclobutadienecobalt-C,N-palladium(II)(D)-Proline

![Chemical structure](image)

A solution of \( S_p^-\)-di-\( \mu \)-chloro-bis(\( \pi \)-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N)tetraphenylcyclobutadienecobalt) 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\(_2\)Cl\(_2\) (5 mL). The phases were separated and the aqueous was washed with further portions of CH\(_2\)Cl\(_2\) (2 \times 2 mL). The organic phases were combined, dried over MgSO\(_4\) and solvent was removed in \textit{vacuo} yielding the product as an orange solid (0.011 g, 50%). Ratio of \( R,R_p \)-270: \( R,S_p^-\)-270 = 1:99. [\( \alpha \)]\(_D\)\(^{23} = +72 \ (c = 0.5 \text{ mg/mL in CH}_2\text{Cl}_2)\); m.p. 206–208 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 7.69 \ (d, J = 6.4 \text{ Hz, Ar} \rightarrow \text{H}), 7.29–7.26 \ (m, 12 \text{H, Ar} \rightarrow \text{H}), 4.45 \ (t, J = 2.3 \text{ Hz, 1H, Cp} \rightarrow \text{H}), 4.33 \ (d, J = 2.6 \text{ Hz, 1H, Cp} \rightarrow \text{H}), 4.20 \ (d, J = 2.5 \text{ Hz, 1H, Cp} \rightarrow \text{H}), 3.44 \ (dt, J = 11.5, 7.6 \text{ Hz, 1H, NHCH}), 3.34 \ (ddt, J = 13.5, 9.1, 4.9 \text{ Hz, 2H, 2 \times NHCHH}), 3.13–2.91 \ (m, 4 \text{H, CH}_2), 2.71–2.61 \ (m, 1 \text{H, CHH}), 2.47\text{–}2.35 \ (m, 1 \text{H, CHH}), 2.18–2.10 \ (m, 1 \text{H, CHH}), 2.05–1.95 \ (m, 2 \text{H, CH}_2), 1.94–1.89 \ (m, 2 \text{H, CH}_2), 1.88–1.79 \ (m, 1 \text{H, CHH}), 1.78–1.72 \ (m, 1 \text{H, CHH}), 1.64 \ (\text{brs, 1H, NH}), 1.51–1.38 \ (m, 1 \text{H, CHH}); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta = 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 C₄₃H₄₄CoN₂O₂Pd: 783.1623 [M+H]⁺; found: 783.1614.

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

To a solution of *Sp-di-μ-chloro-bis[π-1-(pyrrolidinylmethyl)cyclopentadienyl-2C,N]tetraphenylcyclobutadienecobalt* 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 CH₂Cl₂. The solvent was then removed *in vacuo* to give the product as an orange solid (88 mg, 0.06 mmol, 88%). [α]D²³ = -146 (c = 1.0 mg/mL, in CH₂Cl₂); m.p. 162–164 °C; ¹H NMR (500 MHz, CDCl₃): 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, CH₃N), 3.00–2.88 (m, 2H, CHH), 2.44–2.35 (m, 2H, CHH), 2.34–2.25 (m, 2H, CHH), 1.76 (s, 6H, O₂CC₂H₃), 1.56 (s, 6H, CHH), 1.35–1.22 ppm (m, 6H, CHCH); ¹³C NMR (126 MHz, CDCl₃): 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 C₈₀H₇₂Co₂N₂O₄Pd₂: C 65.98, H 4.99, N 1.92; found C 65.75, H 4.96, N 1.95.
To a solution of \( p \)-di-\( \mu \)-chloro-bis(\( p \)-1-((dimethylaminomethyl)cyclopentadienyl-2C,N)tetr phenylcyclobutadiene)cobalt) dipalladium(II) (10 mg, 0.02 mmol) in CH\(_2\)Cl\(_2\) (1 mL) was added 2-(diphenylphosphino)phenylferrocene (7 mg, 0.01 mmol) and the solution was stirred for 16 h. The solvent was removed \textit{in vacuo} and the product was purified by column chromatography (SiO\(_2\), 49:1 CH\(_2\)Cl\(_2\)/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\(_2\)Cl\(_2\) solution (~50:1 hexane: CH\(_2\)Cl\(_2\)). [\( \alpha \)]\(_D\)\(^{21}\) = +26 (c = 0.5 mg/mL in CH\(_2\)Cl\(_2\)); m.p. 171 °C; 1H NMR (500 MHz, CDCl\(_3\)): \( \delta \) = 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, \( CHHNMe_2 \)), 2.92 (dd, \( J \) = 14.0, 2.5 Hz, 1H, \( CHHNMe_2 \)), 2.65 (s, 3H, \( CH_3 \)), 2.38 ppm (d, \( J \) = 2.4 Hz, 3H, \( CH_3 \)); \(^{31}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) = 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\(_3\)): \( \delta \) = 32.22 ppm; IR (neat): \( \nu \) = 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.
A flask was charged with crude \( \eta^5 \)-carboxycyclopentadienyl)-(\( \eta^4 \)-tetraphenylcyclobutadiene)cobalt(I) (200 mg, 0.38 mmol) and dissolved in CH\(_2\)Cl\(_2\) (5 mL). Oxalyl chloride (0.07 mL, 0.76 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated \textit{in vacuo} redissolved in CH\(_2\)Cl\(_2\) and re-concentrated \textit{in vacuo} to give the crude acid chloride. To a solution of \( \text{(S)} \) -alaninol (0.04 mL, 0.53 mmol) and triethylamine (0.32 mL, 2.28 mmol) in CH\(_2\)Cl\(_2\) (8 mL) was added a solution of the crude acid chloride in CH\(_2\)Cl\(_2\) (20 mL) \textit{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 \textit{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\(_3\)): \( \delta = 7.49–7.43 \) (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<sup>237</sup>

![Diagram of (S)-Valinol](image)

To a flask charged with NaBH<sub>4</sub> (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 °C and a solution of iodine (21.5 g, 85.36 mmol) in THF (50 mL) was added dropwise whilst maintaining a temperature below 5 °C. 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 <em>in vacuo</em>. The resultant residue was redissolved in aqueous 50% potassium hydroxide solution and stirred for 4 h. The aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub> (4 × 100 mL) and the organic layers were combined, dried over MgSO<sub>4</sub>, 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 °C (5 mbar); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): \(\delta = 3.63 \text{ (dd, } J = 10.5, 4.0 \text{ Hz, } 1\text{H, CHOOH}), 3.27 \text{ (dd, } J = 10.4, 8.8 \text{ Hz, } 1\text{H, CHOOH}), 2.54 \text{ (ddd, } J = 8.8, 6.4, 4.0 \text{ Hz, } 1\text{H, NCH}), 1.79 \text{ (br s, } 2\text{H, } H_2N), 1.64-1.49 \text{ (m, } 1\text{H, CH(CH}_3)_2\text{)}, 0.91 \text{ ppm (2 x d, } J = 5.5 \text{ Hz, } 6\text{H, CH(CH}_3)_2\text{)\. Spectral data matched that previously reported.}

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

\[\eta^5-(S)-2-(4\text{-methylethyl})\text{oxazolinylcyclopentadienyl})-(\eta^4-\text{tetraphenylcyclobutadiene)cobalt(I)\text{}}\text{\textsuperscript{17}}\]

![Diagram of (S)-117](image)
A flask was charged with crude \((\eta^5\text{-carboxycyclopentadieny})-(\eta^4\text{-tetraphenylcyclobutadiene})\) cobalt(I) (4.00 g, 7.63 mmol) and dissolved in CH\(_2\)Cl\(_2\) (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\(_2\)Cl\(_2\) 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\(_2\)Cl\(_2\) (80 mL) was added a solution of the crude acid chloride in CH\(_2\)Cl\(_2\) (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\(_3\)): \(\delta = 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, CH(CH\(_3\)_2), 0.97 (d, \(J = 6.7\) Hz, 3H CH(CH\(_3\)_2), 0.77 ppm (d, \(J = 6.7\) Hz, 3H, CH(CH\(_3\)_2). Spectral data matched that previously reported.

\[
\eta^5-(S)-2-(4\text{-tertbutyl})\text{oxazolinylcyclopentadieny})-(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}
\]

\[
\begin{align*}
\text{Ph} & \quad \text{Co} \\
\text{Ph} & \quad \text{Ph} \\
\text{Ph} & \quad \text{Ph} \\
\text{O} & \quad \text{N} \\
(S)-119
\end{align*}
\]

A flask was charged with crude \((\eta^5\text{-carboxycyclopentadieny})-(\eta^4\text{-tetraphenylcyclobutadiene})\) cobalt(I) (0.96 g, 1.83 mmol) and dissolved in CH\(_2\)Cl\(_2\) (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 re-dissolved in CH$_2$Cl$_2$ 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$_2$Cl$_2$ (10 mL) was added a solution of the crude acid chloride in CH$_2$Cl$_2$ (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$_3$): $\delta$ = 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.

\[ \eta^5-(S)-2-(4-isobutyl)oxazolincyclopentadienyl)(\eta^4-tetraphenylcyclobutadiene)cobalt(I) \]

A flask was charged with crude (\(\eta^5\)-carboxycyclopentadienyl)-(\(\eta^4\)-tetraphenylcyclobutadiene)cobalt(I) (2.65 g, 5.05 mmol) and dissolved in CH$_2$Cl$_2$ (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 re-dissolved in CH$_2$Cl$_2$ 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$_2$Cl$_2$ (20 mL) was
added a solution of the crude acid chloride in CH₂Cl₂ (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 MgSO₄, filtered, and concentrated in vacuo. Purification with column chromatography (SiO₂, 9:1 hexanes/EtOAc) yielded the product as a golden solid (2.43 g, 3.99 mmol, 79%). [α]D²³ = –114 (c = 1.4 mg/mL in CH₂Cl₂); m.p. 116 °C; ¹H NMR (400 MHz, CDCl₃): 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, CHHCH(CH₃)₂), 1.30 (dt, J = 13.2, 6.4 Hz, 2H, CHHCH(CH₃)₂), 0.92 (dt, J = 13.7, 6.9 Hz, 1H, CH₂CH(CH₃)₂), 0.82 ppm (t, J = 6.3 Hz, 6H, CH₂CH(CH₃)₂); ¹³C NMR (101 MHz, CDCl₃): 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): ν = 2918, 2850, 2161, 1972, 1655, 1596, 1498, 1446, 1113, 742, 694 cm⁻¹; HRMS (ESI⁺) m/z calculated for C₄₀H₃₇CoNO: 606.2202 [M+H]⁺; found: 606.2197.

η⁵-(S)-(4-methylcyclohexyl)oxazolinylcyclopentadienyl)-(η⁴-
tetraphenylcyclobutadiene)cobalt(I)

A flask was charged with crude (η⁵-carboxycyclopentadienyl)-(η⁴-
tetraphenylcyclobutadiene)cobalt(I) (965 mg, 1.84 mmol) and dissolved in CH₂Cl₂ (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 CH₂Cl₂ 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 CH₂Cl₂ (10 mL) was added a solution of the crude acid chloride in CH₂Cl₂ (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 MgSO₄, filtered, and concentrated in vacuo. Purification with column chromatography (SiO₂, 9:1 hexanes/EtOAc) yielded the product as an orange solid (868 mg, 1.34 mmol, 73%). [α]D²¹ = −33 (c = 0.6 mg/mL in CH₂Cl₂); m.p. 175 °C; ¹H NMR (500 MHz, CDCl₃): 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); ¹³C NMR (126 MHz, CDCl₃): 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): ν = 2917, 2850, 2161, 1972, 1656, 1596, 1498, 1446, 1116, 742, 694 cm⁻¹; HRMS (ESI⁺) m/z calculated for C₄₃H₄₁CoNO: 646.2515 [M+H]⁺; found: 646.2506.

η⁵-(S)-2-(4-benzyl)oxazolinylcyclopentadienyl)-(η⁴-tetraphenylcyclobutadiene)cobalt(I)
A flask was charged with crude \((\eta^5\text{-carboxycyclopentadienyl})-(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)}\) (1.01 g, 1.93 mmol) and dissolved in CH\(_2\)Cl\(_2\) (25 mL). Oxalyl chloride (0.33 mL, 3.85 mmol) and dimethylformamide (3 drops) were added sequentially. After 30 minutes the solution was concentrated \textit{in vacuo} redissolved in CH\(_2\)Cl\(_2\) and re-concentrated \textit{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\(_2\)Cl\(_2\) (10 mL) was added a solution of the crude acid chloride in CH\(_2\)Cl\(_2\) (20 mL) \textit{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 \textit{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\(_2\)Cl\(_2\)); m.p. 131 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 7.49\)–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, oxazoline–H), 3.00 (dd, \(J = 13.7, 4.9\) Hz, 1H, CH\(_2\)Ph), 2.31–2.18 ppm (dd, \(J = 13.7, 9.5\) Hz, 1H, CH\(_2\)Ph); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta = 161.38, 138.66, 135.43, 129.14, 129.05, 128.63, 128.11, 126.62, 126.44, 86.57, 84.81, 82.17, 76.13, 71.28, 67.84, 41.82\) ppm; IR (neat): \(\nu = 2918, 2850, 1972, 1655, 1596, 1498, 1446, 1113, 742, 694\) cm\(^{-1}\); HRMS (ASAP) \(m/z\) calculated for C\(_{43}\)H\(_{35}\)CoNO: 640.2045 [M+H]\(^+\); found: 640.2043.
A flask was charged with \( \eta^5-(S)-2-(4\text{-}methylethyl)\text{oxazoliny}lcyclopentadienyl)-(\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)} \) (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\(_3\)): \( \delta = 7.71–7.62 \) (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\(_2\)CCH\(_3\)), 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.

\( \text{di-\mu-acetatis}[\eta^5-(S)-(R\text{p})-2-(2\text{-}4\text{-}methylethyl)\text{oxazoliny}lcyclopentadienyl, 1\text{-}C, 3\text{-}N](\eta^4\text{-tetraphenylcyclobutadiene})\text{cobalt(I)} \) dipalladium(II)\(^{17} \)
A flask was charged with $\eta^5$-(S)-2-(4-tert-butyl)oxazolinylcyclopentadienyl)-(\eta^4\text{-tetrphenylcyclobutadiene})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$_3$): $\delta = 7.67$ (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, CH$_3$), 0.39 ppm (s, 18H, C(CH$_3$)$_3$). Spectral data matched that previously reported.

di-$\mu$-acetatobis[($\eta^5$-(S)($S_p$)-2-(2'4'-isobutyloxazolinyl)cyclopentadienyl, 1-C, 3'-N)(\eta^4\text{-tetrphenylcyclobutadiene})cobalt(II)]dipalladium(II)

A flask was charged with $\eta^5$-(S)-2-(4-iso-butyl)oxazolinylcyclopentadienyl)-(\eta^4\text{-tetrphenylcyclobutadiene})cobalt(I) (50 mg, 0.08 mmol) and palladium(II) acetate (19 mg, 0.08 mmol) in CH$_2$Cl$_2$ (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$_2$Cl$_2$ solution (~50:1 hexane: CH$_2$Cl$_2$). $[\alpha]_D^{19} = -721$ (c = 1.2 mg/mL in CH$_2$Cl$_2$); m.p. 266 °C; $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.67$–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, O2CCCH2), 1.41–1.31 (m, 2H, CHH'Pr), 1.15–1.04 (m, 2H, CH(CH3)2), 0.71 (d, J = 6.6 Hz, 6H, CH(CH3)2), 0.67 (d, J = 6.6 Hz, 6H, CH(CH3)2), 0.19 ppm (ddd, J = 13.6, 11.3, 4.7 Hz, 2H, CHH'Pr); 13C NMR (126 MHz, CDCl3): 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): ν = 3058, 2956, 1605, 1575, 1505, 694 cm⁻¹; Elemental analysis calcd. (%) for C₈₄H₇₆Co₂N₂O₆Pd₂: 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*

A flask was charged with η⁵-(S)-2-(4-iso-butyl)oxazolinylcyclopentadienyl)-(η⁴-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%). [α]D²⁴ = +151 (c = 2.0 mg/mL in CH₂Cl₂); m.p. 188-190 °C; ¹H NMR (500 MHz, CDCl₃): 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,
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 CH₂Cl₂ (5 mL) and washed with aqueous sodium hydrocarbonate solution (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed in vacuo. Purification by column chromatography on silica eluting with CH₂Cl₂/EtOAc (9:1) gave the product as an orange oil (16 mg, 0.02 mmol, 86%). [α]D²⁶ = +24.4 (c = 1.6 mg/mL in CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃): 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, NH), 5.01 (s, 2H, Cp–H), 4.72–4.63 (m, 2H, Cp–H), 4.09–3.99 (m, 1H, CH₂CN), 3.92 (dd, J = 11.2, 5.6 Hz, 1H, NHCH₂HCH), 3.67 (dd, J = 11.2, 4.7 Hz, 1H, NHCH₂HCH), 2.01 (s, 3H, CH₃), 1.49–1.38 (m, 1H, CH(CH₃)₂), 1.11–1.02 (m, 1H, CHH₃Pr), 0.99–0.91 ppm (m, 1H, CHH₃Pr), 0.86 ppm (t, J = 5.9 Hz, 6H, CH(CH₃)₂); ¹³C NMR (126 MHz, CDCl₃): 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 C₄₂H₄₁CoNO₃: 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)

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)

A flask was charged with η⁵-(S)-2-(4-methylcyclohexyl)oxazolinylcyclopentadienyl)-(η⁴-
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%).  

\[\alpha\] \text{D}^{19} = -407 (c = 1.0 mg/mL in CH$_2$Cl$_2$); m.p. 248 °C (dec.); $^1$H NMR (500 MHz, CDCl$_3$):  

$\delta = 7.63$–$7.46$ (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$_2$CCH$_3$), 1.72–1.17 (m, 30H, CH$_2$CH + 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, CHHCy); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta = 180.93$, 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): $\nu = 3057$, 2921, 2849, 1606, 1577, 1499, 1414, 694 cm$^{-1}$; Elemental analysis calcd. (%) for C$_{90}$H$_{84}$Co$_2$N$_2$O$_6$Pd$_2$: C 66.71, H 5.24, N 1.73; found C 62.77, H 5.04, N 1.91.

A flask was charged with di-µ-chlorobis[η⁵-(S)-(S)$_p$-2-(2'-4'-isobutyl)oxazolinyl]cyclopentadienyl, 1-C, 3'-N)(η⁴-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%). \([\alpha]_{D}^{25} = -1222 \text{ (c = 1.9 mg/mL in CH}_2\text{Cl}_2)\); m.p. 183–185 °C; \(^1\)H NMR (500 MHz, CDCl\(_3\)), 1:1.3 mixture of isomers: \(\delta = 7.72–7.65 \text{ (m, 16H, Ar–H), 7.64–7.57 \text{ (m, 16H, Ar–H), 7.31–7.16 \text{ (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 (dddd, J = 12.9, 10.1, 2.3 Hz, 2H, CHiPr), 1.55–1.48 (m, 2H, CHiPr), 1.37–1.24 (m, 4H, CH(CH\(_3\))\(_2\), 0.94–0.77 (m, 24H, CH(CH\(_3\))\(_2\), 0.38 (4 x d, J = 4.2 Hz, 4H, CHiPr) ppm; \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta = 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): \(\nu = 3058, 2957, 1601, 1506, 1469, 1371, 742, 696 \text{ cm}^{-1}\); Elemental analysis calcd. (%) for C\(_{80}\)H\(_{70}\)Co\(_2\)N\(_2\)O\(_2\)Cl\(_2\)Pd\(_2\): C 64.35, H 4.74, N 1.88; found C 62.81, H 5.15, N 1.76.

\textit{di-μ-chlorobis[\(\eta^5\)-(S)-(S\(_p\))-2-(2′-4′-cyclohexyloxazolinylmethyl)cyclopentadienyl, 1-C, 3′-N)(\(\eta^4\)-tetrphenylcyclobutadiene)cobalt(I)]dipalladium(II)\)

\begin{center}
\includegraphics[width=0.3\textwidth]{di-μ-chlorobis[\(\eta^5\)-(S)-(S\(_p\))-2-(2′-4′-cyclohexyloxazolinylmethyl)cyclopentadienyl, 1-C, 3′-N)(\(\eta^4\)-tetrphenylcyclobutadiene)cobalt(I)]dipalladium(II)}
\end{center}

A flask was charged with \textit{di-μ-acetatobis[\(\eta^5\)-(S)-(S\(_p\))-2-(2′-4′-cyclohexyloxazolinylmethyl)cyclopentadienyl, 1-C, 3′-N)(\(\eta^4\)-tetrphenylcyclobutadiene)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 CH₂Cl₂); m.p. 203 °C; \(^1\)H NMR (500 MHz, CDCl₃), 1:1.4 mixture of isomers: \(\delta = 7.71–7.65\) (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), 4.03 (m, \(J = 8.3, 6.4\) Hz, 2H, oxazoline–H), 3.89–3.74 (m, 6H, oxazoline–H), 1.95–1.85 (m, 2H, CHHCy), 1.83–1.44 (m, 24H, CHHCy + Cy–H), 1.35–0.78 (m, 22H, Cy–H), 0.44–0.25 ppm (m, 4H, CHHCy); \(^{13}\)C NMR (126 MHz, CDCl₃): \(\delta = 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): \(v = 3056, 2923\) 2851, 1601, 1506, 1446, 1183, 741, 696 cm\(^{-1}\); Elemental analysis calcd. (%) for C₈₆H₇₈Co₂N₂O₂Cl₂Pd₂: C 65.66, H 5.01, N 1.78; found C 65.53, H 5.01, N 1.83.

hexafluoroacetylacetonate[(\(\eta^5\)-(S)-(S)p)-2-(2'-4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N](\(\eta^4\)-tetraphenylcyclobutadiene)cobalt(I)palladium(II)

A flask was charged with di-μ-acetatobis[(\(\eta^5\)-(S)-(S)p)-2-(2'-4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N](\(\eta^4\)-tetraphenylcyclobutadiene)cobalt(I)dipalladium(II) (10 mg, 0.01 mmol) and sodium hexafluoroacetylacetonate (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 CH₂Cl₂ (5 mL) and washed with water (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed in vacuo to yield the product as an orange solid (10 mg, 0.01 mmol, >99%). [α]ᵦ̂₂⁵ = −919 (c = 1.6 mg/mL in CH₂Cl₂); m.p. 253 °C; ¹H NMR (500 MHz, CDCl₃): 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, CHH’Pr), 1.40–1.30 (m, 1H, CH(CH₃)₂), 0.87 (2 x d, J = 2.4 Hz, 6H, CH(CH₃)₂), 0.57–0.46 ppm (m, 1H, CHH’Pr); ¹³C NMR (126 MHz, CDCl₃): δ = 174.77, 174.07 (d, J_C-F = 4.7 Hz), 173.80 (d, J_C-F = 4.8 Hz), 135.78, 129.22, 127.92, 126.59, 118.93 (d, J_C-F = 55.7 Hz), 116.66 (d, J_C-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; ¹⁹F NMR (471 MHz, CDCl₃): δ = −74.69, −75.63 ppm; IR (neat): ν = 3060, 2960, 1627, 1600, 1512, 1480, 1259, 1209, 1151, 704 cm⁻¹; Elemental analysis calcd. (%) for C₄₅H₃₆CoNO₃F₆Pd: C 58.87, H 3.96, N 1.53; found C 58.71, H 4.05, N 1.68.

**hexafluoroacetylacetonate[(η⁵-(S)-(S′)-2-(2′-(4′-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3′-N)(η⁴-tetraphenylcyclobutadiene)cobalt(I)]palladium(II)**

A flask was charged with di-μ-acetatobis[(η⁵-(S)-(S′)-2-(2′-4′-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3′-N)(η⁴-tetraphenylcyclobutadiene)cobalt(I)]dipalladium(II) (30 mg, 0.02 mmol) and sodium hexafluoroacetylacetonate (43 mg, 0.19 mmol) in acetone/water (2:1 solution, 2 mL).
solution was stirred vigorously for 16 h in which time a precipitate had formed. The solution was diluted with CH₂Cl₂ (5 mL) and washed with water (5 mL). The organic layer was collected, dried over MgSO₄ and the solvent was removed in vacuo to yield the product as an orange solid (31 mg, 0.02 mmol, 99%). [α]D = −532 (c = 5.2 mg/mL in CH₂Cl₂); m.p. 204 °C; ¹H NMR (500 MHz, CDCl₃): 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, CHCy), 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, CHHCy); ¹³C NMR (126 MHz, CDCl₃): δ = 174.66, 174.02 (d, J_C-F = 10.0 Hz), 173.75 (d, J_C-F = 10.6 Hz), 135.77, 129.20, 127.90, 126.57, 118.92 (d, J_C-F = 54.9 Hz), 116.66 (d, J_C-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; ¹⁹F NMR (471 MHz, CDCl₃): δ = −74.69, −75.56 ppm; IR (neat): ν = 3060, 2926, 2854, 1634, 1601, 1574, 1258, 1209, 1150, 704 cm⁻¹; Elemental analysis calcd. (%) for C₄₈H₄₀CoNO₃F₆Pd: C 60.16, H 4.22, N 1.46; found C 57.25, H 4.36, N 1.81.

General Methods for Palladation and ¹H-NMR/¹⁹F 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 hexafluoroacetylacetonate (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$_2$Cl$_2$ (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.

$\text{di-\mbox{-}\mu\text{-acetatobis[}(\eta^5\mbox{-}(S)\text{-}2\mbox{-}(2'\mbox{-}4'\mbox{-}methylethyl)oxazoliny]cyclopentadieny, 1\text{-C}, 3'\text{-}N)(\eta^4\mbox{-}tetraphenylcyclobutadiene)cobalt(I)\text{dipalladium(II)}}$

(S,$S_p$)$_2$: $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.71$–$7.62$ (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, CH$_3$), 1.77 (m, 2H, CH(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,$R_p$)$_2$: $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 7.70$–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, CH$_3$), 1.46–1.34 (m, 2H, CH(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[(η⁵-(S)-2-(2’-(4’-methyl)oxazolinyl)cyclopentadienyl, 1-C, 3’-N)(η⁴-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)

\[
\begin{align*}
&\text{(S,S) - 294} \\
&\text{(S,R) - 294} \\
&\text{(S,S)}: \text{^{1}H NMR (500 MHz, CDCl\textsubscript{3})}: \delta = 7.54-7.50 (m, 8H, Ar-H), 7.21-7.13 (m, 12H, Ar-H), 5.94 (s, 1H, C-H hfacac), 5.11 (dd, J = 2.4, 1.0 Hz, 1H, Cp-H), 4.88 (dd, J = 2.7, 1.0 Hz, 1H, Cp-H), 4.49 (t, J = 2.6 Hz, 1H, Cp-H), 4.07 - 3.95 (m, 3H, oxazoline-H), 1.19 ppm (d, J = 6.5 Hz, 3H, CH₃); \text{^{19}F NMR (471 MHz, CDCl\textsubscript{3})}: \delta = -74.29, -75.70 ppm.
\end{align*}
\]

\[
\begin{align*}
&\text{(S,R) - 295} \\
&\text{(S,R) - 295} \\
&\text{(S,S) - 295} \\
&\text{(S,S) - 295}: \text{^{1}H NMR (500 MHz, CDCl\textsubscript{3})}: \delta = 7.62-7.56 (m, 8H, Ar-H), 7.29-7.20 (m, 12H, Ar-H), 5.91 (s, 1H, C-H hfacac), 4.97 (dd, J = 2.4, 1.0 Hz, 1H, Cp-H), 4.82 (dd, J = 2.7, 1.0 Hz, 1H, Cp-H), 4.62 (t, J = 2.6 Hz, 1H, Cp-H), 3.65 (t, J = 8.1 Hz, 1H, oxazoline-H), 3.55-3.45 (m, 2H, oxazoline-H), 1.00 ppm (d, J = 6.5 Hz, 3H, CH₃); \text{^{19}F NMR (471 MHz, CDCl\textsubscript{3})}: \delta = -74.70, -75.67 ppm.
\end{align*}
\]

hexafluoroacetylacetonate[(η⁵-(S)-2-(2’-(4’-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3’-N)(η⁴-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)

\[
\begin{align*}
&\text{(S,S) - 295} \\
&\text{(S,R) - 295} \\
&\text{(S,S) - 295} \\
&\text{(S,S) - 295}: \text{^{1}H NMR (500 MHz, CDCl\textsubscript{3})}: \delta = 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, CHHPr), 1.53–1.41 (m, 1H, CH(CH₃)₂), 1.24–1.14 (m, 1H, CHHPr), 0.85 ppm (2 × d, J = 2.4 Hz, 6H, CH(CH₃)₂); ¹⁹F NMR (471 MHz, CDCl₃): δ = −74.23, −75.55 ppm.

(S,Sₚ): ¹H NMR (500 MHz, CDCl₃): 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, CH(CH₃)₂), 1.38–1.28 (m, 1H, CH(CH₃)₂), 0.85 (2 × d, J = 2.4 Hz, 6H, CH(CH₃)₂), 0.55–0.44 ppm (m, 1H, CH(CH₃)₂); ¹⁹F NMR (471 MHz, CDCl₃): δ = −74.69, −75.63 ppm.

hexafluoroacetylacetonate[(η⁵-(S)-2-(2’-(4’-cylohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3’-N)(η⁴-tetraphenylcyclohexadiene)cobalt(I)]palladium(II)

(S,Sₚ): ¹H NMR (500 MHz, CDCl₃): 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, oxazoline–H), 1.81–1.45 (m, 8H, CHHcy + Cy–H), 1.23–1.09 (m, 2H), 0.98–0.77 ppm (m, 3H, CHHcy + Cy–H); ¹⁹F NMR (471 MHz, CDCl₃): δ = −74.25, −75.52 ppm.

(S,Rₚ): ¹H NMR (500 MHz, CDCl₃): 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, CHHcy), 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, CHHcy); 19F NMR (471 MHz, CDCl3): \( \delta = -74.69, -75.56 \) ppm.

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

(S,S)-297
(S,Rp)-297

(S,Sp)-297

(298

(S,Sp): \(^1\)H NMR (500 MHz, CDCl3): \( \delta = 7.51 \) (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, CHHPh), 2.55 ppm (dd, \( J = 13.6, 9.4 \) Hz, 1H, CHHPh); 19F NMR (471 MHz, CDCl3): \( \delta = -74.22, -76.51 \) ppm.

(S,Sp): \(^1\)H NMR (500 MHz, CDCl3): \( \delta = 7.66–7.59 \) (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, CHHPh), 1.57 ppm (dd, \( J = 12.9, 11.1 \) Hz, 1H, CHHPh); 19F NMR (471 MHz, CDCl3): \( \delta = -74.64, -76.50 \) ppm.

**Exo palladation product:** \(^1\)H NMR (500 MHz, CDCl3): \( \delta = 7.42–7.38 \) (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 = 7.1, 1.6 Hz, 1H, oxazoline–H), 3.64–3.50 (m, 2H, oxazoline–H + CHPh), 2.49 ppm (d, J = 14.5 Hz, 1H, CHPh); 19F NMR (471 MHz, CDCl3): δ = −74.85, −76.05 ppm.

(η4-I-(4'-Acetylphenyl)-2,3,4-triphenylcyclobutadiene)(η5-carbomethoxy-cyclopentadienyl)cobalt(I)

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. (η5-carbomethoxycyclopentadienyl)-(η4-tetraphenylcyclobutadiene)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 MgSO4 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; 1H NMR (300 MHz, CDCl3): 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)OCH3), 2.57 ppm (s, 3H, Ar–C(O)CH3); 13C NMR (75 MHz, CDCl3): δ = 196.49, 166.45, 141.38, 137.78, 135.53, 134.65.
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. ($\eta^5$-carbomethoxycyclopentadienyl)-($\eta^4$-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 MgSO₄ 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; ¹H NMR (300 MHz, CDCl₃): $\delta$ = 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)OCH₃); ¹³C NMR (75 MHz, CDCl₃): $\delta$ = 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): $\nu = 3060, 2920, 2850, 1704, 1685, 1653, 1597, 1277$ cm$^{-1}$; HRMS (ESI$^+$) $m/z$ calculated for $\text{C}_{42}\text{H}_{32}\text{CoO}_3$ [M+H]$^+$: 643.1678; found: 643.1676.

$(\eta^4-1-(4''\text{-Bromobenzoyl})\text{phenyl})-2,3,4\text{-triphenylcyclobutadiene})(\eta^5$-carbomethoxycyclopentadienyl)cobalt(I)

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. $(\eta^5$-carbomethoxycyclopentadienyl)-(\eta^4\text{-tetrphenyl-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$_3$): $\delta = 7.71$ (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)OCH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 195.29, 166.36, 141.90,$
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 C₄₂H₃₁CoO₃Br [M+H]⁺: 721.0783; found: 721.0785.

(η⁴-1,2,3,4-(4′-Acetylphenyl)(cyclobutadiene)(η⁵-carbomethoxy-cyclopentadienyl)cobalt(I)

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. (η⁵-carbomethoxycyclopentadienyl)-(η⁴-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 MgSO₄ 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, CDCl₃): 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)OCH₃), 2.61 ppm (s, 12H, Ar-C(O)CH₂); ¹³C NMR (75 MHz, CDCl₃): 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 C₄₃H₃₉CoNO₆ [M+NH₄]⁺: 724.2104; found: 724.2082.
(η²-1,2,3,4-(4'-Benzoylphenyl)(cyclobutadiene)(η⁵-carbomethoxy-cyclopentadienyl)cobalt(I)

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. (η⁵-carbomethoxycyclopentadienyl)-(η⁴-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 MgSO₄ 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 CH₂Cl₂:petroleum ether (1:50) yielded crystals eligible for x-ray analysis; m.p. 168 °C; ¹H NMR (400 MHz, CDCl₃): 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)OCH₃); ¹³C NMR (100 MHz, CDCl₃): 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 C₆₃H₄₄CoO₆[M+H]⁺: 955.2464; found: 955.2459.
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. 

\((\eta^5\text{-carbomethoxycyclopentadienyl})-(\eta^4\text{-tetraphenyl-cyclobutadiene})\text{cobalt(I)}\) (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 MgSO₄ 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, CDCl₃): \(\delta = 7.70 (dt, J = 17.0, 5.3 \text{ Hz}, 24\text{H, Ar–H}), 7.54 \text{(d, } J = 8.5 \text{ Hz, 8H, Ar–H}), 5.29 \text{(s, 2H, Cp–H)}, 4.89 \text{(s, 2H, Cp–H)}, 3.30 \text{ ppm, (s, 3H, C(O)OCH₃)}; \(^{13}\)C NMR (100 MHz, CDCl₃): \(\delta = 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 \text{ ppm}; \text{IR (neat): } v = 3051, 1713, 1652, 1595, 1583, 1278, 924, 758 \text{ cm}^{-1}; \text{LCMS (ESI\(^+\)) } m/z \text{ calculated for C}_{63}H_{39}CoO_{6}Br_{4} [M]^{+}: 1271.9; \text{found: 1271.9. Molecular formulae confirmed via theoretical isotope pattern.}
Trimethyl(o-tolylethynyl)silane\textsuperscript{238}

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\text{\includegraphics[width=0.2\textwidth]{trimethyltolylethynylsilane.png}}
\]

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 °C. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated \textit{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\%); \textsuperscript{1}H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.60–7.52\) (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\textsuperscript{239}

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\text{\includegraphics[width=0.2\textwidth]{trimethylisopropylethynylsilane.png}}
\]

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 °C. The mixture was then stirred at room temperature overnight. On completion, the mixture was passed through a pad of Celite. The filtrate was concentrated \textit{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\%); \textsuperscript{1}H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.45\) (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, CH(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

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$_2$CO$_3$ (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$_2$O (2 $\times$ 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$_3$): $\delta$ = 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≡CH), 2.50 ppm (s, 3H, Ar–CH$_3$). Spectral data matched that previously reported.

1-Ethynyl-2-isopropylbenzene

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$_2$CO$_3$ (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$_2$O (2 $\times$ 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$_3$): $\delta$ = 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, CH(CH$_3$)$_2$), 3.30 (s, 1H, CCH), 1.33 ppm (d, J = 6.9 Hz, 6H, CH(CH$_3$)$_2$). Spectral data matched that previously reported.
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$_3$N (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$_3$): $\delta$ = 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

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$_3$N (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$_3$): $\delta = 7.59$–$7.51$ (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, CH(CH$_3$)$_2$), 1.34 ppm (d, $J = 6.9$ Hz, 6H, CH(CH$_3$)$_2$). Spectral data matched that previously reported.

*Alternative Synthesis of (2-Isopropylphenyl-ethynyl)benzene*$_{242}$

![Chemical Structure](image)

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$_3$N (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$_3$): $\delta = 7.59$–$7.51$ (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, CH(CH$_3$)$_2$), 1.34 ppm (d, $J = 6.9$ Hz, 6H, CH(CH$_3$)$_2$). Spectral data matched that previously reported.

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

![Chemical Structure](image)

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$_2$Cl$_2$/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$_2$Cl$_2$: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$_3$): $\delta =$ 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), 7.00–6.88 (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)OCH$_3$), 2.18 ppm (s, 6H, Ar–CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta =$ 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): $\nu$ = 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.

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

$^1$H NMR cis (minor) stereoisomer: (400 MHz, CDCl$_3$): $\delta =$ 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)OCH$_3$), 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)

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 ^1H 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; ^1H 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, CH(CH_3)_2), 3.11 (s, 3H, C(O)OCH_3), 0.94–0.89 ppm (d, J = 6.9 Hz, 12H, CH(CH_3)_2);

^13C 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): ν = 3059, 2961, 1703, 1466, 1283, 1143 cm⁻¹;

HRMS (ESI⁺) m/z calculated for C_{41}H_{60}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, CH(CH_3)_2), 3.24 (s, 3H, C(O)OCH_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)

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)OCH3), 2.45–2.40 (d, J = 1.0 Hz, 3H, C(O)CH3), 2.20–2.14 ppm (s, 6H, Ar–CH3); 13C NMR (100 MHz, CDCl3): 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): ν = 3065, 2923, 1704, 1598, 1463, 1280 cm–1; HRMS (ESI⁺) m/z calculated for C39H37CoNO3 [M+NH4⁺]: 626.2100; found: 626.2086.

(η⁴-1-(4'-acetylphenyl)-3-phenyl-2,4-(o-isopropylphenyl)cyclobutadiene)(η⁵-carbomethoxycyclopentadieny)cobalt(I)

Acetyl chloride (0.06 mL, 0.88 mmol) and aluminium chloride (117 mg, 0.88 mmol) were stirred at room temperature in CH2Cl2 (20 mL) for 30 minutes. (η⁴-1,3-(2-isopropylphenyl)-2,4-phenylcyclobutadiene) (η⁵-carbomethoxycyclopentadieny)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 MgSO4 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; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta = 8.34-8.27 \) (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, CH(CH\textsubscript{3})\textsubscript{2}), 3.05–3.01 (d, \(J = 1.3 \) Hz, 3H, C(O)OCH\textsubscript{3}), 2.39–2.35 (d, \(J = 1.3 \) Hz, 3H, C(O)CH\textsubscript{3}), 0.88–0.82 ppm (dt, \(J = 6.8, 1.4 \) Hz, 12H, CH(CH\textsubscript{3})\textsubscript{2}); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta = 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): \(\nu = 2960, 2924, 1712, 1678, 1597, 1465, 1268 \) cm\textsuperscript{-1}; HRMS (ESI\textsuperscript{+}) \(m/z\) calculated for C\textsubscript{43}H\textsubscript{42}CoO\textsubscript{3}[M+H]\textsuperscript{+}: 665.2460; found: 665.2456.

\((\eta^4\cdot1,3\cdot(4'\cdotacetylphenyl)\cdot2,4\cdot(o\cdottolyl)cyclobutadiene)(\eta^5\cdotcarbomethoxy\cdot cyclopentadienyl)cobalt(I)\)

Acetyl chloride (0.13 mL, 1.85 mmol) and aluminium chloride (247 mg, 1.85 mmol) were stirred at room temperature in CH\(_2\text{Cl}_2\) (20 mL) for 30 minutes. (\(\eta^4\cdot1,3\cdot o\cdotTolyl\cdot2,4\cdot phenylcyclobutadiene)(\eta^5\cdotcarbomethoxy\cdot cyclopentadienyl)cobalt(I)\) (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\textsubscript{4} and the solvent was removed \textit{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\(_3\)): \(\delta = 8.31-8.26\) (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)OCH\(_3\)), 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\(_3\)): \(\delta = 197.57, 166.12, 143.47, 138.09, 134.88, 133.54, 130.25, 128.85, 128.78, 126.61, 124.89, 85.93, 84.73, 76.91, 51.44, 29.90, 26.65, 21.25\) ppm; IR (neat): \(\nu = 2918, 2850, 1707, 1596, 1265\) cm\(^{-1}\); HRMS (ESI\(^+\)) \(m/z\) calculated for C\(_{41}\)H\(_{36}\)CoO\(_4\) [M+H\(^+\)]: 651.940; found: 651.1937.

\((\eta^4\text{-1,3-(4'-acetylphenyl)-2,4-(o-isopropylphenyl)cyclobutadiene})(\eta^5\text{-carbomethoxycyclopentadienyl})\text{cobalt(I)}\)

Acetyl chloride (0.12 mL, 1.68 mmol) and aluminium chloride (224 mg, 1.68 mmol) were stirred at room temperature in CH\(_2\)Cl\(_2\) (20 mL) for 30 minutes. \((\eta^4\text{-1,3-(2-isopropylphenyl)-2,4-phenylcyclobutadiene})\ \((\eta^5\text{-carbomethoxy-cyclopentadienyl})\text{cobalt(I)}\) (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 \emph{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$_3$): $\delta = 8.35$–$8.26$ (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, CH(CH$_3$)$_2$), 3.03 (s, 3H, C(O)OCH$_3$), 2.40–2.36 (m, 6H, H, 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$_3$): $\delta = 197.64$, 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): $\nu = 2958$, 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.

$\eta^5$-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(\eta$^4$-I-(4'-acetylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)

\begin{center}
\includegraphics[width=0.3\textwidth]{s331.png}
\end{center}

(S)-331

Acetyl chloride (60 $\mu$L, 0.89 mmol) and aluminium chloride (234 mg, 1.78 mmol) were stirred at room temperature in CH$_2$Cl$_2$ (10 mL) for 30 minutes. $\eta^5$-(S)-2-(4-methylethyl)oxazolinylcyclopentadienyl)-(\eta$^4$-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%). \([\alpha]_D^{24} = -23\ (c = 4.2 \text{ mg/mL in CH}_2\text{Cl}_2)\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 7.80–7.76\) (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, oxazoline–H), 2.59 (s, 3H, COCH\(_3\)), 1.43–1.34 (m, 1H, CH(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\(_3\)): \(\delta = 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.

\(\eta^5\)-(S)-2-(4-methylethyl)oxazolincyclopentadienyl)-(\(\eta^4\)-1-(4’-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)

\[\text{Co} \quad \text{Ph} \quad \text{Ph} \quad \text{Ph} \quad \text{OH} \quad \text{N} \quad \text{Cp} \]

To a flask charged with \(\eta^5\)-(S)-2-(4-methylethyl)oxazolincyclopentadienyl)-(\(\eta^4\)-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\(_2\)Cl\(_2\) (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%). \([\alpha]_D^{25} = +46\ (c = 9.4 \text{ mg/mL in CH}_2\text{Cl}_2)\); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.48–7.39\) (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–
$H), 4.87 (qd, J = 6.4, 2.0 Hz, 1H, CHO), 4.80–4.76 (m, 1H, Cp–H), 4.70 (td, J = 2.6, 1.6 Hz, 1H, Cp–H), 3.54–3.37 (m, 3H, oxazoline–$H), 1.54 (dd, J = 6.5, 1.0 Hz, 3H, CH$_3$), 1.47–1.36 (m, 1H, CH(CH$_3$)$_2$), 0.95 (d, J = 6.7 Hz, 3H, CH(CH$_3$)$_2$), 0.74 ppm (d, J = 6.7 Hz, 3H, CH$_3$)$_2$; $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ = 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): $\nu$ = 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.

$^\eta^5$-(S)-2-(4-methylethyl)oxazolincyclopentadienyl)-(\$^\eta^4$-1-(4$'$-phenylethylhex-5-ynoate)-2,3,4-triphenylcyclobutadiene)cobalt(I)

To a flask charged with 5-hexynoic acid (42 μl, 0.38 mmol) dissolved in CH$_2$Cl$_2$ (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. $^\eta^5$-(S)-2-(4-methylethyl)oxazolincyclopentadienyl)-(\$^\eta^4$-1-(4$'$-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I) (200 mg, 0.32 mmol) was added in one portion and the solution was stirred at r.t. for 16 h. On completion, water (5 mL) was added. The aqueous layer was extracted with CH$_2$Cl$_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$_3$): $\delta$ = 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, ArCHO), 4.55 (t, J
\[ \text{= 8.7 Hz, 1H, ArCHCH}_3; \text{ 4.49 (t, } J = 2.5 \text{ Hz, 1H, Cp-H), 4.35 (t, } J = 2.5 \text{ Hz, 1H, Cp-H), 3.96 (dd, } J = 8.1, 6.5 \text{ Hz, 1H, oxazoline-H), 3.91-3.75 (m, 3H, oxazoline-H), 2.20 (s, 1H, C=CH), 1.90-1.79 (m, 1H,OCCH}_2(CH}_3)_2, 1.61-1.50 (m, 1H, OC(CH}_2)_3CH}_3, 1.40-1.26 (m, 2H, OCCH}_2CH}_2CH}_3, 0.93 (d, } J = 6.6 \text{ Hz, 3H, CH}_3, 0.90-0.78 (m, 12H, 2 x CH(CH}_3)_2), 0.50-0.32 \text{ ppm (m, 2H, 2 x CH(CH}_3)_2); }^{13}\text{C NMR (126 MHz, CDCl}_3): } \delta = 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 \text{ ppm; IR (neat): } \nu = 3297, 3059, 2961, 1732, 1712, 1599, 1158, 1244, 708, 639 \text{ cm}^{-1}; \text{ HRMS (ESI') } m/z \text{ calculated for } C_{47}H_{45}CoNO}_3 [M+H]^+: 731.2759; \text{ found: 731.2751.}

hexafluoroacetylacetonate[(\eta^5-(S)-(R)_p)-2-(2'-4', \text{ methylethyl}oxazolinyl)cyclopentadienyl, 1-C, 3'-N)](\eta^4-1-(4',1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadiene)cobalt(I)]palladium(II)

A flask was charged with \( \eta^5-(S)-2-(4\text{-methylethyl}oxazolinyl)cyclopentadienyl)-(\eta^4-1-(4',1\text{-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 \textit{in vacuo} to give a crude orange solid. The crude product was redissolved in acetone (2 mL) and sodium hexafluoroacetylacetonate (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\(_2\)Cl\(_2\) (2 x 5 mL) and the
organic phases were combined, washed with brine (5 mL) and dried over MgSO₄.
Purification by column chromatography eluting with hexanes/EtOAc (5:1) gave the product as an orange/red solid (410 mg, 0.43 mmol, 64%). \([\alpha]^{20.7}_D = +589\) (c = 8.9 mg/mL in CH₂Cl₂); \(^1\)H NMR (400 MHz, CDCl₃): \(\delta = 7.55–7.48\) (m, 8H, Ar–H), 7.25–7.21 (m, 2H, Ar–H), 7.22–7.12 (m, 9H, Ar–H), 5.92 (s, 1H, CH), 5.17–5.06 (m, 1H, Cp–H), 4.92–4.83 (m, 2H, CHO& 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, CH(CH₃)₂), 1.53 (d, \(J = 6.4\) Hz, 3H, CH₃), 0.80 (d, \(J = 7.0\) Hz, 3H, CH(CH₃)₂), 0.76 ppm (d, \(J = 6.9\) Hz, 3H, CH(CH₃)₂); \(^1^9\)F NMR (471 MHz, CDCl₃): \(\delta = -74.21, -75.72\) ppm.

*Mosher’s Ester Method*²³⁵

To a flask charged with (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoic acid (3 mg, 0.01 mmol) dissolved in CH₂Cl₂ (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. \(\eta^5\)-(S)-2-(4-methylethyl)oxazolincyclopentadienyl)-(\(\eta^1\)-1-(4′-1-hydroxyethylphenyl)-2,3,4-triphenylcyclobutadienecobalt(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 CH₂Cl₂ (2 × 5 mL) and the organic phases were combined, washed with brine (5 mL) and dried over MgSO₄. A crude \(^1\)H-NMR was used to determine diastereoselectivity, using peaks seen for methoxy methyls at 3.57 and 3.50 ppm.
**General Procedure for Transcyclopalladation**

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$_2$Cl$_2$, 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.

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$_3$): $\delta = 7.62$ (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, CH), 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$_3$): $\delta = 36.17$ ppm. Spectral data matched that previously reported.
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$_3$): $\delta$ = 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, CH), 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, CH$_3$), 1.61 ppm (s, 3H, CH$_3$); $^{31}$P NMR (202 MHz, CDCl$_3$): $\delta$ = 30.78 ppm. Spectral data matched that previously reported.

N-(p-Anisyl)-2,2,2-trifluoroacetimidoyl chloride

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$_3$): $\delta$ = 7.34–7.29 (m, 2H, Ar─H), 7.00–6.93 (m, 2H, Ar─H), 3.85 ppm (s, 3H, OCH$_3$); $^{19}$F NMR (471 MHz, CDCl$_3$): $\delta$ = −71.29 ppm. Spectral data matched that previously reported.

(E)-2,2,2-Trifluoroacetimidic acid hex-2-enyl ester$^{11}$

\[ \text{O} \quad \text{N} \quad \text{O} \]
\[ \text{F}_3\text{C} \quad \text{C} \quad \text{H} \]
\[ \text{H} \quad \text{H} \quad \text{H} \]
\[ \text{(E)-271} \]

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$_3$): $\delta$ = 6.85 (d, $J$ = 8.5 Hz, 2H, Ar─H), 6.81–6.72 (m, 2H, Ar─H), 5.93–5.81 (m, 1H, HC=CH), 5.74–5.63 (m, 1H, HC=CH), 4.70 (brs, 1H, OCH$_2$), 3.79 (s, 3H, OCH$_3$), 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$_3$): $\delta$ = −65.23 ppm. Spectral data matched that previously reported.
**(Z)-2,2,2-Trifluoroacetimidic acid hex-2-enyl ester**

![Chemical Structure](image)

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 (SiO₂, 98.5/1.5 hexanes/EtOAc) gave the product as a pale yellow oil (1.04 g, 3.46 mmol, 82%). 

**¹H NMR (500 MHz, CDCl₃):** 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=CH₂), 4.82 (brs, 1H, OCH₂), 3.79 (s, 3H, OCH₃), 2.19–2.06 (m, 2H, CH₂CH₂CH₃), 1.43 (sext, *J* = 7.3 Hz, 2H, CH₂CH₂CH₃), 0.94 ppm (t, *J* = 7.3 Hz, 3H, CH₂CH₂CH₃); 

**¹⁹F NMR (471 MHz, CDCl₃):** δ = -65.23 ppm. Spectral data matched that previously reported.

**(E)-2,2,2-Trichloroacetimidic acid but-2-enyl ester**

![Chemical Structure](image)

A solution of crotyl alcohol (2.35 mL, 27.74 mmol) and DBU (0.83 mL, 5.55 mmol) in CH₂Cl₂ (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$_3$):
$\delta =$ 8.26 (s, 1H, NH), 5.94–5.83 (m, 1H, HC=CH), 5.74–5.65 (m, 1H, HC=CH), 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](image)

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$_2$Cl$_2$ (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$_3$): $\delta =$ 8.26 (s, 1H, NH), 5.90–5.80 (m, 1H, HC=CH), 5.72–5.62 (m, 1H,
HC=CH), 4.73 (d, $J =$ 6.3 Hz, 2H, OCH$_2$CH=CH), 2.05 (q, $J =$ 7.1 Hz, 2H, CH$_2$CH$_2$CH$_3$),
1.42 (sext., $J =$ 7.4 Hz, 2H, CH$_2$CH$_2$CH$_3$), 0.90 ppm (t, $J =$ 7.4 Hz, 3H, CH$_2$CH$_2$CH$_3$).
Spectral data matched that previously reported.

$^{(Z)}$-2,2,2-Trichloroacetimidic acid hex-2-enyl ester$^{203}$

![Z-299](image)

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$_2$Cl$_2$ (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 (SiO₂, 49:1 hexanes/EtOAc) to give the product as a colourless oil (5.30 g, 22.8 mmol, 96%). ¹H NMR (500 MHz, CDCl₃): δ = 8.28 (s, 1H, NH), 5.76–5.63 (m, 2H, HC=CH), 4.84 (d, J = 6.1 Hz, 2H, OCH₂), 2.12 (q, J = 7.1 Hz, 2H, CH₂CH₂CH₃), 1.42 (sext, J = 7.3 Hz, 2H, CH₂CH₂CH₃), 0.91 ppm (t, J = 7.4 Hz, 3H, CH₂CH₂CH₃). Spectral data matched that previously reported.

(E)-2,2,2-Trichloroacetimidic acid 3-phenylprop-2-enyl ester²⁰³

![Chemical structure](image.png)

A solution of cinnamyl alcohol (2.00 g, 14.91 mmol) and DBU (0.45 mL, 2.98 mmol) in CH₂Cl₂ (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 (SiO₂, 97:3 hexanes/EtOAc) to give the product as a yellow oil (2.75 g, 9.84 mmol, 66%). ¹H NMR (500 MHz, CDCl₃): δ = 8.28 (s, 1H, NH), 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, PhCH=CH), 6.39–6.24 (m, 1H, PhCH=CH), 4.88 ppm (dt, J = 6.1, 1.3 Hz, 2H, CH₂). Spectral data matched that previously reported.

(E)-2,2,2-Trichloroacetimidic acid 4-phenylbut-2-enyl ester²⁰³

![Chemical structure](image.png)

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 CH₂Cl₂ (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...
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$_3$): \( \delta = 8.32 \) (s, 1H, NH), 7.32 (t, \( J = 7.0 \) Hz, 2H, Ar–H), 7.25–7.17 (m, 3H, Ar–H), 6.12–6.00 (m, 1H, HC=CH), 5.85–5.72 (m, 1H, HC=CH), 4.83–4.76 (m, 2H, OCH$_2$), 3.45 ppm (d, \( J = 6.7 \) Hz, 2H, CH$_2$Ph). Spectral data matched that previously reported.

\( (E)-2,2,2\text{-Trichloroacetimidic acid hex-2,5-dienyl ester}^{243} \)

\[
\text{Cl}_3\text{C}=\text{O} \rightleftharpoons \text{CH}=\text{C} \rightleftharpoons \text{NH}
\]

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$_2$Cl$_2$ (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$_3$): \( \delta = 8.28 \) (s, 1H, NH), 5.98–5.63 (m, 3H, 3 x C=CH), 5.09–5.01 (m, 2H, C=CH$_2$), 4.76 (d, \( J = 6.1 \) Hz, 2H, OCH$_2$), 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**$^{203}$

![Diagram](attachment:diagram.png)

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\textsuperscript{11}

Isolated as pale yellow oil, enantiomeric excess was determined after removal of the trifluoroacetyl group. \textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}): \(\delta = 6.75\) (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, HC=CH\textsubscript{2}), 5.18 (dt, \(J = 17.2, 1.3\) Hz, 1H, HC=CH\textsubscript{2}), 5.10 (dt, \(J = 10.3, 1.2\) Hz, 1H, HC=CH\textsubscript{2}), 5.02 (q, \(J = 7.6\) Hz, 1H, NCH\textsubscript{3}), 3.73 (s, 3H, OCH\textsubscript{3}), 1.63–1.50 (m, 2H, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 1.49–1.40 (m, 2H, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}), 0.94 ppm (t, \(J = 7.3\) Hz, 3H, CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{3}). Spectral data matched that previously reported.

General Procedure for Deprotection of Trifluoroacetyl Group\textsuperscript{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\textsubscript{2}Cl\textsubscript{2}. The organic phases are combined and dried over MgSO\textsubscript{4} and the solvent is removed in vacuo. Purification of the residue by flash chromatography (SiO\textsubscript{2}, 19:1 hexanes/EtOAc) gave the products as oils.

\(N\)-(4-Methoxyphenyl)-3-amino-1-hexene\textsuperscript{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$_3$):

$\delta = 6.76$ (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, HC=CH$_2$), 5.19 (td, $J = 17.2, 1.3$ Hz, 1H, HC=CHH-trans), 5.11 (td, $J = 10.3, 1.1$ Hz, 1H, HC=CHH-cis), 3.71–3.76 (m, 1H, NCH), 3.74 (s, 3H, OCH$_3$), 3.37 (broad s, 1H, NH), 1.48–1.63 (m, 2H, CH$_2$CH$_2$CH$_3$), 1.40–1.48 (m, 2H, CH$_2$CH$_2$CH$_3$), 0.95 ppm (t, $J = 7.3$ Hz, 3H, CH$_3$CH$_2$CH$_3$). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(but-3-en-2-yl)acetamide$^{203}$

\[
\begin{align*}
\text{HN} & \quad \text{Cl}_3\text{C} \\
\end{align*}
\]

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$_3$):

$\delta = 6.56$ (brs, 1H, NH), 5.87 (ddd, $J = 17.2, 10.5, 5.1$ Hz, 1H, HC=CH$_2$), 5.29–5.22 (m, 1H, HC=CH), 5.22–5.15 (m, 1H, HC=CHH), 4.54 (dddt, $J = 8.4, 6.8, 5.0, 1.6$ Hz, 1H, NCH), 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$^{203}$

\[
\begin{align*}
\text{HN} & \quad \text{Cl}_3\text{C} \\
\end{align*}
\]

(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$_3$):

$\delta = 6.49$ (brs, 1H, NH), 5.78 (ddd, $J = 16.0, 9.8, 5.6$ Hz, 1H, HC=CH$_2$), 5.22 (dd, 1H, $J = 15.8, 0.9$ Hz, HC=CHH-trans), 5.17 (dd, $J = 9.8, 0.9$ Hz, 1H, HC=CHH-cis), 4.47–4.43 (m,
1H, NCH), 1.67 (q, J = 7.1 Hz, 2H, CH₂CH₂CH₃), 1.40 (sext., J = 7.4 Hz, 2H, CH₂CH₂CH₃), 0.94 ppm (t, J = 7.4 Hz, 3H, CH₂CH₂CH₃). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(1-phenylallyl)acetamide

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). ¹H NMR (500 MHz, CDCl₃): δ = 7.46–7.25 (m, 5H, Ar–H), 6.95, (brs, 1H, NH), 6.05 (ddd, J = 16.0, 10.3, 5.42 Hz, 1H, HC=CH₂), 5.59–5.51 (m, 1H, NCH), 5.36 (d, J = 10.3 Hz, 1H, HC=CHH-cis), 5.30 ppm (dd, J = 16.8 Hz, 1H, HC=CHH-trans). Spectral data matched that previously reported.

2,2,2-Trichloro-N-(1-benzylallyl)acetamide

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). ¹H NMR (500 MHz, CDCl₃): δ = 7.33–7.17 (m, 5H, Ar–H), 6.56 (brs, 1H, NH), 5.85 (ddd, J = 16.5, 10.8, 5.4 Hz, 1H, HC=CH₂), 5.19 (ddd, J = 10.3, 1.2 Hz, 1H, HC=CHH-cis), 5.18 (dd, J = 17.7, 1.2 Hz, 1H, HC=CHH-trans), 4.76–4.67 (m, 1H, NCH), 3.01 (dd, J = 13.8, 6.6 Hz, 1H, CHHPh), 2.92 ppm (dd, 1H, J = 13.6, 6.6 Hz, CHHPh). Spectral data matched that previously reported.
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$_3$): $\delta$ = 6.63 (brs, 1H, NH), 5.89–5.74 (m, 2H, 2 x HC=CH$_2$), 5.74–5.62 (m, 1H, C=CHH), 5.28–5.13 (m, 1H, HC=CHH), 5.12–5.01 (m, 2H, 2 x HC=CHH), 4.81 (d, $J = 6.5$ Hz, 6H), 4.54 (p, $J = 7.1$ Hz, 1H, NCH), 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-\(\mu\)-acetatobis[\((\eta^5\cdot(S)\cdot2\cdot(2'\cdot4'\cdot\text{methylene})\text{oxazolinyl})\text{cyclopentadienyl}, \ 1\cdot\text{C}, \ 3'\cdot\text{N}(\eta^4\cdot\text{tetraphenylcyclobutadiene})\text{cobalt(I)})\text{dipalladium(II)}\)

\[(S,S_p)\sim 118 \quad (S,R_p)\sim 118\]

Crude \(^1H\)-NMR of mixture of acetate dimers (solvent = \(\text{CH}_2\text{Cl}_2\), temp = rt, time = 16h, ratio ca. 2:1 \([S_p:R_p]\)):

\([\alpha]_D^{26} = -600 \ (c = 0.3 \text{ mg/mL in CH}_2\text{Cl}_2).\)
hexafluoroacetylacetonate[(η⁵-(S)-2-(2′-(4′-methyl)oxazolinyl)cyclopentadienyl, 1-C, 3′-N)(η⁴-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)

Crude ¹H-NMR of mixture of hfacac monomers (solvent = AcOH, temp = 95 °C, time = 30 min, ratio ca. 1.5:1 [Sₚ:Rₚ]):

[α]D²⁴ = −443 (c = 0.7 mg/mL in CH₂Cl₂).
Crude $^1$H-NMR of mixture of hfacac monomers (solvent = CH$_2$Cl$_2$, temp = rt, time = 16h, ratio ca. 1:2.5 [S$_p$-R$_p$]):

$[^a]_D^{24} = +467$ (c = 0.6 mg/mL in CH$_2$Cl$_2$).

hexafluoroacetylacetonate{$\eta^5$-(S)-2-(4'-isobutyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N}{$\eta^4$-tetraphenylcyclo- butadiene)cobalt(I)]palladium(II)
Crude $^1$H-NMR of mixture of hfacac monomers (solvent = AcOH, temp = 95 °C, time = 30min, ratio ca. 10:1 $[S_p^o:R_p]$):

$\alpha_D^{26} = -545$ (c = 1.5 mg/mL in CH$_2$Cl$_2$).
Crude $^1$H-NMR of mixture of hfacac monomers (solvent = CH$_2$Cl$_2$, temp = rt, time = 16h, ratio ca. 13:1 [$S_p$:R$_p$]):

$[\alpha]_D^{26} = -586$ (c = 2.2 mg/mL in CH$_2$Cl$_2$).
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[$(\eta^5-(S)-2-(2'-(4'-cyclohexylmethyl)oxazolinyl)cyclopentadienyl, 1-C, 3'-N(\eta^4$-tetraphenylcyclo- butadiene)cobalt(I))palladium(II)])
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$_2$Cl$_2$).
Crude $^1$H-NMR of mixture of hfacac monomers (solvent = CH$_2$Cl$_2$, temp = rt, time = 16h, ratio ca. 2:1 [S$_p$:R$_p$]):

$[\alpha]_D^{26} = -91.6$ (c = 1.2 mg/mL in CH$_2$Cl$_2$).
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($\eta^5$-(S)-2'-(4'-benzyl)oxazolinyl)cyclopentadienyl, 1'-C, 3'-N($\eta^4$-tetraphenylcyclobutadiene)cobalt(I)palladium(II)
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$_2$Cl$_2$).
Crude $^1$H-NMR of mixture of hfacac monomers (solvent = CH$_2$Cl$_2$, 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

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Injection Volume : 5 μL
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Method File Name : IPA 0.5S0.8flow.lem
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Quantitative Results:
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Quantitative Results:

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Chromatogram:

Quantitative Results:

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Chromatogram:

Quantitative Results:
PDA

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<th>Ret. Time</th>
<th>Area</th>
<th>Height</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RT6.459</td>
<td>6.459</td>
<td>18700412</td>
<td>1121239</td>
<td>89.452</td>
</tr>
<tr>
<td>2</td>
<td>RT8.519</td>
<td>8.519</td>
<td>2205018</td>
<td>91497</td>
<td>10.548</td>
</tr>
</tbody>
</table>

[Chemical structures and reaction equations]
**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,Se-249:**

**CCDC-931363**
X-Ray representation and data for R.R.249:

Table 14. Crystal data and structure refinement.

<table>
<thead>
<tr>
<th>Identification code</th>
<th>2013ncs0001/ DJC-387</th>
</tr>
</thead>
<tbody>
<tr>
<td>Empirical formula</td>
<td>C41H43CoN2O4Pd</td>
</tr>
<tr>
<td>Formula weight</td>
<td>793.10</td>
</tr>
<tr>
<td>Temperature</td>
<td>100(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71075 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
</tbody>
</table>
Space group $P2_12_12_1$

Unit cell dimensions

\[
a = 28.653(2) \, \text{Å} \quad a = 90^\circ
\]

\[
b = 8.5350(7) \, \text{Å} \quad b = 90^\circ
\]

\[
c = 14.5829(11) \, \text{Å} \quad g = 90^\circ
\]

Volume $3566.3(5) \, \text{Å}^3$

$Z$ 4

Density (calculated) 1.477 Mg / m$^3$

Absorption coefficient 1.014 mm$^{-1}$

$F(000)$ 1632

Crystal Blade; orange

Crystal size $0.160 \times 0.050 \times 0.010 \, \text{mm}^3$

\(\theta\) range for data collection $3.110 - 27.482^\circ$

Index ranges \(-30 \leq h \leq 33, -11 \leq k \leq 10, -18 \leq l \leq 10\)

Reflections collected 14604

Independent reflections 7438 [$R_{int} = 0.0963$]

Completeness to \(\theta = 25.242^\circ\) 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$^{-3}$

---


**Special details:** There are 2 water molecules in the asymmetry 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 $S_{e265}$:

CCDC-931365
X-Ray representation for rac-257:

CCDC-931364
Chapter 8 - References


(84) Zhao, G.; Yang, Q.; Mak, T. C. W. *Organometallics* **1999**, *18*, 3623–3636.


(102) Zhao, G.; Feng Xue; Zhang, Z.-Y.; Mak, T. C. W. *Organometallics* 1997, 16, 4023–4026.


