FROM OLEFIN METATHESIS TO ORGANORUTHENIUM HOMOGENEOUS CATALYSIS: SYNTHESIS, APPLICATIONS AND MECHANISTIC UNDERSTANDING

Simone Manzini

A Thesis Submitted for the Degree of PhD at the University of St Andrews

2014

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From olefin metathesis to organoruthenium homogeneous catalysis: Synthesis, applications and mechanistic understanding

Simone Manzini

This thesis is submitted in partial fulfilment for the degree of PhD at the University of St Andrews

July 16th 2014
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<td>‡</td>
<td>Transition state</td>
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<tr>
<td>2-MeTHF</td>
<td>2-methyl tetrahydrofuran</td>
</tr>
<tr>
<td>Ac</td>
<td>Acetyl</td>
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<tr>
<td>ADMET</td>
<td>Acyclic Diene Metathesis</td>
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<td>Ar</td>
<td>General aromatic group</td>
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<td>BArF</td>
<td>Tetrakis[3,5-bis(trifluoromethyl)phenyl]borate</td>
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<td>BINOL</td>
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<td>Bn</td>
<td>Benzyl</td>
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<td>Bu</td>
<td>Butyl</td>
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<td>cat.</td>
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<td>COD</td>
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<tr>
<td>conc.</td>
<td>Concentrated</td>
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<td>Cp</td>
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<tr>
<td>CPME</td>
<td>Cyclopentyl methyl ether</td>
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<tr>
<td>Cy</td>
<td>Cyclohexyl</td>
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<td>d</td>
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dd  Double of doublets
δ   Chemical shift
ΔE  Energy span
DCM Dichloromethane
DFT Density functional theory
DKR Dynamic kinetic resolution
DMSO Dimethyl sulfoxide
DMF N,N-Dimethylmethanamide
DCE 1,2-dichloroethane
E   General heteroatom
E_A Activation Energy
ee Enantiomeric excess
EM Effective molarity
Et Ethyl
Eta-5 RuCl(PPh₃)₂(3-phenylindenyl)
Eta-5-H RuH(PPh₃)₂(3-phenylindenyl)
Eta-5-BArF Ru(PPh₃)₂(3-phenylindenyl)(BArF)
Eta-5-SiR₃ RuH₂(SiR₃)₂(3-phenylindenyl)
EVE Ethyl vinyl ether
EXSY Exchange spectroscopy
GI RuCl₂(PCy₃)₂(benzylidene)
GI-py RuCl₂(PCy₃)(3-bromopyridine)₂(benzylidene)
GII RuCl₂(SIMes)(PCy₃)(benzylidene)
GII-SIPr RuCl₂(SIPr)(PCy₃)(benzylidene)
GII-py RuCl₂(SIMes)(3-bromopyridine)₂(benzylidene)
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<td>N-Heterocyclic carbenes</td>
</tr>
<tr>
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<td>Ortho</td>
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<tr>
<td>p-</td>
<td>Para</td>
</tr>
<tr>
<td>PI</td>
<td>RuCl&lt;sub&gt;2&lt;/sub&gt;(PCy&lt;sub&gt;3&lt;/sub&gt;)(tricyclohexylphosphoniumethylidene)(BF&lt;sub&gt;4&lt;/sub&gt;)</td>
</tr>
<tr>
<td>PII</td>
<td>RuCl&lt;sub&gt;2&lt;/sub&gt;(SIMes)(tricyclohexylphosphoniumethylidene)(BF&lt;sub&gt;4&lt;/sub&gt;)</td>
</tr>
<tr>
<td>PCM</td>
<td>Polarizable continuum solvation model</td>
</tr>
<tr>
<td>PCy&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Tricyclohexylphosphine</td>
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<tr>
<td>PES</td>
<td>Potential-energy surfaces</td>
</tr>
<tr>
<td>Phob</td>
<td>Phosphabicyclo[3.3.1]nonane</td>
</tr>
<tr>
<td>Pin</td>
<td>tetramethylene glycol (pinacol)</td>
</tr>
<tr>
<td>PPh&lt;sub&gt;3&lt;/sub&gt;</td>
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</tr>
<tr>
<td>py</td>
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<tr>
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</tr>
<tr>
<td>RCM</td>
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</tr>
<tr>
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<td>Ring Opening Cross Metathesis</td>
</tr>
<tr>
<td>ROMP</td>
<td>Ring Opening Metathesis Polymerization</td>
</tr>
<tr>
<td>RMM</td>
<td>Ring Rearrangement Metathesis</td>
</tr>
<tr>
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<td>Room temperature</td>
</tr>
<tr>
<td>S</td>
<td>entropy</td>
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</table>
s  Singlet
sat. aq.  Saturated aqueous
SHOP  Shell® higher olefin process
SICy  1,3-Biscyclohexylimidazolidin-2-ylidene
SIMes  1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene
SIPr  1,3-Bis(2,6-di-iso-propylphenyl)imidazolidin-2-ylidene
SIlBu  1,3-Bis(tert-butyl)imidazolidin-2-ylidene
SVB  Split-valence basis set
t  Triplet
'tBu  Tert-butyl
TBA  Tetrabutylammonium
TDI  Turnover determining intermediate
TDTS  Turnover determining transition state
TEP  Tolman electronic parameter
THF  Tetrahydrofuran
TON  Turnover number
TOF  Turnover frequency
TPT  1,3,4-triphenyl-4,5-dihydro-1H-1,2,4-triazol-5-ylidene
Ts  4-methylbenzene-1-sulfonyl
TZVP  Triple zeta valence plus polarisation
%Vbur  Buried volume
X  General anionic group
ABSTRACT

Olefin metathesis is a valuable synthetic tool, widely used in several fields of science. Due to the importance of this transformation several contributions have been made in this field in order to understand mechanistic aspects, reactivity and applicability of this process.

In this topic, ruthenium indenylidene complexes have shown great activity and stability in metathesis, making them very valuable pre-catalysts. However, several aspects of these pre-catalysts have not been evaluated yet. For example, even though reports of active second generation ruthenium indenylidene complexes bearing bulky N-heterocyclic carbenes are present in the literature, no studies have been done to understand how steric hindrance affects the process. For these reasons, [RuCl₂(IPr*)(PPh₃)(3-phenylindenylidene)] (IPr*-PPh₃) and [RuCl₂(IPr*)(Py)(3-phenylindenylidene)] (IPr*-Py), bearing the very bulky ligand, IPr* have been synthesised and compared with [RuCl₂(IPr)(PPh₃)(3-phenylindenylidene)] (IPr-PPh₃) and the new [RuCl₂(IPr)(Py)(3-phenylindenylidene)] (IPr-Py).

Another important aspect, presented in this thesis, is the investigation of the stability of indenylidene pre-catalysts in alcohol solvents. Surprisingly, several different decomposition processes occur depending on the starting complex and the alcohol used. Mechanistic investigation into this decomposition, allowed us to develop a better understanding of this process, and to predict the decomposition product based on the environment. In particular, this study revealed that [RuCl(η⁵-3-phenylindenyl)(PPh₃)₂] (Eta-5) is accessed from [RuCl₂(3-phenylindenylidene)(PPh₃)₂] (M₁₀) via a novel indenylidene to η²-indenyl rearrangement. This formal decomposition product has been found to be active in at least 20 different catalytic transformations, rendering it a versatile catalytic tool.
Chapter I: Introduction to Ruthenium Catalysed Olefin Metathesis

Olefin metathesis is a valuable synthetic transformation. It consists of a scrambling of two double bonds, via a series of bond breaking and bond making, promoted by an organometallic catalyst (Scheme 1.1).

![Scheme 1.1: Metathesis reaction.](image)

The first olefin metathesis reaction was reported in the 1960’s where a research group at Du Pont described the polymerisation of norbornene in the presence of lithium tetraheptyl aluminium titanium tetrachloride.¹ Four years later, Natta and co-workers reported the formation of an unsaturated polymer in the polymerisation of cyclopentene using molybdenum and tungsten halides.² In the same year, researchers at Phillips Petroleum Company described an olefin disproportionation process with tungsten and molybdenum carbonyl complexes.³ However, it was not until 1967, when Calderon and co-workers at the Goodyear Tire and Rubber Company described this metal-catalysed redistribution of carbon-carbon atoms as “metathesis” (form Greek word “μετάθεσις”, which means change of position).⁴ Three years later, Chauvin and Hérisson proposed that the olefin metathesis proceeds through formation of metallacyclobutane intermediates (V and VIII), which form after coordination of olefin(s) to
metal alkylidenes (III and VII) via a series of alternating [2+2]-cycloadditions and cycloreversions (Scheme 1.2).

Scheme 1.2: General olefin metathesis mechanism.

From these early investigations, several efforts from several research groups have contributed to the field, making olefin metathesis an important and valuable transformation for academia and industry and leading ultimately to award of the Nobel Prize in Chemistry to Yves Chauvin, Robert Grubbs and Richard Schrock for their work in this area in the year 2005.

Olefin metathesis can be divided in different subclasses based on the transformation considered: Cross Metathesis (CM), Ring Closing Metathesis (RCM), Ring Opening Cross Metathesis (ROCM), Ring Opening Metathesis Polymerisation (ROMP), Acyclic Diene Metathesis (ADMET), Ring Rearrangement Metathesis (RMM) and Enyne Metathesis (Scheme 1.3).
As well as these reactions, there are other metathesis transformations that should be noted. The alkyne analogues of RCM, CM and ROMP are known as ring closing alkyne metathesis, cross alkyne metathesis and ring opening alkyne metathesis polymerisation, respectively (Scheme 1.4).\(^7\)

While the early stages in olefin metathesis relied on ill-defined heterogeneous titanium, rhenium, molybdenum or tungsten catalysts, culminating in the development of the SHOP process (shell higher olefin process) in the laboratories of Shell\(^9,8\) the major improvements for
synthetic chemistry have been accomplished by homogeneous systems using ruthenium, tungsten and molybdenum complexes as catalysts.

**WELL DEFINED MOLYBDENUM AND TUNGSTEN CATALYSTS FOR OLEFIN METATHESIS**

Molybdenum and tungsten olefin metathesis systems, mainly developed by Schrock and Hoveyda, are typically high oxidation state $d^0$-metal alkylidene complexes having a set of amido or oxo ligands which stabilise the electrophilic metal centre (Figure 1.1).

![Figure 1.1: Examples of molybdenum and tungsten based olefin metathesis precatalysts.](image)

These complexes reveal sensitivity towards temperature, oxygen and moisture. Also, acidic compounds such as aldehydes and alcohols can deactivate these catalysts, mainly due to the high oxophilicity of the metal centre. However, their stability can be increased by using chelating pyridine based ligands, like 1,10-phenanthroline. The bench stable catalyst **Mo-3** requires the use of ZnCl$_2$ to be activated (Scheme 1.5).
Despite the aforementioned drawbacks, this family of complexes shows remarkable selectivity towards stereospecific reactions. In particular, molybdenum complexes were the first systems to efficiently access Z-olefins via the cross-metathesis reaction. An interesting application of a Z-selective molybdenum catalyst (compound **Mo-4**, Scheme 1.6) is the synthesis of **KRN7000**, an antitumor agent and potent immune stimulant, firstly isolated in 1990 at Kirin Pharmaceuticals.

**Scheme 1.5:** Bench stable molybdenum pre-catalyst.

**Scheme 1.6:** Z-selective molybdenum catalyst applied for the synthesis of KRN7000.
Regarding this olefin stereoselectivity, only recently have Ru-based complexes accessed similar selectivity (see ruthenium section), albeit with lower activities. In addition, molybdenum and tungsten show remarkable activity in alkyne metathesis,\(^{13}\) which still remains a challenging transformation for ruthenium analogues.

**WELL-DEFINED RUTHENIUM CATALYSTS FOR OLEFIN METATHESIS**

Since 1965, ruthenium(III) trichloride, as well as the corresponding osmium(II) and iridium(I) chloride salts, were considered to be active in olefin metathesis.\(^{14}\) However, their reactivity was limited to the ROMP of 7-oxa-norbornene derivatives at high temperatures. Only several years later, in 1992, Grubbs et al. accessed the first well defined Ru-alkylidene complex Ru-2, which proved to be active in ROMP reactions of strained olefins like norbornene at room temperature. Easily accessible from the reaction of dichlorotris(triphenylphosphine)-ruthenium(II) and 2,2'-diphenylcyclopropene, the alkenylidene complex Ru-2 was also found to be more tolerant in several functional groups (scheme 1.7).\(^{15}\)

![Scheme 1.7: Ruthenium alkenylcarbene complexes.](image)

Substituting the triphenylphosphine ligands in Ru-2 with the more electron-donating tricyclohexylphosphine (PCy\(_3\)) (Scheme 1.7) led to a significant improvement of reactivity, enabling the ROMP of a larger number of olefins. In addition, complex Ru-3 showed activity towards different metathesis reactions like RCM.\(^{16}\)

The big breakthrough in this field was the introduction of ruthenium complexes bearing benzylidene ligands in place of alkenylidene ligands. This class of complexes is accessed by
reacting complex Ru-1 with phenyl diazomethane affording complex Ru-4 and, by subsequent phosphine exchange, complex GI (Scheme 1.8).\(^\text{17}\)

![Scheme 1.8: Ruthenium benzylidene complexes.](image)

Benzylidene catalysts are more functional group tolerant than Ru-3 and Ru-4 and remarkably stable towards oxygen and moisture in the solid state. Yet, despite the properties of GI, the use of phenyl diazomethane, which is a highly explosive chemical, limits the large scale preparation of these catalysts in this way. In order to make ruthenium olefin metathesis systems more valuable, the scientific community put in important efforts to gain faster access to active pre-catalysts bearing the alkylidene moiety starting from less harmful reagents.\(^\text{18}\) An interesting example of this approach can be found in the synthesis of ruthenium vinylidene (Ru-8)\(^\text{19}\) and allenylidene (Ru-7)\(^\text{20}\) complexes by reacting ruthenium complexes with terminal alkyl/aryl alkynes or propargylic alkynes, respectively (Scheme 1.9).
Scheme 1.9: Allenylidene and vinylidene Ruthenium complexes.

Although Ru-8 and Ru-7 are obtainable from non-hazardous reagents, they are less active than their benzylidene counterparts, requiring longer reaction times and often harsher conditions.

Inspired by the use of alkynes for the synthesis of ruthenium carbenes, Hill and co-workers described the synthesis of the coordinately unsaturated allenylidene complex Ru-10 (Scheme 1.10 a). Surprisingly, the spectroscopic data were not in agreement with the structure proposed by the authors. In fact, in the same year, the correct structure was elucidated in our group, in the synthesis of a 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) derivative of Ru-10 via X-ray analysis. The data revealed that the allenylidene moiety had actually rearranged to form a 3-phenylindenylidene ligand, thereby giving complex [RuCl₂(3-phenylidinylidene)(IPr)(PCy₃)] (Ru-13) as shown in scheme 1.10 b. These indenylidene complexes are easily accessed by reacting [RuCl₂(PPh₃)₃] (Ru-1) and 1,1-diphenyl-2-propyn-
1-ol, in the presence of a Lewis acid, yielding the bistriphenylphosphine Ru-indenylidene complex, commercialised by UMICORE© with the name of M_{10} (Scheme 1.10 a).^{23}

Scheme 1.10: Ruthenium indenylidene complexes.

The mechanism proposed for this transformation involves the formation of the allenylidene complex Ru-10, which reacts rapidly with catalytic amounts of acid to afford intermediate Ru-11, which quickly coordinates a molecule of THF to form the cationic carbide species Ru-12. The carbyne-carbon atom in complex Ru-12 is highly electrophilic and therefore reacts with one of the benzene rings attached to C_γ, forming the 3-phenylindenylidene moiety via nucleophilic intramolecular attack.^{23} These Ru-indenylidene complexes show high air and moisture stability, good thermal stability, and excellent tolerance toward functional groups. In addition, a wide selection of Ru-indenylidene precursors is commercially available.^{18b}
HETEROPLETIC N-HETEROCYCLIC CARBENE (NHC)/PHOSHINE RUTHENIUM COMPLEXES

Despite the numerous successes achieved with GI and other alkylidene derivatives, the breakthrough for allowing ruthenium-catalysed olefin metathesis to be used as a valuable synthetic tool in organic chemistry was the introduction of N-heterocyclic carbenes (NHCs) as ligands.

N-heterocyclic carbenes (NHCs) are by far the most studied members of the family of nucleophilic carbenes. Easily to synthesise, usually from stable precursors, these compounds have found several applications in numerous fields of homogeneous catalysis either as ligands or as catalysts themselves.7,24

Early work on their coordination to metal centres dates back to the 1960s by Ofele25 and Wanzlick26 and was followed by important organometallic studies by Lappert and co-workers.27 The real breakthrough facilitating forays into catalytic applications came in 1991 when the group of Arduengo reported the isolation of “free” IAd (Figure 1.2).28
Figure 1.2: Most frequently used N-Heterocyclic Carbenes.

NHCs are singlet carbenes featuring a sp$^2$-hybridised carbene carbon atom, with two nonbonding electrons occupying the sp$^2$-orbital with antiparallel spin orientation, while the p-orbital remains unoccupied. In principle, NHCs display an ambiphilic behaviour, but they are mostly σ-donating ligands. The singlet ground state of an NHC is stabilised by the electron withdrawing nitrogen atoms at the carbene carbon atom. In addition, mesomeric effects are fundamental for the stabilisation of NHCs. In fact, the nonbonding electron pairs of the π-donors can effectively interact with the empty π-orbital at the carbene carbon atom resulting in the formation of a four electron three-centre π-system, where the X–C bonds obtain a partial double bond character (Figure 1.3).
Consequently, planar nitrogen substituents which are more electronegative than carbon and possess a free electron pair with p-symmetry are perfectly suited to stabilise a singlet carbene carbon atom.\textsuperscript{7,24b}

The first application of NHCs in ruthenium-based olefin metathesis dates back to 1998 when Herrmann and co-workers used N-alkyl substituted NHCs to replace both phosphine ligands in GI to generate a series of highly stable homoleptic complexes (Figure 1.4).\textsuperscript{30}

Despite their high stability, these complexes did not show a significant improvement in metathesis activity, mostly due to their slow initiation rates, which was attributed to the NHCs being more strongly bound to the metal centre than phosphines.\textsuperscript{30}

Different results were observed with mixed NHC/phosphine heteroleptic ruthenium complexes. First, reported simultaneously by Grubbs and Nolan, a non-labile 3-bis(2,4,6-
trimethylphenyl)imidazol-2-ylidene (IMes) was combined with a labile ligand such as tricyclohexylphosphine or triphenylphosphine to generate the mixed NHC and phosphine complexes, Ru-19 and Ru-20, respectively. These complexes exhibit not only higher RCM activity affording even tetrasubstituted cycloolefins, but also improved thermal stability compared to the parent bis(tricyclohexylphosphine) complex (Figure 1.5). \(^{31}\)

![Figure 1.5: Heteroleptic NHC-Phosphine ruthenium catalysts.](image)

From these early achievements with mixed NHC/phosphine systems, a plethora of new complexes bearing different NHC ligands have been reported in the literature, revealing continuously improved activities, supported systems and stereoselective reactions. Among them, the introduction of saturated NHCs revealed outstanding increases in reactivity, allowing RCM at very low catalyst loading, stability to air and moisture in the solid state and tolerance towards different functional groups.\(^{9a,33}\) From this family, the Ru-benzylidene complex bearing 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene (SIMes) and tricyclohexylphosphine is one of the frequently used ruthenium pre-catalysts, due to its balanced performance in several reactions. This complex is also known as Grubbs’ second generation catalyst (GII) (Figure 1.6). \(^{33-34}\)
In line with these observations, also in the case of phenylindenylidene complexes the introduction of heteropletic systems leads to an important improvement of reactivity and stability, even beyond those of the benzylidene type complexes. Recent achievements in the use of these compounds in catalysis and in understanding their reactivity will be discussed in chapter II.

CHELATING-ALKYLIDENE BEARING RUTHENIUM COMPLEXES FOR OLEFIN METATHESIS

This class of complexes was first discovered by Hoveyda et al. reacting GII and 1-isopropoxy-2-vinylbenzene in a ROCM reaction. Surprisingly, instead of accessing the expected metathesis product, the formation of GHIII was achieved (Figure 1.6).\textsuperscript{35}

These complexes show remarkable robustness, due to the slow activation rate, resulting in high activities in several transformations where a thermal induction is necessary to promote the reaction (for example sterically hindered substrates).\textsuperscript{9a,33}
Several variations of this class of complex have been reported in the literature, for example by tuning the aryl moiety, increasing the aromaticity (naphthalene based Hoveyda-Grubbs complexes) or simply introducing electron-withdrawing or electron donating groups.\textsuperscript{33,36} Another modification of these alkoxylidene complexes was reported by Grela et al., who prepared a different O-chelating moiety. Their complexes $\text{M}_1$ and $\text{M}_2$ possess a keto-ether functionality, which also coordinates via the carbonyl-oxygen to the ruthenium metal, generating a six-coordinate species (Figure 1.6).\textsuperscript{37}

**N-, S- AND X- CHELATED COMPLEXES**

Another approach to access latent complexes is the introduction of nitrogen-, sulphur- or halide-based chelating alkylidenes (Scheme 1.11).\textsuperscript{18b,36d,38} These complexes are highly stable and, due to their low activity under ambient conditions, can easily be handled before activation, which is usually done using light, heat, or additives.\textsuperscript{18b,38} In contrast to the Hoveyda-Grubbs
type complexes, these pre-catalysts exhibit *cis-trans* isomerisation in order to activate, in which, generally the *trans*-isomer is the active pre-catalyst in metathesis.\(^{39}\)

![Chemical structures](image)

**Scheme 1.11:** Examples of N-, S- and X- chelated complexes.

This behaviour is more pronounced in the sulphur- and halide-chelated pre-catalysts, where the *trans*-isomer is not observable in some cases.\(^{40}\)

**Vinylicinium Complexes**

Cationic 14e\(^{-}\) vinylicinium complexes can be obtained by reacting first or second generation Grubbs catalyst with very active substrates such as the Feist ester followed by acid addition (see the decomposition section).\(^{41}\) The initiation mechanism takes place via \([2+2]\) cycloaddition with ethylene, releasing the corresponding vinylicinium, which is a non-reactive side product, and generating the 14e\(^{-}\) methylidene (Scheme 1.12).\(^{42}\) Connected to the high initiation activity, these complexes show high instability; in particular competing dimerisation can occur (see the decomposition section). These deactivation processes can be mitigated with the appropriate phosphonium substitution pattern. The use of
triisopropylphosphine-based complexes shows the best compromise between stability and reactivity.\textsuperscript{43}

\begin{center}
\textbf{Scheme 1.12:} Initiation of Piers-type complexes.
\end{center}

**MECHANISM IN RUTHENIUM CATALYSED OLEFIN METATHESIS.**

Even though the mechanism of olefin metathesis was proposed for the first time in 1971 by Chauvin, this process, and in particular the one involved in ruthenium-based catalysis, is far from being fully understood,\textsuperscript{5} due to the wide range of pre-catalysts, the majority of which bear N-heterocyclic carbene (NHC) ligands,\textsuperscript{28c,32} different ancillary ligands, alkylidenes, halides and sacrificial ligands such as a chelating alkoxy styrene group or a phosphine (Figure 1.8).\textsuperscript{17b,32b,33b,35b,41,44} Therefore, several further mechanistic studies have been disclosed in order to fully elucidate this process.
CHAPTER I: INTRODUCTION TO RUTHENIUM CATALYSED OLEFIN METATHESIS

Figure 1.8. Common metathesis pre-catalysts; G indicates Grubbs-type; Gr Grela type, N, Nolan, M, Umicore ‘M’ series indenylidene complexes; GH, Grubbs-Hoveyda type, Piers type.

The mechanism of ruthenium-catalysed olefin metathesis can be divided into three main parts: pre-catalyst initiation, propagation and termination/decomposition.

The initiation step consists of the activation of a stable pre-catalyst (typically 16e− RuII) to an active 14e− species in which, on the basis of the combination of ancillary ligands present, affects the different reactivity of the system. The propagation step was shown to be the key for gaining high selectivity in several metathesis reactions, while the termination process is related to catalyst decomposition (Scheme 1.13).
Scheme 1.13: Key stages of alkene metathesis reactions.

**PRE-CATALYST INITIATION**

The initiation step of a pre-catalyst determines the rate at which the active 14e⁻ species is formed; this factor has a significant impact on the overall reaction. Generally, these precatalysts are 16e⁻ species which must first lose a ligand to generate a (typically unobservable) 14e⁻ alkylidene. Due to the importance of this step in terms of reactivity, several contributors have heavily studied this process, particularly in recent years. The initiation of 16e⁻ pre-catalysts is considered to follow three possible pathways: associative, dissociative, or interchange (Scheme 1.14).
In the *associative* mechanism, the alkene binds the metal centre to yield an $18e^-$ intermediate before loss of a ligand; in the *dissociative* mechanism, a $14e^-$ species is formed before the binding of the alkene. In the *interchange* mechanism the binding of the alkene and loss of a ligand occur simultaneously. These processes will be discussed based on the sacrificial ligand.

**PHOSPHINE-CONTAINING PRE-CATALYSTS (GRUBBS-TYPE)**

Despite initial studies in which it was suggested that Grubbs-type catalysts activate *via* an associative mechanism, several NMR kinetic studies by Grubbs and co-workers have shown that the initiation step involves a phosphine dissociation prior to alkene coordination (Scheme 1.15). The analysis was based on the exchange rate between free phosphine and the bound phosphine in the presence of ethyl vinyl ether (EVE). Under these conditions an inactive alkylidene complex (see decomposition section) forms. In addition, the results revealed that less electron-donating phosphines dissociate more readily and highly $\sigma$-donating phosphines are more capable of stabilising the metallacyclobutene (MCB) active species.

Interestingly, GII initiates *slower* than GI, despite the increased $\sigma$-donating ability of SIMes.
The origin of the higher activity of second generation complexes was found to be due to the preference to coordinate alkenes, propagating the catalytic cycle, over the dissociated phosphine, generating the methyldiene resting state (see propagation).

\[ \text{Scheme 1.14: Initiation rate measurements via reaction with ethyl vinyl ether.} \]

Initiation rates for GII are known in several solvents, including some fluorinated aromatic solvents that have been found to enhance reactivity. Notably, the nature of the sacrificial phosphine ligand does not change the active species; the same 14e alkylidene is generated upon initiation.

Several studies have been conducted in order to understand why second generation catalysts initiate slower than the previous generation. In fact, initially there was an assumption that the activation of GII should be faster than GI because of the higher trans-effect of the NHC versus the phosphine. However, X-ray absorption spectroscopy experiments revealed that the metal centre of GII is more electron deficient than in GI due to d to π* back-bonding in GII. Several DFT studies have attempted to reproduce the experimental initiation data reaching reasonable agreement. An interesting explanation was proposed by Truhlar and co-workers, who proposed that carbene rotamers are the underlying cause of the intriguing initiation rate differences between GI and GII.

Nolan and co-workers have studied the initiation of indenylidene species such as M\textsubscript{20} and M\textsubscript{23} using \[^{31P},^{31P}\] EXSY and EVE quenching experiments. The indenylidene moiety reveals a decrease in initiation rate compared to the analogous benzylidene complexes. Interestingly, M\textsubscript{20} was shown to initiate via an interchange mechanism rather than a dissociative mechanism. The activation parameters obtained reveal a negative entropy of
activation ($\Delta S^\ddagger = -13 \pm 5 \text{ cal K}^{-1} \text{ mol}^{-1}$) for $\text{M}_{20}$ versus a positive entropy of activation for complexes such as $\text{M}_1$ ($\Delta S^\ddagger = 8 \pm 8 \text{ cal K}^{-1} \text{ mol}^{-1}$), $\text{GII}$ ($\Delta S^\ddagger = 12 \pm 10 \text{ cal K}^{-1} \text{ mol}^{-1}$), and $\text{M}_{23}$ ($\Delta S^\ddagger = 21 \pm 3 \text{ cal K}^{-1} \text{ mol}^{-1}$).\textsuperscript{53} DFT calculations were performed to support this work, which indicated a rather fine balance between dissociative and interchange mechanisms, with typically only a few kcal mol$^{-1}$ difference between the two pathways.\textsuperscript{53}

**CHELATING BENZYLIDENE PRE-CATALYSTS (HOVEYDA-TYPE)**

These types of complexes have been widely used in several applications due to the improved stability given by the chelated oxy-alkylidene bonded to the ruthenium centre. Firstly synthesised by Hoveyda et al.\textsuperscript{35b} these chelated species initiate at a slower rate than the Grubbs type catalysts and sometimes thermal activation is required for initiation. Despite the initially proposed mechanisms which reported a dissociative initiation to be operative,\textsuperscript{48} later work revealed that the entropy of activation was actually negative ($\Delta S^\ddagger$ for $\text{GIII} = -19 \pm 3 \text{ cal K}^{-1} \text{ mol}^{-1}$),\textsuperscript{32a} consistent with either an interchange or associative mechanism. Several contributors tried to describe this process using different approaches.\textsuperscript{54} Even though these studies provide reasonable results for the activation process of these complexes, more recent studies have shown that the understanding of this step for Grubbs-Hoveyda pre-catalysts is far from trivial.

\textsuperscript{55}

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**Figure 1.9:** Transition states for Hoveyda-type pre-catalyst initiation.
PROPAGATION STEP

Although the initiation process is critical for the rate of formation of the 14e\textsuperscript{-} active species, affecting their activity and their thermal stability, the chemo-, regio-, stereoselectivity and some substrate compatibility depends on the propagation step.

REACTIVITY DIFFERENCE BETWEEN FIRST AND SECOND GENERATION GRUBBS CATALYSTS

As mentioned before, since the introduction of the first NHC-bearing complexes, strong differences in reactivity between these second generation complexes and the bis(phosphine) first generation pre-catalysts have been observed. In fact, the former show higher activity in olefin metathesis than the first generation analogues, even though they report a slower initiation. The reason for this difference in reactivity has been elucidated by studying the reaction rate between metathesis pre-catalysts with a defined amount of ethyl vinyl ether (EVE) and phosphine.\textsuperscript{46,56} The concept behind these competition experiments was to evaluate if the reversible phosphine binding could compete with the irreversible reaction with EVE (Scheme 1.15).\textsuperscript{46a,47} The experiments showed that GI\textsubscript{II} is equally selective for phosphine and alkene, while GI is 10\textsuperscript{3} times more selective for phosphine coordination. Therefore, even though GI initiates more rapidly, it is less prone to generate “productive metathesis cycles” before being trapped by the dissociated phosphine.\textsuperscript{46a}

\textbf{Scheme 1.15:} Probing the selectivity of GI and GI\textsubscript{II} for alkene versus phosphine.
OLEFIN REACTIVITY IN CROSS METATHESIS

Olefin metathesis catalysts react differently on basis of the substitution patterns in the substrates considered. In fact, it is possible to classify the reactivity and type of alkene termini, predicting or rationalising CM reaction outcomes. Four different types of reactivity are considered:

*Type I*: alkenes react (and dimerise) quickly, but dimers are consumable; *type II*: alkenes react (and dimerise) more slowly, and the corresponding dimers are consumed slowly; *type III*: alkenes are still reactive in CM, but will not dimerise; *type IV*: alkenes do not react, but will not poison catalysts, acting as ‘spectators’. The class in which a determined olefin is classified is dependent on the pre-catalyst considered. Indeed, different behaviour is observed with molybdenum, and for first- and second-generation ruthenium complexes. In addition, the reactivity of the NHC bearing ruthenium complexes varies, depending on the nature of the sacrificial ligand and on the type of the N-heterocyclic carbene considered. For example, complexes with less hindered NHCs have been considered to access heavily-substituted alkenes, like in Stoltz’s synthesis of (+)-elatol, where complex **Ru-30** is employed in the synthesis of the challenging tetrasubstituted cyclohexene unit (Scheme 1.23).

![Scheme 1.16: Stoltz’s synthesis of (+)-elatol.](image)
RING CLOSING METATHESIS SELECTIVITY

Even though olefin metathesis reactions are all based on [2+2] cycloaddition mechanism, different processes may sometimes compete with the acyclic diene metathesis (ADMET) or the ring closed product can ring open again and lead to polymerisation (ROMP). This complicated series of competitive reactions, can be rationalised using a parameter applied widely in the study of acid- and base-catalysed nucleophilic ring-closing chemistry, the effective molarity (EM) (Scheme 1.17).59

\[
\begin{align*}
\text{(a)} & \quad \frac{k_{\text{intra}}}{k_{\text{inter}}} \\
\text{(b)} & \quad \underset{\text{GII}}{\text{CDCl}_3 \text{ or CD}_2\text{Cl}_2} \quad 298 \text{ K}
\end{align*}
\]

**Scheme 1.17:** Effective molarity to measure cyclisation efficiency.

This approach is very effective with simple substrates where the RCM can be conducted via thermodynamic control. In fact, in these cases it is possible to predict the mixture of products achievable, using thermodynamic data available in the literature or extrapolated DFT calculations and the optimal initial reaction concentration on the basis of straightforward calculations, rather than by expensive and time-consuming trial and error.60

Regarding the stereoselectivity in RCM, smaller (ca. 5-8 membered) rings almost always produce Z-alkenes.61 RCM reactions to produce larger rings (such as macrocycles), and in CM reactions, both isomers can be obtained.62
**E/Z selectivity in CM**

An important factor in Cross Metathesis is the selectivity of the product obtained, which usually for ruthenium metathesis is $E$-selective. The reason for this high selectivity is due to the geometry of the metallacycle formed, in *bottom on* instead of *side on*. 

![Diagram showing E/Z selectivity](image)

**Scheme 1.18**: Selectivity on CM based on MCB conformation

Several contributors have tried to access the most unfavourable products. The key development to access $Z$-selective pre-catalysts, was initially assessed by Hoveyda and Schrock reporting on molybdenum- and tungsten-based $Z$-selective catalysts in 2009. Grubbs described the first ruthenium-based $Z$-selective catalyst $\text{Ru-32}$ in 2011 (Scheme 1.19). $\text{Ru-31}$, bearing an unsymmetrical 1-adamantyl-3-mesityl-substituted NHC, underwent reaction with $\text{AgO}_2\text{C}^\text{tBu}$ to yield cyclometallated complex $\text{Ru-32}$. When tested in the CM reaction of allylbenzene with acetyl-protected but-2-ene-1,4-diol, $\text{Ru-32}$ led to $E/Z$ ratios as low as 0.14. However, $\text{Ru-32}$ was shown to be far slower for the RCM of diethyl diallylmalonate than $\text{GHIII}$, even at higher temperatures and with much higher catalyst loadings, so less active overall.
An improvement of the cyclometalated Grubbs complex has been found in the introduction of bidentate $κ^2$-nitrato ligands accessing modest to excellent yields and $E/Z$ ratios of typically 0.25 or lower.\textsuperscript{63a,64b,66}

Another approach has been used by Jensen and co-workers, disclosing the synthesis and study of an accessible $Z$-selective metathesis pre-catalyst, by simple exchange of a chloride ligand on GHII with an arylthiolate potassium salt leading to complex Ru-34. The complex showed excellent $Z$-selectivity (Scheme 1.20).\textsuperscript{67}
CHAPTER I: INTRODUCTION TO RUTHENIUM CATALYSED OLEFIN METATHESIS

Scheme 1.20: Synthesis of a simple Z-selective metathesis catalyst.

In the same line, Hoveyda and co-workers disclosed the synthesis of a highly selective and active ruthenium complex by using the 2,3-dimercaptomaleonitrile ligand which forces the complex into a cis-anion conformation, promoting the formation of Z-olefins (Scheme 1.21).^{64a}

Scheme 1.21: Synthesis of Hoveyda type Z-selective metathesis catalyst.

Very recently Hoveyda et al. disclosed a very interesting computational study, analysing the CM process of several types of (a)chiral ruthenium carbene complexes. The calculations suggested that the preference for E- or Z- selectivity is dependent on the type of metallacyclobutene formed (side-on or bottom-on) and the preferences between one of the two depends on the conformation of the two anionic ligands: trans- for the bottom on and cis for the side on (Scheme 1.18).^{63d,e} The effect of the cis- conformation on the MCB is due to the electron-electron repulsion and a large dipole moment. Ligand spheres which destabilise the usual square-based pyramidal geometry of metathesis catalysts can favour side-bound MCBs and therefore Z-selective metathesis. In the case of chelated NHC complexes such as Ru-38,
the other anionic ligand is proposed to prefer to coordinate trans to the NHC rather than the alkyl ligand, favouring a side-bound MCB.\textsuperscript{63a,63d}

**CATALYST DECOMPOSITION**

The last step in the metathesis reaction is the termination step, which very often involves decomposition of the active/resting species to a deactivated one. However decomposition pathways can occur at several stages of the metathesis process. For this reason, the design and utilization of ligand environments that reduce deactivation pathways is one of the greatest challenges, not only in the metathesis field but in all of homogeneous catalysis. For these reasons the complete understanding of decomposition processes is fundamentally important.

**METHYLIDENE COMPLEXES**

Methylidene complexes are the possible resting state during catalytic turnover and, often, the most fragile species in metathesis reactions. The formation of these species occurs when, during the propagation step Ru-36 and Ru-37, instead of coordinating an olefin, and continuing the catalytic cycle, the active species re-coordinates the phosphine ligand, forming the corresponding 16e’ methylidene species Ru-38 and Ru-39 (Scheme 1.22).\textsuperscript{9a}

\[
\begin{align*}
\text{Ru-36} & : \text{L} = \text{PCy}_3 \\
\text{Ru-37} & : \text{L} = \text{SIMes} \\
\end{align*}
\]

**Scheme 1.22:** Phosphine capture of methylidene complexes.

Even though these methylidene species cannot be considered as decomposition products, because the binding process is theoretically reversible, they are prone to rapid decomposition, rendering it impossible to determine the initiation rate.\textsuperscript{46a} The decomposition rate of these complexes is highly dependent on the ligand structure, being more stable than the
second generation analogues, leading, usually, to the formation of the corresponding phosphonium ylide species and a ruthenium decomposition product that is still unknown for the first generation catalysts; Ru-37 has been found to form the di nuclear ruthenium species Ru-40 which has been claimed to have some activity in alkene isomerization.

Scheme 1.23: Decomposition of methylidene complex Ru-37.

The proposed mechanism initiates via phosphine dissociation, which reacts with the alkylidene moiety, forming phosphonium ylide Cy₃P=CH₂. The achieved 12e⁻ ruthenium
product can dimerise via co-ordination to the mesityl ring of another molecule of Ru-37, leading to hydride complex Ru-40 after HCl removal by Cy₃P=CH₂ liberated previously.⁶⁸ When Ru-39 is exposed to an atmospheric pressure of ethylene gas, the intermediate Ru-37 dimerises to form a chloride bridged cyclometallated species.⁶⁸ Methylidene complexes are also known to be sensitive to pyridine; for example, Ru-39 reacts rapidly to form tris(pyridine) complex Ru-41 (Scheme 1.24).⁶⁸

![Scheme 1.24: Decomposition of Ru-39 by reaction with pyridine.](image)

**DEACTIVATION BY SUBSTRATES**

Methylidene complexes are not the only vectors for decomposition: reactions with certain substrates can lead to unwanted side reactions.

**CYCLOPROPENYL SUBSTRATES**

Particularly reactive olefins, such as the Feist ester, have been found to decompose G1 and GII to form the ruthenium carbide complexes Ru-44 and Ru-45 respectively. These complexes are formed via rearrangement of the species Ru-42 or Ru-43, eliminating dimethyl fumarate and the carbide product (Scheme 1.25).⁷⁰
Scheme 1.25: Decomposition of alkene metathesis pre-catalysts via reaction with cyclopropenyl substrates.

This particular species can be protonated using Jutzi’s acid, [H(OEt)$_2$][B(C$_6$F$_5$)$_4$], leading to the fast initiating Piers-type catalysts.\textsuperscript{41} Interestingly, [RuCl$_2$(PPh$_3$)$_2$(CHPh)] reacts with the ester to yield only the Ru-42 analogue.

**ELECTRON-RICH ALKENES**

Electron rich alkenes have also been shown to promote decomposition in the cases when, after the MCB formation, the electron-rich alkylidene formed has a major Fischer-type character and, for this reason, is inactive in metathesis.\textsuperscript{71} Thanks to those properties, these olefins are often used as a catalyst quench (see initiation step determination for example of this application).

A proof of this inactivity has been reported by Grubbs et al. by the preparation of a series of Fischer carbene complexes \textit{via} the metathesis of vinyl ethers (Scheme 1.26).\textsuperscript{47} These complexes were found to be much less reactive than the parent benzylidene derivatives, requiring higher temperatures to achieve turnover. In addition, when these complexes are
exposed to high temperatures for a long period, a ruthenium hydride species can be formed. These hydride species are active in terminal alkene isomerisation reactions.\textsuperscript{49a,69b,72}

**Scheme 1.26:** Metathesis of electron-rich alkenes.

The Piers-type complexes have been found to decompose in the presence of 1,1-dichloroethene, leading to the halide bridged complex **Ru-48** (Scheme 1.27).\textsuperscript{43}

**Scheme 1.27:** Reaction of 1,1-dichloroethene with PII.

In addition, catalytically-inactive species **Ru-44**, **Ru-45**, **Ru-49** and **Ru-50** have been obtained from the reaction of vinyl halides and vinyl esters with metathesis pre-catalysts (Scheme 1.28).\textsuperscript{73}
Another challenging olefin, which usually leads to the formation of inactive complexes such as Ru-51, is acrylonitrile. In order to overcome this issue, Grubbs et al., showed that GII-py can preclude the capture of 14e alkylidenes by phosphine and promote the metathesis reaction.\textsuperscript{44c}

![Scheme 1.28: Metathesis of electron-rich alkenes.](image_url)

**Scheme 1.28:** Metathesis of electron-rich alkenes.

**LIGAND C-H ACTIVATION**

C-H activation of the N-aryl substituents on the imidazolium ring is a very common deactivation pathway when at least one of the arene moieties is able to rotate and interact with the ruthenium centre.

Two possible types of C-H insertion can occur: ruthenium metallacycle formation, or insertion of the alkylidene moiety.

An interesting example of the first type of activation has been reported by Grubbs where complex Ru-52 spontaneously decomposes \textit{via} double C-H activation to form Ru-53 (Scheme 1.29).\textsuperscript{74} This deactivation has been computationally studied by Cavallo and Suresh separately.\textsuperscript{75}
The DFT calculations suggest that when the $N$-phenyl substituent rotates in a position close enough to be ortho-metallated, the intermediate Ru-54 is formed. This complex immediately rearranges to access complex Ru-55 via a series of $\alpha$-hydrogen abstraction/insertion shown in scheme 1.29. The other $N$-phenyl moiety on complex Ru-55, can rotate as well and be C-H activated, achieving the final product Ru-53. To avoid this type of C-H activation, the introduction of bulkier $N$-aryl substituents disfavours the possible arene rotation.

Scheme 1.29: C-H insertion in complex Ru-52.
A different C-H insertion process can occur via the alkylidene moiety. The asymmetric Hoveyda-Grubbs complex Ru-56 when exposed to air can undergo a pericyclic intramolecular C-H insertion of the aryl substituent into the alkylidene moiety to give the inactive complex Ru-57 (Scheme 1.30).\(^7\)

![Scheme 1.30: Intramolecular C-H insertion of Ru-56.](attachment:image1.png)

This C-H insertion has also been observed with the phosphonium ylide type complexes. In fact, some of these pre-catalysts, like Ru-58, reveal thermal decomposition after two day in solution at room temperature, dimerising to a bimetallic complex like Ru-59 (Scheme 1.31).\(^3\)

![Scheme 1.31: Decomposition of Ru-58.](attachment:image2.png)
A C-H activation and cyclometallation does not always lead to deactivation. In fact in the case of complex \textbf{Ru-31}, in the presence of $^t$BuCO$_2$Ag, the \textit{N}-adamantyl substituent can be inserted on the ruthenium \textit{via} C-H activation to form complex \textbf{Ru-32}, active in olefin metathesis, reporting \textit{Z}-selectivity in CM reactions (Scheme 1.19) (see propagation discussion).$^{66,77}$

This synthetic C-H activation process has been heavily investigated, showing a high dependence on the NHC considered. Indeed, varying the bulkiness of the \textit{N}-aryl substituent or changing the adamantyl substituent to an aromatic moiety, instead of forming the desired product, leads to decomposition (Scheme 1.32).$^{78}$

\textbf{Scheme 1.32.} Decomposition of pre-catalysts promoted by Ag$^t$BuCO$_2$.

\textbf{II-ACIDS}

\pi-Acids such as CO or isocyanates react with ruthenium metathesis catalysts, deactivating them. For example, exposing \textbf{GII} or its methyldiene analogue to atmospheric pressure of CO at room temperature, leads to a rapid rearrangement and insertion of the alkylidene moiety in to one of the \textit{N}-aryl substituent, \textit{via} a Buchner-type mechanism, leading to complexes such as \textbf{Ru-60} (Scheme 1.33).$^{79}$
This deactivation process can be used as a catalyst scavenger, using CNCH\textsubscript{2}CO\textsubscript{2}K which generates complexes such as $\text{Ru-61}$, easily removable from the reaction mixture.\textsuperscript{80}

This rearrangement has been computationally investigated by Cavallo et al., suggesting that reaction proceeds via the attack of the ipso carbon of the $N$-aryl substituent from the benzylidene moiety, promoted by the $\pi$-acidity of the ligand trans- to the alkylidene.\textsuperscript{81}

The cyclometallated complex $\text{Ru-32}$ was also found to be deactivated by CO. In fact under a CO atmosphere at -78 °C, it de-cyclometallates, promoting C-H insertion of the $N$-adamantyl substituent into the alkylidene moiety, yielding complex $\text{Ru-62}$ (Scheme 1.34).\textsuperscript{78} The $\pi$-acidity of the CO ligands decrease the ability of the metal centre to stabilise the alkylidene by back-bonding, promoting the C-H processes in order to increase the stabilisation on the metal centre.
Metathesis pre-catalysts and catalysts can also be deactivated in alcohol solutions, generating highly active compounds for several transformation. This particular decomposition pathway and, in particular, the alcoholysis of indenylidene pre-catalysts will be discussed in chapter III.

AIMS OF THE PROJECT

A brief overview of the current stage of research in olefin metathesis has been disclosed, highlighting the most recent discoveries on the mechanism of the ruthenium catalysed process and how every single step, initiation, propagation and termination, can effect this transformation. In light of this topic, the aim of the research presented in this thesis is focussed in two main areas, strongly related to the mechanism of this transformation.

The first part of this thesis will focus on the evaluation of the catalytic performance of ruthenium indenylidene complexes bearing sterically encumbered N-heterocyclic carbenes. The second topic, which is also the main part of this thesis, discloses the recent discoveries regarding the decomposition of ruthenium indenylidene complexes in alcohol solutions. As an important outcome from this study, a novel indenyl complex was obtained. This formal decomposition product revealed high and unique activity in several transformations.
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CHAPTER I: INTRODUCTION TO RUTHENIUM CATALYSED OLEFIN METATHESIS


CHAPTER I: INTRODUCTION TO RUTHENIUM CATALYSED OLEFIN METATHESIS


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CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

*Organometallics* 2012, 31, 6514.
*Dalton Trans.* 2013, 42, 7433.

**STATEMENT**

The X-ray experiments were carried out by Prof. Alexandra M. Z. Slawin.

The DFT-calculations were performed by Dr. Albert Poater (Cavallo group)

The synthesis of the ruthenium complexes and the connected catalytic applications have been performed in collaboration with Dr. Cesar A. Urbina-Blanco.
SYNTHETIC ASPECT OF RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS

As mentioned in section I, in order to access active ruthenium-alkylidene complexes, avoiding the use of hazardous reagents such phenylidiazomethane, several methodologies have been reported in the literature. Among them the development of phenylindenylidene complexes for olefin metathesis, is probably one of the most successful. In fact, even though they initiate slower that the corresponding benzylidene analogues, these complexes are generally more stable, active and accessible from a simple tertiary propagylic alcohol, which is a cheap and inexpensive starting material (Scheme 2.1). However, the synthesis of this indenylidene moiety is less than trivial. In fact the methodology employed to access the commercially available M10, takes account of several factors that are important in order to achieve the desired product. For example, if the reaction is carried out in the absence of acid, which can be generated by AcCl \textit{in situ}, instead of allowing access to the desired product, a $\mu^3$-chlorobridged bimetallic ruthenium allenylidene complex Ru-63 is achieved (Scheme 2.1, Route A). In the absence of ethereal solvent the rearrangement to the desired indenylidene ligand is inhibited, forming complex Ru-64 (Scheme 2.1 route C and D).
Scheme 2.1: Ruthenium indenylidene complex synthesis

The choice of the propargylic alcohol is also important: indeed, substitution on the aryl moiety of the propargylic alcohols can inhibit the indenylidene rearrangement, as Bassetti et al. reported analysing the reaction rate of the acid catalysed cyclisation rate of a series of allenylidene complexes like Ru-66 to the corresponding indenylidene derivatives (Scheme 2.2).³

Scheme 2.2: Substituent evaluation on the indenylidene rearrangement

R= EDG cyclisation disfavoured
R= EWG cyclisation favoured
CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

RUTHENIUM SYNTHETIC PROCEDURE TO SECOND AND THIRD GENERATION INDENYLIDENE CATALYSTS

$\text{M}_{10}$ is not metathesis active,$^5$ but is a good synthon to synthesise other Ru-indenylidene pre-catalysts.$^{4,5}$ The usual synthetic process to access second generation system from $\text{M}_{10}$ is usually performed by ligand exchange between the phosphine and the free carbene that can be isolated or generated in situ, either by using potassium tert-butoxide or the chloroform adduct (Scheme 2.3).$^{6b,6f,7}$

![Scheme 2.3: Synthesis of second generation catalysts by direct phosphine exchange](image)

Even though the in situ free carbene generation methodology has evident advantages (the ligand precursors are air, moisture and temperature stable, the free NHC be stored at low temperature and under strictly inert conditions), generally this methodology can easily generate side products, lowering the final yields. Therefore the free carbene route is preferable. However
this procedure was limited to unsaturated NHCs such as IPr or IMes. Only recently was this methodology extended to saturated NHCs such as SIPr or SIMes, avoiding the derivatisation of $M_{10}$ to the bis(tricyclohexyl)phosphine derivative ($M_1$) and the use of CuCl as PCy$_3$ abstractor (usually used when the NHC is highly sterically demanding) (Scheme 2.4).  

**Scheme 3:** Old synthetic route for Ru-indenyldene pyridine adducts

In addition, the novel procedure not only allows access to the second generation complexes directly from $M_{10}$ in good yields (88% and 62%), reducing the amount of waste, but if the same complex was achieved with the old process, it was necessary to generate the pyridine adduct and add an additional equivalent of PPh$_3$ as Verpoort *et al.* reports for the synthesis of $M_{20}$.  

Regarding the pyridine adducts, it is possible to access these types of complex without isolating the phosphine precursor just adding pyridine in a telescoped manner (Scheme 2.5).
Scheme 2.5: Novel protocol for unsaturated NHC and for the synthesis of [RuCl₂(NHC)(Py)(Ind)] complexes

Regarding indenylidene pyridine adducts, this class of pre-catalysts has found utility either as a synthon for chelating/latent pre-catalysts, or as active catalysts themselves, showing very high activity in metathesis reactions at low catalyst loadings with less hindered substrates and remarkable results in polymerisation chemistry.4,6b,8-9

Regarding the NHC ligand, it has been found that either with second or third generation pre-catalysts, sterically demanding carbenes such as SIPr are extremely beneficial in the catalysis allowing, for example, the RCM of less hindered dienes using ppm catalyst loadings.4b,8,10
EVALUATION OF STERIC EFFECTS OF HIGHLY STERICALLY DEMANDING NHCS IN CATALYSIS

In order to understand how much the steric effects of N-heterocyclic carbenes can influence olefin metathesis the highly sterically demanding 1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene (IPr*) ligand was considered.

Scheme 2.6: Synthesis of IPr*

Firstly reported by Markò in 2010, its synthesis was achieved through a dialkylation of p-toluidine (1) using benzhydrol (2), in the presence of stoichiometric amounts of HCl(conc) and ZnCl₂, affording the aniline 3, which was subsequently reacted with aqueous glyoxal to afford the diimine 4. The most critical step in this synthesis is the cyclisation to form IPr*HCl. The diimine 4 exists preferentially in the s-trans conformation, which does not undergo cyclisation, so it is necessary to isomerise it to the s-cis conformer. In order to afford this HCl/ZnCl₂/(CH₂O)ₙ were used in a 2:1:1 ratio affording IPr*HCl in moderate yields. Once
formation of the imidazolium chloride is achieved, the synthesis of the free carbene is achieved via, first, counteranion exchange, accessing a more organic solvent soluble imidazolium salt and deprotonation using sodium hydride and a catalytic amount of potassium tert-butoxide as phase transfer reagent (Scheme 2.6).\textsuperscript{12} IPr* revealed beneficial effects in several processes, particularly in Pd and Ni catalysed cross-coupling reactions.\textsuperscript{12-13}

SYNTHESIS AND STRUCTURAL ANALYSIS OF [RuCl\textsubscript{2}(IPr*)(L)(3-phenylindenylidene)] complexes\textsuperscript{4a,14}

Following the previously reported protocol to synthesise second and third generation catalysts,\textsuperscript{4b} 1.5 equivalents of free IPr* were added to a solution containing [RuCl\textsubscript{2}(PPh\textsubscript{3})\textsubscript{2}(3-phenylindenylidene)] (M\textsubscript{10}) in toluene (Scheme 2.7). After stirring for 10 h at 40 °C, [RuCl\textsubscript{2}(IPr*)(PPh\textsubscript{3})(3-phenylindenylidene)] (IPr*-PPh\textsubscript{3}) was obtained in 43% yield after removal of the solvent under vacuum and subsequent recrystallisation from dichloromethane/hexane. As for the SIPr and SIMes containing Ru-indenylidene complexes, a one-pot reaction was developed, affording the pyridine adduct [RuCl\textsubscript{2}(IPr*)(Py)(3-phenylindenylidene)] (IPr*-Py) in good yield (73%) (Scheme 2.7).

Scheme 2.7: Synthesis of complexes bearing IPr and IPr*.

In order to have an appropriate complex to evaluate the steric influence of IPr*, the smaller IPr ligand was considered.\textsuperscript{13d} Despite the lower activity of the pre-catalysts bearing
unsaturated NHCs, to date, it was not possible to access the saturated version of IPr* to have a proper comparison with the SIPr derivatives.

[\text{RuCl}_2(\text{IPr})(\text{PPh}_3)(\text{3-phenylindenylidene})] (\text{IPr*-PPh}_3) and the novel [\text{RuCl}_2(\text{IPr})(\text{Py})(\text{3-phenylindenylidene})] (\text{IPr*-Py}) were synthesised using the previously described protocol. \textit{sf,15}

From these four complexes, it was possible to grow crystals suitable for X-ray analysis; the structures are shown in Figure 2.1.\textit{35}

**Figure 2.1:** Molecular structures of IPr*-PPh$_3$, IPr*-Py, IPr-PPh$_3$ and IPr-Py (the hydrogen atoms are omitted for clarity). Selected bond lengths [Å] and angles [°]: IPr*-PPh$_3$: Ru1-Cl1 2.377(3), Ru1-Cl2 2.346(3), Ru1-P1 2.418(3), Ru1-C1 2.135(10), Ru1-C72 1.836(10); Cl1-Ru1-Cl2 159.40(9), P1-Ru1-C1 168.3(3), P1-Ru1-C72 89.9(4), C1-Ru1-C72 100.4(4); IPr*-Py: Ru1-Cl1 2.3716(19), Ru1-Cl2 2.3635(18), Ru1-N87 2.123(6), Ru1-C1
The X-ray analysis reveals that, although IPr* is very bulky, it is accommodated easily in the system on the basis of the environment present. In fact, evaluating the steric hindrance, determined using the buried volume parameter ($\%V_{\text{bur}}$),\textsuperscript{16} of IPr* in IPr*-PPh\textsubscript{3} reveals that is smaller compared to IPr in IPr-PPh\textsubscript{3} and similar Ru-C1 bond distance (2.135(10) Å vs 2.094(7) Å).

### Table 2.1: Buried volumes of IPr*-PPh\textsubscript{3}, IPr*-Py, IPr-PPh\textsubscript{3} and IPr-Py\textsuperscript{a}

<table>
<thead>
<tr>
<th>Complex</th>
<th>$%V_{\text{bur}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPr*-PPh\textsubscript{3}</td>
<td>30.3%</td>
</tr>
<tr>
<td>IPr*-Py</td>
<td>33.9%</td>
</tr>
<tr>
<td>IPr-PPh\textsubscript{3}</td>
<td>31.1%</td>
</tr>
<tr>
<td>IPr-Py</td>
<td>31.2%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}$\%V_{\text{bur}}$ determined on basis of the Ru-C1 distance for each complexes.

The pyridine derivatives show a typical square based pyramidal geometry, with the two chloride ligands in a mutual trans- arrangement, while the apical position is occupied by the indenylidene moiety, similar to the previously reported complexes.\textsuperscript{8,9d,17} Due to the presence of a smaller ligand (pyridine) IPr* and IPr can be closer to the metal center, increasing the volume occupied in the coordination sphere ($\%V_{\text{Bur}}$). This effect is evident in the case of IPr*-Py, where the NHC moiety is more bent than in the other analogues and the $\%V_{\text{Bur}}$ is bigger than the PPh\textsubscript{3} correspondent. Interestingly, IPr-Py does not show any $\pi$-stacking interaction between the NHC and the indenylidene moiety; this stabilising interaction is usually present in heteroleptic ruthenium-indenylidene complexes.\textsuperscript{1,6f,8,9d,9m}

The electronic properties of IPr and IPr*, evaluated on Ni carbonyl complexes using the Tolman electronic parameter (TEP),\textsuperscript{18} are similar (TEP = 2052.7 cm$^{-1}$ for IPr* and TEP= 2051.5 cm$^{-1}$ for IPr).\textsuperscript{13d,19}
CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

EVALUATION OF IPr* COMPLEXES IN CATALYSIS\textsuperscript{4a}

The activity of the pre-catalysts is influenced mostly by steric properties. To evaluate their behaviour in catalysis, a comparative study was performed and the results are reported in Schemes 2.8 and 2.9.

Scheme 2.8: Comparative RCM reaction with complexes bearing IPr* and IPr ligand.

In ring closing metathesis, IPr*-PPh\textsubscript{3} and IPr*-Py show similar reactivity to form di- and tri-substituted double bonds. The difference in reactivity between IPr-PPh\textsubscript{3} and IPr-Py is more evident, revealing that more hindered substrates are more difficult to react with the pyridine analogue. The effect of IPr* in this system is detrimental, resulting in, generally, longer reaction times to reach full conversions (Scheme 2.8). In enyne metathesis, the same
trend is observed, although, in the formation of compound 9, IPr*-Py shows the best activity, reaching full conversion in 3 h (Scheme 2.8).

<table>
<thead>
<tr>
<th>Compound</th>
<th>Conv% (E/Z ratio)</th>
<th>Conv%</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPr*-PPh₃</td>
<td>77% (&gt;20:1)</td>
<td>2%</td>
</tr>
<tr>
<td>IPr*-Py</td>
<td>78% (&gt;20:1)</td>
<td>0%</td>
</tr>
<tr>
<td>IPr-PPh₃</td>
<td>91% (&gt;20:1)</td>
<td>4%</td>
</tr>
<tr>
<td>IPr-Py</td>
<td>54% (&gt;20:1)</td>
<td>8%</td>
</tr>
</tbody>
</table>

**Scheme 2.9:** Comparative CM reaction with complexes bearing IPr* and IPr ligand.

In olefin cross metathesis (Scheme 2.9) a significant difference in reactivity and selectivity is also observed. The IPr* complexes show lower reactivity than the corresponding IPr pre-catalysts, however, in both transformations, there is no significant difference between IPr*-PPh₃ and IPr*-Py. Differently, in the CM with IPr derivatives, a marked difference between the pyridine and the phosphine derivatives can be observed. In fact, IPr-Py displays low activity in both CM reaction, also lower than the IPr* derivatives. IPr-PPh₃ achieves high conversion and selectivity in both transformations, confirming how the combination of IPr and a phosphine is beneficial in cross metathesis, as previously reported in the literature.\(^ {15,20}\)

Remarkably, The CM with 13 and methyl acrylate catalysed by IPr-PPh₃ reaches almost full conversion in 5 h, with only 1 mol% of catalyst, which is one of the best results reported in the literature for these substrates. \(^ {15,20}\)

The results of the comparison of the catalytic activities, shown that the steric hindrance of IPr* highly affects the catalytic system decreasing the reaction rate. However, in the case of
the IPr*-Py, IPr* seems to slightly favour certain transformations, probably stabilising the active species. In order to better understand the effect of this highly encumbered system, a computational analysis was carried out in collaboration with the Cavallo group.

**DFT INVESTIGATION OF STERIC EFFECTS OF IPr* IN OLEFIN METATHESIS**

For the sake of consistency, the results achieved will be discussed in the next section, but without discussing in detail the methodology and approach used, which goes beyond the focus of this thesis. The IPr and IPr* were analysed in silico, evaluating how the steric hindrance can affect the steps of a metathesis reaction. DFT calculations revealed that the steric hindrance affects all steps of the process. In particular IPr*-PPh₃ and IPr-PPh₃ were studied in the overall metathesis mechanism using ethylene as the model substrate. Interestingly, IPr* was revealed to have a detrimental effect during the dissociation process, however the bigger NHC is better able to stabilise the generated 14e⁻ species B and F (Figure 2.2).

![DFT Calculation of the generation of the methylidene 14e⁻ species F for IPr and](image)

**Figure 2.2:** DFT Calculation of the generation of the methylidene 14e⁻ species F for IPr and IPr*.
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IPr* systems. Free energies in kcal/mol in DCM as solvent (M06L/TZVP//BP86/SVP level of theory; PCM model for the solvent).

In addition, IPr* was revealed to disfavour not only the generation of the active species F, but also the approach of the new substrate, which is less favoured than in the IPr systems (Figure 2.3).

![Energy Diagram](image)

**Figure 2.3:** DFT Calculation of the propagation step leading to metallacycle H. Free energies in kcal/mol in DCM as solvent (M06L/TZVP//BP86/SVP level of theory; PCM model for the solvent).

**CONCLUSION**

Steric hindrance of the NHC was shown to have a fundamental influence on the reactivity, enhancing the reactivity in several transformations. However a balance is necessary. In fact the comparison between IPr and IPr* derivatives shows that when the steric bulk is too significant, the reactivity is reduced, due to a more difficult activation process, and to an inhibit approach of new substrates during the propagation step. However, highly hindered ligands like IPr* can stabilise better the 14e⁻ active species, resulting in faster initiating pre-catalysts.
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Therefore, a perfect combination of bulkiness and flexibility is necessary to lead to positive effects in olefin metathesis.

EXPERIMENTAL SECTION

GENERAL CONSIDERATIONS

All reagents were used as received. Dichloromethane and toluene were dispensed from a solvent purification system from MBraun. Catalyst syntheses were performed in a MBraun glovebox containing dry Ar and less than 1 ppm oxygen. $^1$H, $^{31}$P, and $^{13}$C Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker Avance 300 or Bruker Avance II 400 Ultrashield NMR spectrometers. Elemental analyses were performed at the London Metropolitan University. The substrates for products from 5 to 10, 12 and 13 and the corresponding products have previously been described in the literature.$^{15,21}$

SYNTHESIS OF [RuCl$_2$(IPr*)(PPh$_3$)(3-phenylindenylidene)](IPr*-PPh$_3$)

In the glovebox, M$_{10}$ (1.00 g, 1.13 mmol) and IPr* (914 mg, 1.2 mmol) were charged to a Schlenk flask and dissolved in toluene (3 mL). The reaction was taken out of the glovebox and stirred at 40 °C for 10 h under Ar. After this time, the mixture was allowed to cool to RT and the solvent was removed under vacuum. The remaining solid was recrystallised from a mixture of dichloromethane/pentane. The mixture was filtered, washed with cold methanol (2 x 5 mL) and cold hexane (8 x 25 mL), affording [RuCl$_2$(IPr*)(PPh$_3$)(3-phenylindenylidene)](IPr*-PPh$_3$) (750 mg, 0.49 mmol, 44%) as a microcrystalline solid. $^1$H NMR (C$_6$D$_6$, 400 MHz): $\delta$ = 8.13 (d, J=7.3 Hz, 1 H), 7.67 - 8.00 (m, 7 H), 7.57 (t, J=7.8 Hz, 5 H), 6.55 - 7.42 (m, 60 H), 6.24 (s, 1 H), 6.03 (s, 1 H), 5.90 (s, 1 H), 4.93 (s, 1 H), 4.51 (s, 1 H), 2.05 (s, 2 H),
CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

1.77 (s, 3 H) ppm. $^{13}$C($^1$H) NMR (CD$_2$Cl$_2$, 75 MHz): δ = 301.0, 185.1, 183.8, 146.9, 146.7, 145.7, 145.2, 144.1, 141.0, 138.2, 135.8, 135.0, 134.8, 132.1, 131.6, 130.0, 129.3, 129.0, 128.6, 128.3, 128.1, 128.1, 126.5, 123.6, 116.7, 50.8, 50.4, 22.5, 21.9, ppm, $^{31}$P($^1$H) NMR (162 MHz, C$_6$D$_6$) δ = 27.54 ppm. Anal. Calcd for C$_{103}$H$_{85}$Cl$_2$N$_2$PRu C, 79.62; H, 5.51; N 1.80; Found: C, 79.77; H, 5.25; N, 1.73.

**SYNTHESIS OF [RuCl$_2$(IPr*)(Py)(3-phenylindenylidene)](IPr*-Py)**

In the glovebox, M$_{10}$ (1.00 g, 1.13 mmol) and IPr* (914 mg, 1.2 mmol) were weighed to a Schlenk flask and dissolved in toluene (3 mL), taken out of the glovebox, connected to a Schlenk line and stirred at 40 °C for 10 h under Ar. Pyridine (0.45 mL) was then added by syringe, the resulting solution was left stirring for 0.5 h, after which time pentane was added (35 mL) and the reaction left stirring for another 0.5 h. The resulting suspension was then cooled to -40°C, filtered and recrystallised from dichloromethane/pentane. The mixture was filtered, washed with cold methanol (1 x 10 mL) and cold hexane (3 x 10 mL) affording compound [RuCl$_2$(IPr*)(Py)(3-phenylindenylidene)] (IPr*-Py) (940 mg, 0.69 mmol, 73% yield).$^1$H NMR (CD$_2$Cl$_2$, 400 MHz): δ = 8.12 (d, J=7.2 Hz, 1 H), 7.85 (br. s., 2 H), 7.77 (d, J=5.1 Hz, 2 H), 6.42 - 7.57 (m, 60 H), 6.31 (br. s., 2 H), 6.09 - 6.19 (m, 1 H), 5.95 (s, 1 H), 5.72 - 5.86 (m, 1 H), 5.69 (s, 1 H), 4.97 - 5.01 (m, 1 H), 4.93 (d, J=1.9 Hz, 1 H), 4.08 (d, J=1.7 Hz, 1 H), 2.24 (s, 3 H), 2.10 - 2.18 (m, 1 H), 1.22 ppm (s, 3 H) $^{13}$C($^1$H) NMR (CD$_2$Cl$_2$, 75 MHz): δ = 153.6, 146.3, 143.1, 142.7, 142.0, 140.7, 140.2, 140.0, 139.8, 137.3, 136.5, 135.6, 133.8, 131.7, 130.7, 130.0, 129.3, 128.6, 128.0, 126.8, 126.4, 126.2, 124.6, 124.5, 123.9, 118.1, 22.7, 22.0, 20.8 ppm. Anal. Calcd for C$_{89}$H$_{71}$Cl$_2$N$_2$Ru C, 78.86; H, 5.35; N 3.10; Found: C, 78.81; H, 5.16; N, 3.05.
CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

SYNTHESIS OF [RuCl₂(IPr)(PPh₃)(3-phenylindenylidene)](IPr-PPh₃)

In the glovebox, M₁₀ (0.500 g, 0.56 mmol) and IPr (240 mg, 0.62 mmol) were charged to a Schlenk flask and dissolved in toluene (3 mL). The reaction was taken out of the glovebox, stirred at 40 °C for 4 h under Ar. After this time, the mixture was allowed to cool to RT and the solvent removed under vacuum. The remaining solid and recrystallised in a mixture of dichloromethane / pentane. The mixture was filtered, washed with cold methanol (2 x 5 mL) and cold hexane (8 x 25 mL), affording [RuCl₂(IPr)(PPh₃)₃(phenylindenylidene)] (IPr-PPh₃) (410 mg, 0.41 mmol, 81%) as a microcrystalline solid. Spectroscopic data for the product were in accordance with the literature.⁶f Anal. Calcd. for C₆₁H₆₅Cl₂N₂PRu C, 71.19; H, 6.37; N, 2.72; Found: C, 71.52; H, 6.19; N, 2.62.

SYNTHESIS OF [RuCl₂(IPr*)(Py)(3-phenylindenylidene)](IPr*-Py)

In the glovebox, M₁₀ (1.00 g, 1.13 mmol) and IPr (480 mg, 1.2 mmol) were weighed to a Schlenk flask and dissolved in toluene (3 mL), taken out of the glovebox, connected to a Schlenk line and stirred at 40 °C for 4 h under Ar. Pyridine (0.45 mL) was then added by syringe, the resulting solution was left stirring for 0.5 h, after which time pentane was added (35 mL) and the reaction left stirring for another 0.5 h. The resulting suspension was then cooled to -40°C. Filtration and recrystallisation in dichloromethane/pentane. The mixture was filtered, washed with cold methanol (1 x 10 mL) and cold hexane (3 x 10 mL) affording compound [RuCl₂(IPr*)(Py)(3-phenylindenylidene)] (IPr*-Py) (630 mg, 0.76 mmol, 66% yield).¹H NMR (400 MHz, C₆D₆) δ = 0.66 - 0.94 (m, 4 H) 1.00 - 1.39 (m, 6 H) 1.52 - 1.91 (m, 5 H) 2.80 - 2.97 (m, 1 H) 3.12 - 3.23 (m, 1 H) 3.23 - 3.38 (m, 1 H) 4.63 - 4.81 (m, 1 H) 6.06 (t, J=6.9 Hz, 1 H) 6.31 - 6.42 (m, 2 H) 6.60 (s, 1 H) 6.64 - 6.75 (m, 1 H) 6.87 - 6.95 (m, 2 H) 7.02 - 7.13 (m, 1 H) 7.32 - 7.45 (m, 2 H) 7.74 (d, J=7.5 Hz, 1 H) 8.19 (d, J=5.1 Hz, 1 H) 8.67 (d,
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$J = 7.2 \text{ Hz, } 1 \text{ H}) \text{ ppm } ^{13}\text{C}[^{1}\text{H}] \text{ NMR (75 MHz, CD}_2\text{Cl}_2) \delta = 24.0, 25.2, 25.5-26.1, 26.5-26.9, 27.6, 28.9, 29.8, 30.1-30.7, 124.1, 127.0, 127.7, 128.44, 129.19, 129.5, 130.8-131.6, 132.4, 132.5, 132.6-132.7, 137.2, 137.4, 140.0, 141.2, 141.8, 142.2, 145.7, 153.3, 181.6, 300.7 \text{ ppm.}$

Anal. Calcd. for C$_{48}$H$_{55}$Cl$_2$N$_3$Ru, 68.15; H, 6.55; N, 4.97; Found: C, 67.68; H, 6.72; N, 5.04.

**GENERAL PROCEDURE FOR RCM AND ENYNE REACTIONS**

In a Radley carousel under argon or nitrogen, a reaction tube was charged with the substrate (0.25 mmol) and the solvent (2.5 mL) (CH$_2$Cl$_2$ for reaction at RT and 40 °C, toluene for reactions at 80 °C), then pre-catalyst (0.0025 mmol). The progress of the reaction was monitored by $^1\text{H NMR spectroscopy. Conversion was determined by } ^1\text{H NMR spectroscopy by integrating the characteristic signals for allylic proton resonances.}$

**GENERAL PROCEDURE FOR CM REACTIONS**

In a Radley carousel under argon or nitrogen, a reaction tube was charged with one equivalent of the electron rich substrates (0.25 mmol) and two equivalents of the electron poor olefin (0.5 mmol), solvent (2.5 mL), then pre-catalyst (0.0025 mmol). The progress of the reaction was monitored by $^1\text{H NMR spectroscopy. At reaction completion solvent was removed under vacuum and the crude residue was checked by } ^1\text{H NMR spectroscopy. Conversion determined by } ^1\text{H NMR spectroscopy by integrating the characteristic signals for allylic proton resonances.}$
CHAPTER II: RUTHENIUM INDENYLIDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

COMPUTATIONAL DETAILS

All the DFT static calculations were performed at the GGA level with the Gaussian09 set of programs,\textsuperscript{22} using the BP86 functional of Becke and Perdew.\textsuperscript{23} The electronic configuration of the molecular systems was described with the standard split-valence basis set with a polarization function of Ahlrichs and co-workers for H, C, N, O, and Cl (SVP keyword in Gaussian).\textsuperscript{24} For Ru we used the small-core, quasi-relativistic Stuttgart/Dresden effective core potential, with an associated valence basis set contracted (standard SDD keywords in gaussian09).\textsuperscript{25} The geometry optimisations were performed without symmetry constraints, and the characterisation of the located stationary points was performed by analytical frequency calculations. Bearing in mind the entropic contribution calculated in the gas phase ($p = 1$ atm) is likely exaggerated in dissociative steps.\textsuperscript{5,26} All the thermochemical analysis was performed at $p = 1254$ atm, as suggested by Martin et al.\textsuperscript{27} The reported energies have been optimised \textit{via} single point calculations on the BP86 geometries with triple zeta valence plus polarisation (TZVP keyword in Gaussian) using the M06L functional,\textsuperscript{28} however estimating solvent effects with the polarisable continuous solvation model PCM using CH$_2$Cl$_2$ as solvent.\textsuperscript{29} Zero point energies and thermal corrections calculated at the BP86 level were added to the M06 in solvent energies to approximate free energies in the solvent.

\textbf{Table 2.1}: Free energy relative to the generation of the propagating species $G$ and propagation step to metallacycle $L$ for IPr*-PPh$_3$ and IPr-PPh$_3$ in kcal/mol. Thermochemical terms calculated in solvent (PCM model).

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<tr>
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<td>16.9</td>
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</tr>
<tr>
<td>F</td>
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</table>
CHAPTER II: RUTHENIUM INDENYLDENE COMPLEXES FOR OLEFIN METATHESIS BEARING HIGHLY HINDERED LIGANDS

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REFERENCES

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CHAPTER III: ALCOHOLYSIS OF RUTHENIUM

INDENYLIDENE PRE-CATALYSTS


STATEMENT

The X-ray experiments were carried out by Prof. Alexandra M. Z. Slawin.

The low temperature 2D NMR and NMR kinetic experiments were performed in collaboration with Dr. Tomas Lebl.

The DFT-calculations were performed by Dr. Albert Poater (Cavallo group)

The work regarding the synthesis of Eta-5 and mechanistic investigations have been performed in collaboration with Dr. Cesar A. Urbina-Blanco.

The work regarding the synthesis of \textit{phobEta-5}, the evaluation of the decomposition of the indenylidene pre-catalysts have been performed in collaboration with Dr. David J. Nelson.
INTRODUCTION TO DECOMPOSITION OF METATHESIS CATALYSTS VIA ALCOHOLYSIS REACTION

Despite several decomposition processes being known to occur with metathesis pre-catalysts, the deactivation via alcoholysis reactions is probably one of the most investigated. This process generally consists of a double or single oxidation of a primary alcohol such as methanol, which leads to the formation of ruthenium complexes that may be active in “parasite” reactions. For example, products from the alcoholysis of benzyldiene pre-catalysts are generally hydrido carbonyl complexes, which are active in alkene isomerisation reactions (Scheme 3.1). However, different to the others decay pathways, alcoholysis reaction can be used as tools for tandem transformations such as metathesis/hydrogenation or metathesis/isomerisation.¹

ALCOHOLYSIS OF BENZYLIDENE PRE-CATALYSTS

The first detection of these hydride complexes as decomposition products in alcohol conditions was reported in 2001 by Furstner et al.² However the difficult characterisation of these decomposed products, led the author to assign the structure as [RuH₂Cl₂(PCy₃)₂] as a diasteromeric mixture, in analogy to the known structure of [RuH₂Cl₂(PiPr₃)₂] (Ru-9).³ A year later, Grubbs et al. described the formation of the ruthenium hydrido carbonyl Ru-46, achieved by prolonged heating of [RuCl₂(PCy₃)₂(=CHOEt)] (See scheme 1.26 in chapter I).⁴ Differently from what was observed by Furstner, Mol et al. isolated Ru-46 as a decomposition product, by stirring GI in alcohol solvents.⁵ In the same year, Grubbs et al. isolated the hydrido carbonyl
complexes Ru-67 and Ru-47 during the purification of Ru-19 and GII with alcoholic solutions (Scheme 3.1).\(^6\)

![Scheme 3.1: Alcoholysis of first and second generation Grubbs’ catalysts.](image)

In order to confirm the real nature of the alcoholysis product of first generation benzylidene catalysts, and to understand the mechanism, Mol et al. performed a decomposition reaction using separately isotopically labelled complexes and primary alcohols. In particular, from the results of these experiments, it has been found that the alcohol was the source of the CO, determined using \(^{13}\)C labelled ethanol. The presence of the base accelerates the rate of this transformation. The same insight can be extended also for second generation catalysts.\(^5,7\) Only recently Percy, Hillier and Tuttle reported a detailed study of the decomposition of GII with primary alcohols using DFT calculations (Scheme 3.2).\(^8\)
Scheme 3.2: Proposed mechanism for the alcoholyis of GI and GII.

The proposed mechanism involves an initial phosphine dissociation and coordination of the primary alcohol through the oxygen to the ruthenium centre. Then, via elimination of HCl, (quenched by the base present), the methoxy compound III immediately reacts with the alkylidene moiety via hydride transfer. Then, a series of hydride transfers to the benzyl moiety form toluene and the ruthenium formyl species VI, which rearranges to form the hydrido carbonyl VII. Finally, the re-coordination of the dissociated PCy3 leads to the formation of hydrido carbonyl complex VIII (Scheme 3.2).5,7b,8

Treating GI and GII with benzyl alcohol, in the presence of triethylamine, instead of forming the expected hydrido carbonyl complexes, complexes Ru-68 and Ru-69, where the phenyl is directly bonded to the ruthenium centre in a η-1 fashion, were achieved (Scheme 3.3 a).7b

Even though less correlated with the alcoholyis reaction, oxygen can decompose metathesis catalysts. Mol and co-workers reported the formation of Ru-69, which is the same
side product obtained from decomposition by benzyl alcohols, by exposing GII to an oxygen atmosphere in solution and in the solid state. Interestingly, in the same year, Grubbs published the formation of the SIMes cyclometallated carbonyl complex Ru-70 obtained in presence of oxygen during the synthesis of GII (Scheme 3.3). The reason for such different products under oxygen can be due to the different conditions carried out to achieve the complexes, allowing the possibility that different factors and not only the presence of oxygen can lead to these species.

Scheme 3.3: Decomposition of GI and GII in presence of benzyl alcohol and in presence of oxygen.

Connected with the decomposition of metathesis catalysts in primary alcohols, the use of alkoxide base has been revealed to be highly useful for several synthetic transformations. For
example, the use of KO'Bu is often considered for the synthesis of metathesis catalysts, in order to generate the free NHC ligands towards the ruthenium complexes.\textsuperscript{9} However, KO'Bu can react directly with the ruthenium species, generating 14 e\textsuperscript{-} tetracoordinated complexes, like Ru-71 (Scheme 3.4),\textsuperscript{10} which is very difficult to isolate as a pure compound due to its instability.\textsuperscript{11}

\begin{center}
\includegraphics[width=\textwidth]{scheme34}
\end{center}

**Scheme 3.4:** Decomposition of GI in presence of potassium tert-butoxide.

In the way of analogously, Fogg and co-workers evaluated the decomposition of GI and Ru-19 in the presence of sodium methoxide. The overreaction with NaOMe generates three novel ruthenium species (Ru-72, Ru-73 and Ru-74) (Scheme 3.5).\textsuperscript{12}

\begin{center}
\includegraphics[width=\textwidth]{scheme35}
\end{center}

**Scheme 3.5:** Decomposition of GI and Ru-19 in presence of sodium methoxide.

The concept of using alkoxide ligands to tune the activity of the metathesis catalysts has been widely developed in the past decade.\textsuperscript{13} The use of aryloxides, like phenol or even chiral BINOL derivatives, has been found, in certain cases, to have a non-innocent behaviour, generating decomposition products which are inactive in metathesis.\textsuperscript{13c,14} Caulton reported the
formation of the tetracoordinated ruthenium carbynes Ru-78 and Ru-79. These decomposition products are achieved by treating GI or Ru-75 with sodium phenoxide, which immediately reacts, generating the bis-phenoxide complexes Ru-76 and Ru-77 via anion exchange. These complexes are unstable in the reaction condition decomposing to the benzyne complexes Ru-78 and Ru-79 via elimination of a molecule of phenol (Scheme 3.6). This unwanted reaction can been avoided using the second generation pyridine complex Ru-81 (Scheme 3.6).

![Scheme 3.6: Decomposition of GI and Ru-75 in presence of phenoxides.](image)

Fogg reported another interesting decomposition of ruthenium benzylidene pre-catalysts, which takes place in presence of BINOL. It has been found that the BINOL ligand can bind the metal centre in two ways: $\kappa^2$-$O,O$ coordination or $\kappa$-$O$, $\eta^1$-enolate coordination. The two isomers are present along with an unknown decomposition product (Scheme 3.7). This type of $\delta$ to $\pi$ isomerism, it has been found to be common for the ruthenium bearing aryloxide ligands, in which they can rearrange up $\eta^6$ coordination on the Ru species.
In order to reduce the amount of the enolate product, pyridine was used as the solvent, which promotes the $\kappa^2$-O,O coordination to form product. This isomerism has been revealed to be dynamic. For example, Ru-85 can be irreversibly converted to Ru-88, which is less active in metathesis, in dichloromethane (DCM) in 5 h. However in the presence of pyridine, Ru-88 is reconverted to Ru-85 (Scheme 3.8). \textsuperscript{13c,15}

Scheme 3.7: Synthesis of ruthenium benzylidene complexes bearing BINOL as X ligand.

HYDROGENOLYSIS OF BENZYLIDENE PRE-CATALYSTS

As was mentioned before in this introduction, the use of alcohols can generate new species that can be active in catalysts like hydrido carbonyl and arenyl derivatives. However it is possible to use hydrogen to generate, via hydrogenolysis, different hydrido dihydrogen species active in isomerization and hydrogenation. Stirring first and second generation metathesis catalysts in dichloromethane, in the presence of triethylamine (Et\textsubscript{3}N) or a proton sponge such as 1,8-bis(dimethylamino)naphthalene, under a hydrogen atmosphere (1000 psi) the hydrido dihydrogen analogues (for GI and Ru-19, Ru-89 and Ru-90) are achievable in
quantitative yields (Scheme 3.8). The following complexes can be converted into the corresponding hydrido carbonyl derivatives by adding methanol to the reaction mixture (Scheme 3.8). Ru-89 and Ru-90 have been found to be active in the hydrogenation of double bonds and the isomerisation of alkenes. Interestingly, starting from GI it is possible to develop multiple tandem hydrogenation/metathesis reactions, performing first the metathesis transformation, using hydrogen to generate Ru-89, active in hydrogenation and, with the use of the alkyne 14, generating complex Ru-91, active in metathesis (Scheme 3.7).

ALCOHOLYSIS OF RUTHENIUM INDENYlidene PRE-CATALYSTS

Despite the seminal studies on the decomposition of benzylidene complexes, the evaluation of possible deactivation pathways of ruthenium indenyldene pre-catalysts was still unexplored. Intrigued to investigate any possible behaviour of these complexes in different conditions, several indenyldene pre-catalysts were exposed to alcoholic solutions. These complexes have revealed an alternative alcoholysis pathway, where the indenyldene is reduced to η¹-indenyl, followed by a rearrangement to η⁵-indenyl. This decomposition pathway is
dependent on the phosphine ligand coordinated, with a special regard to ligand flexibility (Scheme 3.9).^{18}

Second generation metathesis pre-catalysts showed the same behaviour as the bisphosphine analogues under alcoholysis reaction conditions. However, the possible N-heterocyclic carbene dissociation makes the system more complicated and difficult to analyse.^{15} The decomposition of $M_{10}$, $M_{11}$ and $M_1$ will be considered separately, evaluating how the different phosphines affect the indenyl rearrangement.

**ALCOHOLYSIS OF [RuCl(PPh$_3$)$_2$(3-phenylindenylidene)] ($M_{10}$)$^{17c}$**

$M_{10}$ is a very valuable synthon for the synthesis of first and second generation ruthenium indenylidene complexes (see chapter II).^{19} Complex $M_{10}$ is easily accessible from [RuCl$_2$(PPh$_3$)$_3$-4] and diphenyl propargylic alcohol. In its preparation as well as in the synthesis of its corresponding first and second generation derivatives, it is necessary to use alcohols (MeOH and iPrOH), in order to remove the generated free phosphine and the excess of the ligand present.^{19-20} For these reasons, the evaluation of the stability of this complex under...
alcoholic reaction conditions is mandatory, in order to avoid side products. By stirring $M_{10}$ in the presence of a primary alcohol, such as ethanol, after 14 days, the formation of a new ruthenium species is detected. This new complex shows two doublets at $\delta = 42.3$ and 48.7 ppm with a coupling constant of $J_{P-P} = 46.1$ Hz, in the $^{31}\text{P}\{^{1}\text{H}\}$ NMR spectrum, which means the presence of two spectroscopically non-equivalent phosphorus centres. Interestingly, the $^{1}\text{H}$ NMR spectrum does not indicate the formation of a hydride species. In order to evaluate if the process involved in this decomposition process was a real alcohol oxidation, a series of tests with $M_{10}$ were carried out (see experimental section). The reaction is accelerated in the presence of a stoichiometric amount of triethylamine (to sequester any possible HCl formed). In the presence of tert-butanol no reaction was observed and by using iso-propanol the formation of acetone was detected, which suggests a single oxidation of the alcohol. The novel microcrystalline ruthenium complex was analysed by $^{1}\text{H}$ and $^{13}\text{C}\{^{1}\text{H}\}$ NMR and, surprisingly, the data suggest that the indenyl moiety is coordinated to the ruthenium centre in a different coordination mode. Due to the reduction of the indenylidene to indenyl, confirmed by $^{13}\text{C}\{^{1}\text{H}\}$ NMR spectrum, there is the disappearance of the carbene resonance between $\delta = 240$ and 330 ppm.$^{21}$ The confirmation of the novel ruthenium complex was determined via single crystal X-ray diffraction, confirming a rearranged indenyl moiety into a $\eta^5$-coordinated fashion in $[\text{RuCl(PPh}_3)(\eta^5\text{-3-phenylindenyl})](\text{Eta-5})$ (Figure 3.1).
Figure 3.1: X-ray structure of Eta-5 (H atoms are omitted for clarity).

Selected bond lengths [Å] and angles [°]: Ru1–C1 2.182(5), Ru1–C2 2.194(4), Ru1–C3 2.271(4), Ru1–C4 2.348(4), Ru1–C9 2.345(4), Ru1–P1 2.3430(11), Ru1–P2 2.2960(11), Ru1–Cl1 2.4407(12); P2–Ru1–P1 96.49(4), P1–Ru1–Cl1 92.34(4), P2–Ru1–Cl1 96.82(4).

The complex bears a distorted piano stool geometry with C1 symmetry. Complex Eta-5 showed a smaller P-Ru-P bond angle (96.49(4)°) than its ruthenium indenyl congener [RuCl(PPh3)2(η5-indenyl)]22 (Ru-92) (99.205(18)°), which could be presumably a result of the steric hindrance of the phenyl substituent on the indenyl ligand.

Due to the ruthenium arene analogues complexes reported in the literature being widely used in catalysis as well as a synthon,23 we considered the development of a straightforward synthesis of complex Eta-5 to be of interest. After optimizing the protocol, Eta-5 can be obtained almost quantitatively (92% yield of isolated compound) by refluxing M10 in ethanol for 2 hours in the presence of a stoichiometric amount of triethylamine (Scheme 3.10 a). The methodology developed allowed for multi-gram scale synthesis simply by changing ethanol for iso-propyl alcohol. In addition, it is possible to synthesise Eta-5 starting from [RuCl2(PPh3)3] (Ru-1) and the corresponding propargylic alcohol to access M10 in a one-pot manner with good yield (77% overall yield) (Scheme 3.10 b).23
In order to have a deeper understanding of the reaction mechanism involved in this rearrangement, a series of kinetic experiments were carried out using $^{31}$P$\{^1$H$\}$ NMR spectroscopy, determining the overall rate of the reaction as $n = k[M_{10}][EtOH]$. It has been found that the concentration of triethylamine does not affect the rate of the reaction. In addition, the presence of free phosphine affects the reaction rate, which means that phosphine dissociation is possibly involved in the reaction mechanism. However, different concentrations of PPh$_3$ do not vary the reaction rates, determining that any possible phosphine dissociation does not take place in the rate-determining step. From the kinetic experiments at different temperature it was possible to extract the thermodynamic parameters through the Eyring equation: $\Delta H^\neq = 25.1(2)$ kcal mol$^{-1}$; $\Delta S^\neq = 113(5)$ cal mol$^{-1}$ K$^{-1}$, and $E_A = 25.7(2)$ kcal mol$^{-1}$.

In order to support the experimental results and to propose a reaction mechanism, this indenylidene rearrangement was computationally calculated by Cavallo et al. (Scheme 3.11).
The coordination of the alcohol molecule to the metal centre is preceded by the dissociation of one phosphine (B-PPh₃). Then, one equivalent of HCl is released, promoted by the presence of triethylamine in the reaction media (D-PPh₃ and E-PPh₃). After re-coordination of the phosphine (F-PPh₃), one hydride is presumably transferred from the alkoxide to the indenylidene moiety, via an agostic hydrogen transfer, releasing one molecule of the corresponding aldehyde and forming the η¹-indenyl species (G-PPh₃), which quickly rearranges to the final complex Εta-5 (Scheme 3.11). From the calculations, the rate determining step is the hydrogen atom transfer from the methyl group of the methoxy ligand to the ylidene carbon atom of the indenylidene ligand (from F to G), which takes place through a transition-state of 27.6 kcal mol⁻¹, leading to intermediate G. These data are in good
agreement with the experimental $E_A = 25.7$ kcal mol$^{-1}$, as well as with the experimental evidence. However the computational results exclude the effect of the ethanol in the reaction rate. This result is not in agreement with the reaction order experimentally achieved, which consider the RDS dependent on the concentration of alcohol present. In the absence of a nearby NEt$_3$ molecule the overall energy required to access Eta-5 is calculated to be 39.9 kcal mol$^{-1}$, which clearly indicates the crucial role of NEt$_3$ in the process (Scheme 3.11).

**Alcoholysis of** [RuCl(ISO-butyrophoban)$_2$(3-phenylindenylidene)]
(M$_{11}$)$_{18}^{18a,b}$

In order to understand the generality and the applicability of the rearrangement, complexes [RuCl$_2$(PCy$_3$)$_2$(3-phenylindenylidene)] (M$_1$)$_{25}^{25}$ and [RuCl$_2$(Bu-Phoban)$_2$(3-phenylindenylidene)]$_{26}^{26}$ (M$_{11}$), which are indenylidene-bearing analogous metathesis catalysts, were subjected to the same reaction conditions (Scheme 3.12). The latter was chosen due to the industrial applicability of phoban type ligands.$^{27}$ Complex M$_1$ showed the same behaviour as GI, yielding Ru-46 (Scheme 3.12, a). However, complex M$_{11}$ yielded an indenyl complex which overreacts, forming a hydride species as mixture of isomers (Scheme 3.12, b).
Scheme 3.12: Alcoholysis products from $M_1$ and $M_{11}$.

X-ray analysis from a single crystal of $M_{11}$ indenyl, obtained from a concentrated solution in pentane at low temperature, confirmed that the product is a novel complex $[\text{Ru(H)(}^{t}\text{Bu-Phoban)}_2(\eta^5-3\text{-phenylindenylidene})]\text{phobEta-5}$ (Figure 3.2).

Figure 3.2: X-ray structure of complex $\text{phobEta-5}$. (H atoms are omitted for clarity). Selected bond lengths [Å] and angles [°]: Ru1-H1m 1.48(3), Ru1-P1 2.2906(7), Ru1-P2 2.2587(8), Ru1-C1 2.228(3), Ru1-C2 2.200(3), Ru1-C3 2.286(3), Ru1-C4 2.406(3), Ru1-C9 2.413(3); P1-Ru1-P2 96.51(3), P1-Ru1-H1m 82.5(10), P2-Ru1-H1m 80.6(10).
The Ru–P bond distances of $^{\text{phob}}$Et₅-5 are shorter (2.2587(7) and 2.2906(7) Å) than observed in complex Et₅-5 (2.296(1) and 2.343(1) Å), probably due to the more electron donating capability of $^t$Bu-Phoban, compared to triphenyl phosphine.

By switching from EtOH to $^t$PrOH, in order to avoid the formation of any hydrido carbonyl species, it is possible to isolate $^{\text{phob}}$Et₅-5 as a red powder in 76% yield (Scheme 3.12). The elemental analysis was consistent with $^{\text{phob}}$Et₅-5.

However, as mentioned above, complex $^{\text{phob}}$Et₅-5 is isolated as a mixture of isomers. The $^1$H NMR spectrum showed three hydride signals (where two of them are enough intense to be determined in C₆D₆: $\delta_H = -15.95$ ppm, $t, J = 32.2$ Hz and $\delta_H = -17.25$ ppm, $t, J = 32.2$ Hz), while six signals were evident on the $^{31}$P{$^1$H} NMR spectrum.

In order to have a clearer idea of the mixture achieved, more detailed NMR studies were carried out. 2D $^{31}$P-EXSY and [$^1$H, $^{31}$P]-HMBC experiments (Figure 3.3) recorded at 265 K, confirmed that the multiple signals observed were a result of different rotamers of the complex in solution, due to hindered restriction around a bond.
Unfortunately, it was not possible to assign the structure of each rotamer by NMR methods. Therefore, in collaboration with Cavallo et al., DFT calculations were used to identify the three lowest energy rotamers. Three low-lying minima, have been found in which the phoban ligand adopts three different conformations (Figure 3.4).

**Figure 3.3:** (top) 2D $^1$H, $^{31}$P-HMBC spectrum of $^{\text{phob}}$Eta-5 optimised for $J_{HP} = 30$ Hz recorded at 265 K; (bottom) 2D $^{31}$P-EXSY spectrum of $^{\text{phob}}$Eta-5 recorded at 265 K.
Figure 3.4: DFT-calculated conformers for complex $\text{phobEta-5}$ and their relative energies normalized to $I$ (in kcal mol$^{-1}$) in DCM as solvent (M06L/TZVP//BP86/SVP level of theory; PCM model for the solvent).

One shows the two iso-butyl groups on the opposite side from the hydride ($I$), another one where the iso-butyl groups are in trans-relative position to each other ($II$), and the third one where both iso-butyl groups and the hydride are on the same side ($III$). The relative energies normalized to $I$ are $0$, $2.6$ and $5.5$ kcal mol$^{-1}$, with barriers to interconversion of $15.7$ kcal mol$^{-1}$. This type of conformational isomerism is known for ruthenium complexes bearing phoban-type ligands.$^{28}$ Notably, this complex bears a hydride ligand rather than a chloride ligand. One of the reasons of the direct formation of the hydride can be found in the bulkier nature of the ligands present in $\text{phobEta-5}$, which may favour the placement of a smaller ligand. In comparison, to access $[\text{Ru(H}(\eta^5-3\text{-phenyl-indenyl})(\text{PPh}_3)_2]$ (Eta-5-H), the analogous hydride of Eta-5, it is necessary to re-expose the complex to the reaction conditions for a prolonged time (days) (Scheme 3.13).
Scheme 3.13: Formation of Eta-5-H after prolonged exposure of Eta-5 in the alcoholysis conditions

It is possible to get complex Eta-5-H in MeOH with an excess of NaOMe at room temperature in an overnight reaction,\(^ {29}\) suggesting that \(\text{phobEta-5}\) may be formed from the corresponding chloride, which could not be isolated. To confirm the stated hypothesis, in collaboration with the Cavallo group, DFT calculations of the formation of the \(\text{phobEta-5}\) were carried out and compared with the formation of Eta-5 and Eta-5-H (Figure 3.5).

Figure 3.5: Potential-energy surfaces (PES) for the reaction of the chloride complexes \(H\) to yield hydride species \(M\). Energies are free energies, in kcal mol\(^{-1}\) (M06L\(\text{ATZP} \backslash \text{BP86} \text{SVP}\) level of theory). The relative energy is referred for the energy state chloride species \(H\) for the independent processes.
Despite all the alcoholysis process for $\text{M}_{11}$ to $\text{H}$ being slightly uphill (see Figure 3.7 in the next section) and, in thermodynamic control the formation intermediate $\text{I}$ would be more favourable, in the reaction conditions considered, the excess of alcohol in the reaction mixture promotes the formation of $\text{phobE}ta\text{-}5$, which is slightly favoured by 0.4 kcal mol$^{-1}$, probably by the reduced steric effect the hydride vs the chloride correspondent. In comparison, the reaction pathway to form $\text{Eta-5-H}$ from the $\text{Eta-5}$ it is less favourable (18.3 kcal mol$^{-1}$), which makes the stronger conditions to access the hydride species and the possibility to access the chloride complex without overreaction reasonable.

**ALCOHOLYSIS OF $[\text{RuCl(PCy}3)_2(3\text{-phenylindenylidene})]$ (M$_1$)$^{18a}$**

As mentioned before, the complex $[\text{RuCl}_2(\text{PCy}_3)_2(3\text{-phenylindenylidene})]$ (M$_1$) decomposes to $\text{Ru-46}$ in the presence of primary alcohol, in the same way as GI. To understand if it is possible to access the corresponding indenyl derivative, the use of secondary alcohols was considered, to avoid any possible over alcohol oxidation to carbon monoxide (Scheme 3.14).

**Scheme 3.14:** Alcoholysis of $\text{M}_1$ in primary and secondary alcohols.
Interestingly, instead of accessing the expected indenyl product, \([\text{RuCl(H}_2\text{)(PCy}_3\text{)}_2]\) (Ru-89) was formed in 76% yield. In order to understand if this unexpected decomposition product can be formed with other PCy\(_3\) bearing metathesis complexes, this alcoholysis procedure was extended to GI and the methylidene derivative Ru-38, which is easily achievable using a modified version of Fogg’s protocol,\(^{30}\) (Scheme 3.15).\(^{31}\)

**Scheme 3.15:** Alcoholysis of GI and Ru-40 in secondary alcohols.

In both cases, Ru-89 was obtained, confirming that this pathway is general to ruthenium alkylidene complexes bearing tricyclohexylphosphine. Notably, Ru-89 is usually achieved via hydrogenolysis of metathesis catalysts (see Scheme 3.7),\(^{16a}\) through the dehydrogenation of \([\text{RuH}_2\text{(H}_2\text{)}_2\text{(PCy}_3\text{)}_2]\).\(^{32}\) This is the first example where this complex is obtained without the direct use of dihydrogen. Fogg and co-workers have shown that by treating Ru-89 with a primary alcohol, it is possible to achieve Ru-46 from a methanolysis reaction.\(^{33}\) These data suggest that alcoholysis and hydrogenolysis may proceed by similar pathways and Ru-91 can be a potential intermediate in the primary-alcohol-mediated decomposition of metathesis catalysts.

For the sake of consistency, also second-generation indenylidene catalysts (M\(_2\) and M\(_{20}\)) were also evaluated in the presence of primary and secondary alcohols (Scheme 3.16).
The decomposition of the second generation catalysts reveals similar trends as the first generation, but the possible NHC dissociation makes the resulting mixture more complicated than expected. \( M_2 \) is slowly decomposed in primary alcohols, most likely as a consequence of its low initiation rate,\(^{34} \) achieving \( \text{Ru-47} \) in small amounts. \( M_{20} \), which features a more labile phosphine, decomposed quickly in primary alcohol, yielding mainly the corresponding hydridocarbonyl species \( \text{Ru-93} \) (Scheme 3.16). Then, the same set of complexes were exposed to iso-propyl alcohol (Scheme 3.16). In both cases, the NHC dissociation is predominant, obtaining for complex \( M_{20} \) a mixture of \( \text{Eta-5}, \text{Eta-5-H} \) (major product) and an unidentified mixture of products. In the case of \( M_2 \), \( \text{Ru-89} \) is accessed together with a mixture of unidentified products (Scheme 3.17).
The nature of the phosphine appears to have a role in the reactivity of this transformation. PPh$_3$ and PCy$_3$ are quite different in terms of both steric and electronic properties (cone angles of 145° and 170°, respectively, and TEP of 2068.9 cm$^{-1}$ and 2056.4 cm$^{-1}$, referred to the respective $[\text{Ni(CO)}_3(\text{PR}_3)]$ complexes$^{35}$. However, coordinated to M$_{10}$ and M$_1$, they show a similar steric bulk, having a percent buried volumes of ($\%V_{\text{bur(avs)}}$) = 26.5% (M$_{10}$; Ru-P = 2.39 Å) and 27.6% (M$_1$; Ru-P = 2.42 Å)$^{34,36,37}$ $i$-Bu-Phoban in M$_{11}$, shows a very similar $\%V_{\text{bur}}$ compared to PCy$_3$ ($\%V_{\text{bur}}$ = 27.4%) (Figure 3.6)$^{18b}$.

Figure 3.6: X-ray structure of M$_{10}$, M$_1$ and M$_{11}$. Hydrogen atoms omitted for clarity. Selected bonds (Å) and angles (°): M$_{10}$: Ru1-C1 1.867(4), Ru1-Cl1 2.3518(12), Ru1-Cl2 2.3741(12), Ru1-P1 2.3851(12), Ru1-P2 2.4021(12); C1-Ru1-Cl2 156.51(4), C1-Ru1-P1 91.15(12), C1-Ru1-P2 97.86(12), P1-Ru1-P2 170.99(4). M$_1$: Ru1-C1 1.881(6), Ru1-Cl1 2.3892(18), Ru1-Cl2 2.4081(17), Ru1-P2 2.416(2), Ru1-P1 2.427(2); Cl2-Ru1-Cl1, 163.92(6), C1-Ru1-P1 91.15(12), C1-Ru1-Cl2 97.86(12), P1-Ru1-P2 170.99(4). M$_{11}$: Ru1-Cl1 2.395(5), Ru1-Cl2 2.405(5), Ru1-P2 2.396(5), Ru1-P1 2.427(5); Cl1-P1 159.52(15), P1-Ru1-P2 163.83(15), P1-Ru1-P1 98.9(5), P2-Ru1-C1 96.9(5).

The electronic properties of $i$-Bu-Phoban are very similar to PCy$_3$ as well. The average of the carbonyl stretching frequencies are 2029 cm$^{-1}$ for $i$-Bu-Phoban, 2028 cm$^{-1}$ for PCy$_3$ and 2044 cm$^{-1}$ for PPh$_3$ on [IrCl$_2$(CO)$_2$(PR$_3$)]. Despite the effective electronic difference between PPh$_3$ and PCy$_3$, this type of descriptor cannot rationalise the exact effect of these ligands in the decomposition process. For this reason, in collaboration with the Cavallo group, the indenyl rearrangement was computationally calculated for M$_1$, M$_{10}$ and M$_{11}$ (Figure 3.7).
**Figure 3.7:** PES of the indenyl rearrangement for complexes $M_1$, $M_{10}$ and $M_{11}$. Energy normalized to $A$ plus NEt$_3$ and methanol. Level of theory M06L\TZP\BP86\SVP.

In the presented calculations, it can be easily found that the rate determining reaction step in the energy barrier profile is the formation of intermediate $G$, via hydrogen transfer from intermediate $F$, which is remarkably different between $M_{10}$, $M_1$, and $M_{11}$. Another important value to consider the feasibility of the whole process is the formation of the final compound $H$, which in the case of $M_{10}$ is favoured by 14.5 kcal mol$^{-1}$. In the case of $M_1$ and $M_{11}$ this is
unfavourable by 10.8 and 5.5 kcal mol\(^{-1}\), respectively. As mentioned before, for \(\text{M}_{11}\), \(\text{H}\) overreacts forming the hydride species \(\text{phob}_{\text{Eta}-5}\), favoured by 0.5 kcal mol\(^{-1}\). In light of these results, one for the explanations of the different stability and energy barriers observed can be due to the configurations of \(\text{A}\) and \(\text{H}\). In the indenylidene complex, the two phosphines are \textit{trans} to each other; meanwhile in \(\text{H}\) they are placed \textit{cis}. Probably the stability of \(\text{H}\) decreases on the basis of the capability of the phosphines to accommodate each other, reducing the steric hindrance, favouring the configurational change.

\[\text{Figure 3.8: DFT-calculated transition state } \Phi \text{ for } \text{M}_1 \text{ (selected distances in } \text{Å}, \text{cyclohexyl moieties are omitted for the sake of clarity).}\]

In fact, a computational evaluation of the energy difference between \(\text{A}\) and \(\text{H}\) using the smaller PMe\(_3\) has been considered. This study showed that the \(\text{F}\) to \(\text{G}\) barrier should be only 20.2 kcal mol\(^{-1}\), and that \(\text{H}\) is 26.5 kcal mol\(^{-1}\) more stable than \(\text{A}\). Therefore, the capability to accommodate steric hindrance in the \textit{cis} conformation is the key factor for this rearrangement, providing a valuable way to predict the capability of new complexes to undergo rearrangement to the indenyl derivatives. In addition, the same explanation can be used to understand the over-reactivity of \(\text{M}_{11}\) to \(\text{phob}_{\text{Eta-5}}\), probably even more favourable due to the less sterically hindered hydride species.
CONCLUSION

Decomposition processes allow a better understanding of catalytic systems. Regarding this topic, alcoholsysis reactions have been proven to be important side-reactions either for the formation of highly active decomposition products, or for tandem systems like metathesis/isomerisation processes. The decomposition of first and second-generation metathesis pre-catalysts has been evaluated, finding a novel rearrangement which led to two new complexes, Eta-5, a valuable catalyst for several transformations (see next chapter) and phobEta-5. In addition, the decomposition of indenylidene and benzylidene complexes in secondary alcohols has been studied, determining the formation of an unexpected decomposition product from PCy3 bearing complexes, which connects hydrogenolysis and alcoholsysis reactions, with possible implications for tandem systems and in catalyst regeneration. The different behaviour observed for the alcoholsysis reaction with indenylidene complexes is dependent on the ability of the phosphine to accommodate steric effects from the trans- conformation of the metathesis pre-catalyst to the cis conformation of the desired product. A detailed mechanistic evaluation has been disclosed, allowing us to predict the capability of indenylidene complexes undergo to this rearrangement depending on the phosphine present.

EXPERIMENTAL SECTION

GENERAL CONSIDERATIONS:

Benzene was purchased from Alfa Aesar as anhydrous under argon and used as supplied. Methanol, ethanol and iso-propanol were purchased as anhydrous under argon from Sigma-
Aldrich and used as supplied. Pentane was dried by refluxing over phosphorus pentoxide and distilled. 1,7-Octadiene was dried by passage through a column of activated alumina and degassed with a stream of argon. Triethylamine was purchased from Acros Organics and used as supplied. M_{10}, M_{11}, M_{2}, M_{20} and iso-butylphoban were purchased from Umicore AG. GI was purchased from Sigma-Aldrich and used as supplied. Elemental analyses were performed at the London Metropolitan University. Catalyst syntheses were performed in an MBraun glovebox containing dry argon and less than 1 ppm oxygen. $^1$H, $^{31}$P, and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance 300 or Bruker Avance II 400 or 500 NMR spectrometers.

**SYNTHESIS OF RuCl(PPh$_3$)$_2$(3-phenylindenyl) (Eta-5):**

In the glovebox a solution of $\text{M}_{10}$ (600 mg, 0.67 mmol) in ethanol (10 mL) was prepared in a Schlenk flask. To this suspension triethylamine (1.015 mmol, 1.5 equiv., 0.130 mL) was added. The reaction mixture was taken out of the glovebox, stirred at reflux for 1.5 h under Ar atmosphere. The suspension was cooled down to room temperature and methanol (10 mL) was added. It was cooled down at -40 °C. Filtration and washing with cold pentane (3 x 15 mL) afforded RuCl(PPh$_3$)$_2$(η$_5$-3-phenylindenyl) (Eta-5) (523 mg, 94%) as microcrystalline red solid.

$^1$H NMR (CD$_2$Cl$_2$ 400 MHz): δ = 7.84 (d, $J$=8.4 Hz, 1 H, H$_{indenyl}$), 7.66 - 7.69 (m, 2 H, H$_{indenyl}$), 7.46 (s, 1 H, H$_{indenyl}$), 7.28 - 7.43 (m, 18 H), 7.13 - 7.22 (m, 10 H), 6.94 - 7.04 (m, 20 H) 6.76 (s, 1 H, H$_a$), 6.67 (dd, $J$=9.3, 7.8 Hz, 9 H), 5.96 (s, 1 H), 5.22 (ddd, $J$=5.4, 2.3, 0.8 Hz, 1 H, H$_{indenyl}$), 3.03 ppm (s, 1 H, H$_{indenyl}$) $^{13}$C { [$^1$H] NMR (75.5 MHz, CD$_2$Cl$_2$): 58.9 (C$_{indenyl}$), 87.3, 90.0 (C$_{indenyl}$), 109.9, 112.2, 123.8, 124.7 (C$_{indenyl}$), 126.7, 127.3 (C$_{indenyl}$), 127.4, 127.7,
127.8, 128.7(C\textsubscript{indenyl}), 129.0, 129.2(C\textsubscript{indenyl}), 129.7(C\textsubscript{indenyl}), 133.5, 133.6, 134.7, 134.8, 135.7, 136.2, 136.6, 136.4, 138.5, 139.1 ppm \textsuperscript{31}P \{\textsuperscript{1}H\} NMR (162 MHz, CD\textsubscript{2}Cl\textsubscript{2}) $\delta = 42.31$ (d, J = 46.1 Hz) 48.72 (d, J = 46.1 Hz) ppm Anal. Calcd for C\textsubscript{51}H\textsubscript{40}ClP\textsubscript{2}Ru C, 71.95; H, 4.74; Found: C, 71.87; H, 4.60;

**LARGE SCALE SYNTHESIS OF RuCl(PPh\textsubscript{3})\textsubscript{2}(3-phenylindenyl) (\textit{Eta}-5):**

In the glovebox a solution of M\textsubscript{10} (30 g 33.9 mmol) was prepared in a Schlenk flask. Outside the glovebox, anhydrous and degassed iso-propanol (100 mL) and triethylamine (50.8 mmol, 1.5 equiv. 7.1 mL) was added to this suspension. The suspension achieved was left to stir at reflux for 3 h under Ar atmosphere. Then it was cooled down to room temperature, filtered, washed with additional iso-propanol (3 x 10 mL), cold pentane (3 x 40 mL) affording RuCl(PPh\textsubscript{3})\textsubscript{2}(\eta^5-3-phenylindenyl) (\textit{Eta}-5) (25.7 g, 89% yield) as microcrystalline red solid.

**ONE-POT SYNTHESIS OF RuCl(PPh\textsubscript{3})\textsubscript{2}(3-phenylindenyl) (\textit{Eta}-5):**

In the glovebox, a solution of Ru(PPh\textsubscript{3})\textsubscript{3}.4Cl\textsubscript{2} (Ru-1, 0.46 mmol, 500 mg) and 1,1-diphenylprop-2-yn-1-ol (0.549 mmol, 0.114 g) in THF (40 mL) was prepared in a Schlenk flask. The reaction mixture was taken out of the glovebox, some drops of acetyl chloride were added and refluxed for 5 h under Ar. Triethylamine (7.82 mmol, 1 ml) and ethanol (20 ml) were added. Then the reaction was left stirring for another 2h. The mixture was cooled down to room temperature and another amount of ethanol (10 mL) was added and cooled at -40 °C. The suspension was filtered and washed with pentane affording RuCl(PPh\textsubscript{3})\textsubscript{2}(\eta^5-3-phenylindenyl) (\textit{Eta}-5) (300 mg, 77% yield based on Ru content in the starting material) as microcrystalline red solid.
MECHANISTIC INVESTIGATION ON THE ALCOHOLYSIS REACTION WITH M\textsubscript{10}:

REACTIVITY TOWARDS DIFFERENT ALCOHOLS:

GENERAL CONDITIONS

In a j-young NMR tube was charged with M\textsubscript{10} (0.023 mmol, 20 mg) in d\textsuperscript{2}-dichloromethane (0.046 M, 0.5 mL), triethylamine (0.035 mmol, 0.05 mL) and the appropriate alcohol (0.025 mmol). The reaction was monitored by NMR after 1 h, 16 h and 36 h.

Table 3.1 Alcoholysis reaction with different alcohol source\textsuperscript{a}

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-propanol (0.02ml)</td>
<td>Acetone formation</td>
</tr>
<tr>
<td>tert-butanol (0.02ml)</td>
<td>No reaction observed</td>
</tr>
<tr>
<td>Without alcohol</td>
<td>No reaction observed</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Determined by \textsuperscript{1}H NMR spectroscopy

REACTIVITY TOWARDS DIFFERENT BASES:

GENERAL CONDITIONS

In a j-young NMR tube was charged with M\textsubscript{10} (0.023 mmol, 20 mg) in d\textsuperscript{2}-dichloromethane (0.046 M, 0.5 mL), methanol (0.025 mmol, 0.01 mL) and the appropriate base (0.23 mmol). The reaction was periodically monitored by NMR.

Table 3.1 Alcoholysis reaction with different bases\textsuperscript{a}

<table>
<thead>
<tr>
<th>Base</th>
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<tr>
<td>triethylamine (0.032 ml)</td>
<td>16 h &gt;99% conversion</td>
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</tbody>
</table>

\textsuperscript{a}Determined by \textsuperscript{1}H NMR spectroscopy

DETERMINATION OF REACTION RATE AND ACTIVATION PARAMETERS:

GENERAL CONDITIONS:
A screw cap fitted NMR tube was charged with $\text{M}_{10}$ (0.023 mmol, 20 mg) $d^8$-toluene (0.032 M, 0.7 mL) and triethylamine (0.23 mmol, 0.032 mL). When the mixture is homogenous and at the appropriate temperature, ethanol was added (0.23 mmol, 0.015 mL). The reaction was monitored by $^{31}$P NMR spectroscopy, every 10 minutes.
**Eyring plot**

- Equation: \( y = -12654x + 30.295 \)
- \( R^2 = 0.9819 \)

**Activation energy**

- Equation: \( y = -12951x + 36.99 \)
- \( R^2 = 0.9827 \)

### Table: Eyring plot and activation energy

<table>
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<th>Error STD</th>
<th>k/T</th>
<th>1/T</th>
<th>Ln(k/T)</th>
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CHAPTER III: ALCOHYLYSIS OF RUTHENIUM INDENYLIDENE PRE-CATALYSTS

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<td>ΔS (J* mol⁻¹*K⁻¹)</td>
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</table>

Equations used in the determination of the activation parameters:³⁹

Arrhenius Equation:

\[ k = A e^{-\frac{AE}{RT}} \]

\[ \ln k = \frac{-AE}{R} \cdot \frac{1}{T} + \ln A \]

Free energy equation:

\[ \Delta G^\ddagger = \Delta H^\ddagger - T \Delta S^\ddagger \]

Erying Equation:

\[ k = K = 1 \]

\[ \ln \left( \frac{k}{T} \right) = \frac{-\Delta H^\ddagger}{R} \cdot \frac{1}{T} + \frac{k_b}{h} + \frac{\Delta S^\ddagger}{R} \]

\[ k = \text{constant rate} \]

Equations used in the determination of activation parameter error:³⁹

\[ S_{y/x} = \sqrt{\frac{\sum (y_i - \bar{y})^2}{n-2}} \]

\[ S_b = \frac{S_{y/x}}{\sqrt{\sum(x_i - \bar{x})^2}} \]

\[ S_a = S_{y/x} \sqrt{\frac{\sum x_i^2}{n \cdot \sum(x_i - \bar{x})^2}} \]

\[ \text{Error}_a = t_{95\%} \cdot S_a \]

\[ \text{Error}_{\Delta H^\ddagger} = R \cdot \text{Error}_b \]

\[ \text{Error}_{AE} = R \cdot \text{Error}_b \]

\[ \text{Error}_{\Delta S^\ddagger} = \Delta S^\ddagger \cdot \frac{\text{Error}_a}{a} \]

\[ t_{95\% \ (N=3)} = 2.353 \]

\[ S_{y/x} = \text{Model STD} \]

\[ S_b = \text{slope STD} \]
CHAPTER III: ALCOHOLYSIS OF RUTHERNIUM INDENYLIDENE PRE-CATALYSTS

\[ S_a = \text{intercept STD} \]
\[ y_i = \text{experimental values on the y axis} \]
\[ \hat{y}_i = \text{calculated values on the y axis} \]
\[ n = \text{number of experimental value} \]
\[ N = n-2= \text{freedom degrees} \]
\[ x_i = \text{experimental values on the x axis} \]
\[ \bar{x} = x_i \text{average values} \]

**PHOSPHINE DISSOCIATION ANALYSIS AND REACTION ORDER DETERMINATION:**

**GENERAL CONDITIONS:**

A NMR tube was charged with \( \text{M}_{10} \) (0.023 mmol, 20 mg) d\textsuperscript{8}-toluene (0.032 M, 0.7 mL) a defined amount of triphenylphosphine and triethylamine (0.23 mmol, 0.032 mL). When the mixture is homogeneous and at the appropriate temperature, ethanol was added (0.23 mmol, 0.015 mL). The reaction was monitored by \( ^{31}\text{P} \) NMR spectroscopy, every 10 minutes.
Determination of Alcohol Reaction Order:

A NMR tube was charged with $M_{10}$ (0.023 mmol, 20 mg) d$^8$-toluene (0.032 M, 0.7 mL) and triethylamine (0.23 mmol, 0.032 mL). When the mixture is homogeneous and at the appropriate temperature, ethanol was added (0.46 mmol, 0.030 mL). The reaction was monitored by $^{31}$P NMR spectroscopy, every 10 minutes.

\[ y = -0.0112x - 3.4563 \]
\[ R^2 = 0.9915 \]

\[ y = -0.0037x - 3.5109 \]
\[ R^2 = 0.9967 \]

Determinación de la orden de reacción de base:

A NMR tube was charged with $M_{10}$ (0.023 mmol, 20 mg) d$^8$-toluene (0.032 M, 0.7 mL) and triethylamine (0.46 mmol, 0.064 mL). When the mixture is homogeneous and at the appropriate temperature, ethanol was added (0.46 mmol, 0.030 mL). The reaction was monitored by $^{31}$P NMR spectroscopy, every 10 minutes.
**CHAPTER III: ALCOHOLYSIS OF RUTHENIUM INDENYLIDENE PRE-CATALYSTS**

**ALCOHOLYSIS OF M11: DECOMPOSITION EXPERIMENTS.**

**GENERAL PROCEDURE:**

In the glovebox, the pre-catalyst was weighed (ca. 0.25 mmol) into a PTFE septum fitted vial and the appropriate solvent was added (3 mL). Outside of the glovebox, triethylamine (0.5 mL, 3.5 mmol) was added. The vial was then heated to reflux overnight, cooled to room temperature and, inside the glovebox, the contents were worked up and analyzed by $^1$H and $^{31}$P{$_^1$}H NMR spectroscopy. NMR spectra from each experiment are provided herein; experimental details are provided below where yields were recorded.

**SYNTHESIS OF [RUH(PHOB)$_2$(3-PHENYLINDENYL)] (PHOB$^\text{Eta}$-5):**

The reaction mixture (in iso-propanol) was evaporated under vacuum. To the crude oil, pentane was added and the solution was filtered through celite. The mother liquor was evaporated until one third of the original volume, which was then cooled to -38°C. Red crystals were obtained by decanting the mother liquor, washing the solid with cold pentane and drying it *in vacuo* (137 mg, 76% yield). Complex PHOB$^\text{Eta}$-5 has been obtained as a mixture of three
rotamers (see EXSY experiments). Anal. Calcd for C_{39}H_{57}RuCl_{2}P_{2}: C, 68.00; H, 8.34. Found: C, 67.88; H, 8.41.

$^1$H NMR in C$_6$D$_6$

![$^1$H NMR in C$_6$D$_6$](image)

$^{31}$P{$^1$H} NMR in C$_6$D$_6$

![$^{31}$P{$^1$H} NMR in C$_6$D$_6$](image)
Using the previously reported procedure for the synthesis of complex $^{\text{phob}}$Eta-5, 150 mg of red powder was obtained, consisting of a 1:1 mixture of complex $^{\text{phob}}$Eta-5 and presumably other (presumably hydride) derivatives of M$_{11}$. The signals are consistent with analogous complexes reported in the literature.$^4$

2D NMR Experiments for Identification of the Rotamers

NMR experiments were conducted using a Bruker AV500 NMR spectrometer equipped with a QNP ($^1$H, $^{13}$C, $^{19}$F, $^{31}$P) probe (500 MHz $^1$H observe frequency; 202 MHz $^{31}$P observe frequency). Chemical shifts are reported relative to external standards Me$_4$Si ($\delta_\text{H} = 0$ ppm) and 85% H$_3$PO$_4$ in H$_2$O ($\delta_\text{p} = 0$ ppm).
2D $^1$H,$^{31}$P-HMBC spectrum of $\text{phobE}ta-5$ optimized for $J_{HP} = 30$ Hz recorded at 265 K. Three hydride triplets are resolved showing correlations with three pairs of doublets in the $^{31}$P dimension, implying the existence of three conformers in solution.

2D $^{31}$P-EXSY spectrum of $\text{phobE}ta-5$ recorded at 265 K showing an exchange pattern of $^{31}$P resonances that complement the $^1$H,$^{31}$P-HMBC correlation and supports the hypothesis about three conformers in solution. In accordance with theoretical calculations, the spectrum
shows that the most abundant conformer ($\delta_P = 35$ and 45 ppm) exchanges with less abundant ones ($\delta_P = 32, 40, 37$ and 41, respectively).

**SYNTHESIS OF [RuCl$_2$(=CH$_2$)(PC$_{2}$)$_2$] RU-38:**

In the glovebox, GI (1.0169 g, 1.236 mmol) was dissolved in benzene (15 mL) in a Schlenk flask. The flask was removed from the glovebox and attached to a Schlenk line. The stopper was exchanged for a septum under a flow of argon, then the flask was closed and a balloon was attached to the side-arm. The tap was opened, and 1,7-octadiene (2.5 mL) was added via syringe. The solution began to effervesce and a pressure of ethene was built up in the balloon. The reaction was stirred at room temperature for 3 h, during which time the deep pink-purple solution turned brown. The volatiles were stripped under high vacuum, and the residue was returned to the glovebox, re-dissolved in benzene and transferred to a vial. The benzene was removed *in vacuo* and the residue was washed with acetone (3 x 5 mL) and pentane (2 x 5 mL) and dried *in vacuo*. The resulting pink solid (603.4 mg) was analysed by $^1$H and $^{31}$P NMR, revealing a 20:1 mixture of methylidene Ru-38 and GI (therefore 94.8% Ru-38 by wt; 572.0 mg yield; 0.766 mmol; 62%). NMR spectroscopic data was in agreement with the literature.$^{30}$ Anal. Calcd. for C$_{37}$H$_{68}$RuCl$_2$P$_2$: C, 59.50; H, 9.18. Found: C, 59.57; H, 9.09.

**DECOMPOSITION EXPERIMENTS WITH M$_1$, M$_2$, M$_{20}$**

**GENERAL PROCEDURE:**

In the glovebox, the pre-catalyst was weighed into a PTFE septum fitted vial and the appropriate solvent was added (3 mL). Outside of the glovebox, triethylamine (0.5 mL) was added. The vial was then heated to reflux overnight, cooled to room temperature and, inside
the glovebox, the contents were worked up and analysed by $^1$H and $^{31}$P NMR spectroscopy. NMR spectra from each experiment are provided herein, which allow identification of the major products of each reaction. Experimental details are provided below where yields were recorded.

**Synthesis of [RuCl(H)(H$_2$)(PC$_3$)$_2$] (Ru-89):**

The reaction mixture was filtered, and the solid obtained was washed with *iso*-propanol and pentane and dried under vacuum, achieving a yellow powder (yields are variable depending on the pre-catalyst considered: from M$_1$ 76% yield, 133 mg; from GI 46% yield, 81 mg. From Ru-38 81 mg, 46% yield). Anal. Calcd for C$_{36}$H$_{69}$RuClP$_2$: C, 61.73; H, 9.93. Found: C, 61.51; H, 10.15. $^1$H NMR (400 MHz, C$_6$D$_6$) $\delta$ = 2.18-2.05 (m, 17H), 1.75-1.29 (m, 30H), 1.26-1.13 (m, 19H), $-16.4$ (s, 2H); $^{31}$P{$^1$H} NMR (162 MHz, C$_6$D$_6$) $\delta$ = 53.4. The $^1$H and $^{31}$P NMR data are in accordance with the reported spectra in the literature.$^{16a}$

**Decomposition of M$_1$ in EtOH:**

The yellow precipitate in the reaction mixture was isolated by filtration and washed with cold ethanol, pentane and dried under vacuum (150 mg obtained). The solid is predominantly the hydridocarbonyl complex Ru-46, with traces of an unknown product, which reports a doublet peak at $\delta$= -11.65 ppm with a J coupling of 30 Hz in the $^1$H NMR spectrum and singlet peak at $\delta$= 59.0 ppm in the $^{31}$P{$^1$H} NMR spectrum (recorded at 400 MHz using C$_6$D$_6$ as solvent).

**Decomposition of M$_2$ in EtOH:**

The yellow precipitate in the reaction mixture was isolated by filtration and washed with cold ethanol, pentane and dried under vacuum (50 mg obtained). The solid is hydrido carbonyl complex Ru-46, and an unknown compound at 32 ppm in the $^{31}$P NMR spectrum. The mother
liquors were concentrated until dryness and dissolved in pentane to remove the triethylammonium chloride present. After filtration through celite, the liquid was concentrated under vacuum, obtaining a powder (150 mg) which shows complex Ru-47 as a major product.

**DECOMPOSITION OF M20 IN EtOH:**

The red solid from the reaction mixture was isolated by filtration and washed with cold ethanol, pentane and dried under vacuum (15 mg obtained). The solid is complex Eta-5. The mother liquors were concentrated until dryness and dissolved in pentane to remove the triethylammonium chloride present. After filtration through celite, this liquid was concentrated under vacuum, obtaining a powder (170 mg) which shows complex Ru-93 as a major product.

$^1$H NMR in C$_6$D$_6$ of the mother liquid
\[ ^{31}\text{P}\{^1\text{H}\}\text{ NMR in C}_6\text{D}_6 \text{ of the mother liquid} \]

\[
\begin{align*}
\text{[RuHCl(CO)(SIMes)(PPh}_3\text{)]} & \quad \text{[RuHCl(CO)(PPh}_3\text{)]} \\
\text{[RuH(PPh}_3\text{)}_2(3\text{-phenyldenyl})] & \quad \text{[RuHCl(CO)(PPh}_3\text{)]}_3
\end{align*}
\]

**DECOMPOSITION OF M\textsubscript{2} IN ISO-PROPANOL:**

The reaction mixture was evaporated until dryness and toluene was added, obtaining a white suspension, which was filtered off. The white solid was SIMes·HCl (100 mg) (determined by $^1$H NMR). The mother liquor remaining was evaporated and the crude was with suspended in pentane and filtered, obtaining 100 mg of a mixture of complex \textbf{Ru-89} and triethylammonium chloride. The mother liquid was evaporated again until dryness. The remaining solid was a mixture of multiple complexes, where one of the main compounds was found to be complex \textbf{Ru-89} (40 mg).
$^1$H NMR in C$_6$D$_6$ of the mother liquor

$^{31}$P NMR in C$_6$D$_6$ of the mother liquor
DECOMPOSITION OF M$_2$O IN PrOH:

The red solid was isolated from the reaction mixture by filtration and washed with cold ethanol, pentane and dried under vacuum (30 mg obtained). The solid was complex Eta-5. The mother liquors were concentrated until dryness and dissolved in pentane to remove the triethylammonium chloride present. After filtration through celite the liquid was concentrated under vacuum, obtaining a powder (150 mg) which shows complex Eta5-H as a major product.

$^1$H NMR in C$_6$D$_6$ of the mother liquor
**CHAPTER III: ALCOHOLYSIS OF RUTHENIUM INDIENYLDENE PRE-CATALYSTS**

$^{31}$P$^1$H NMR in C$_6$D$_6$ of the mother liquor

![NMR Spectra]

**DECOMPOSITION OF [RUCl$_2$(PCy$_3$)$_2$(CH$_2$)] IN MEOH, ETOH AND iPROH:**

In each case, the precipitate was collected on a frit, carefully washed with the alcohol used for the experiment and pentane. The solid was analysed by NMR spectroscopy. The mother liquors were then concentrated and analysed by NMR spectroscopy.

**MeOH:** $^1$H NMR of solid in C$_6$D$_6$: [RuCl(CO)(PCy$_3$)$_2$] Ru-46

**EtOH:** $^1$H NMR of solid in C$_6$D$_6$: [RuCl(CO)(PCy$_3$)$_2$] Ru-46

**iPrOH:** $^1$H NMR of solid in C$_6$D$_6$: [RuCl(H$_2$)(PCy$_3$)$_2$] Ru-89.
CHAPTER III: ALCOHOLYSIS OF RUTHENIUM INDENYLIDENE PRE-CATALYSTS

CHARACTERISATION OF THE TEP OF iso-BUTYLPHOBAN

SYNTHESIS OF [IrCl(COD)(iso-butyaphoban)]

In the glovebox, [IrCl(COD)]$_2$ (67.0 mg, 0.100 mmol) and iso-butylphoban (72.4 mg of a 70:30 mixture of 9-iso-butyl-9-phosphabicyclo[3.3.1]nonane and 9-iso-butyl-9-phosphabicyclo[4.2.1]nonane, thus 0.256 mmol, 2.6 equiv.) were dissolved in THF (1 mL) and stirred overnight at room temperature. The volatiles were then removed *in vacuo*, and the residue was taken up in diethyl ether (*ca.* 1.5 mL) outside of the glovebox. The solution was filtered through a pad of silica, followed by further portions of diethyl ether (*ca.* 2 mL). The solvents were removed *in vacuo* and the resulting residue was washed with pentane (3 × 0.5 mL) and dried under high vacuum to yield a red-orange solid. Yield: 56.0 mg (0.105 mmol, 52%). $^1$H NMR (CDCl$_3$): δ 4.85 - 4.72 (m, 2H, COD C$_\text{H}$), 3.04 - 2.93 (m, 2H, COD C$_\text{H}$), 2.76 - 0.83 (m, 31H, COD C$_\text{H}_2$ and phoban). $^{13}$C{$^1$H} NMR (CDCl$_3$): δ 90.3 (br.), 51.8 (br.), 34.7 (br.), 34.0 (d, $J_{\text{CP}}$ = 22.1), 33.0 (br.), 30.6 (br.), 29.7 (br.), 29.5 (br.), 28.4 (br.), 27.0 (d, $J_{\text{CP}}$ = 4.5), 26.5 (d, $J_{\text{CP}}$ = 5.4), 23.9 (br.), 22.3 (d, $J_{\text{CP}}$ = 8.8), 20.6 (d, $J_{\text{CP}}$ = 4.6). $^{31}$P{$^1$H} NMR (CDCl$_3$): -2.4. Anal. Calcd for C$_{20}$H$_{35}$ClIrP: C, 44.97; H, 6.60. Found: C, 45.04; H, 6.73.

SYNTHESIS OF [IrCl(CO)$_2$(iso-butyaphoban)]

Attempts to prepare this complex under ambient conditions led to decomposition of the complex during work-up. In the glovebox, [IrCl(COD)(iso-butylphoban)] (32.5 mg, 0.061 mmol) was dissolved in DCM (1.5 mL) and transferred to a flask fitted with J. Young tap. The flask was removed from the glovebox, the solution was frozen, and the headspace was removed under vacuum. Carbon monoxide was then introduced, and the solution was stirred at RT overnight. The flask was re-introduced to the glovebox, the volatiles were stripped *in vacuo* and the residue was washed with cold (-40 °C) pentane to yield a pale yellow solid. Yield: 18.8 mg (0.039 mmol, 64%). $^1$H NMR (C$_6$D$_6$): δ 2.60 – 0.77 (m, 23H, phoban). $^{13}$C{$^1$H} NMR
(C₆D₆): δ 179.7 (d, J_{CP} = 118.0, trans-CO), 170.0 (d, J_{CP} = 12.4, cis-CO), 32.6 (d, J_{CP} = 25.0, phoban), 30.4 (phoban), 27.4 (d, J_{CP} = 2.2, phoban), 26.2 (d, J_{CP} = 5.4, phoban), 24.6 (br., phoban), 22.1 (d, J_{CP} = 6.0, phoban), 20.9 (d, J_{CP} = 4.9, phoban). \(^{31}\)P\(^{1}\)H\) NMR (C₆D₆): 7.5. IR (υ, CH₂Cl₂) = 2072.4, 1985.4 cm⁻¹.

**COMPUTATIONAL DETAILS**

All the DFT static calculations were performed at the GGA level with the Gaussian09 set of programs,\(^{41}\) using the BP86 functional of Becke and Perdew.\(^{42}\) The electronic configuration of the molecular systems was described with the standard split-valence basis set with a polarization function of Ahlrichs and co-workers for H, C, N, O, and Cl (SVP keyword in Gaussian).\(^{43}\) For Ru we used the small-core, quasi-relativistic Stuttgart/Dresden effective core potential, with an associated valence basis set contracted (standard SDD keywords in gaussian09).\(^{44}\) The geometry optimizations were performed without symmetry constraints, and the characterization of the located stationary points was performed by analytical frequency calculations. Bearing in mind the entropic contribution calculated in the gas phase (p = 1 atm) is likely exaggerated in dissociative steps.\(^{34,45}\) All the thermochemical analysis was performed at p = 1254 atm, as suggested by Martin et al.\(^{46}\) The reported energies have been optimized via single point calculations on the BP86 geometries with triple zeta valence plus polarization (TZVP keyword in Gaussian) using the M06L functional,\(^{47}\) however estimating solvent effects with the polarizable continuous solvation model PCM using CH₂Cl₂ as solvent.\(^{48}\) MeOH was included in the PCM model. Furthermore diffuse basis sets have been incorporated for O and Cl.\(^{49}\)

The relative M06L/TZVP//BP86/SVP Gibbs energies reported in this work include solvent contribution computed at M06L/TZVP level together with zero-point energies, thermal
corrections, and entropy effects calculated with the BP86/SVP level. The singlet state was found to be the multiplicity ground state for all studied species.

Table 3.3: Free energy relative to structure II, in kcal/mol, of the species rotamer isomerisation of phobEta-5. Thermochemical terms calculated in solvent (PCM model).

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Table 3.4: Free energy relative to structure A, in kcal/mol, of alcoholysis process to H. Thermochemical terms calculated in solvent (PCM model).

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Table 3.5: Free energy relative to structure H, in kcal/mol, of alcoholysis process to M. Thermochemical terms calculated in solvent (PCM model).

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<td>12.2</td>
<td>2.4</td>
</tr>
<tr>
<td>#KL</td>
<td>28.5</td>
<td>23.1</td>
<td>15.8</td>
</tr>
<tr>
<td>L</td>
<td>19.6</td>
<td>13.5</td>
<td>11.2</td>
</tr>
<tr>
<td>#LM</td>
<td>24.4</td>
<td>15.3</td>
<td>13.0</td>
</tr>
<tr>
<td>M</td>
<td>18.3</td>
<td>-0.4</td>
<td>12.7</td>
</tr>
</tbody>
</table>
CHAPTER III: ALCOHOLYSIS OF RUTHENIUM INDENYLIDENE PRE-CATALYSTS

REFERENCES


(11) Due to the high solubility of Ru-71 in alkenes and its high instability in solution, the authors report the use of copper chloride to remove the free phosphine remained. However, due probably to the high difficulty to remove the copper residues, they can provide a maximum purity of 95% by 31P NMR.


(24)Eta-5 now is commercially available in small quantities by strem (cat. number 44-0138). Large quantity can be supplied by UMICORE.


(37) The \( \%V_{\text{bur}} \) reported are obtained as average between the \( \%V_{\text{Bur}} \) of the two equivalent phosphines.


CHAPTER IV: EVALUATION OF THE ACTIVITY OF 

[RuCl(PPh₃)₂(3-Phenyldienyl)]

Organometallics 2013, 32, 660.
Chemcatchem 2013, 5, 2848.

STATEMENT

The X-ray experiments were carried out by Prof. Alexandra M. Z. Slawin.

The DFT-calculations were performed by Dr. Albert Poater (Cavallo group)

The work regarding to the racemization, transfer hydrogenation, alcohol oxidation process with Eta-5 have been performed in collaboration with Dr. Cesar A. Urbina-Blanco.

The work regarding the synthesis of Eta-5-BAr⁢F and the isomerisation processes have been performed in collaboration with Dr. David J. Nelson.

The work regarding the synthesis of Eta-5-R₃Si, hydrosilylation, dehydrogenative coupling and C-B bond formation have been performed in collaboration with Dr. Jose. A. Fernandez-Salas.

The work regarding the synthesis of Eta-5-SiR₃ and C-B bond formation have been performed in collaboration with Lorenzo Piola.
PHENYLINDENYL AS EFFICIENT MULTI-TASKING CATALYST

What has emerged from the study of alcoholysis of indenylidene complexes that a major decomposition product can be obtained quantitatively in a valuable synthetic procedure (Chapter III). Taking account of the features of the complex, closely analogous to several ruthenium arenes, we thought that Eta-5 may be a valuable complex and that it could be worth investigating the possible and novel chemistry that can be developed from it. Some may call it an example of “making lemonade from lemons”. Some of us, of a more optimistic nature saw that maybe novel vistas in reactivity could be explored (Scheme 4.1).

![Scheme 4.1: Portfolio of reaction catalysed by the Eta-5 family.](image)

In this section, some of the transformations accessed with Eta-5 will be discussed, putting the focus on the properties of this simple complex, but with unique reactivity.

**RACEMISATION OF CHIRAL ALCOHOLS**

Related to the reactivity in alcoholysis reactions, Eta-5 appears capable of transfer hydrogen atoms via $\alpha$-hydrogen elimination/insertion of alkoxides. A quick test reaction for this purpose is the racemisation of chiral secondary alcohols.
Racemisation protocols are often involved in industrial syntheses to obtain enantiomerically pure compounds where, in combination with the appropriate enzyme, it is possible to resolve a racemic mixture of alcohols into an enantiomerically pure compound in a dynamic kinetic resolution (DKR) process.\textsuperscript{2} Using (S)-phenylethanol as a model substrate, the reaction was carried out in toluene at room temperature in the presence of sodium tert-butoxide, in order to activate the catalyst. Complete racemisation was achieved using 1 mol\% of \textbf{Eta-5} in less than 20 minutes, comparable with the indenyl analogue used by Park \textit{et al.}\textsuperscript{2\textit{e,f}} The catalytic activity at low catalyst loading revealed that \textbf{Eta-5} can promote near-complete racemisation with a catalyst loading as low as 10 ppm (95\%) in 14 h at room temperature, reporting a turnover number (TON) of $7 \cdot 10^8$ and turnover frequency (TOF) of $5 \cdot 10^7$ h\textsuperscript{-1} (Scheme 4.2).

\begin{center}
\begin{tikzpicture}
  \node[above=of current bounding box] (reaction) {
    \begin{tabular}{c}
      OH \\
      (s)
    \end{tabular}
  };
  \node[below=of reaction] (catalyst) {
    Eta-5 (1 mol\%) \\
    Toluene \\
    NaO\textsuperscript{Bu} \\
    rt, 20 min
  };
  \node[below=of catalyst] (reaction2) {
    \begin{tabular}{c}
      OH \\
      (s)
    \end{tabular}
  };
  \node[below=of reaction2] (products) {
    99\% ee \\
    15 \\
    0\% ee \\
    16
  };
\end{tikzpicture}
\end{center}

\textbf{Scheme 4.2:} Racemization of (S)-phenylethanol.

**HYDROGENATION OF KETONES, ALDEHYDES AND IMINES VIA TRANSFER HYDROGENATION\textsuperscript{3}**

Taking account of the fact that racemisation processes are based on consecutive alcohol oxidation and hydrogenation of the resulting carbonyl, in order to understand the efficiency of both processes separately and develop new transformations with \textbf{Eta-5}, a sacrificial substrate is introduced. Indeed, the addition of isopropanol (hydrogen source) for the hydrogenation of
carbonyl moieties, or a ketone (hydrogen acceptor) for the oxidation of alcohols, allows the separate study of the two processes involved in the racemisation (Scheme 4.3).  

\[
\begin{align*}
&\text{O} + \text{OH} \xrightarrow{\text{Alcohol oxid.}} \text{O} + \text{OH} \\
&\xrightarrow{\text{hydrogenation}} \end{align*}
\]

Scheme 4.3: Hydrogenation and oxidation processes via sacrificial donor/acceptor.

As a first transformation, the reduction of carbonyl complexes via transfer hydrogenation has been evaluated. This eco-friendly process avoids the amount of waste generated by the use of stoichiometric reagents such as in the use of aluminium and boron hydride reducing reagents.\textsuperscript{5} Ruthenium complexes have been widely used for this transformation, mainly due to their being the best compromise between price\textsuperscript{6} and reactivity.\textsuperscript{7} Regarding ruthenium arene complexes, one of the first very efficient catalysts is [Ru\textsubscript{2}(CO)\textsubscript{4}(\mu-H)(\text{C}_\textsubscript{6}\text{H}_\textsubscript{4}\text{COHOCC}_\textsubscript{6}\text{H}_\textsubscript{4})]\textsuperscript{(Ru-94)} (Ru-94), synthesised in 1984 by Shvo, also known as Shvo’s catalyst,\textsuperscript{8} which has several applications including hydrogen transfer reactions.\textsuperscript{9} In 2007, Frost reported an interesting variation of the [Ru(Cl)(PPh\textsubscript{3})\textsubscript{2}(indenyl)] (Ru-93),\textsuperscript{10} a well-known complex in literature.\textsuperscript{11} Ru-95 is remarkably active in transfer hydrogenation in formic acid. Casey has reported a novel complex (Ru-96) bearing an OTMS substituted indenyl ligand, showing relevant activity in transfer hydrogenation reactions (Figure 4.1).\textsuperscript{12}
**Figure 4.1:** Some examples of ruthenium complexes active in transfer hydrogenation.

*Etα-5* was tested in the hydrogenation of carbonyls *via* transfer hydrogenation, showing remarkable activity compared to several commercially available arene analogues under the optimised reaction conditions (Scheme 4.4). In particular, the introduction of the phenyl group at the 3-position of the indenyl moiety greatly enhance the reactivity, probably due to an electronic effect.
Scheme 4.4: Transfer hydrogenation of benzophenone with several ruthenium complexes.

Notably, Eta-5 shows high activity for this transformation, reaching a maximum TON of 1920 using benzhydrol as the substrate. In addition, Eta-5 shows good compatibility with various functional groups, allowing the hydrogenation of either aromatic or aliphatic ketones, aldehydes or aldimines. However, with sterically hindered and electron poor ketones, a higher catalyst loading is necessary to achieve reasonable conversions (Scheme 4.5).
Scheme 4.5: Hydrogenation of ketones, aldehydes and imines via transfer hydrogenation mechanism.

**ALCOHOL OXIDATION VIA OPPENAUER MECHANISM**

The reverse process, the oxidation of alcohols to the corresponding carbonyl compound, is affected differently by using Eta-5. Despite several hydrogen scavenger free oxidation procedures, or others using more reactive reagents such as peroxides or oxygen, demand still exists for a simple and industrially applicable process. Complex Eta-5 was evaluated in the Oppenauer oxidation, where the substrate is easily oxidised via the transfer of two hydrogen atoms by a metal complex to a sacrificial ketone (Scheme 4.3).
Complex Eta-5 was found to be catalytically active for alcohol oxidation at room temperature using acetone as a hydrogen acceptor. However, in order to access the desired product efficiently, the optimum reaction conditions was found to be at 110 °C using toluene as a co-solvent. In fact, in the optimised system, benzophenone is oxidized in only 0.5 h with 0.5 mol% of catalyst. Also in this case the effect of the phenyl substituent on the indenyl ligand is beneficial to the reaction, allowing complex Eta-5 to surpass the reactivity of its analogues, complex Ru-92 and Ru-97 (Scheme 4.3) in the Oppenauer oxidation, achieving a maximum TON of 1250 and a relatively high TOF of 400 h$^{-1}$. These results demonstrate the beneficial effect, of using phenylindenyl as a ligand in this transformation (Scheme 4.6).

Scheme 4.6: A comparison of alcohol oxidation catalysts.

The system displays high compatibility towards several bases and “green” solvents. In particular, it is possible to carry out the alcohol oxidation using iso-butyl methyl ketone, which is considered as a greener hydrogen acceptor than acetone (Scheme 4.7).\textsuperscript{17}
Scheme 4.7: Alcohol oxidation with *iso*-butyl methyl ketone as hydrogen acceptor

Secondary alcohols can be easily oxidised, achieving full conversion to the desired aliphatic and aromatic ketones in 1 h. Electron-withdrawing substituents disfavour the oxidation process making it less effective than with their electron-rich analogues. More sterically demanding aromatic compounds are slightly more difficult to oxidise, showing similar behaviour as in the reduction of carboxyls (Scheme 4.8).

Scheme 4.8: Oxidation of secondary alcohols via Oppenauer oxidation mechanism.
Surprisingly, complex **Eta-5** shows no activity in the oxidation of primary alcohols to aldehydes (Scheme 4.8). This high chemoselectivity has been highlighted by two competition experiments, in which only the secondary (vs primary) alcohol was oxidised in both cases (Scheme 4.9).

Scheme 4.9: Chemoselective oxidation of secondary alcohols

**ISOMERISATION OF ALLYLIC ALCOHOLS TO KETONES**

Parallel to hydrogen transfer processes, the isomerisation of allylic alcohols catalysed by transition metal complexes represents a powerful, elegant and green method to prepare carbonyl compounds, where otherwise a two-step sequence of oxidation and reduction would be required.
Several complexes of Fe, Os, Ru, Rh, Co, Ni, Mo, Ir, and Pt have been shown to catalyse this rearrangement; however, most of them show restricted scope with regard to reaction conditions and substitution at the 1- and 3-positions (R' and R''). Primary allylic alcohols are typically the most challenging substrates. Regarding the Ru-catalysed isomerization of allylic alcohols, the first Ru\(^{II}\)-cyclopentadienyl-like complex employed in this reaction was [RuCl(Cp)(PPh\(_3\))] (Ru-97) by Kulawec and Trost in the 1990s.

**Figure 4.2:** Examples of ruthenium allylic isomerisation catalysts.

Ru-97, in combination with [Et\(_3\)NH][PF\(_6\)] in dioxane at 100 °C, is able to catalyse the isomerization of allylic alcohols, with the exception of primary alcohols and unsubstituted vinyl groups. Slugovc et al., using a well-defined cationic complex of the form...
[Ru(Cp)(MeCN)$_2$(PR$_3$)][PF$_6$] in CDCl$_3$, were able to improve the activity, reaching high conversions at 57 °C.$^{23}$ A relevant step forward in this transformation was shown by Cadierno and Gimeno using a series of Ru$^{	ext{IV}}$ complexes such as [Ru(η$_3$-η$_2$-η$_3$-C$_{12}$H$_{18}$)Cl$_2$] and derivatives, reaching high activity in aqueous media and in ionic liquids at 75 °C.$^{24}$ However, all of these complexes display activity with only a limited substitution pattern and they still need high temperatures to perform the isomerisation.

In 2005, Bäckvall shown that [RuCl(Cp*)(CO)$_2$] is able to isomerise substituted allylic alcohols at room temperature. However, this catalyst requires relatively high loadings (5 mol%), to access full conversions.$^{25}$ In the same year, Ikariya introduced a series of Ru(Cp*)(P-N) complexes that were very active at 30 °C with 1 mol% of catalyst.$^{26}$

Despite the many contributions to the field reported in the literature,$^{19c,d,20}$ the operational conditions and substrate compatibility still present significant limitations in particular for the isomerisation of primary allylic alcohols.

Regarding Eta-5, we were pleased to see that it displays extremely high activity in this transformation, isomerising secondary allylic alcohols at room temperature and tolerating a reasonable degree of substitution at the vinyl moiety (Scheme 4.11).

![Scheme 4.11: Isomerisation of secondary allylic alcohols.](image-url)
Internal and terminal benzyl and aliphatic allylic alcohols are easily isomerised with 0.25 mol% of Eta-5 in 1 h. Aryl allylic alcohols bearing electron-donating substituents on the phenyl group are more difficult to isomerise. With aliphatic allylic alcohols or when the phenyl substituent is on the olefin moiety, a higher catalyst loading (0.5 mol%) is required to reach full conversion. Monosubstituted and 1,1- or 1,2- disubstituted alkenes isomerise readily, but trisubstituted alkenes do not react under these conditions. With Eta-5 this methodology is restricted to secondary allylic alcohols, as the corresponding primary alcohols cannot be isomerised. In addition, the system was tested with different green solvents such as, cyclopentyl methyl ether (CPME) and iso-butyl methyl ketone (IBK) and with several bases, reaching in most of the cases full conversion at room temperature in only 1 h with substrate 48 (see experimental section).

In order to probe the limits of reactivity of Eta-5, the performance of the system was evaluated at lower catalyst loadings, revealing Eta-5 to be highly competitive with the state-of-the-art, achieving a turnover number (TON) of $1.0 \cdot 10^4$ and a turnover frequency (TOF) of $3.6 \cdot 10^4$ h$^{-1}$ at high temperatures (100ºC).\textsuperscript{19a-c,27}

As already highlighted in the previous transformations, the substitution of the arene ligand plays a crucial role in this transformation; in fact complex Eta-5 shows high activity, while the congeners Ru-92 and Ru-97 are totally inactive under the same conditions (Scheme 4.12).
In order to understand this marked difference in reactivity a series of mechanistic investigations, supported with a DFT calculation of the mechanism, in collaboration with the Cavallo group was evaluated.

For this transformation, three possible pathways have been suggested in the literature (Scheme 4.13). In the alkyl mechanism (Scheme 4.13 a), the metal hydride complex is the active species. This reaction proceeds via reversible addition of metal hydride across the alkene moiety, followed by reversible β-hydride elimination to effectively move the double bond down the chain, resulting in a formal 1,3-hydrogen shift. However the formal 1,2-hydrogen shift may also result. Alternatively the system can exhibit a π₃-allyl mechanism (Scheme 4.13 b), which proceeds via abstraction of an allylic proton by a metal that is bound to the alkene via η²-coordination. The hydride achieved can then deposited at the terminus of the allyl complex, yielding a new η²-complex. The π₃-oxo-allyl mechanism (Scheme 4.13 c) proceeds in a similar way, but it requires to having an alkohoxy moiety in the allylic position coordinated to the metal. The alcohol co-ordinates to the metal, which is followed by η²-complexation of the alkene, abstraction of the allylic proton, and generation of a new π₃-allyl complex by depositing the hydride on the terminal carbon.
Scheme 4.13: Possible mechanism in the allylic alcohol isomerization.

In order to discriminate between the alkyl hydride mechanism and the π-allyl system, selectively-labelled substrate 47-d1 was employed in the transformation. The reaction showed only the 1,3-deuterium shift, meaning that the reversible metal hydride addition/elimination shown in Scheme 4.14 a does not occur; if it did, both 1,2- and 1,3-deuterium shifts would be expected.
A crossover experiment was also performed in which 48-d\textsubscript{1} and 55 were exposed to the same charge of Eta-5 (0.25 mol\%, based on the sum of substrates) for 24 h (Scheme 4.14 b). No deuterium scrambling between compounds was detected, excluding the presence of an unbound metal hydride (or deuteride) in the reaction, which completely excludes the possibility to have an alkyl hydride mechanism (Scheme 4.14 a).

To discriminate between the two $\pi^3$-allyl mechanism (Scheme 4.14 b and c), the isomerisation was performed using $O$-methylated allylic alcohol 60 (Scheme 4.15). If the reaction involves only a $\pi^3$-allyl intermediate, the isomerization of 60 should yield enol ether 61, thermodynamically favoured by $ca.$ $1.7$ kcal mol$^{-1}$ (determined via DFT calculations; level of theory M06L/TZVP//BP86/SVP).

**Scheme 4.14:** Isotopic labelling experiments.

**Scheme 4.15:** Isomerisation of allyl ether.
The reaction showed no conversion, even after 24 h, suggesting that the alcohol functionality is necessary to enable the isomerisation at room temperature with low catalyst loadings, and therefore a $\pi^3$-oxo-allyl mechanism is involved (Scheme 4.13 c).

Considering three possible mechanism, a potential energy surfaces (PES) were evaluated, by the Cavallo group, for the isomerisation of three model substrates. In each case, the $\pi^3$-oxo-allyl mechanism was found to be the most favourable (Figure 4.3).

**Figure 4.3**: PES of the isomerisation of different allylic alcohols with Eta-5 from A to F

**Eta-5** undergoes a series of steps to form the active species, which is dependent on the substrate. Phosphine dissociation is relatively facile (16.8 kcal mol$^{-1}$), followed by coordination of the substrate and deprotonation by the base. Chloride abstraction leads to intermediate F, and thus into the catalytic cycle. Alternative mechanisms showed that the base is necessary at this point to remove the HCl produced by initiation of the pre-catalyst and the removal of the second phosphine (from C) leads to much higher energy intermediates ($G_{\text{rel}} = 25 – 35$ kcal mol$^{-1}$) on the PES of the catalytic cycle itself, so this possibility was discounted.
Figure 4.4: PES of the isomerisation of different allylic alcohols with Eta-5 from F to F. Energies in kcal/mol. Level of theory M06L/TZVP//BP86/SVP. Thermochemical terms calculated at $p = 1254$ atm.

From F the reaction proceeds via abstraction of the second allylic proton forming the enone $\eta^2$-coordinated to a ruthenium hydride species (G) in a potential energy well (Figure 4.4). Rotation of this $\eta^2$-ligand has a considerable (20 kcal mol$^{-1}$) barrier via GH‡, yet presents the alkene terminus for delivery of the hydride via a rather facile process, with H to H‡ barrier being only 2-3 kcal mol$^{-1}$. The complex then rearranges to bind the enol product via the oxygen, setting the scene for a series of steps to liberate the enol product and co-ordinate a subsequent molecule of substrate. The isomerisation reaction of primary and secondary allylic alcohols show similar energetics, suggesting that the inability of Eta-5 to isomerise primary allylic alcohols does not depend to a kinetic barrier. The energetic spans of the catalytic cycles can be calculated by subtracting the energy of G (the turnover-determining intermediate, or TDI) from that of LF‡ (the turnover-determining transition state, or TDTS) ($\Delta E = T_{TDTS} - I_{TDI}$). 29
The values calculated are 28.0, 31.5 and 28.9 kcal mol\(^{-1}\) for allyl alcohol, but-1-ene-3-ol and α-vinyl benzyl alcohol, respectively. Therefore, it would be expected that primary alcohol isomerisation should be even faster than that of the secondary alcohols.

![Diagram of energy profiles](image)

**Figure 4.5:** PES of allylic alcohol isomerisation with Eta-5, Ru-92 and Ru-97. From A to F. Energies in kcal/mol. Level of theory M06L/TZVP//BP86/SVP. Thermochemical terms calculated at p = 1254 atm.

The effect of catalyst structure on reactivity has been calculated (Figure 4.5 and 4.6). Surprisingly, even though the phosphine dissociation is favoured for Eta-5, the deprotonation and chloride abstraction steps for this complex, exhibited the highest barriers, in contrast with the experimental observations.

In general, the calculations suggest that the intermediates on the reaction pathway catalysed by the cyclopentadienyl analogue Ru-97 are much lower in energy, although the overall energetic span (ΔE) is similar (31.5, 27.3 and 28.7 kcal mol\(^{-1}\) for Eta-5, Ru-92 and Ru-
97, respectively). However, the barriers to each of the individual steps for Eta-5 are typically smaller, compared to Ru-92 and Ru-97, e.g. J to JK\(^{‡}\) versus J\(^{†}\) to JK\(^{‡}\). An explanation of this different reactivity may be due to the reduced decomposition of Eta-5 (or intermediates derived from it) under the reaction conditions than for Ru-92 and Ru-97.

Scheme 4.5: PES of allylic alcohol isomerisation with Eta-5, Ru-92 and Ru-97, From F to F. Energies in kcal/mol. Level of theory M06L/TZVP//BP86/SVP. Thermochemical terms calculated at p = 1254 atm.

The small difference in energetics between secondary allylic alcohols and primary allylic alcohols revealed that reactivity differences are not a consequence of thermodynamic or kinetic effects, and a faster isomerisation of primary allylic alcohols would be expected. One of the causes of this inhibition may be due to the presence of base as catalyst initiator, which might promote a side reaction and deactivate the system. In order to avoid the requirement of base to activate the system, the use of a cationic complex derived from Eta-5 was considered.

Treating Eta-5 with sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate in dichloromethane for 1 h led to the formation of the cationic complex Eta-5-BAr\(^{‡}\). This
complex efficiently isomerised primary allylic alcohols to the corresponding aldehydes at room temperature, confirming the negative effect of the base. (Scheme 4.16).

**Scheme 4.16: Isomerisation of primary allylic alcohols with Eta-5-BArF.**

**ISOMERISATION OF TERMINAL ALKENES**

The isomerisation of terminal alkenes is a very useful reaction, employed in industrial processes to equilibrate feedstocks or to achieve high-value molecules starting from easily accessible precursors. Numerous catalytic systems have been employed for this transformation, however most of these complexes are not particularly robust, especially in the presence of moisture, air or impurities in the starting substrate.

**Eta-5**, under optimized conditions, revealed high activity in the conversion of terminal alkenes to the internal alkene at 300 ppm of catalyst loading at 60°C in THF (1:1
solvent/substrate) with 1-octene as the substrate. However, the use of bases to activate the desired complex can be detrimental for more sensitive substrates. For this reason, complex Eta-5-BArF was used (Scheme 4.17). In addition, Eta-5-BArF was found to be air- and moisture-stable in the solid-state and reagent grade substrates can be used without the need for purification.

Scheme 4.17: Isomerisation of terminal alkenes.

The system is sensitive to the steric bulk about the alkene moiety, showing reduced reactivity and stereoselectivity with more hindered substrates. Allyl ethers are less prone to isomerise; in the case of allylic amines, probably due to chelating effects, a higher catalyst loading (1 mol%) is required. The efficiency of Eta-5-BArF at low catalyst loading was evaluated with important industrial feedstocks, showing remarkable activity with 1-octene.
(TON= $5.5 \times 10^4$) (oil feedstock), methyl-1-undecenoate (TON= $4.5 \times 10^4$) (fatty ester feedstock) and allylbenzene (TON= $7.6 \times 10^4$) (essential oil feedstock).

**Eta-5-BArF** is very active with allylic arenes yielding the corresponding vinyl arenes which can be easily derivatised to high value molecules used in various fields (such as medicinal chemistry, polymer chemistry, fragrances, pesticides, etc). Examples of this approach can be found from the groups of Bruneau and Fogg, which have explored the functionalisation of isoeugenol, isosafrole and anethole via cross-metathesis, achieving valuable products. Therefore, by combining the isomerisation process, with an ethenolysis reaction it has been possible to access the corresponding styrene derivatives that can be further functionalised via various reactions, such as epoxidation, dihydroxylation or oxidative cleavage, for example.

The isomerisation of eugenol and estragole was performed on up to a 3 g scale under neat conditions using standard glovebox and Schlenk techniques; material prepared in this way was washed through silica with toluene, which was evaporated to yield the desired product. The product retained some colour, but was deployed directly in subsequent metathesis reactions; impurities remaining in this material did not compromise further steps, validating a telescoped isomerisation-metathesis procedure. After initial screening of a number of metathesis precatalysts, $M_{20}$ was selected as the most efficacious catalyst for the ethenolysis of isoeugenol and anethole (Figure 4.6).

![Figure 4.6](image_url)

**Figure 4.6:** Metathesis precatalysts explored in this study.
Ethenolysis reactions were conducted using 1,7-octadiene as the solvent, which allows *in situ* generation of ethylene from the rapid and thermodynamically-favoured metathesis reaction to form cyclohexene.\(^{36}\) The system avoids the use of ethylene gas directly and consequently precludes the need for high-pressure apparatus, making it a valuable laboratory methodology. Optimised conditions allowed the corresponding styrene compounds to be obtained in high yield (Scheme 4.18).

![Scheme 4.18: Functionalization of allylarene feedstocks *via* ethenolysis.](image)

**SYNTHESIS OF S-E COMPOUNDS *VIA* DEHYDROGENATIVE COUPLING\(^{37}\)**

Organosulfur compounds have been widely used in organic chemistry\(^ {38}\) and their transformations/application have always generated interest in the scientific community. For example, disulfides play very important roles in both nature\(^ {39}\) (since they are involved in DNA cleavage, stabilisation of protein folding,....) and industrial applications (drugs, vulcanising agents, oils, rubber and rechargeable lithium batteries).\(^ {38,39e,40}\) These compound can be achieved *via* oxidation of the corresponding thiols, using stoichiometric amounts of oxidants such as Br\(_2\) or thionyl chloride.\(^ {41}\) However these types of oxidants are usually hazardous, toxic, or expensive reagents, requiring long reaction times, generating a considerable amount of waste and very often over-oxidised undesired products can be formed.\(^ {42}\) Aiming to have greener and
more valuable methodologies, some metal-catalysed methodology have been reported in the literature. For example, by using oxygen as oxidant, it is possible to access disulfides, using Fe or Co based catalysts (such as Fe(BTC) in MOF\textsuperscript{43} and Co(II)/phthalocyanine\textsuperscript{44}). Also aerobic heterogeneous catalytic systems have also been developed.\textsuperscript{45} Combining [Rh(COD)\textsubscript{2}]BF\textsubscript{4} or CpMn(CO)\textsubscript{3}/h\textsubscript{2}\textsuperscript{47} it is possible to synthesise disulfides without using any additional oxidant. However, these methodologies possess some drawbacks: for instance, high catalyst loadings (5 mol\%) of expensive Rh complex is required, or the use of laser radiation to form the active species is needed in the case of the Mn system.

In the case of Eta-5, the complex is capable of oxidising thiols into disulfides, with remarkable activity, without using any additional oxidants. The system can convert aryl as well as primary and secondary alkyl thiols to the corresponding disulphides in good yields. Even sterically hindered tertiary alkyl thiols proved to be suitable substrates in the reaction, providing the corresponding disulphide in modest yields. However electronic factors were shown to play a role in the reactivity. For example, the presence of an electron-withdrawing group on the aromatic ring led to shorter reaction times but a slight erosion in yield (Scheme 4.19).

![Scheme 4.19: Oxidation of thiols to disulfides](image-url)
Another important class of organosulfur compounds are silyl and boron sulfide. For instance, silylthioethers are widely employed in organic chemistry as valuable tools, due to their unique properties and reactivity, being, for example, used as a protecting group for carbonyl compounds,\textsuperscript{48} in the preparation of unsymmetrical sulfide,\textsuperscript{48-49} or even for the synthesis of anomeric thioacetals in oligosaccharide chemistry.\textsuperscript{50}

Generally thiosilanes are obtained through the stoichiometric reaction between chlorosilanes and a metal thiolate, such as lithium thiolate.\textsuperscript{41a} This procedure requires the formation of the metal thiolate to react with the chlorosilane, resulting in a drawback on atom economy. In order to develop a more convenient and atom-efficient methodology, a few catalytic approaches have been reported. However, these processes requires expensive and highly sensitive reagents such as B(C\textsubscript{6}H\textsubscript{5})\textsubscript{3}\textsuperscript{51} or the use of light activated transition-metal complexes such as CpFe(CO)\textsubscript{3}Me\textsuperscript{52} or Ru\textsubscript{3}(CO)\textsubscript{12}\textsuperscript{53} and high catalyst loadings.

Complex Eta-5 has been found to be also capable of coupling thiols with silanes and boronates, generating the corresponding thioethers. Several thiols and silanes are well tolerated by the dehydrogenative coupling system, achieving high conversion in all cases. In fact, this transformation gave the best TON to date (TON = 200) (Scheme 4.20).

This procedure can also be extended also to access sulfur-boronates. These compounds present potential utility, particularly as borylation reagents, and the reported transformation using Eta-5 is the first catalytic process developed for the coupling of thiols with pinacol and catechol borane (Scheme 4.21).
Scheme 4.21: Synthesis of thiaboronates via dehydrogenative coupling.

Complex Eta-5 shows high versatility in this transformation, enabling the use of alkyl, benzyl and aryl thiols and accessing the coupling products in good yields and high turnover number (TON: 200).

**CHEMOSELECTIVE REDUCTION OF CARBOXYLIC ACIDS TO ALCOHOLS VIA HYDROSILYLATION**

The reduction of carboxylic acids to alcohols is a valuable transformation, usually carried out by using stoichiometric amounts of hydride reducing agents. However, the high sensitivity/reactivity of these reagents to air and moisture, makes them very impractical in large scale processes. In addition, due to their high reactivity, stoichiometric reagents are usually poorly chemoselective and renders them unattractive; the catalytic hydrogenations reported to date, which may represent an alternative usually require harsh conditions presenting a serious practical drawback. Among these procedures, the catalytic hydrosilylation of carbonyl compounds, has become an important alternative reduction strategy.
Several metal- and metal-free catalysed hydrosilylations of esters or amides to the corresponding alcohols and amines have been reported.\textsuperscript{58} However, only a limited number of catalytic systems have been described for the hydrosilylation of free carboxylic acids.\textsuperscript{59}

Complex \textbf{Eta-5} shows very high activity and chemoselectivity in the hydrosilylation of benzoic acids in the presence of a broad range of substituents in either \textit{ortho} or \textit{para} positions, using phenylsilane as reducing reagent. In addition, heteroaromatic carboxylic acids are generally well tolerated, with the exception of picolinic acid, where a complex mixture of products was obtained (Scheme 4.22).

\begin{center}
\begin{tikzpicture}
\node (A) at (0,0) {\textbf{Scheme 4.22}: Reduction of carboxylic acids via hydrosilylation mechanism.};
\end{tikzpicture}
\end{center}

Surprisingly, several sensitive functional groups, like alkenes, nitriles, tertiary amides, esters and even ketones, which are usually much more reactive than the carboxylic acids under other hydrosilylation or reduction conditions, are not reduced by the catalytic system, showing remarkable chemoselectivity (Scheme 4.23 a). The chemoselectivity was investigated in a series of competitive reactions, reducing benzoic acid in the presence of three ketones. The
system was found to be highly chemoselective, and only acetophenone is slightly reduced under the conditions employed (Scheme 4.23 b).

Scheme 4.23: Chemoselective hydrosilylation of carboxylic acids.

In order to understand the reaction mechanism in this process, several experiments were conducted. Firstly, using dimethylphenylsilane in the presence of Eta-5, the silyl ester 134 can be easily achieved (Scheme 4.24, reaction a). However, due to its high moisture-sensitivity, the possible formation of poly-dehydrogenative coupled products and the observed redistribution associated with the phenylsilane, the analogous silyl ester intermediate I cannot be easily detected. Performing this reaction in a shorter reaction time (15 min) than the optimised condition, and after the hydrolysis of the disilylacets (II), the corresponding
aldehyde was detected by $^1$H-NMR spectroscopy. In light of these results, the following mechanism has been proposed (Scheme 4.24).

![Scheme 4.24: Proposed mechanism of hydrosilylation of carboxylic acids](image)

The carboxylic acid reacts with phenylsilane in the presence of Eta-5, in three steps (Scheme 4.24, reaction b).$^{59f}$ The desired primary alcohols are proposed to be produced by (I) a dehydrogenative coupling between the carboxylic acid and the silane, (II) a reduction of the silyl ester derivative (I) by a Si-H addition in the C=O bond, followed by (III) reductive cleavage of a C-O bond of the disilylacetal intermediate (II), and the final hydrolysis of the corresponding silyl ether (III). It is generally assumed that the silane is activated by the metal complex via oxidative addition to produce a metal silyl complex able to transfer the silyl group to a carbonyl moiety.$^{58c,62}$
Ruthenium Catalysed Borylation of Phenylpyridines via C-H Activation

Aiming to gain information regarding the active species and the possible intermediates in the Eta-5 catalysed silylation reaction, a stoichiometric reaction with Et₃SiH was carried out, achieving a novel yellow pale complex bearing one phosphine, confirmed by $^{31}$P NMR and one silane, confirmed the $^1$H NMR. Moreover a wide $^1$H NMR spectra revealed the presence of two hydrides, which, due probably due to the possible interchanging of the hydrides around the ruthenium centre, are detected as two broad signals. In order to confirm the suggested structure, a single crystal of one of the complex of the series suitable for X-ray diffraction analysis was obtained, showing the structure to be the $[RuH_2(SiEt_3)(PPh_3)(3$-phenylindenyl)] (Eta-5-SiEt₃) (Figure 4.7).⁶⁴

![Figure 4.7: X-ray structure of complex Eta-5-SiEt₃. Most hydrogen are omitted for clarity. Selected bonds (Å) and angles (°): Ru1-P1 2.2876(13), Ru1-Si1 2.3997(12), Ru1-H1M 1.380(13), Ru1-H2M 1.37(3), Si1-H2M 1.95(3); P1-Ru1-Si1 105.35(4), P1-Ru1-H1M 78.9(17), P1-Ru1-H2M 80.1(15), Si1-Ru1-H1M 63.1(17), Si1-Ru1-H2M 54.3(14), H1M-Ru1 H2M-104(2).](image-url)
This effective synthetic procedure was extended to a series of different silanes, showing higher compatibility and avoiding the usual multi-step synthesis than the literature reported preparation of analogous hydrido silyl ruthenium complexes.\textsuperscript{62-64}

\begin{align*}
\text{Scheme 4.25: Synthesis of } [\text{RuH}_2(\text{SiR}_3)(\text{PPh}_3)(3\text{-phenylindenyl})].
\end{align*}

The mechanism proposed for the formation of \textbf{Eta-5-SiR}_3 proceeds through oxidative addition of the Si-H bond of the silane to ruthenium, after dissociation of one of the two phosphine ligands; a consecutive reductive elimination of a molecule of R\textsubscript{3}SiCl is driven by the stronger Si-Cl (90 kcal mol\textsuperscript{-1}) than the Si-H bond (75 kcal mol\textsuperscript{-1}).\textsuperscript{65} The addition of a molecule of R\textsubscript{3}SiH then, lead to the desired product (Scheme 4.25). The second oxidative addition of a molecule of R\textsubscript{3}SiH is in competition with the irreversible re-coordination of a molecule of PPh\textsubscript{3}, generating \textbf{Eta-5-H}. This side product can be avoided by adding a large excess of silane in the reaction media. However this synthetic protocol cannot be applied to the most sterically hindered silanes such as TBDMS or TIPS or to too reactive silanes like PhSiH\textsubscript{3} or Cl\textsubscript{3}SiH.
These complexes were tested in C-H activation reactions, more specifically in arene C-H bond borylation reactions. Despite several rhodium and iridium catalysed reports in the literature, this represents the first methodology involving a ruthenium catalyst. Among the whole series of \textbf{Eta-5-SiR}_3 reported, \textbf{Eta-5-SiEt}_3 showed the best result, promoting the borylation using a pyridine as directing group in high yields and at the lowest catalyst loading reported for a ruthenium-mediated C-H activation reaction.\textsuperscript{67}
Complex \textit{Eta-5-SiEt}_3 shows remarkable activity with several phenylpyridine derivatives. Additionally, high regioselectivity is observed, yielding the 2-substituted product in all cases considered. The borylation procedure catalysed by \textit{Eta-5-SiEt}_3 also compatible with other transformations in sequential reactions, such as Suzuki-Miyaura cross-coupling (Scheme 4.28).\textsuperscript{63}

\textbf{Scheme 4.28:} Sequential Borylation- Suzuki-Miyaura cross-coupling of phenylpyridine.
CONCLUSION

In summary, the 3-phenylindenyl complex reports remarkable versatility and we propose that this formal decomposition product may potentially become more valuable than the starting alkyldiene material. In fact, the recently commercial availability of [RuCl(PPh$_3$)$_2$(3-phenylindenyl)] (Eta-5) by STREM$^{©}$ and UMICORE$^{©}$ (and the ease of synthesis of its derivatives) and the fact that these are active in at least 20 different transformations is truly remarkable. Meandering through the exploration of its reactivity we have discovered more than a decomposition product but a veritable multi-tasking catalyst.

EXPERIMENTAL SECTION

GENERAL CONSIDERATIONS:

Silanes, bases, sodium tetrakis(3,5-(trifluoromethyl)phenyl)borate, starting materials to compounds 2, from 15 to 23, from 26 to 45, from 71 to 133, from 135, 136, 140 and substrates 48, 49, 52, 53, 57, 62, 63, 64, from 66 to 69 were purchased from Sigma Aldrich or Alfa Aesar; Bis(pinacolato)diboron was purchased from BASF. All the reagent above mentioned were used as received, with the exception the starting aldehydes to compound 18 and 26, which were purified according to the procedure reported in literature.$^{68}$ Complexes Ru-1, Ru-5, Ru-92, Ru-94, Ru-97, were purchased from commercial suppliers and used as received. Complexes Ru-98, Ru-99, Ru-100, Ru-101, and were synthesised according to previously described procedures.$^{69}$ The starting imine to compounds 24 and 25 were synthesised in according to the procedure reported in the literature.$^{70}$ Compound 46 was synthesised in according to the reported procedure.$^{71}$ Compounds 54, 55, 56, 48-d$_1$, 65 and 70 were synthesised via reduction of the corresponding aldehyde according to the reported procedure.$^{72}$ Compounds 51 and 52
were synthesised from benzaldehyde and the correspondent vinyl Grignard reagent.\textsuperscript{73} Compound 60 was synthetized in according with the reported procedure.\textsuperscript{74} The starting pyridines to compounds from 137 to 139 and from 141 to 144 were prepared according to the literature.\textsuperscript{75}

Anhydrous toluene, THF, dichloromethane, pentane, were dispensed from a solvent purification system from Innovative Technology. Other solvents considered were purified in according with the reported procedure. Catalyst syntheses were performed in an MBraun glovebox containing dry argon and less than 1 ppm oxygen or using standard Schlenk techniques.\textsuperscript{1}H, \textsuperscript{13}C, \textsuperscript{31}P, \textsuperscript{19}F, \textsuperscript{11}B and \textsuperscript{19}Si Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance 300 or Bruker Avance II 400 or 500 NMR spectrometers Ultrashield NMR spectrometers. Chemical shifts are reported in δ ppm. Mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre at Swansea University, Grove building, Singleton Park, Swansea, SA2 8PP, Wales, UK. Elemental analyses were performed at the London Metropolitan University. The racemisation reaction were analysed by HLPC at room temperature with a CHIRALCEL OD-H column. Method 99:1 Hexane/Isopropanol 1 ml min\textsuperscript{-1} flow. The GC conversions and yields are determined using the following method and column: 90°C to 300°C rate 45°C min\textsuperscript{-1} column HP-5 5% phenyl methyl siloxane.

**SYNTHESIS OF [RUH(PPh\textsubscript{3})\textsubscript{2}(3-PHENYLINDENYL)] (Eta-5-H).**

In a round-bottomed flask, inside an Argon-filled glovebox, complex Eta-5 (0.47 mmol, 400 mg) and NaOMe (0.47 mmol, 25 mg) were added and dissolved in methanol (23.5 mL). The reaction mixture was stirred at room temperature for 3 h. The suspension was filtered and the solid collected was washed with methanol (2 x 5 mL) and then with pentane (5 mL). The solid was collected and dried under vacuum, yielding Eta-5-H as yellow solid (277 mg 77%
yield). $^1$H NMR (300 MHz, C$_6$D$_6$) $\delta$ ppm -14.58 -14.27 (m, 1 H) 4.58 - 4.66 (m, 1 H) 6.03 (s, 1 H) 6.23 (dd, $J$=8.2, 3.6 Hz, 2 H) 6.74 - 6.82 (m, 7 H) 6.83 - 6.96 (m, 15 H) 6.97 - 7.12 (m, 12 H) 7.31 (ddd, $J$=9.8, 7.1, 2.2 Hz, 6 H) 7.81 (d, $J$=7.3 Hz, 2 H) $^{13}$C NMR (75 MHz, C$_6$D$_6$) $\delta$ ppm 74.24 - 75.14 86.79 - 87.69 88.72 - 89.49 106.63 - 107.08 110.88 119.87 125.27 125.46 125.82 126.97 127.08 127.35 127.47 127.90 128.55 129.52 139.19 139.43 139.94 140.85 141.37 $^{31}$P NMR (121 MHz, C$_6$D$_6$) $\delta$ 62.78 (d $J$= 25.5 Hz) 65.65 (d $J$= 25.5 Hz) ppm. Anal. Calcd. for C$_{51}$H$_{41}$P$_2$Ru C, 74.99; H, 5.06; Found: C, 74.83; H, 4.95;

**SYNTHESIS OF [Ru(PPPh$_3$)$_2$(3-phenylindenyl)][tetrakis(3,5-(trifluoromethyl)phenyl)borate] (Eta-5-BAr$^F$)**

In the glovebox, complex Eta-5 (1 g, 1.17 mmol) was combined with sodium tetrakis(3,5-(trifluoromethyl)phenyl)borate (1.1 g, 1.2 mmol, 1.1 equiv.) in dichloromethane. The reaction was stirred for 1 h at room temperature, then the volatiles were removed *in vacuo*. The resulting residue was carefully washed with pentane to yield [Ru(PPPh$_3$)$_2$(3-phenylindenyl)][tetrakis(3,5-(trifluoromethyl)phenyl)borate] (Eta-5-BAr$^F$) as a very dark purple powder in analytically-pure form. Yield: 1.8 g (1.08 mmol, 98%). $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.74 (s 1H), 7.65 (s, 12H), 7.43 (m, 8H), 7.35 (m, 2H), 7.27 (m, 10H), 7.04 (m, 15H) 6.64 (t, $J$= 10.4 Hz 2H), 6.42 (m, 13H), 5.70 (d, $J$= 11.2 Hz 1H), 4.72 (d $J$= 2.8 Hz, 1H), 3.96 (d $J$= 2.8 Hz, 1H); $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$): $\delta$ 47.6, 86.6, 105.4, 106.9, 117.9, 119.6, 123.2, 127.7, 128.7, 129.2, 129.3, 129.5, 129.9, 131.4, 131.7, 132.8, 135.2, 161.2, 162.5, 161.9; $^{19}$F NMR (250 MHz, CD$_2$Cl$_2$) $\delta$ 63.2; $^{31}$P NMR (162 MHz, CD$_2$Cl$_2$): $\delta$ 38.4. Anal. elem. for C$_{83}$H$_{52}$BF$_{24}$P$_2$Ru calcd C 59.37 H 3.12 obtained C 59.15 H 3.10.

**GENERAL PROCEDURE TO THE SYNTHESIS OF COMPLEXES Eta-5-SiR$_3$**
In the glovebox, complex Eta-5 (500 mg, 0.58 mmol) was dissolved in toluene (10 ml) in a schlenk flask. Outside the glovebox the desired silane was added (6 equiv.). The reaction was stirred for the determined time at 100°C, then the volatiles were removed in vacuo. The resulting residue was washed with pentane for several time, yielding Eta-5-SiR₃ in the reported yield.

**Table 4.1: Reaction time and yield for the synthesis of Eta-5-SiR₃**

<table>
<thead>
<tr>
<th>Complex</th>
<th>Silane</th>
<th>t (h)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eta-5-SiEt₃</td>
<td>Et₃SiH</td>
<td>16 h</td>
<td>85 %</td>
</tr>
<tr>
<td>Eta-5-Si(OEt)₃</td>
<td>(EtO)₃SiH</td>
<td>3 h</td>
<td>69 %</td>
</tr>
<tr>
<td>Eta-5-SiMe₂Ph</td>
<td>PhMe₂SiH</td>
<td>3 h</td>
<td>60 %</td>
</tr>
<tr>
<td>Eta-5-SiMePh₂</td>
<td>Ph₂MeSiH</td>
<td>16 h</td>
<td>65 %</td>
</tr>
<tr>
<td>Eta-5-SiPh₃</td>
<td>Ph₃SiH</td>
<td>16 h</td>
<td>70 %</td>
</tr>
</tbody>
</table>

[RuH₂(PPH₃)(3-phenylindenyl)(SiEt₃)] (ETA-5-SiEt₃):

1H NMR (400 MHz, C₆D₆): δ 7.570 (m, 2H), 7.46 (m, 1H), 7.19 (m, 7H), 7.01 (m, 4H), 6.89 (m, 10H) 6.64 (m, 1H), 6.52 (m, 1H), 5.47 (m, 2H), 5.02 (m, 1H), 1.16 (t J= 8.3 Hz, 9H), 0.74 (sext. J = 7.11 Hz 3H), 0.63 (sext. J = 7.11 Hz 3H) -12.89 (bs, 1H), -13.83 (bs, 1H); ¹³C NMR (101 MHz, C₆D₆): δ 138.0, 137.5, 137.4, 134.1 (d, J = 11.4 Hz), 129.3, 129.1 (d J = 1.5 Hz), 128.6, 127.5, 126.1, 125.5, 125.3, 123.4, 121.6, 108.6, 106.5, 93.0, 89.9 (d, J = 3.0 Hz), 73.7 (d, J=8.8 Hz), 13.5, 9.8; ³¹P NMR (162 MHz, C₆D₆): δ 66.2. Anal. Calcd. for C₃₉H₄₃PRuSi: C, 69.72%; H, 6.45%. Found: C, 69.62%; H, 6.48%.

[RuH₂(PPH₃)(3-phenylindenyl)(SiOEt₃)] (ETA-5-SiOEt₃):
$^1$H NMR (400 MHz, C$_6$D$_6$): δ 7.56 (m, 2H), 7.48 (m, 1H), 7.15 (m, 7H), 7.01 - 6.83 (m, 13H) 6.66 (m, 1H), 6.42 (m, 1H), 5.69 (m, 1H), 3.89 (m, 6H), 1.26 (t, $J = 7.9$ Hz, 9H) -12.26 (bs, 1H), -13.24 (bs, 1H); $^{13}$C NMR (101 MHz, C$_6$D$_6$): δ 138.0, 137.5, 137.0, 134.0 (d, $J = 11.4$ Hz), 129.6, 129.2, 129.1 (d, $J = 1.5$ Hz), 128.6, 127.6, 127.5, 126.4, 126.3, 125.9, 123.7, 121.6, 110.6, 106.5, 94.0, 89.9 (d, $J = 4.4$ Hz), 73.1 (d, $J = 8.8$ Hz), 57.8, 18.8; $^{31}$P NMR (162 MHz, C$_6$D$_6$): δ 60.6. Anal. Calcd. for C$_{39}$H$_{43}$PRuSi: C, 65.16; H, 5.89. Found: C, 65.25; H, 5.95.

$[\text{RuH}_2(\text{PPH}_3)(-3\text{-phenylindenyl})(\text{SiMe}_2\text{PH})](\text{E}ta-5\text{-SiMe}_2\text{PH})$:

$^1$H NMR (400 MHz, C$_6$D$_6$): δ 7.87 (m, 2H), 7.46 (m, 1H), 7.39 (m, 2H), 7.27 - 7.12 (m, 9H), 6.99 (m, 3H), 6.89 (m, 9H), 6.75 (m, 1H), 6.69 (m, 1H), 6.58 (m, 1H), 5.28 (m, 1H), 4.88 (m, 1H), 0.65 (s, 3H), 0.36 (s, 3H), -13.00 (bs, 2H); $^{13}$C NMR (101 MHz, C$_6$D$_6$): δ 152.1, 138.1, 137.6, 137.5, 134.5 (d, $J = 11.4$ Hz), 134.4, 129.7 (d, $J = 4.0$Hz), 129.1, 128.5, 128.3, 128.2, 128.1, 127.9, 126.4, 126.7, 126.3, 124.1, 122.0, 109.3, 107.0, 94.1, 91.2 (d, $J = 4.4$ Hz), 76.5 (d, $J = 8.8$ Hz), 10.7, 10.4; $^{31}$P NMR (162 MHz, C$_6$D$_6$): δ 66.5. Anal. Calcd. for C$_{41}$H$_{38}$PRuSi: C, 71.28; H, 5.54. Found: C, 71.15; H, 5.65.

$[\text{RuH}_2(\text{PPH}_3)(3\text{-phenylindenyl})(\text{SiMePh}_2)](\text{E}ta-5\text{-SiMePh}_2)$

$^1$H NMR (400 MHz, C$_6$D$_6$): δ 7.82 (m, 4H), 7.46 (m, 5H), 7.29 (m, 5H), 7.17 (m, 5H) 7.04 (m, 7H), 6.99-6.75 (m, 16H), 6.68 (m, 1H), 6.50 (m, 1H), 4.96 (m, 2H), 0.60 (s, 3H), -11.81 (bs, 1H), -13.20 (bs, 1H); $^{13}$C NMR (101MHz, C$_6$D$_6$): δ 149.5, 148.1, 137.4, 137.0, 136.9, 135.7, 134.8, 135.2, 134.4, 133.9, 133.8, 130.0, 129.8, 129.2, 128.7, 127.7, 127.5, 126.2, 126.0, 123.8, 121.8, 109.6, 106.7, 93.5, 92.4 (d, $J = 4.4$ Hz), 75.5 (d, $J = 8.8$ Hz), 8.62; $^{31}$P
NMR (162MHz, C₆D₆): δ 63.3. Anal. Calcd. for C₄₆H₄₀PRuSi: C, 73.24; H, 5.35. Found: C, 73.23; H, 5.43.

[RuH₂(PPH₅)(3-phenylindenyl)(SiPh₃)] (Eτa-5-SiPh₃):

¹H NMR (400 MHz, CD₂Cl₂): δ 7.66 (m, ¹H), 7.49 (m, 8H), 7.28 (m, 6H), 7.13 (m, 18H) 6.86 (m, 9H), 6.58 (m, 7H), 5.89 (m, 1H), 4.76 (m, 1H), 4.10 (m, 1H), 4.22 (m, 1H), -11.55 (d, J = 30.0 Hz, 1H), -13.25 (d, J = 30.0 Hz, 1H); ¹³C NMR (101 MHz, CD₂Cl₂): δ 145.9, 137.3, 136.7, 136.7, 136.3, 136.1, 135.3, 133.8, 133.7, 130.4, 130.2, 129.5, 129.3, 128.6, 128.4, 128.5, 128.2, 127.5, 127.4, 127.3, 126.6, 126.4, 125.9, 124.1, 122.0, 111.1, 107.4, 93.6 (d, J = 3.6 Hz), 93.5, 74.1 (d, J = 338.8 Hz); ³¹P (162MHz, CD₂Cl₂) δ 58.7. Anal. Calcd. for C₅₁H₄₂PRuSi: C, 75.16; H, 5.19. Found: C, 69.88, H, 5.20.

LOW CATALYST LOADING RACEMISATION EXPERIMENTS:

In the glovebox, a 5 mL vial was charged with a defined amount of a stock solution of the catalyst in toluene, sodium tert-butoxide (0.005 mmol, 1 mg) and toluene were added up to 1 mL of reaction solution. After 10 minutes (S)-phenylethanol (15) was added (0.5 mmol, 60 µL). The racemisation reaction was monitored by HPLC analysis.

HPLC CHROMATOGRAM OF (S)-PHENYLETHANOL AND RAC-PHENYLETHANOL:

Method 99:1 hexane/iso-propanol 1 ml min⁻¹ flow (S)-phenylethanol tᵣ=34.01min
Method 99:1 hexane/iso-propanol 1 ml*min-1 flow (S)-phenylethanol \( t_r = 28.75 \) min, (R)-phenylethanol \( t_r = 21.46 \) min

**GENERAL PROCEDURE FOR THE HYDROGENATION OF KETONES, IMINES AND ALDEHYDES.**

In a vial fitted with a screw cap, the substrate (1 mmol), catalyst \textbf{Eta-5} (0.005 mmol, 4.4 mg) and KHMDS (0.025 mmol, 4.8 mg) were charged inside the glovebox and dissolved in iso-propyl alcohol (2 mL). The solution was stirred at 89°C for a period of time indicated in of time indicated on Scheme 4.5. The reaction was monitored by \(^1\)H NMR analysis of aliquots. The solvent was removed under vacuum, and the product was purified by silica gel chromatography (pentane / ethyl acetate from 98:2 to 50:50).

**General procedure for optimization of reactions and catalyst comparisons.** In a vial fitted with a screw cap, benzophenone (17) (0.25 mmol), catalyst (0.00125 mmol) and the proper amount of base were charged inside the glovebox and dissolved in organic solvent (0.5
mL). To this mixture the hydrogen source was added (0.5 mL). The solution was stirred at given temperature for 1 h hour (in the case of Table 4.1 the reactions are analysed for 1 h and 5 h). The solvent was removed under vacuum and the crude reaction was analysed by $^1$H NMR.

**Table 4.2: Base optimisation.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Conv. after 1h (%)$^b$</th>
<th>Conv. after 5h (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>K$_3$PO$_4$</td>
<td>30</td>
<td>45</td>
</tr>
<tr>
<td>3</td>
<td>Cs$_2$CO$_3$</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>NaOH</td>
<td>58</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>CsOH</td>
<td>25</td>
<td>55</td>
</tr>
<tr>
<td>6</td>
<td>KOH</td>
<td>23</td>
<td>30</td>
</tr>
<tr>
<td>7</td>
<td>NaOAc</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>8</td>
<td>NaOMe</td>
<td>67</td>
<td>78</td>
</tr>
<tr>
<td>9</td>
<td>NaO$^t$Bu</td>
<td>71</td>
<td>83</td>
</tr>
<tr>
<td>10</td>
<td>KO$^t$Bu</td>
<td>48</td>
<td>79</td>
</tr>
<tr>
<td>11</td>
<td>KO$^t$Am</td>
<td>66</td>
<td>72</td>
</tr>
<tr>
<td>12</td>
<td>KHMDS</td>
<td>75</td>
<td>91</td>
</tr>
</tbody>
</table>

$^a$ Reaction conditions: benzophenone (0.25 mmol), **Eta-5** (0.5 mol%) and base (10 mol%) dissolved in 1:1 toluene / isopropyl alcohol (1 mL). $^b$ Conversion determined by $^1$H NMR from an average of at least two runs.

**Table 4.3: Base optimisation.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Base loading</th>
<th>Conv. (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>None</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td><strong>Eta-5</strong></td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td><strong>Eta-5</strong></td>
<td>10</td>
<td>70</td>
</tr>
<tr>
<td>5</td>
<td><strong>Eta-5</strong></td>
<td>5</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td><strong>Eta-5</strong></td>
<td>2.5</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td><strong>Eta-5</strong></td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td><strong>Eta-5</strong></td>
<td>0.5</td>
<td>0</td>
</tr>
</tbody>
</table>
Reaction conditions: benzophenone (0.25 mmol), Eta-5 (0.5 mol%), KHMDS (X mol%) dissolved in 1:1 toluene. Conversion determined in $^1$H NMR.

**Table 4.4: Solvent optimisation.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Conv(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>H$_2$O</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>iPrOH</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>DMSO</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>CH$_3$CN</td>
<td>8</td>
</tr>
<tr>
<td>5</td>
<td>DMF</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>DCE</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>DME</td>
<td>79</td>
</tr>
<tr>
<td>8</td>
<td>Toluene</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>Dioxane</td>
<td>72</td>
</tr>
<tr>
<td>10</td>
<td>cC$<em>6$H$</em>{12}$</td>
<td>89</td>
</tr>
</tbody>
</table>

**Table 4.5: Hydrogen source screening.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Hydrogen source</th>
<th>Conv.(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>iPrOH</td>
<td>90</td>
</tr>
<tr>
<td>2</td>
<td>EtOH</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>HCOOH</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>H$_2$</td>
<td>0</td>
</tr>
</tbody>
</table>

Conversion determined by $^1$H NMR from an average of at least two runs.
Table 4.6: Temperature optimisation.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Conv. (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>89 (reflux)</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>93</td>
</tr>
<tr>
<td>3</td>
<td>40</td>
<td>52</td>
</tr>
<tr>
<td>4</td>
<td>Rt</td>
<td>8</td>
</tr>
</tbody>
</table>

\(^a\)Reaction conditions: benzophenone (0.25 mmol), Eta-5 (0.5 mol%), KHMDS (2.5 mol%) dissolved in isopropyl alcohol (1 mL). \(^b\)Conversion determined by \(^1\)H NMR from an average of at least two runs.

**LOW CATALYST LOADING PROCEDURE FOR THE TRANSFER HYDROGENATION REACTION.**

In a vial fitted with a screw cap, inside the glovebox, an aliquot of Eta-5, from a stock solution of catalyst Eta-5 in dichloromethane (2.6 mg in 5 mL) was added. The solvent was removed under vacuum and the benzophenone (0.25 mmol), KHMDS (0.0625 mmol 1.2 mg) were added and dissolved in isopropyl alcohol (1 mL). The solution was stirred at 89°C for a period of time indicated in. The solvent was removed under vacuum and the crude reaction was analysed by \(^1\)H NMR.
Table 4.7: Low catalyst loading screening.\(^a\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst loading (mol%)</th>
<th>Time (h)</th>
<th>Conv. (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>0.25</td>
<td>3</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>0.15</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>24</td>
<td>92</td>
</tr>
<tr>
<td>5</td>
<td><strong>0.05</strong></td>
<td><strong>48</strong></td>
<td><strong>96</strong></td>
</tr>
<tr>
<td>6</td>
<td>0.025</td>
<td>72</td>
<td>48</td>
</tr>
</tbody>
</table>

\(^a\)Reaction conditions: benzophenone (0.25 mmol), Eta-5 (X mol\%), KHMDS (2.5 mol\%) dissolved in isopropyl. \(^b\)Conversion determined by \(^1\)H NMR.

NMR DATA FOR HYDROGENATED COMPOUNDS:

**Benzhydrol (2)**

Yield: 93%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 7.31-7.21 (m, 10H), 5.80 (s, 1H), 2.24 (bs, 1H). \(^1\)H NMR Spectroscopic data for the product were in accordance with the literature.\(^76\)

**Phenylethanol (16)**

Yield: 88%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 7.22-7.11 (m, 5H), 4.77 (q, J= 6.3 Hz 1H), 1.70 (bs, 1H), 1.37 (d, J= 6.6 Hz 1H). \(^1\)H NMR Spectroscopic data for the product were in accordance with the literature.\(^76\)

**Benzyl Alcohol (18)**

Yield: 87%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 7.22 (m, 4H), 7.28 (m, 1H), 4.60 (s, 2H), 1.86 (bs, 1H). \(^1\)H NMR Spectroscopic data for the product were in accordance with the literature.\(^76\)
Cyclohexanol (19)

Yield: 88%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 3.64- 3.58 (m, 1H), 1.93-1.87 (m, 2H) -1.71-1.69 (m, 2H), 1.57-1.52 (m, 1H), 1.42 (m, 1H), 1.15-1.34 (m, 5H).

Spectroscopic data for the product were in accordance with the literature. 

1-Indanol (20)

Yield: 77%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.42-7.39 (m, 1H), 7.27-7.22 (m, 3H), 5.23 (m, 1H), 3.03 (m, 1H), 2.82 (m, 1H), 2.47 (m, 1H), 1.97 (m, 2H).

Spectroscopic data for the product were in accordance with the literature.

$a$-Tert-butylbenzyl alcohol (21)

Yield: 62%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.32-7.60 (m, 5H), 4.40 (s, 1H), 1.84 (s, 1H), 1.57 (s, 1H), 0.92 (s, 9H). Spectroscopic data for the product were in accordance with the literature.

$o$-Chlorophenyethanol (22)

Yield: 87%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.35-7.33 (m, 1H), 7.31-7.20 (m, 3H), 4.40 (s, 1H), 5.32 (q, J= 6.3 Hz 1H), 2.02 (s, 1H), 1.51 (d, J= 6.3 3H).

Spectroscopic data for the product were in accordance with the literature.

N-Benzylandiline (23)

Yield: 86%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.26 (dd, J= 7.5 Hz and 7.5 Hz 1H), 7.19-7.15 (m 2H), 6.71 (dd, J= 7.3Hz and J= 7.3Hz 1H), 6.63 (d, J=6.4 Hz, 2H), 4.32 (s, 1H), 4.02 (brs 1H). Spectroscopic data for the product were in accordance with the literature.
N-(4-methylbenzyl)aniline (24)

Yield: 83%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.43-7.30 (m 5H), 7.07 (d, J= 8.4 H 2H), 6.65 (d, J= 8.4 2H), 4.39 (s, 1H), 3.98 (brs, 1H), 2.33 (s 3H). Spectroscopic data for the product were in accordance with the literature.$^{80}$

N-benzyl-4-methylaniline (25)

Yield: 75%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.38-7.34 (m 2H), 6.98 (m 2H), 6.59 (dd, J= 4.8 Hz and J= 13.5 Hz 2H), 4.31 (s, 2H), 3.48 (brs, 1H), 2.41 (s 3H). Spectroscopic data for the product were in accordance with the literature.$^{81}$

p-tolylmethanol (26)

Yield: 98%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.26 (m, 3H), 4.65 (s, 2H), 2.35 (s, 3H), 1.58 (bs, 1H). Spectroscopic data for the product were in accordance with the literature.$^{76}$

$m$-Bromophenyethanol (27)

Yield: 44%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.39-7.38 (m, 1H), 7.31-7.29 (m, 1H), 7.28-7.19 (m, 2H), 4.87 (q, J= 6.3 Hz 1H), 1.48 (d, J= 6.3 3H). Spectroscopic data for the product were in accordance with the literature.$^{78}$

4-(1-hydroxyethyl)benzonitrile (28)

Conversion was determined by analysing the methyl signal for both compounds in the $^1$H NMR ($\delta$ 2.65 ppm from starting material and 1.49 ppm for compound 15). The signal are in accordance with the literature.$^{82}$
5-Nonanol (29)

Yield: 81%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 3.59-3.47 (m, 1H), 1.43-1.31 (m, 14H), 0.89-0.93 (m 6H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{76}

\textit{p-Methyl-1-phenyl ethanol} (30)

Yield: 85%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.27 (d, J= 6.7 Hz 2H), 7.15 (d, J= 6.7 Hz 2H), 4.87 (q, J= 6.3Hz 1H), 2.34 (s, 3H), 1.71 (brs, 1H), 1.48 (d, J= 6.3Hz 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{76}

\textit{\textalpha{-Isopropyl-benzyl alcohol}} (31)

Yield: 68%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.34-7.25 (m, 5H), 4.36 (d, J= 6.9 Hz 1H), 1.96 (sept, J= 6.9 Hz 1H), 1.75 (brs, 1H), 0.99 (d, J= 6.6 Hz 3H), 0.80 (d, J= 6.6 Hz 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{83}

\textit{2',4',6'-Trimethylphenylethanol} (32)

Yield: 69%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 6.82 (s, 2H), 5.36 (q, J= 6.4 Hz 1H), 2.42 (s, 6H), 2.25 (s, 3H), 1.62 (brs, 1H), 1.52 (d, J= 6.4 Hz 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{84}

\textit{p-Methoxy-1-phenyl ethanol} (33)

Yield: 66%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.29 (d, J= 8.8 Hz 2H), 6.88 (d, J= 8.8 Hz 2H), 4.86 (q, J= 6.4Hz 1H), 3.80 (s, 3H), 1.80 (brs, 1H), 1.47 (d, J= 6.4 Hz 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{76}

\textit{p-Iodophenylethanol} (34)
Conversion determined by analyzing the methyl signal for both compounds in the $^1$H NMR ($\delta$ 2.58 ppm for compound starting material and 1.47 ppm for compound 21). The signal are in accordance with the literature.$^{85}$

**GENERAL PROCEDURE FOR OXIDATION REACTION OPTIMISATION.**

In a vial fitted with a screw septum cap, benzhydrol (2) (0.25 mmol), Eta-5 (0.00125 mmol) and base (0.005 mmol) were charged inside the glovebox and dissolved in organic solvent (0.25 mL). To this mixture acetone (or isobutyl methyl ketone) was added (0.25 mL). The solution was stirred at a given temperature for 1 hour (in the case of Table 4.8 the reactions were analyzed at 0.5 h and 1 h). The solvent was removed under vacuum and the crude reaction was analysed by $^1$H NMR spectroscopy.

**Table 4.8:** Activity of catalyst Eta-5 under various conditions.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Cat. Loading (mol %)</th>
<th>Conv. (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>RT</td>
<td>16</td>
<td>0.5</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>Toluene</td>
<td>56</td>
<td>1</td>
<td>0.5</td>
<td>72</td>
</tr>
<tr>
<td>3</td>
<td>Toluene</td>
<td>56</td>
<td>0.5</td>
<td>0.5</td>
<td>86</td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>89</td>
<td>0.5</td>
<td>0.5</td>
<td>79</td>
</tr>
<tr>
<td>5</td>
<td>Toluene</td>
<td>110</td>
<td>0.5</td>
<td>0.5</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>Toluene</td>
<td>110</td>
<td>0.5</td>
<td>0.5</td>
<td>&gt;99</td>
</tr>
<tr>
<td>7</td>
<td>Toluene</td>
<td>110</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Toluene</td>
<td>110</td>
<td>1</td>
<td>0.25</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>Toluene</td>
<td>110</td>
<td>5</td>
<td>0.1</td>
<td>91</td>
</tr>
<tr>
<td>10</td>
<td>Toluene</td>
<td>110</td>
<td>24</td>
<td>0.05</td>
<td>63</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: benzhydrol (0.25 mmol), KHMD (2.5 mol%) dissolved in 1:1 toluene / acetone (0.5 mL). $^b$Conversion determined by $^1$H NMR from an average of at least two runs.
Table 4.9: Activity of catalyst **Eta-5** with different bases.\textsuperscript{a}

\begin{tabular}{|c|c|c|}
\hline
Entry & Base & Conv. (\%)\textsuperscript{b} \\
\hline
1 & KHMDS & >99 \\
2 & KO\textsuperscript{t}Bu & 97 \\
3 & KOH & 94 \\
4 & K\textsubscript{2}CO\textsubscript{3} & 90 \\
\hline
\end{tabular}

\textsuperscript{a} Reaction conditions: benzhydrol (0.25 mmol), base (2.5 mol\%) dissolved in 1:1 toluene / acetone (0.5 mL). \textsuperscript{b} Conversion determined by \textsuperscript{1}H NMR from an average of at least two runs.

Table 4.10: Activity of catalyst **Eta-5** in different conditions.\textsuperscript{a}

\begin{tabular}{|c|c|c|}
\hline
Entry & Solvent & Conv. (\%)\textsuperscript{b} \\
\hline
1 & Toluene & >99 \\
2 & Heptane & 96 \\
3 & CPME & 80 \\
4 & Acetone & 79 \\
5 & 2-MeTHF & 96 \\
6 & H\textsubscript{2}O & 77 \\
\hline
\end{tabular}

\textsuperscript{a} Reaction conditions: benzhydrol (0.25 mmol), KHMDS (2.5 mol\%) dissolved in 1:1 solvent / acetone (0.5 mL). \textsuperscript{b} Conversion determined by \textsuperscript{1}H NMR from an average of at least two runs.

**General Procedure for Oxidation Reactions in Scheme 4.8**

In a 10 mL J-Young type schlenk flask, the substrate considered (1 mmol), **Eta-5** (0.005 mmol) and KHMDS (0.02 mmol) were charged inside the glovebox and dissolved in toluene
(1 mL). To this mixture acetone was added (1 mL). The solution was stirred at 110 °C for the time reported in Scheme 4.8. The solvent was removed under vacuum and the crude reaction was purified by column chromatography using as eluent a mixture of pentane/ethylacetate 95:5 (with the exception substrate 43, where dichloromethane was used as eluent)

LOW CATALYST LOADING PROCEDURE

In a 10 mL J-Young type schlenk flask, inside the glovebox, an aliquot of Eta-5, from a stock solution of catalyst Eta-5 in toluene (2.6 mg in 5 mL) was added and diluted with toluene to a total volume of 0.25 ml. Benzhydrol (2) (0.25 mmol), KHMDS (0.0625 mmol 1.2 mg) and acetone (0.25 ml) were added. The solution was stirred at 110°C for a period of time indicated in Table 1. The solvent was removed under vacuum and the crude reaction was analyzed by 1H NMR spectroscopy.

NMR DATA FOR HYDROGENATED COMPOUNDS:

Benzophenone (17)

Yield: 97%. 1H NMR (300 MHz, CDCl3): δ 7.72-7.68 (m, 4H), 7.40-7.35 (m, 4H) 7.51-7.45 (m, 2H). Spectroscopic data for the product were in agreement with the literature.86

Acetophenone (35)

Yield: 96%. 1H NMR (300 MHz, CDCl3): δ 7.96 (d, J=7.6 Hz, 2H), 7.56-7.54 (m, 1H), 7.48-7.44 (m, 2H), 2.605 (s, 3H). Spectroscopic data for the product were in agreement with the literature.86
1-Indanone (37)

Yield: 97%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.74-7.72 (m, 1H), 7.58-7.54 (m, 1H), 7.47-7.45 (m, 1H), 7.36-7.32 (m, 1H), 3.12 (t, J= 6 Hz 2H), 2.63 (m, 2H).

Spectroscopic data for the product were in agreement with the literature.$^{87}$

Cyclohexanone (38)

Yield: 91%. $^1$H NMR (300 MHz, CDCl$_3$): δ 2.35 (m, 4H), 1.88 (m, 4H), 1.71 (m, 2H). Spectroscopic data for the product were in agreement with the literature.$^{86}$

5-Nonanone (39)

Yield: 87%. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.34 (t, J=5.4 Hz 4H), 1.53 (q, J= 5.4 Hz 4H), 1.32 (q, J= 5.7, 4H), 0.90 (t, J= 7.2 Hz 6H). Spectroscopic data for the product were in agreement with the literature.$^{88}$

2’-Methylacetophenone (41)

Yield: 86%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.68 (d, J= 6 Hz 1H), 7.38-7.35 (m, 1H), 7.27-7.23 (m, 2H), 2.57 (s, 3H), 2.52 (s, 3H). Spectroscopic data for the product were in agreement with the literature.$^{89}$

4’-Acetylanisole (42)

Yield: 98%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.93 (dd, J=6.9 Hz and 2.1 Hz, 2H), 6.92 (dd, J= 2.1 Hz and 6.9 Hz 2H), 3.86 (s, 3H), 2.55 (s, 3H). Spectroscopic data for the product were in agreement with the literature.$^{86}$

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4’-Trifluoromethylacetophenone (43)

Yield: 67%. \( ^1\text{H NMR (300 MHz, CDCl}_3\): } \delta 8.05 (dd, J=6.4, 2H), 6.92 (dd, J= 6.4 Hz 2H), 2.65 (s, 3H). Spectroscopic data for the product were in agreement with the literature.\(^89\)

Cholest-4-en-3-one (44)

Yield: 84% , \( ^1\text{H NMR (400 MHz, CDCl}_3\): } \delta 5.72 (1H, s), 2.43-2.27 (4H, m), 2.06-1.99 (2H, m), 1.87-1.81 (2H, m), 1.68-1.23 (12 H, m), 1.18 (3H, s), 1.15-1.00 (8H, m), 0.91 (3H, d, \( J = 6.4 \text{ Hz)\), 0.87 (3H, d, \( J = 2.0 \text{ Hz)\), 0.85 (3H, d, \( J = 1.6 \text{ Hz)\), 0.71 (3H, s). Spectroscopic data for the product were in agreement with the literature.\(^90\)
GENERAL PROCEDURE FOR THE OPTIMISATION OF THE ISOMERISATION OF ALLYLIC ALCOHOLS

In a vial fitted with a screw cap, in the glovebox, *trans*-1,3-diphenyl-2-propen-1-ol (32) (0.5 mmol), *Eta*-5 (0.00125 mmol) and base (0.02 mmol) were charged and dissolved in organic solvent (1 mL). The solution was stirred for 1 h. The solvent was removed under vacuum and the crude reaction was analysed by $^1$H NMR spectroscopy.

Table 4.11 Screening of bases.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Base</th>
<th>Conv. %$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NaO'Bu</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>KO'Bu</td>
<td>&gt;99</td>
</tr>
<tr>
<td>3</td>
<td>KHMDS</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>KOH</td>
<td>&gt;99</td>
</tr>
<tr>
<td>5</td>
<td>K$_2$CO$_3$</td>
<td>31</td>
</tr>
</tbody>
</table>

$^a$ Conditions: substrate (0.5 mmol), base (0.02 mmol), *Eta*-5 (1.25 μmol) and toluene (1 mL) added. Reactions stirred at ambient temperature for 1 h.

$^b$ Conversion determined from $^1$H NMR analysis; average of at least two experiments.
Table 4.11 Screening of solvents.\textsuperscript{a}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solv.</th>
<th>Conv. %\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Toluene</td>
<td>&gt;99</td>
</tr>
<tr>
<td>2</td>
<td>CPME</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>2-MeTHF</td>
<td>96</td>
</tr>
<tr>
<td>4</td>
<td>IBK</td>
<td>97</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Conditions: substrate (0.5 mmol), NaO\textsubscript{t}Bu (0.02 mmol), \textbf{Eta-5} (1.25 \textmu mol) and solvent (1 mL) added. Reactions stirred at ambient temperature for 1 h. \textsuperscript{b}Conversion determined from \textsuperscript{1}H NMR analysis; average of at least two experiments.

**REPRESENTATIVE PROCEDURE FOR ISOMERISATION OF ALLYLIC ALCOHOLS**

In a vial fitted with a screw cap, in the glovebox, allylic alcohol (1 mmol), \textbf{Eta-5} (0.0025 mmol) and NaO\textsubscript{t}Bu (0.04 mmol) were charged and dissolved in toluene (2 mL). The solution was stirred for 1 h. The solvent was removed under vacuum and the crude reaction was analysed by \textsuperscript{1}H NMR spectroscopy. For lower catalyst loadings a stock solution of \textbf{Eta-5} (2 mg in 2.5 mL) in toluene was used.

**NMR DATA FOR HYDROGENATED COMPOUNDS:**

1,3-diphenyl-1,4-propanedione (58)

Yield: 97%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 7.96-7.94 (m, 2H), 7.56-7.53 (m, 1H), 7.45-7.43 (m, 2H), 7.31-7.102 (m, 5H), 3.30 (t, \(J= 6.4\) Hz 2H), 3.06 (t, \(J= 6.4\) Hz 2H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{91}
Propiophenone (147)

Yield: 95%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.97-7.95 (m, 2H), 7.56-7.53 (m, 1H), 7.48-7.45 (m, 2H), 3.00 (t, J = 6 Hz 2H), 1.22 (t, J = 6 Hz 3H).

Spectroscopic data for the product were in accordance with the literature.86

Propyl phenyl ketone (148)

Yield: 97%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.97-7.95 (m, 2H), 7.57-7.54 (m, 1H), 7.48-7.44 (m, 2H), 2.95 (t, J = 2H), 1.77 (q, J = 6.5 Hz 2H), 1.01 (t, J = 5.6 Hz 3H). Spectroscopic data for the product were in accordance with the literature.92

1-phenyl-2-methyl-1-propanone (149)

Yield: 89%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.64-7.47 (m, 1H), 7.56-7.53 (m, 2H), 7.48-7.46 (m, 2H), 3.56 (sept, J = 6 Hz 1H), 1.21 (d, J = 6 Hz 3H).

Spectroscopic data for the product were in accordance with the literature.93

Cyclohexanone (38)

Yield 81 % (see above for the peak list). Spectroscopic data for the product were in accordance with the literature.94

Octan-3-one (150)

Yield: 94%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.44-2.37 (m, 4H), 1.55 (q, J = 6 Hz 4H), 1.05, (t J = 6 Hz, 3H), 0.86 (t, J = 6 Hz 3H).

Spectroscopic data for the product were in accordance with the literature.95
4-Pheny-butane-2-one (151)

Yield: 96%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.33-7.30 (m, 2H), 7.24-7.21 (m, 3H), 2.93 (t, J= 6 Hz 2H), 2.78, (t, J= 6 Hz, 2H), 2.15 (s, 3H).

Spectroscopic data for the product were in accordance with the literature.$^96$

1-(4-methoxyphenyl)-3-phenyl-1-propanone (59)

Yield: 92%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.99-7.91 (m, 2H), 7.35-7.23 (m 6H), 6.95 (d, J= 7.2 Hz 2H), 3.10 (s, 3H), 3.27, (t J= 6.8 Hz, 3H), 3.09 (t, J= 6.8 Hz 2H). Spectroscopic data for the product were in accordance with the literature.$^97$

1-(4-fluorophenyl)-3-phenylpropan-1-one (152)

Yield: 92%. $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.00-7.97 (m, 2H), 7.24-7.14 (m 6H), 7.13-7.10 (m, 2H), 3.27, (t J= 6.3 Hz, 2H), 3.06 (t, J= 6.3 Hz 2H). Spectroscopic data for the product were in accordance with the literature.$^98$

MECHANISTIC STUDIES FOR THE ALLYLIC ALCOHOL ISOMERISATION

GENERAL PROCEDURE FOR ISOMERISATION IN PRESENCE OF TBACl

In a vial fitted with a screw cap, in the glovebox, trans-1,3-diphenyl-2-propen-1-ol (48) (0.5 mmol), Eta-5 (0.00125 mmol), NaO'Bu (0.04 mmol) and tetrabutylammonium chloride (the amount is reported below) were charged and dissolved in isobutyl methyl ketone (1 mL). The solution was stirred for 1 h. The solvent was removed under vacuum and the crude reaction was analyzed by $^1$H NMR spectroscopy.
Table 4.12: conversion on basis of the concentration of Cl⁻

<table>
<thead>
<tr>
<th>TBACl (mol%)</th>
<th>Conv. %</th>
</tr>
</thead>
<tbody>
<tr>
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<td>97</td>
</tr>
<tr>
<td>10</td>
<td>91</td>
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<tr>
<td>25</td>
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</tr>
<tr>
<td>100</td>
<td>52</td>
</tr>
</tbody>
</table>

GENERAL PROCEDURE FOR ISOMERISATION WITH VARIABLE AMOUNT OF BASE

In a vial fitted with a screw cap, in the glovebox, trans-1,3-diphenyl-2-propen-1-ol (48) (0.5 mmol), Eta-5 (0.00125 mmol) and NaO'Bu (see below) were charged and dissolved in toluene (1 mL). The solution was stirred at given temperature for 1 h. The solvent was removed under vacuum and the crude reaction was analysed by ¹H NMR spectroscopy.

Table 4.12: conversion on basis of amount of base

<table>
<thead>
<tr>
<th>NaO'Bu (mol%)</th>
<th>Conv. %</th>
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<tr>
<td>1</td>
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</tr>
<tr>
<td>2</td>
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<td>&gt;99</td>
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<tr>
<td>8</td>
<td>96</td>
</tr>
<tr>
<td>50</td>
<td>Decomp.</td>
</tr>
<tr>
<td>100</td>
<td>Decomp.</td>
</tr>
</tbody>
</table>
**Figure 4.8:** Isomerization of 48 in the presence of various equivalents of NaO'Bu (black points) and TBACl (grey points).

**DETERMINATION OF THE ALLILIC ALCOHOL ISOMERISATION MECHANISM VIA DFT ANALYSIS**

**COMPUTATIONAL DETAILS**

All the DFT static calculations were performed at the GGA level with the Gaussian09 set of programs, using the BP86 functional of Becke and Perdew. The electronic configuration of the molecular systems was described with the standard split-valence basis set with a polarization function of Ahlrichs and co-workers for H, C, N, O, and Cl (SVP keyword in Gaussian). For Ru we used the small-core, quasi-relativistic Stuttgart/Dresden effective core potential, with an associated valence basis set contracted (standard SDD keywords in gaussian09). The geometry optimizations were performed without symmetry constraints, and the characterization of the located stationary points was performed by analytical frequency calculations. The reported energies have been optimized via single point calculations on the BP86 geometries with triple zeta valence plus polarization (TZVP keyword in Gaussian) using the M06 functional however estimating solvent effects with the polarizable continuous solvation model PCM using DCM as solvent.

Since in this work we had to compare a dissociative versus an associative/interchange mechanism, careful treatment of the entropic contribution to the free energy was fundamental. In this respect, it is clear that the contribution calculated in the gas phase (p = 1 atm) most likely exaggerates the entropic contribution. Thus, some kind of correction is needed when mechanisms of different molecularity have to be compared, or calculations will be biased in favor of the dissociative mechanism. Various recipes have been proposed in the literature, like
using only a fraction of the gas-phase entropy,\textsuperscript{104f,g} or using a higher pressure that would represent better the liquid state. In the present work we adopted the latter, and all the thermochemical analysis was performed at \( p = 1254 \) atm, as suggested by Martin et al.\textsuperscript{104g,h25a,b}

**Table 4.13:** Free energy of the isomerisation mechanism catalysed by Eta-5 with the substrates below stated. Values expressed in kcal/mol. Thermochemical terms calculated at \( p = 1254 \) atm.

<table>
<thead>
<tr>
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<td>0.0</td>
<td>0.0</td>
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<tr>
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<td>F’</td>
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**Table 4.14:** Free energy of the isomerisation mechanism catalysed by Eta-5, Ru-92 and Ru-97. Values expressed in kcal/mol. Thermochemical terms calculated at \( p = 1254 \) atm.

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<td>0.1</td>
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<tr>
<td>F'</td>
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<td>-9.0</td>
<td>-5.3</td>
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**ISOMERISATION OF PRIMARY ALLYLIC ALCOHOLS**

**METHOD A:**

Substrate solution (0.6 mL of a 0.5 mol L\(^{-1}\) solution in toluene-\(d_8\)) added to solid Eta-5-BAr\(^F\) in an NMR tube equipped with J. Young valve and mixed at room temperature for the specified time. Conversion was determined by integration of the \(^1\)H NMR spectrum.

**METHOD B:**

In a vial fitted with a screw cap, in the glovebox, the allylic alcohol (1 mmol), Eta-5-BAr\(^F\) (0.01 mmol) were charged and dissolved in toluene (1 mL). The solution was stirred at room temperature for the determine time. The solvent was removed under vacuum and the crude reaction was analyzed by \(^1\)H NMR in order to determine reaction conversion.

**ALKENE ISOMERISATION REACTIONS WITH COMPLEX Eta-5**

In the glovebox, an appropriate solution of substrate in solvent (if a solvent was used) was added to solid Eta-5, followed by a stirrer bar. The reactions were removed from the glovebox and stirred at 60 °C in closed vials for the specified time, and then quenched by exposure to air. A sample was diluted with chloroform-\(d\) and analysed by \(^1\)H NMR spectroscopy.
Table 4.15: Alkene isomerisation with complex Eta-5.$^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Eta-5 (mol%)</th>
<th>Solvent$^b$</th>
<th>Time</th>
<th>Conversion$^c$</th>
</tr>
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<tbody>
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<td>1$^{[d]}$</td>
<td>0.2</td>
<td>(neat)</td>
<td>24 h</td>
<td>48%</td>
</tr>
<tr>
<td>2</td>
<td>0.2</td>
<td>(neat)</td>
<td>24 h</td>
<td>66%</td>
</tr>
<tr>
<td>3</td>
<td>0.1</td>
<td>(neat)</td>
<td>24 h</td>
<td>69%</td>
</tr>
<tr>
<td>4</td>
<td>0.1</td>
<td>Toluene</td>
<td>24 h</td>
<td>50%</td>
</tr>
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<td>5</td>
<td>0.1</td>
<td>DCM</td>
<td>24 h</td>
<td>76%</td>
</tr>
<tr>
<td>6</td>
<td>0.1</td>
<td>IPA</td>
<td>24 h</td>
<td>98%</td>
</tr>
<tr>
<td>7</td>
<td>0.1</td>
<td>THF</td>
<td>24 h</td>
<td>91%</td>
</tr>
<tr>
<td>8</td>
<td>0.1</td>
<td>THF</td>
<td>12 h</td>
<td>92%</td>
</tr>
<tr>
<td>9</td>
<td>0.06</td>
<td>THF</td>
<td>24 h</td>
<td>90%</td>
</tr>
<tr>
<td>10</td>
<td>0.03</td>
<td>THF</td>
<td>24 h</td>
<td>87%</td>
</tr>
</tbody>
</table>

$^a$General conditions: substrate and 1 heated to 60 °C with stirring for the specified time. $^b$1:1 v/v with 1-octene. $^c$Determined by $^1$H NMR integration. $^d$0.9 mol% KHMDS added.

**General Procedure for Alkene Isomerisation with Complex Eta-5-BArF.**

In the glovebox, neat substrate and Eta-5-BArF were weighed into a vial. The vial was sealed, removed from the glovebox, and stirred at 110 °C for 16 h. Upon cooling, the reaction was analysed by $^1$H NMR spectroscopy (and GC if required) to assess conversion and E/Z stereoselectivity.

**Large Scale Alkene Isomerisation Reaction:**

In the glovebox, neat substrate (20 mmol) and Eta-5-BArF were weighed into a schlenk flask. Outside the glovebox, the solution was heated at 110 °C for 16 h. Upon cooling, the reaction was filtered through silica gel and washed with toluene. The mother liquor was evaporated under vacuum.
Isoeugenol (71)

Yield: 99%. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 6.87-6.84 (m, 3H), 6.35-6.29 (m, 1H), 6.12-6.02 (m, 1H), 5.57 (s, 1H), 3.90 (s, 3H), 1.85 (dd, J= 2.5 Hz and 11 Hz 3H). The $^1$H NMR is in accordance with the literature.$^{105}$

Anethole (72)

Yield: 99%. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.29-7.26 (m, 2H), 6.89-6.84 (m, 2H), 6.40-6.35 (m, 1H), 6.18-6.08 (m, 1H), 3.80 (s, 3H), 1.87 (t, J= 2.5 Hz and J= 11 Hz 3H). The $^1$H NMR is in accordance with the literature.$^{106}$

**GENERAL PROCEDURE FOR ETHENOLYSIS REACTION.**

An anhydrous and degassed solution of the phenylpropene substrate and 1,7-octadiene was added to the precatalysts in a small septum-fitted vial previously purged with inert gas. A syringe barrel fitted with a balloon and a needle was attached to the vial, which was stirred at room temperature for 2 h before being quenched by the addition of 1 mL ethyl vinyl ether. The mixture was then filtered through a pad of silica, followed by ethyl acetate. The volatiles were removed and the crude material was analysed by $^1$H NMR with the use of diethyl malonate as internal standard.

**GENERAL PROCEDURE FOR OPTIMISATION OF ETHENOLYSIS REACTION**

An anhydrous and degassed solution of the isoeugenol (46 mg, 0.25 mmol) substrate and 1,7-octadiene was added to the solid precatalysts in a small septum-fitted vial previously purged with inert gas. A syringe barrel fitted with a balloon and a needle was attached to the vial and stirred at the defined temperature for the reported time, before being quenched by the addition of 1 mL ethyl vinyl ether. The mixture was then filtered through a pad of silica,
followed by a portion of ethyl acetate. The volatiles were removed and a defined portion of crude of reaction was analysed by \textsuperscript{1}H NMR.

<table>
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<th>Entry</th>
<th>[Ru]</th>
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<th>T (h)</th>
<th>1,7-octadiene (equiv.)</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Conv. (%)</th>
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<td>M\textsubscript{2}</td>
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</table>

**GENERAL PROCEDURE FOR THE DISULFIDE SYNTHESIS**

In a vial fitted with a screw cap, in the glove box, \textbf{Eta-5} (0.00625 mmol) and KOH (0.25 mmol) were dissolved in MeOH (0.5 mL). Then, outside of the glovebox, the corresponding thiol (0.25 mmol) and \textit{n}-tetradecane (10 μL) were added and the resulting mixture was stirred at 60°C. The reaction progress was monitored by GC. After the indicated time (Scheme 4.) the solvent was removed under vacuum and the crude reaction was analysed by GC.

**GENERAL PROCEDURE FOR OPTIMIZATION OF THE DISULFIDE SYNTHESIS**

In a vial fitted with a screw cap, in the glove box, \textbf{Eta-5} (0.00625 mmol) and base (0.25 mmol) were dissolved in the reported solvent (0.5 mL). Then, outside of the glovebox, the corresponding cyclohexanthiolthiol (0.25 mmol) and \textit{n}-tetradecane (10 μL) were added and the resulting mixture was stirred at 60°C. The reaction progress was monitored by GC. After the
indicated time in table the solvent was removed under vacuum and the crude reaction was analysed by GC.

**Table 4.16: Solvent optimisation.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>T (ºC)</th>
<th>t (h)</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>DCM</td>
<td>r.t.</td>
<td>3</td>
<td>60</td>
<td></td>
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<tr>
<td>2</td>
<td>DCM</td>
<td>r.t.</td>
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<td>&gt;99 (50)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Acetone</td>
<td>60</td>
<td>24</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Toluene</td>
<td>60</td>
<td>24</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>iPrOH</td>
<td>60</td>
<td>24</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>H₂O</td>
<td>60</td>
<td>24</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>MeOH</td>
<td>60</td>
<td>1.5</td>
<td>&gt;99 (79)</td>
<td></td>
</tr>
</tbody>
</table>

*a*Reactions conditions: CySH (0.25 mmol), Eta-5 (5 mol %), KOH (0.25 mmol), dissolved in toluene (0.5 mL). *b*Conversion determined by ¹H NMR. *c*Determined by GC using n-tetradecane as internal standard.

**Table 4.17: Base and catalyst loading optimization.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat. loading, (mol %)</th>
<th>Base</th>
<th>Conv. (%)</th>
<th>Yield (%)</th>
</tr>
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<tbody>
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<td>KHMDS</td>
<td>&gt;99</td>
<td>54</td>
</tr>
<tr>
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<td>5</td>
<td>KO'Bu</td>
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</tr>
<tr>
<td>3</td>
<td>5</td>
<td>K₂CO₃</td>
<td>&gt;99</td>
<td>48</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>Et₃N</td>
<td>77</td>
<td>42</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>CsOH</td>
<td>&gt;99</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
<td>KOH</td>
<td>&gt;99</td>
<td>79</td>
</tr>
<tr>
<td>7</td>
<td>2.5</td>
<td>KOH</td>
<td>&gt;99</td>
<td>82</td>
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<tr>
<td>8</td>
<td>1</td>
<td>KOH</td>
<td>60</td>
<td>36</td>
</tr>
</tbody>
</table>

*a*Reactions conditions: CySH (0.25 mmol), Eta-5 (X mol %), KOH (0.25 mmol), dissolved in toluene (0.5 mL). *b*Conversion determined by ¹H NMR. *c*Determined by GC using n-tetradecane as internal standard.
**Dehydrogenative Coupling Reaction of Thiols with Silanes**

**Catalyzed by Eta-5.**

In a vial fitted with a screw cap, in the glovebox, Eta-5 (0.00125 mmol) and the silane (0.55 mmol) were dissolved in toluene (0.5 mL). Then, outside of the glovebox, the thiol (0.25 mmol) was added and the resulting mixture was stirred at 110ºC for 16h. After this time, the solvent was removed under vacuum. The residue was dissolved in pentane and filtered through a pad of celite to remove the catalyst (Eta-5). The volatile materials were removed under vacuum to afford the desired silylthioethers.

The silylthioethers CySSiEt$_3$ (110),$^{52}$ BnSSiEt$_3$ (105),$^{52}$ PhSSiEt$_3$ (100),$^{52}$ CySSiPh$_3$ (113),$^{52}$ and PhSSiPh$_3$ (103),$^{107}$ produced were identified by the comparison of the NMR spectra of the authentic compounds prepared according to the literature method.

**Triethyl(pentylthio)silane (98)**

![Triethyl(pentylthio)silane](image)

Yield: 96% (colorless oil). $^1$H NMR (400 MHz, CD$_2$Cl$_2$): δ 2.46 (t, $J = 7.4$ Hz, 2H), 1.64-1.54 (m, 2H), 1.42-1.25 (m, 3H), 1.02-0.97 (m, 9H), 0.89 (t, $J = 7.1$ Hz, 3H), 0.74 (dt, $J = 16.3, 6.2$ Hz, 6H). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$): δ 32.9, 31.0, 25.7, 22.3, 14.0, 7.3, 5.4. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ 22.6. HRMS (EI+): m/z calcd for C$_{11}$H$_{26}$SSi: 218.1519, found 218.1518.

**Cyclopentylthio)triethylsilane (99)**

![Cyclopentylthio)triethylsilane](image)

Yield: 94%. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): δ 3.00-2.92 (m, 1H), 1.99 – 1.89 (m, 2H), 1.74 – 1.63 (m, 2H), 1.53 – 1.43 (m, 4H), 0.94 (t, $J = 7.9$ Hz, 9H), 0.69 (dt, $J = 12.1, 7.8$ Hz, 6H). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$): δ 39.6, 37.9, 24.6, 7.3, 5.7. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ 21.5. HRMS (EI+): m/z calcd for C$_{11}$H$_{24}$SSi: 216.1368, found 216.1369.

**Dimethyl(phenyl)(phenylthio)silane (101)**

![Dimethyl(phenyl)(phenylthio)silane](image)

Yield: 95%. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): δ 7.51-7.46 (m, 2H), 7.34-7.29 (m, 3H), 7.23-7.19 (m, 3H), 7.14-7.09 (m, 2H), 0.47 (s, 3H), 0.28 (s, 3H).
\(^{13}\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 138.4, 136.9, 135.6, 134.9, 132.9, 131.7, 130.5, 129.7, 129.5, 128.7, 0.9. \(^{29}\)Si (79.3 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 9.9. HRMS (EI\(+\)): \textit{m/z} calcd for C\(_{14}\)H\(_{16}\)Si: 244.0736, found 244.0739.

**Methyldiphenyl(phenylthio)silane (102)**

\[ \text{Yield: 96\%.} \]

\(^1\)H NMR (400 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 7.55-7.49 (m, 4H), 7.35-7.25 (m, 6H), 7.18-7.13 (m, 2H), 7.10-6.98 (m, 3H), 0.65 (s, 1H). \(^{13}\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 137.7, 134.9, 134.8, 134.7, 133.9, 130.7, 130.1, 129.8, 129.6, 129.5, 129.2, 129.1, 128.7, 128.0, 127.9, 127.8, 126.9, 125.5, -2.3. \(^{29}\)Si (79.3 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 3.2. HRMS (EI\(+\)): \textit{m/z} calcd for C\(_{19}\)H\(_{18}\)Si: 306.0893, found 306.0899.

**O,O,O-Triethyl S-phenyl orthosilicothioate (104)**

\[^{1}\text{H NMR (400 MHz, CD}_{2}\text{Cl}_{2}) : \delta 7.47-7.39 (m, 2H), 7.21-7.12 (m, 3H), 3.79 (q, J = 7.0 Hz, 6H), 1.11 (t, J = 7.0 Hz, 9H).\]

\(^{13}\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 134.2, 129.5, 129.3, 127.1, 60.1, 18.3. \(^{29}\)Si (79.3 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) -58.2. HRMS (EI\(+\)): \textit{m/z} calcd for C\(_{12}\)H\(_{20}\)O\(_3\)Si: 272.0902, found 272.0903.

**(Benzylthio)dimethyl(phenyl)silane (106)**

\[^{1}\text{H NMR (400 MHz, CDCl}_{3}) : \delta 7.58-7.53 (m, 2H), 7.36-7.29 (m, 3H), 7.16-7.07 (m, 5H), 3.51 (s, 2H), 0.44 (s, 6H).\]

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 142.3, 138.3, 135.6, 134.7, 131.5, 130.2, 130.1, 129.7, 129.4, 128.5, 32.6, 0.9. \(^{29}\)Si (79.3 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 9.6. HRMS (EI\(+\)): \textit{m/z} calcd for C\(_{15}\)H\(_{18}\)SSi: 258.0893, found 258.0892.

**Benzylthio)(methyl)diphenylsilane (107)**

\[^{1}\text{H NMR (400 MHz, CDCl}_{3}) : \delta 7.57-7.53 (m, 2H), 7.34-7.27 (m, 7H), 7.15-7.09 (m, 2H), 7.09-7.03 (m, 2H), 3.51 (s, 2H), 0.68 (s, 3H).\]

\(^{13}\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)) \(\delta\) 140.3, 134.8, 134.8, 134.7, 133.9, 133.9, 130.1, 129.8,
129.6, 129.5, 128.5, 128.4, 128.1, 127.9, 127.7, 126.8, 31.3, -2.01. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ 3.6. HRMS (EI+): $m/z$ calcd for C$_{20}$H$_{26}$SSi: 320.1049, found 320.1052.

**(Benzylthio)triphenylsilane (108)**

108 could not be separated from the triphenylsilane. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.65-7.62 (m, 6H), 7.44-7.39 (m, 3H), 7.39-7.33 (m, 6H), 7.19-7.15 (m, 3H), 7.08-7.03 (m, 2H), 3.57 (s, 2H). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$): δ 140.0, 135.7, 133.0, 130.2, 128.5, 128.4, 128.1, 126.7, 31.6. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ -1.98. HRMS (EI+): $m/z$ calcd for C$_{25}$H$_{22}$SSi: 382.1206, found 382.1207.

**S-benzyl O,O,O-triethyl orthosilicothioate (109)**

Yield: 99%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.29-7.11 (m, 5H), 3.81-3.74 (m, 8H), 1.15 (t, $J = 7.0$ Hz, 9H), 0.69 (dt, $J = 12.1, 7.8$ Hz, 6H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 140.6, 129.0, 128.9, 127.5, 77.9, 77.4, 77.0, 59.8, 30.6, 18.4.

$^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ -53.9. HRMS (EI+): $m/z$ calcd for C$_{13}$H$_{22}$O$_3$SSi: 286.1053, found 286.1053.

**(Cyclohexylthio)dimethyl(phenyl)silane (111)**

Yield: 97%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.60-7.57 (m, 2H), 7.34-7.31 (m, 3H), 2.65-2.58 (m, 1H), 1.81-1.74 (m, 2H), 1.66-1.58 (m, 2H), 1.48-1.42 (m, 1H), 1.36-1.27 (m, 2H), 1.18-1.11 (m, 3H), 0.50 (s, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 138.8, 134.8, 134.0, 130.6, 128.9, 128.7, 42.0, 38.7, 27.3, 26.5, 0.90. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ 7.6. HRMS (EI+): $m/z$ calcd for C$_{14}$H$_{22}$SSi: 250.1206, found 250.1207.

**(Cyclohexylthio)(methyl)diphenylsilane (112)**

Yield: 96%. $^1$H NMR (400 MHz, CDCl$_3$): δ 7.61-7.57 (m, 4H), 7.35-7.31 (m, 6H), 2.69-2.60 (m, 1H), 1.78-1.73 (m, 2H), 1.62-1.58 (m, 2H), 1.43-1.25 (m, 3H), 1.14-1.06 (m, 3H), 0.80 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 137.2, 136.1,
136.0, 131.2, 129.3, 129.3, 42.8, 38.9, 27.6, 26.8, -0.0. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ 4.1. HRMS (EI+): $m/z$ calcd for C$_{19}$H$_{24}$SSi: 312.1362, found 312.1365.

**S-Cyclohexyl O,O,O-triethyl orthosilicothioate (114)**

![S-Cyclohexyl O,O,O-triethyl orthosilicothioate](image)

Yield: 99%. $^1$H NMR (400 MHz, CDCl$_3$): δ 3.79 (q, $J = 7.0$ Hz, 6H), 2.92-2.85 (m, 1H), 1.96-1.89 (m, 2H), 1.71-1.62 (m, 2H), 1.54-1.45 (m, 1H), 1.42-1.31 (m, 2H), 1.31-1.19 (m, 3H), 1.15 (t, $J = 7.0$ Hz, 9H). $^{13}$C NMR (100 MHz, CDCl$_3$): δ 59.3, 40.8, 37.4, 26.5, 25.6, 17.9. $^{29}$Si (79.3 MHz, CD$_2$Cl$_2$): δ -56.2. HRMS (EI+): $m/z$ calcd for C$_{12}$H$_{26}$O$_3$SSi: 278.1288, found 278.1284.

**DEHYDROGENATIVE COUPLING REACTIONS OF THIOLS WITH PINACOLBORANE CATALYZED BY ETA-5**

In a vial fitted with a screw cap, in the glove box, *Eta*-5 (0.00125 mmol) and pinacolborane (0.55 mmol) were dissolved in toluene (0.5 mL). Then, outside of the glovebox, the thiol (2) (0.25 mmol) was added and the resulting mixture was stirred at 60ºC for 16h. After this time, the solvent and the pinacolborane were removed under vacuum. The compounds were so hygroscopic that the correct elemental analysis or HRMS data could not be obtained, though satisfactory spectroscopic data were obtained.

**2-(Cyclohexylthio)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (120)**

![2-(Cyclohexylthio)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane](image)

$^1$H NMR (400 MHz, CD$_2$Cl$_2$): δ 3.05-2.92 (m, 1H), 1.93-1.83 (m, 2H), 1.68-1.58 (m, 2H), 1.49-1.45 (m, 1H), 1.29 (m, 5H), 1.2 (s, 12H). $^{13}$C NMR (100 MHz, CD$_2$Cl$_2$) δ 85.2, 41.3, 37.2, 27.0, 26.3, 25.1, 25.0. $^{11}$B NMR (128 MHz, CD$_2$Cl$_2$) 33.5.
4,4,5,5-Tetramethyl-2-(pentylthio)-1,3,2-dioxaborolane (115)

\[
\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{): } \delta 2.58 \text{ (t, } J = 7.3 \text{ Hz, 2H), 1.57-1.46 (m, 2H), 1.31-1.23 \text{ (m, 4H), 1.21 \text{ (s, 12H), 0.85-0.78 \text{ (m, 3H). }} \text{C NMR (100 MHz, CD}_2\text{Cl}_2\text{) } \delta 85.0, 32.5, 31.0, 27.0, 24.9, 22.6, 14.3. } B \text{ NMR (128 MHz, CD}_2\text{Cl}_2\text{) } \delta 33.7.\
\]

2-(Benzy1thio)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (118)

\[
\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{): } \delta 7.27-7.07 \text{ (m, 4H), 3.78 \text{ (s, 2H), 1.19 (s, 12H). C NMR (100 MHz, CD}_2\text{Cl}_2\text{) } \delta 141.6, 129.3, 129.2, 127.6, 85.9, 31.3, 25.1. } B \text{ NMR (128 MHz, CD}_2\text{Cl}_2\text{) } \delta 33.5.\
\]

4,4,5,5-Tetramethyl-2-(phenylthio)-1,3,2-dioxaborolane (116)

\[
\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{): } \delta 7.51-7.48 \text{ (m, 2H), 7.32-7.26 \text{ (m, 3H), 1.31 \text{ (s, 12H). C NMR (100 MHz, CD}_2\text{Cl}_2\text{) } \delta 133.3, 129.6, 128.7, 126.9, 85.4, 24.3. } B \text{ NMR (128 MHz, CD}_2\text{Cl}_2\text{) } \delta 32.8.\
\]

DEHYDROGENATIVE COUPLING REACTIONS OF THIOLS WITH

CATECHOLBORANE CATALYZED BY Eta-5.

In a vial fitted with a screw cap, in the glove box, Eta-5 (0.00125 mmol) and catecholborane (0.55 mmol) were dissolved in toluene (0.5 mL). Then, outside of the glovebox, the thiol (0.25 mmol) was added and the resulting mixture was stirred at 60ºC for 16h. After this time, the solvent was removed under vacuum. Due to the obtained partial conversion and the instability of these compounds, they could not be isolated as pure compounds. Thus, the correct characterization could not be completely carried out.
2-(Phenylthio)benzo[d][1,3,2]dioxaborole (117)

$$\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{: }\delta 7.51-7.47 \text{ (m, 1H), 7.40-7.34 (m, 2H), 7.28-7.22 (m, 6H).}$$

2-(Benzylthio)benzo[d][1,3,2]dioxaborole (119)

$$\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{: }\delta 7.34-7.31 \text{ (m, 1H), 7.27-7.19 (m, 3H), 7.16-7.08 (m, 3H), 7.02-6.95 (m, 2H), 3.98 (s, 2H).}$$

2-(Cyclohexylthio)benzo[d][1,3,2]dioxaborole (121)

$$\text{H NMR (400 MHz, CD}_2\text{Cl}_2\text{: }\delta 7.15-7.13 \text{ (m, 1H), 7.11-7.09 (m, 1H), 7.03-7.01 (m, 1H), 6.99-6.96 (m, 1H), 3.4-3.32 (m, 1), 2.04-1.98 (m, 2H), 1.73-1.67 (m, 2H), 1.52-1.42 (m, 3H), 1.37-1.29 (m, 3H).}$$

**GENERAL PROCEDURE FOR HYDROSILYLATION OF CARBOXYLIC ACIDS:**

In a vial fitted with a screw cap, in the glove box, **Eta-5** (1 mol% or 2 mol%) and the corresponding carboxylic acid (0.25 mmol) were dissolved in THF (0.5 mL). Then, outside of the glovebox, the PhSiH$_3$ was added (2-4 equiv.) and then, an empty balloon was placed on the vial, in order to compensate the pressure generated. The resulting mixture was stirred 16 h at 60°C. The reaction was hydrolysed with aqueous HCl (1 mL, 1M) in THF (0.5 mL) at r.t. for 1h. Then, the aqueous phase was extracted with Et$_2$O (3x5mL). The organic layer was washed with brine and dried over MgSO$_4$. The solvent was removed under reduced pressure. The residue was purified by flash chromatography on silica gel. The eluent is indicated below.
Table 4.18: Optimisation of the conditions for the reduction of benzoic acid.

\[ \text{Entry} \quad \text{Silane (equiv.)} \quad \text{Solvent} \quad \text{Conv.} \,(\%)^b \]

<table>
<thead>
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<th></th>
<th>Entry</th>
<th>Silane (equiv.)</th>
<th>Solvent</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
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<td>1</td>
<td>1</td>
<td>PhSiH(_3) (3)</td>
<td>MeOH</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>PhSiH(_3) (3)</td>
<td>iPrOH</td>
<td>60</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>PhSiH(_3) (3)</td>
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<td>Toluene</td>
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<tr>
<td>5</td>
<td>5</td>
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<td>Toluene(^c)</td>
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</tr>
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<td>6</td>
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</tr>
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<td>7</td>
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</tr>
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<td>8</td>
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<tr>
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<td>10</td>
<td>PhMe(_2)SiH(_2) (3)</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>11</td>
<td>11</td>
<td>Et(_3)SiH (3)</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>12</td>
<td>PMHS (3)</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>13</td>
<td>(EtO)(_2)MeSiH(_2) (3)</td>
<td>THF</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>14</td>
<td>PhSiH(_3) (2)</td>
<td>THF</td>
<td>&gt;98</td>
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<tr>
<td>15</td>
<td>15</td>
<td>PhSiH(_3) (1)</td>
<td>THF</td>
<td>70</td>
</tr>
</tbody>
</table>

\(^a\)Reaction conditions: \textbf{Eta}-5 (1 mol%), benzoic acid (0.25 mmol) and silane (1-3 equiv.). Hydrolysis was performed using HCl (1 mL, 1M) in THF (0.5 mL).
\(^b\)Conversion determined by \(^1\)H-NMR spectroscopy.
\(^c\)At 80ºC. \(^d\)In the absence of catalyst (\textbf{Eta}-5).

Benzyl alcohol (18)

Chromatography: pentane/Et\(_2\)O, 9:1. Yield: 84%. Spectroscopic data for the product were in accordance with the literature.\(^{108}\)

2-Phenylethanol (45)

Chromatography: pentane/Et\(_2\)O, 4:1. Yield: 80%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.38-7.33 (m, 2H), 7.29-7.25 (m, 3H), 3.88 (t, \(J = 6.6\) Hz, 1H), 2.90 (t, \(J = 6.6\) Hz, 1H). Spectroscopic data for the product were in accordance with the literature.\(^{109}\)

(2-Fluorophenyl)methanol (121)

Chromatography: pentane/Et\(_2\)O, 7:1. Yield: 79%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.47-7.38 (m, 1H), 7.33-7.24 (m, 1H), 7.19-7.11 (m, 1H), 7.08-7.03
(m, 1H), 4.76 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{110}

\textbf{(4-Methoxyphenyl)methanol (122)}

Chromatography: pentane/Et\textsubscript{2}O, 8:1. Yield: 78\%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.31 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.3 Hz, 2H), 4.62 (s, 2H), 3.84 (s, 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{111}

\textbf{(2-Hydroxyphenyl)methanol (123)}

Chromatography: pentane/Et\textsubscript{2}O, 2:1. Yield: 78\%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.22 (ddd, J = 8.0, 7.3, 1.7 Hz, 1H), 7.04 (dd, J = 7.7, 1.6 Hz, 1H), 6.89 (dd, J = 8.1, 1.1 Hz, 1H), 6.86 (td, J = 7.4, 1.2 Hz, 1H), 4.87 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{112}

\textbf{(2-Methylphenyl)methanol (124)}

Chromatography: pentane/Et\textsubscript{2}O, 4:1. Yield: 73\%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.38-7.33 (m, 2H), 7.24-7.16 (m, 3H), 4.70 (s, 2H), 2.36 (s, 3H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{108}

\textbf{(4-Bromophenyl)methanol (125)}

Chromatography: pentane/Et\textsubscript{2}O, 7:1. Yield: 80\%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 7.51-7.46 (m, 2H), 7.26-7.22 (m, 2H), 4.66 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{108}

\textbf{1-Adamantanylmethanol (126)}

Chromatography: pentane/Et\textsubscript{2}O, 4:1. Yield: 78\%. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ 3.20 (s, 2H), 2.00-1.97 (m, 3H), 1.70-1.62 (m, 6H), 1.50 (d, J = 2.4 Hz, 6H). Spectroscopic data for the product were in accordance with the literature.\textsuperscript{113}

192
Furfuryl alcohol (127)

Chemical structure: \( \text{H}_2\text{O} \)

Chromatography: pentane/Et\(_2\)O, 4:1. Yield: 65%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.40 (dd, \( J = 1.9, 0.9 \) Hz, 1H), 6.35 (dd, \( J = 3.2, 1.8 \) Hz, 1H), 6.30 (dd, \( J = 3.2, 0.7 \) Hz, 1H), 4.61 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\(^{114}\)

Thiencylmethanol (128)

Chemical structure: \( \text{S} \)

Chromatography: pentane/Et\(_2\)O, 5:1. Yield: 60%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.29 (dd, \( J = 5.0, 1.3 \) Hz, 1H), 7.02 (ddt, \( J = 3.5, 1.3, 0.8 \) Hz, 1H), 6.98 (dd, \( J = 5.0, 3.5 \) Hz, 1H), 4.84 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\(^{108}\)

Undec-10-en-1-ol (130)

Chemical structure: \( \text{H}_2\text{O} \)

Chromatography: pentane/Et\(_2\)O, 4:1. Yield: 79%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 5.87 (ddt, \( J = 16.9, 10.2, 6.7 \) Hz, 1H), 5.10-4.95 (m, 2H), 3.69 (t, \( J = 6.6 \) Hz, 2H), 2.14-2.05 (m, 2H), 1.70-1.56 (m, 3H), 1.49-1.29 (m, 13H). Spectroscopic data for the product were in accordance with the literature.\(^{108}\)

4-(Hydroxymethyl)benzonitrile (131)

Chemical structure: \( \text{NC} \)

Chromatography: pentane/Et\(_2\)O, 3:1. Yield: 79%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.65 (d, \( J = 8.3 \) Hz, 2H), 7.53 - 7.44 (m, 2H), 4.78 (s, 2H). Spectroscopic data for the product were in accordance with the literature.\(^{115}\)

Methyl 4-(hydroxymethyl)benzoate (132)

Chemical structure: \( \text{MeO}_2\text{C} \)

Chromatography: pentane/Et\(_2\)O, 2:1. Yield: 80%. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.98-7.91 (m, 2H), 7.38-7.31 (m, 2H), 4.69 (s, 2H), 3.84 (s, 3H). Spectroscopic data for the product were in accordance with the literature.\(^{116}\)
4-Hydroxy-1-(piperidin-1-yl)butan-1-one (133)

Chromatography: AcOEt. Yield: 73%. $^1$H NMR (300 MHz, CDCl$_3$): δ 3.69 (br s, 2H), 3.58-3.54 (m, 2H), 3.43-3.40 (m, 2H), 2.51 (t, J = 6.5 Hz, 2H), 1.96-1.83 (m, 2H), 1.66-1.42 (m, 8H). $^{13}$C NMR (75 MHz, CDCl$_3$): δ 171.8, 62.9, 46.8, 42.9, 31.1, 27.6, 26.5, 25.6, 24.5. Spectroscopic data for the product were in accordance with the literature.$^{117}$

3-(Hydroxymethyl)benzophenone (47)

Chromatography: pentane/Et$_2$O, 3:1. Yield: 82%. $^1$H NMR (300 MHz, CDCl$_3$): δ 7.82-7.78 (m, 3H), 7.71 (dt, J = 7.7, 1.4 Hz, 1H), 7.64-7.56 (m, 2H), 7.52-7.45 (m, 3H), 4.78 (s, 2H). Spectroscopic data for the product were in accordance with the literature.$^{118}$

Dimethyl(phenyl)silyl benzoate (134)

In a vial fitted with a screw cap, in the glove box, Eta-5 (1 mol%) and benzoic acid (0.25 mmol) were dissolved in THF (0.5 mL). Then, outside of the glovebox, the PhMe$_2$SiH was added (0.25 mmol). The resulting mixture was stirred 16 h at room temperature. $^1$H NMR (300 MHz, CDCl$_3$): δ 8.26-8.20 (m, 2 H), 7.90-7.86 (m, 2 H), 7.68-7.62 (m, 1 H), 7.52-7.49 (m, 5H) 0.83 (s, 6 H). Spectroscopic data for the product were in accordance with the literature.$^{60}$

GENERAL PROCEDURE FOR THE RUTHENIUM-CALAYSED BORYLATION

In a vial fitted with a screwcap, in the glovebox, bis(pinacolato)diboron (0.25 mmol), the corresponding pyridine (0.25 mmol) and Eta-5-SiEt$_3$ (0.00375 mmol, 1.5 mol%) were dissolved in 1,4-dioxane (0.5 mL). Then, outside of the glovebox, the resulting mixture was
stirred 16 h at 110°C. Solvent was removed under reduced pressure. The crude material was purified by recrystallization from dichloromethane/hexane.

**Table 4.19:** Optimisation of the conditions for the borylation of 2-phenylpyridine.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Ru] (mol %)</th>
<th>Solvent</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>Toluene</td>
<td>20</td>
</tr>
<tr>
<td>2</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>NMP</td>
<td>-b</td>
</tr>
<tr>
<td>3</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>DMF</td>
<td>-b</td>
</tr>
<tr>
<td>4</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>DMAc</td>
<td>-b</td>
</tr>
<tr>
<td>5</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>1,4-dioxane</td>
<td>&gt;95</td>
</tr>
<tr>
<td>6</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>1,4-dioxane&lt;sup&gt;c&lt;/sup&gt;</td>
<td>-b</td>
</tr>
<tr>
<td>7</td>
<td>Eta-5-SiEt3 (2.5)</td>
<td>1,4-dioxane&lt;sup&gt;d&lt;/sup&gt;</td>
<td>-b</td>
</tr>
<tr>
<td>8</td>
<td>Eta-5-Si(OEt)3 (2.5)</td>
<td>1,4-dioxane</td>
<td>19</td>
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<tr>
<td>9</td>
<td>Eta-5-SiMe2Ph (2.5)</td>
<td>1,4-dioxane</td>
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<tr>
<td>10</td>
<td>Eta-5-SiMePh2 (2.5)</td>
<td>1,4-dioxane</td>
<td>12</td>
</tr>
<tr>
<td>11</td>
<td>Eta-5-SiPh3 (2.5)</td>
<td>1,4-dioxane</td>
<td>27</td>
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<tr>
<td>12</td>
<td>Eta-5-SiEt3 (2.0)</td>
<td>1,4-dioxane</td>
<td>&gt;95</td>
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<tr>
<td>13</td>
<td>Eta-5-SiEt3 (1.5)</td>
<td>1,4-dioxane</td>
<td>&gt;95</td>
</tr>
<tr>
<td>14</td>
<td>Eta-5-SiEt3 (1.0)</td>
<td>1,4-dioxane</td>
<td>85</td>
</tr>
</tbody>
</table>

<sup>a</sup>Conversion determined by <sup>1</sup>H-NMR spectroscopy. <sup>b</sup>Starting material was recovered unchanged. 60°C. 80°C.

**Table 4.17:** Borylation of 2-phenylpyridine using [Ru(p-cymene)Cl<sub>2</sub>]<sub>2</sub> (Ru-5).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive</th>
<th>Solvent</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AdCO&lt;sub&gt;2&lt;/sub&gt;H</td>
<td>toluene</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>AdCO&lt;sub&gt;2&lt;/sub&gt;H</td>
<td>1,4-dioxane</td>
<td>68</td>
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<tr>
<td>3</td>
<td>AdCO&lt;sub&gt;2&lt;/sub&gt;H</td>
<td>NMP</td>
<td>-b</td>
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<tr>
<td>4</td>
<td>KOAc</td>
<td>1,4-dioxane</td>
<td>76</td>
</tr>
<tr>
<td>5</td>
<td>MesCO&lt;sub&gt;2&lt;/sub&gt;H</td>
<td>1,4-dioxane</td>
<td>23</td>
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<tr>
<td>6</td>
<td>PhCO&lt;sub&gt;2&lt;/sub&gt;H</td>
<td>1,4-dioxane</td>
<td>63</td>
</tr>
<tr>
<td>7</td>
<td>PPh&lt;sub&gt;3&lt;/sub&gt;</td>
<td>1,4-dioxane</td>
<td>-b</td>
</tr>
</tbody>
</table>
2-[2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine (135)

\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}):} & \quad \delta \ 8.67 (d, J = 5.5 \text{ Hz}, 1\text{H}), 8.01-7.92 (m, 1\text{H}), \\
& \quad 7.80 (d, J = 7.7 \text{ Hz}, 1\text{H}), 7.72 (d, J = 7.4 \text{ Hz}, 1\text{H}), 7.66 (d, J = 7.7 \text{ Hz}, 1\text{H}), 7.41 \\
& \quad (td, J = 7.4, 1.2 \text{ Hz}, 1\text{H}), 7.36 (ddd, J = 7.2, 5.5, 1.2 \text{ Hz}, 1\text{H}), 7.29 (td, J = 7.4, \\
& \quad 1.2 \text{ Hz}, 1\text{H}), 1.43 \text{ s}, 12\text{H}).
\end{align*}

Spectroscopic data for the product were in accordance with the literature.\textsuperscript{119}

2-[4-Methoxycarbonyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine (136)

\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}):} & \quad \delta \ 8.72 (d, J = 5.0 \text{ Hz}, 1\text{H}), 8.36 (d, J = \\
& \quad 1.0 \text{ Hz}, 1\text{H}), 8.06-7.98 (m, 2\text{H}), 7.88 (d, J = 8.0 \text{ Hz}, 1\text{H}), 7.72 (d, J = \\
& \quad 8.0 \text{ Hz}, 1\text{H}), 7.45 (ddd, J = 7.5, 5.6, 1.0 \text{ Hz}, 1\text{H}), 3.93 \text{ s}, 3\text{H}, 1.44 \text{ s}, 12\text{H}).
\end{align*}

\textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \delta 167.8, 155.5, 143.9, 142.5, 141.5, 133.0, 132.7, 130.0, \\
124.1, 121.5, 118.7, 80.9, 52.6, 27.4. \textbf{MS} (ESI): \textit{m/z} 340 (M+H\textsuperscript{+}, 93); \textbf{HRMS} (ESI): Calcd. for 
\textit{C}_{19}\textit{H}_{23}\textit{BNO}_{4}(M+H\textsuperscript{+}), 340.1715; found 340.1718.

2-[5-Methoxycarbonyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine (137)

\begin{align*}
\text{\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}):} & \quad \delta \ 8.74-8.65 (m, 1\text{H}), 8.35-8.33 (m, 1\text{H}), \\
& \quad 8.12-7.97 (m, 2\text{H}), 7.92 (dt, J = 8.0, 1.1 \text{ Hz}, 1\text{H}), 7.80 (dd, J = 7.6, \\
& \quad 0.7 \text{ Hz}, 1\text{H}), 7.44 (ddd, J = 7.5, 5.6, 1.3 \text{ Hz}, 1\text{H}), 3.94 \text{ s}, 3\text{H}, 1.43 \\
& \quad (s, 12\text{H}).
\end{align*}

Spectroscopic data for the product were in accordance with the literature.\textsuperscript{119}
2-[4-Methoxy-2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-pyridine

(138)

\[ \text{1H NMR (300 MHz, CDCl}_3): \delta 8.59 (d, J = 5.7 \text{ Hz, } 1\text{H}), 7.90 (t, d, J = 8.0, 1.5 \text{ Hz, } 1\text{H}), 7.67 (d, J = 8.0 \text{ Hz, } 1\text{H}), 7.58 (d, J = 8.4 \text{ Hz, } 1\text{H}), 7.28-7.23 \text{ (m, } 2\text{H}), 6.81 (dd, J = 8.4, 2.5 \text{ Hz, } 1\text{H}), 3.88 (s, 3\text{H}), 1.42 (s, 12\text{H}); \]

\[ \text{13C NMR (100 MHz, CDCl}_3): \delta 162.7, 156.6, 142.9, 141.8, 129.9, 122.8, 121.4, 116.8, 116.4, 113.8, 80.2, 55.3, 27.1; \]

\[ \text{MS (ESI): } m/z 312 (M+H}^+, 100); \text{ HRMS (ESI): Calcd. for C}_{18}H_{23}BNO}_3 (M+H}^+, 312.176; \text{ found 312.1768.} \]

2-[5-Methoxy-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine

(139)

\[ \text{1H NMR (300 MHz, CDCl}_3): \delta 8.65 (ddd, J = 5.6, 1.6, 1.0 \text{ Hz, } 1\text{H}), 7.95 \]

\[ \text{(dd, } J = 8.0, 7.4, 1.6 \text{ Hz, } 1\text{H}), 7.75 (dt, J = 8.0, 1.0 \text{ Hz, } 1\text{H}), 7.61 (d, J = 8.0 \text{ Hz, } 1\text{H}), 7.35 (ddd, J = 7.5, 5.6, 1.2 \text{ Hz, } 1\text{H}), 7.17 (d, J = 2.3 \text{ Hz, } 1\text{H}), 6.98 (dd, J = 8.0, 2.3 \text{ Hz, } 1\text{H}), 3.84 (s, 3\text{H}), 1.41 (s, 12\text{H}). \text{ Spectroscopic data for the product were in accordance with the literature.}^{119} \]

10-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzo[h]quinolone (140)

\[ \text{1H NMR (300 MHz, CDCl}_3): \delta 8.90 (dd, J = 4.6, 1.6 \text{ Hz, } 1\text{H}), 8.19 (dd, J = 7.9, 1.6 \text{ Hz, } 1\text{H}), 7.87 (d, J = 7.9 \text{ Hz, } 1\text{H}), 7.81 (d, J = 8.9 \text{ Hz, } 1\text{H}), 7.77 (d, J = 7.0 \text{ Hz, } 1\text{H}), 7.73-7.66 \text{ (m, } 1\text{H}), 7.66 (d, J = 8.9 \text{ Hz, } 1\text{H}), 7.52 (dd, J = 7.9, 4.5 \text{ Hz, } 1\text{H}), 1.55 (s, 12\text{H}). \text{ Spectroscopic data for the product were in accordance with the literature.}^{119} \]

2-[4-Fluoro-2-(4,4,5,5-Tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-pyridine

(141)

197
$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.65 (d, $J = 5.9$ Hz, 1H), 8.03-7.91 (m, 1H), 7.75 (d, $J = 8.0$ Hz, 1H), 7.63 (dd, $J = 8.4$, 4.7 Hz, 1H), 7.39-7.33 (m, 2H), 6.96 (td, $J = 8.7$, 2.5 Hz, 1H), 1.41 (s, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 165.6 (d, $J = 252.4$ Hz), 155.6, 143.1, 142.2, 132.9, 123.1 (d, $J = 8.6$ Hz), 122.4, 118.2 (d, $J = 19.9$ Hz), 117.2, 115.0 (d, $J = 23.8$ Hz), 80.3, 27.0; $^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -110.0; MS (ESI): $m/z$ 300 (M+H$^+$, 81); HRMS (ESI): Calcd. for C$_{17}$H$_{19}$BFNO$_2$ (M+H$^+$), 300.1567; found 300.1566.

2-[5-Fluoro-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]pyridine (142)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.64 (d, $J = 5.7$ Hz, 1H), 7.99 (td, $J = 7.7$, 1.5 Hz, 1H), 7.81 (d, $J = 8.0$ Hz, 1H), 7.48 (d, $J = 7.5$ Hz, 1H), 7.48-7.37 (m, 1H), 7.30 (dd, $J = 7.9$, 2.7 Hz, 1H), 7.03 (t, $J = 8.1$ Hz, 1H), 1.45 (s, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 165.1 (d, $J = 245.1$ Hz), 155.0, 142.9, 141.9, 140.0 (d, $J = 12.7$ Hz), 130.3 (d, $J = 7.8$ Hz), 123.4, 118.7 (d, $J = 26.4$ Hz), 117.8, 117.5 (d, $J = 2.9$ Hz), 81.0, 27.4; $^{19}$F NMR (282 MHz, CDCl$_3$): $\delta$ -105; MS (ESI): $m/z$ 300 (M+H$^+$, 100); HRMS (ESI): Calcd. for C$_{17}$H$_{19}$BFNO$_2$ (M+H$^+$), 300.1567; found 300.1567.

2-(2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)naphthalen-1-yl)pyridine (143)

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.77 (dd, $J = 5.5$, 0.7 Hz, 1H), 8.34-8.26 (m, 2H), 8.01 (ddd, $J = 8.1$, 7.5, 1.6 Hz, 1H), 7.93-7.86 (m, 3H), 7.55 (ddd, $J = 8.5$, 6.8, 1.5 Hz, 1H), 7.47 (ddd, $J = 8.0$, 6.8, 1.2 Hz, 1H), 7.39 (ddd, $J = 7.5$, 5.5, 1.1 Hz, 1H), 1.42 (s, 12H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 157.8, 144.5, 142.0, 135.1, 133.9, 131.9, 130.0, 130.1, 128.8, 127.4, 125.6, 123.2, 122.2, 81.1, 27.5. MS (ESI): $m/z$ 332 (M+H$^+$, 100); HRMS (ESI): Calcd. for C$_{21}$H$_{23}$BNO$_2$ (M+H$^+$), 300.1816; found 332.1820.
2-[4-Methyl-2-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-phenyl]-pyridine (144)

\[\text{H NMR (300 MHz, CDCl}_3\):} \delta 8.63 (\text{ddd, } J = 5.6, 1.5, 1.0 \text{ Hz, } 1\text{H}), 7.92 (\text{ddd, } J = 8.0, 7.4, 1.5 \text{ Hz, } 1\text{H}), 7.74 (\text{d, } J = 8.0 \text{ Hz, } 1\text{H}), 7.55 - 7.49 (m, 2\text{H}), 7.31 (\text{ddd, } J = 7.4, 5.6, 1.0 \text{ Hz, } 1\text{H}), 7.11 - 7.07 (m, 1\text{H}), 2.39 (s, 3\text{H}), 1.43 (s, 12\text{H}). \]

Spectroscopic data for the product were in accordance with the literature.\(^{120}\)

**General procedure for the one pot borylation Suzuki-Miyaura coupling.**

In a vial fitted with a screwcap, in the glovebox, bis(pinacolato)diboron (0.25 mmol), the 2-phenylpyridine (145) (0.25 mmol) and \(\text{Eta-5-SiEt}_3\) (0.00375 mmol, 1.5 mol%) were dissolved in 1,4-dioxane (0.5 mL). Then, outside of the glovebox, the resulting mixture was stirred 16 h at 110°C. Volatiles was removed under reduced pressure. Then Suzuki-Miyaura coupling was carried out following a procedure developed in our laboratory.\(^{121}\) In the glovebox, KOH (0.375 mmol, 1.5 equiv) was added to the mixture. A solution of the palladium pre-catalyst [\(\text{Pd(IPr^\#)(cinnamyl)Cl}\)] in DME (1 mL of DME, 3.0 mol%) and the chloroanisole (0.375 mmol, 1.5 equiv.) were added sequentially. The reaction mixture was then stirred (800 rpm) at room temperature or 60°C during 16 h. Then the solution was cooled, quenched with water (5 mL), and the aqueous layer was extracted with DCM (3 x 10 mL). The combined organic layers were dried over \(\text{MgSO}_4\) and the volatiles were evaporated under vacuum. The crude product was finally purified by flash chromatography on silica gel.

2-(4'-methoxy-[1,1'-biphenyl]-2-yl)pyridine (146)

\[\text{H NMR (300 MHz, CDCl}_3\):} \delta 8.64 (\text{ddd, } J = 4.9, 1.8, 0.9 \text{ Hz, } 1\text{H}), 7.71-7.62 (m, 1\text{H}), 7.47-7.36 (m, 4\text{H}), 7.15-7.04 (m, 3\text{H}), 6.90 (d, \text{J} = 7.9 \text{ Hz,}}

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1H), 6.82-6.72 (m, 2H), 3.79 (s, 3H). Spectroscopic data for the product were in accordance with the literature.122

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APPENDIX: SCIENTIFIC CONTRIBUTIONS

FEATURE ARTICLES


ACCOUNT


PUBLICATIONS


**COMMUNICATION IN CONFERENCES**


**OTHER SCIENTIFIC CONTRIBUTIONS**
**Scientific Awards**

2014 Selected to the **La Roche-Hoffman RSC organic division symposium**
2013 **JSPS** short-term fellowship (short term) awarded.
2012 Selected to the **CaRLa/BASF winterschool**