Iron and Ruthenium Catalysts for Hydrogen Transfer Reactions

By

Tarn Cormac Johnson

A thesis submitted in partial fulfilment of the degree of Doctor of

Philosophy in Chemistry

University of Warwick, Department of Chemistry

May 2012

Contents.

Acknowledgements.

Firstly, I would like to thank Professor Martin Wills for giving me the opportunity to carry out this work and for all his help, support and patience throughout my studies.

I would also like to thank the group members past and present for all their help and for making the Wills group an enjoyable and productive place to work. In particular, I would like to thank Katherine Jolley, Dr. David Morris, Dr. Rina Soni, Dr. Vimal Parekh, Dr. Charles Manville, Dr. Jonathan Hopewell, Dr. José Eduardo Damas Martins, Dr. Silvia Gosiewska, Moftah Darwish, Alexander Bisset, Vicky Marlow, Zhijia Fang, Jamie Godfrey and William Totty.

Secondly, I would like to thank Dr. Guy Clarkson for X-ray crystallography and Dr. Adam Clarke, Dr. Ivan Prokes, Edward Tunnah, Dr. Lijiang Song and Philip Aston for NMR spectroscopy and mass spectrometry.

I would also like to thank Professor Pat Unwin and Dr. Massimo Peruffo at the University of Warwick and Dr. Mariolino Carta and Professor Neil McKeown at Cardiff University for their assistance in some collaborative work that is not included in this thesis.

Finally, I would like to thank my family and friends for all their support throughout my PhD.

Declaration.

The research described in this thesis is solely the work of the author unless otherwise stated. These studies were carried out at the Department of Chemistry, University of Warwick between November 2008 and April 2012. The content of this thesis has not been submitted, either wholly or partially for a degree at any other academic institution.

Some of this work has appeared in the scientific literature in the following publications:

1. T. C. Johnson, D. J. Morris and M. Wills, *Chem. Soc. Rev*, 2010, **39**, 81-88.

2. T. C. Johnson, G. J. Clarkson and M. Wills, *Organometallics*, 2011, **30**, 1859-1868.

3. J. P. Hopewell, J. E. D. Martins, T. C. Johnson, J. Godfrey and M. Wills, *Org. Biomol. Chem*, 2012, **10**, 134-145.

Abstract.

The ruthenium catalysed oxidation of 1-phenylethanol derivatives with the release of hydrogen gas has been studied. A hydrogen acceptor was introduced in an effort to elucidate the rate-determining step of the reaction.

The transfer of hydrogen from complex alcohols to simple aldehydes and ketones was pursued as a process for obtaining simple alcohols for fuel cell applications. The Shvo catalyst was identified as being the most efficient catalyst for the oxidation of difficult substrates.

A family of iron analogues of the Shvo catalyst were synthesised and studied as precatalysts for the oxidation of alcohols. Catalyst activation was achieved by the removal of a CO ligand using trimethylamine-*N*-oxide and the oxidation of 1-phenylethanol derivatives with acetone was studied. Simple aldehydes were evaluated as hydrogen acceptors and a novel formylation reaction was discovered.

Asymmetric iron analogues of the Shvo catalyst were synthesised and applied to the asymmetric transfer hydrogenation of acetophenone using 5:2 formic acid/triethylamine. The synthesis of further analogues with a tethering group was investigated to improve catalyst stability and enantioselectivity.

Novel chiral diamine and amino-alcohol ligands containing 1,2,3-triazole functionalities were developed as ligands for the asymmetric transfer hydrogenation of ketones. Tridentate diaminotriazoles provided the best activity and selectivity in the reduction reactions with $Ru_3(CO)_{12}$.

Abbreviations.

δ_C	^{13}C NMR chemical shift (ppm)
δ_H	^1H NMR chemical shift (ppm)
δ_P	^{31}P NMR chemical shift (ppm)
$[\alpha]_D$	Optical rotation
Å	Angstroms
Ac	Acetyl
aq	Aqueous
Ar	Aryl
ATH	Asymmetric transfer hydrogenation
atm	Atmospheric
BINAP	2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl
Bn	Benzyl
Boc	*tert*-Butoxycarbonyl
BPin	Pinacol borane
BQC	2,2'-biquinoline-4,4'-dicarboxylic acid
Bu	Butyl
C	Concentration
CBS	Corey-Bakshi-Shibata
COD	Cyclooctadiene
conv	Conversion
Cp	Cyclopentadienyl
Cp*	Pentamethylcyclopentadienyl
CuAAC	Cu(I) catalysed azide-alkyne cycloaddition

Cy	Cyclohexyl
d	Doublet
DCC	Dicyclohexyl carbodiimide
DCM	Dichloromethane
dd	Doublet of doublets
DKR	Dynamic kinetic resolution
DMAP	4-Dimethylaminopyridine
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
DPEN	1,2-Diphenylethylenediamine
dppb	Diphenylphosphinobutane
dppf	Diphenylphosphinoferrocene
dppp	Diphenylphosphinopropane
e.e.	Enantiomeric excess
en	Ethylenediamine
ESI	Electospray ionisation
Et	Ethyl
FA	Formic acid
FT-IR	Fourier transform infrared
GC	Gas chromatography
h	Hour
HMB	Hexamethylbenzene
HPLC	High pressure liquid chromatography
i	Iso
IBX	*o*-Iodoxybenzoic acid

IMes	1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene
IR	Infrared
J	Coupling constant (Hz)
lit	Literature
Ln	Ligands
m	Multiplet
m	Meta
M+	Molecular ion
M	Mol dm^{-3}
mDa	Milli Daltons
Me	Methyl
MHz	Megahertz
mins	Minutes
mp	Melting point
MPV	Meerwein-Ponndorf-Verley
MPVO	Meerwein-Ponndorf-Verley-Oppenauer
Ms	Mesyl
m/z	Mass to charge ratio
n	Primary
NHC	*N*-Heterocyclic carbene
NMO	*N*-Methylmorpholine-*N*-oxide
NMR	Nuclear magnetic resonance
o	Ortho
p	Para
pet	Petroleum

Ph	Phenyl
PMA	Phosphomolybdic acid
PMHS	Polymethylhydrosiloxane
ppm	Parts per million
Pr	Propyl
psi	Pound-force per square inch
q	Quartet
rt	Room temperature
s	Singlet
t	Triplet
T	Temperature
t or *tert*	Tertiary
TBAF	Tetrabutylammonium fluoride
TBS or TBDMS	*tert*-Butyldimethylsilyl
Tf	Triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TIPS	Triisopropylsilyl
TLC	Thin layer chromatography
TMANO	Trimethylamine *N*-oxide
TMSCl	Trimethylsilyl chloride
TOF	Turnover frequency
TON	Turnover number
TPAP	Tetrapropylammonium perruthenate
Ts	*p*-Toluenesulphonyl

TsDPEN   1,2-Diphenyl-*N*-(*p*-toluenesulfonyl)ethylenediamine

UV   Ultraviolet

ν_{max} Wave number (cm^{-1})

W   Watt

1 Introduction.
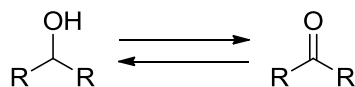
The oxidation of alcohols and the reduction of ketones are fundamental organic transformations available to the synthetic chemist. As such, many different procedures for these transformations are known and the development of new and improved procedures is always of interest.

1.1 Oxidation of Alcohols.

Historically, stoichiometric (or greater) quantities of chromium or manganese reagents have been used for the oxidation of both primary and secondary alcohols. The Jones oxidation[1] (CrO_3, H_2SO_4, acetone), Collins reagent[2] (CrO_3, pyridine), pyridinium chlorochromate[3] and MnO_2[4] are all prominent examples.
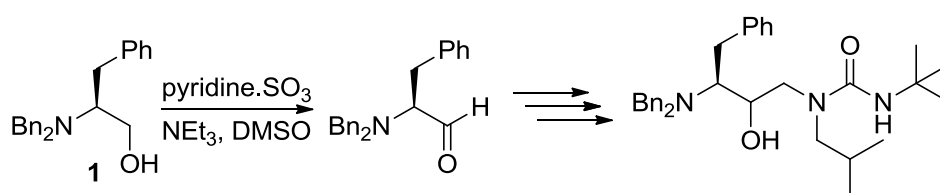
Scheme 1. A Parikh-Doering oxidation en route to a pharmaceutical intermediate.

More contemporary methods are not reliant on the use of stoichiometric metal reagents. Activated DMSO reagents are widely used for the oxidation of both primary and secondary alcohols. Many different electrophilic activating agents can be used but the most commonly used are oxalyl chloride (Swern oxidation),[5] carbodiimides (Pfitzner-Moffatt oxidation)[6] and pyridine-sulphurtrioxide (Parikh-

Doering oxidation).[7] The Parikh-Doering oxidation was performed on 190 kg of alcohol **1** to give the product aldehyde in >95 % purity en route to a key intermediate of an HIV protease inhibitor (Figure 1).[8]
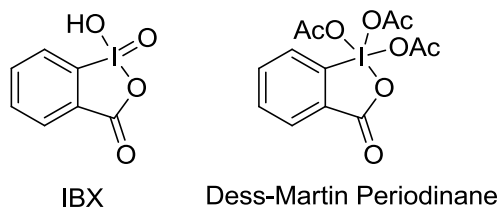
Figure 1. Hypervalent iodine compounds for alcohol oxidation reactions.

Hypervalent iodine compounds have also been well studied; *o*-iodoxybenzoic acid[9] (IBX) and the related Dess-Martin periodinane[10] readily and selectively oxidise primary and secondary alcohols at room temperature in high yield.
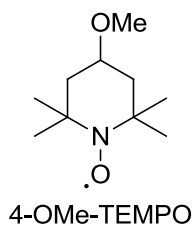
Figure 2. A stable *N*-oxyl radical catalyst for the oxidation of primary alcohols.

The development of catalytic procedures for the oxidation of alcohols is desirable in terms of cost and in order to reduce the quantities of waste generated. The Anelli oxidation, reported in 1987,[11] involves the use of a catalytic amount of the stable *N*-oxyl radical, 4-OMe-TEMPO, in conjunction with sodium hypochlorite as the terminal oxidant for the oxidation of primary alcohols to aldehydes or acids (when longer reaction times are used).
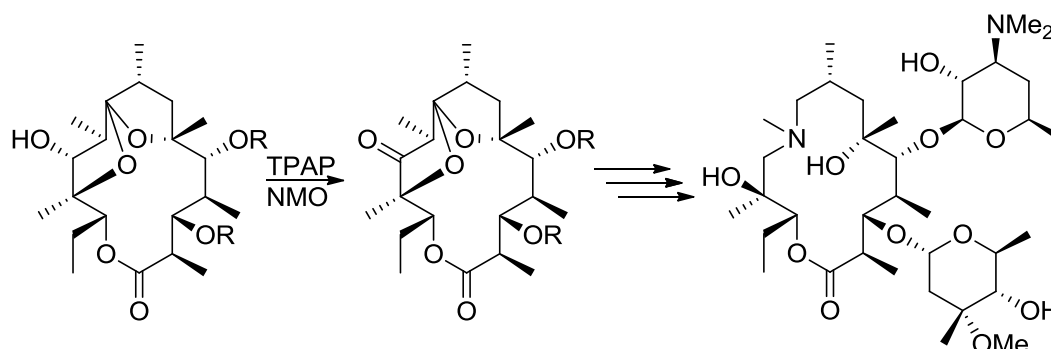
Scheme 2. Oxidation of a secondary alcohol with TPAP in the synthesis of an azithromycin analogue.

Transition metal catalysed procedures are also known, typically utilising ruthenium and a variety of different terminal oxidants including O_2,[12-15] iodosylbenzene[16] and amine-*N*-oxides.[17] A well known example is the Ley oxidation, in which primary and secondary alcohols are oxidised by tetrapropylammoniumperruthenate (TPAP) and *N*-methylmorpholine-*N*-oxide (NMO) as the terminal oxidant.[18] The oxidation of a macrolide in the synthesis of an azithromycin analogue for antibiotic applications was performed using TPAP[19] (Scheme 2).

1.2 Reduction of Ketones.

The reduction of ketones to secondary alcohols is most commonly carried out with $NaBH_4$[20] or $LiAlH_4$.[21] In the reduction of prochiral ketones, however, this results in the formation of a racemic product. The isolation of chiral compounds in enantiomerically pure form is of great importance as one enantiomer of a compound can have very different properties in biological systems compared to the other enantiomer despite having the same constitution. This is due to the inherent chirality of biological systems. A well known example is the drug thalidomide

which was prescribed for the treatment of morning-sickness during pregnancy. One enantiomer of thalidomide had the desired therapeutic properties but the other enantiomer was responsible for causing birth defects.[22] One example of an important enantioselective transformation is the asymmetric reduction of ketones to give enantiomerically enriched secondary alcohols which will be discussed below.
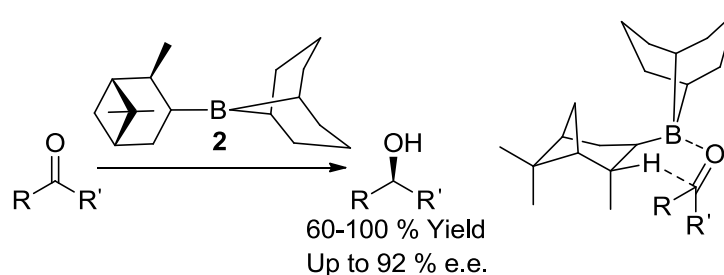
Scheme 3. Alpine borane and its interaction with ketones.

α,β-Acetylenic ketones can be reduced in high enantiomeric excess (e.e.) by a chiral borane reagent, alpine borane (**2**).[23] Hydride transfer occurs from the chiral α-pinene substituent of the borane reagent to the ketone (Scheme 3). This method has also been used for the reduction of 1-deuterio aldehydes to produce chiral 1-deuterio primary alcohols for mechanistic studies.[24]
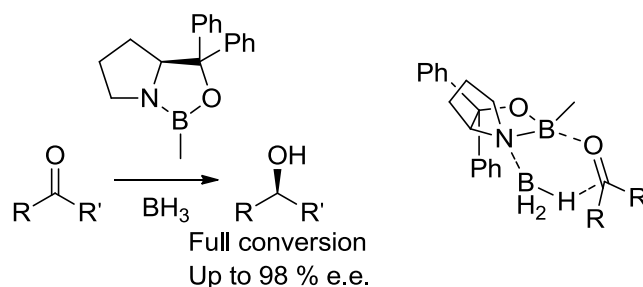
Scheme 4. The CBS reduction of prochiral ketones to chiral alcohols with a Lewis acidic and Lewis basic oxazaborolidine.

The Corey-Bakshi-Shibata (CBS) reduction utilises a chiral oxazaborolidine catalyst to mediate the asymmetric reduction of ketones by borane.[25] Aliphatic, allylic and benzylic ketones can be reduced in high yield and high e.e. in very short

reaction times.[26] The Lewis acidic boron coordinates to the ketonic substrate and the Lewis basic amine holds the borane in place to direct the reduction to one face of the ketone (Scheme 4).
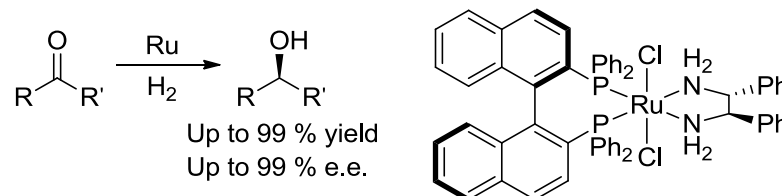
Scheme 5. Noyori's Ru/diphosphine/diamine catalyst for asymmetric pressure hydrogenation.

The use of transition metal catalysts for the hydrogenation of ketones under pressure of hydrogen gas is another successful way of introducing asymmetry. Noyori and co-workers developed one of the first pressure hydrogenation catalysts capable of selectively reducing ketones in preference to olefins.[27-29] Utilising ruthenium (II) complexes containing both a chiral diamine and chiral diphosphine, a wide range of ketones can be reduced in high e.e. including benzylic and allylic ketones. Earlier work omitting the chiral diamine component was also successful but substrates required a nearby directing group such as an acid, ester, or hydroxyl.[30]

1.3 Transfer Hydrogenation.

Transfer hydrogenation is a mild catalytic process for oxidation and reduction reactions in which hydrogen is removed from a donor molecule and used to reduce an acceptor molecule. It is generally regarded as a safer and more practical alternative to hydrogenation since high pressures of hydrogen gas are not required.

$$DH_2 \ + \ \underset{R \quad R}{\overset{X}{\|}} \ \xrightleftharpoons{\text{Catalyst}} \ D \ + \ \underset{R \quad R}{\overset{XH}{\bigvee}}$$
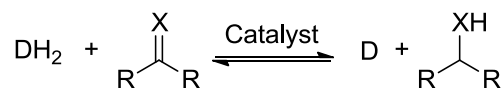
Scheme 6. A transfer hydrogenation reaction where X = O, NR or CR$_2$. DH$_2$ = hydrogen donor.

1.3.1 The Meerwein-Ponndorf-Verley Reduction.

The first reported example of a transfer hydrogenation reaction was the Meerwein-Ponndorf-Verley (MPV) reduction which was independently reported by Meerwein and Schmidt,[31] Ponndorf[32] and Verley[33] in the mid-1920s. It was found that a stoichiometric amount of an aluminium alkoxide reagent would facilitate the transfer of hydrogen from 2-propanol to aldehydes and ketones to give the corresponding primary and secondary alcohols selectively. Over a decade later, Oppenauer reported the reverse reaction, where alcohols were oxidised to aldehydes and ketones by aluminium *tert*-butoxide using acetone as the hydrogen acceptor.[34]

$$\underset{}{\overset{OH}{\bigvee}} \ + \ \underset{R \quad R}{\overset{O}{\|}} \ \underset{\underset{\text{Oppenauer}}{\xleftarrow{\hspace{1cm}}}}{\overset{\text{MPV}}{\xrightarrow{\text{Al(OR)}_3}}} \ \underset{}{\overset{O}{\|}} \ + \ \underset{R \quad R}{\overset{OH}{\bigvee}}$$
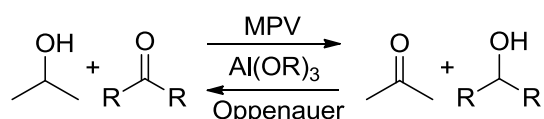
Scheme 7. The MPV reduction and Oppenauer oxidation reactions.

The reaction is thought to proceed through a six-membered cyclic transition state in which the hydrogen donor is coordinated to the aluminium centre as an alkoxide and the hydrogen acceptor is coordinated by a Lewis acidic interaction. Direct hydride transfer from the donor to the acceptor takes place to give an

alkoxide product which is released from the metal by an alcoholysis reaction with the bulk solvent.
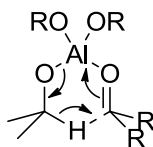
Figure 3. Mechanism of the MPV reduction.

Early publications concerning the MPVO reaction required stoichiometric quantities of the aluminium reagent for the reaction to proceed but the reaction was made catalytic in 1977 by Rathke and co-workers.[35] Performing an Oppenauer oxidation with 5 mol % $Al(O^tBu)_3$ and 2.5 mol % TFA, cyclohexanol was oxidised in 80 % yield after 1 min at 0 °C with benzaldehyde as the hydrogen acceptor. Akamanchi and Noorani demonstrated a similar approach for the MPV reduction using 8.3 mol % $Al(O^iPr)_3$ as the catalyst, 0.3 mol % TFA as the co-catalyst and 2-propanol as the hydrogen donor.[36] A range of aldehydes and ketones were reduced with moderate to high conversions in up to 24 h.

More recent work in this field has focussed on the use of ligands to generate catalysts with higher activities or to promote asymmetric induction to give enantiomerically enriched products.[37-40]

In 1993 Evans and co-workers devised a C_2-symmetric aminodiol ligand for the samarium (III) catalysed MPV reduction of acetophenone derivatives. With 5 mol % of the *in situ* generated catalyst, ketones were reduced in 1-2 h at 25 °C with a high level of enantioselectivity (Table 1).[41]

5 mol % Sm catalyst
25 equiv 2-propanol
THF, rt, 1-2 h

$Ar \overset{O}{\underset{}{\|}} R \longrightarrow Ar \overset{OH}{\underset{}{}} R$
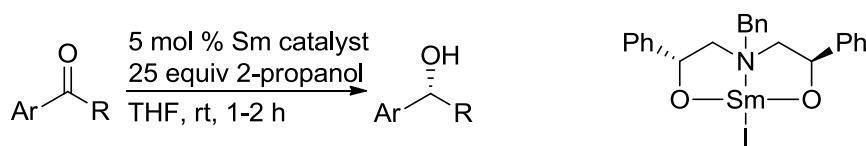
Aryl	R	Conversion (%)	e.e. (%)
Ph	Me	83	96 (R)
2-ClC$_6$H$_4$	Me	100	97 (R)
2-MeOC$_6$H$_4$	Me	100	96 (R)
4-ClC$_6$H$_4$	Me	91	94 (R)
4-MeOC$_6$H$_4$	Me	43	92 (R)
4-NO$_2$C$_6$H$_4$	Me	100	94 (R)
Ph	Et	66	73 (R)
2-ClC$_6$H$_4$	Et	95	68 (R)
1-Naphthyl	Me	98	97 (R)
2-Naphthyl	Me	84	96 (R)

Table 1. The asymmetric MPV reduction of ketones with a chiral samarium catalyst.

1.3.2 Transition Metal-Catalysed Transfer Hydrogenation.

The use of transition metals to catalyse transfer hydrogenation reactions is a familiar concept, with examples from as early as the 1950s.[42] The mechanism of hydrogen transfer by transition metal complexes is distinct from the direct transfer mechanism seen in the MPV reduction, transfer of hydrogen from donor to acceptor takes place via a metal hydride intermediate. A general mechanism is illustrated in Scheme 8, beginning with the substitution of chloride in the catalyst precursor by the hydrogen donor, followed by β-elimination to generate a metal hydride complex. Insertion of the ketonic substrate into the metal-hydride bond generates

the product which is displaced by the hydrogen donor to complete the catalytic cycle. The addition of base is known to accelerate these reactions by increasing the concentration of alkoxide present and therefore increasing the rate at which the pre-catalyst is activated.[43-45]
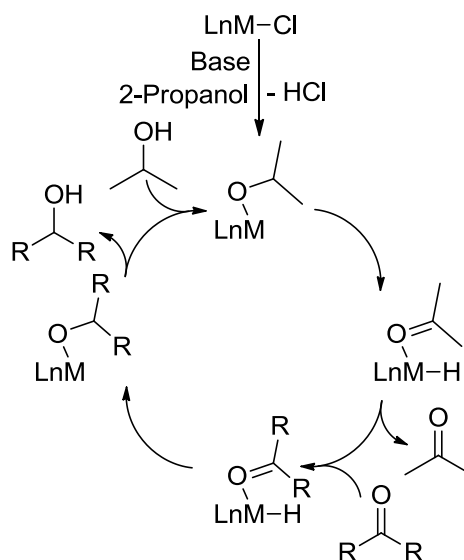
Scheme 8. The monohydride mechanism for transfer hydrogenation.

An alternative mechanism involving metal dihydride intermediates is also possible. The replacement of chloride in a dichloride complex by the hydrogen donor followed by β-elimination generates a metal dihydride complex. Insertion of the ketonic substrate into a metal-hydride bond followed by a reductive elimination generates the product alcohol. Oxidative addition across the O-H bond of the hydrogen donor followed by β-elimination regenerates the metal dihydride complex.
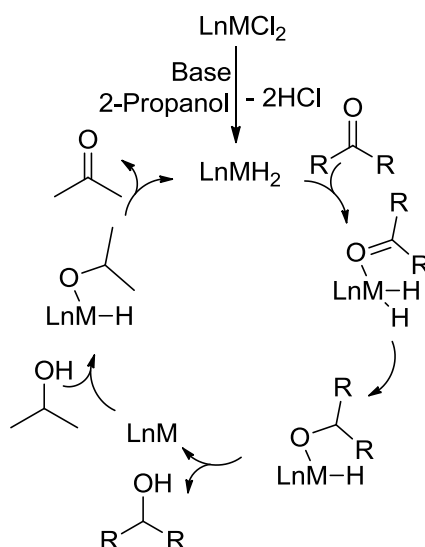
Scheme 9. The dihydride mechanism for transfer hydrogenation.

It is possible to differentiate between these mechanisms experimentally by a deuterium labelling study as shown by Bäckvall and co-workers for a range of ruthenium, rhodium and iridium catalysts.[46] In the reaction shown in Scheme 10 (S)-α-deutero-1-phenylethanol is racemised in the presence of acetophenone by a transition metal catalyst. If the monohydride mechanism is operating then the metal hydride originates from the α-proton of the alcohol and so deuterium should be retained in the α-position after the racemisation has taken place. If the dihydride mechanism is operating then both the hydroxyl proton and the α-proton are transferred to the metal centre to generate a metal dihydride and so scrambling of the deuterium atom is observed.
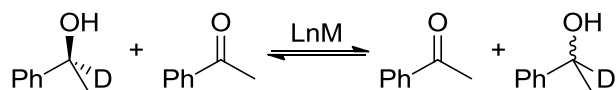
Scheme 10. Racemisation of (S)-α-deutero-1-phenylethanol.

The mechanisms discussed so far have been inner-sphere mechanisms; mechanisms in which the substrate binds to the metal centre during catalysis. Outer-sphere mechanisms for transfer hydrogenation in which the substrate does

not bind to the metal centre are also known. Noyori and co-workers described the ruthenium catalyst **3** shown in Figure 14 for the asymmetric transfer hydrogenation of ketones.[47, 48] Reaction with base eliminates HCl from the catalyst precursor to generate 16-electron intermediate **4** via an $E1_{cB}$ mechanism. This intermediate abstracts a proton and hydride from the hydrogen donor in a concerted manner via a 6-membered cyclic transition state to generate 18-electron ruthenium hydride complex **5**. A concerted transfer of a hydride from the metal centre and a proton from a bound amine to the substrate takes place to generate the alcohol product and **4**. The amine functionality in the ligand plays an important role in the catalytic cycle, taking the hydroxyl proton from the hydrogen donor and delivering it to the oxygen atom of the ketonic substrate. The term "metal-ligand bifunctional catalysis" is often used to describe catalysts in which the ligand plays a role in the catalytic cycle.[48-50]
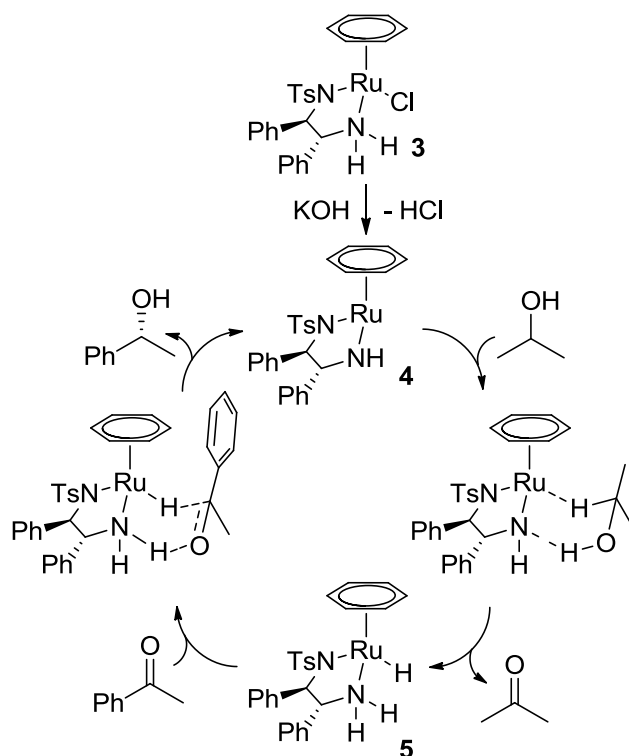
Scheme 11. The mechanism of transfer hydrogenation by Noyori's catalyst, **3**.

1.4 The Oxidation of Alcohols with a Hydrogen Acceptor.

1.4.1 Ruthenium Catalysts.

The first transfer hydrogenation for the oxidation of alcohols to be catalysed by a transition metal complex was reported by Wang and Bäckvall in 1992.[51] A range of aliphatic, benzylic and cyclic secondary alcohols were oxidised to the corresponding ketones by $RuCl_2(PPh_3)_3$ with K_2CO_3 in refluxing acetone (Table 2).
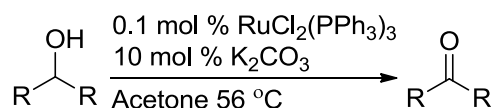
Substrate	Conversion (%)	Time (h)
Indan-1-ol	98	1
1-Tetralol	99	7
1-Phenylethanol	97	2
1-Phenylpropan-1-ol	86	12
Cyclopentanol	94	1.5
Cyclohexanol	62	12
Octan-2-ol	27	40

Table 2. The oxidation of alcohols catalysed by $RuCl_2(PPh_3)_3$.

The oxidation of primary alcohols was not possible with this catalytic system, possibly due to decarbonylation of the product aldehydes to give an inactive carbonyl complex.
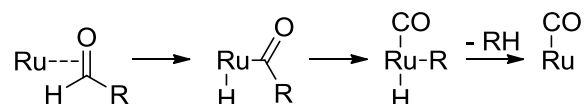
Scheme 12. Decarbonylation of an aldehyde by a ruthenium complex.

The oxidation of primary alcohols to aldehydes was achieved by Hulshof *et al*. by heating at 130 °C in *p*-xylene with RuCl$_2$(*S*-BINAP) as the catalyst and diphenylacetylene as the hydrogen acceptor.[52] A selection of the substrates tested are listed in Table 3. Linear aliphatic, allylic and benzylic alcohols were oxidised with high conversions, aliphatic alcohols with branches close to the hydroxyl group had lower conversions. The presence of an internal alkyne does not erode the selectivity of the reaction even though it could act as a hydrogen acceptor; a terminal alkyne however, resulted in a significant drop in selectivity.
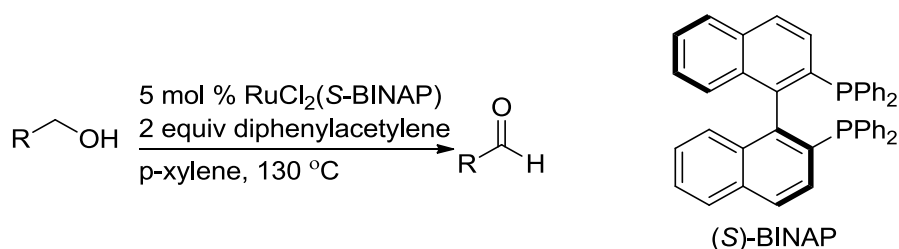
Substrate	Time (h)	Conv (%)	Selectivity (%)
	2	100	81
	2	94	73
	4	100	40
	2	100	97
	5	85	84
	2	79	87
	4	100	92
	2	60	53
	2	100	100

Table 3. The oxidation of primary alcohols by RuCl$_2$(*S*-BINAP).

1.4.2 Iridium Catalysts.

The oxidation of secondary alcohols in aqueous media by an iridium catalytic system was reported by Ajjou in 2001.[53] Utilising 0.4 mol % [Ir(COD)Cl]$_2$, 6 mol % 2,2'-biquinoline-4,4'-dicarboxylic acid dipotassium salt (BQC) and 1 equivalent of Na$_2$CO$_3$ in a 2:1 water/acetone mixture at 90 °C, a range of aliphatic, benzylic and cyclic secondary alcohols were oxidised to the corresponding ketones over 4 h. Benzylic alcohols were oxidised in > 90 % conversion with the more sterically hindered 1-phenylpropan-1-ol not performing as well, giving an 80 % conversion. Ring size had an effect on the oxidation of cyclic alcohols with cyclooctanol achieving a much higher conversion, 76 %, than cyclohexanol, 15 %. Chain length appeared not to affect the oxidation of aliphatic alcohols with octanol and decanol both having a conversion of 21 %.

Substrate	Conversion (%)
1-Phenylethanol	98
1-Phenylpropan-1-ol	80
1-(4-methoxyphenyl)ethanol	96
1-(4-bromophenyl)ethanol	90
1-Tetralol	97
9-Hydroxyfluorene	96
Benzhydrol	90
Cyclooctanol	76
Cyclohexanol	15
Octanol	21
Decanol	21
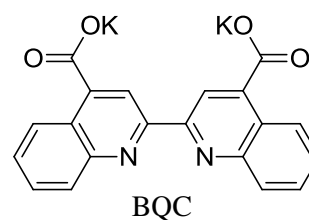
Table 4. The oxidation of secondary alcohols by an aqueous iridium catalyst. 0.4 mol % [Ir(COD)Cl]$_2$, 6 mol % BQC, 1 equivalent Na$_2$CO$_3$, 2:1 water/acetone, 90 °C.

In 2002 Fujita, Furukawa and Yamaguchi reported on the oxidation of primary and secondary alcohols with [Cp*IrCl$_2$]$_2$ as the catalyst, K$_2$CO$_3$ and acetone as the solvent and hydrogen acceptor.[54] With 1 mol % of the iridium dimer and 10 mol % K$_2$CO$_3$, benzyl alcohol was oxidised by 71 %. Decreasing the substrate concentration from 0.1 M to 0.033 M resulted in an increase in conversion to 87 %. A range of substituted benzylic primary alcohols were oxidised in moderate to high conversion with alcohols bearing an electron-donating group in the *para* position giving the highest conversions and electron-withdrawing groups giving the lowest. Substitution at the *ortho* position led to a drop in conversion whereas *meta* substitution had no effect. Aliphatic primary alcohols gave only modest conversions. Secondary alcohols could also be efficiently oxidised, only requiring 0.25 mol % [Cp*IrCl$_2$]$_2$ and a substrate concentration of 1 M to reach high conversions.

1.4.2.1 *N*-Heterocyclic Carbene Complexes.
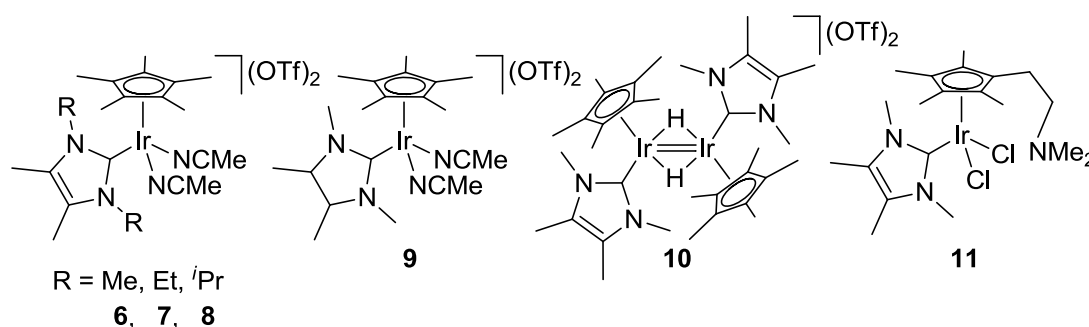
Figure 4. Iridium complexes for the oxidation of alcohols.

In subsequent publications Yamaguchi *et al*. synthesised and tested various iridium *N*-heterocyclic carbene (NHC) complexes for the oxidation of alcohols using acetone as the hydrogen acceptor.[55-57] The activity of each complex for the oxidation of 1-phenylethanol to acetophenone is shown in Table 5. Increasing steric bulk around the NHC ligand caused a decrease in activity for the oxidation reaction and the same was true of a saturated derivative. The dimeric complex **10** was shown to be almost inactive. A good result was obtained with complex **11**, bearing a pendant dimethylamino group which served the role of base for the reaction making the addition of K_2CO_3 unnecessary. A control experiment in the presence of K_2CO_3 surprisingly showed a much lower conversion than in its absence.
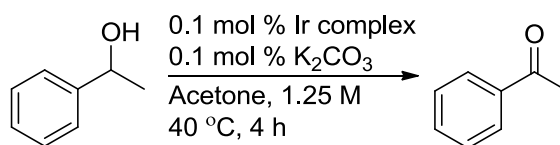
Complex	6	7	8	9	10	11[a]	11[b]
Conversion (%)	95	92	29	87	7	95	63

Table 5. The oxidation of 1-phenylethanol by iridium complexes. [a] Carried out with 0.2 mol % AgOTf and without K_2CO_3. [b] Carried out with 0.2 mol % AgOTf.

1.4.2.2 Pincer Complexes.

A report published by C. M. Jensen and co-workers in 2001 detailed the use of PCP pincer iridium complex **12** for the oxidation of alcohols with *tert*-butylethylene as the hydrogen acceptor.[58] The reactions were carried out in toluene in a sealed tube at 200 °C over 18 h with a catalyst loading of 14 mol % and 5.9 equivalents of *tert*-butylethylene. A few examples of primary and secondary

aliphatic alcohols were fully converted to the corresponding aldehydes and ketones. Benzyl alcohol and 1-phenylethanol were also fully converted.
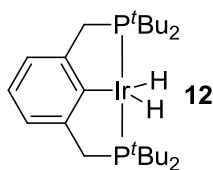
Figure 5. A PCP pincer iridium complex used by Jensen for the oxidation of alcohols.

An efficient PCP pincer iridium catalyst for the oxidation of benzylic secondary alcohols has been developed by Gelman and co-workers.[59] With 0.1 mol % complex **13** and 5 mol % KO^{t}Bu in refluxing acetone as the solvent and hydrogen acceptor a range of benzylic alcohols were oxidised to acetophenone derivatives. 1-Phenylethanol was 92 % converted after 0.5 h and after a total of 6 h had reached 96 % under an atmosphere of nitrogen. Surprisingly when the same reaction was conducted under an atmosphere of air the result was almost identical, giving conversions of 91 and 98 % after 0.5 and 6 h respectively. The presence of electron-donating methyl and methoxy groups and an electron-withdrawing bromine substituent in the *para* position have little impact on the conversion, being over 92 % in each case, although a strongly electron-withdrawing cyano group resulted in a lower conversion of only 45 %. A bromine substituent in the *ortho* position resulted in a lower conversion of 34 %; this was attributed to an electron-withdrawing effect rather than sterics after observing high conversion with a methoxy group in the *ortho* position. The oxidation of a primary alcohol, benzyl alcohol, resulted in the formation of an ester and only traces of the aldehyde product. This complex is also highly efficient for the racemic reduction of ketones with 2-propanol, achieving turnover frequencies of up to 3600000 h^{-1}.[60]
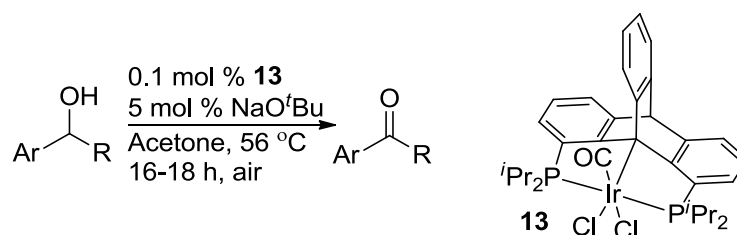
Aryl	R	Conversion (%)
Ph	Me	98
4-MeC$_6$H$_4$	Me	97
4-MeOC$_6$H$_4$	Me	98
4-BrC$_6$H$_4$	Me	92
3-BrC$_6$H$_4$	Me	90
2-BrC$_6$H$_4$	Me	34
4-CNC$_6$H$_5$	Me	45
2,4-(MeO)$_2$C$_6$H$_3$	Me	94
2-Naphthyl	Me	99
Ph	Ph	98
4-MeC$_6$H$_4$	Ph	99
C$_6$H$_5$	H	N/D

Table 6. The oxidation of benzylic secondary alcohols catalysed by an iridium complex.

1.4.2.3 Aminoalcohol Complexes.

The bifunctional iridium aminoalcohol complex **14** was shown by Hiroi *et al*. to catalyse the oxidation of primary alcohols to aldehydes using 2-butanone as the solvent and hydrogen acceptor.[61] A low substrate concentration (0.08 M) was found to be beneficial with more concentrated solutions leading to lower conversions and the formation of esters. Refluxing in 2-butanone (80 °C) for 16-18

18

h with a catalyst loading of 1 mol %, a range of benzylic alcohols were oxidised in moderate to high conversion. Benzyl alcohol was 71 % converted; introducing an electron-donating methyl or methoxy group in the *para* position gave higher conversions of 92 and 91 % respectively and an electron-withdrawing bromine substituent gave a lower conversion of 40 %. An aliphatic alcohol, octan-1-ol, was only 33 % converted and an allylic alcohol, cinnamyl alcohol, was oxidised with a conversion of 72 %. Interestingly base was not required for the reactions to proceed, this could be attributed to the iridium complex being an unsaturated 16-electron complex which is analogous to the 16-electron intermediate **4** found in Noyori's catalytic system described earlier; Complex **14** is the 'true' catalyst rather than a catalyst precursor which needs activation.
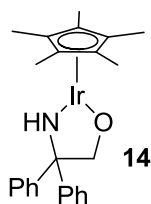
Figure 6. A bifunctional iridium catalyst for the oxidation of primary alcohols.

1.4.3 Bimetallic Catalysts.
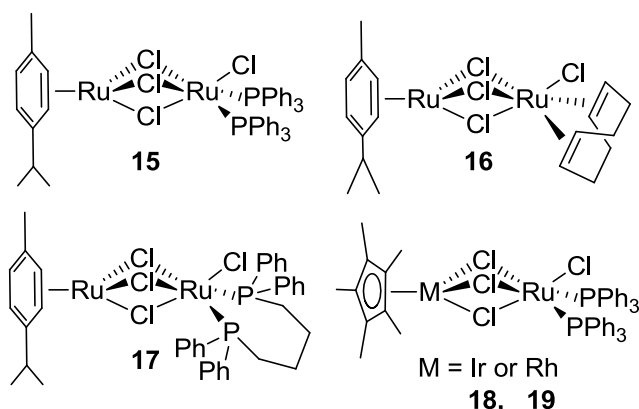
Figure 7. Bimetallic complexes used by Severin for the oxidation of secondary alcohols.

A series of bimetallic complexes were synthesised by Severin and co-workers and their activities in the oxidation of benzhydrol were reported.[62] At a catalyst loading of 0.2 mol % with 1 equivalent of K_2CO_3 in refluxing 2-butanone, benzhydrol was oxidised in 92 and 94 % conversion by complexes **15** and **19** after a period of 3 h. The other complexes were less successful, reaching 20-30 % conversion. The individual 'halves' of the complexes that were used in the syntheses of **15-19** were also tested and showed less than 20 % conversion, which could imply that a bimetallic species is catalysing the reaction instead of splitting to form two catalytically active monomers. The most active catalyst, complex **19**, was tested with other substrates and the results are listed in Table 7. Notably, all of the other substrates tested reached high conversions after 1 h, including aliphatic and cyclic alcohols. The oxidation of a primary alcohol, benzyl alcohol, however, was unsuccessful.

Substrate	Conversion (%)
Benzhydrol	94[a]
1-Phenylethanol	99
1-Indanol	99
1-Tetralol	97
Cyclopentanol	95
Cyclohexanol	85
Cycloheptanol	99
Octan-2-ol	86

Table 7. The oxidation of secondary alcohols catalysed by **19**. 0.2 mol % **19**, 1 equivalent K_2CO_3, 2-butanone, reflux, 1 h. [a] Conversion after 3 h.

In a subsequent paper a mixed Rh/Ru complex was identified as an active catalyst for alcohol oxidations at room temperature with acetone as the hydrogen

acceptor.[63] With 0.5 mol % **20** and 1 equivalent K$_2$CO$_3$, 1-phenylethanol was oxidised with a conversion of 94 % after 6 h at room temperature in a 1:1 acetone/benzene mixture. Aliphatic and cyclic alcohols could also be oxidised but required a longer reaction time of 24 h to achieve good conversions. Primary alcohols were also applicable to this system with benzyl alcohol achieving a 54 % conversion after 24 h. An electron-donating group was necessary to reach high conversions with primary alcohols; 4-methoxybenzyl alcohol was 90 % converted after 24 h.
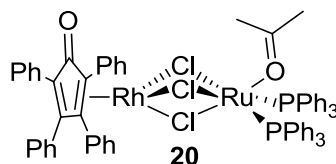
Figure 8. A heterobimetallic complex for the oxidation of alcohols at room temperature.

1.5 The Oxidation of Alcohols Without a Hydrogen Acceptor.

If an alcohol is oxidised by a transition metal complex in the absence of a hydrogen acceptor or other oxidant the elimination of hydrogen gas may occur. This is currently of great interest due to the higher atom economy of the reaction caused by the absence of a terminal oxidant and because of the potential of the reaction for generating hydrogen gas for use as a renewable fuel source.[64, 65] The mechanism of this process becomes distinct from transfer hydrogenation after the generation of a metal hydride species, at this point protonation occurs from an acidic proton, followed by hydrogen gas release or in the case of a metal dihydride species a reductive elimination may occur. This reaction is often referred to as a 'dehydrogenation'.
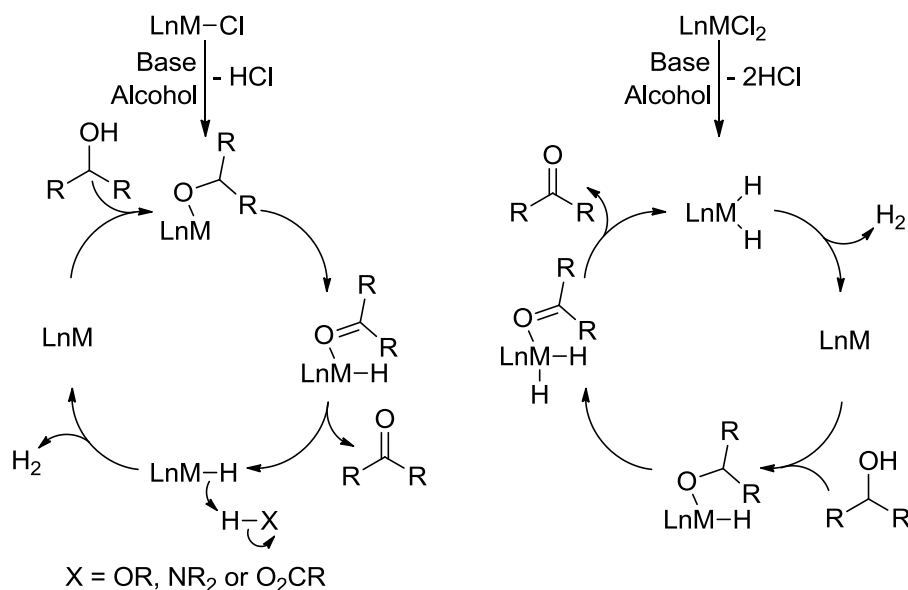
Scheme 13. Hydrogen evolution from alcohols via metal mono- and dihydride species.

1.5.1 Carboxylic Acid Complexes.

An early example of this process, published in 1977 by Dobson and Robinson, demonstrated the activity of the complex [Ru(OCOCF$_3$)$_2$(CO)(PPh$_3$)$_2$] (**21**) for the dehydrogenation of a range of primary and secondary alcohols.[66, 67] The proposed mechanism involves the attack of alkoxide on the metal centre and loss of trifluoroacetic acid, followed by a β-elimination step to give a metal hydride species. Reaction with acid liberates dihydrogen and regenerates the catalyst. Each reaction was carried out at the boiling point of the alcohol being studied with catalyst loadings in the order of ~0.03 mol % and 12 equivalents of trifluoroacetic acid to promote the reaction. Initial turnover frequencies of 2952 h^{-1} for heptan-1-ol and 1620 h^{-1} for cyclooctanol were reported. Rates for lower molecular weight

primary and secondary alcohols were low (<100 h^{-1}) although notably, the highest initial TOF was achieved for benzyl alcohol with a value of 8172 h^{-1}.

This system has also been studied by Rybak and Ziółkowski who heterogenised the catalyst on a polystyrene support[68] and also by Jung and Garrou who reported a series of analogous catalysts replacing triphenylphosphine with bidentate diphosphine ligands.[69] An initial rate 3.5 times higher than the original catalyst was reported for the oxidation of cyclohexanol when diphenylphosphinoethane was used. Catalyst deactivation was also studied with loss of activity being attributed to the formation of metal carbonyl complexes following decarbonylation of product aldehydes and also to loss of the volatile trifluoroacetic acid ligands from the system.
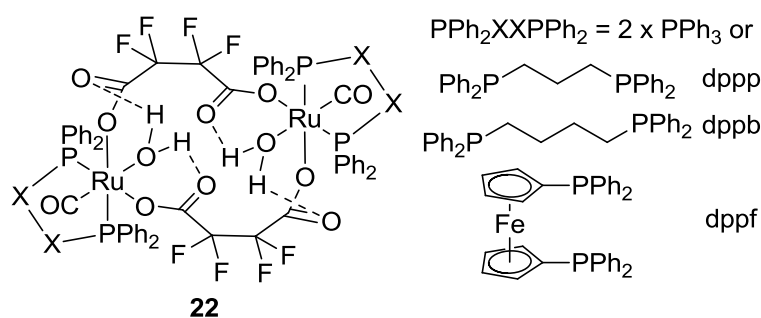
Figure 9. Complexes used by Hulshof for the acceptorless dehydrogenation of alcohols.

Later studies performed by Hulshof *et al*. addressed the problem of volatility of the acid component by utilising a bidentate acid ligand that negates the need for excess acid in the system.[70] Increased activity for the oxidation of 1-phenylethanol relative to **21** was reported with the diphenylphosphinoferrocene (dppf) complex proving the most active, giving a 70 % conversion after 24 h at a loading of 0.1 mol % in *p*-xylene at 130 °C. In an experiment with a lower catalyst loading of 0.025 % a turnover number of 651 was observed; this indicates a more stable catalytic

system in comparison to **21** which stopped converting after 72 turnovers. A speculated catalytic cycle (Scheme 14) involves the coordination of an alcohol to the metal centre and deprotonation by a carboxylate function of the ligand to give a carboxylic acid which dissociates to generate a vacant coordination site for β-elimination to take place, resulting in a hydride complex. After dissociation of the ketone, reaction with the acid eliminates H_2 and regenerates the catalyst.
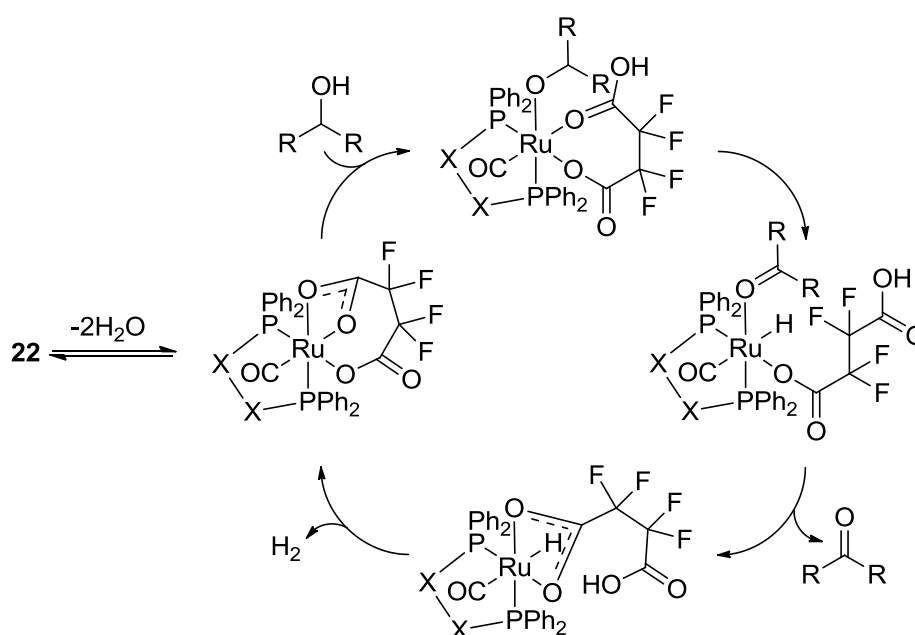
Scheme 14. The mechanism of alcohol dehydrogenation catalysed by **22**.

1.5.2 Phosphine and Amine Ligands.

Beller *et al*. identified two complexes; [RuCl$_3$.xH$_2$O] and [RuCl$_2$(p-cymene)]$_2$ as suitable precursors for the dehydrogenation of 2-propanol under basic conditions.[71] A series of phosphine ligands were then screened with 315 ppm [RuCl$_3$.xH$_2$O] and 0.8 M NaO^{i}Pr or NaOH at 90 °C with a 2:1 ligand to metal ratio in order to identify an efficient catalyst. Ligand **27** proved the most effective giving a turnover frequency of 155 h^{-1} after 2 h which dropped to 78 h^{-1} after a total of 6 h.

In a later publication a series of amine ligands were also screened for the dehydrogenation of 2-propanol with 16 ppm [RuCl$_2$(p-cymene)]$_2$ and 0.8 M NaO^{i}Pr at 90 °C with a 1:1 ligand to metal ratio.[72] In general the amine ligands studied provided more active catalysts than the previously studied phosphines and it was observed that trialkylamines generally were the best performing, however, aminoalcohol **29** gave the highest turnover frequency of 373 h^{-1} after 2 h which fell to 236 h^{-1} after a total of 6 h. The use of **32** gave the most stable catalyst, giving a total of 17215 turnovers after 268 h with 4 ppm [RuCl$_2$(p-cymene)]$_2$ and a 10:1 ligand to metal ratio.
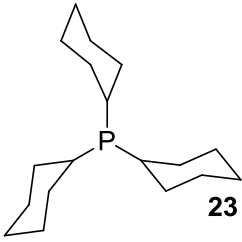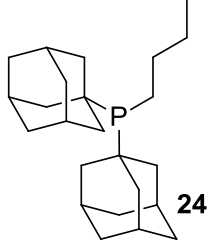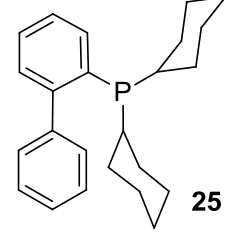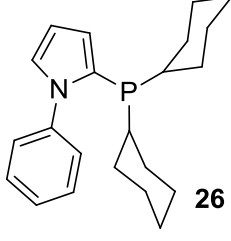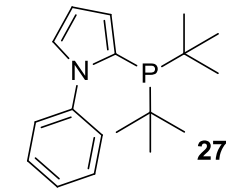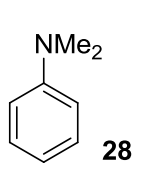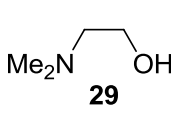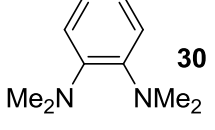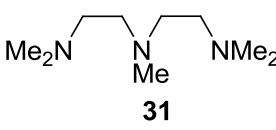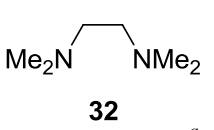
Ligand	Base	Time (h)	TOF (h^{-1})
23[a]	NaO^{i}Pr	2	101
		6	57
24[a]	NaOH	2	104
		6	55
25[a]	NaO^{i}Pr	2	114
		6	61
26[a]	NaO^{i}Pr	2	120
		6	64
27[a]	NaO^{i}Pr	2	155
		6	78
28[b]	NaO^{i}Pr	2	348
		6	211
29[b]	NaO^{i}Pr	2	373
		6	236
30[b]	NaO^{i}Pr	2	296
		6	177
31[b]	NaO^{i}Pr	2	322
		6	203
32[b]	NaO^{i}Pr	2	309
		6	190

Table 8. The dehydrogenation of 2-propanol with Ru phosphine/amine catalysts. [a] 315 ppm [RuCl$_3$.xH$_2$O], 0.8 M NaO^{i}Pr or NaOH, 90 °C, 2:1 ligand:Ru. [b] 16 ppm [RuCl$_2$(p-cymene)]$_2$, 0.8 M NaO^{i}Pr, 90 °C, 1:1 ligand:Ru.

1.5.3 Arene and Carbene Complexes.

Adair and Williams demonstrated that a range of ruthenium aryl, cyclopentadienyl and carbene complexes are active for the dehydrogenation of 1-phenylethanol under basic conditions in refluxing toluene.[73] Grubbs' 1st generation catalyst, PhCH=Ru(PCy$_3$)$_2$Cl$_2$ and [RuCl$_2$(p-cymene)]$_2$ were found to be the most efficient.

Ru Complex	Conversion (%)
CpRuCl(PPh$_3$)$_2$	16
(Indenyl)RuCl(PPh$_3$)$_2$	22
[(Benzene)RuCl$_2$]$_2$	24
[(p-Cymene)RuCl$_2$]$_2$	58
PhCH=Ru(PCy$_3$)$_2$Cl$_2$	71
Ru(IMes)(PPh$_3$)$_2$CO(H)$_2$[a]	17

Table 9. The oxidation of 1-phenylethanol catalysed by ruthenium complexes. 5 mol % Ru, 5 mol % KOH, toluene, reflux, 24 h. [a] No base was used.

During optimisation studies, the [RuCl$_2$(p-cymene)]$_2$ complex proved to be more efficient in the presence of 4 equivalents of triphenylphosphine per ruthenium. Experiments with other substrates under optimised conditions showed that benzylic alcohols were more easily oxidised than aliphatic alcohols and a primary alcohol, benzyl alcohol, was essentially inactive. The [RuCl$_2$(p-cymene)]$_2$/PPh$_3$ system was more effective at oxidising the more sterically demanding alcohol, benzhydrol.
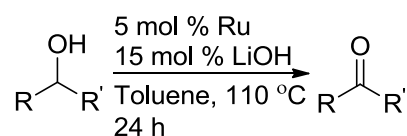
R	R'	PhCH=Ru(PCy$_3$)$_2$Cl$_2$ Conversion (%)	[RuCl$_2$(p-cymene)]$_2$ Conversion (%)[a]
Ph	Me	100	100
4-FC$_6$H$_4$	Me	100	100
4-MeOC$_6$H$_4$	Me	100	100
Ph	H	2	3
Ph	Ph	54	100
Ph(CH$_2$)$_2$	Me	58	91
α-Tetralol		100	100

Table 10. The oxidation of other alcohols. [a] With 20 mol % PPh_3.

An efficient catalyst for the dehydrogenation of primary alcohols was reported by Prades, Peris and Albrecht under base-free conditions.[74] Complex **33**, containing a 1,2,3-triazolylidene ligand, was able to oxidise a range of benzylic alcohols in refluxing toluene at a 5 mol % catalyst loading. Electron-withdrawing groups in the *para* position gave lower conversions but electron-donating groups had little impact. Increasing steric hindrance by introducing a group in the *ortho* position gave a lower conversion. Aliphatic alcohols gave only low conversions (< 5 %). A secondary alcohol, 1-phenylethanol, was also dehydrogenated but required a longer reaction time.
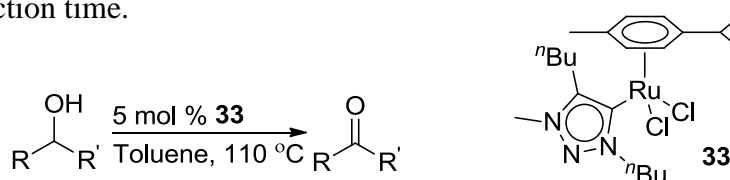
R	R'	Time (h)	Conversion (%)
Ph	H	16	> 95
Ph	Me	24	> 95
CH_2Ph	H	20	< 5
C_7H_{15}	H	20	< 5
$4\text{-}NO_2C_6H_4$	H	22	65
$4\text{-}ClC_6H_4$	H	22	68
$2\text{-}ClC_6H_4$	H	22	70
$4\text{-}BrC_6H_4$	H	16	91
$4\text{-}MeC_6H_4$	H	16	> 95
$4\text{-}MeOC_6H_4$	H	16	90

Table 11. The dehydrogenation of primary alcohols with a 1,2,3-triazolylidene complex.

1.5.4 Hydroxypyridine Complexes.

In 2007 Fujita, Tanino and Yamaguchi reported an iridium complex containing a 2-hydroxypyridine ligand for the dehydrogenation of secondary alcohols.[75] With 0.2 mol % **34**, 1-phenylethanol was oxidised in a 95 % yield after 20 h in refluxing toluene. Different substituted 1-phenylethanol derivatives were also oxidised in high yield. The 4-bromo and 4-nitro derivatives, however, required 50 h to reach 82 and 86 % yield respectively and the 4-nitro derivative also required a slightly increased catalyst loading of 0.33 mol %. Various other alcohols including aliphatic and cyclic alcohols were also oxidised in high yields but in some cases required longer reaction times and catalyst loadings up to 1 mol %. A primary alcohol, benzyl alcohol, could only reach a yield of 24 %. This complex is also effective for the dehydrogenation of tetrahydroquinolines.[76]
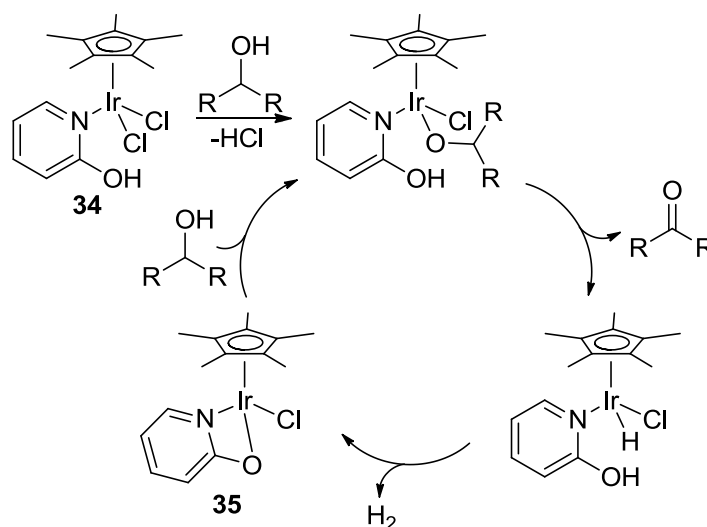
Scheme 15. Complex **34** and its catalytic cycle for the oxidation of alcohols.

A proposed mechanism shown in Scheme 15 involves the initial coordination of alkoxide followed by a β-elimination step to generate an iridium hydride species. Reaction of the hydride with the hydroxyl proton of the ligand

eliminates H_2 to give cyclic intermediate **35** which is ring-opened by an alcohol to complete the catalytic cycle. Intermediate **35** was independently synthesised and showed comparable catalytic activity to **34**. Analogues containing the hydroxyl group in the 3 and 4-positions of the pyridine ring were far less efficient catalysts. This catalyst has been the subject of recent mechanistic study both experimentally[77] and computationally.[78] An alternative mechanism suggested by computational results involves an outer-sphere interaction shown in Figure 10.
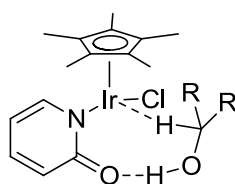
Figure 10. A proposed outer-sphere dehydrogenation.

In a more recent publication Yamaguchi and co-workers reported the improved catalyst **36** for the dehydrogenation of both primary and secondary alcohols.[79] Using 0.1 mol % **36** in refluxing *p*-xylene for 20 h, 1-phenylethanol was oxidised in a 96 % yield. A range of other substrates including aliphatic and cyclic alcohols also gave high yields, in some cases requiring catalyst loadings up to 0.5 mol %. Primary alcohols, however, required a catalyst loading of 2 mol % and 5 mol % NaOMe in refluxing toluene for 20 h. Benzylic alcohols were the most effective substrates with benzaldehyde being obtained in 90 % yield.
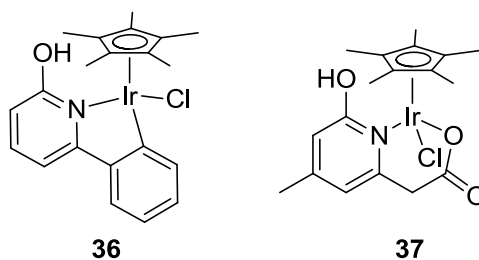
Figure 11. 2-Hydroxypyridine iridium catalysts for the dehydrogenation of alcohols.

A similar complex, **37**, was devised by Royer, Rauchfuss and Wilson utilising a ligand modelled on the organometallic cofactor of a dehydrogenase enzyme.[80] With 0.1 mol % **37** in refluxing toluene with 1-phenylethanol as the substrate a turnover number of 339 was achieved after 24 h.

1.5.5 Diaminodiphosphine Complexes.
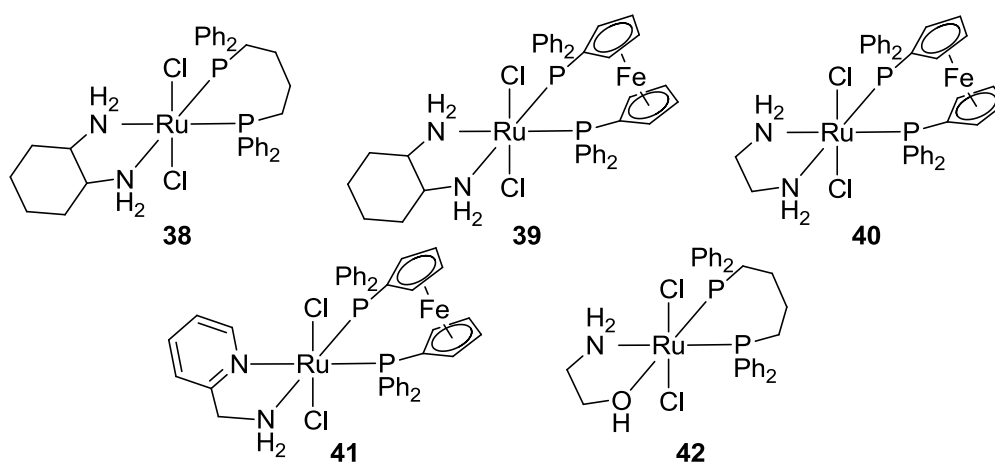
Figure 12. Diaminodiphoshine complexes used for the dehydrogenation of alcohols.

The use of diaminodiphosphine complexes, commonly used for asymmetric hydrogenation reactions, for the dehydrogenation of alcohols was demonstrated by Baratta and co-workers.[81] A family of complexes were synthesised and tested for the oxidation of α-tetralol in ^{t}BuOH at 130 °C with 2 mol % KO^{t}Bu and a catalyst loading of 0.4 mol %. Complexes bearing the dppf ligand were the most active and variations in the diamine ligand have little impact on the activity. Replacing the diamine with an amino-alcohol ligand gives a complex which is far less efficient, taking 45 h to reach 86 % conversion.

Table 12. The oxidation of α-tetralol by diaminodiphosphine ruthenium complexes.
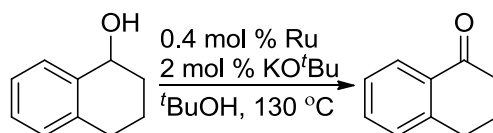
Complex	Time (h)	Conversion (%)
38	22	97
39	3	97
40	3	98
41	4	97
42	45	86

Complex **40** proved efficient for the dehydrogenation of further substrates, including aliphatic, allylic and benzylic secondary alcohols with aliphatic alcohols requiring longer reaction times. The analogous osmium complexes were also prepared and proved to be less efficient, requiring longer reaction times than the ruthenium complexes. For a few select substrates including 5-en-3β-hydroxysteroids, higher conversions are achieved with an osmium complex.

1.5.6 Pincer Complexes.
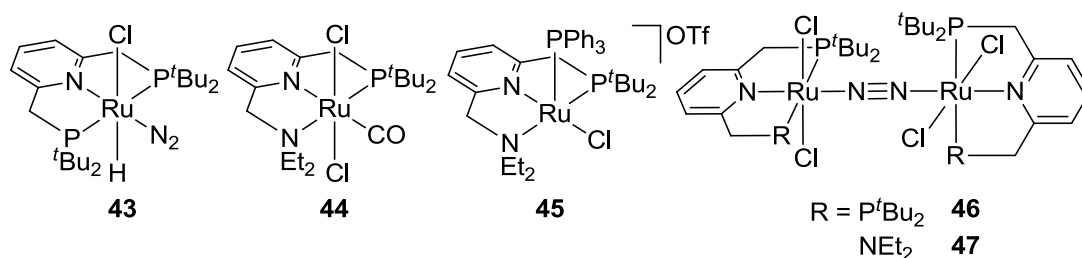
Figure 13. Pincer complexes for the dehydrogenation of alcohols.

A series of PNP and PNN pincer ruthenium complexes have been prepared by Milstein and co-workers and applied to the dehydrogenation of alcohols.[82, 83] Variations in the ligands had little impact on the activity of the complexes in refluxing 2-propanol. Lowering the catalyst loading and increasing the reaction time from 24 to 70 h demonstrated the stability of **43**, achieving a total of 924 turnovers (Table 13, entry 2).
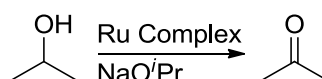
Entry	Complex	Ratio base:cat	Conversion (%)	TON^a
1	**43**	2	27	265
2^b	**43**	2	27	924
3	**44**	2	26	241
4	**45**	2	23	230
5	**46**	4	24	235
6	**47**	4	30	304

Table 13. The dehydrogenation of 2-propanol with Ru complexes. 0.1 mol % **43**-**45** or 0.05 mol % **46**-**47**, reflux, 24 h. ^{a} Turnover number per ruthenium atom. ^{b} 0.025 mol % **43**, 70 h.

In order to achieve high conversions, higher temperatures and longer reaction times were required; 2-propanol needed 70 h at 100 °C in dioxane to reach 94 % conversion with complex **47**. The investigation of other substrates identified an unusual trend in reactivity; aliphatic alcohols were more readily oxidised than a benzylic alcohol, 1-phenylethanol, which is in turn more readily oxidised than a cyclic alcohol, cyclohexanol. The oxidation of primary alcohols was also possible but resulted in almost exclusive formation of the ester product arising from a Tischenko-type reaction.

Substrate	Time (h)	Conversion (%)
2-Propanol	70	94
2-Butanol	100	85
2-Hexanol	100	90
Cyclohexanol	100	58
1-Phenylethanol	100	64

Table 14. Further substrates. 0.2 mol % **47**, 0.8 mol % NaO^{i}Pr, dioxane, 100 °C.

The rate of hydrogen production from 2-propanol was measured by Beller *et al*. for a range of ruthenium and iridium pincer complexes.[84] A well-defined ruthenium complex with an aliphatic backbone, **48**, was found to be an efficient catalyst for the dehydrogenation of 2-propanol at reflux with 32 ppm of catalyst and 1.3 equivalents of NaO^{i}Pr relative to the catalyst, giving a turnover frequency of 1231 h^{-1} after 2 h. Further catalysts were formed *in situ* for subsequent experiments by mixing the ligand with an appropriate ruthenium precursor. By tuning the substituents of the phosphines and selecting a ruthenium precursor that does not require base to activate, significant improvement in the rate was possible for the dehydrogenation of 2-propanol under neutral conditions. The combination of **50** and **52** gave a turnover frequency of 2048 h^{-1} after 2 h.
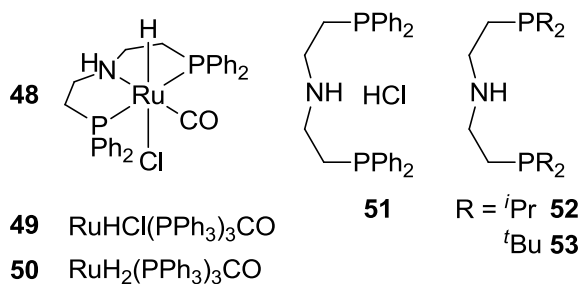
Catalyst	NaO^{i}Pr equiv	TOF 2 h (h^{-1})	TOF 6 h (h^{-1})
48	1.3	1231	644
49+**51**	1.3	460	384
49+**52**	1.3	1187	351
50+**52**	1.3	1843	1009
50+**52**	0	2048	1109
50+**53**	0	< 100	-

Table 15. The dehydrogenation of 2-propanol catalysed by ruthenium pincer complexes. 32 ppm Ru, 32 ppm ligand, reflux.

Gelman and co-workers hypothesised that the addition of a pendant hydroxyl group to a previously successful catalyst[59] (**13**) for alcohol oxidations in acetone would result in an active catalyst for dehydrogenation reactions via a bifunctional mechanism.[85] Using 0.1 mol % **54** in refluxing *p*-xylene under neutral conditions, 1-phenylethanol, benzhydrol and octan-2-ol were each oxidised in > 90 % yield. Primary alcohols could also be oxidised but this resulted in the formation of esters. Complex **54** was found to slowly decompose in solution by loss of H$_2$ to form **55**, this observation hints at a catalytic cycle shown in Scheme 16.
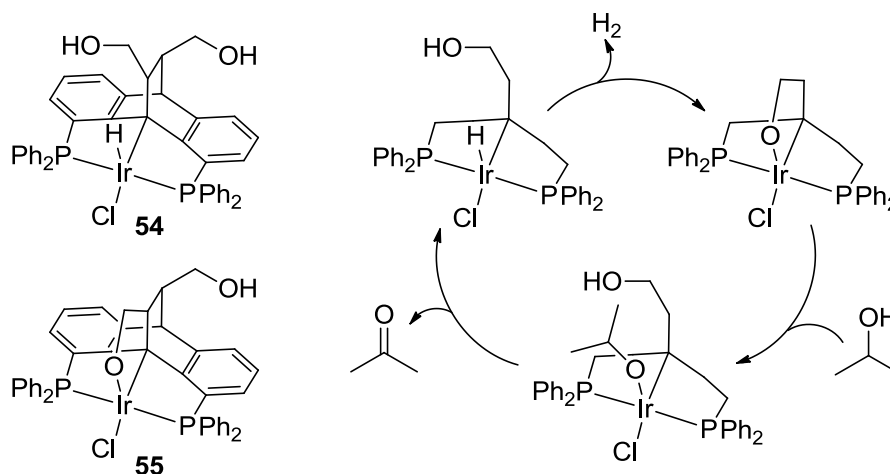
Scheme 16. A bifunctional catalyst for alcohol dehydrogenation, an isolated intermediate and the catalytic cycle (ligand structure simplified for clarity).

1.5.7 Photocatalysis.

Cole-Hamilton and co-workers reported a series of ruthenium and rhodium complexes for the oxidation of primary and secondary alcohols.[45, 86-88] The most effective catalyst reported, $[RuH_2N_2(PPh_3)_3]$, had a turnover frequency of 148 h^{-1} for the oxidation of ethanol at 150 °C, which increased to 210 h^{-1} under illumination with a 500 W tungsten-halogen lamp. The most remarkable increase was seen for ethylene glycol with an increase from 516 h^{-1} to 1185 h^{-1} under illumination. The effect of illumination may be twofold; light may promote evolution of CO from metal carbonyl complexes, thus preventing catalyst poisoning from CO generated by decarbonylation of aldehyde products. Light may also promote the elimination of hydrogen from the catalyst following dehydrogenation.

Saito and co-workers demonstrated the use of *in situ* generated metal-tin complexes for the dehydrogenation of 2-propanol under illumination conditions.[89-91] Reactions were conducted by dissolving an appropriate metal salt (RhCl$_3$.3H$_2$O,

$IrCl_3.3H_2O$, K_2PtCl_4 or $RuCl_3.3H_2O$) in 2-propanol containing $SnCl_2.2H_2O$ and heating to reflux after which, illumination with 3 x 24 W low pressure mercury lamps was begun. The iridium system was by far the most effective with a rate of 109 h^{-1} under illumination and a total of 3430 turnovers. A turnover frequency of 4.5 h^{-1} was measured when the reaction was performed without illumination. The use of ^{119}Sn NMR spectroscopy alluded to the presence of $[IrCl_2(SnCl_3)_4]^{3-}$ and $[IrH(SnCl_3)_5]^{3-}$ in the reaction mixture. Excess uncoordinated $SnCl_2$ was found to be detrimental to the reaction.[90] The dehydrogenation of methanol was also possible although the reaction proceeded more slowly.[92]

Arakawa and Sugi demonstrated the efficiency of Wilkinson's catalyst $(RhCl(PPh_3)_3)$ for the dehydrogenation of 2-propanol under illumination with a 100 W high pressure mercury lamp at 21 °C.[93] An unusual observation was that the turnover frequency for the reaction was almost 5 times higher (670 h^{-1} rather than 138 h^{-1}) when the reaction mixture was prepared under an oxygen atmosphere instead of nitrogen. Griggs and Smith reported a much higher rate of 5415 h^{-1} for Wilkinson's catalyst using a 125 W medium pressure mercury lamp at 21 °C.[94] The difference was attributed to differences in the experimental apparatus and optimisation of the rate of stirring. Other rhodium complexes were also found to be effective catalysts for this process, a turnover frequency of 6410 h^{-1} was measured for $RhCl(P(OPh)_3)_3$.

1.6 The Reduction of Ketones.

1.6.1 Hydrogen Donors.

The most commonly used hydrogen donor for the transfer hydrogenation of ketones is 2-propanol due to its stability, low cost, low toxicity, ability to dissolve a wide range of substrates and ease of removal of it and its oxidation product, acetone, from the reaction mixture. One problem arising from the use of 2-propanol as a hydrogen donor, however, is the problem of reversibility. Once a ketone has been reduced to the corresponding alcohol, the acetone by-product produced from 2-propanol can act as a hydrogen acceptor and allow the reverse reaction to take place. This can act as a limiting factor for the conversion achieved by the catalytic system, the position of the chemical equilibrium being controlled by the oxidation potentials[95] of the substrates. A 100 % conversion is theoretically impossible without distillation of the acetone by-product. This reverse process is promoted by long reaction times and can erode the enantioselectivity in asymmetric reductions. The use of 2-propanol as the reaction solvent and at high dilutions can help to drive the equilibrium towards the desired product.

The use of formic acid as the hydrogen donor can alleviate the problem of reversibility. Formic acid can be viewed as an adduct of H_2 and CO_2; the dehydrogenation of formic acid provides hydrogen for the reduction of the substrate and produces CO_2 as a gaseous by-product which is released from the system. As such, reductions utilising formic acid as the hydrogen donor are essentially irreversible which allows for conversions of up to 100 % and can prevent racemisation of enantiomerically enriched product alcohols. Formic acid is in the

majority of cases used as a 5:2 azeotrope with triethylamine, which has been described as an activated form of formic acid.[96]

A striking comparison of 2-propanol and 5:2 formic acid/triethylamine (FA/TEA) as hydrogen donors was made by Noyori *et al*. in the reduction of *p*-methoxyacetophenone with complex **56**. Notably, even with the long reaction time (60 h) required to reach full conversion with FA/TEA the e.e. is high, therefore, very little or no racemisation is taking place (Table 16).
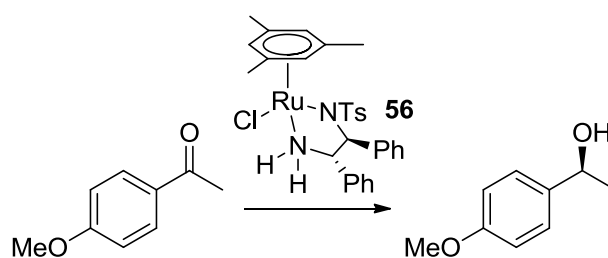
Hydrogen Donor	Time (h)	Yield (%)	e.e. (%)	Ref
2-Propanol[a]	20	53	72 (*S*)	47
5:2 FA/TEA[b]	60	99	97 (*S*)	97

Table 16. The reduction of *p*-methoxyacetophenone with different hydrogen donors. [a]0.5 mol % **56**, 1.25 mol % KOH, 28 °C, 0.1 M. [b]0.5 mol % **56**, 28 °C, 2M.

1.6.2 Oxazolines.
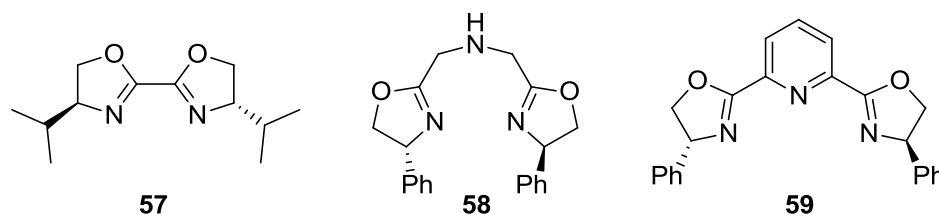
Figure 14. Bisoxazoline ligands for the ATH of ketones.

In 1991 Pfaltz and co-workers reported on a series of bisoxazoline ligands for the asymmetric transfer hydrogenation (ATH) of ketones with [Ir(COD)Cl]$_2$.[98] With 0.5 mol % of the iridium dimer, 1 mol % of the most successful ligand, **57** and 2 mol % KOH in refluxing 2-propanol acetophenone was reduced to 1-phenylethanol in 89 % conversion and 58 % e.e. after 3 h. A better result of 70 % conversion and 91 % e.e. was obtained with *iso*-propyl phenyl ketone as the substrate.

A related ligand, **58**, was developed by Jiang, Jiang and Zhang and proved to form an efficient ATH catalyst with RuCl$_2$(PPh$_3$)$_3$ and NaO^{i}Pr.[99] With 1 mol % of each component acetophenone was reduced in 91 % conversion and 97 % e.e. in just 10 mins. Crucially it was found that PPh$_3$ released when the active catalyst is formed was detrimental to the reaction, an Et$_2$O wash was necessary to remove it prior to the addition of acetophenone and NaO^{i}Pr. When the Et$_2$O wash was not performed the reaction reached 67 % conversion and 84 % e.e. after 1 h. Phosphine-bridged bisoxazoline ligands have also been reported by Zhang *et al*. but were less effective.[100]

The combination of Sn(II) triflate and pybox derivative **59** with polymethylhydrosiloxane (PMHS) as the hydrogen donor proved to be effective for the reduction of benzylic ketones.[101] With a 10 mol % catalyst loading and 200 mol % PMHS in MeOH at room temperature acetophenone was reduced in 95 % conversion and 58 % e.e.
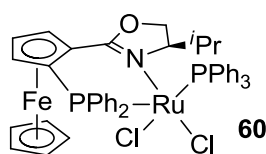
Figure 15. A highly selective ruthenium catalyst for the reduction of ketones.

In 1999 A ruthenium (II) oxazolinylferrocenylphosphine complex (**60**) was shown by Hidai and co-workers to be a highly efficient and selective catalyst for the ATH of ketones.[102] A wide range of ketones could be reduced in up to 99 % conversion and > 99 % e.e. with 0.5 mol % of catalyst at room temperature in 2-propanol (Table 17). Notably, the catalyst was capable of reducing pinacolone and 2,2-dimethylcyclohexanone in 99 and 98 % e.e. respectively. The planar chirality of the ligand was an important factor; this was demonstrated by replacing the ferrocenyl portion of the ligand with a benzene ring. Low conversion and selectivity were found in the reduction of acetophenone with the modified ligand.
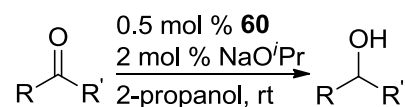
R	R'	Time (h)	Conv (%)	e.e. (%)
Ph	Me	2	94	> 99 (R)
Ph	Et	8	99	> 99 (R)[a]
Ph	^{n}Bu	4	99	99 (R)[b]
4-MeC$_6$H$_4$	Me	4	98	> 99 (R)
4-ClC$_6$H$_4$	Me	2	99	99 (R)
3-ClC$_6$H$_4$	Me	2	99	> 99 (R)
2-ClC$_6$H$_4$	Me	1	99	> 99 (R)
2,4-(Me)$_2$C$_6$H$_3$	Me	5	99	> 99 (R)
Furan	Me	2	66	95 (R)
^{t}Bu	Me	16	81	> 99 (S)[a]
c-Hexyl	Me	24	68	52 (S)
2,2-Dimethylcyclohexanone		3	78	98 (S)[a]

Table 17. The ATH of ketones catalysed by Ru(II) catalyst **60**. [a] At 50 °C. [b] At 70 °C.

1.6.3 Isonitrile Complexes.
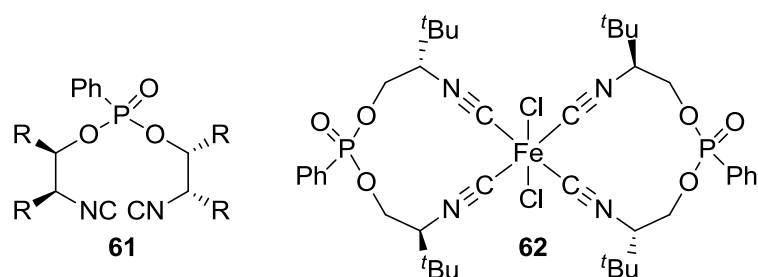
Figure 16. A bis(isonitrile) ligand and its complex of $FeCl_2$.

A rather unusual bis(isonitrile) ligand has been developed by Naik, Maji and Reiser and applied to the iron (II) catalysed ATH of ketones.[103] Several ligands of general structure **61** were prepared and their $FeCl_2$ complexes were synthesised. Variation of the R substituents of the ligands had a large effect on the activity and selectivity of the complexes with **62** giving the best results; acetophenone was reduced in 90 % conversion and 64 % e.e. with a catalyst loading of 5 mol % and 50 mol % KO^{t}Bu after 8 h in 2-propanol at room temperature. A range of other ketones could be reduced with varying selectivities from 10-91 % e.e.
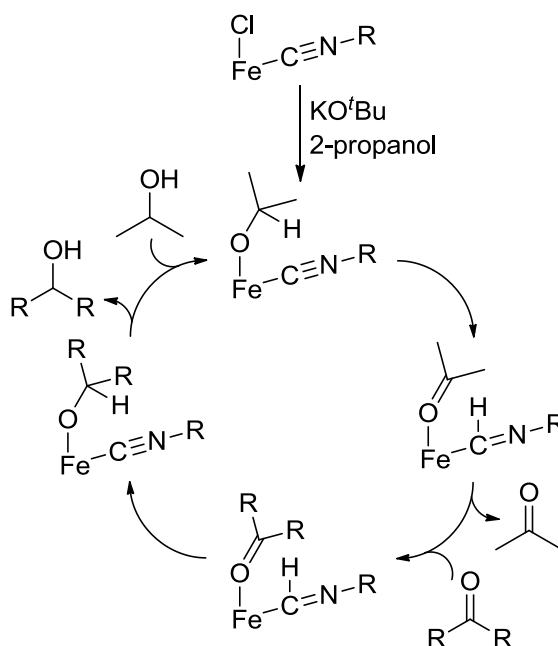
Scheme 17. The speculated catalytic cycle of ketone reduction by iron isonitrile complex **62**.

To gain a mechanistic insight attempts were made to observe an iron hydride species by ^{1}H NMR but no such species was observable, similarly the IR spectrum was devoid of an expected characteristic Fe-H stretch. What was observed however, was the disappearance of the isonitrile signal in the IR spectrum and the appearance of a new band indicative of a C=N bond. Based on these observations a catalytic cycle was proposed involving the reduction of a nitrile group to the corresponding imine which could reduce the coordinated substrate by transfer of hydride and regeneration of the isonitrile group (Scheme 17).

1.6.4 Benzylic Amine Complexes.
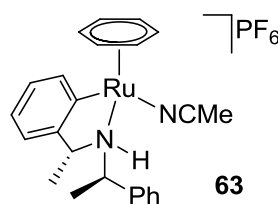
Figure 17. A cyclometallated benzylic amine ruthenium (II) catalyst for the reduction of ketones.

Cationic ruthenium (II) complexes of cyclometallated benzylic amines have been developed by Pfeffer *et al.* and applied to the asymmetric reduction of ketones in 2-propanol.[104] With 1 mol % of **63** and 5 mol % KO^{t}Bu, acetophenone was reduced in 95 % conversion and 85 % e.e. after 2 h at 0 °C. A range of other chiral benzylic amines were tested as ligands but no significant improvements were made, however, the presence of an NH function was found to be necessary for activity and selectivity. A potential drawback of this system is that complexes are isolated as a mixture of diastereoisomers with differing configurations at the ruthenium centre. This could have a detrimental effect on the selectivity of the catalyst. This is in contrast to the Noyori-type catalysts discussed later in which complex formation is always diastereoselective.

1.6.5 Diamine Ligands.
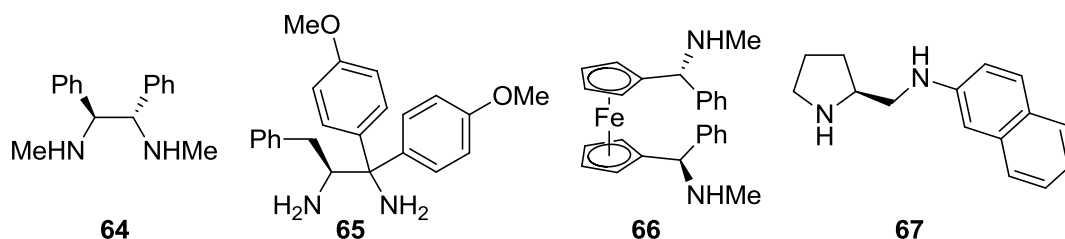
Figure 18. Chiral diamine ligands for the enantioselective reduction of ketones.

A series of C_2-symmetrical chiral diamines based on diphenylethylenediamine and diaminocyclohexane were screened for the reduction of acetophenone with $[Rh(C_6H_{10})Cl]_2$ and KOH by Lemaire *et al.*[105, 106] With diamine **64**, acetophenone was reduced in full conversion and 67 % e.e. after 7 days at room temperature in 2-propanol. When a β-ketoester, methylphenylglyoxylate, was the substrate, full conversion and 97 % e.e. was recorded after 1 h.

A similar diamine, **65**, was found by Noyori and co-workers to reduce a range of ketones with high enantioselectivity in conjunction with $[Ir(COD)Cl]_2$.[107] Stirring acetophenone with 2 mol % catalyst and 10 mol % KOH in 2-propanol afforded 1-phenylethanol in 96 % yield and 93 % e.e. after 12 h at room temperature. A ligand to iridium ratio of 2:1 was found to be necessary for a fast reaction.

Knochel and co-workers synthesised a whole family of ferrocene-derived chiral diamines for the enantioselective reduction of ketones with $[RuCl_2(p\text{-}cymene)]_2$.[108] With ligand **66** a conversion of 98 % and 71 % e.e. was obtained for the reduction of acetophenone after 0.5 h. When the temperature was lowered to -30 °C an e.e. of 80 % was obtained although a longer reaction time of 120 h was required to reach 95 % conversion. Similarly, 1'-acetonaphthone was reduced in 99 % conversion and 78 % e.e. after 0.5 h at room temperature but was able to reach 91 % conversion and 90 % e.e. after 120 h at -30 °C.

Chiral diamines derived from the α-amino acid proline form highly selective catalysts for the reduction of ketones with $[RuCl_2(p\text{-}cymene)]_2$ as shown by Karim *et al.*[109] With a catalyst loading of 2 mol % and 5 mol % NaO^{i}Pr, acetophenone was reduced in 89 % yield and 91 % e.e. after 0.5 h using ligand **67** in 2-propanol at

room temperature. Similar proline-based aminoalcohols were also synthesised but made relatively ineffective ligands, achieving only moderate enantioselectivities.

1.6.6 Tetradentate Ligands.
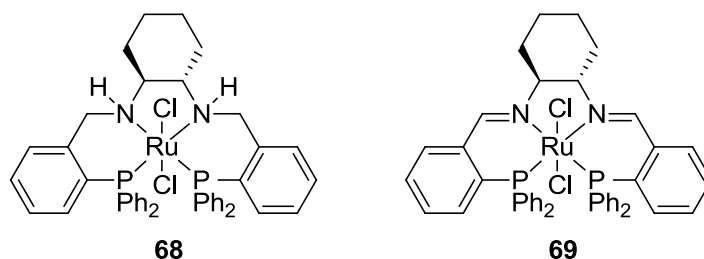
Figure 19. Tetradentate ligands for ruthenium catalysed ATH.

Ruthenium complex **68**, containing a tetradentate diaminodiphosphine ligand was synthesised by Gao, Ikariya and Noyori and applied to the ATH of acetophenone derivatives.[110] Using 0.5 mol % catalyst and 0.25 mol % KO^{i}Pr in 2-propanol at 45 °C, acetophenone was reduced in 93 % yield and 97 % e.e. after 7 h. The analogous diiminodiphosphine complex, **69**, was an ineffective catalyst, reducing acetophenone in only 7 % conversion and 5 % e.e. after 4 h at 82 °C. This implies that the NH present in **68** is necessary for effective catalysis to take place. A series of similar diimine ligands has been used previously for the ATH of ketones with [Ru(C$_6$H$_6$)Cl$_2$]$_2$ but despite good yields of the desired alcohol products only poor to moderate enantioselectivities were observed.[111]
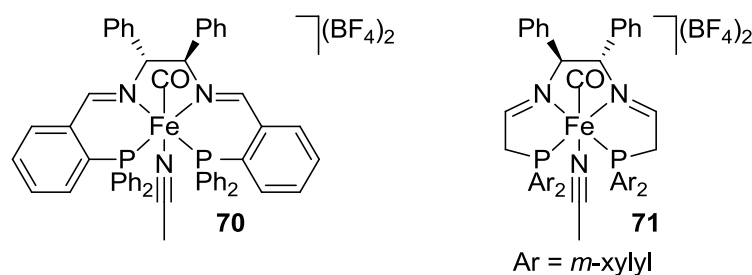
Figure 20. Fe(II) catalysts for the ATH of ketones.

Meyer, Lough and Morris reported the synthesis and activity of iron (II) complex **70** for the ATH of ketones.[112] With a catalyst loading of 0.17 mol % and 1.3 mol % KO^{t}Bu in 2-propanol, acetophenone was reduced in 68 % yield and 63 % e.e. after 15 mins at room temperature. To reach full conversion it was necessary to remove the solvent from the reaction mixture and add fresh 2-propanol. The use of more sterically hindered substrates gave better results; *iso*-propyl phenyl ketone and *tert*-butyl phenyl ketone were reduced in 94 and 96 % e.e. respectively (Table 18).
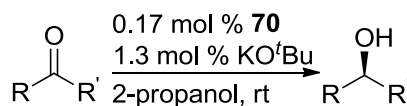
R	R'	Time (mins)	Conv (%)	e.e. (%)
Ph	Me	15	68	63
Ph	Et	30	75	70
Ph	^{i}Pr	30	58	94
Ph	^{t}Bu	15	93	96[a]
4-ClC$_6$H$_4$	Me	30	81	38
3-ClC$_6$H$_4$	Me	30	68	45
2-ClC$_6$H$_4$	Me	30	93	29
1-Naphthyl	Me	30	73	61[a]
Ph(CH$_2$)$_2$	Me	15	91	57[a]
^{t}Bu	Me	60	48	21[a]

Table 18. The reduction of ketones with chiral Fe(II) catalyst **70**. All products have an *S*-configuration. ^{a} 0.5 mol % **70**.

Simplifying the side-chain of the ligand and tuning the aryl groups on the phosphine substituents led to a more active and selective catalyst.[113] Complex **71** was able to reduce acetophenone in 94 % yield and 90 % e.e. after only 7 mins with a catalyst loading of 0.1 mol %. During studies on pressure hydrogenation with analogous achiral Fe(II) complexes similar activities were seen for diamine and diimine based ligands, perhaps suggesting that *in situ* reduction to the diamine may take place and the mechanism of ketone reduction may resemble that of the analogous Ru(II) catalysts discussed previously.[114]

1.6.7 Tridentate Ligands.
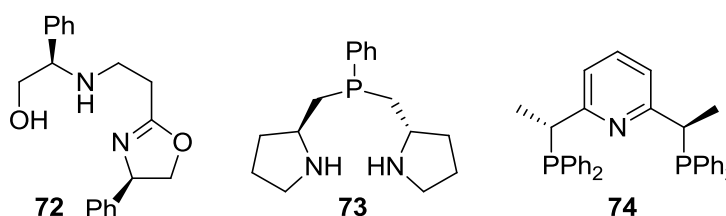
Figure 21. Tridentate ligands developed by Zhang and co-workers.

The tridentate NNO ligand, **72**, was developed by Zhang *et al.* for the ATH of ketones with [RuCl$_2$(C$_6$H$_6$)]$_2$ and NaO^{i}Pr in 2-propanol.[115] With 1 mol % of catalyst acetophenone could be reduced in 97 % conversion after 14 h at room temperature but a poor e.e. of only 13 % was obtained. An NPN ligand, **73**, reported in the same publication gave an improved e.e. of 20 % but the reaction took a longer time of 24 h to reach 96 % conversion. Rather unusually an aliphatic ketone, pinacolone, was reduced with greater enantioselectivity, giving a 92 %

conversion and 46 % e.e. after 24 h for **72** and giving a 75 % conversion and 61 % e.e. for **73** after a total of 160 h. A PNP ligand, **74**, fared slightly better, giving 91 % yield and 35 % e.e after 24 h using NaOMe rather than NaO^{i}Pr.[116] A concentration of 2 M was required to reach high conversion which is unusually high for a 2-propanol reduction.
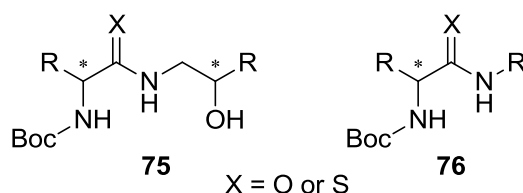
Figure 22. Amino acid-derived ligands developed by Adolfsson.

A family of amino acid-derived NNO ligands have been developed by Bøgevig, Pastor and Adolfsson for the reduction of ketones with [RuCl$_2$(*p*-cymene]$_2$.[117] The general structure (**75**) is shown in Figure 22. It was found that both chiral centres in the ligand needed to have the same configuration to ensure high activity and selectivity in the reduction of acetophenone. Typically > 85 % conversion and > 90 % e.e. was obtained for ligands with matching stereocentres after stirring for 2 h at room temperature in 2-propanol. In subsequent work an analogous thioamide ligand was shown to give the opposite enantiomer of 1-phenylethanol as the major product in the reduction of acetophenone although the conversion and selectivity were modest.[118] However as bidentate ligands of general structure **76**, the thioamide-based ligands perform well, often achieving > 90 % conversion and > 90 % e.e. with [RhCl$_2$Cp*]$_2$.[119, 120]

1.6.8 Binaphthyl Derivatives.
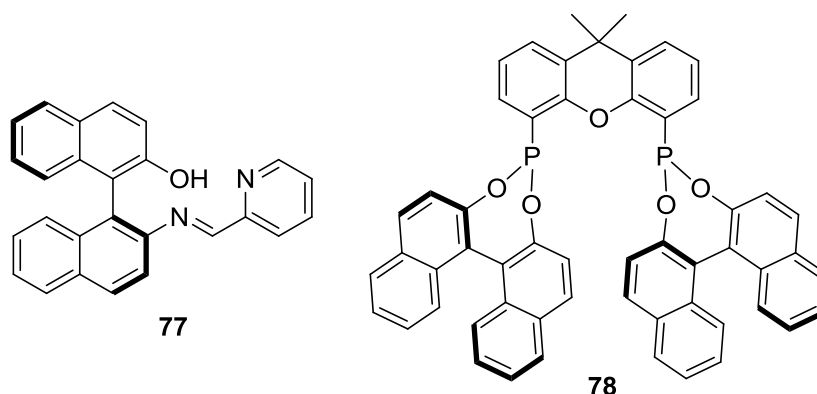
Figure 23. Binaphthyl-derived ligands for the reduction of ketones.

Brunner *et al*. utilised a pyridine substituted (S)-2-Amino-2'-hydroxy-1,1'-binaphthyl compound, **77**, for the ATH of ketones with Ru(PPh$_3$)$_3$Cl$_2$ in 2-propanol.[121] Acetophenone was reduced in 94 % conversion and 96 % e.e. after 15 h at 28 °C. Reduction of the imine functionality of **77** to the corresponding secondary amine resulted in a ligand that gave almost identical conversion and selectivity so the *in situ* reduction of the imine under catalytic conditions cannot be ruled out.

The xanthene-bridged diphosphonite ligand **78** was developed by Reetz and Li for the enantioselective reduction of ketones with [RuCl$_2$(*p*-cymene)]$_2$.[122] The rigidity of the ligand proved crucial for catalyst activity as more flexible analogues achieved only low conversions (5-10 %) for the reduction of acetophenone. Ligand **78** is highly selective for a wide range of ketones including aliphatic ketones, > 90 % conversion and > 90 % e.e. was achieved in most cases.

$$R-CO-R' \xrightarrow[\substack{10 \text{ mol \% NaOH} \\ 2\text{-propanol, } 40\ ^{\circ}C}]{\substack{0.5 \text{ mol \% Ru dimer} \\ 2.5 \text{ mol \% } \mathbf{78}}} R-CH(OH)-R'$$
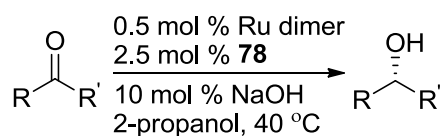
R	R'	Time (h)	Conv (%)	e.e. (%)
Ph	Me	20	88	97
Ph	Et	26	65	93
4-ClC$_6$H$_4$	Me	16	98	95
3-BrC$_6$H$_4$	Me	16	100	96
2-ClC$_6$H$_4$	Me	26	83	99
c-Hexyl	Me	22	97	99
n-Hexyl	Me	16	96	90
^{i}Pr	Me	22	99	99
Ph(CH$_2$)$_2$	Me	26	97	76

Table 19. The Ru(II) catalysed reduction of ketones with a diphosphonite ligand. All products have an *R*-configuration.

1.6.9 Diamine-Diphosphine Complexes.
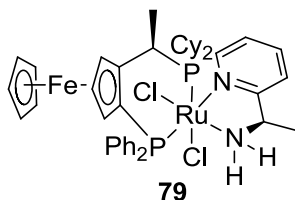
Figure 24. A highly active ATH catalyst reported by Baratta.

The chiral ruthenium (II) complex **79** was found by Baratta *et al*. to be an exceptional catalyst for the reduction of ketones.[123] With a very low catalyst loading of 0.05 mol %, acetophenone was reduced in 97 % conversion and 96 % e.e. after 5 mins at 60 °C in 2-propanol. Various derivatives were also prepared and showed similar activities and selectivities, notably, turnover frequencies of up to 70000 h^{-1} were measured.

1.6.10 β-Amino Alcohol Ligands.
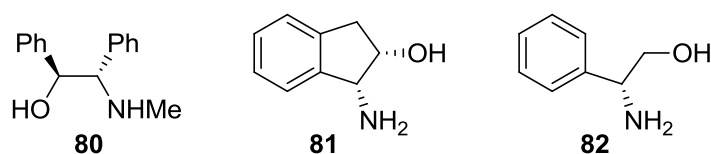
Figure 25. β-Amino alcohols used as ligands for the ATH of ketones.

In 1996 Noyori and co-workers reported on the use of β-amino alcohols as ligands for the ruthenium (II) catalysed asymmetric reduction of ketones.[124] A small range of β-amino alcohols were evaluated in the reduction of acetophenone with [RuCl$_2$(arene)]$_2$ where the aryl substituent was benzene, *p*-cymene, mesitylene or hexamethylbenzene (HMB). Ligand **80** with [RuCl$_2$(HMB)]$_2$ was found to be the most effective catalytic system, giving 1-phenylethanol in 94 % yield and 92 % e.e. after 1 h in 2-propanol at room temperature. Significantly lower enantioselectivities were obtained with the other arenes.

The use of the stereochemically rigid indane-derived β-amino alcohol **81**, for ATH under similar conditions was reported soon after by Palmer, Walsgrove and Wills.[125] With [RuCl$_2$(*p*-cymene)]$_2$, 1-phenylethanol was obtained in 70 % yield and 91 % e.e. after 1.5 h. To test the effect of rigidity in the system (*R*)-phenylglycinol (**82**) was used and proved to be more active, achieving 95 % yield and a disappointing 23 % e.e.
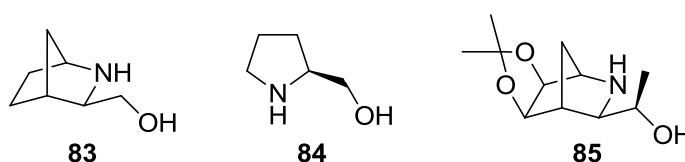
Figure 26. Ligands utilised by Andersson for the reduction of ketones.

Andersson *et al.* demonstrated that a conformationally constrained β-amino alcohol was a very effective ligand for the reduction of ketones with [RuCl$_2$(HMB)]$_2$.[126] In 2-propanol at room temperature, acetophenone was reduced in 92 % yield and 95 % e.e. after 5 h with ligand **83** compared to 16 % yield and 8 % e.e. for the conformationally more flexible **84**. Changing the arene group on ruthenium to *p*-cymene gave a similar result with a shorter reaction time of 1.5 h and gave slightly enhanced selectivities for more hindered ketones. The introduction of a dioxolane ring in the backbone of the ligand (**85**) proved beneficial, giving rise to a significantly more active catalytic system, reducing acetophenone in 97 % conversion and 96 % e.e. with a turnover frequency of 8500 h^{-1} after 15 mins.[127] Lowering the catalyst loading from 0.1 mol % to 0.02 mol % gave an almost identical result but the reaction took 1.5 h. At 0.014 mol % the reaction stopped after 110 mins at 85 % conversion.

1.6.11 Monosulphonated Diamine Complexes.
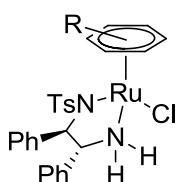
Figure 27. Noyori's asymmetric transfer hydrogenation catalyst. The aryl group is usually benzene, *p*-cymene or mesitylene.

The use of *N*-*p*-tosyl-1,2-diphenylethylenediamine (TsDPEN) with [RuCl$_2$(mesitylene)]$_2$ for the reduction of benzylic ketones was reported by Noyori and co-workers in 1995.[47] Moderate to high yields of chiral alcohols in up to 98 % e.e. were obtained after stirring in basic 2-propanol for 14-24 h. The utility of this

catalytic system was demonstrated in a subsequent publication in which 5:2 FA/TEA was used as the solvent and hydrogen donor.[97] Most of the ketones tested gave > 90 % yield and up to 99 % e.e. of the corresponding chiral alcohols. The substrate scope was later extended to include α,β-acetylenic ketones[128] and benzil[129] derivatives.
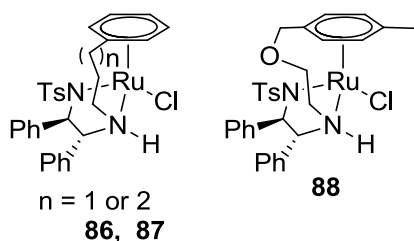
Figure 28. Tethered Ru(II) catalysts for the ATH of ketones.

The catalyst structure was refined by Wills *et al*. by the introduction of a tether between the arene ring on ruthenium and the diamine ligand.[130-132] The resulting complex benefits from increased stability due to the three-point attachment of the ligand and is also able to reduce ketones more rapidly than the untethered complex. With complex **86**, acetophenone is fully converted with an e.e. of 96 % after 3 h at room temperature in FA/TEA compared to 20 h and a 98 % e.e. for Noyori's catalyst. Increasing the tether length to 4 carbons (**87**) gives a faster catalyst with the same selectivity. A recent modification incorporates an oxygen atom into the tether (**88**) and results in higher selectivity for the reduction of acetophenone; > 99 % conversion and 99 % e.e. can be obtained overnight.[133, 134]

$$R \overset{O}{\underset{}{\|}} R' \xrightarrow[\text{FA/TEA, 40 °C}]{0.5 \text{ mol \% } \mathbf{86}} R \overset{OH}{\underset{}{|}} R'$$
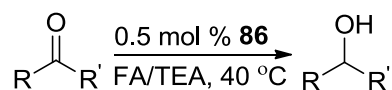
R	R'	Time (h)	Conv (%)	e.e. (%)
Ph	Me	3	100	96 (R)
Ph	Et	3	100	94 (R)
Ph	^{i}Pr	24	92	95 (R)
Ph	^{t}Bu	24	95	77 (R)
Ph	c-Hexyl	24	90	94 (R)
c-Hexyl	Me	10	100	69 (S)[a]
4-MeOC$_6$H$_4$	Me	1.67	100	94 (S)[b]
3-MeOC$_6$H$_4$	Me	1	100	94 (S)[b]
2-MeOC$_6$H$_4$	Me	1.25	100	70 (S)[b]
Furan	Me	1.17	100	98 (S)[b,c]
Ph	CH$_2$Cl	1.5	100	95 (R)[a,b]

Table 20. The ATH of ketones catalysed by tethered Ru(II) complex **86**. [a] At 28 °C. [b] With (S,S)-**86**. [c] 0.02 mol % catalyst.
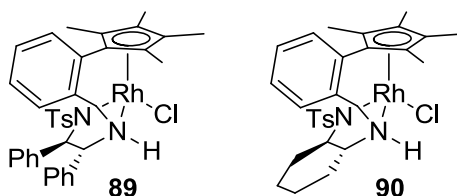
Figure 29. Tethered Rh(III) catalysts for the ATH of ketones.

The use of rhodium and iridium in the form of [Cp*MCl$_2$]$_2$ with TsDPEN for the basic 2-propanol reduction of ketones has also been described but lower activities were found in comparison to Ru(II).[135, 136] For a range of ketones, conversions from 40-90 % are obtained over 12-48 h and enantioselectivities up to 99 % are achievable. Tethered rhodium complexes **89**-**90**, however, are far more active.[137, 138] Acetophenone is reduced in full conversion and 98 % e.e. in FA/TEA

by complex **89** after 10 h. Complex **90** reduces ketones more rapidly but is slightly

less selective, giving 100 % conversion to 1-phenylethanol in 96 % e.e. in only 2 h.

1.7 The Shvo Catalyst.
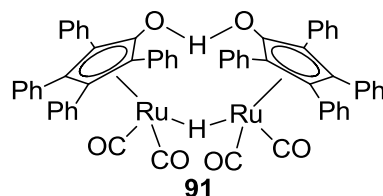
Figure 30. The Shvo catalyst.

The Shvo catalyst, **91**, is a hydroxycyclopentadienyl ruthenium dimer

bearing a bridging hydride ligand that is known to catalyse a number of processes

including the reduction of ketones, imines, alkenes and alkynes, the Oppenauer-

type oxidation of alcohols and the dynamic kinetic resolution of alcohols and

amines among others.[139]
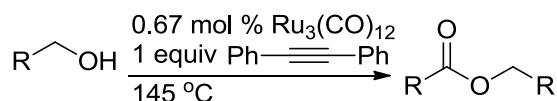
Scheme 18. The ruthenium-catalysed formation of esters from alcohols.

In the 1980s Shvo and co-workers synthesised esters from the

homocoupling of alcohols using $Ru_3(CO)_{12}$ as the catalyst and diphenylacetylene as

the hydrogen acceptor (Scheme 18).[140, 141] Eventually **91**, which was originally

incorrectly assigned as $[(\eta^4\text{-}Ph_4C_4CO)(CO)_2Ru]_2$, and a related complex, **92**, were

isolated from the reaction mixture and found to be catalysts for the formation of

esters from alcohols.[142, 143] Re-examination of the ^{1}H NMR spectrum of the isolated

ruthenium dimer revealed a resonance at -17.75 ppm indicative of a hydride

ligand.[144] This prompted a more detailed examination of the catalyst so the X-ray

crystal structure of analogous complex **93** was determined and revealed the bridging hydride and hydroxyl proton.
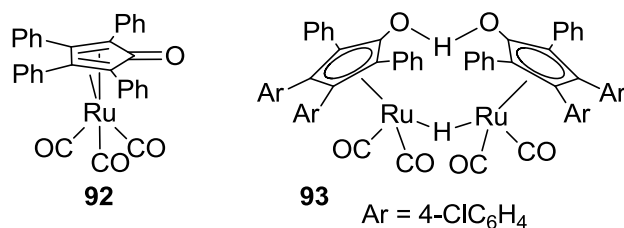
Figure 31. Complexes synthesised by Shvo.

Complex **92** had been synthesised previously[145] and the cyclopentadienone ligand is formed by a [2 + 2 + 1] cycloaddition reaction between 2 molecules of diphenylacetylene and 1 molecule of CO mediated by the ruthenium cluster.[145, 146] Complex **92** was found to serve as a precursor to **91**, the latter complex being formed upon reaction with aqueous sodium carbonate.[147]

1.7.1 Mechanism.
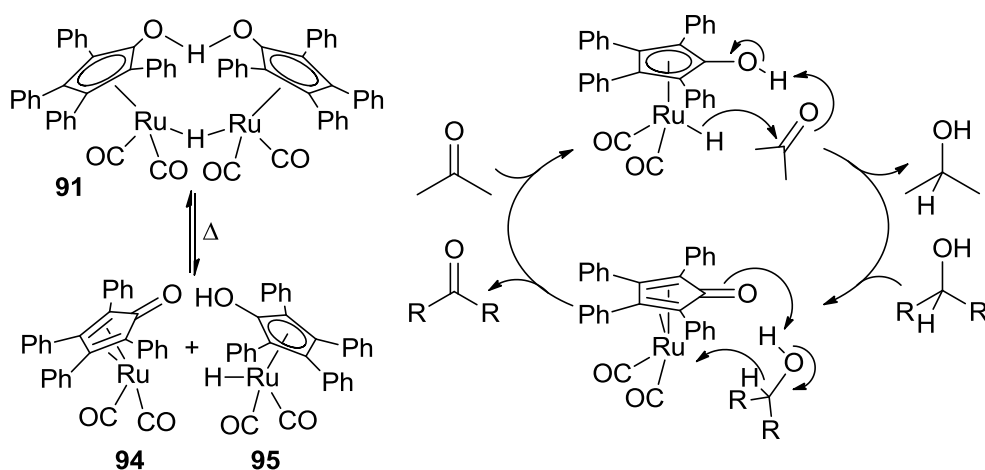
Scheme 19. The outer-sphere mechanism for the oxidation of alcohols by the Shvo catalyst.

The hydride-bridged dimer **91** is a resting state for the catalyst, upon heating it disproportionates into the 16-electron Ru(0) cyclopentadienone **94**, featuring a vacant coordination site and the 18-electron Ru(II) hydroxycyclopentadienyl hydride **95**. The oxidation of an alcohol by the Shvo catalyst is illustrated in Scheme 19. The pendant ketone functionality of **94** attacks the hydroxyl proton of the substrate and the metal centre abstracts the α-proton in a concerted manner to give the oxidised product and another molecule of **95**. Complex **95** donates a proton and hydride to the hydrogen acceptor to reform **94** and complete the catalytic cycle. Although **94** is too reactive to be isolated, its existence has been implied from trapping experiments with triphenylphosphine.[142, 148]
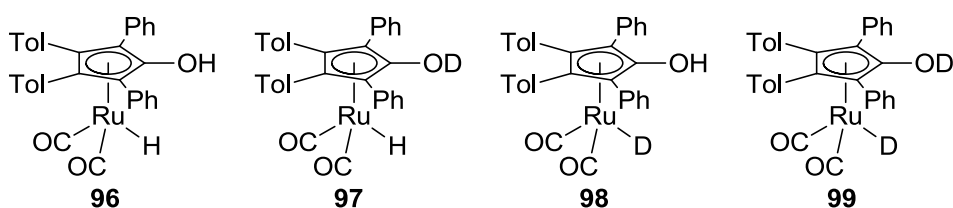
Figure 32. Complexes studied by Casey to determine kinetic isotope effects.

Kinetic isotope effects were measured for the reduction process by Casey and co-workers.[149] Tolyl analogues of the Shvo catalyst were chosen for ease of study due to the distinctive tolyl-CH_3 signal in the ^{1}H NMR spectrum. Benzaldehyde was reduced by a stoichiometric amount of ruthenium hydride **96** in an NMR tube and the reaction was monitored over time to determine the rate. The rates of reduction by isotopologues **97**-**99** were also measured and the kinetic isotope effects were calculated. Strong isotope effects were found for the ligand OH ($k_H/k_D = 2.2(1)$) and for the ruthenium hydride ($k_H/k_D = 1.5(2)$) and these values multiply to give $k_H/k_D = 3.3(2)$ which matches within experimental error the measured combined value of $k_H/k_D = 3.6(3)$. This indicates that the ligand hydroxyl

proton and the ruthenium hydride are both participating in the rate-determining step of the reduction, therefore, the transfer of proton and hydride to the substrate is concerted.

Similar findings for the reverse process, the oxidation of an alcohol, were reported by Johnson and Bäckvall in 2003.[150] The catalytic oxidation of 1-(4'-fluoro)phenylethanol and its isotopologues deuterated at the α-position, the hydroxyl position and both positions were carried out with **91** and tetrafluorobenzoquinone as the hydrogen acceptor. Isotope effects of $k_H/k_D = 1.9(2)$ and $k_H/k_D = 2.6(3)$ were measured for the OH and CH respectively and these values multiply to give $k_H/k_D = 4.8(5)$ which is within experimental error of the measured combined value ($k_H/k_D = 4.6(4)$). These results also point towards a concerted mechanism for proton and hydride transfer by the Shvo catalyst.
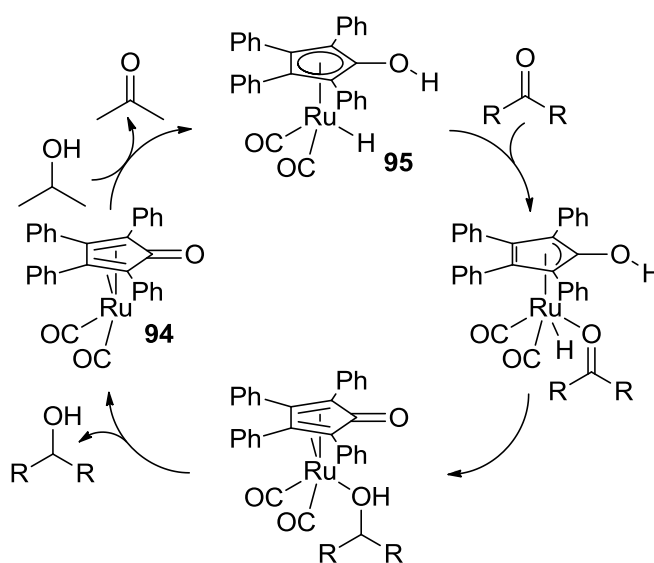
Scheme 20. The inner-sphere mechanism for ketone reductions by the Shvo catalyst. One of several possible ring-slips shown.

In addition to the outer-sphere mechanism for hydrogen transfer previously discussed (Scheme 19), an inner-sphere mechanism can also be envisaged as shown for the reduction of a ketone in Scheme 20. This mechanism involves the

coordination of the ketone prior to reduction therefore a ring-slip of the hydroxycyclopentadienyl ligand is necessary to provide a vacant coordination site. Alternatively the temporary loss of a CO ligand could also take place to provide a vacant coordination site, however this is unlikely since Casey demonstrated that CO exchange with ^{13}CO for complex **96** is a slow process.[149]

Differentiating between the inner-sphere and outer-sphere mechanisms is difficult to accomplish by experiment, although the application of density functional theory can provide some insight. In 2007 Comas-Vives, Ujaque and Lledós published their computational studies on the mechanism of ketone reductions by the Shvo catalyst.[151] The outer-sphere mechanism was found to be the most viable with an energy barrier of + 9.1 kcal/mol compared to a value of + 34.3 kcal/mol for the inner-sphere, ring-slip mechanism. The energy barrier to dissociation of CO was calculated to be + 51.2 kcal/mol which is consistent with Casey's experimental findings of slow CO exchange.

1.7.2 Applications.

1.7.2.1 Oxidations.

The Shvo catalyst was utilised by Bäckvall *et al*. for the oxidation of alcohols.[152] With catalyst loadings from 0.1-0.5 mol % in refluxing acetone, a range of secondary alcohols including aliphatic, allylic and benzylic alcohols were oxidised with yields ranging from 73-96 %. The results compared with $RuCl_2(PPh_3)_3/K_2CO_3$ but proved superior for the oxidation of aliphatic alcohols.

This method was also applied to the oxidation of 5-en-3β-hydroxysteroids.[153] Substrates with various different pendant functionalities were tested and the expected 4-en-3-ones were obtained in yields of 74-93 %. This method significantly improves upon a previously developed catalytic system for the oxidation of alcohols using the Shvo catalyst, 2,6-di-*tert*-butylbenzoquinone and MnO$_2$ as the terminal oxidant in which only poor conversions were obtained for steroidal substrates.[154]

100
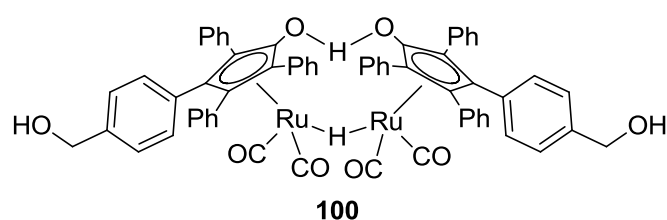
Figure 33. A Shvo catalyst analogue that was supported on silica and used for the dehydrogenation of alcohols.

The oxidation of alcohols in the absence of a hydrogen acceptor is also possible. Park and co-workers synthesised Shvo catalyst analogue **100** and immobilised it on silica.[155] The newly-supported catalyst (4.4 mol %) was then applied to the dehydrogenation of aliphatic and benzylic secondary alcohols in refluxing toluene, achieving 96-100 % conversion to the corresponding ketone products in up to 8 h. Cyclohexanol required a longer reaction time of 20 h to reach 100 % conversion. Benzyl alcohol was a less effective substrate, achieving only a 41 % conversion. The catalyst could be recovered and reused albeit with a small loss of activity with each subsequent use (Table 21).

Run	1	2	3	4	5
Yield (%)	100	97	96	91	87

Table 21. The dehydrogenation of 1-phenylethanol catalysed by silica supported **100** with catalyst recycling. 4.4 mol % catalyst, toluene, reflux.
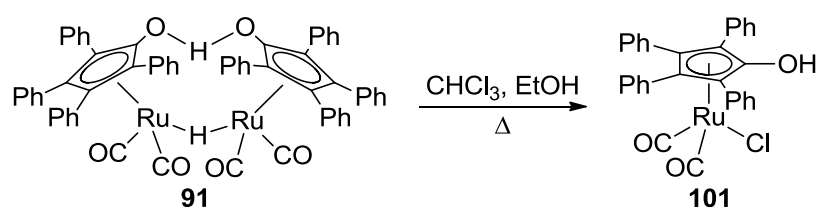
Scheme 21. Conversion of the Shvo catalyst to a hydroxycyclopentadienyl chloride complex.

An alternative catalytic system for the oxidation of alcohols using chloroform as the terminal oxidant was discovered by Park and co-workers after making the unexpected observation that the Shvo catalyst converts to hydroxycyclopentadienyl chloride complex **101** after heating in chloroform.[156] A small amount of ethanol was found to be necessary for clean conversion to **101**. Heating 2 mol % of **101** with 1.5 equivalents of Na_2CO_3 in $CHCl_3$ at 90 °C in a closed vessel led to the quantitative conversion of a range of secondary alcohols to the corresponding ketones in 6-24 h. The primary alcohols; benzyl alcohol and 1-octanol could be oxidised selectively to aldehydes and diols could be quantitatively oxidised to lactones.
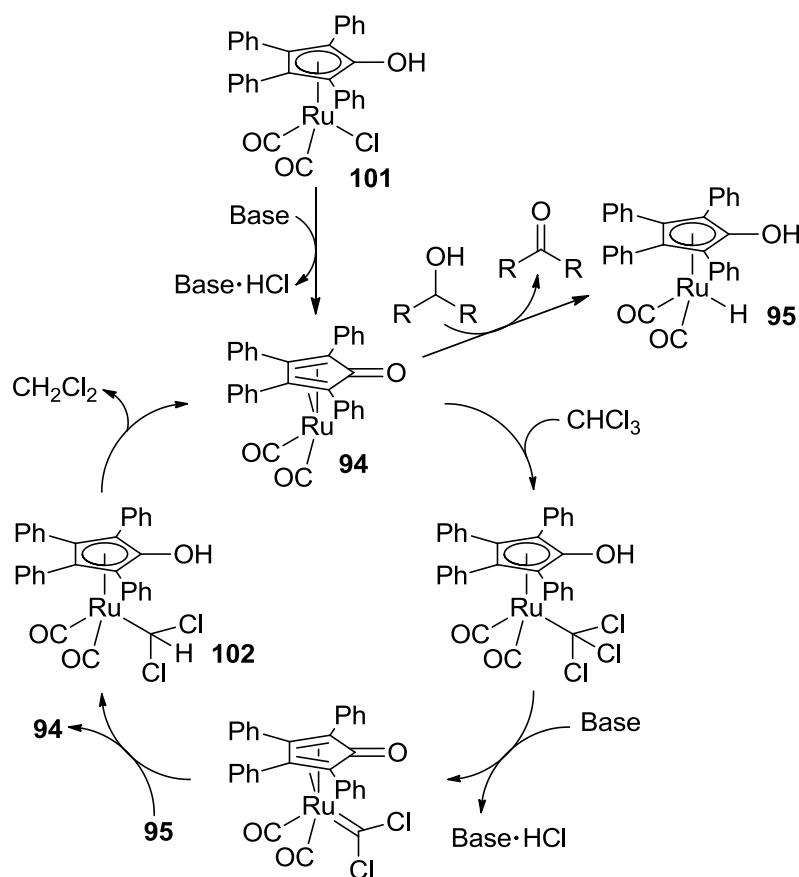
Scheme 22. A speculated catalytic cycle for the oxidation of alcohols with chloroform as the terminal oxidant.

The catalytic cycle for the oxidation of alcohols with chloroform is shown in Scheme 22. The action of base on **101** eliminates HCl to generate unsaturated species **94** which performs the oxidation. Further **94** reacts with $CHCl_3$ to generate a CCl_3 complex which is converted to dichlorocarbene by base. Ruthenium hydride **95**, generated by the alcohol oxidation, reduces the dichlorocarbene complex to regenerate **94** and produce complex **102**, which reductively eliminates DCM to generate more **94** and complete the cycle. The NMR spectra of the reaction mixture showed the presence of the Shvo catalyst, which could in fact be used directly, avoiding the need to synthesise **101** first. DCM was also observed and it was shown that if $CDCl_3$ is used in the reaction then $CDHCl_2$ is generated.

1.7.2.2 Reductions.

The Shvo catalyst is also a very efficient catalyst for the reduction of ketones by formic acid.[157] Aliphatic, allylic and benzylic ketones could be reduced at 100 °C with turnover numbers of up to 7400. Notably, the reduction of benzaldehyde had an initial turnover frequency of 20563 h^{-1} and reached a total of 8000 turnovers. Aliphatic aldehydes, however, were not reduced cleanly and significant aldol side-products were observed. It was found that 10 mol % of water and 20 mol % of sodium formate were required to suppress the formation of formate esters which were otherwise the major products of the reaction. Allylic ketones were selectively reduced at the C=C double bond, the carbonyl was only reduced if an excess of formic acid was present.
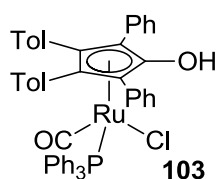
Figure 34. A phosphine-substituted analogue of the Shvo catalyst.

The Shvo catalyst is also a competent pressure hydrogenation catalyst for alkenes and alkynes in addition to aldehydes and ketones with 500 psi H_2 although a higher temperature of 145 °C and longer reaction times are required.[158] A phosphine-substituted analogue (**103**), however, is capable of reducing benzaldehyde at room temperature due to the suppression of dimer formation by the steric bulk of the phosphine.[159, 160]
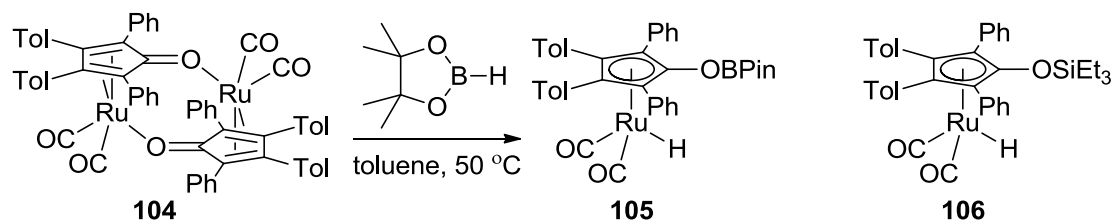
Scheme 23. The synthesis of a boron analogue of the Shvo catalyst and an analogous silyl-substituted complex.

The reduction of aldehydes by the Shvo catalyst can also be achieved under milder conditions (50-70 °C) via a hydroboration with pinacolborane.[161] Casey *et al*. found that ruthenium dimer **104** reacted with pinacol borane to form **105** which was capable of hydroborating aldehydes. The reaction was rendered catalytic by applying 2 mol % of **104** and 1.5 equivalents of pinacolborane. A range of substituted benzaldehydes yielded the corresponding benzylic alcohols in moderate to high yield after workup in up to 40 h. The hydroboration of 3-phenylpropionaldehyde to give 3-phenylpropan-1-ol demonstrated that aliphatic primary alcohols could also be accessed by this reaction. The lower than normal temperatures required for this process in comparison to other reactions catalysed by the Shvo catalyst was attributed to the steric bulk of the BPin unit of complex **105**. As such the formation of a stable hydride-bridged dimer is suppressed, therefore a higher temperature is not required for dissociation. The analogous silyl-substituted complex, **106**, was unreactive towards the hydrosilylation of aldehydes.[149]

1.7.2.3 Dynamic Kinetic Resolution.

In a typical kinetic resolution of a racemic alcohol a lipase enzyme, usually Novozym 435 (*Candida Antarctica* component B lipase), will selectively acylate

one enantiomer of the substrate. A limitation of this process is that a maximum yield of only 50 % is attainable. The application of a transition metal catalyst to continuously racemise the alcoholic substrate provides more of the required enantiomer for the enzyme to acylate and raises the theoretical yield to 100 % in what is now termed a dynamic kinetic resolution (DKR).

Bäckvall *et al.* have demonstrated that the Shvo catalyst is an efficient racemising agent for this process, providing aliphatic and benzylic acetates in up to 99 % e.e. and in 60-88 % yield with 4-chlorophenyl acetate as the acyl donor at 70 °C.[162, 163] An advantage of this method is that enantiopure aliphatic alcohols can be obtained which are difficult to access via the ATH of ketones. Park and co-workers have shown that chiral acetates can also be obtained directly from ketones or enol acetates by performing a DKR in the presence of FA/TEA or H_2.[164, 165]

107
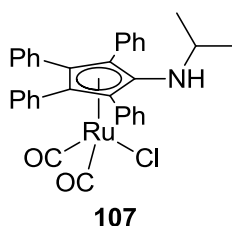
Figure 35. An aminocyclopentadienyl complex for DKR.

The analogous aminocyclopentadienyl complex **107** has also been used for DKR with Novozym 435, isopropenyl acetate and Na_2CO_3 achieving yields of up to 97 % and up to 99 % e.e. at room temperature.[166, 167] The weaker acidity of the NH compared to OH and the steric bulk of the *iso*-propyl group prevent dimer formation, allowing the catalyst to operate at lower temperatures than the Shvo catalyst. Casey attempted to use a similar complex for the reduction of benzaldehyde but due to the low acidity of the NH the reduction was very slow.[168]

Prior protonation of the amine allowed benzaldehyde to be reduced rapidly at - 80

°C but the process could not be made catalytic.

1.7.3 Other Metals.

1.7.3.1 Osmium.
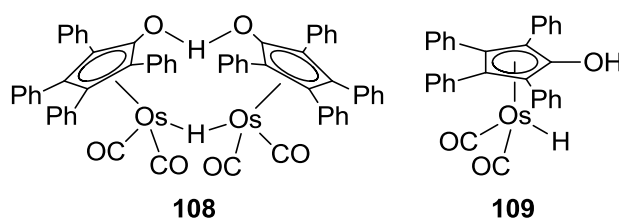
Figure 36. Osmium analogues of the Shvo catalyst.

The analogous osmium complexes **108** and **109** were synthesised by Shvo

and co-workers.[169] Interestingly, whereas the ruthenium hydride **95** is air-sensitive

and quickly decomposes to the more stable dimer **91**, the osmium hydride **109** is

air-stable and requires refluxing in acetone to convert it to dimer **108**. In fact, **108**

and **109** can be separated by column chromatography. Unsurprisingly, catalysis

with **109** proved to be sluggish; the hydrogenation of benzaldehyde at 105 °C with

25 atm H_2 gave a yield of 30 % after 96 h.

1.7.3.2 Iron.
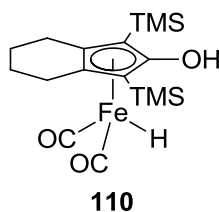
Figure 37. An iron analogue of the Shvo catalyst.

In 2007 Casey and Guan reported on the use of an iron analogue of the Shvo catalyst for the pressure hydrogenation of aldehydes and ketones.[170] With 2 mol % of **110**, benzaldehyde and a range of ketones were reduced in up to 100 % conversion under 3 atm H_2 at room temperature. Notably, isolated alkenes and alkynes are not hydrogenated under the reaction conditions. Partial reduction of the double bond was observed however, in the hydrogenation of an α,β-unsaturated ketone. The catalyst was also active under transfer hydrogenation conditions; acetophenone was reduced in 87 % yield after 16 h by 1 mol % of **110** in 2-propanol at 75 °C.

1.8 Summary.

Various methods for the oxidation of alcohols and the reduction of ketones, including asymmetric reductions, have been described. Transfer hydrogenation has emerged as a synthetically useful tool for the interconversion of alcohols and ketones with the advantages of mild reaction conditions, the use of catalytic quantities of a metal reagent and the use of benign oxidants and reductants.

Of particular interest, the catalytic dehydrogenation of alcohols negates the need for a terminal oxidant such as acetone which makes the reaction atom economic and gives rise to an essentially irreversible reaction after hydrogen gas is lost from the system. The catalytic system of $[RuCl_2(p\text{-cymene})]_2$ and PPh_3 reported by Adair and Williams[73] is simple and effective and our efforts to probe mechanistic aspects of this system will be described in the following section.

The asymmetric transfer hydrogenation of ketones was shown to be an efficient way of accessing chiral alcohols in high optical purity under mild reaction

conditions. Recent developments include efforts to substitute the precious metals used as catalysts such as ruthenium, rhodium and iridium for cheaper and more abundant first-row transition metals such as iron. Notably, iron complexes developed by Morris *et al*. compare favourably with successful precious metal-based catalysts.[113]

The Shvo catalyst is a very versatile and efficient transfer hydrogenation catalyst, capable of a range of different transformations including both oxidations and reductions. Although the Shvo catalyst itself is well-studied, catalytic studies of derivatised ligand structures are comparatively rare, leaving much potential for further study. Of particular note is that at the outset of this project no asymmetric examples had yet been described. An exciting development to this end is the discovery by Casey and Guan that an iron complex with an analogous ligand structure is an effective catalyst for both pressure and transfer hydrogenation.[170] The investigation of new ligand structures based on the Shvo catalyst utilising ruthenium and iron will be discussed in the following section.

2 Results and Discussion.

2.1 Studies on the Dehydrogenation of Alcohols.

A developing interest within the Wills group is the sustainable generation of hydrogen gas as a renewable fuel source. Previous work has included the catalytic decomposition of formic acid to form hydrogen and carbon dioxide.[171, 172] The generation of hydrogen from alcohols is the next logical step in this research programme and forms the first part of this PhD.

For the previously mentioned work on formic acid decomposition, gas evolution was measured by the movement induced on the plungers of attached syringes to a closed reaction vessel.[171] This proved to be impractical for the far slower alcohol dehydrogenation reaction so evolved gasses could not be detected directly and as such reactions were monitored by sampling of the reaction mixture and integration of the ^{1}H NMR spectra. Other workers have demonstrated the presence of hydrogen gas in similar systems by infrared and mass spectrometry[67] and gas chromatography (GC) measurements.[88] In this instance however, the generation of hydrogen gas is implied by the clean conversion of alcohol to ketone (Scheme 24).
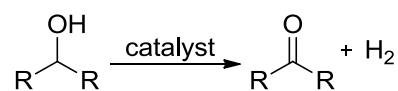
Scheme 24. The oxidation of an alcohol to a ketone and hydrogen.

The possibility remains that an aerobic oxidation could take place with the generation of water as a by-product (rather than hydrogen). This possibility was eliminated by carrying out an oxidation once under a nitrogen atmosphere and once

open to the air. The catalytic system for the dehydrogenation of alcohols reported by Adair and Williams[73] and discussed in section 1.5.3 was chosen for further study due to its effectiveness and operational simplicity. The use of a lower catalyst loading in comparison to the published work gives less than complete conversions and as such allows for a more detailed study of the system. Using 1 mol % [RuCl$_2$(p-cymene)]$_2$, 8 mol % PPh$_3$ and 15 mol % LiOH.H$_2$O, 1-phenylethanol was oxidised in 56 % conversion after 15 h in refluxing toluene under an atmosphere of nitrogen. In a vessel open to the air the conversion was 45 % after 15 h. The lower conversion reflects the air sensitivity of likely ruthenium hydride intermediates.

2.1.1 Substituent Effects.

The electronics of the substrate were shown to be an important factor in the dehydrogenation reaction by carrying out a competition reaction in which 1-phenylethanol and two *para*-substituted derivatives were oxidised simultaneously in one pot. The expected trend was observed with the most electron-rich alcohol being oxidised to the greatest extent. The graph in Figure 38 shows the reaction progress over time.

Figure 38. The simultaneous one-pot oxidation of 3 alcohols, each line represents the conversion of alcohol to the corresponding ketone. Conditions; 0.3 mmol each alcohol, 1 mol % [RuCl$_2$(p-cymene)]$_2$, 8 mol % PPh$_3$, 15 mol % LiOH.H$_2$O, toluene, 110 °C, 15 h.

This trend was demonstrated more noticeably when the experiments were performed in the absence of triphenylphosphine (Figure 39) As Adair and Williams had found, the catalyst was far less efficient; much lower conversions were observed but the most electron-rich alcohol, 1-(4'methoxyphenyl)ethanol, was still oxidised to a reasonable extent, achieving a conversion of 56 % compared to 17 % and 10 % for 1-(4'-methylphenyl)ethanol and 1-phenylethanol respectively.

Figure 39. The oxidation of 3 alcohols, each line represents the conversion of alcohol to the corresponding ketone. Conditions; 3 mmol alcohol, 1 mol % [RuCl$_2$(p-cymene)]$_2$, 15 mol % LiOH.H$_2$O, toluene, 110 °C, 15 h.

A curious feature of the graphs shown in Figures 38 and 39 is that the conversions level off and the reactions do not go to completion. This could imply either catalyst decomposition or that the reactions reach equilibrium. Hydrogen evolution and loss from solution should, however, make the reaction irreversible.

2.1.2 Mechanism of Dehydrogenation.

In considering the mechanism of alcohol dehydrogenation (Scheme 13), two discrete processes take place: in the first process the active catalyst removes two hydrogen atoms from the alcoholic substrate, resulting in a metal hydride species and a carbonyl compound, in the second process hydrogen gas is released from the metal hydride intermediate by reaction with an acidic proton in the case of a monohydridic species or a reductive elimination in the case of a dihydridic species.

By exploiting the reversible nature of transfer hydrogenation it is possible to identify which process is the rate-determining step. If another carbonyl compound is added to the reaction mixture it will be hydrogenated by the metal hydride intermediate, resulting in the formation of a new alcohol (Figure 40). Observation of the conversions of each of the original substrates over time allows for a crude comparison of the relative rates of the two mechanistic steps.
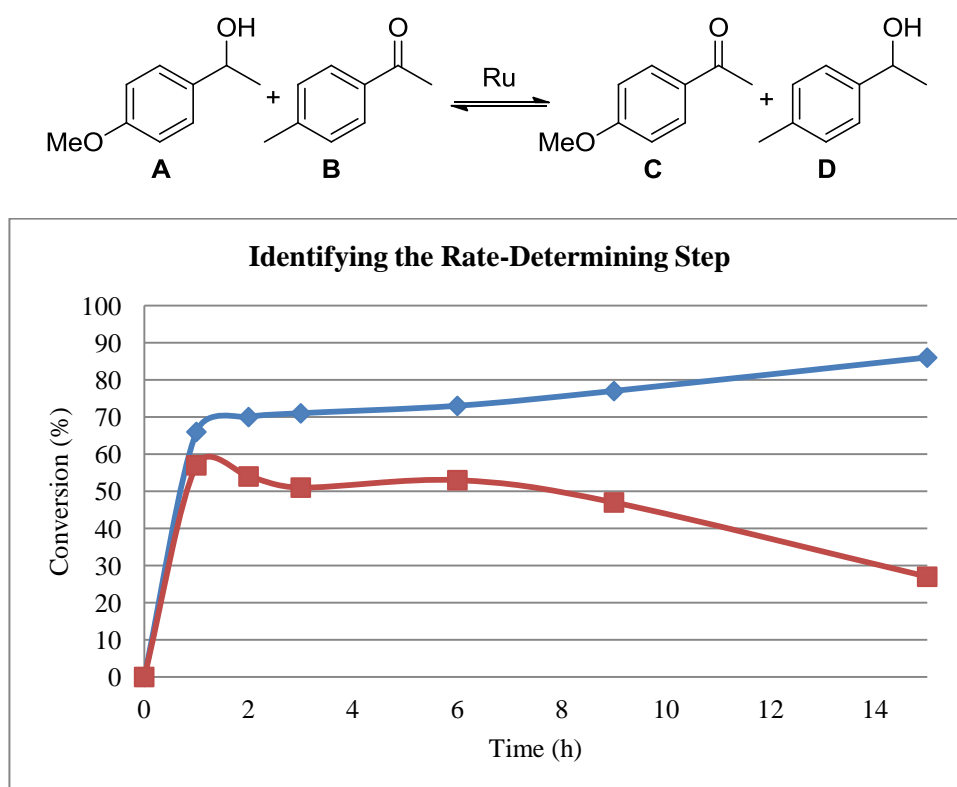
Figure 40. The blue line represents the percentage of ketone **C** relative to alcohol **A** and the red line represents the percentage of alcohol **D** relative to ketone **B** in the reaction mixture. Conditions; 3 mmol **A**, 3 mmol **B**, 1 mol % [RuCl$_2$(p-cymene)]$_2$, 8 mol % PPh$_3$, 15 mol % LiOH.H$_2$O, toluene, 110 °C, 15 h.

The graph illustrated in Figure 40 shows the conversions of **A** and **B** over time. The conversions are high after the first hour which indicates a fast equilibration process between species **A**, **B**, **C** and **D**. This shows that the first process, the oxidation of an alcohol, is fast. The slow rise of the blue line and

decline of the red line as the reaction progresses shows a decrease in the quantities of alcohols **A** and **D** as hydrogen gas is gradually lost from the system. This shows that the second process, the release of hydrogen gas, is slow and therefore, the rate-determining step.

To investigate this further, Noyori's ATH catalyst **111** was chosen to see if it displayed the same slow hydrogen release behaviour. The presence of acidic protons in the NH_2 functionality could be hypothesised to aid in hydrogen gas release. Compound **111**, was synthesised by heating $[RuCl_2(p\text{-cymene})]_2$ and (R,R)-TsDPEN with triethylamine in 2-propanol at reflux for 1 h and was isolated in an 82 % yield by recrystallisation from methanol. The oxidations of 1-phenylethanol, 1-(4'-methoxyphenyl)ethanol and 1-(4'-methylphenyl)ethanol were attempted and the results are displayed in Figure 41. Notably the reaction temperature was lowered from 110 °C to 70 °C to avoid catalyst decomposition. The conversions level off after 2-3 h which could indicate that after a sufficient quantity of ketone is generated hydrogen transfer between the alcohol and the newly formed ketone is so rapid as to suppress further hydrogen gas production. The raised temperatures typically seen (> 100 °C) in dehydrogenation reactions may be necessary to drive hydrogen gas release from the catalyst.
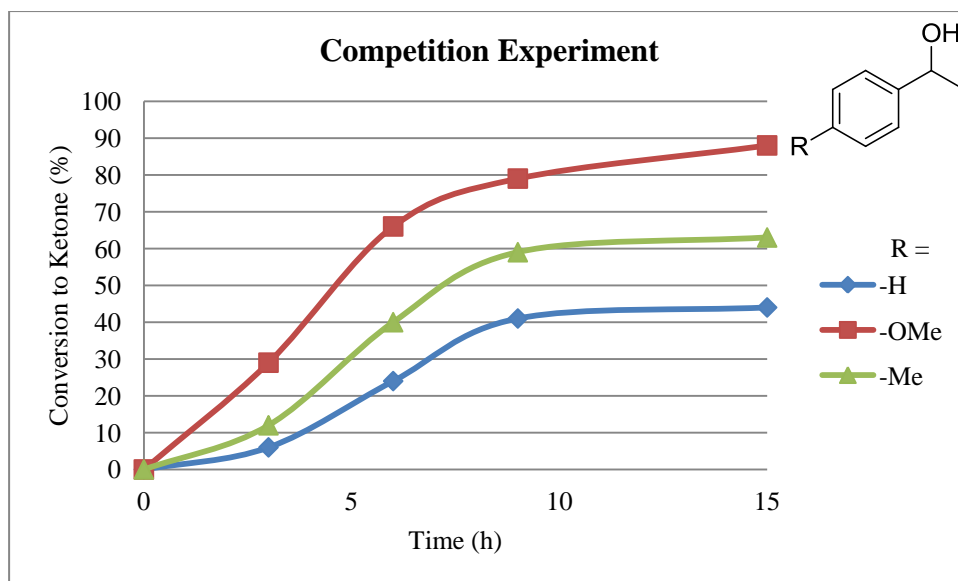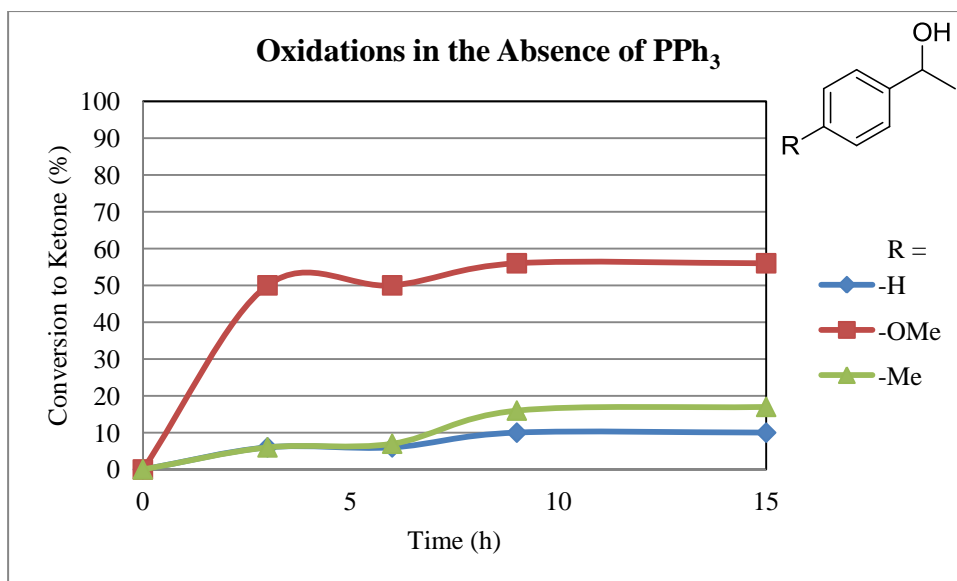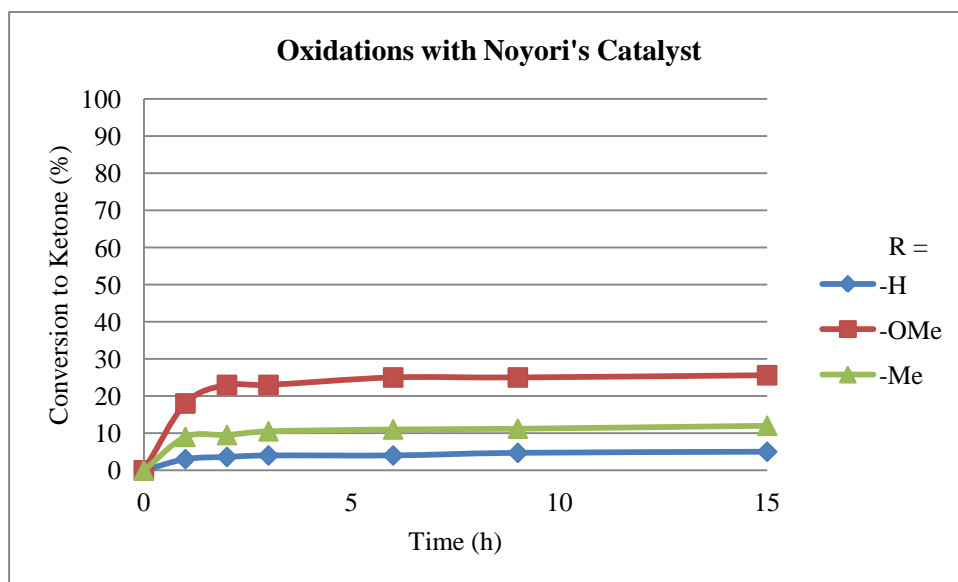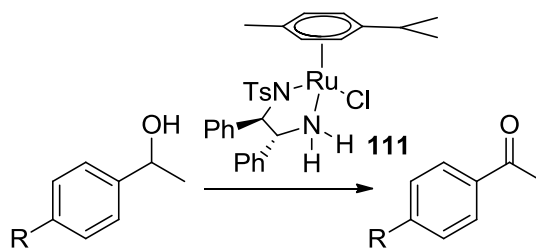
Figure 41. The oxidation of 3 alcohols, each line represents the conversion of alcohol to the corresponding ketone. Conditions; 3 mmol alcohol, 1 mol % **111**, 15 mol % LiOH.H$_2$O, toluene, 70 °C, 15 h.

To eliminate the possibility of catalyst decomposition causing the low conversions observed the same oxidations were repeated in the presence of 5 molar equivalents of acetone as a hydrogen acceptor. Figure 42 shows that significantly higher conversions were achieved which indicates that the reversible transfer of hydrogen is much faster than hydrogen gas release as was found for the [RuCl$_2$(p-cymene)]$_2$/PPh$_3$ system.
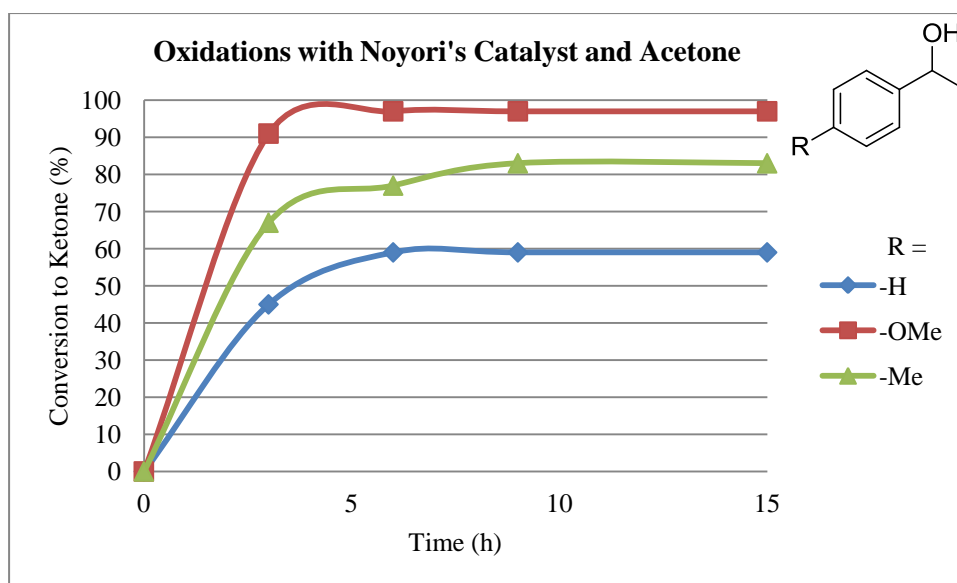
Figure 42. The oxidation of 3 alcohols, each line represents the conversion of alcohol to the corresponding ketone. Conditions; 3 mmol alcohol, 15 mmol acetone, 1 mol % **111**, 15 mol % LiOH.H_2O, toluene, 70 °C, 15 h.

2.2 Alcohol Oxidations with an Acceptor.

The observed efficiency in hydrogen transfer behaviour presents an opportunity; hydrogen could potentially be transferred from complex alcohols from waste or biomass to generate much more simple alcohols for use in fuel cell applications. For example, if hydrogen can be transferred from a complex alcohol, such as glycerol or sucrose, to formaldehyde then the methanol formed could be used in direct methanol fuel cells.

A selection of catalysts were compared in the oxidation of 1-phenylethanol with 10 molar equivalents of acetone in toluene at 70 °C and the results are shown in Figure 43. Interestingly an achiral variant of **111** was more sluggish than its chiral counterpart but reached the same conversion. The Shvo catalyst (**91**) was by far the most efficient, achieving an 88 % conversion after 3 h. The use of

paraformaldehyde as a hydrogen acceptor was also possible with **91**; a 94 % conversion was achieved after 3 h.
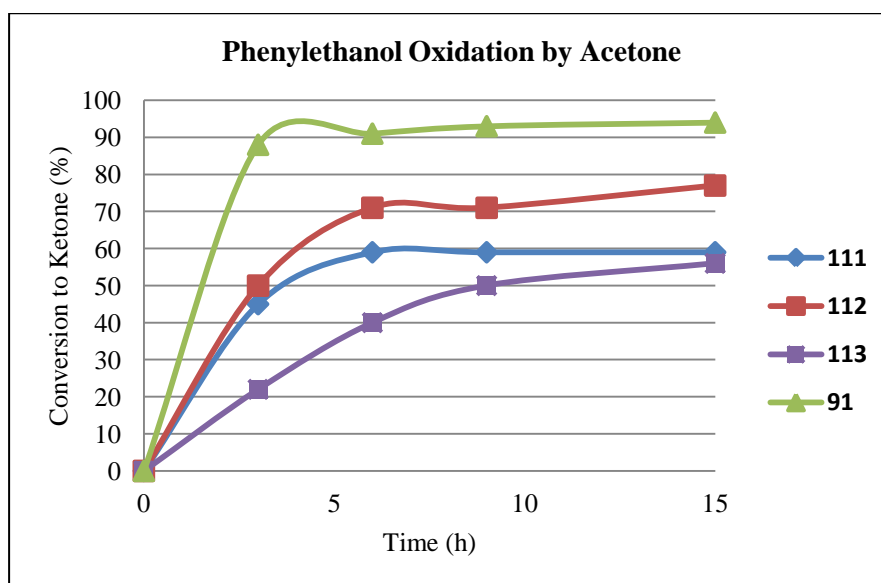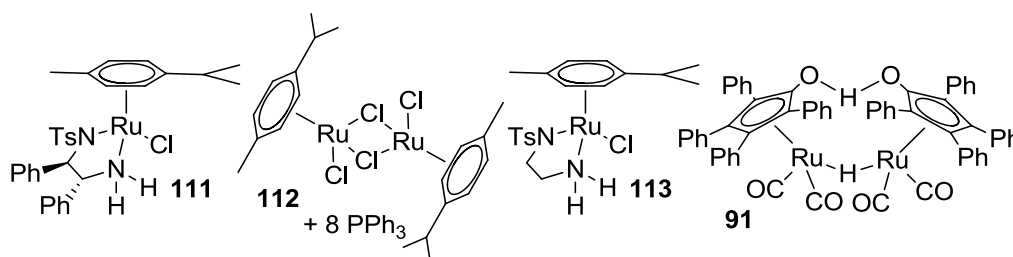
Figure 43. The oxidation of 1-phenylethanol. Conditions; 1 mol % **111**, **113**, 0.5 mol % **112**, **91**, 15 mol % LiOH.H$_2$O (except **91**), toluene, 70 °C, 15 h.

With an efficient transfer hydrogenation catalyst in hand, the oxidation of more complex substrates was attempted. Glycerol (**114**) is a by-product of the biodiesel industry and is cheap, readily available and each mole could potentially provide 3 moles of hydrogen. The oxidation of glycerol was attempted using 0.5 mol % **91** in *tert*-amyl alcohol at 70 °C with a 20-fold excess of acetone, achieving a 15 % conversion to 1,3-dihydroxyacetone (**115**). The use of paraformaldehyde as the hydrogen acceptor resulted in no conversion. Using refluxing acetone as the solvent to drive the equilibrium to the product side led to a small improvement.

Performing the reaction in acetone at 100 °C in a sealed tube gave the best result; a conversion of 44 %. For comparison **111** and **112** were also tested for glycerol oxidation in refluxing acetone but no conversion was observed in either case. Other groups have since reported on the use of glycerol as a solvent and hydrogen donor for the transfer reduction of aldehydes[173] and ketones.[174] The thermal decomposition of **115** was reported to be significant at 100 °C.[174]
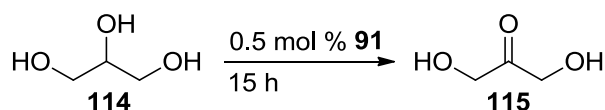
Additive	Solvent	T (°C)	Conversion (%)
20 Equiv acetone	*tert*-Amyl alcohol	70	15
5 Equiv paraformaldehyde	*tert*-Amyl alcohol	70	0
-	Acetone	56	18
-	Acetone	100[a]	44

Table 23. The oxidation of glycerol by **91**. [a] Reaction performed in a sealed tube.

The oxidation of sucrose (Figure 44) was attempted using 1 mol % **111** and 15 mol % LiOH.H_2O in 2:1 *tert*-amyl alcohol/H_2O at 70 °C for 15 h, once in the presence of 5 equivalents of acetone and once without, both of which resulted in no reaction. The use of **112** at a higher temperature of 100 °C with 10 equivalents of acetone also resulted in no reaction. When 4'-methylacetophenone was chosen as a hydrogen acceptor, the oxidation of sucrose could be observed indirectly by the conversion of 4'-methylacetophenone to 1-(4'-methylphenyl)ethanol. Under the aforementioned conditions, **111** achieved a 7 % conversion of 4'-methylacetophenone to 1-(4'-methylphenyl)ethanol and with **112** achieving 2 %. The use of **91** under similar conditions resulted in no conversion.
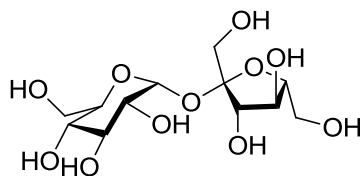
Figure 44. Sucrose, a disaccharide of glucose and fructose with an α-1,2 glycosidic linkage.

2.3 Shvo Catalyst Analogues.
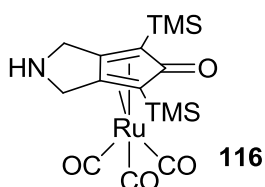
Figure 45. A Shvo catalyst analogue bearing a pendant amine group.

Intrigued by the high reactivity of **91** towards the oxidation of alcohols, efforts were made to synthesise and test complexes with modified ligand structures. Complex **116**, incorporating a pendant amine functionality, was postulated to catalyse the oxidation of alcohols with the subsequent release of hydrogen gas via the intramolecular donation of an amine proton to the ruthenium hydride intermediate **117** (Scheme 25). A proton transfer step would regenerate **118** and complete the catalytic cycle.
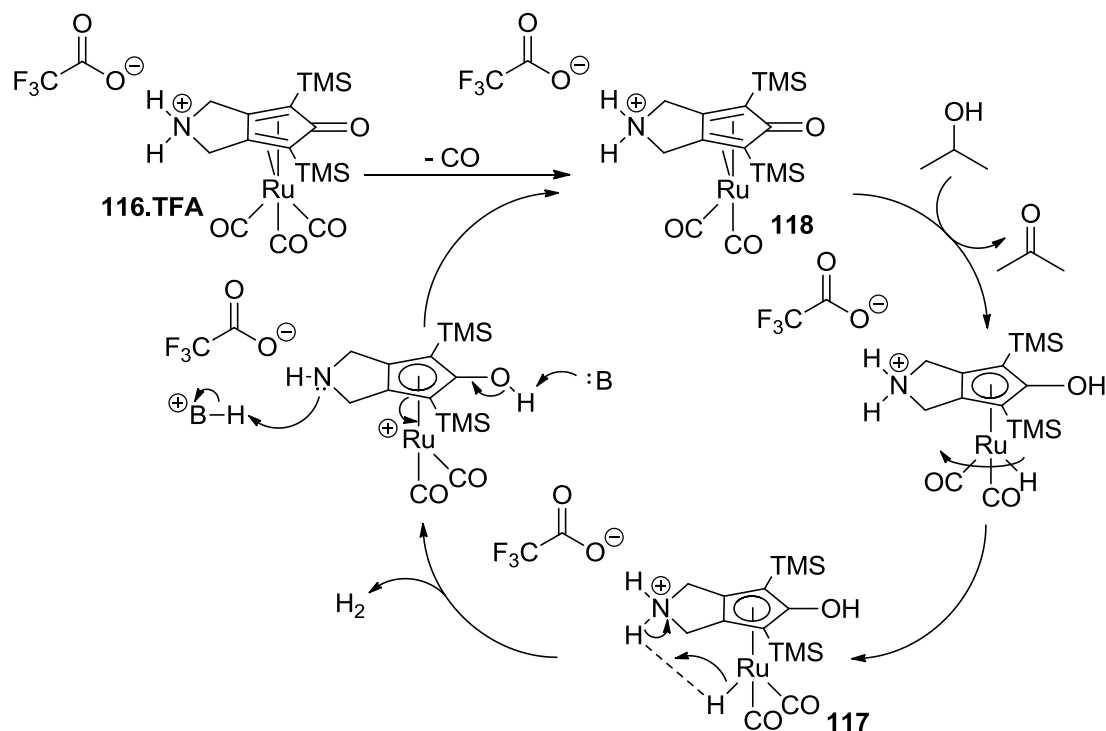
Scheme 25. A speculated catalytic cycle for hydrogen gas release from a hydroxycyclopentadienyl hydride generated from **116.TFA**.

Hydrogen gas release from **96** was studied by Casey *et al.* and was found to be slow and required elevated temperatures.[148] The rate was found to increase significantly in the presence of H_2O or ethanol owing to the interaction illustrated in Scheme 26. Rapid exchange of the hydride and hydroxyl protons was demonstrated by a labelling experiment and alludes to the intermediacy of a dihydrogen complex.
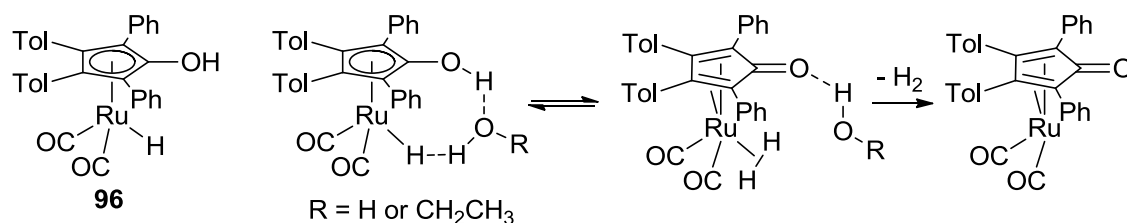
Scheme 26. Hydrogen loss from a hydroxycyclopentadienyl hydride.

The aminocyclopentadienyl complex **119** has also been shown to release hydrogen rapidly at -25 °C but the amine must be protonated for the reaction to occur; the free amine does not have the required acidity.[168]
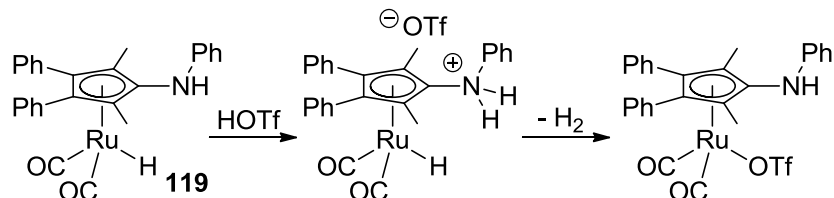
Scheme 27. Hydrogen gas release from an aminocyclopentadienyl complex.

The synthetic route to access **116** is illustrated in Scheme 28. An alkylation of the starting material with sodium hydride and propargyl bromide followed by a lithiation to install trimethylsilyl groups provided the ligand precursor which was reacted with $Ru_3(CO)_{12}$ in a sealed tube to give complex **120**. Following reaction with trifluoroacetic acid (TFA) to remove the *tert*-butoxycarbonyl (Boc) protecting group the volatiles were removed and the resulting complex (**116.TFA**) was used for catalytic reactions without further purification.
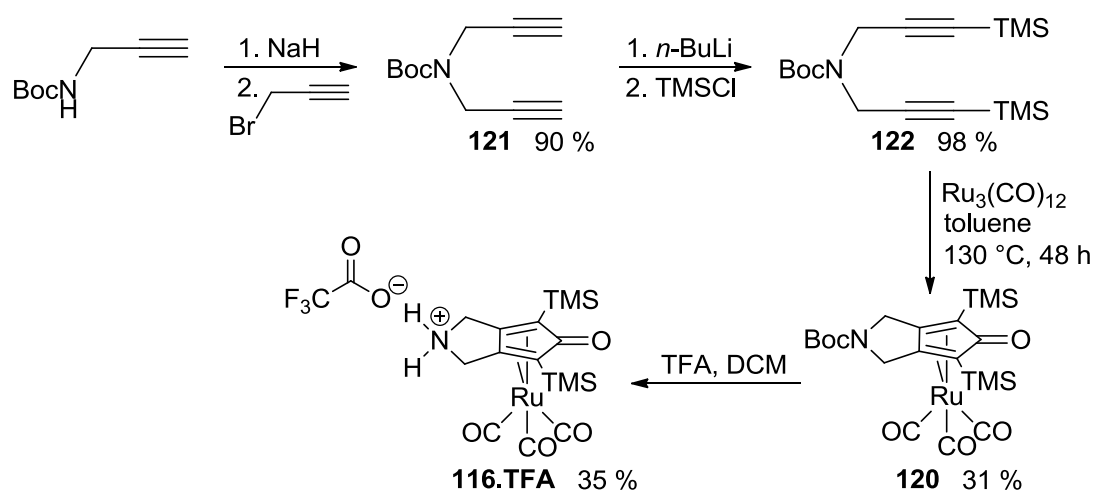
Scheme 28. The synthetic route to Shvo analogue **116.TFA**.

Complexes **91**, **116.TFA** and **120** were applied to the oxidation of 1-phenylethanol in the absence of a hydrogen acceptor in toluene at 70 °C, giving conversions of 7 %, 3 % and 1 % respectively after 15 h. The fact that complexes **116.TFA** and **120** gave lower conversions than **91** indicate that the pendant amine does not have a significant impact on the catalysis.

Complexes **116.TFA** and **120** were also tested for the oxidation of 1-phenylethanol in the presence of 20 molar equivalents of acetone in toluene at 70 °C, achieving conversions of 14 % and 19 % after 15 h. Raising the temperature to 110 °C gave conversions of 50 % and 91 %. The higher temperatures required for a high conversion could imply that the complexes are less competent catalysts than **91**. Another possibility is that thermal activation by loss of a CO ligand is a slow process. To probe this, **120** was heated at 110 °C for 50 minutes prior to performing the catalysis at 70 °C. A conversion of 43 % was achieved, compared to 19 % without the pre-treatment, indicating that CO loss must be slow.

2.4 (Cyclopentadienone)iron Tricarbonyl Complexes.
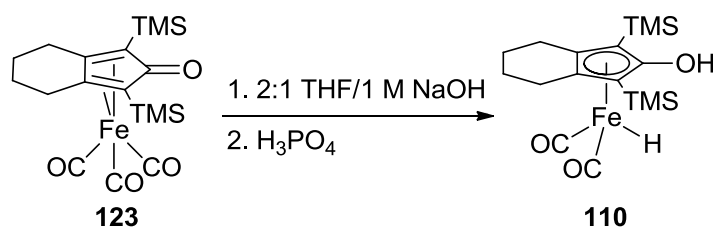
Scheme 29. The basic hydrolysis of a CO ligand to generate an iron hydride complex.

Casey and Guan[170] reported on the application of an iron analogue (**110**) of the Shvo catalyst for the reduction of aldehydes and ketones as discussed in section

1.7.3.2. An intriguing point about this work is that the active catalyst **110** is synthesised from a tricarbonyl precursor (**123**) prior to use. We have demonstrated that a similar ruthenium tricarbonyl complex is a catalyst precursor for transfer hydrogenation and so set out to test if a (cyclopentadienone)iron tricarbonyl complex can also function as a catalyst precursor.
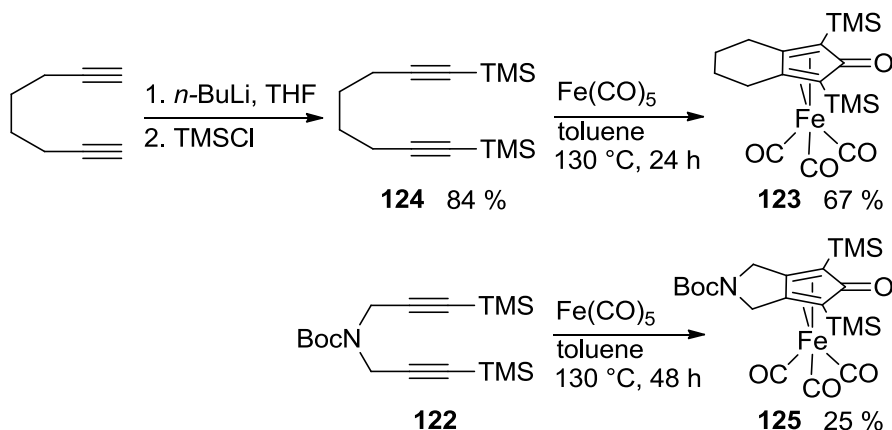
Scheme 30. The synthesis of iron complexes **123** and **125**.

Initially two different iron complexes were synthesised; complex **123** was made according to the original literature procedure[175] and **125** which is the iron analogue of **120**. Attempts to use these complexes to form an active catalyst *in situ* for the oxidation of 1-phenylethanol in refluxing acetone for 48 h resulted in no conversion of the starting material. Refluxing in toluene with 5 equivalents of acetone was also unsuccessful.

These results suggest that the thermal loss of CO is more difficult from iron than from ruthenium. This is supported by the observation by Takats and coworkers that M-CO bond strength with transition metals varies in the order 1st row > 3rd row > 2nd row.[176] Evidence for this can be seen in the IR data; the C≡O stretching frequencies are 2081, 2023 and 2002 for **120** and 2070, 2016 and 1994 for **125**. The lower stretching frequencies for iron indicate a weaker C≡O bond as a result of

increased back-donation from iron relative to ruthenium, causing the M-CO bond to be stronger.

126 91 %
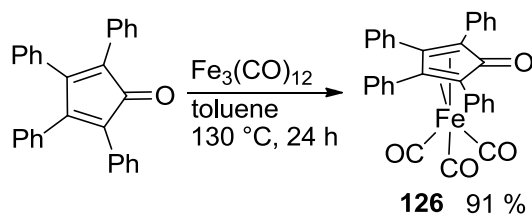
Scheme 31. An iron catalyst for the oxidation of alcohols.

The *in situ* catalytic activity of **126** (Scheme 31) in the oxidation of alcohols was reported by Williams *et al.*[177] Using 10 mol % **126** in acetone at 54 °C, 1-phenylethanol was oxidised in 44 % conversion after 4 days. The reaction mixture was prepared in air and performed in a sealed NMR tube so the CO lost from **126** to form the active catalyst was still present and may have had a detrimental effect on the reaction. Complex **126** was synthesised directly from tetraphenylcyclopentadienone and $Fe_3(CO)_{12}$ and was used for the oxidation of 1-phenylethanol under oxygen-free conditions and the results are summarised in Table 24. Complex **126** can also be synthesised using $Fe(CO)_5$ but ultraviolet radiation is required.[178]
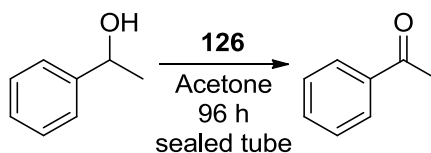
Entry	126 (mol %)	Conc (M)	H_2O	T (°C)	Conversion (%)
1	10	0.19	-	60	29
2	5	0.38	-	60	29
3	10	0.19	-	80	63
4	5	0.38	-	80	45
5	10	0.19	1 drop	60	82
6	5	0.38	1 drop	60	67
7	10	0.19	1 drop	80	95
8	5	0.38	1 drop	80	92
9^a	10	0.19	10 mol %	60	85^b

Table 24. The oxidation of 1-phenylethanol catalysed by **126**. [a] Reaction was performed in a schlenk tube. [b] Conversion is after 48 h, quantitative conversion after 72 h.

Entries 1-8 were performed in a sealed pressure tube. It was found that the addition of H_2O is beneficial, giving much improved conversions (Entries 5-8). Williams suggested that H_2O might hydrolyse one of the CO ligands of **126**, liberating CO_2. The lower conversions in the absence of H_2O might suggest that the thermal loss of CO is more reluctant than hydrolysis or that lost CO may re-coordinate on account of the sealed system. An experiment in an open system (Entry 9) allowed the reaction to be monitored over time; an 85 % conversion was attained after 48 h and the reaction was complete after 72 h, the corresponding experiment in a sealed tube (Entry 5) did not reach completion, stopping after 82 % conversion.

Encouraged by these results, further derivatives were prepared with the goal that *in situ* activation by H_2O might be possible for complexes other than **126**. The alkylation of a propargylic alcohol with propargyl bromide provided a dipropargylic ether which was either silylated via a lithiation or a phenyl ring was installed via a palladium-catalysed Sonogashira coupling. Reaction with $Fe(CO)_5$ gave the desired cyclopentadienone complexes in moderate yield after chromatography. This synthesis allows for modification of the ligand structure in three different places which should allow the complexes to be easily tuned to optimise catalytic activity.
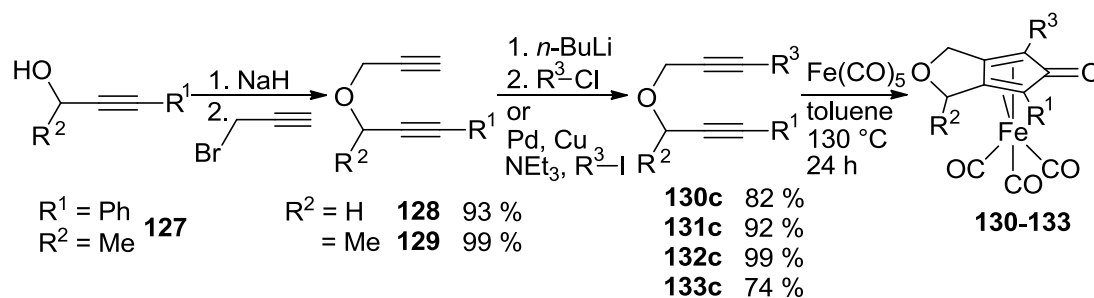
Complex	R^1	R^2	R^3	Yield (%)	a/b
130	Ph	H	Ph	39	-
131	Ph	Me	Ph	23	1.3:1
132	Ph	Me	TMS	45	2.8:1
133	Ph	Me	TBDMS	53	2.7:1

Table 25. The synthetic approach to iron complexes **130**-**133**.
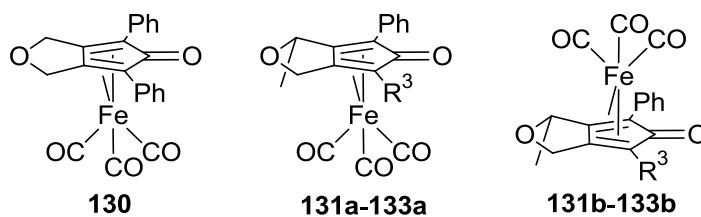
Figure 46. The structures of complexes **130**-**133**.

Complexes **131**-**133** contain a chiral centre in addition to planar chirality due to the unsymmetrical cyclopentadienone ligands and as such were formed as a mixture of diastereoisomers. When a phenyl ring was present in the R^1 position and a methyl group was in the R^2 position the diastereoisomers were separable by column chromatography. The addition of this chiral centre is important for asymmetric applications that will be discussed later. A series of closely-related ruthenium complexes bearing TBDMS or TIPS groups at R^1 were synthesised by a postdoctoral research assistant in the group, Jonathan Hopewell, in addition to a series of complexes bearing a phenyl ring in the R^2 position and in all such cases an inseparable mixture of diastereoisomers was obtained.

The ^{1}H NMR spectra of both diasteroisomers of **133** are shown in Figure 47. Some notable differences are that the CH quartet at ~5.5 ppm and the CH_3 doublet at ~1.6 ppm are shifted slightly reflecting their different orientations with respect to the metal centre. There is also a distinctive downfield shift of a resonance in the aromatic region of **133b** which is characteristic of the **b** diastereoisomers. The two methyl groups present in the silyl functionality are inequivalent as evidenced by the two singlets at ~0 ppm and ~0.5 ppm implying that rotation about the C-Si bond is restricted.
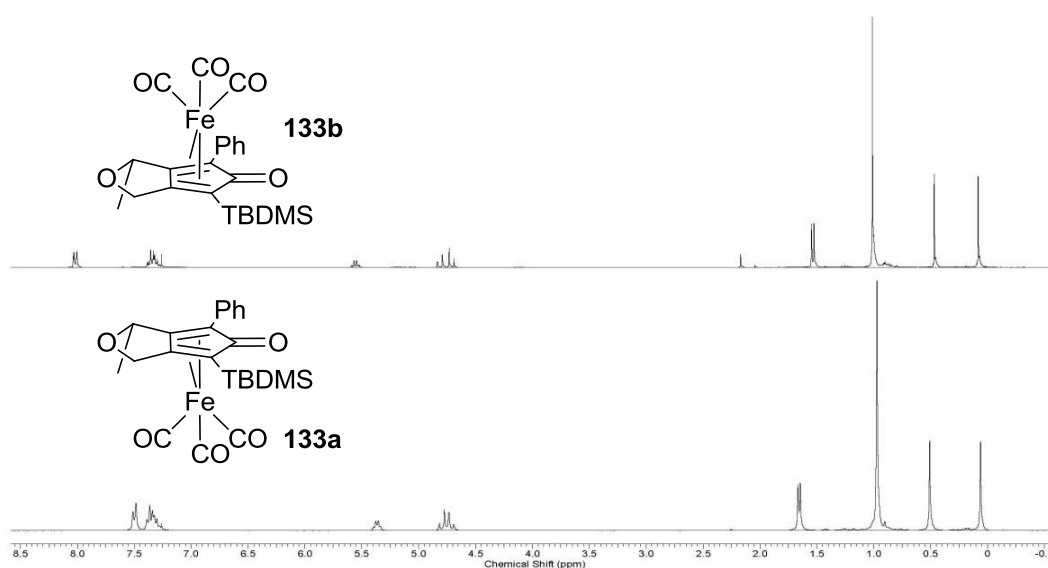
Figure 47. The ^{1}H NMR spectra of **133a** and **133b**.

In order to assign which structure belonged to which diasteroisomer it was necessary to obtain an X-ray crystal structure. Suitable crystals of **133b** were grown from an acetone/H$_2$O mixture and the structure is illustrated in Figure 48. Both enantiomers are present in the unit cell and the methyl group can be seen to point away from the metal centre. The diastereoisomers of **131** and **132** were assigned by analogy to this structure and the ^{1}H NMR spectra.
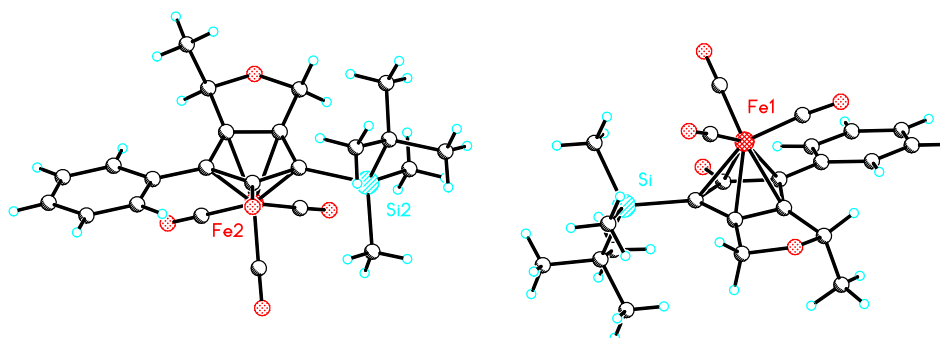
Figure 48. The X-ray crystal structure of **133b**.

Complexes **123**, **125** and **130**-**133** were submitted to the most successful reaction conditions found for **126** (Table 24, Entry 9) for the oxidation of 1-

phenylethanol in acetone and in all cases only traces of acetophenone were observed. Of the iron complexes studied, **126** appears to be unique in its ability to lose a CO ligand under mild conditions. The oxidation of 1-phenylethanol was carried out using **123** in the presence of LiOH.H_2O in an attempt to hydrolyse a CO ligand *in situ* to initiate catalysis but this proved to be unsuccessful. A stronger base, NaOH, was similarly ineffective; the prior synthesis of an iron hydride complex may be necessary to facilitate catalysis.

2.4.1 Catalyst Activation.

The method for transforming iron tricarbonyl complex **123** to iron dicarbonyl hydride **110** (Scheme 29) was first reported by Knölker[179] and can be achieved under strictly anaerobic conditions. The product however, is not formed cleanly and is extremely air sensitive making purification difficult. Therefore a new method for this transformation is desirable.
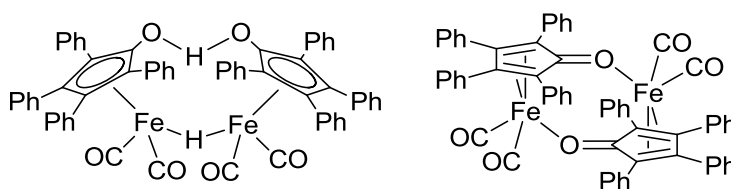
Figure 49. Hypothesised iron dimers.

The air stability of the Shvo catalyst (**91**) can be attributed to its dimeric structure; the monomeric reducing form of the catalyst, **95**, is air sensitive. If a dimeric form of an analogous iron complex could be synthesised then an air stable catalyst precursor would be realised (Figure 49). A mixture of aqueous Na_2CO_3 and acetone is capable of converting the tricarbonyl precursor (**92**) to **91**. The hydrolysis of a CO ligand of **92** results in the formation of ruthenium hydride **95**

which can reduce acetone to form the unsaturated ruthenium species **94** which traps another molecule of **95** to generate **91** (Scheme 32). Subjecting iron complex **126** to the same conditions did not result in the formation of the expected dimeric species.
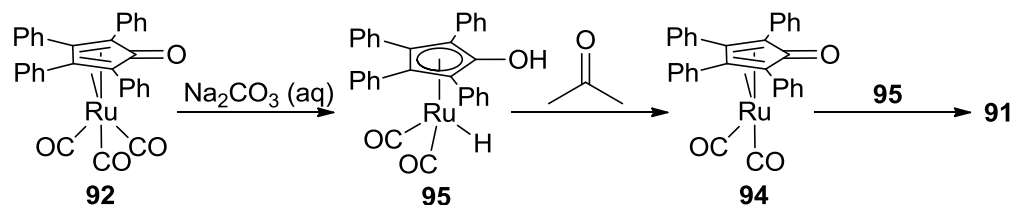
Scheme 32. Synthesis of **91** from a tricarbonyl complex.

A novel approach to the desired hydride synthesis was envisaged by analogy to a reaction reported by Ogoshi *et al*. for the synthesis of an acyl derivative of **92** using AlMe$_3$.[180] The coordination of borane to the cyclopentadienone carbonyl and subsequent donation of a hydride to one of the CO ligands would generate a formyl complex which would be expected to decompose to the desired hydride (Scheme 33). Hydride donation could also take place to the metal centre via a ring-slip mechanism followed by CO dissociation. When attempted with **92**, weak signals at -9.86 ppm and -18.37 ppm were observed in the ^{1}H NMR spectrum indicative of the presence of ruthenium hydrides **95** and **91** respectively.[149] With complex **126**, however, a broad signal at 13.81 ppm was observed which is near the expected range for a metal formyl proton.[181-183] No signals indicative of hydrides were observed.
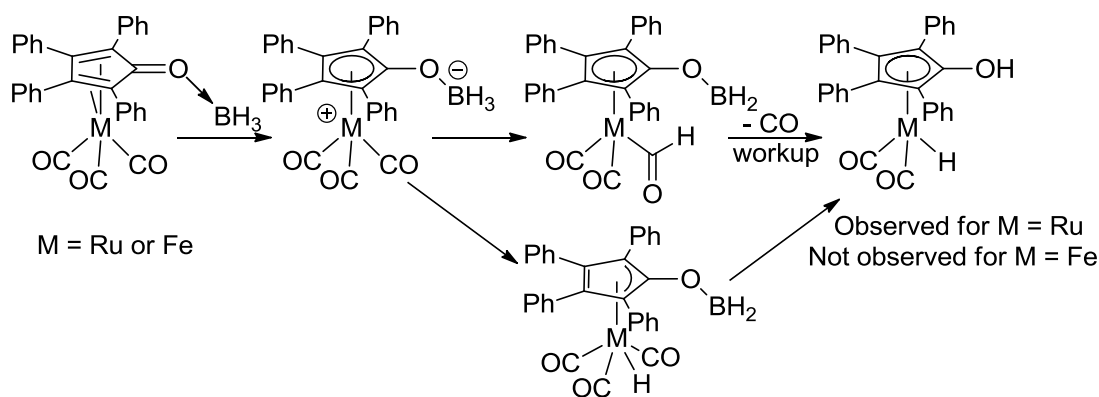
Scheme 33. Attempted hydride formation by addition of borane. One of several possible ring-slips shown.

Following unsuccessful attempts to form hydroxycyclopentadienyl hydride complexes efforts were focussed on the use of additives for *in situ* activation. Trimethylamine *N*-oxide (TMANO) is a well-known reagent for the decarbonylation of metal carbonyl complexes[184] and has been used to mediate ligand substitution reactions of cyclopentadienone carbonyl complexes[185, 186] and demetalation to isolate the free cyclopentadienone.[187] TMANO reacts with metal carbonyls by nucleophilic attack at the carbonyl carbon followed by elimination of CO_2 and Me_3N as shown in Scheme 34.
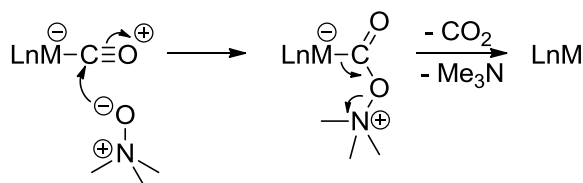
Scheme 34. The removal of CO from a metal complex by TMANO.

2.4.2 Alcohol Oxidations with Acetone.

Using one molar equivalent of TMANO per mole of complex, the *in situ* activation of (cyclopentadienone)iron tricarbonyl complexes towards hydrogen-

transfer was achieved. Data for the oxidation of 1-phenylethanol in acetone at 60 °C are shown in Table 26. Complex **126** gave the highest conversion at 99 %, followed by complex **133b** at 63 %. Notably, there is a pronounced difference in reactivity between diastereoisomers of the same complex with the **b** diastereoisomers of complexes **132** and **133** outperforming the **a** diastereoisomers whilst the **b** diastereoisomer of complex **131** is almost inactive.
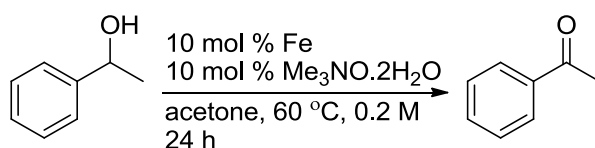
Complex	123	125	126	130	131a	131b	132a	132b	133a	133b
Conv (%)	61	17	99	15	14	2	11	34	11	63

Table 26. The iron catalysed oxidation of 1-phenylethanol.

During the course of this work two papers were published by other researchers concerning the use of iron cyclopentadienone complexes for the oxidation of alcohols. Guan and co-workers used preformed hydride **110** for the oxidation of a wide range of alcohols.[188] Funk and Moyer had a similar idea and reported on the use of **123** with TMANO for the oxidation of a range of allylic, aliphatic and benzylic alcohols in acetone.[189] Two further complexes were also synthesised and tested and a comparison for the oxidation of 1-phenylethanol is reproduced in Table 27. Exchanging the TMS substituents of the ligand for phenyl rings resulted in a lower conversion. Going from a 6-membered ring to a 5-membered ring was similarly detrimental.
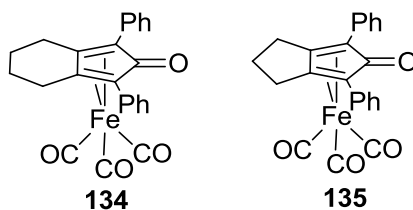
Complex	123	134	135
Conversion (%)	97	79	36

Table 27. The oxidation of 1-phenylethanol as reported by Moyer and Funk. 10 mol % catalyst, 10 mol % $Me_3NO.2H_2O$, acetone, 0.5 M, reflux, 18 h.

Bearing in mind the publication of very similar work, our own studies of substrate scope were limited to a few selected examples to avoid too much repetition. The oxidation of further substrates with **126** was carried out and the results are listed in Table 28. The oxidation of the electron-rich 1-(4-methoxyphenyl)ethanol proceeds rapidly, reaching essentially quantitative conversion after 6 h. 1-Phenylethanol is fully converted after 24 h but a conversion of 78 % after 6 h is listed for comparison. The electron-poor 1-(4-chlorophenyl)ethanol was only 48 % converted after 24 h. An aliphatic alcohol, 1-cyclohexylethanol could also be oxidised, reaching 86 % conversion after 24 h. Notably, the primary alcohol *p*-anisyl alcohol could be oxidised selectively to the aldehyde product without the formation of an ester.

R	C_6H_5	4-MeOC_6H_4	4-MeOC_6H_4	4-ClC_6H_4	Cyclohexyl
R'	Me	Me	H	Me	Me
Conv (%)	78 (6 h)	99 (6 h)	92 (6 h)	48 (24 h)	86 (24 h)

Table 28. The oxidation of various alcohols by **126**.

2.4.3 Alcohol Oxidations with Aldehydes.

The use of other hydrogen acceptors was also investigated. Table 29 shows the conversions obtained for the oxidation of 1-phenylethanol with **126** in the presence of 5 molar equivalents of some simple aldehydes in toluene solvent. In general, the aldehydes tested were less effective hydrogen acceptors than acetone with the exception of paraformaldehyde which was able to achieve a higher conversion after 6 h than acetone.

R	H	Me	Et	^{n}Pr
Conversion (%)	88	40	22	32
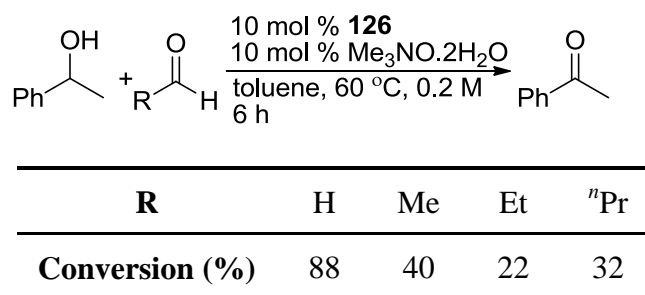
Table 29. The oxidation of 1-phenylethanol with various aldehydes as hydrogen acceptors.

When the complexes were tested using paraformaldehyde as an acceptor an interesting behaviour was observed; the formation of acetophenone took place but the reaction was not selective. The major product of the reaction in most cases was another compound which was identified by independent synthesis as 1-phenylethyl formate. Only traces of this product were identified in reactions with the Shvo catalyst and paraformaldehyde discussed earlier. Table 30 lists the conversion and the selectivity for both products. Complexes **132b** and **133b** showed increased selectivity for 1-phenylethyl formate relative to the corresponding major diastereoisomers whereas both diastereoisomers of complex **131** exhibit a relatively low activity and similar selectivity. After conversion of 1-phenylethanol has been completed the selectivity of the product mixture does not change, indicating that the

products are formed in competing processes rather than further reaction of the acetophenone product. In a control reaction without the iron complex no reaction took place.
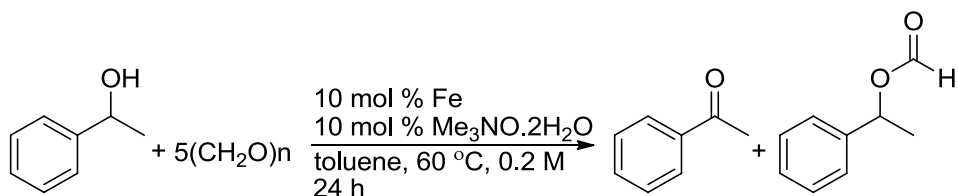
Complex	Conv (%)	Selectivity (%)	
		Acetophenone	1-Phenylethyl formate
123	62	25	75
125	80	41	59
126	99	56	44
130	48	25	75
131a	29	29	71
131b	13	33	67
132a	98	52	48
132b	93	21	79
133a	36	40	60
133b	77	20	80

Table 30. The oxidation of 1-phenylethanol with iron catalysts and paraformaldehyde.

To further probe the selectivity of this formylation process complex **136** was synthesised which is analogous to complex **132** but lacking a methyl group in the backbone of the ligand. The selectivity for 1-phenylethyl formate over acetophenone was expected to fall in between the values seen for the two diastereoisomers of **132**. The synthesis of **136** is shown in Scheme 35. When applied to the oxidation of 1-phenylethanol with paraformaldehyde, **136** showed the

expected selectivity; 70 % of the product formed was 1-phenylethyl formate compared to 48 % for **132a** and 79 % for **132b** (Table 30). Notably, **136** performed the reaction more rapidly than anticipated, achieving a 96 % conversion after 5 h compared to 88 % in 6 h for **126**.
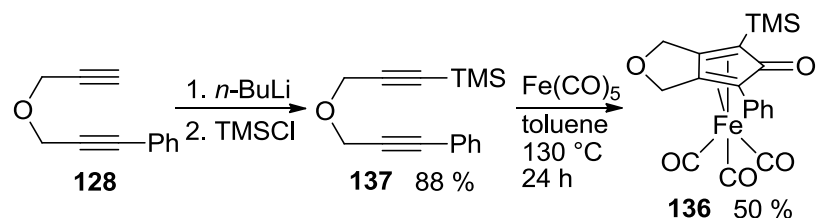
Scheme 35. The synthesis of complex **136**.

Substrate	Complex	Conv (%)	Selectivity (%)	
			Acetophenone	1-Phenylethyl formate
	126	88 (6 h)	56	44
	136	96 (5 h)	30	70
	126	93 (6 h)	70	30
	136	96 (6 h)	50	50
	126	97 (3 h)	55	45
	136	99 (3 h)	19	81
	126	94 (3 h)	65	35
	136	91 (6 h)	24	76

Table 31. The oxidation of various alcohols by **126** and **136** with paraformaldehyde. 10 mol % catalyst, 10 mol % $Me_3NO.2H_2O$, 5 equiv paraformaldehyde, toluene, 0.2 M, 60 °C.

Other substrates were also tested in the oxidation reaction with paraformaldehyde and the results are shown in Table 31. The selectivities vary

from one substrate to another and do not appear to adhere to a noticeable trend. In regard to activity, however, all of the substrates tested appear to react rapidly, achieving high conversions in 3-6 h. Most surprisingly, the electron donating and withdrawing effects in the substrates do not appear to be influential on activity which is quite unusual. In fact the electron-poor 1-(4-chlorophenyl)ethanol reached 94 % conversion after 3 h with **126** with 65 % selectivity in favour of the ketone product compared to 93 % conversion after 6 h and 70 % selectivity for the ketone in the oxidation of the electron-rich 1-(4-methoxyphenyl)ethanol. After 3 h 1-(4-methoxyphenyl)ethanol was at 70 % conversion so the electron-poor alcohol was actually oxidised more rapidly which opposes the trend observed with acetone as the hydrogen acceptor. The same comparison cannot be made for **136**, however.

Attempts to drive the selectivity of the reaction towards the formyl ester products were made by increasing the number of equivalents of paraformaldehyde present (Table 32). In the oxidation of 1-phenylethanol with **136** a selectivity of 81 % in favour of the formate product can be achieved by increasing the equivalents of paraformaldehyde from 5 to 10. Increasing it to 15 provides a further increase in selectivity to 85 %. With 25 equivalents no significant improvement is noted and the conversion begins to suffer, falling to 80 %.

Table 32. Varying the amount of paraformaldehyde.
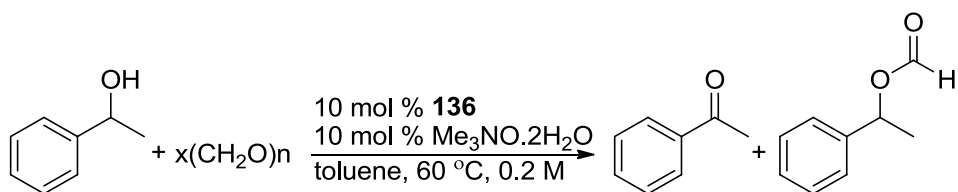
x	Conv (%)	Selectivity (%)	
		Acetophenone	1-Phenylethyl formate
5	96 (5 h)	30	70
10	94 (5 h)	19	81
15	99 (4 h)	15	85
25	80 (6 h)	14	86

Although no ester formation was observed for the oxidation of 1-phenylethanol with aldehydes other than paraformaldehyde, the possibility was investigated that ester formation might take place with other substrates. Table 33 shows the oxidation of other alcohols with **126** using n-butanal as the hydrogen acceptor. Only low to moderate conversions were achieved and in no case was ester formation observed.

R	C_6H_5	4-MeOC$_6$H$_4$	4-MeOC$_6$H$_4$	4-ClC$_6$H$_4$	Cyclohexyl
R'	Me	Me	H	Me	Me
Conv (%)	32	63	15	26	21

Table 33. The oxidation of alcohols using **126** and n-butanal. 5 Equivalents of n-butanal.

The use of an amine as a nucleophile in this process was investigated using α-methylbenzylamine but no reaction took place. The formylation of amines has

been reported using paraformaldehyde with $[Cp*IrI_2]_2$.[190] The formylation was thought to take place via hemiaminal formation between the amine and paraformaldehyde followed by oxidation by the iridium catalyst (Scheme 36).

$$R\diagup NH_2 \quad \xrightarrow{CH_2O} \quad R\diagup N(H)\diagup OH \quad \xrightarrow[CH_2O]{Catalyst} \quad R\diagup N(H)\diagdown O$$
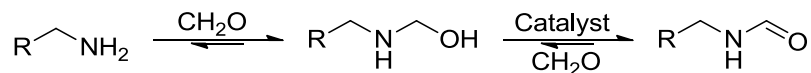
Scheme 36. The formylation of amines.

A tentative catalytic cycle for the iron catalysed formylation of alcohols with paraformaldehyde is shown in Scheme 37. After activation of the iron complex by TMANO, a Lewis acidic-type activation of formaldehyde would allow for nucleophilic attack by the alcoholic substrate to take place. Following a proton transfer step a ring-slip of the hydroxycyclopentadienyl ligand could take place to generate a vacant coordination site, allowing a β-hydride elimination to occur. This would generate the formate product and an iron hydride which could reduce a molecule of formaldehyde to complete the catalytic cycle. Alternatively, the mechanism could deviate following the proton transfer; a reductive elimination would generate a hemi-acetal intermediate which could subsequently be oxidised to generate the product and an iron hydride which would re-enter the catalytic cycle by reducing a molecule of formaldehyde (Scheme 38).
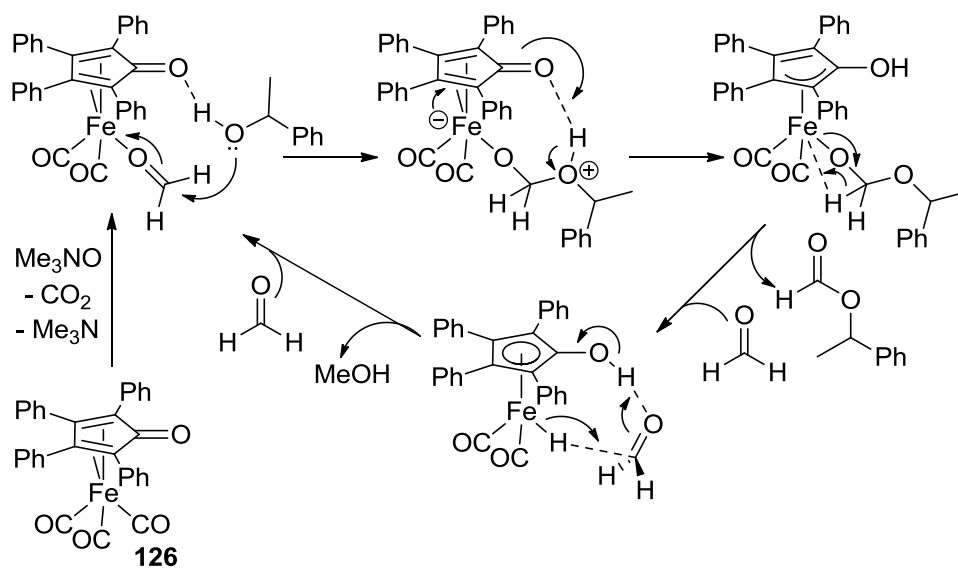
Scheme 37. A speculative mechanism for the formylation of alcohols catalysed by iron cyclopentadienone complexes. One of several possible ring-slips shown.
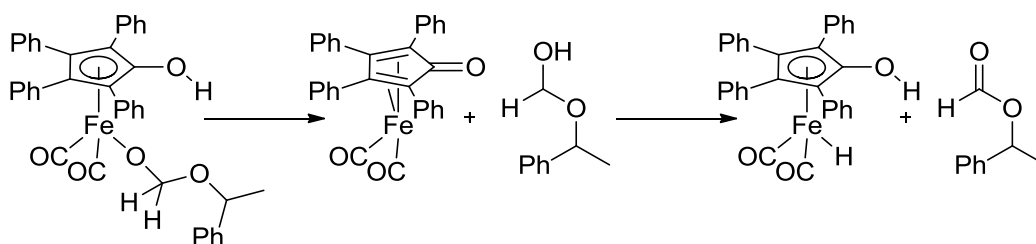
Scheme 38. An alternative pathway in the formylation of alcohols.

2.4.4 Ketone Reductions.

With the completion of a body of work on alcohol oxidation reactions with (cyclopentadienone)iron tricarbonyl complexes, attention was now directed towards the asymmetric reduction of ketones.
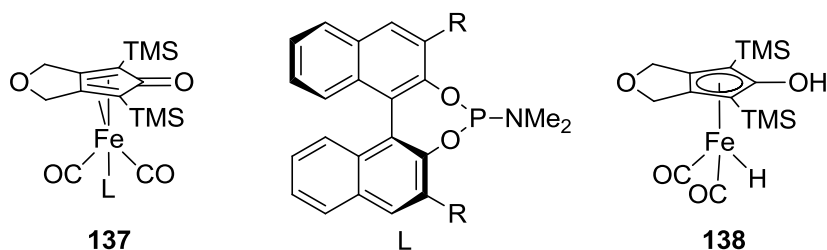
Figure 50. A chiral iron cyclopentadienone complex and a related achiral complex.

An example of iron cyclopentadienone complexes for asymmetric ketone reductions was published during the course of this project by Berkessel and co-workers who described the synthesis and application of iron cyclopentadienone complexes modified by the substitution of a carbonyl ligand for a chiral phosphoramidite ligand.[191] Complex **137** was converted to an active catalyst *in situ* by the photolysis of one of the carbonyl ligands with 350 nm UV light. The pressure hydrogenation of acetophenone took place with 10 bar H_2 at room temperature with a 10 mol % catalyst loading and 1-phenylethanol was formed in up to 90 % conversion and 31 % e.e. Under the reaction conditions a mixture of complexes were observed by ^{1}H NMR spectroscopy assigned to two diastereomeric iron hydrides and also the presence of **138** and signals tentatively assigned to an iron hydride complex bearing two phosphoramidite ligands. The low selectivity of the reduction is attributed to this complex mixture of species, including the achiral **138**.
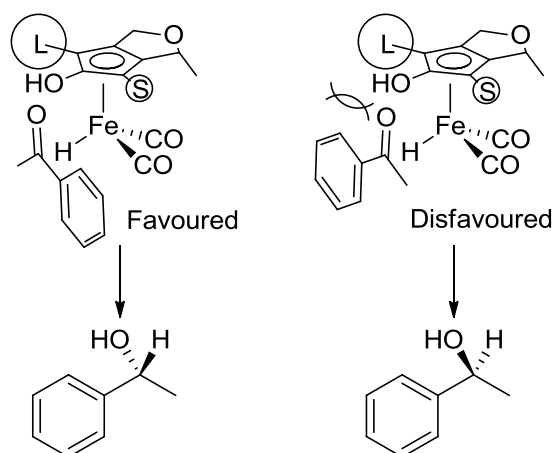
Figure 51. Hypothesised asymmetric induction via planar chiral cyclopentadienone ligands. L = large, S = small.

Our approach towards the asymmetric reduction of ketones with iron cyclopentadienone complexes relies on the planar chirality of unsymmetrical cyclopentadienone ligands. By having groups of different relative size flanking the central C=O of the cyclopentadienone ligand it might be possible to induce asymmetry via a steric interaction between the substrate and the ligand; only one orientation of the substrate is favoured. This approach is illustrated in Figure 51.

Having established that the presence of a chiral centre in the backbone of complexes **131**-**133** gives rise to separable diastereoisomers, it should be possible to synthesise the same complexes in high enantiomeric excess by using optically-enriched starting materials.
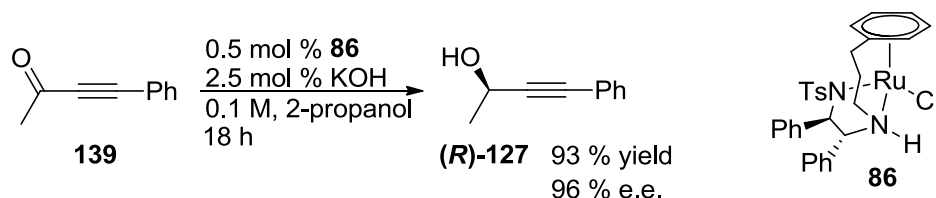
Scheme 39. The asymmetric reduction of an acetylenic ketone.

The starting material for the synthesis of **131**-**133** is an acetylenic alcohol, 4-phenyl-3-butyn-2-ol. The asymmetric synthesis of this compound can be achieved by the asymmetric reduction of the acetylenic ketone 4-phenyl-3-buty-2-one by transfer hydrogenation.[128, 132] The reduction was carried out using a well-established ruthenium ATH catalyst (**86**) developed in the Wills group (Scheme 39). With our chiral alcohol in hand, complexes (**R**)**-131**-**133** were synthesised as per the earlier synthesis (Table 25). The optical purity of complex (**R**)**-132a** was established as 92 % by NMR spectroscopy with a chiral shift reagent (Europium tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]) to rule out the possibility of racemisation during the synthesis. Expansions of the CH quartet in the NMR spectra of racemic **132a** and (**R**)**-132a** with a chiral shift reagent are shown in Figure 52.
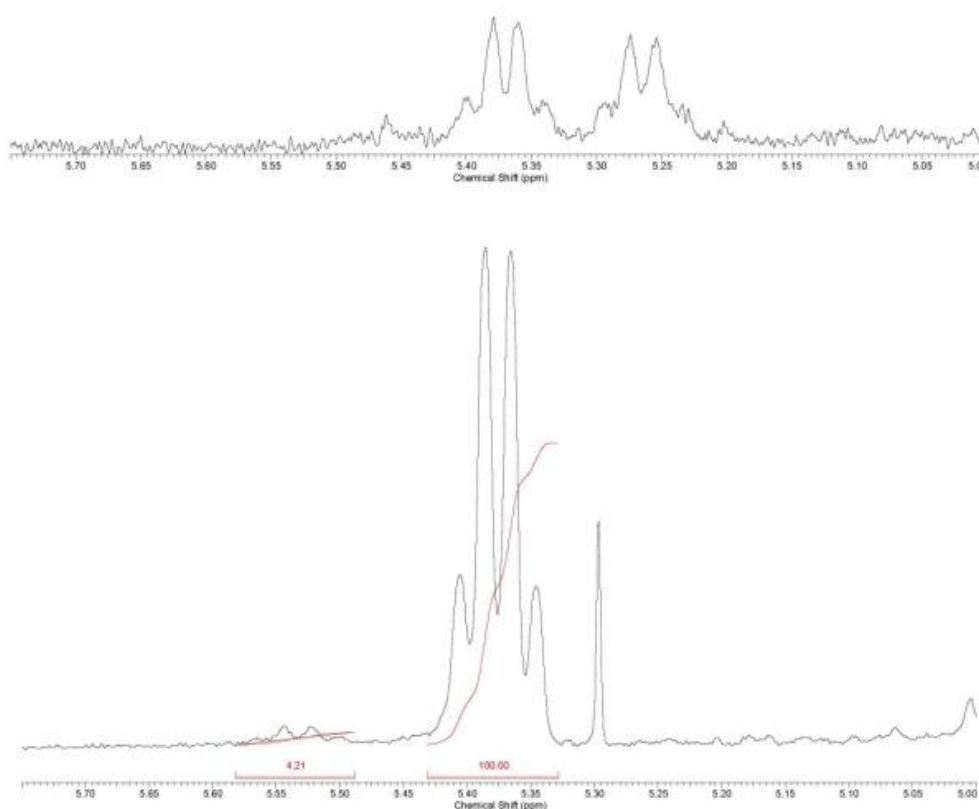
Figure 52. The NMR spectra of the CH quartet of racemic **132a** (top) and (**R**)**-132a** (bottom) with a chiral shift reagent.

A range of conditions for the reduction of acetophenone were tested with racemic complex **136** and the results are listed in Table 34. Using 2-propanol as a hydrogen donor required raised temperatures for catalytic turnover but 5:2 formic acid/triethylamine, however, was much more successful, achieving 90 % conversion to 1-phenylethanol after 18 h at 40 °C with minimal formylation of the product alcohol. Raising the temperature to 60 °C resulted in full conversion of the starting material but a significant amount of formate (10 %) was generated.
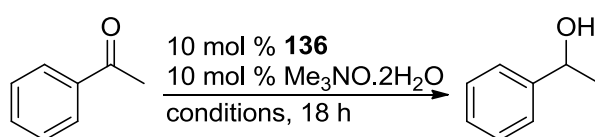
Conditions	Conversion (%)
2-Propanol, 28 °C, 0.2 M	7
2-Propanol, 60 °C, 0.2 M	52
5:2 FA/TEA, 28 °C, 1 M	60
5:2 FA/TEA, 40 °C, 1 M	90 (+ 2 % formate)
5:2 FA/TEA, 60 °C, 1 M	89 (+ 10 % formate)

Table 34. Different conditions for the reduction of acetophenone with **136**.

Using the optimal conditions, the reduction of acetophenone was carried out with complexes (**R**)-**131**-**133** and the results are displayed in Table 35. In general the activities of the complexes are lower than racemic complex **136**; the methyl group in the backbone is in some way detrimental to reactivity. High conversions can still be achieved with (**R**)-**132a** and (**R**)-**132b** but longer reaction times (48-96 h) are required. Surprisingly complexes (**R**)-**133a** and (**R**)-**133b** were far less reactive than their TMS-substituted congeners, which is in contrast with the alcohol oxidation data in which **133b** was the most active in the series for the oxidation of 1-phenylethanol in acetone (Table 26).

Complex	Time (h)	Conversion (%)	e.e. (%)
(**R**)-**131a**	96	66 (+ 10 % formate)	25 (R)
(**R**)-**131b**	96	17	5 (R)
(**R**)-**132a**	96	80 (+ 5 % formate)	23 (R)
(**R**)-**132b**	48	91 (+ 5 % formate)	11 (R)
(**R**)-**133a**	48	36	10 (R)
(**R**)-**133b**	96	10	10 (R)

Table 35. The iron-catalysed reduction of acetophenone. 10 mol % catalyst, 10 mol % $Me_3NO.2H_2O$, 5:2 FA/TEA, 1 M, 40 °C.

Unfortunately the enantioselectivities obtained in the reduction are low, the highest being 25 % e.e. obtained with (**R**)-**131a**. Monitoring of the e.e. over time showed that racemisation was not taking place. What is important to note, however, is that 1-phenylethanol of (R) configuration is the major product in all cases. This reflects the fact that each of the complexes has an (R) stereocentre in the backbone but this is not what was expected. Comparing an **a** diastereoisomer to a **b** diastereoisomer, they each have the opposing sense of planar chirality, i.e. the 'large' and 'small' groups are flipped and should give the opposite enantiomer of product as per the interaction in Figure 51.

These results mirror findings by Yamamoto *et al.* for a series of similar ruthenium complexes in a paper published during the course of this project.[192] The authors synthesised a series of (cyclopentadienone)ruthenium tricarbonyl complexes bearing a ribose moiety (Figure 53). The corresponding hydroxycyclopentadienyl hydride complexes were produced by reaction with aqueous NaOH in THF and their catalytic activities were evaluated in the reduction of acetophenone under hydrogen pressure (Table 36). The enantioselectivities achieved are similar to our own findings and although the authors did not state

which enantiomer of 1-phenylethanol was the major product they did state that it was the same enantiomer in all cases.
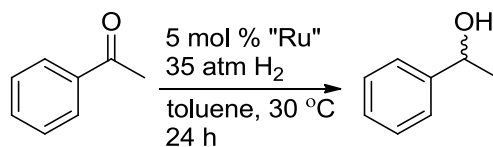
Complex	R^1/R^2	Conv (%)	e.e. (%)
140	TMS/TMS	100	0
140a	Ph/TMS	41	18
140b	Ph/TMS	100	14
140a	Ph/TIPS	100	19
140b	Ph/TIPS	29	21

Table 36. The reduction of acetophenone as reported by Yamamoto *et al*.
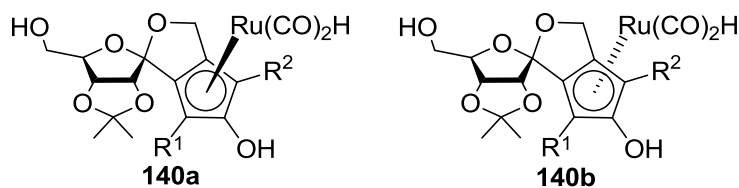
Figure 53. Complexes used by Yamamoto *et al*. for the reduction of acetophenone.

2.4.4.1 Influence of Steric Effects.

An interesting result reported by Yamamoto is that complex **140** containing two of the same group flanking the C=O group of the ligand, two TMS groups, provides a racemic product in the reduction. This provides some support for the proposal that groups of different relative size are required for asymmetric induction even though the enantiomer of product formed is determined by the configuration of the stereocentre in the backbone of the cyclopentadienone ligand.

Interestingly, complexes (**R**)-**131a** and (**R**)-**131b** which have the same group flanking the C=O of the ligand, two phenyl groups, do show asymmetric induction, producing 1-phenylethanol in 25 % and 5 % e.e. respectively. This could be explained by the phenyl rings having different orientations and therefore, providing different steric environments that could affect the approach of the substrate. This idea was probed by synthesising complexes (**R**)-**141a** and (**R**)-**141b** with one phenyl group and one *o*-tolyl group to see if the steric influence of the extra methyl group would cause a change in conformation and affect the enantioselectivity of the reduction (Scheme 40).
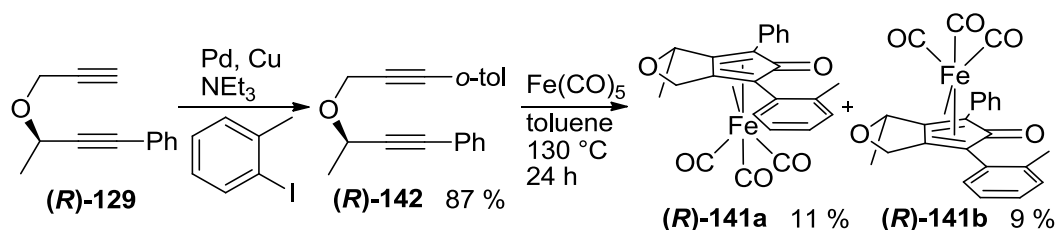
Scheme 40. The synthesis of (**R**)-**141a** and (**R**)-**141b**.

Complex	Time (h)	Conversion (%)	e.e. (%)
(**R**)-**141a**	96	50 (+ 5 % formate)	12 (*R*)
(**R**)-**141b**	96	62 (+ 7 % formate)	32 (*R*)

Table 37. The iron-catalysed reduction of acetophenone. 10 mol % catalyst, 10 mol % Me$_3$NO.2H$_2$O, 5:2 FA/TEA, 1 M, 40 °C.

The results for the reduction of acetophenone with (**R**)-**141a** and (**R**)-**141b** are shown in Table 37. In comparing (**R**)-**141a** to (**R**)-**131a** the activity is similar; 50 % conversion after 96 h versus 66 % conversion after 96 h. The main difference lies in the enantioselectivity. 1-Phenylethanol was produced in 12 % e.e. by (**R**)-**141a** compared to 25 % e.e. for (**R**)-**131a**. When comparing the **b** diastereoisomers the differences are even more pronounced; (**R**)-**141b** achieved a 62 % conversion

and 32 % e.e. compared to 17 % conversion and 5 % e.e. for **(R)-131b**. These results highlight the sensitivity of the reduction to the steric environment around the metal centre. Attempts to introduce more hindered substituents using commercially available substituted iodobenzenes: *o*-iodobiphenyl and 2-iodo-1,3-dimethylbenzene were unsuccessful. In both cases the Sonogashira coupling reaction between **(R)-129** and the aryl iodide resulted in an inseparable mixture of products.

143
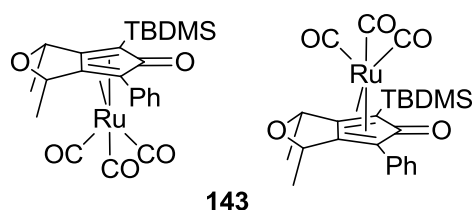
Figure 54. Ruthenium cyclopentadienone complexes with (*R*) and (*S*) stereocentres.

The influence of the two groups flanking the C=O of the cyclopentadienone ligand was further emphasised by work performed by Jonathan Hopewell, who synthesised a complex with two chiral centres in the backbone of the ligand with opposing configurations so as to eliminate the effect of the ligand stereocentre on the selectivity of the reduction. Complex **143** was isolated in crude form as a pair of diastereoisomers but only one of which could be isolated following chromatography. The identity of the diastereoisomer that was isolated was not proven. Following synthesis of the corresponding hydroxycyclopentadienyl hydride complex, acetophenone was reduced using 1 mol % catalyst in 5:2 FA/TEA at 60 °C with a concentration of 1.6 M. After 150 h, a conversion of 19 % and e.e. of 15 % were measured. Interestingly the product had an (*S*) configuration. This proves that the planar chirality of the ligand alone is enough to induce asymmetry.

2.4.4.2 Ligand Ring Size.
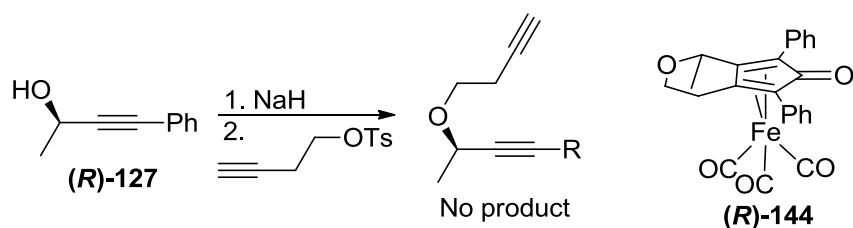
Scheme 41. The unsuccessful synthesis of a cyclopentadienone complex with a 6-membered ring in the backbone.

Taking inspiration from Moyer and Funk's finding that a complex containing a 6-membered ring in the backbone of the cyclopentadienone ligand outperformed a ligand with a 5-membered ring in the oxidation of alcohols, efforts were directed towards the synthesis of chiral (cyclopentadienone)iron tricarbonyl complexes containing a 6-membered ring. The initial target was complex (**R**)-**144** which would only require a small modification of the existing synthesis, exchanging propargyl bromide for 3-butynyl *p*-toluenesulphonate. Unfortunately the expected nucleophilic substitution did not take place; instead an elimination reaction proceeded to generate a conjugated enyne and (**R**)-**127** was recovered (Scheme 41).
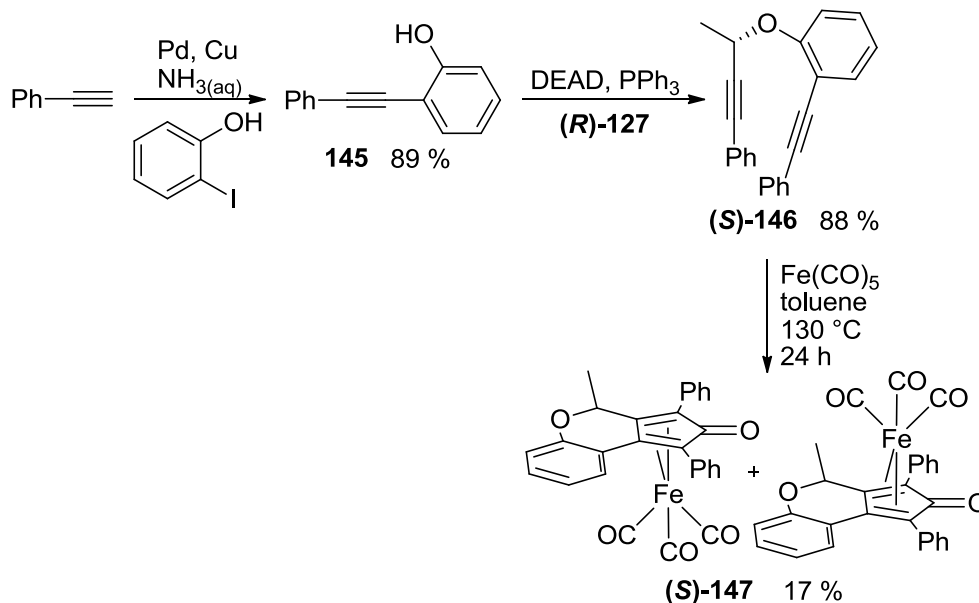
Scheme 42. The synthesis of (*S*)-**147**.

Following this setback a new target complex was devised. Complex (*S*)-**147** incorporates a 6-membered ring into the backbone of the ligand whilst also incorporating another aryl group, making the complex a closer analogue of the Shvo catalyst and complex **126** which was the most competent iron catalyst studied for the oxidation of alcohols in acetone. A Sonogashira coupling between phenylacetylene and *o*-iodophenol provided **145** in high yield. A subsequent Mitsunobu reaction with (*R*)-**127** gave the ligand precursor with inversion of configuration. Reaction with iron pentacarbonyl yielded the expected mixture of diastereomeric complexes ((*S*)-**147**) which proved to be inseparable by chromatography and could not be purified. In the reduction of acetophenone, the mixture of complexes (*S*)-**147** achieved a 66 % conversion, giving the (*S*) enantiomer of 1-phenylethanol in 14 % e.e. after 96 h. Unfortunately the activity of (*S*)-**147** offered no improvement over the previous series of catalysts.
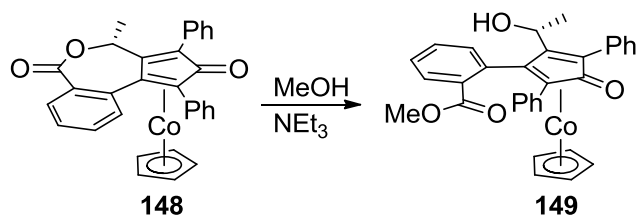
Scheme 43. Cobalt cyclopentadienone complexes prepared by Taylor, Montevalli and Richards.
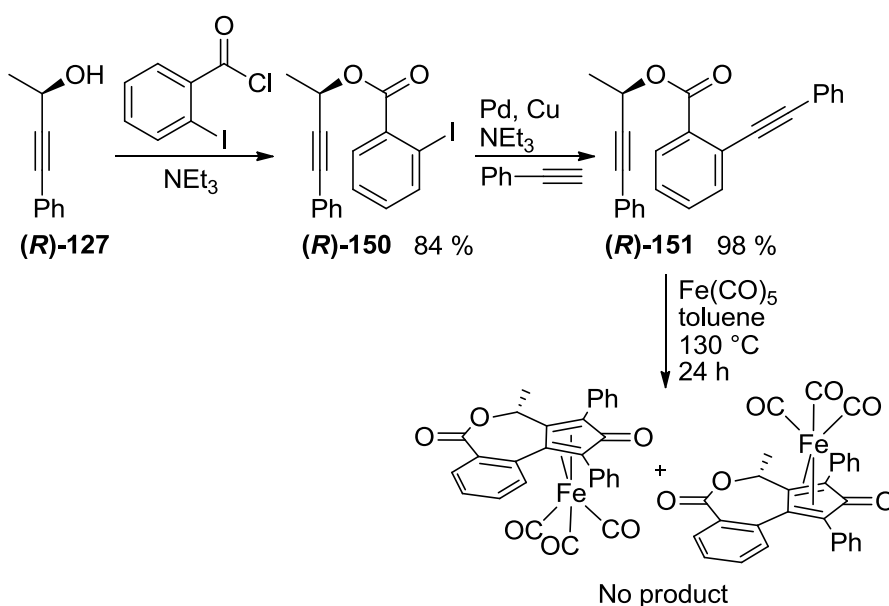
Scheme 44. The attempted synthesis of an iron cyclopentadienone complex with a 7-membered ring.

In 2006 Taylor, Montevalli and Richards synthesised chiral cobalt cyclopentadienone complex **148** containing a 7-membered ring in the backbone and demonstrated a ring-opening reaction to generate complex **149**.[193] If the same ring-opening procedure can be applied to an analogous iron complex it would provide access to an even closer asymmetric analogue of the Shvo catalyst. The synthesis of the ligand precursor was carried out following the procedure of Taylor, Montevalli and Richards and is shown in Scheme 44. An esterification followed by a Sonogashira coupling gave the ligand precursor in high yield. Heating **(R)-151** with

iron pentacarbonyl at 130 °C in a sealed tube resulted in the isolation of unreacted starting material.

2.4.4.3 Tethered Complexes.

X = linker
Y = neutral 2 e⁻ donor
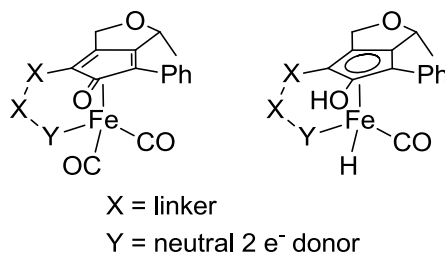
Figure 55. A tethered cyclopentadienone complex and a chiral-at-metal hydroxycyclopentadienyl hydride complex.

Another avenue that was pursued was the synthesis of complexes bearing a tethering group to provide another point of attachment between the cyclopentadienone ligand and the metal centre (Figure 55). This would serve two purposes: the stability of the complexes would be expected to increase and upon formation of a hydride complex under catalytic conditions the complex would be chiral at the metal centre which could affect greater enantioselectivity. The first target utilised a benzene ring as the linker and a phosphine as the donor (Scheme 45). A Sonogashira coupling of (*R*)-129 with 1-iodo-2-bromobenzene reacts selectively with the aryl iodide to give *ortho*-bromo substituted (*R*)-152 in 92 % yield. Subsequent lithiation and quenching with chlorodiphenylphosphine did not produce the desired phosphine-containing product. Analysis of the ^{1}H NMR spectrum of the crude reaction mixture showed the presence of (*R*)-131c which demonstrates that the lithiation proceeded as expected. The compound is likely to be too hindered for addition of the phosphine to take place. Complex formation was

attempted using (**R**)-**152** but proved to be unsuccessful, resulting in the isolation of starting material.
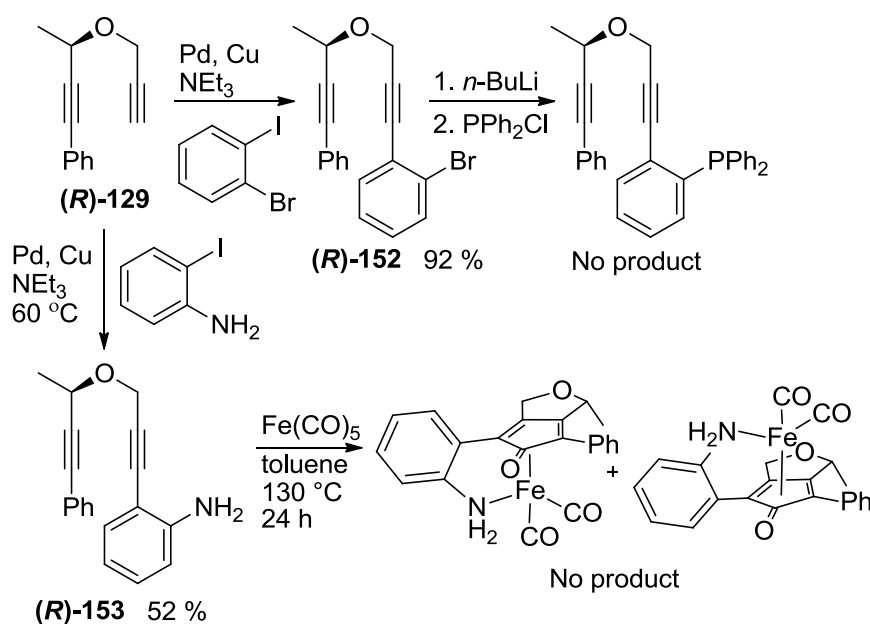
Scheme 45. The attempted synthesis of tethered iron cyclopentadienone complexes.

Attempts were also made to use an amine as a donor. Scheme 45 details the synthetic route to amine-containing ligand precursor (**R**)-**153**. The Sonogashira coupling with *o*-iodoaniline would not proceed at room temperature. Raising the temperature to 60 °C provided the product in moderate yield. The attempted formation of iron complexes from (**R**)-**153** resulted in the isolation of starting material.

X = linker
Y = neutral 2 e⁻ donor
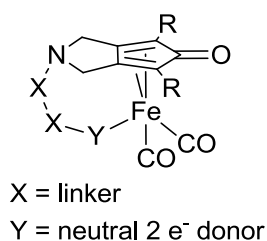
Figure 56. A symmetrical tethered iron cyclopentadienone complex.

Following the previously unsuccessful attempts to form tethered complexes a new approach was devised (Figure 56). A tether attached to the backbone of the

ligand may be less likely to interfere with the complexation reaction. If the chiral centre is contained in the tether then this approach also has the added advantage that the ligand is symmetrical which will avoid the generation of diastereoisomers and as such will simplify purification.
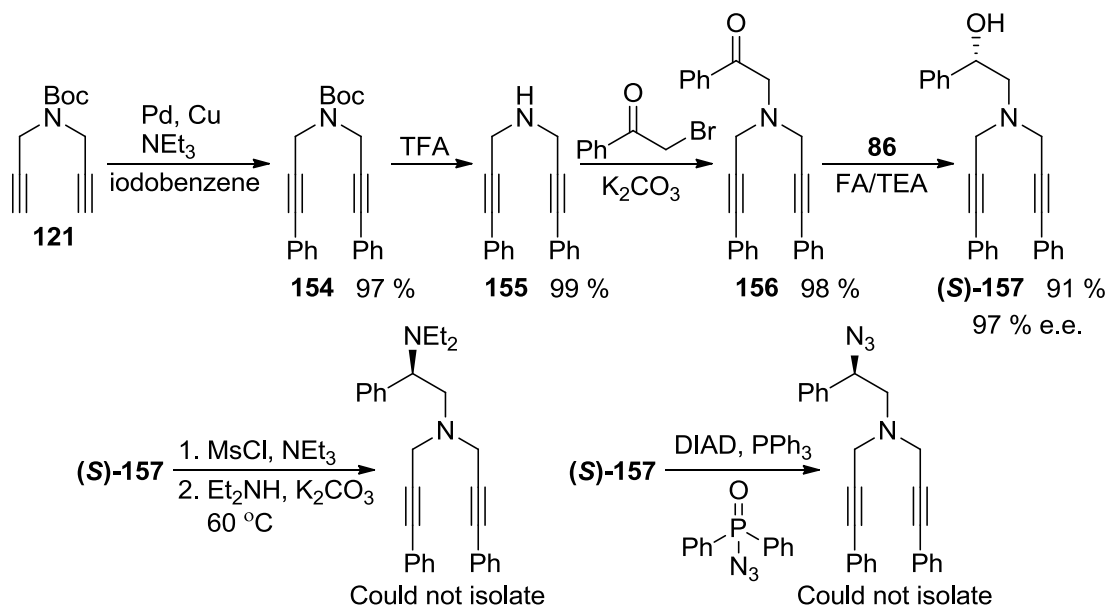
Scheme 46. The synthetic route to a ligand precursor with a tether in the backbone.

The synthetic route to a new ligand precursor is shown in Scheme 46. Compound **121** is made by the alkylation of *N*-Boc-propargylamine with propargyl bromide. Subsequent Sonogashira coupling and deprotection gave **155** which was alkylated with α-bromoacetophenone in high yield. The asymmetric reduction of the ketone functionality proceeded smoothly using **86** in 5:2 FA/TEA to give the expected chiral alcohol (**(S)-157**) in high yield and enantioselectivity. The attempted conversion of the alcohol to an amine via mesylation and displacement with diethylamine was unsuccessful. The ^{1}H NMR spectrum of the crude reaction mixture contained signals which could be attributed to the desired product but purification was not possible. The attempted Mitsunobu reaction to install an azide which could later be reduced to an amine was also unsuccessful. Likewise the [1]H

NMR spectrum of the crude product also showed encouraging signals but purification was not possible.
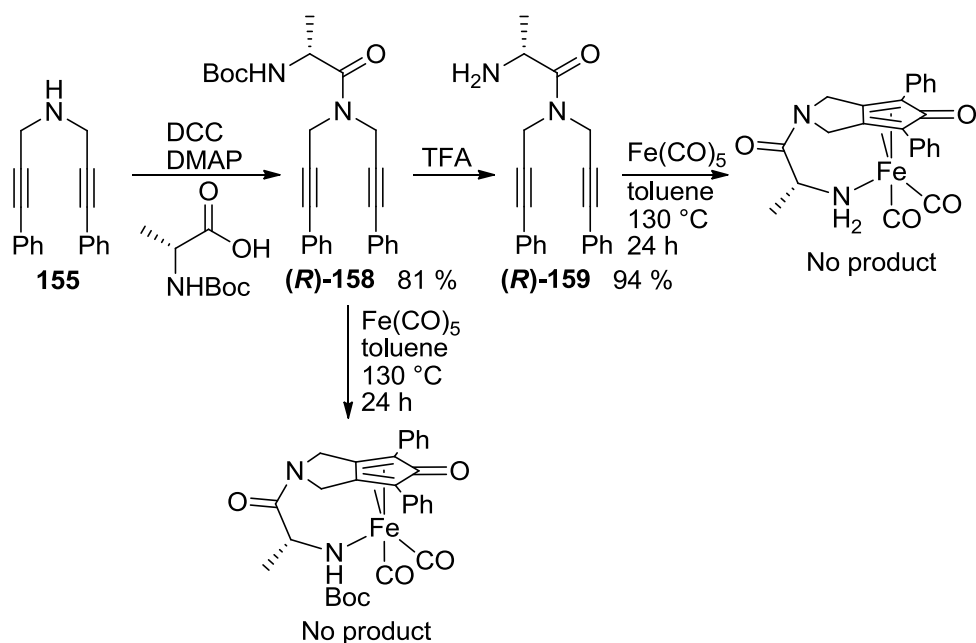
Scheme 47. The synthesis of α-amino acid-derived ligand precursors.

An alternative synthesis diverged at compound **155**. A peptide coupling reaction with *N*-Boc-D-alanine provided compound (***R***)-**158** in 81 % yield. The attempted formation of an iron complex from (***R***)-**158** was unsuccessful. The less bulky compound (***R***)-**159** was made by deprotection of (***R***)-**158** but complex formation was still unsuccessful. In the event of a successful complex formation a tether would be unlikely with compounds (***R***)-**158** and (***R***)-**159**; the sp^2 nature of the amide would not allow sufficient flexibility. Attempts to reduce the amide, however, resulted only in hydrolysis to regenerate **155**.

Somewhat surprisingly it was possible to form a complex from the chiral alcohol (***S***)-**157**. The NMR spectra of the crude reaction mixture showed clear signals indicative of product formation; however, attempts to purify by column chromatography or recrystallisation resulted in decomposition. Use of the crude

product for the reduction of acetophenone gave a conversion of 88 % after 96 h but the 1-phenylethanol product was racemic.
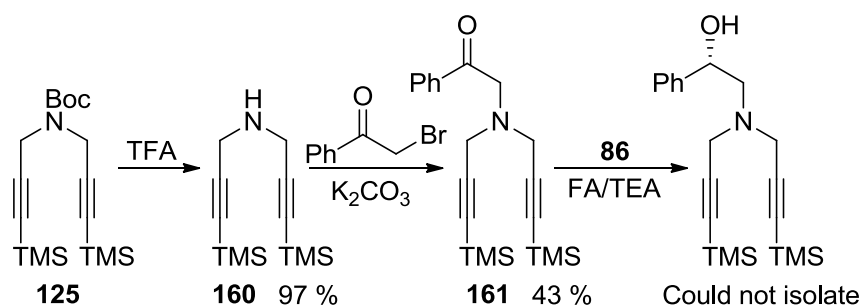
Scheme 48. The synthetic route to a TMS-substituted ligand precursor.

The synthesis was attempted using TMS groups instead of phenyl rings to see if the resulting complex was more stable. Compound **125** was deprotected with TFA to give **160** which was alkylated with α-bromoacetophenone. Significant desilylation took place during the alkylation reaction which accounts for the modest yield. The use of K_2CO_3 for the deprotection of TMS-substituted alkynes is known.[194, 195] The asymmetric reduction step also proceeded with desilylation to give an inseparable mixture of products.
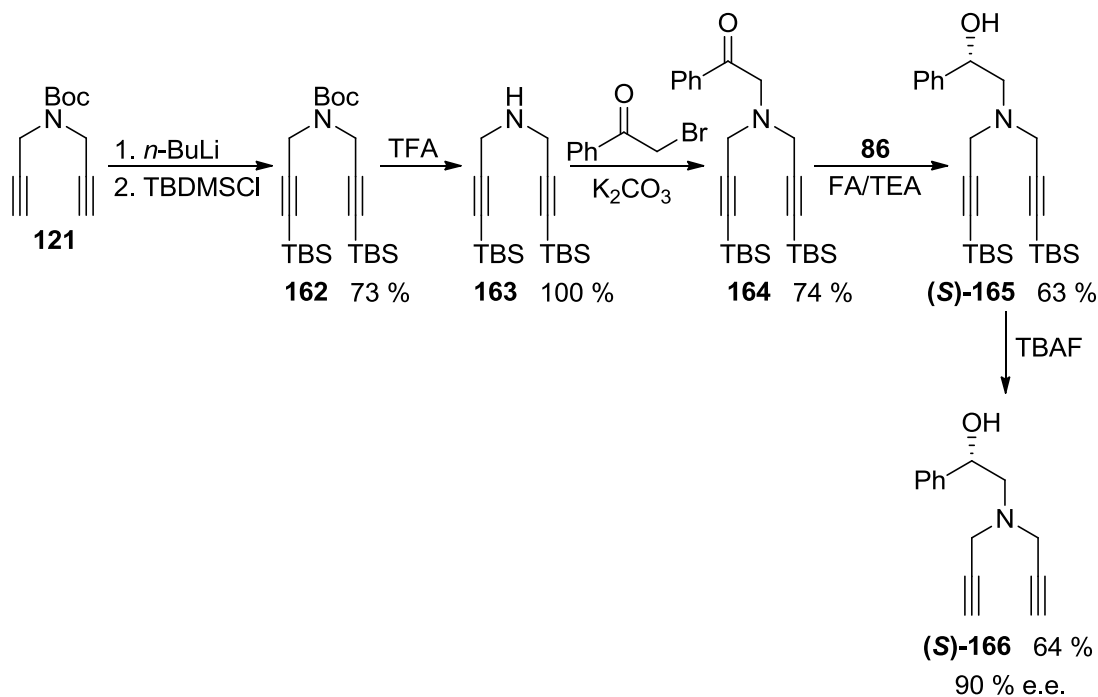
Scheme 49. The synthetic route to a TBDMS-substituted ligand precursor.

The use of the more bulky TBDMS instead of TMS avoided the problem of desilylation and allowed access to chiral alcohol (*S*)-165. The enantiomeric excess of (*S*)-165 could not be determined by chiral GC, HPLC or by derivatisation with Mosher's acid chloride. Removal of the TBDMS groups with tetrabutylammonium fluoride (TBAF) gave (*S*)-166 which gave sufficient separation by HPLC for determination of the e.e. which was found to be 90 %. A complex was synthesised from the reaction of (*S*)-165 with iron pentacarbonyl but proved to be as unstable to purification as the phenyl-substituted complex.
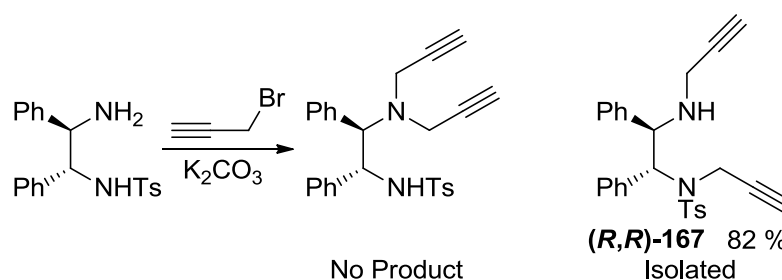
Scheme 50. The unsuccessful synthesis of a dialkylated TsDPEN derivative.

Further attempts were made to synthesise a ligand precursor with an amine tether following a new approach. Scheme 50 shows the attempted synthesis of a desired ligand precursor starting from the commercially available chiral diamine (*R,R*)-TsDPEN. Surprisingly the dialkylation proceeded to give the undesired regioisomer (**(R,R)-167**). Dialkylations of TsDPEN have previously been reported to substitute only at the basic amine with a variety of different alkylating agents.[196] Mindt *et al.* performed a similar dialkylation of *N*-Boc lysine with propargyl bromide and observed selective reaction at the basic amine.[197] Attempts to Boc-protect DPEN resulted exclusively in the isolation of the di-protected product and unreacted starting material so a different diamine was used, (*R,R*)-diaminocyclohexane.
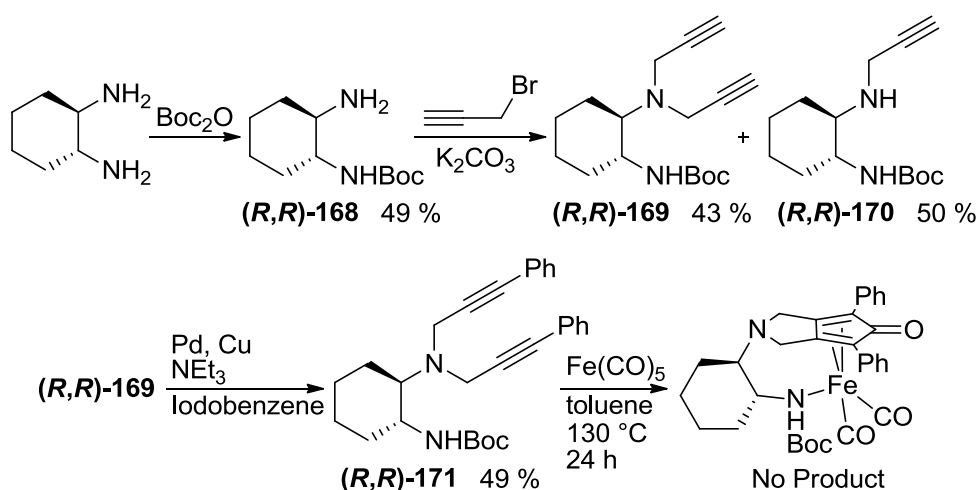
Scheme 51. The synthetic route to a chiral diamine-containing iron complex.

Reaction of (*R,R*)-diaminocyclohexane with Boc-anhydride gave the mono-protected product in 49 % yield. Gratifyingly, the dialkylation proceeded with the desired regioselectivity although there was a significant amount of mono-alkylation product formed during the reaction. A Sonogashira coupling with iodobenzene yielded the desired ligand precursor in moderate yield. The complexation reaction was unsuccessful, resulting in the recovery of starting material.
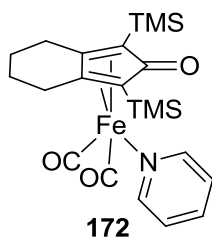
Figure 57. A pyridine-ligated complex synthesised by Casey and Guan.

A potential reason for the failure of all the amine-containing ligand precursors to undergo complexation could be that coordination of the amine to the iron pentacarbonyl reagent could take place and inhibit the cycloaddition reaction. To explore this idea two reactions were carried out; In one reaction compound **124** was reacted with one equivalent of iron pentacarbonyl instead of the usual excess under the otherwise normal conditions of 130 °C in toluene in a sealed tube for 24 h. The second reaction was the same but with one equivalent of pyridine present. Pyridine has been used as a ligand in complex **172** by Casey and Guan.[186] After 24 h the reaction mixtures were filtered through celite, the solvent was removed under reduced pressure and the ^{1}H NMR spectra were acquired. In the reaction without pyridine the starting material was 34 % converted to the product complex. Rather unexpectedly, in the reaction with pyridine the starting material was 58 % converted to the tricarbonyl complex **123**. No **172** was observed and the reaction was enhanced by the addition of pyridine. This result implies that the failure of amine-containing ligand precursors to form cyclopentadienone complexes is not caused by the presence of a coordinating group and may be as a result of steric effects.

The implication of these results is that further progress towards the development of asymmetric iron cyclopentadienone complexes should focus on the completed synthesis of the cyclopentadienone prior to coordination with iron.

2.4.4.4 Preformed Cyclopentadienones.
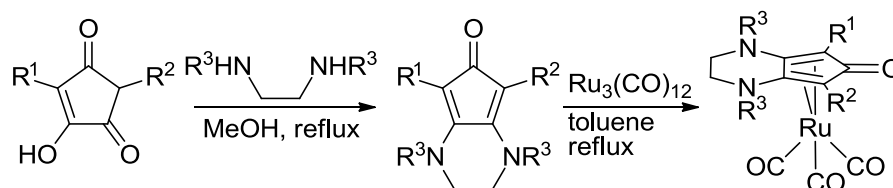
Scheme 52. The synthesis of ruthenium complexes utilised by Haak.

Edgar Haak has published several papers concerning the reactions of acetylenic alcohols with (cyclopentadienone)ruthenium tricarbonyl complexes of the type shown in Scheme 52.[198-201] A modified synthetic route could make use of a chiral diamine component to access C_2-symmetrical chiral iron complexes.
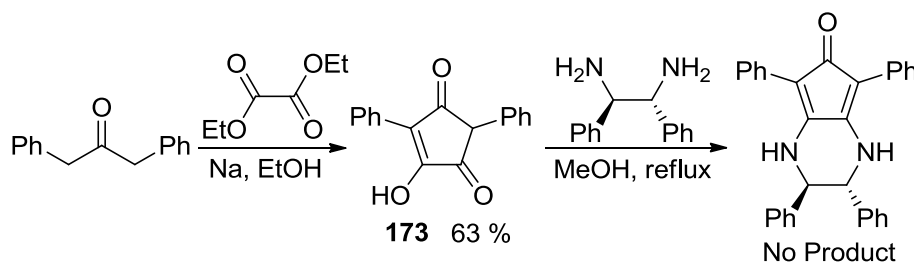
Scheme 53. The attempted synthesis of a chiral cyclopentadienone.

Reaction of 1,3-diphenylpropanone with diethyl oxalate and sodium in ethanol gave the expected cyclic product in moderate yield. Reaction with (*R,R*)-DPEN in refluxing methanol yielded a complicated mixture of products. A secondary amine is desirable to keep the reaction as similar as possible to Haak's procedure so the dimethylated derivative of (*R,R*)-DPEN was prepared by the published procedure[202] shown in Scheme 54. Unfortunately the reaction of **(R,R)-176** with **173** gave a mixture of products and the desired cyclopentadienone was not isolated.
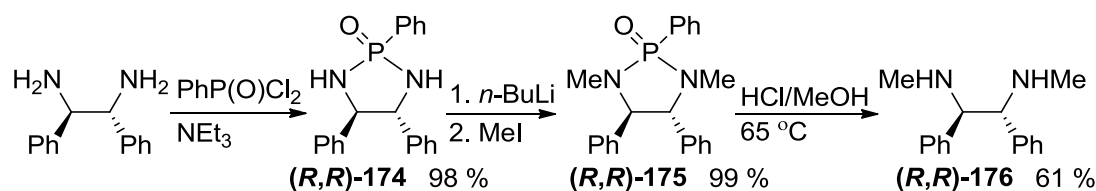
Scheme 54. The synthesis of dimethylated DPEN.
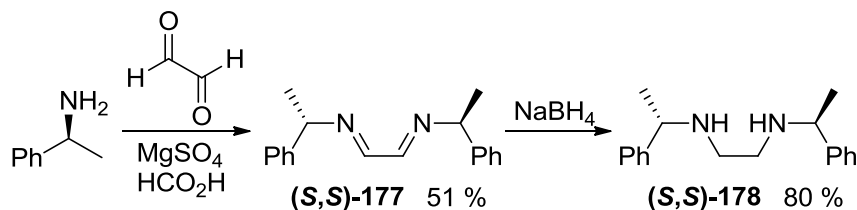
Scheme 55. The synthesis of a C_2-symmetrical chiral diamine.

The synthesis of an alternative chiral diamine with the chirality moved out of the backbone of the molecule is shown in Scheme 55. Imine formation between (S)-α-methylbenzylamine and glyoxal generated (*S,S*)-177 which was reduced by NaBH$_4$ to form the desired amine. Reaction with **173** also failed to yield a cyclopentadienone product.

The lack of further progress on iron cyclopentadienone chemistry led to a decision to change direction.

2.5 1,2,3-Triazole Ligands.

1,2,3-Triazoles are nitrogen-containing heterocycles formed by the Cu(I) catalysed azide-alkyne cycloaddition (CuAAC). These heterocycles have been widely used as a component of chelating ligands for transition metals.[203] Applications include ligands for the CuAAC reaction,[204] for cross-coupling reactions,[205] allylic alkylations,[206] and for radiopharmaceuticals.[197] To date only

two examples of 1,2,3-triazole ligands for transfer hydrogenation have been reported.[207, 208]
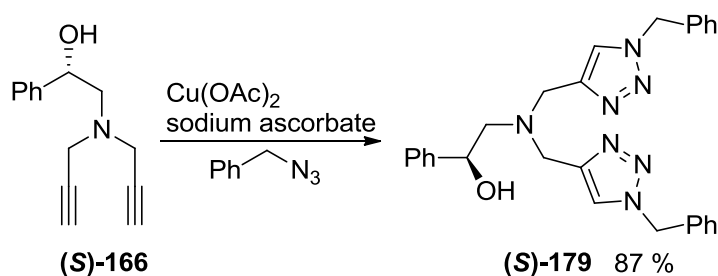
Scheme 56. The synthesis of a triazole-containing ligand.

Performing the CuAAC reaction on the previously prepared chiral amino alcohol (*S*)-166 with benzyl azide provided access to tetradentate triazole ligand (*S*)-179. The new ligand was applied to the reduction of acetophenone in 2-propanol with various ruthenium and iron complexes and the results are shown in Table 38.
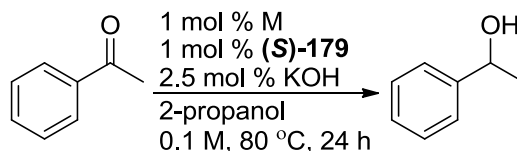
Metal Precursor	Conv (%)	e.e. (%)	Conv without ligand (%)
$RuCl_3 \cdot 3H_2O$	0	0	0
$(PPh_3)_3RuCl_2$	96	0	98
$(DMSO)_4RuCl_2$	17	6 (*S*)	28
$Ru_3(CO)_{12}$	18	18 (*R*)	32
$Fe_3(CO)_{12}$	0	0	0
$Fe_2(CO)_9$	0	0	0
$Fe(CO)_5$	0	0	0

Table 38. The reduction of acetophenone with (*S*)-179.

No conversion to product was observed with the simple $RuCl_3 \cdot 3H_2O$ as the metal precursor. The reduction proceeded almost to completion with $(PPh_3)_3RuCl_2$

but with no enantioselectivity. A control experiment without the ligand reached a similar conversion indicating that the metal and the ligand are unlikely to be interacting. The use of $(DMSO)_4RuCl_2$ and $Ru_3(CO)_{12}$ resulted in modest conversions and a small enantiomeric excess, giving opposing enantiomers as the major product. Notably the conversions were lower than in the absence of ligand. Some simple iron precursors were also tested but showed no activity.
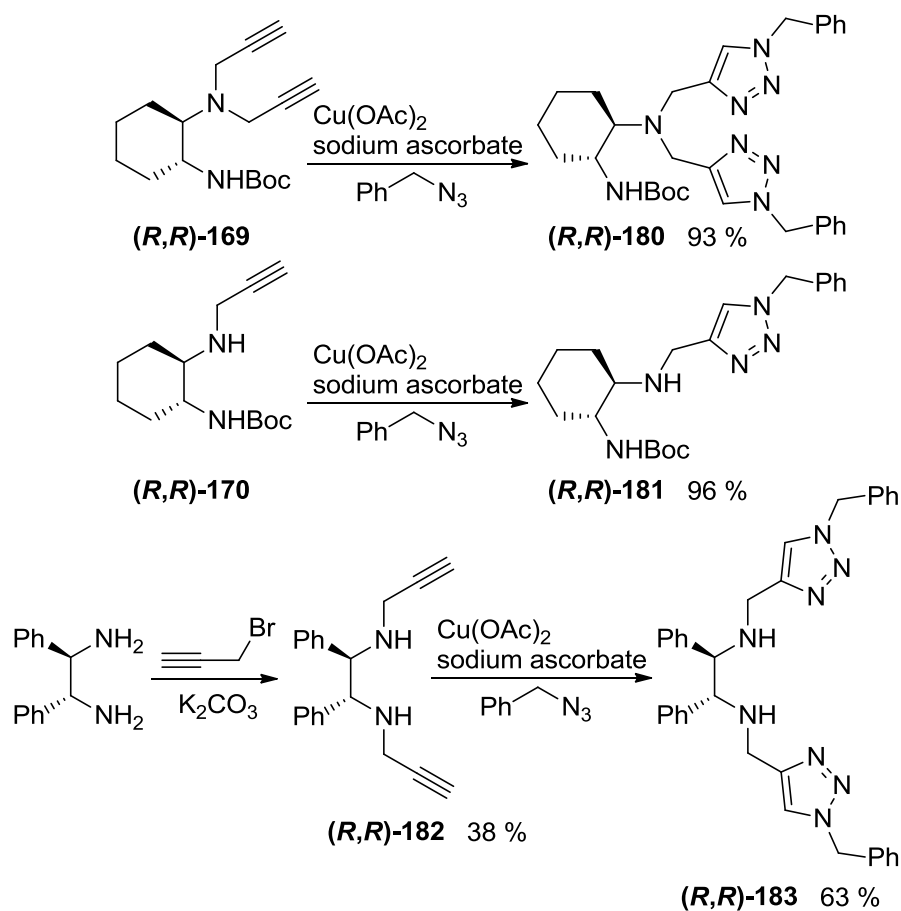
Scheme 57. Chiral diamine-derived triazole ligands.

Further ligands were prepared by performing the CuAAC reaction on the previously prepared diaminocyclohexane-derived terminal alkynes (**R,R**)-**169** and (**R,R**)-**170** with benzyl azide as shown in Scheme 57. A C_2-symmetrical ligand derived from (R,R)-DPEN was synthesised by a dialkylation followed by CuAAC with benzyl azide. The dialkylation was initially attempted with (R,R)-

diaminocyclohexane but resulted in an inseparable mixture of products. The bis(triazole) ligand **(R,R)-180** achieved a 70 % conversion in the reduction of acetophenone with $Ru_3(CO)_{12}$ after 48 h with an e.e. of 44 % (Table 39). Compound **(R,R)-183** was far more active, achieving full conversion after 24 h and the enantioselectivity was also improved. A better performance was seen for **(R,R)-181**, achieving 96 % conversion and 75 % e.e. in 24 h. Interestingly the tetradentate ligands produced a different enantiomer of product to the tridentate **(R,R)-181**. Compound **(R,R)-168**, lacking a triazole functionality, performed poorly, thus emphasising the necessity of the triazole.

Ligand	Conv (%)	e.e. (%)
(R,R)-180	70^a	44 (S)
(R,R)-181	96	75 (R)
(R,R)-183	99	69 (S)
(R,R)-168	16	2 (R)

Table 39. The reduction of acetophenone with diaminotriazole ligands. 0.33 mol % $Ru_3(CO)_{12}$, 1 mol % ligand, 2.5 mol % KOH, 2-propanol, 0.1 M, 80 °C, 24 h. ^{a} 48 h.

Further metal precursors were tested with the most successful ligand, **(R,R)-181**, and the results are listed in Table 40. All of the precursors tested failed to produce an enantiomerically enriched product with the exception of $[RhCp*Cl_2]_2$ which provided an e.e. of 67 % when the reaction was performed at room temperature and the e.e. was falling as the reaction progressed.
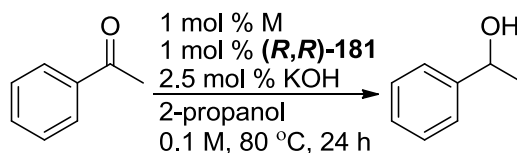
Metal Precursor	Conv (%)	e.e. (%)	Conv without ligand (%)
[Ru(benzene)Cl$_2$]$_2$	53	0	35
RuCl$_3$.3H$_2$O	0	0	0
Fe(CO)$_5$	0	0	0
[RhCp*Cl$_2$]$_2$	74	0	98
[RhCp*Cl$_2$]$_2$[a]	80	67 (R)	-

Table 40. The reduction of acetophenone with (**R,R**)-**181** and different metal precursors. [a] Performed at 28 °C.

Reactions were performed with (**R,R**)-**181** to optimise the reduction conditions (Table 41). Changing the metal to ligand ratio resulted in lower conversions, a ratio of 1:1 proved to be optimal. In a related system a 3:1 metal to ligand ratio was used and a cluster complex was proposed to be the active catalyst.[209] Lowering the temperature to 60 °C resulted in a lower conversion, lowering the temperature further resulted in the loss of all catalytic activity; a higher temperature might be necessary to form the active catalyst. Control experiments showed that a base is not required for reduction to take place and no reaction occurs in the absence of Ru$_3$(CO)$_{12}$. No reaction occurred when 5:2 FA/TEA was used as the solvent and hydrogen donor.

Ru$_3$(CO)$_{12}$ (mol %)	Temp (°C)	Time (h)	Conv (%)	e.e. (%)
0.33	80	6	88	78 (R)
0.66	80	6	48	81 (R)
1	80	6	48	80 (R)
0.33^a	80	6	71	77 (R)
0.33	28	24	0	-
0.33	40	24	0	-
0.33	60	24	63	76 (R)
0.33	80	24	98^b	79 (R)
0.33	80	24	0^c	-
0.33	28	24	0^d	-

Table 41. Varying the metal to ligand ratio and reaction temperature in the reduction of acetophenone. 1 mol % (**R,R**)-**181**, 2.5 mol % KOH, 2-propanol, 0.1 M. ^{a} 1.2 mol % (**R,R**)-**181**. ^{b} No KOH. ^{c} No Ru$_3$(CO)$_{12}$. ^{d} 1 mol % (**R,R**)-**181**, 5:2 FA/TEA, 1 M.

Another series of compounds were synthesised to tune the reactivity of the ligands (Scheme 58). Compound (**R,R**)-**184** was formed by the deprotection of (**R,R**)-**181** with TFA. Compound (**R,R**)-**185** was produced by the alkylation of (R,R)-diaminocyclohexane with propargyl bromide followed by CuAAC with benzyl azide. A TsDPEN-derived ligand ((**R,R**)-**186**) was synthesised in the same manner. Compound (**R,R**)-**187** was made by the alkylation of (R,R)-DPEN, followed by Boc protection and CuAAC with benzyl azide. Their activities in the reduction of acetophenone are listed in Table 42.
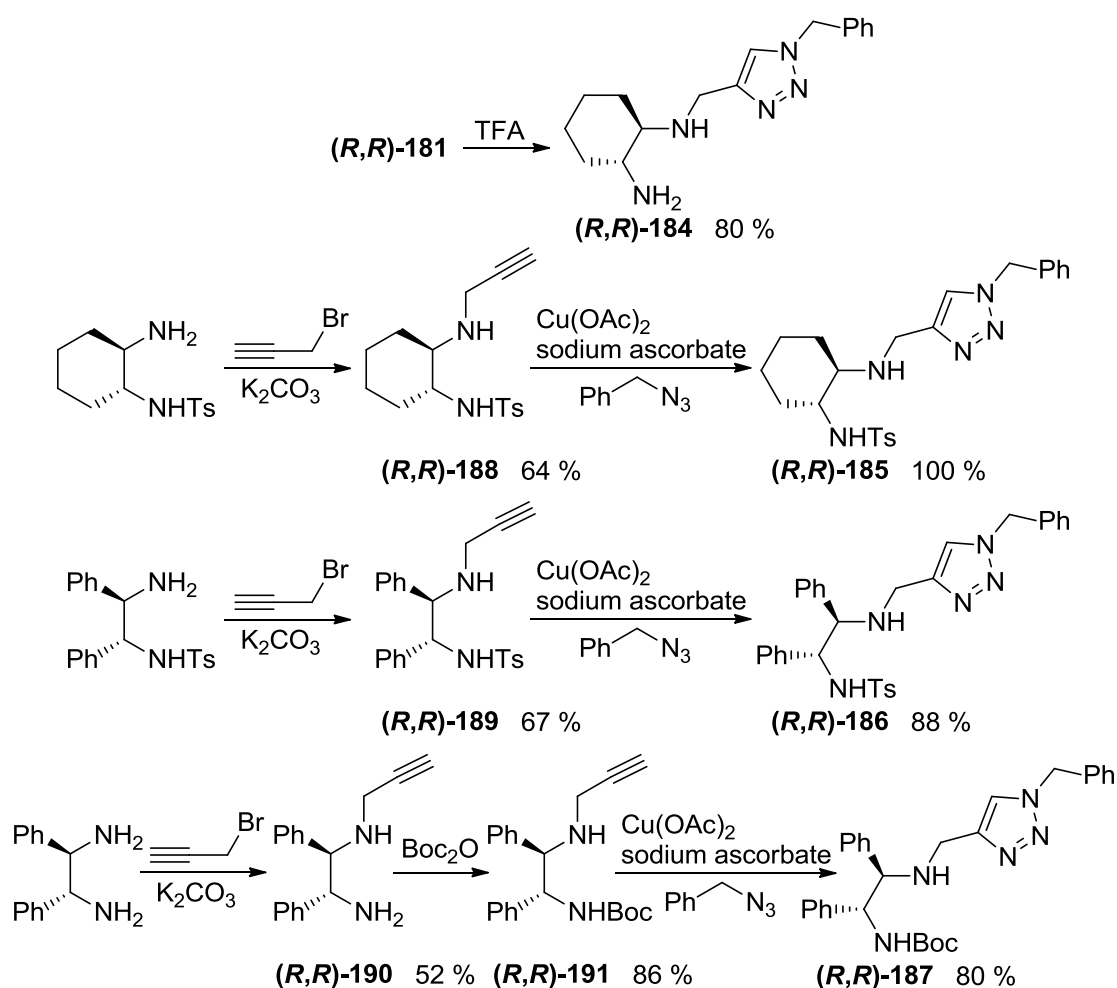
Scheme 58. The synthesis of several diaminotriazole ligands.

Ligand	Conv 8 h (%)	Conv 24 h (%)	e.e. (%)
(*R*,*R*)-181	82	98	78 (*R*)
(*R*,*R*)-184	6	12	3 (*R*)
(*R*,*R*)-185	34	94	80 (*R*)
(*R*,*R*)-186	35	97	92 (*R*)
(*R*,*R*)-187	96	97	76 (*R*)

Table 42. The reduction of acetophenone with diaminotriazole ligands. 0.33 mol % Ru$_3$(CO)$_{12}$, 1 mol % ligand, 2-propanol, 0.1 M, 80 °C.

The primary amine-containing (*R*,*R*)-184 showed very little activity and produced an essentially racemic product. The tosyl-substituted (*R*,*R*)-185 achieved

a similar conversion and enantioselectivity to its Boc-substituted congener but the reaction proceeded more slowly. Changing the chiral diamine component to TsDPEN resulted in an increase in enantioselectivity; acetophenone was reduced in 97 % conversion and 92 % e.e. Since the reduction with **(R,R)-181** proceeded more rapidly than with **(R,R)-185**, a Boc-containing DPEN-derived ligand was predicted to show a greater activity in the reduction and this was shown to be true, however, the enantioselectivity was inferior.
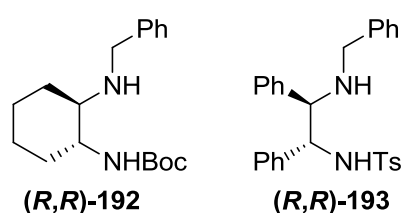
Figure 58. Benzyl-substituted diamines.

As a control, the reduction was carried out with benzyl-substituted diamines **(R,R)-192** and **(R,R)-193**. (R,R)-TsDPEN was also tested and for all three compounds only trace conversion of acetophenone to 1-phenylethanol was observed. The benzyl group is of a comparable size to the triazole substituent but lacks the capacity for bonding so the absence of activity demonstrates that the triazole must be bound to the metal centre in the active catalyst.

The reduction of other substrates using **(R,R)-186** was carried out and the results are listed in Table 43. Having an electron-withdrawing trifluoromethyl group in the *para* position has little effect on the reaction, achieving essentially quantitative conversion and 91 % e.e. after 16 h. An electron-donating methoxy group requires a significantly longer reaction time of 65 h to reach 91 % conversion without significant racemisation taking place. Having a methoxy group in the *ortho* or *meta* positions did not impact on the reactivity, in both cases the reaction was

complete after 16 h. For a series of *ortho*-substituted acetophenones good enantioselectivities are achieved and the electronics do not affect reactivity. A bulky bromine substituent in the *ortho* position, however, results in a longer reaction time and reduced selectivity. Substitution in the alpha position is not tolerated, with propiophenone and α-tetralone being reduced in low conversion after long reaction times. No reduction took place with a chlorine substituent in the alpha position. Cyclohexyl methyl ketone could be reduced in 93 % conversion but required 88 h and the enantioselectivity was low.

$$\underset{R\overset{\displaystyle O}{\diagup}R'}{}\quad\xrightarrow[\substack{\text{2-propanol}\\0.1\text{ M, 80 °C}}]{\substack{0.33\text{ mol \% }Ru_3(CO)_{12}\\1\text{ mol \% }(\mathbf{R,R})\text{-}\mathbf{186}}}\quad\underset{R\overset{\displaystyle OH}{\diagup}R'}{}$$
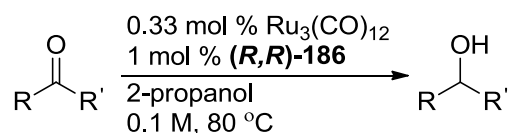
R	R'	Time (h)	Conv (%)	e.e. (%)
C_6H_5	Me	16	97	92 (*R*)
$4\text{-}CF_3C_6H_4$	Me	16	99	91 (*R*)
$4\text{-}MeOC_6H_4$	Me	65	91	89 (*R*)
$3\text{-}MeOC_6H_4$	Me	16	97	93 (*R*)
$2\text{-}MeOC_6H_4$	Me	16	98	85 (*R*)
$2\text{-}FC_6H_4$	Me	16	99	83 (*R*)
$2\text{-}ClC_6H_4$	Me	16	96	84 (*R*)
$2\text{-}BrC_6H_4$	Me	65	99	77 (*R*)
Cyclohexyl	Me	88	93	13 (*R*)
C_6H_5	Et	88	4	0
C_6H_5	CH_2Cl	88	0	-
α-Tetralone		88	27	79 (*R*)

Table 43. The substrate scope of (*R,R*)-186.

A speculated catalytic cycle is shown in Scheme 59. The formation of an 18-electron Ru(II) pincer complex ((*R,R*)-194) by the oxidative addition of a

ruthenium species across the TsN-H bond is thought to occur based on the reaction stoichiometry. The reduction of acetophenone could then proceed in a concerted manner via a 6-membered cyclic transition state, resulting in the generation of unsaturated 16-electron Ru(II) amide **(R,R)-195** which can oxidise 2-propanol to regenerate **(R,R)-194**.
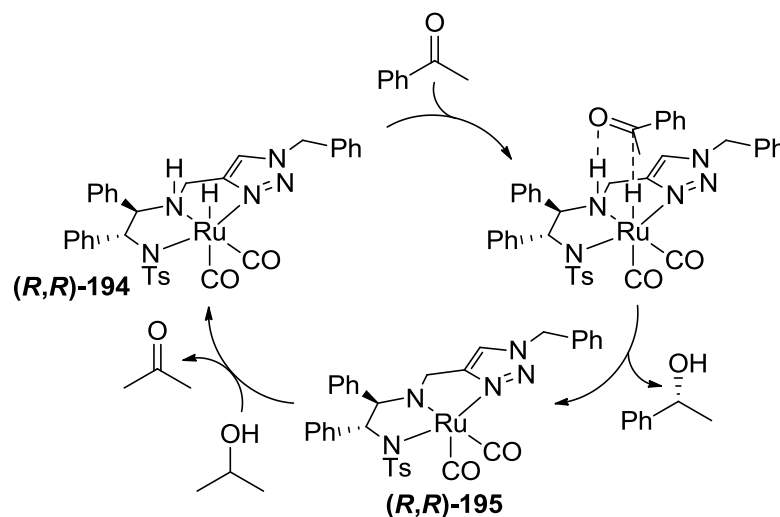
Scheme 59. A speculated catalytic cycle for the reduction of ketones by **(R,R)-186** and $Ru_3(CO)_{12}$.

Attempts to isolate a complex from the reaction of **(R,R)-186** and $Ru_3(CO)_{12}$ under a variety of conditions were unsuccessful but an interesting observation was made; after heating the two compounds together at 80 °C in toluene for 5 h and removing the solvent *in vacuo*, signals at about -16 and -17 ppm were observed in the ^1H NMR spectrum. These signals are indicative of metal hydride species and give some credence to the proposed structure **(R,R)-194** since activation of an N-H bond is the most likely source of hydride. To test the validity of the mechanistic proposal, ligands **(R,R)-196** and **(R,R)-197** were synthesised in which an NH proton had been replaced with a methyl group. The syntheses were carried out as shown in Scheme 60. Similar attempts at complex formation showed a signal at

about -11 ppm in the ^{1}H NMR spectrum for (***R***,***R***)-**196** but not for (***R***,***R***)-**197**. When applied to the reduction of acetophenone neither ligand showed significant activity (<5 %) which demonstrates the necessity for both NH protons to be present in order for a competent catalyst to be formed.
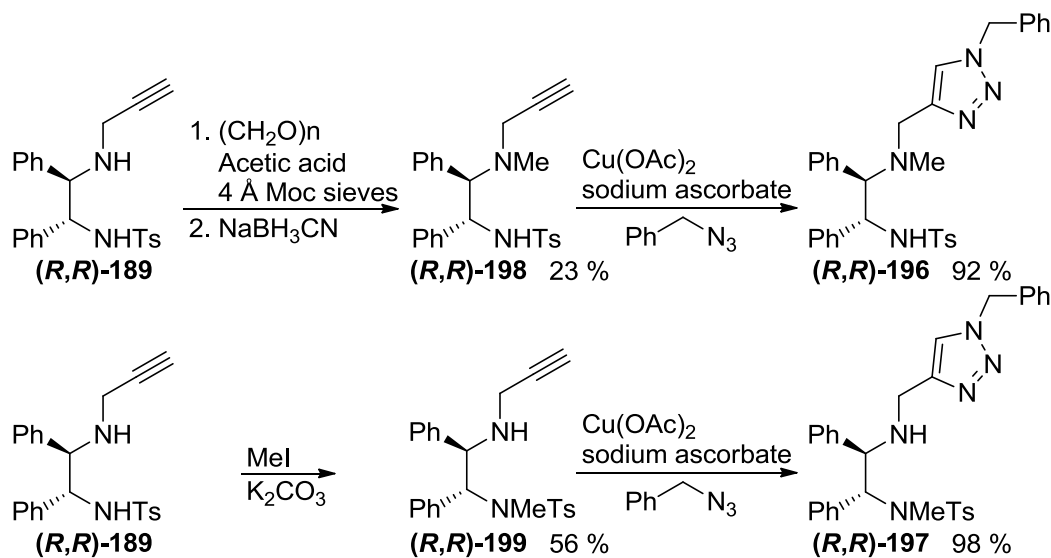
Scheme 60. The synthesis of methyl-substituted triazole ligands.

2.6 Conclusions.

The dehydrogenation of 1-phenylethanol derivatives using [RuCl(*p*-cymene)]₂ and PPh₃ under basic conditions was studied and a strong dependency on the electronics of the substrate was observed. Introducing a hydrogen acceptor to the system served to identify the release of hydrogen gas from the catalyst as the rate-determining step. High temperatures are required to drive the reaction.

The Shvo catalyst was identified as being a highly efficient transfer hydrogenation catalyst. A difficult substrate, glycerol, was oxidised to 1,3-dihydroxyacetone in up to 44 % conversion. An analogue was prepared bearing a pendant amine functionality (**116**) designed to aid in hydrogen gas release but proved to be unsuccessful.

A family of iron analogues of the Shvo catalyst were synthesised and studied as precatalysts for the oxidation of alcohols. Catalyst activation by thermal loss of CO, dimer formation and hydride formation were all explored but were unsuccessful. The removal of a CO ligand was achieved using TMANO and provided access to catalytically active iron species which were evaluated for the oxidation of 1-phenylethanol with acetone. Complex **126** achieved essentially quantitative conversion. The use of simple aldehydes as hydrogen acceptors was investigated and the use of paraformaldehyde led to high conversions and the discovery of an unusual formylation reaction.

The synthesis of asymmetric iron analogues of the Shvo catalyst was achieved and the ATH of acetophenone was carried out in 5:2 FA/TEA. It was possible to reduce acetophenone to (*R*)-1-phenylethanol in up to 91 % conversion and up to 32 % e.e. The steric influence of substituents on the cyclopentadienone

ligand was shown to affect the enantioselectivity of the reduction and the configuration of the chiral centre on the ligand controls the configuration of product that is formed. The syntheses of elaborated structures with more hindered substituents, different ring sizes and tethered derivatives were largely unsuccessful with the major limitation being the sensitivity of the complexation reaction in which a diyne undergoes a $[2 + 2 + 1]$ cycloaddition with CO.

Chiral diamines and an amino-alcohol containing 1,2,3-triazole functionalities were investigated as ligands for the ATH of ketones. Tridentate diaminotriazoles in conjunction with $Ru_3(CO)_{12}$ in 2-propanol provided the best activity and selectivity in the reduction reactions. The reductions proceed without the need for base and enantioselectivities of up to 93 % were obtained. Notably, a range of *ortho* substituted acetophenones could be reduced in up to 99 % conversion and 85 % e.e.

2.7 Future Work.

Although tethered iron cyclopentadienone complexes have proven elusive they could still potentially be accessed by the synthesis of the completed cyclopentadienone prior to complexation. Scheme 61 shows the application of known chemistry to ligand precursor (**R,R**)-**171** that could provide access to a cyclopentadienone bearing an amine tether. Treatment of a diyne with *in situ* generated Cp_2Zr creates a zirconacyclopentadiene which can react with iodine to form a diiododiene.[210, 211] Lithiation followed by bubbling CO_2 through the reaction mixture should result in the desired cyclopentadienone.[212]
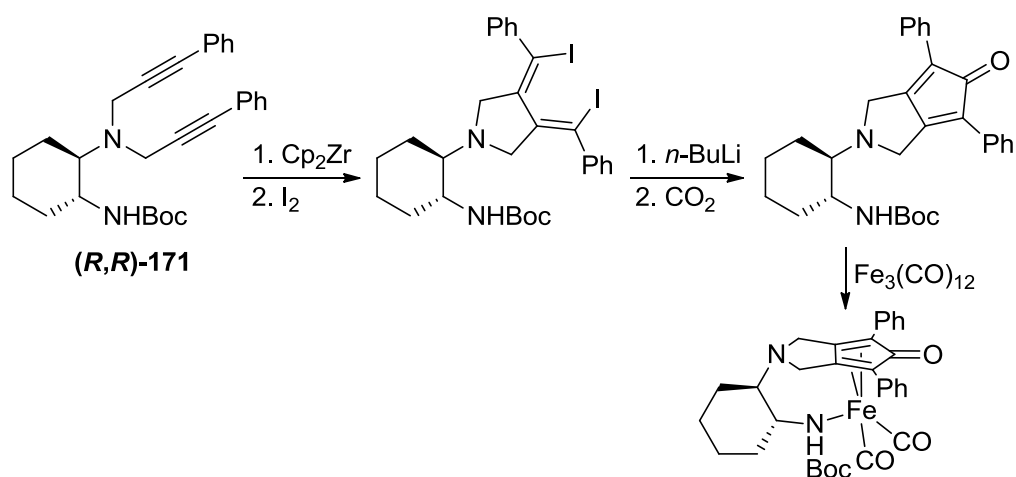
Scheme 61. The synthesis of a tethered cyclopentadienone complex from an easily accessed precursor.

A different route to a tethered cyclopentadienone is shown in Scheme 62. The regioselective [3 + 2] cycloaddition between an alkyne and a cyclopropenone (commercially available or accessed from a propan-2-one derivative in two steps) with a rhodium catalyst to form a cyclopentadienone was reported by Williams in 2006.[213] The use of a chiral alkyne derived from a protected amino alcohol could provide rapid access to tethered cyclopentadienones. The desired complex would

form as a mixture of diastereoisomers which could potentially be separated by chromatography or recrystallisation.
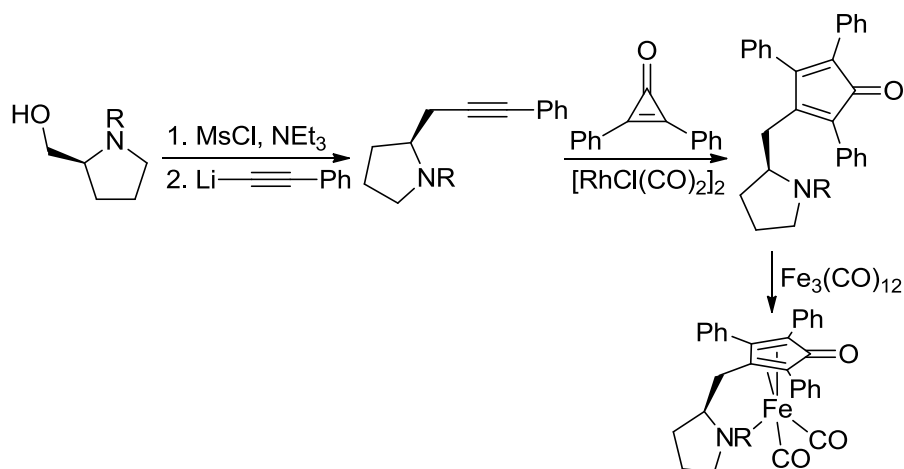
Scheme 62. Cyclopentadienone synthesis via a [3 + 2] cycloaddition between an alkyne and a cyclopropenone.

Many further modifications could be made to the chiral diamine-derived tridentate ligands studied in section 2.5 to tune the reactivity and selectivity. The 1,2,3-triazole group could be substituted for a variety of different aliphatic and aromatic heterocycles. Equally, the toluenesulphonyl group could be substituted for various other sulphonyl derivatives and amides. Variation of the chain length between the diamine and the heterocycle could also impact on the reactivity of these ligands.
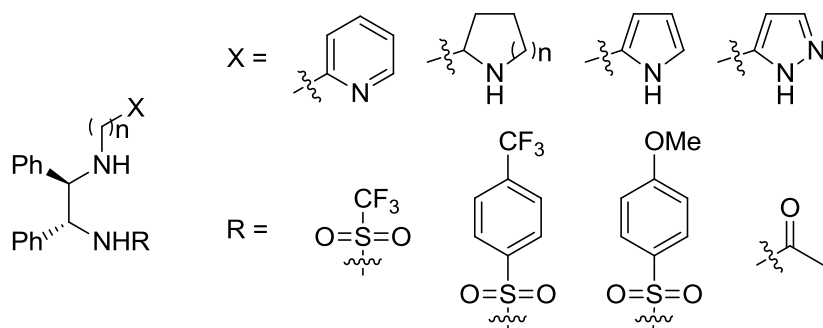
Figure 59. Further modification of diamine ligands for ATH with $Ru_3(CO)_{12}$.

3 Experimental.

General Considerations.

Solvents and reagents for the synthesis of complexes and catalytic reactions were degassed prior to use and all reactions were carried out under either a nitrogen or argon atmosphere. Room temperature refers to ambient room temperature (20-22 °C), 0 °C refers to an ice slush bath and −78 °C refers to a dry ice-acetone bath. Heated experiments were conducted using thermostatically controlled oil baths. Reactions were monitored by TLC using aluminum backed silica gel 60 (F254) plates, visualized using UV 254 nm and phosphomolybdic acid, ninhydrin, potassium permanganate or vanillin dips as appropriate. Flash column chromatography was carried out routinely using 60 Å silica gel (Merck). Reagents were used as received from commercial sources unless otherwise stated. NMR spectra were recorded on a Bruker DPX (300 or 400 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform. Coupling constants (*J)* are measured in Hertz. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Mass spectra were recorded on a Bruker Esquire 2000 or a Bruker MicroTOF mass spectrometer. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected. GC analysis was performed using a Hewlett Packard 5890. Optical rotations were measured on an AA-1000 polarimeter. Dry solvents were purchased and used as received.

3.1 Procedures from Section 2.1.

Noyori's Catalyst, **111**.
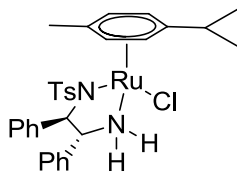
This compound is known but not fully characterised.[48] [RuCl$_2$(p-cymene)]$_2$ (0.199 g, 0.325 mmol), (R,R)-TsDPEN (0.238 g, 0.649 mmol) and NEt$_3$ (0.18 cm^3, 1.29 mmol) were dissolved in dry 2-propanol (40 cm^3) and heated at 80 °C for 1 h 25 mins. The solution was allowed to cool to room temperature, after which the solvent was removed *in vacuo*. The resultant orange solid was triturated with water (2 x 10 cm^3) and the product was recrystallised from MeOH to give orange crystals (0.170 g, 0.267 mmol, 82 %). Mp 181-185 °C; $[\alpha]_D^{28}$ -78.5 (c 0.025 in CHCl$_3$) (R,R); (Found (ESI): M$^+$ - Cl 601.1480, C$_{31}$H$_{35}$N$_2$O$_2^{102}$RuS requires 601.1465); ν_{max} 3272, 3211, 2961, 2365, 2344, 1598, 1493, 1452, 1375, 1265, 1126, 1083, 1003, 989, 911, 858, 807, 751, 696, 679, 653 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 6.85-7.02 (5H, m, Ar), 6.57-6.73 (5H, m, Ar), 6.49-6.57 (2H, m, Ar), 6.24-6.35 (2H, m, Ar), 5.84 (1H, broad s, Ar), 5.66-5.79 (3H, m, Ar), 3.62-3.70 (1H, m, C*H*NTs), 3.48-3.60 (1H, m, C*H*NH$_2$), 3.28 (1H, broad s, N*H*$_2$), 3.02-3.13 (1H, m, C*H*(CH$_3$)$_2$), 2.29 (3H, s, SO$_2$C$_6$H$_4$C*H*$_3$), 2.19 (3H, s, ^{i}PrC$_6$H$_4$C*H*$_3$), 2.00 (1H, broad s, N*H*$_2$), 1.33 (6H, d, J 6.4, CH(C*H*$_3$)$_2$); δ_C (75 MHz, CDCl$_3$) 143.3, 139.6, 138.9, 138.6, 129.0, 127.9, 127.7, 127.3, 127.2, 126.6, 126.5, 125.8, 94.7, 94.4, 85.3, 82.1, 80.1, 71.7, 69.2, 30.5, 21.1, 18.9; *m/z* (ESMS+) 601 [M - Cl]$^+$.

General Procedure for the Oxidation of alcohols with [RuCl$_2$(*p*-cymene)]$_2$/PPh$_3$, **112**.

This is based on a literature procedure.[73] [RuCl$_2$(*p*-cymene)]$_2$ (20.0 mg, 32.7 μmol), PPh$_3$ (62.0 mg, 0.236 mmol) and LiOH.H$_2$O (20.0 mg, 0.477 mmol) were dissolved in toluene (10 cm^3) and heated at reflux (110°C). After 30 mins 1-phenylethanol (0.365 g, 2.99 mmol) in toluene (5 cm^3) and added to the mixture. The reaction was monitored after 3, 6, 9 and 15 h by ^{1}H NMR and the conversion was calculated by integration of the CH$_3$ signals.

Competition Experiment

[RuCl$_2$(*p*-cymene)]$_2$ (0.018 g, 0.294 μmol), PPh$_3$ (0.064 g, 0.244 mmol) and LiOH.H$_2$O (0.019 g, 0.453 mmol) were dissolved in toluene (10 mL) and heated at reflux (110 °C). 1-Phenylethanol (0.122 g, 0.998 mmol), 1-(4'-methoxyphenyl)ethanol (0.152 g, 0.998 mmol) and 1-(4'methylphenyl)ethanol (0.136 g, 0.998 mmol) in toluene (5 mL) were added. The reaction was monitored by ^{1}H NMR and the conversion was calculated by integration of the CH$_3$ signals.

General Procedure for the Oxidation of alcohols with Noyori's Catalyst, **111**.

Complex **111** (10.0 g, 15.7 μmol) and LiOH.H$_2$O (10.0 g, 0.238 mmol) were dissolved in toluene (10 cm^3) and heated at 70 °C. After 30 mins 1-phenylethanol (0.192 g, 1.57 mmol) in toluene (5 cm^3) was added. The reaction was monitored

after 3, 6, 9 and 15 h by ^{1}H NMR and the conversion was calculated by integration of the CH_3 signals.

3.2 Procedures from Section 2.2.

4-Toluenesulphonylethylenediamine.
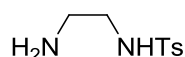
This compound is known and has been fully characterised.[214, 215] A solution of tosyl chloride (2.222 g, 11.7 mmol) in DCM (25 cm^3) was added dropwise to a solution of ethylenediamine (7.50 cm^3, 0.111 mol) in DCM (25 cm^3). After stirring for 15 mins the solution was washed with H_2O (2 x 50 cm^3), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* to give a white solid (1.305 g, 6.09 mmol, 52 %). The reported data is in agreement with the literature. δ_H (300 MHz, CDCl$_3$) 7.72-7.77 (2H, m, Ar), 7.28-7.33 (2H, m, Ar), 3.21 (1H, broad s, NHTs), 2.93-2.98 (2H, m, CH_2NHTs), 2.76-2.81 (2H, m, CH_2NH$_2$), 2.42 (3H, s, CH_3), 2.18 (2H, s, NH_2); δ_C (75 MHz, CDCl$_3$) 143.3, 136.9, 129.7, 127.0, 45.4, 40.9, 21.5.

[RuCl(*p*-cymene)Tsen], **113**.
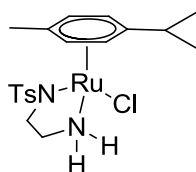
This compound is known but not fully characterised.[216] [RuCl$_2$(*p*-cymene)]$_2$ (0.249 g, 0.407 mmol), 4-toluenesulphonylethylenediamine (0.174 g, 0.812 mmol) and NEt$_3$ (0.40 cm^3, 2.88 mmol) were dissolved in dry 2-propanol (40 cm^3) and heated at 80 °C for 1 h. The solution was allowed to cool to room temperature, after which

the solvent was removed *in vacuo*. The resultant orange solid was dissolved in DCM (10 cm^3), washed with water (2 x 10 cm^3) and the solvent was removed *in vacuo*. Recrystallisation from MeOH gave the product as red crystals (0.106 g, 0.219 mmol, 54 %). Mp 204-206 °C; (Found (ESI): M$^+$ - Cl 449.0835, C$_{19}$H$_{27}$N$_2$O$_2$^{102}RuS requires 449.0836); ν_{max} 3267, 3215, 3139, 2858, 2363, 1586, 1492, 1459, 1374, 1280, 1256, 1199, 1154, 1130, 1094, 1039, 1002, 981, 908, 861, 838, 817, 728, 710, 657 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.73-7.79 (2H, m, Ar), 7.14-7.19 (2H, m, Ar), 5.72 (1H, broad s, Ar), 5.47-5.56 (2H, broad m, Ar), 5.39 (1H, broad s, Ar), 4.49 (1H, broad s, N*H*$_2$), 3.23 (1H, broad s, C*H*$_2$), 3.02 (1H, broad s, C*H*$_2$), 2.72-2.83 (1H, m, C*H*(CH$_3$)$_2$), 2.68 (1H, broad s, C*H*$_2$), 2.34 (3H, s, SO$_2$C$_6$H$_4$C*H*$_3$), 2.28 (1H, broad s, C*H*$_2$), 2.14 (3H, s, ^{i}PrC$_6$H$_4$C*H*$_3$), 1.26 (6H, broad s, CH(C*H*$_3$)$_2$); δ_C (75 MHz, CDCl$_3$) 140.8, 140.5, 128.7, 127.2, 102.1, 96.2, 82.7, 81.6, 81.1, 79.9, 48.6, 47.3, 30.5, 21.4, 18.6; *m/z* (ESMS+) 449 [M - Cl]$^+$.

General Procedure for the Oxidation of alcohols with an Acceptor.

Complex **111** (10.0 g, 15.7 μmol) and LiOH.H$_2$O (10.0 g, 0.238 mmol) were dissolved in toluene (10 cm^3) and heated at 70 °C. After 30 mins 1-phenylethanol (0.192 g, 1.57 mmol) and acetone (1.15 cm^3, 15.7 mmol) in toluene (5 cm^3) was added. The reaction was monitored after 3, 6, 9 and 15 h by ^{1}H NMR and the conversion was calculated by integration of the CH$_3$ signals.

Oxidation of Glycerol in a Sealed Tube.

Complex **91** (5.0 mg, 4.61 μmol) was dissolved in acetone (5 cm^3) and added to a pressure tube charged with glycerol (83.0 mg, 0.901 mmol). The tube was sealed and the mixture was heated at 100 °C for 24 h. The conversion was calculated from integration of the ^{1}H NMR spectrum.

3.3 Procedures from Section 2.3.

N-tert-Butoxycarbonyl-dipropargylamine, **121**.
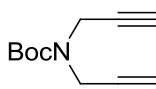
This product is known but has not been fully characterised.[217] *N*-Boc-Propargylamine (1.504 g, 9.69 mmol) in dry THF (10 cm^3) was added dropwise to a suspension of NaH (0.279 g, 11.6 mmol) in dry THF (20 cm^3) at 0 °C. After 30 mins 80 % propargyl bromide in toluene (1.36 cm^3, 12.6 mmol) was added and the solution was left to stir for 18 h. The reaction was quenched with a saturated NaHCO$_3$ solution (30 cm^3) and the product was extracted into Et$_2$O (3 x 30 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography on silica with a gradient elution from 0-16 % EtOAc in pet. ether gave the product as a yellow oil (1.684 g, 8.72 mmol, 90 %). (Found (ESI): M$^+$ + H 216.0992, C$_{11}$H$_{15}$NaO$_2$ requires 216.0995); ν_{max} 3300, 2978, 2934, 1693, 1478, 1447, 1403, 1367, 1340, 1244, 1159, 1121, 949, 926, 861, 766 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 4.17 (4H, broad s, C*H*$_2$), 2.21 (2H, m, CC*H*), 1.47 (9H, s, C*H*$_3$); δ_C (75 MHz, CDCl$_3$) 154.1, 81.1, 78.7, 71.9, 35.1, 28.2; *m/z* (ESMS+) 216 [M + Na]$^+$.

1,7-Bis(trimethylsilyl)-*N*-*tert*-butoxycarbonyl dipropargylamine, **122**.
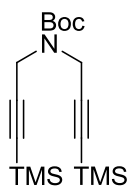
This compound is novel. Compound **121** (0.500 g, 2.59 mmol) was dissolved in dry THF (10 cm^3) and cooled to -78 °C. 1.6 M *N*-Butyllithium in hexanes (3.40 cm^3, 5.44 mmol) was added cautiously and the mixture was allowed to stir for 30 mins after which time chlorotrimethylsilane (0.72 cm^3, 5.67 mmol) was added and the solution was allowed to warm to room temperature. The reaction was quenched after 3 h with H$_2$O (10 cm^3) and the product was extracted into Et$_2$O (3 x 15 cm^3), dried over MgSO$_4$, filtered and the solvent was removed in vacuo to give a dark orange oil (0.854 g, 2.53 mmol, 98 %). (Found (ESI): M$^+$ + Na, 360.1802. C$_{17}$H$_{31}$NNaO$_2$Si$_2$ requires 360.1791); ν_{max} 2965, 2178, 1703, 1444, 1400, 1365, 1334, 1240, 1162, 1118, 1006, 837, 758, 697 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 4.14 (4H, broad s, C*H$_2$*), 1.47 (9H, s, (C*H$_3$*)$_3$C), 0.16 (18H, s, Si(C*H$_3$*)$_3$); δ_C (100 MHz, CDCl$_3$) 165.5, 154.4, 100.9, 80.8, 36.0, 28.3, -0.1; *m/z* (ESMS+) 360 [M + Na]$^+$.

Tricarbonyl(2,4-bis(trimethylsilyl)-7-*N*-*tert*-butoxycarbonylamine-bicyclo[3.3.0]hepta-1,4-dien-3-one)ruthenium, **120**.
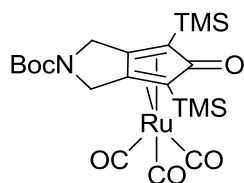
This compound is novel. Ru$_3$(CO)$_{12}$ (0.647 g, 1.01 mmol) and **122** (0.512 g, 1.52 mmol) were dissolved in dry toluene (14 cm^3) and heated at 130 °C in a sealed pressure tube for 48 h. The solution was allowed to cool to room temperature

before releasing the pressure. Hot filtration and removal of the solvent under reduced pressure gave a brown solid. The product was purified by column chromatography on silica with a gradient elution from 0-15 % EtOAc in hexane, followed by trituration with hexane to give the product as a yellow solid (0.259 g, 0.470 mmol, 31 %). Mp 172-173 °C; (Found (ESI): M^+ + H, 552.0818. $C_{21}H_{32}NO_6{}^{102}RuSi_2$ requires 552.0811); ν_{max} 2962, 2081, 2023, 2002, 1695, 1623, 1412, 1365, 1297, 1245, 1166, 1110, 1039, 918, 839, 767, 745, 695 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 4.39-4.59 (4H, m, CH_2), 1.51 (9H, s, (CH_3)$_3$CCO$_2$N), 0.27 (9H, s, Si(CH_3)$_3$), 0.26 (9H, s, Si(CH_3)$_3$); δ_C (100 MHz, CDCl$_3$) 193.8, 184.7, 154.4, 114.4, 113.2, 81.0, 66.7, 66.4, 48.2, 48.1, 31.3, 28.4, -0.4, -0.5; m/z (ESMS+) 552 [M + H]$^+$.

Tricarbonyl(2,4-bis(trimethylsilyl)-7-amino-bicyclo[3.3.0]hepta-1,4-dien-3-one)ruthenium, **116**.
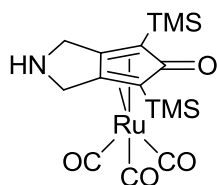
This compound is novel. Trifluoroacetic acid (3.0 cm^3, 39.2 mmol) was added in 1.0 cm^3 aliquots to a solution of **120** (88.0 mg, 0.160 mmol) in DCM (5 cm^3) with periodic monitoring by TLC. When the reaction was complete the solvent was removed under reduced pressure and the product was redissolved and the solvent was removed 5 times to remove the excess trifluoroacetic acid to give the product as a yellow-brown oil which was used for catalytic experiments without further purification. A small sample (50 mg) was dissolved in EtOAc (5 cm^3) and washed with H$_2$O (3 x 5 cm^3), dried over Na$_2$SO$_4$, filtered and the solvent was removed

under reduced pressure to give the product as a yellow-brown oil (25 mg 55.5

µmol, 35 %) for characterisation. (Found (ESI): $M^+ + H$, 452.0292.

$C_{16}H_{24}NO_4{}^{102}RuSi_2$ requires 452.0286); ν_{max} 2085, 2014, 1963, 1671, 1632, 1447,

1406, 1381, 1247, 1198, 1119, 836, 796, 766, 746, 720, 694 cm^{-1}; δ_H (400 MHz,

CDCl$_3$) 4.37-4.43 (4H, broad s, CH_2), 0.26 (18H, s, Si(CH_3)$_3$), NH not found; δ_C

(100 MHz, CDCl$_3$) 192.9, 185.0, 111.0, 66.6, 46.9, -0.5; m/z (ESMS+) 452 [M +

H]$^+$.

3.4 Procedures from Section 2.4.

1,8-Bis(trimethylsilyl)-1,7-octadiyne, **124**.
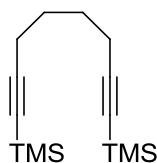
This compound is known and has been fully characterised.[218] 1,7-Octadiyne (2.18 g,

20.6 mmol) was dissolved in dry THF (50 cm^3) and cooled to -78 °C. 1.6 M *N*-

Butyllithium in hexanes (24.0 cm^3, 38.4 mmol) was added cautiously and the

mixture was allowed to stir for 2 h after which time chlorotrimethylsilane (4.80

cm^3, 37.8 mmol) was added and the solution was allowed to warm to room

temperature. After 72 h the reaction was quenched with a saturated NH$_4$Cl solution

(50 cm^3) and the product was extracted into Et$_2$O (3 x 50 cm^3) and the solvent was

removed *in vacuo* to give a yellow oil (4.31 g, 17.2 mmol, 84 %). The reported data

is in agreement with that reported in the literature. ν_{max} 2957, 2173, 1428, 1324,

1248, 1046, 999, 963, 944, 908, 835, 757, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 2.22-

2.27 (4H, m, CH$_2$CH_2C) 1.59-1.64 (4H, m, CH_2CH$_2$C), 0.14 (18H, s, Si(CH_3)$_3$); δ_C

(75 MHz, CDCl$_3$) 107.0, 84.7, 27.7, 19.4, 0.2.

Tricarbonyl(2,4-bis(trimethylsilyl)bicyclo[4.3.0]nona-1,4-dien-3-one)iron, **123**.
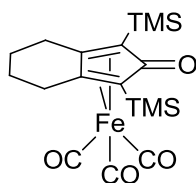
This compound is known and has been fully characterised.[175] Fe(CO)$_5$ (2.6 cm^3, 19.8 mmol) was added to a solution of **124** (0.498 g, 1.99 mmol) in toluene (10 cm^3) and heated at 130 °C in a sealed pressure tube. After 24 h the reaction mixture was allowed to cool to room temperature before releasing the pressure, after which it was hot filtered. The product was purified by column chromatography on silica with a gradient elution from 0-15 % EtOAc in hexane to give the product as a yellow solid (0.556 g, 1.33 mmol, 67 %). The reported data is in agreement with that reported in the literature. Mp 138-139 °C; (Found (ESI): M$^+$ + H, 419.0790. C$_{18}$H$_{27}$FeO$_4$Si$_2$ requires 419.0792); ν_{max} 2053, 1989, 1606, 1241, 843, 828 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 2.52-2.59 (4H, broad m, CH$_2$C*H*$_2$C), 1.82 (4H broad s, C*H*$_2$CH$_2$C), 0.27 (18H, s, Si(C*H*$_3$)$_3$); δ_C (75 MHz, CDCl$_3$) 209.0, 181.2, 111.0, 71.7, 24.8, 22.4, -0.3; *m/z* (ESMS+) 418 [M + H]$^+$.

Tricarbonyl(2,4-bis(trimethylsilyl)-7-*N*-*tert*-butoxycarbonlamine-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, **125**.
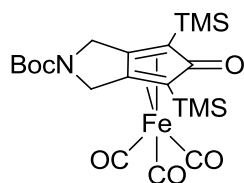
This compound is novel. Fe(CO)$_5$ (1.56 cm^3, 11.9 mmol) and **122** (0.499 g, 1.48 mmol) were dissolved in dry toluene (10 cm^3) and heated at 130 °C in a sealed pressure tube for 24 h. The solution was allowed to cool to room temperature

before releasing the pressure. Hot filtration and removal of the solvent under reduced pressure gave a brown solid. The product was purified by column chromatography on silica with a gradient elution from 0-15 % EtOAc in hexane to give the product as a yellow solid (0.189 g, 0.374 mmol, 25 %). Mp 166-167 °C; (Found (ESI): M$^+$ + H, 506.1122. C$_{21}$H$_{32}$FeNO$_6$Si$_2$ requires 506.1112); ν_{max} 2968, 2070, 2016, 1994, 1695, 1620, 1415, 1363, 1243, 1165, 1109, 1044, 922, 840, 766, 746, 696 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 4.32-4.52 (4H, broad m, CH$_2$), 1.51 (9H, s, (CH$_3$)$_3$CCO$_2$N), 0.26 (18H, s, Si(CH$_3$)$_3$); δ_C (100 MHz, CDCl$_3$) 207.8, 181.6, 154.6, 112.2, 111.8, 81.0, 69.6, 69.3, 47.6, 28.4, -1.0; m/z (ESMS+) 506 [M + H]$^+$.

Tricarbonyl(tetraphenylcyclopentadienone)iron, **126**.
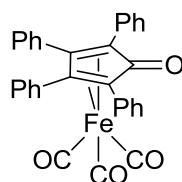
This compound is known but not fully characterised.[178] Fe$_3$(CO)$_{12}$ (0.362 g, 0.653 mmol) and tetraphenylcyclopentadienone (0.250 g, 0.650 mmol) were dissolved in dry toluene (3 cm^3) and heated at 80 °C in a sealed pressure tube for 20 h after which the solution was allowed to cool to room temperature and the solvent was removed under reduced pressure. The black solid was dissolved in EtOAc, filtered through celite and the solvent was removed under reduced pressure to give the product as a yellow solid (0.311 g, 0.593 mmol, 91 %). Mp 174-175 °C; (Found (ESI): M$^+$ + Na, 547.0604. C$_{32}$H$_{20}$FeNaO$_4$ requires 547.0604); ν_{max} 3058, 2061, 1987, 1639, 1498, 1444, 1386, 1187, 1158, 1124, 1075, 1029, 1005, 920, 840, 803, 752, 729, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.55-7.61 (4H broad m, Ar) 7.20-7.28 (8H, broad m, Ar), 7.13-7.19 (8H, broad m, Ar); δ_C (75 MHz, CDCl$_3$) 208.5, 169.7,

131.7, 130.7, 130.2, 129.8, 128.6, 128.0, 127.97, 127.8, 104.0, 82.4; m/z (ESMS+) 525 $[M + H]^+$.

3-Phenyl-2-propyn-1-yloxy(prop-2-yne), **128**.
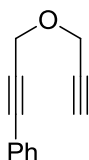
This compound is known and has been fully characterised.[219] 3-Phenyl-2-propyn-1-ol (3.01 g, 22.8 mmol) in dry THF (12 cm^3) was added to NaH (0.656 g, 27.4 mmol) in dry THF (10 cm^3) cooled to 0 °C and left to stir. After 30 minutes 80 % propargyl bromide in toluene (3.19 cm^3, 37.0 mmol) was added and the solution was allowed to warm to room temperature. The reaction was quenched after 24 h with saturated NaHCO$_3$ solution (25 cm^3) and the THF was removed under reduced pressure. The product was extracted into Et$_2$O (4 x 30 cm^3), dried over Na$_2$SO$_4$ and the solvent was removed under reduced pressure to give a brown oil (3.643 g, 21.4 mmol, 93 %). The reported data is in agreement with that reported in the literature. (Found (ESI): M^+ + Na, 193.0616. C$_{12}$H$_{10}$NaO requires 193.0624); ν_{max} 3292, 2852, 1598, 1490, 1442, 1344, 1257, 1245, 1075, 1029, 1000, 966, 928, 917, 883, 755, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.42-7.49 (2H, m, Ar), 7.29-7.35 (3H, m, Ar), 4.50 (2H, s, PhCCCH_2O), 4.32 (2H, d, J 2.6, CHCCH_2O), 2.47 (1H, t, J 2.6, CHCCH$_2$O); δ_C (75 MHz, CDCl$_3$) 131.8, 128.6, 128.3, 122.4, 86.8, 84.0, 79.0, 75.0, 57.3, 56.5; m/z (ESMS+) 193 $[M + Na]^+$.

4-Phenyl-3-butyn-2-yloxy(prop-2-yne), **129**.
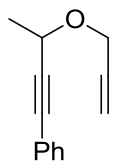
This compound is known and has been fully characterised.[193] Compound **129** was synthesised by the same procedure as for **128** using 4-Phenyl-3-butyn-2-ol (4.73 g, 32.4 mmol), NaH (0.932 g, 38.9 mmol) and 80 % propargyl bromide in toluene (4.50 cm^3, 41.8 mmol). The product was isolated as a brown oil (5.958 g, 32.3 mmol, 99 %). The reported data is in agreement with that reported in the literature. (Found (ESI): M$^+$ + Na, 207.0774. $C_{13}H_{12}NaO$ requires 207.0780); ν_{max} 3293, 2855, 1714, 1598, 1574, 1489, 1443, 1372, 1331, 1263, 1128, 1093, 1064, 1029, 917, 902, 824, 755, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.41-7.47 (2H, m, Ar), 7.29-7.34 (3H, m, Ar), 4.64 (1H, q, *J* 6.4, CC*H*(CH$_3$)O) 4.40 (1H, dd, *J* 2.3, 15.8, CC*H*HO) 4.32 (1H dd, *J* 2.3, 15.8, CCH*H*O), 2.5 (1H, t, *J* 2.3, C*H*CCH$_2$O), 1.56 (3H, d, *J* 6.4, CCH(C*H$_3$*)O); δ_C (75 MHz, CDCl$_3$) 131.7, 128.4, 128.3, 122.5, 87.9, 85.6, 8.5, 74.4, 64.6, 55.7, 22.0; *m/z* (ESMS+) 207 [M + Na]$^+$.

The asymmetric derivative of **129** was prepared by the same procedure using **(R)-127** (3.86 mmol) and provided **(R)-129** in 99 % yield. [α]$_D^{28}$ +222.2 (c 0.4 in CHCl$_3$) (*R*).

3-Phenyl-2-propyn-1-yloxy(3-phenylprop-2-yne), **130c**.
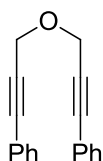
This compound is known and has been fully characterised.[220] Compound **128** (1.00 g, 5.88 mmol) and iodobenzene (1.64 cm^3, 14.7 mmol) were dissolved in NEt$_3$ (12 cm^3) and added to a solution of PdCl$_2$(PPh$_3$)$_2$ (83.0 mg, 0.118 mmol) and CuI (56.0 mg, 0.294 mmol) in NEt$_3$ (10 cm^3) and left to stir for 72 h after which time the NEt$_3$ was removed under reduced pressure. The brown residue was dissolved in DCM (30 cm^3) and washed with saturated Na$_2$S$_2$O$_3$ solution (30 cm^3) and brine (30 cm^3) before drying over MgSO$_4$, filtration and removal of the solvent under reduced pressure. The product was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in hexane to give the product as a yellow oil (1.185 g, 4.81 mmol, 82 %). The reported data is in agreement with that reported in the literature. (Found (ESI): M$^+$ + Na, 269.0932. C$_{18}$H$_{14}$NaO requires 269.0937); ν_{max} 3057, 2849, 2240, 1598, 1571, 1489, 1441, 1347, 1256, 1243, 1177, 1157, 1070, 1028, 1000, 959, 916, 886, 753, 688 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.43-7.50 (4H, m, Ar), 7.29-7.35 (6H, m, Ar), 4.56 (4H, s, CH_2); δ_C (75 MHz, CDCl$_3$) 131.8, 128.5, 128.3, 122.5, 86.8, 84.3, 6.4; m/z (ESMS+) 269 [M + Na]$^+$.

4-Phenyl-3-butyn-2-yloxy(3-phenylprop-2-yne), **131c**.
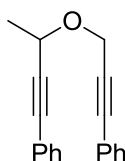
This compound is known and has been fully characterised.[193] Compound **131c** was synthesised by the same procedure as for **130c** using **129** (0.250 g, 1.36 mmol), iodobenzene (0.38 cm^3, 3.40 mmol), PdCl$_2$(PPh$_3$)$_2$ (19.0 mg, 27.1 μmol) and CuI (13.0 mg, 68.2 μmol). The product was purified by column chromatography on silica with a gradient elution from 0-10 % EtOAc in hexane to give the product as a yellow oil (0.323 g, 1.24 mmol, 92 %). The reported data is in agreement with that

reported in the literature. (Found (ESI): M$^+$ + Na, 283.1105. C$_{19}$H$_{16}$NaO requires 283.1093); ν_{max} 3056, 2851, 2224, 1597, 1572, 1489, 1442, 1371, 1358, 1329, 1256, 1126, 1092, 1061, 1028, 999, 960, 914, 826, 753, 688 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.43-7.49 (4H, m, Ar), 7.29-7.35 (6H, m, Ar), 4.70 (1H, q, J 6.4, CCH(CH$_3$)O), 4.63 (1H, d, J 15.8, CCHHO) 4.55 (1H, d, J 15.8, CCHHO), 1.59 (3H, d, J 6.4, CCH(CH_3)O); δ_C (75 MHz, CDCl$_3$) 131.8, 131.8, 128.4, 128.4, 128.3, 128.3, 122.6, 122.6, 88.2, 86.2, 85.6, 84.9, 64.7, 56.6, 22.1; m/z (ESMS+) 283 [M + Na]$^+$.

4-Phenyl-3-butyn-2-yloxy(3-(trimethylsilyl)prop-2-yne), **132c**.
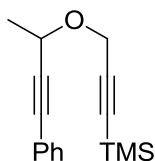
This compound is novel. Compound **129** (1.00 g, 5.45 mmol) was dissolved in dry THF (15 cm^3) and cooled to -78 °C. 2.5 M *N*-Butyllithium in hexanes (2.61 cm^3, 6.53 mmol) was added cautiously and the mixture was allowed to stir for 1 h after which chlorotrimethylsilane (0.90 cm^3, 7.09 mmol) was added. After 17 h the reaction was quenched with H$_2$O (10 cm^3), the THF was removed under reduced pressure and the product was extracted into Et$_2$O (3 x 20 cm^3). The combined organic phase was dried over Na$_2$SO$_4$, filtered and the solvent was removed under reduced pressure to give the product as a brown oil (1.385 g, 5.40 mmol, 99 %). (Found (ESI): M$^+$ + Na, 279.1182. C$_{16}$H$_{20}$NaOSi requires 279.1176); ν_{max} 2960, 2851, 2174, 1599, 1489, 1443, 1371, 1355, 1330, 1250, 1127, 1094, 1067, 1022, 990, 915, 839, 754, 689 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.42-7.46 (2H, m, Ar), 7.30-7.33 (3H, m, Ar), 4.60 (1H, q, J 6.5, CCH(CH$_3$)O), 4.41 (1H, d, J 15.6, CCHHO), 4.30 (1H, d, J 15.6, CCHHO), 1.55 (3H, d, J 6.5, (CCH(CH_3)O), 0.19 (9H, s,

Si(CH_3)$_3$); δ_C (75 MHz, CDCl$_3$) 131.7, 128.4, 128.3, 122.6, 101.3, 91.3, 88.1, 85.5, 64.7, 56.6, 22.1, -0.2); m/z (ESMS+) 279 [M + Na]$^+$.

4-Phenyl-3-butyn-2-yloxy(3-(*tert*-butyldimethylsilyl)prop-2-yne), **133c**.
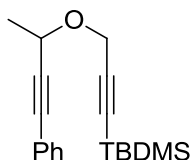
This compound is novel. Compound **133c** was synthesised by the same procedure as for **132c** using **129** (0.350 g, 1.90 mmol), 1.6 M *N*-butyllithium in hexanes (1.40 cm^3, 6.53 mmol) and *tert*-butyldimethylsilylchloride (0.373 g, 2.48 mmol) and was purified by column chromatography on silica with a gradient elution from 0-20 % EtOAc in hexane to give the product as a yellow oil (0.421 g, 1.41 mmol, 74 %). (Found (ESI): M$^+$ + Na, 321.1637. C$_{19}$H$_{26}$NaOSi requires 321.1645); ν_{max} 2953, 2930, 2856, 2173, 1773, 1599, 1490, 1471, 1463, 1443, 1361, 1330, 1251, 1094, 1068, 1022, 1006, 990, 938, 915, 836, 824, 810, 775, 754, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.42-7.46 (2H, m, Ar), 7.28-7.34 (3H, m, Ar), 4.64 (1H, q, *J* 6.8, CC*H*(CH$_3$)O), 4.41 (1H, d, *J* 15.8, CC*H*HO), 4.33 (1H, d, *J* 15.8, CCH*H*O), 1.55 (3H, d, *J* 6.8, (CCH(C*H$_3$*)O), 0.95 (9H, s, Si(CH$_3$)$_2$C(C*H$_3$*)$_3$) 0.12 (6H, s, Si(C*H$_3$*)$_2$C(CH$_3$)$_3$); δ_C (75 MHz, CDCl$_3$) 131.8, 128.4, 128.2, 122.5, 102.0, 89.7, 88.2, 87.3, 85.9, 64.4, 56.6, 26.1, 22.0, -4.7); m/z (ESMS+) 321 [M + Na]$^+$.

Asymmetric derivatives of compounds **131c**-**133c** were prepared by the same procedures as for the racemic compounds using (*R*)-**129** and the scale (mmol of substrate), yields and optical rotation data are summarised below. All optical rotations were performed in CHCl$_3$.

Compound	Scale (mmol)	Yield (%)	T (°C)	c (g/100 cm^3)	$[\alpha]_D$
(R,R)-131c	1.08	79	28	0.5	+283.4
(R,R)-132c	1.85	91	28	0.5	+193.4
(R,R)-133c	1.19	92	24	1.0	+150.7

Tricarbonyl(2,4-bis(phenyl)-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, **130**.
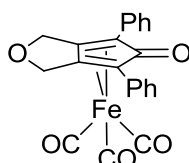
This compound is novel. Compound **130c** (0.300 g, 1.22 mmol) and Fe(CO)$_5$ (0.48 cm^3, 3.65 mmol) were dissolved in dry toluene (3 cm^3) and heated at 130 °C for 24 h after which the solution was allowed to cool to room temperature and the solvent was removed under reduced pressure. The brown residue was filtered through celite using a 9:1 mixture of hexane: EtOAc to give an orange residue. The product was purified by column chromatography on silica with a gradient elution from 0-20 % EtOAc in hexane to give the product as a yellow-brown solid (0.196 g, 0.473 mmol, 39 %). Mp 218-220 °C; (Found (ESI): M$^+$ + Na, 437.0076. C$_{22}$H$_{14}$FeNaO$_5$ requires 437.0083); ν_{max} 2064, 2004, 1634, 1055, 766, 693 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.86-7.92 (4H, m, Ar), 7.33-7.44 (6H, m, Ar), 5.24 (2H, d, *J* 12.1, C*H*H), 5.11 (2H, d, *J* 12.1, CH*H*); δ_C (75 MHz, CDCl$_3$) 207.6, 169.7, 131.5, 129.1, 128.6, 127.3, 100.6, 68.3, 65.8; *m/z* (ESMS+) 415 [M + H]$^+$. A small, broad resonance exists from 6.8-7.8 ppm and a smaller broad resonance at 5.0 ppm in the ^{1}H NMR spectrum that have not been assigned; these may be due to paramagnetic impurities.

Tricarbonyl(2,4-bis(phenyl)-6-methyl-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron **131**.
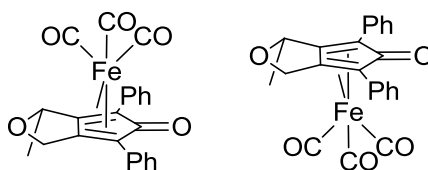
These complexes (two diastereoisomers) are novel. Complexes **131a** and **131b** were synthesised by the same procedure as for **130** using **131c** (0.300 g, 1.15 mmol) and $Fe(CO)_5$ (0.46 cm^3, 3.50 mmol) and was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in hexane to give two separated diastereoisomers. **131b**; brown powder (0.050 g, 0.117 mmol, 10 %). Mp 102-104 °C; (Found (ESI): M$^+$ + Na, 451.0235. $C_{23}H_{16}FeNaO_5$ requires 451.0239); ν_{max} 2066, 1995, 1712, 1645, 1496, 1444, 1069, 913, 837, 752, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.06-8.11 (2H, m, Ar), 7.86-7.93 (2H, m, Ar), 7.32-7.45 (6H, m, Ar), 5.63 (1H, q, *J* 6.4, (CC*H*(CH$_3$)O), 5.17 (2H, s, C*H$_2$*), 1.53(3H, d, *J* 6.4, (CCH(C*H$_3$*)O); δ_C (75 MHz, CDCl$_3$) 207.8, 171.8, 131.7, 131.5, 129.0, 128.9, 128.5, 128.3, 127.3, 127.0, 76.0, 66.3, 19.2; *m/z* (ESMS+) 451 [M + Na]$^+$. A broad resonance exists from 6.5-7.6 ppm in the ^{1}H NMR spectrum that has not been assigned; this may be due to paramagnetic impurities. **131a**; brown powder (0.065 g, 0.152 mmol, 13 %). Mp 130-132 °C; (Found (ESI): M$^+$ + Na, 451.0240. $C_{23}H_{16}FeNaO_5$ requires 451.0239); ν_{max} 2926, 2064, 2003, 1718, 1638, 1449, 1054, 845, 768, 694 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.90-7.96 (2H, m, Ar), 7.53-7.59 (2H, m, Ar), 7.32-7.45 (6H, m, Ar), 5.41 (1H, q, *J* 6.0, (CC*H*(CH$_3$)O), 5.25 (1H, d, *J* 13.2, C*H*H), 5.03 (1H, d, *J* 13.2, CH*H*) 1.67 (3H, d, *J* 6.0, (CCH(C*H$_3$*)O); δ_C (75 MHz, CDCl$_3$) 207.9, 131.3, 129.7, 129.0, 128.6, 128.5, 128.4, 127.3, 104.7, 104.6, 79.2, 75.0, 67.3, 30.9, 21.8; *m/z* (ESMS+) 451 [M + Na]$^+$. A broad resonance exists from

6.6-7.8 ppm in the ^{1}H NMR spectrum that has not been assigned; this may be due to paramagnetic impurities.

Tricarbonyl(2-(trimethylsilyl)-4-phenyl-6-methyl-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, **132**.
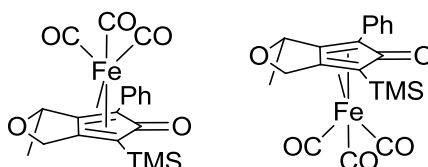
These complexes (two diastereoisomers) are novel. Complexes **132a** and **132b** were synthesised by the same procedure as for **130** using **132c** (0.300 g, 1.17 mmol) and Fe(CO)$_5$ (0.46 cm^3, 3.50 mmol) and was purified by column chromatography on silica with a gradient elution from 0-60 % EtOAc in hexane to give two separated diastereoisomers. **132b**, brown oil (0.060 g, 0.142 mmol, 12 %) (Found (ESI): M$^+$ + H, 425.0497. C$_{20}$H$_{21}$FeO$_5$Si requires 425.0502); ν_{max} 2959, 2065, 2010, 1992, 1633, 1445, 1418, 1249, 1170, 1056, 842, 768, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.99-8.03 (2H, m, Ar), 7.29-7.40 (3H, m, Ar), 5.56 (1H, q, *J* 6.4, CC*H*(CH$_3$)O), 4.82 (1H, d, *J* 12.8, C*H*H), 4.70 (1H, d, *J* 12.8, CH*H*), 1.52 (3H, d, J 6.4, C*H*$_3$), 0.33 (9H, s, Si(C*H*$_3$)$_3$); δ_C (75 MHz, CDCl$_3$) 207.9, 177.2, 131.9, 128.9, 128.2, 126.9, 108.5, 107.9, 77.3, 75.9, 66.1, 65.7, 19.0, -0.9; *m/z* (ESMS+) 425 [M + H]$^+$. **132a**, brown oil (0.166 g, 0.392 mmol, 33 %) (Found (ESI): M$^+$ + H, 425.0501. C$_{20}$H$_{21}$FeO$_5$Si requires 425.0502); ν_{max} 2962, 2064, 1998, 1712, 1635, 1447, 1250, 1168, 1054, 842, 756, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.48-7.52 (2H, m, Ar), 7.30-7.40 (3H, m, Ar), 5.36 (1H, q, *J* 6.4, CC*H*(CH$_3$)O), 4.78 (1H, d, *J* 13.2, C*H*H), 4.71 (1H, d, *J* 13.2, CH*H*), 1.65 (3H, d, J 6.4, C*H*$_3$), 0.31 (9H, s,

Si(CH_3)$_3$); δ_C (75 MHz, CDCl$_3$) 207.9, 174.9, 129.7, 129.4, 128.4, 128.2, 113.2, 108.7, 81.6, 74.9, 66.7, 64.8, 21.7, -01.0; m/z (ESMS+) 425 [M + H]$^+$.

Tricarbonyl(2-(*tert*-butyldimethylsilyl)-4-phenyl-6-methyl-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, **133**.
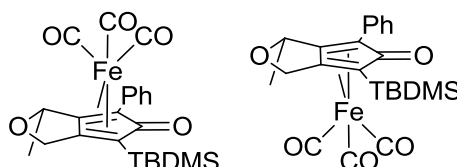
These complexes (two diastereoisomers) are novel. Complexes **133a** and **133b** were synthesised by the same procedure as for **130** using **133c** (0.300 g, 1.01 mmol) and Fe(CO)$_5$ (0.40 cm^3, 3.04 mmol) and was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in hexane to give two separated diastereoisomers. **133b**, yellow solid (0.066 g, 0.142 mmol, 14 %). Mp 124-126 °C; (Found (ESI): M$^+$ + H, 467.0974. C$_{23}$H$_{26}$FeO$_5$Si requires 467.0972); ν_{max} 2928, 2856, 2064, 1991, 1769, 1714, 1635, 1504, 1462, 1445, 1421, 1364, 1331, 1250, 1165, 1056, 1008, 826, 770, 694, 674 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.99-8.05 (2H, m, Ar), 7.29-7.39 (3H, m, Ar), 5.55 (1H, q, J 6.8, CCH(CH$_3$)O), 4.81 (1H, d, J 13.2, CHH), 4.71 (1H, d, J 13.2, CHH), 1.52 (3H, d, J 6.8, CH_3), 1.01 (9H, s, SiC(CH_3)$_3$) 0.47 (3H, s, Si(CH_3)(CH$_3$)C(CH$_3$)$_3$), 0.08 (3H, s, Si(CH$_3$)(CH_3)C(CH$_3$)$_3$); δ_C (75 MHz, CDCl$_3$) 207.8, 176.9, 131.8, 128.9, 128.3, 127.0, 109.3, 108.1, 76.5, 75.8, 66.5, 65.9, 27.2, 19.0, 18.6, -5.0, -5.3; m/z (ESMS+) 467 [M + H]$^+$. **133a**, brown oil (0.181 g, 0.388 mmol, 39 %) (Found (ESI): M$^+$ + H, 467.0974. C$_{23}$H$_{26}$FeO$_5$Si requires 467.0972); ν_{max} 2928, 2856, 2063, 1993, 1634, 1463, 1444, 1416, 1249, 1157, 1082, 1069, 1053, 1007, 825, 763, 694, 673 cm^{-1}; (300 MHz, CDCl$_3$) 7.47-7.53 (2H, m, Ar), 7.29-7.41 (3H, m, Ar), 5.37

(1H, q, *J* 6.0, CC*H*(CH₃)O), 4.80 (1H, d, *J* 13.2, C*H*H), 4.72 (1H, d, *J* 13.2, CH*H*), 1.65 (3H, d, J 6.0, C*H*₃), 0.97 (9H, s, SiC(C*H*₃)₃) 0.51 (3H, s, Si(C*H*₃)(CH₃)C(CH₃)₃), 0.06 (3H, s, Si(CH₃)(C*H*₃)₂C(CH₃)₃); δ$_C$ (75 MHz, CDCl₃) 207.9, 174.7, 129.7, 129.6, 128.5, 128.4, 115.0, 108.0, 81.1, 75.0, 67.2, 65.4, 27.1, 21.8, 18.8, -5.2; *m/z* (ESMS+) 467 [M + H]⁺.

Asymmetric derivatives of complexes **131**-**133** were prepared by the same procedure as for **130** using (*R*)-**131c**-**133c** and the scale (mmol of ligand precursor), yields and optical rotation data are summarised below. All optical rotations were performed in CHCl₃.

Complex	Scale (mmol)	Yield (%)	T (°C)	c (g/100 cm³)	[α]$_D$
(*R,R*)-**131a**	0.63	14	28	0.05	+23.0
(*R,R*)-**131b**	0.63	10	28	0.01	-75.0
(*R,R*)-**132a**	1.53	37	28	0.05	+101.0
(*R,R*)-**132b**	1.53	17	28	0.05	-166.0
(*R,R*)-**133a**	0.69	44	28	0.05	+20.0
(*R,R*)-**133b**	0.69	8	26	0.05	-47.0

Dicarbonyl(2,4-bis(trimethylsilyl)bicyclo[4.3.0]nona-1,4-dien-3-one)iron hydride, **110**.
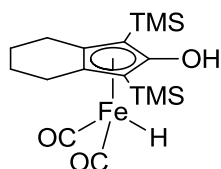
This compound is known and has been fully characterised.[179] Aqueous 1 M NaOH solution (0.96 cm³) was added to a solution of **123** (40.0 mg, 95.6 μmol) in dry

THF (4 cm^3). After 2.5 h a solution of 85 % H$_3$PO$_4$ (0.03 cm^3) in H$_2$O (1 cm^3) was added and the product was extracted into Et$_2$O (3 x 5 cm^3), dried over Na$_2$SO$_4$, filtered and the solvent removed *in vacuo*. A signal at -12.07 attributable to an iron hydride was observed in the ^{1}H NMR spectrum.

Tricarbonyl(tetraphenylcyclopentadienone)ruthenium.
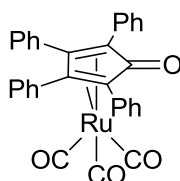
This compound is known and has been fully characterised.[198] Ru$_3$(CO)$_{12}$ (0.254 g, 0.397 mmol) and tetraphenylcyclopentadienone (0.611 g, 1.59 mmol) were dissolved in xylenes (8 cm^3) and heated at 130 °C for 24 h after which the reaction mixture was allowed to cool, degassed and heated at 130 °C for a further 6 h 45 mins before cooling and removal of the solvent *in vacuo*. The product was purified by column chromatography on silica with a gradient elution from 0-100 % EtOAc in DCM to give the product as a yellow solid (0.520 g, 0.913 mmol, 77 %). Mp 187-188 °C; (Found (ESI): M$^+$ + H, 571.0485. C$_{32}$H$_{21}$O$_4$^{102}Ru requires 571.0487); ν_{max} 3060, 2077, 2015, 2001, 1715, 1644, 1623, 1498, 1444, 1404, 1353, 1221, 1197, 1157, 1074, 1028, 1004, 968, 912, 839, 800, 749, 729, 694 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.46-7.49 (4H, m, Ar), 7.16-7.26 (8H, m, Ar), 7.09-7.13 (4H, m, Ar), 7.04-7.07 (4H, m, Ar); δ_C (100 MHz, CDCl$_3$) 194.4, 173.9, 132.0, 131.4, 130.7, 129.8, 128.5, 128.0, 127.9, 127.4, 107.7, 82.0; (ESMS+) 571 [M + H]$^+$.

Dicarbonyl(tetraphenylcyclopentadienone)ruthenium hydride.
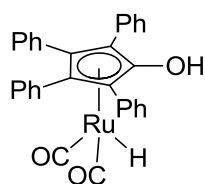
This compound is known but not fully characterised.[221] 2M $BH_3.Me_2S$ in THF (0.02 cm^3, 40.0 μmol) was added to a solution of Tricarbonyl(tetraphenylcyclopentadienone)ruthenium (0.010 g, 17.6 μmol) in dry THF (5 cm^3) cooled to -78 °C. After 1 h H_2O (0.1 cm^3) was added and the solution allowed to warm to room temperature after which the solvent was removed *in vacuo*. Resonances at -9.86 and -18.37 ppm in the ^{1}H NMR spectrum indicate the presence of small quantities of the monomeric and dimeric hydride complexes respectively.[149]

3-Phenyl-2-propyn-1-yloxy(3-(trimethylsilyl)prop-2-yne), **137**.
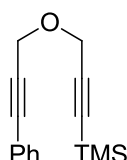
This compound is known but not characterised.[222] Compound **137** was made by the same procedure as for **132c** using **128** (1.00 g, 5.88 mmol), 1.6 M *N*-butyllithium in hexanes (4.38 cm^3, 7.01 mmol) and chlorotrimethylsilane (0.96 cm^3, 7.56 mmol). The product was isolated as an] orange oil (1.249 g, 5.15 mmol, 88 %). (Found (ESI): M^+ + Na, 265.1018. $C_{15}H_{18}NaOSi$ requires 265.1019); ν_{max} 2957, 2899, 2362, 2172, 1719, 1598, 1489, 1442, 1344, 1249, 1077, 1042, 998, 918, 839, 755, 690 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.42-7.49 (2H, m, Ar), 7.28-7.35 (3H, m, Ar), 4.47 (2H, s, C*H*$_2$), 4.32 (2H, s, C*H*$_2$), 0.19 (9H, s, Si(C*H*$_3$)$_3$); δ_C (75 MHz, CDCl$_3$) 131.8,

128.5, 128.3, 122.5, 100.7, 92.0, 86.7, 84.3, 57.4, 57.4, -0.2); m/z (ESMS+) 265 [M + Na]$^+$.

Tricarbonyl(2-(phenyl)-4-trimethylsilyl-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, **136**.
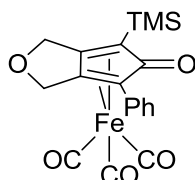
This compound is novel. Complex **136** was made by the same procedure as for **130** using **137** (0.300 g, 1.24 mmol) and Fe(CO)$_5$ (0.49 cm^{-3}, 3.73 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in hexane to give the product as a yellow solid (0.253 g, 0.617 mmol, 50 %). Mp 129-133 °C; (Found (ESI): M$^+$ + H, 411.0365. C$_{19}$H$_{19}$FeO$_5$Si requires 411.0346); ν_{max} 2959, 2058, 1993, 1627, 1508, 1467, 1450, 1430, 1381, 1346, 1266, 1246, 1172, 1081, 1050, 1027, 1008, 987, 939, 890, 843, 791, 761, 691 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.80-7.83 (2H, m, Ar), 7.31-7.38 (3H, m, Ar), 5.18 (1H, d, J 12.6, CHH), 5.04 (1H, d, J 12.6, CHH), 4.80 (1H, d, J 12.6, CHH), 4.75 (1H, d, J 12.6, CHH); δ_C (100 MHz, CDCl$_3$) 207.8, 176.0, 131.5, 129.0, 128.4, 127.2, 108.9, 104.4, 79.0, 68.3, 67.7, 65.8, -1.0; m/z (ESMS+) 411 [M + H]$^+$.

Phenylethylformate.
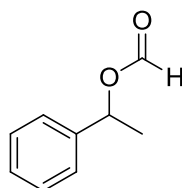
This compound is known but not fully characterised.[223] Phenylethanol (0.150 g, 1.23 mmol) was dissolved in formic acid (5 cm^3) with 3 Å molecular sieves and left to stir for 18 h after which H_2O (5 cm^3) was added. The product was extracted into Et_2O (2 x 10 cm^3), washed with H_2O (3 x 20 cm^3), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica (90:10 hexane:ethyl acetate) to give the product as a colourless oil (0.112 g, 0.746 mmol, 61 %). (Found (ESI): M^+ - CO_2H, 105.0705. C_8H_9 requires 105.0699); ν_{max} 3033, 2982, 2931, 1717, 1496, 1452, 1375, 1308, 1286, 1165, 1059, 1029, 992, 914, 845, 759, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.10 (1H, s, OC(O)H), 7.28-7.41 (5H, m, Ar), 6.03 (1H, q, J 6.6, PhCH), 1.60 (3H, d, J 6.6, CH_3); δ_C (75 MHz, CDCl$_3$) 160.29, 140.83, 128.52, 128.09, 126.09, 72.14, 22.06; m/z (ESMS+) 105 $[M - CO_2H]^+$.

1-(4-Methoxyphenyl)ethylformate.
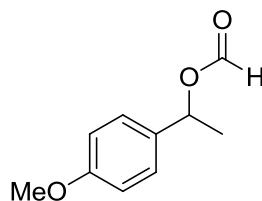
This compound is known but not fully characterised.[224] 1-(4-Methoxyphenyl)ethanol (0.150 g, 0.986 mmol) was dissolved in formic acid (5 cm^3) with 3 Å molecular sieves and left to stir for 18 h after which H_2O (5 cm^3) was added. The product was extracted into Et_2O (2 x 10 cm^3), washed with H_2O (3 x 20 cm^3), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica (90:10 hexane:ethyl acetate) to give the product as a colourless oil (0.089 g, 0.494 mmol, 50 %). (Found (ESI): M^+ + Na, 203.0682. $C_{10}H_{12}NaO_3$ requires 203.0679); ν_{max} 2933, 2837, 1718,

1613, 1586, 1514, 1459, 1375, 1297, 1247, 1169, 1058, 1033, 996, 830 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.07 (1H, s, OC(O)H), 7.28-7.34 (2H, m, Ar), 6.86-6.92 (2H, m, Ar), 5.98 (1H, q, J 6.6, PhCH), 3.81 (3H, s, OCH_3), 1.58 (3H, d, J 6.6, CH_3); δ_C (75 MHz, CDCl$_3$) 160.43, 159.45, 132.91, 127.67, 113.88, 71.93, 55.26, 21.83; m/z (ESMS+) 135 [M − CO$_2$H]$^+$.

Anisyl formate.
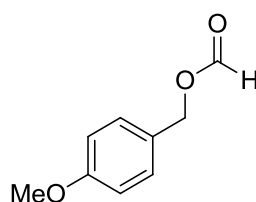
This compound is known but not fully characterised.[223] Anisyl alcohol (0.070 g, 0.507 mmol) was dissolved in formic acid (5 cm^3) with 3 Å molecular sieves and left to stir for 18 h after which H$_2$O (5 cm^3) was added. The product was extracted into Et$_2$O (2 x 10 cm^3), washed with H$_2$O (3 x 20 cm^3), dried over MgSO$_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica (90:10 hexane:ethyl acetate) to give the product as a colourless oil (0.037 g, 0.223 mmol, 44 %). (Found (ESI): M$^+$ + Na, 189.0526. C$_9$H$_{10}$NaO$_3$ requires 189.0522); ν_{max} 2936, 2837, 1716, 1612, 1586, 1514, 1461, 1397, 1303, 1246, 1150, 1112, 1031, 820 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 8.11 (1H, s, OC(O)H), 7.29-7.33 (2H, m, Ar), 6.88-6.92 (2H, m, Ar), 5.14 (2H, s, PhCH_2), 3.81 (3H, s, OCH_3); δ_C (100 MHz, CDCl$_3$) 160.87, 159.80, 130.24, 127.29, 113.99, 65.51, 55.27; m/z (ESMS+) 121 [M − CO$_2$H]$^+$.

1-(4-Chlorophenyl)ethylformate.
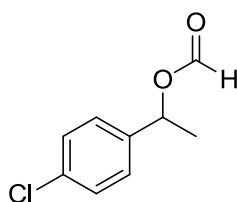
This compound is known but not fully characterised.[225] 1-(4-Chlorophenyl)ethanol (0.150 g, 0.958 mmol) was dissolved in formic acid (5 cm^3) with 3 Å molecular sieves and left to stir for 18 h after which H$_2$O (5 cm^3) was added. The product was extracted into Et$_2$O (2 x 10 cm^3), washed with H$_2$O (3 x 20 cm^3), dried over MgSO$_4$ and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica (90:10 hexane:ethyl acetate) to give the product as a colourless oil (0.102 g, 0.553 mmol, 58 %). (Found (ESI): M$^+$ - CO$_2$H, 139.0310. C$_8$H$_8$Cl requires 139.0309); ν_{max} 2984, 2930, 1719, 1599, 1494, 1452, 1409, 1375, 1342, 1298, 1276, 1162, 1091, 1058, 1014, 996, 823, 752, 718 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 8.07 (1H, s, OC(O)H), 7.28-7.35 (4H, m, Ar), 5.97 (1H, q, J 6.5, PhCH), 1.56 (3H, d, J 6.5, CH_3); δ_C (100 MHz, CDCl$_3$) 160.14, 139.37, 133.85, 128.71, 127.53, 71.38, 22.01; m/z (ESMS+) 139 [M – CO$_2$H]$^+$.

4-Phenyl-3-butyn-2-one, **139**.
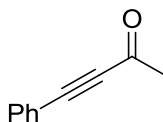
This compound is known and has been fully characterised.[226, 227] 1.6 M N-Butyllithium in hexanes (14.7 cm^3, 23.5 mmol) was added dropwise to a solution of phenylacetylene (2.00 g, 19.6 mmol) in dry THF (30 cm^3) cooled to -78 °C. After 30 mins dry EtOAc (2.49 cm^3, 25.5 mmol) and BF$_3$.Et$_2$O (2.42 cm^3, 19.6 mmol) were added sequentially. After a further 30 mins the reaction was quenched with

saturated NH$_4$Cl solution (30 cm^3) and allowed to warm to room temperature. The product was extracted into EtOAc (3 x 30 cm^3), washed with brine (3 x 90 cm^3), dried over MgSO$_4$ and the solvent was removed under reduced pressure. The product was isolated by kugelrohr distillation (1 mbar, 100 °C) to give a pale yellow oil (2.340 g, 16.2 mmol, 83 %). (Found (ESI): M$^+$ + H 145.0650, C$_{10}$H$_9$O requires 145.0648); ν_{max} 2998, 2199, 2126, 1667, 1489, 1443, 1416, 1357, 1278, 1180, 1154, 1070, 1024, 975, 921, 855, 756, 687 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.54-7.60 (2H, m, Ar), 7.30-7.49 (3H, m, Ar), 2.45 (3H, s, CH_3); δ_C (100 MHz, CDCl$_3$) 163.2, 133.0, 130.7, 128.6, 120.0, 90.3, 88.2, 32.7; m/z (ESMS+) 145 [M + H]$^+$.

(*R*)-4-Phenyl-3-butyn-2-ol, (***R***)-**127**.
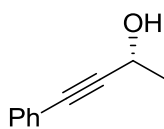
This compound is known and has been fully characterised.[128, 132] A solution of KOH (19.0 mg, 0.339 mmol) in dry 2-propanol (20 cm^3) was added to a solution of **86** (43.0 mg, 69.3 μmol) in dry 2-propanol (100 cm^3) and left to stir for 30 mins at 28 °C. Compound **139** (2.00 g, 13.9 mmol) in dry 2-propanol (20 cm^3) was added and the solution was left to stir for 18 h at 28 °C after which the mixture was filtered through silica which was washed with EtOAc. The solvent was removed under reduced pressure to give a brown oil. The product was purified by kugelrohr distillation (1 mbar, 100 °C) to furnish the product as a colourless oil (1.879 g, 12.9 mmol, 93 %). [α]$_D^{28}$ +28.2 (c 1.0 in CHCl$_3$) 96 % e.e. (*R*) (lit.[128] [α]$_D^{23}$ -35.0 (c 1.0 in CHCl$_3$) 97% ee (*S*); (Found (ESI): M$^+$ + H 147.0812, C$_{10}$H$_{11}$O requires 147.0804); ν_{max} 3318, 2980, 2931, 1595, 1489, 1443, 1369, 1328, 1278, 1255, 1103, 1071, 1035, 1024, 931, 851, 754, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.39-7.45

(2H, m, Ar), 7.27-7.33 (3H, m, Ar), 4.73-4.80 (1H, m, CH(OH)CH$_3$), 2.26 (1H, broad s, OH), 1.56 (3H, d, J 6.8, CH_3); δ_C (75 MHz, CDCl$_3$) 131.6, 128.4, 128.3, 122.5, 90.9, 84.0, 58.8, 24.4; m/z (ESMS+) 147 [M + H]$^+$. The e.e. was determined using chiral GC of the acetyl derivative of the alcohol synthesised by reacting a sample of the alcohol (<10 mg) with acetic anhydride (<0.5 cm^3) and DMAP (<1 mg) in DCM (ca. 1 cm^3) for 30 mins; (Chrompac cyclodextrin-β-236M 50M column, T = 115 °C, inj T = 220 °C, det T = 220 °C, 15 psi H$_2$ carrier gas). R$_T$: 51.3 (*S*), 52.4 (*R*) min.

(*R*)-4-Phenyl-3-butyn-2-yloxy(3-(*o*-tolyl)prop-2-yne), **(*R*)-142**.
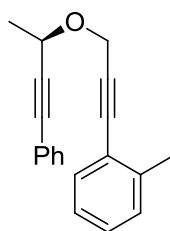
This compound is novel. Compound **(*R*)-142** was made by the same procedure as for **130c** using **(*R*)-129** (0.300 g, 1.63 mmol, 97 % e.e.), 2-iodotoluene (0.52 cm^3, 4.09 mmol), PdCl$_2$(PPh$_3$)$_2$ (23.0 mg, 32.8 μmol) and CuI (16.0 mg, 84.0 μmol). Purification by column chromatography on silica with a gradient elution from 0-5 % EtOAc in pet. ether gave the product as a yellow oil (0.388 g, 1.41 mmol, 87 %). [α]$_D^{29}$ +272.0 (c 0.5 in CHCl$_3$) (*R*); (Found (ESI): M$^+$ + H 275.1435, C$_{20}$H$_{19}$O requires 275.1430); ν_{max} 2984, 2934, 2850, 2222, 1487, 1442, 1357, 1329, 1252, 1092, 1061, 1028, 915, 826, 753, 690 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.42-7.48 (3H, m, Ar), 7.30-7.34 (3H, m, Ar), 7.19-7.24 (2H, m, Ar), 7.11-7.16 (1H, m, Ar), 4.76 (1H, q, J 6.5, CH(OR)), 4.67 (1H, d, J 15.6 CHH), 4.61 (1H, d, J 15.6, CHH), 2.46 (3H, s, ArCH_3), 1.60 (3H, d, J 6.5, CH_3); δ_C (100 MHz, CDCl$_3$) 140.4, 132.2,

131.8, 129.4, 128.43, 128.40, 128.3, 125.5, 122.6, 122.4, 88.7, 88.2, 85.5, 85.2, 64.4, 56.7, 22.1, 20.7; m/z (ESMS+) 297 [M + Na]$^+$.

(*R*)-Tricarbonyl(2-(phenyl)-4-(*o*-tolyl)-6-methyl-7-oxy-bicyclo[3.3.0]hepta-1,4-dien-3-one)iron, (*R*)-141.
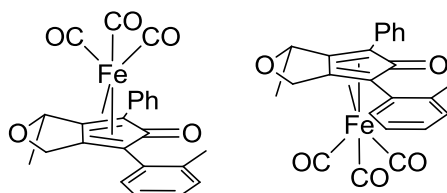
These complexes (two diastereoisomers) are novel. Complexes (*R*)-141a and (*R*)-141b were synthesised by the same procedure as for 130 using (*R*)-142 (0.221 g, 0.806 mmol) and Fe(CO)$_5$ (0.32 cm^3, 2.43 mmol). Purification by column chromatography on silica with a gradient elution from 0-40 % EtOAc in pet. ether gave two separated diastereoisomers. (*R*)-141b, yellow oil (31.0 mg, 70.1 μmol, 9 %). [α]$_D^{26}$ -106.0 (c 0.05 in CHCl$_3$) (*R*); (Found (ESI): M$^+$ + H 443.0574, C$_{24}$H$_{19}$FeO$_5$ requires 443.0577); ν$_{max}$ 3059, 2973, 2927, 2863, 2064, 1995, 1718, 1646, 1498, 1445, 1379, 1114, 1055, 832, 765, 696 cm^{-1}; δ$_H$ (400 MHz, CDCl$_3$) 8.03-8.08 (2H, m, Ar), 7.28-7.42 (5H, m, Ar), 7.20-7.24 (2H, m, Ar), 5.67 (1H, q, *J* 6.5, C*H*), 4.96 (1H, d, *J* 13.1, C*H*H), 4.69 (1H, d, *J* 13.1, CH*H*), 2.42 (3H, s, ArC*H*$_3$), 1.60 (3H, d, *J* 6.5, C*H*$_3$); δ$_C$ (100 MHz, CDCl$_3$) 207.9, 171.5, 138.0, 132.3, 131.6, 130.8, 129.0, 128.9, 128.4, 127.0, 126.2, 104.4, 102.5, 82.7, 76.1, 74.1, 20.9, 18.9; m/z (ESMS+) 443 [M + H]$^+$. (*R*)-141a, yellow oil (39.0 mg, 88.2 μmol, 11 %). [α]$_D^{26}$ +39.0 (c 0.05 in CHCl$_3$) (*R*); (Found (ESI): M$^+$ + H 443.0576, C$_{24}$H$_{19}$FeO$_5$ requires 443.0577); ν$_{max}$ 3057, 2974, 2927, 2864, 2063, 1994, 1718, 1647, 1500, 1450, 1378, 1341, 1116, 1053, 980, 840, 758, 742, 695 cm^{-1}; δ$_H$ (400 MHz, CDCl$_3$) 7.55-7.59 (2H, m, Ar), 7.28-7.43 (5H, m, Ar), 7.19-7.24 (1H, m, Ar), 7.14-7.18

(1H, m, Ar), 5.44 (1H, q, J 6.5, CH), 4.72 (1H, d, J 13.1, CH_2), 4.67 (1H, d, J 13.1, CH_2), 2.33 (3H, s, ArCH_3), 1.72 (3H, d, J 6.5, CH_3); δ_C (100 MHz, CDCl$_3$) 207.9, 170.1, 138.2, 134.7, 132.6, 130.4, 129.6, 129.0, 128.9, 128.7, 128.5, 126.2, 109.7, 102.7, 83.0, 77.7, 75.5, 66.4, 22.1, 20.5; m/z (ESMS+) 443 [M + H]$^+$.

3-Butynyl p-toluenesulphonate.
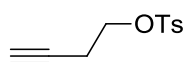
This compound is known and has been fully characterised.[228] 3-Butyn-1-ol (0.800 g, 11.4 mmol) was dissolved in dry pyridine (30 cm^3) and cooled to -20 °C. Tosyl chloride (5.440 g, 28.5 mmol) was added portionwise and the mixture was allowed to warm to room temperature. After 4 h the reaction was quenched with 1 M HCl solution, extracted into Et$_2$O (3 x 30 cm^3), washed with saturated NaHCO$_3$ solution (90 cm^3), CuSO$_4$ solution (90 cm^3) and brine (90 cm^3). The organic layer was dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure to give the product as a yellow oil (1.690 g, 7.55 mmol, 66 %). δ_H (300 MHz, CDCl$_3$) 7.77-7.83 (2H, m, Ar), 7.32-7.38 (2H, m, Ar), 4.10 (2H, t, J 7.2, CH_2OTs), 2.55 (2H, dt, J 2.6 7.2, CH_2CCH), 2.44 (3H, s, CH_3), 1.96 (1H, t, J 2.6, CH); δ_C (75 MHz, CDCl$_3$) 145.0, 132.7, 129.9, 127.9, 78.3, 70.7, 67.4, 21.6, 19.4.

o-Hydroxytolane, **145**.
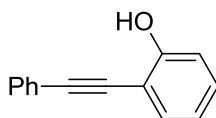
This compound is known but has not been fully characterised.[229] Phenylacetylene (1.00 g, 9.79 mmol) and 2-iodophenol (1.943, 8.83 mmol) in dry THF (5 cm^3) was added to a solution of PdCl$_2$(PPh$_3$)$_2$ (62.0 mg, 88.3 μmol) and CuI (34.0 mg, 0.179

mmol) in dry THF (5 cm^3). 33 % Aqueous NH$_3$ (1.03 cm^3, 17.6 mmol) was added and the mixture was left to stir. After 68 h H$_2$O (10 cm^3) was added and the organic layer was separated. The aqueous layer was further extracted with Et$_2$O (2 x 10 cm^3) and the combined organic extracts were dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. Column chromatography on silica with a gradient elution from 0-4 % EtOAc in pet. ether gave the desired product as an orange solid (1.531 g, 7.88 mmol, 89 %). (Found (ESI): M$^+$ + H 195.0804, C$_{14}$H$_{11}$O requires 195.0804); ν_{max} 3513, 3488, 3059, 1571, 1493, 1478, 1461, 1443, 1344, 1288, 1238, 1194, 1139, 1070, 1027, 945, 915, 860, 800, 752, 688 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.53-7.57 (2H, m, Ar), 7.41-7.45 (1H, m, Ar), 7.35-7.40 (3H, m, Ar), 7.24-7.31 (1H, m, Ar), 6.97-7.02 (1H, m, Ar), 6.89-6.95 (1H, m, Ar), 5.86 (1H, s, OH); δ_C (100 MHz, CDCl$_3$) 156.5, 131.6, 131.5, 130.5, 128.8, 128.5, 122.3, 120.4, 114.7, 109.6, 96.4, 83.0; m/z (ESMS+) 217 [M + Na]$^+$.

(S)-4-Phenyl-3-butyn-2-yloxy(o-tolane), **(S)-146**.
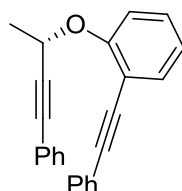
This compound is novel. Compound **145** (0.400 g, 2.06 mmol), (R)-4-phenyl-3-butyn-2-ol (0.301 g, 2.06 mmol, 97 % e.e.) and PPh$_3$ (0.540 g, 2.06 mmol) were dissolved in dry THF (15 cm^3) and cooled to 0 °C. DEAD (0.50 cm^3, 3.18 mmol) was added dropwise and the solution was allowed to warm to room temperature. After 47 h the solvent was removed under reduced pressure and the product was purified by column chromatography on silica with a gradient elution from 0-5 % EtOAc in pet. ether to give a yellow oil (0.565 g, 1.75 mmol, 88 %). [α]$_D^{26}$ +138.5

(c 0.1 in CHCl$_3$) (*S*); (Found (ESI): M$^+$ + Na 345.1247, C$_{24}$H$_{18}$NaO requires 345.1250); ν_{max} 3059, 2986, 2933, 1733, 1593, 1572, 1329, 1276, 1232, 1163, 1084, 1035, 1024, 943, 748, 688 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.51-7.60 (3H, m, Ar), 7.38-7.44 (3H, m, Ar), 7.27-7.37 (6H, m, Ar), 6.99-7.04 (1H, m, Ar), 5.20 (1H, q, *J* 6.5, C*H*) 1.85 (3H, d, *J* 6.5, C*H$_3$*); δ_C (100 MHz, CDCl$_3$) 158.3, 133.3, 131.7, 131.6, 129.4, 128.4, 128.3, 128.2, 128.1, 123.7, 122.4, 121.7, 115.8, 114.3, 93.6, 88.2, 86.2, 85.8, 66.1, 22.5; *m/z* (ESMS+) 345 [M + Na]$^+$.

(*S*)-Tricarbonyl(2,4-diphenyl)-6-methyl-7-oxy-8-(*o*-benzene)bicyclo[3.3.0]octa-1,4-dien-3-one)iron, (*S*)-**147**.
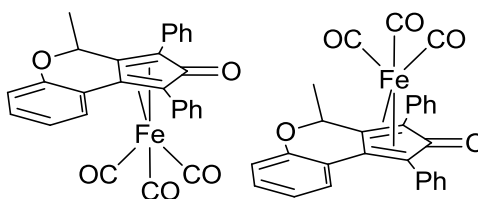
These complexes (two diastereoisomers) are novel. Complexes (*S*)-**147** were synthesised by the same procedure as for **130** using (*S*)-**146** (0.350 g, 1.09 mmol) and Fe(CO)$_5$ (0.43 cm^3, 3.27 mmol). Purification by column chromatography on silica with a gradient elution from 0-20 % EtOAc in pet. ether gave two diastereoisomers which were isolated as a mixture (90.0 mg, 0.184 mmol, 17 %) in a ratio of 0.8:1. (Found (ESI): M$^+$ + H 491.0576, C$_{28}$H$_{19}$FeO$_5$ requires 491.0577); ν_{max} 3058, 2975, 2867, 2062, 1993, 1944, 1648, 1607, 1443, 1228, 1113, 810, 696 cm^{-1}; *m/z* (ESMS+) 491 [M + H]$^+$. Due to signal overlaps assignment of the NMR spectra was not possible but signals attributable to CH protons can be seen at 5.60 and 5.36 ppm and signals attributable to CH$_3$ groups can be seen at 1.54 and 1.47 ppm.

(*R*)-4-Phenyl-3-butyn-2-yloxy(2-iodobenzoate), (***R***)-150.
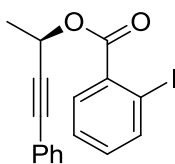
This compound is known and fully characterised.[193] 2-Iodobenzoylchloride (0.674 g, 2.53 mmol) was added to a solution of (***R***)-127 (0.370 g, 2.53 mmol, 95 % e.e.) in dry DCM (5 cm^3) and cooled to 0 °C. Triethylamine (0.46 cm^3, 3.30 mmol) was added and the mixture was left to stir for 19 h. DCM (5 cm^3) and H$_2$O (10 cm^3) were added and the organic layer was separated. The aqueous layer was extracted with DCM (2 x 10 cm^3) and the combined organic extracts were dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure to give a pale yellow oil. Purification by column chromatography on silica with a gradient elution from pet. ether to 95:5 pet. ether: EtOAc gave the produce as a colourless oil (0.795 g, 2.11 mmol, 84 %). $[\alpha]_D^{28}$ +66.3 (c 0.6 in CHCl$_3$) (*R*); (Found (ESI): M$^+$ + Na 398.9855, C$_{17}$H$_{13}$INaO$_2$ requires 398.9852); ν_{max} 2987, 2934, 2228, 1727, 1582, 1489, 1464, 1442, 1429, 1340, 1312, 1280, 1239, 1082, 1013, 919, 847, 738, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.98-8.03 (1H, m, Ar), 7.84-7.89 (1H, m, Ar), 7.44-7.50 (2H, m, Ar), 7.28-7.35 (3H, m, Ar), 7.13-7.20 (1H, m, Ar), 5.95 (1H, q, *J* 6.8, C*H*), 1.74 (3H, d, *J* 6.8 C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 165.4, 141.3, 134.8, 132.7, 131.9, 131.1, 128.6, 128.2, 127.9, 122.2, 94.1, 87.0, 85.1, 62.3, 21.5; *m/z* (ESMS+) 399 [M + Na]$^+$.

(*R*)-4-Phenyl-3-butyn-2-yloxy(2-(ethynylbenzene)benzoate), (***R***)-151.
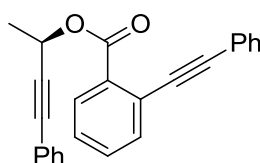
This compound is known and fully characterised.[193] **(R)-150** (0.676 g, 1.80 mmol, 95 % e.e.) and phenylacetylene (0.20 cm^3, 1.82 mmol) in NEt$_3$ (5 cm^3) were added to a solution of PdCl$_2$(PPh$_3$)$_2$ (38.0 mg, 54.1 μmol) and CuI (34.0 mg, 0.179 mmol) in NEt$_3$ (5 cm^3) and heated at 60 °C for 24 h after which the solvent was removed under reduced pressure. The residue was dissolved in DCM (20 cm^3) and washed with a saturated NH$_4$Cl solution (20 cm^3). The aqueous phase was further extracted with DCM (2 x 20 cm^3) and the combined organic extracts were dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica with a gradient elution from 0-20 % EtOAc in pet. ether to give an orange oil (0.614 g, 1.75 mmol, 98 %). $[\alpha]_D^{28}$ +63.3 (c 0.5 in CHCl$_3$) (R); (Found (ESI): M$^+$ + Na 373.1198, C$_{25}$H$_{18}$NaO$_2$ requires 373.1199); ν_{max} 3058, 2987, 2217, 1711, 1597, 1491, 1442, 1280, 1239, 1126, 1083, 1064, 1021, 918, 752, 688 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 8.02-8.05 (1H, m, Ar), 7.65-7.68 (1H, m, Ar), 7.60-7.64 (2H, m, Ar), 7.48-7.53 (1H, m, Ar), 7.39-7.43 (3H, m, Ar), 7.27-7.33 (6H, m, Ar), 6.01 (1H, q, *J* 7.0, C*H*), 1.73 (3H, d, *J* 7.0 C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 165.3, 134.1, 131.9, 131.8, 131.7, 131.6, 130.7, 128.5, 128.4, 128.3, 128.2, 127.9, 123.8, 123.3, 122.3, 94.5, 88.1, 87.5, 84.9, 61.7, 21.7; *m/z* (ESMS+) 373 [M + Na]$^+$.

(R)-4-Phenyl-3-butyn-2-yloxy(3-(2-bromobenzene)prop-2-yne), **(R)-152**.
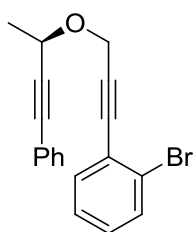
This compound is novel. Compound **(R)-152** was made by the same procedure as for **130c** using **(R)-129** (0.500 g, 2.71 mmol, 97 % e.e.), 2-bromo-iodobenzene

(0.87 cm^3, 6.77 mmol), PdCl$_2$(PPh$_3$)$_2$ (38.0 mg, 54.1 μmol) and CuI (26.0 mg, 0.137 mmol). Purification by column chromatography on silica with a gradient elution from 0-10 % EtOAc in pet. ether gave the product as a yellow oil (0.847 g, 2.50 mmol, 92 %). [α]$_D$^{26} +233.2 (c 0.5 in CHCl$_3$) (R); (Found (ESI): M$^+$ + Na 361.0194, C$_{19}$H$_{15}$^{79}BrNaO requires 361.0198); ν$_{max}$ 2984, 2934, 2849, 2222, 1719, 1597, 1489, 1468, 1434, 1329, 1256, 1091, 1063, 1026, 915, 825, 757, 689, 656 cm^{-1}; δ$_H$ (300 MHz, CDCl$_3$) 7.56-7.61 (1H, m, Ar), 7.44-7.52 (3H, m, Ar), 7.28-7.35 (4H, m, Ar), 7.14-7.21 (1H, m, Ar), 4.82 (1H, q, J 6.8, CH), 4.64 (2H, s, CH$_2$), 1.60 (3H, d, J 6.8, CH$_3$); δ$_C$ (75 MHz, CDCl$_3$) 133.5, 132.4, 131.8, 129.6, 128.4, 128.2, 126.9, 125.5, 124.8, 122.5, 89.7, 88.1, 85.6, 84.8, 64.6, 56.5, 22.1; m/z (ESMS+) 361 [M + Na]$^+$.

(R)-4-Phenyl-3-butyn-2-yloxy(3-(o-aniline)prop-2-yne), **(R)-153**.
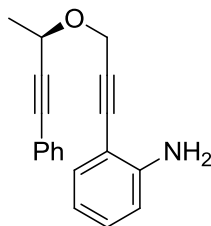
This compound is novel. **(R)-153** (0.600 g, 3.26 mmol) and 2-Iodoaniline (0.713 g, 3.26 mmol) were dissolved in NEt$_3$ (10 cm^3) and added to a solution of PdCl$_2$(PPh$_3$)$_2$ (46.0 mg, 65.5 μmol) and CuI (31.0 mg, 0.163 mmol) in NEt$_3$ (10 cm^3). The solution was heated at 60 °C for 5 h after which the solvent was removed under reduced pressure. Purification by column chromatography on silica with a gradient elution from 0-40 % EtOAc in pet. ether gave a yellow oil (0.462 g, 1.68 mmol, 52 %). [α]$_D$^{26} +301.5 (c 0.1 in CHCl$_3$) (R); (Found (ESI): M$^+$ + Na 298.1200, C$_{19}$H$_{17}$NNaO requires 298.1202); ν$_{max}$ 3465, 3374, 3054, 2985, 2934, 2851, 1614, 1490, 1456, 1442, 1371, 1329, 1313, 1248, 1158, 1091, 1057, 1027, 915, 822, 747, 689 cm^{-1}; δ$_H$ (400 MHz, CDCl$_3$) 7.44-7.48 (2H, m, Ar), 7.29-7.34 (4H, m, Ar),

7.10-7.15 (1H, m, Ar), 6.65-6.71 (2H, m, Ar), 4.72 (1H, q, *J* 6.5, C*H*), 4.67 (1H, d, *J* 15.6, C*H*H), 4.61 (1H, d, *J* 15.6, CH*H*), 4.22 (2H, broad s, N*H₂*), 1.59 (3H, d, *J* 6.5, C*H₃*); δ_C (75 MHz, CDCl₃) 148.1, 132.5, 131.7, 129.9, 128.4, 128.2, 122.4, 117.7, 114.2, 107.1, 90.2, 88.2, 85.6, 83.0, 64.5, 56.7, 22.1; *m/z* (ESMS+) 298 [M + Na]⁺.

N-tert-Butoxycarbonyl-1,7-bis-phenyl-dipropargylamine, **154**.
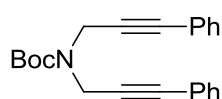
This compound is novel. Compound **154** was made by the same procedure as for **130c** using **121** (0.700 g, 3.62 mmol), iodobenzene (1.22 cm³, 10.9 mmol), PdCl₂(PPh₃)₂ (0.102 g, 0.145 mmol) and CuI (69.0 mg, 0.362 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-10 % EtOAc in pet. ether to give a pale yellow oil (1.213 g, 3.51 mmol, 97 %). (Found (ESI): M⁺ + H 368.1614, C₂₃H₃₃NNaO₂ requires 368.1621); ν_{max} 2976, 2929, 1697, 1490, 1442, 1401, 1365, 1338, 1241, 1158, 1117, 1070, 1028, 969, 914, 864, 753, 689 cm⁻¹; δ_H (300 MHz, CDCl₃) 7.40-7.46 (4H, m, Ar), 7.27-7.33 (6H, m, Ar), 4.45 (4H, broad s, C*H₂*), 1.53 (9H, s, C*H₃*); δ_C (75 MHz, CDCl₃) 154.5, 131.7, 128.24, 128.22, 122.8, 84.5, 80.9, 72.2, 36.1, 28.4; *m/z* (ESMS+) 368 [M + Na]⁺.

1,7-Bis-phenyl-dipropargylamine, **155**.
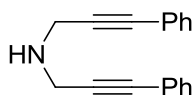
This compound is novel. Compound **154** (2.975 g, 8.61 mmol) was dissolved in DCM (10 cm³) and TFA (6.60 cm³, 86.2 mmol) was added. After 1 h the reaction was quenched with a saturated K₂CO₃ solution (20 cm³) and the product was

extracted into DCM (3 x 20 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo* to give an orange oil (2.097 g, 8.55 mmol, 99 %). (Found (ESI): M$^+$ + H 246.1275, C$_{18}$H$_{16}$N requires 246.1277); ν_{max} 3055, 2915, 2821, 1675, 1597, 1489, 1441, 1353, 1324, 1255, 1100, 1070, 1027, 951, 914, 752, 688 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.41-7.48 (4H, m, Ar), 7.27-7.34 (6H, m, Ar), 3.82 (4H, s, C*H$_2$*), 1.70 (1H, s, N*H*); δ_C (75 MHz, CDCl$_3$) 131.6, 128.2, 128.1, 123.0, 86.7, 83.8, 37.9; *m/z* (ESMS+) 246 [M + H]$^+$.

N,N-Bis(3-phenyl-2-propyne)-α-aminoacetophenone, **156**.
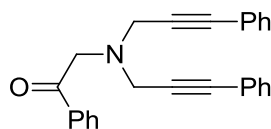
This compound is novel. Compound **155** (0.202 g, 0.823 mmol), α-bromoacetophenone (0.164 g, 0.824 mmol) and K$_2$CO$_3$ (0.171 g, 1.24 mmol) were dissolved in dry MeCN (5 cm^3) and left to stir for 24 h. The solvent was removed under reduced pressure and the residue was dissolved in CHCl$_3$ (10 cm^3), washed with H$_2$O (10 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. The product was purified by column chromatography on silica with a gradient elution from 0-20 % EtOAc in pet. ether to give an orange oil (0.292 g, 0.803 mmol, 98 %). (Found (ESI): M$^+$ + H 364.1694, C$_{26}$H$_{22}$NO requires 364.1696); ν_{max} 3061, 1680, 1597, 1489, 1442, 1315, 1277, 1216, 1176, 1104, 1070, 957, 845, 752, 687 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.04-8.11 (2H, m, Ar), 7.54-7.61 (1H, m, Ar), 7.40-7.50 (6H, m, Ar), 7.27-7.35 (6H, m, Ar), 4.24 (2H, s, C(O)C*H$_2$*), 3.90 (4H, s, NC*H$_2$*); δ_C (75 MHz, CDCl$_3$) 196.4, 135.9, 133.3, 131.7, 128.6, 128.23, 128.21, 128.19, 122.9, 85.8, 84.2, 58.3, 44.1; *m/z* (ESMS+) 364 [M + H]$^+$.

(*S*)-*N*,*N*-Bis(3-phenyl-2-propyne)-2-amino-1-phenylethanol, (*S*)-**157**.
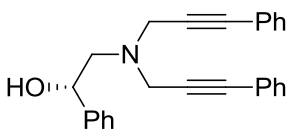
This compound is novel. Complex **86** (5.0 mg, 8.10 μmol) was dissolved in 5:2 FA/TEA (1.5 cm^3) and heated at 28 °C for 30 mins. A solution of **156** (0.553 g, 1.52 mmol) in dry EtOAc (1.5 cm^3) was added and the mixture was left to stir at 28 °C for 4 h. The reaction was quenched with a saturated K$_2$CO$_3$ solution (5 cm^3), the product was extracted into EtOAc (3 x 5 cm^3) and the solvent was removed *in vacuo*. Column chromatography on silica with a gradient elution from 0-20 % EtOAc in pet. ether gave the product as a pale yellow oil (0.505 g, 1.38 mmol, 91 %) with an e.e. of 97 % (*S*). $[\alpha]_D^{25}$ +60.0 (c 0.05 in CHCl$_3$) 96 % e.e. (*S*); (Found (ESI): M$^+$ + H 366.1849, C$_{26}$H$_{24}$NO requires 366.1852); ν_{max} 3060, 2822, 1711, 1598, 1489, 1442, 1252, 1198, 1113, 1062, 1027, 984, 914, 892, 856, 753, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.44-7.50 (6H, m, Ar), 7.36-7.42 (2H, m, Ar), 7.29-7.36 (7H, m, Ar), 4.87 (1H, dd, *J* 3.4 10.6, C*H*), 3.87 (4H, s, NC*H*$_2$), 3.04 (1H, dd, *J* 3.4 12.8, CH(OH)C*H*H), 2.77 (1H, dd, *J* 10.6 12.8, CH(OH)CH*H*); δ_C (75 MHz, CDCl$_3$) 141.8, 131.7, 128.4, 128.24, 128.22, 127.6, 125.9, 122.8, 85.4, 84.2, 69.8, 61.3, 43.6; *m/z* (ESMS+) 366 [M + H]$^+$. The e.e. was determined by chiral HPLC (Chiralpak IB, 30 cm x 6 mm column, hexane:2-propanol 90:10, 0.5 cm^3/min, T = 25 °C, R$_T$: 15.6 (*R*), 18.0 (*S*) min). A racemic standard was prepared via the sodium borohydride reduction of **156**.

N,*N*-Bis(3-phenyl-2-propyne)-*N*'-*tert*-butoxycarbonyl-D-alanine amide, (***R***)-**158**.
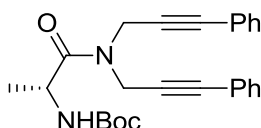
This compound is novel. N-Boc-D-alanine (0.386 g, 2.04 mmol), DCC (0.841 g, 4.08 mmol) and DMAP (25.0 mg, 0.205 mmol) were dissolved in dry DCM (10 cm^3) and cooled to 0 °C. A solution of **155** in dry DCM (5 cm^3) was added. After 18 h the reaction mixture was filtered, washed with brine, dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Column chromatography on silica with a gradient elution from 0-30 % EtOAc in pet. ether gave the product as a pale yellow oil (0.690 g, 1.66 mmol, 81 %). $[\alpha]_D^{25}$ +55.0 (c 0.05 in CHCl$_3$), (*R*); (Found (ESI): M$^+$ + H 439.2016, C$_{28}$H$_{27}$N$_2$O$_3$ requires 439.2016); ν_{max} 3318, 2978, 2933, 1701, 1651, 1490, 1443, 1366, 1249, 1220, 1164, 1065, 1020, 971, 756, 691 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.38-7.45 (4H, m, Ar), 7.25-7.33 (6H, m, Ar), 5.48 (1H, d, *J* 8.3, N*H*), 4.75-4.86 (1H, m, C*H*), 4.62-4.75 (2H, m, C*H*H), 4.44-4.57 (2H, m, CH*H*), 1.41-1.46 (12H, m, C*H*$_3$); δ_C (75 MHz, CDCl$_3$) 172.5, 155.0, 131.8, 131.7, 128.6, 128.4, 128.3, 128.2, 122.4, 122.0, 85.0, 84.4, 83.3, 82.9, 46.6, 37.1, 35.3, 28.3, 19.2; *m/z* (ESMS+) 418 [M + H]$^+$.

N,N-Bis(3-phenyl-2-propyne)-D-alanine amide, (***R***)-**159**.
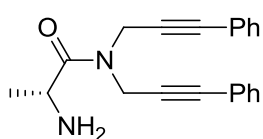
This compound is novel. Compound (***R***)-**159** was made by the same procedure as for **155** using (***R***)-**158** (0.165 g, 0.396 mmol) and TFA (0.30 cm^3, 3.92 mmol). The product was isolated as a pale yellow oil (0.117 g, 0.370 mmol, 94 %). $[\alpha]_D^{24}$ +1.4 (c 0.5 in CHCl$_3$), (*R*); (Found (ESI): M$^+$ + H 317.1653, C$_{21}$H$_{21}$N$_2$O requires 317.1648); ν_{max} 3303, 3053, 2927, 1706, 1648, 1489, 1442, 1348, 1264, 1209, 1170, 1069, 1025, 970, 915, 755, 734, 690 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.36-7.45 (4H, m, Ar), 7.23-7.33 (6H, m, Ar), 4.43-4.73 (4H, m, C*H*$_2$), 3.93 (1H, q, J 6.8,

C*H*), 1.76 (2H, broad s, N*H₂*), 1.36 (3H, d, J 6.8, C*H₃*); δ$_C$ (75 MHz, CDCl₃) 175.8, 131.7, 131.6, 128.6, 128.3, 128.2, 128.1, 122.4, 121.9, 84.7, 84.1, 83.6, 83.1, 52.0, 51.1, 48.9, 47.3, 36.6, 35.2, 33.9, 29.2, 25.7, 24.9, 21.4, 17.6; *m/z* (ESMS+) 317 [M + H]⁺.

1,7-Bis(trimethylsilyl)-dipropargylamine, **160**.
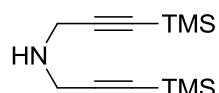
This compound is novel. TFA (1.94 cm³, 25.3 mmol) was added dropwise to a solution of **125** (0.854 g, 2.53 mmol) in DCM (15 cm³). When tlc showed complete consumption of the starting material (5 h) the reaction was quenched with a saturated K₂CO₃ solution (20 cm³), extracted into DCM (3 x 20 cm³), dried over MgSO₄, filtered and the solvent was removed *in vacuo* to give a brown oil (0.583 g, 2.45 mmol, 97 %). (Found (ESI): M⁺ + H 238.1439, C₁₂H₂₄NSi₂ requires 238.1442); ν$_{max}$ 2959, 2900, 1672, 1423, 1348, 1324, 1249, 1110, 989, 835, 757, 698, 657 cm⁻¹; δ$_H$ (300 MHz, CDCl₃) 3.49 (4H, s, C*H₂*), 1.61 (1H, broad s, N*H*), 0.15 (18H, s, Si(C*H₃*)₃); δ$_C$ (75 MHz, CDCl₃) 103.4, 88.3, 38.1, -0.1; *m/z* (ESMS+) 238 [M + H]⁺.

N,N-Bis(3-trimethylsilyl-2-propyne)-α-aminoacetophenone, **161**.
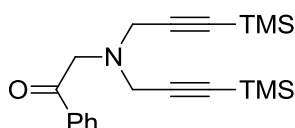
This compound is novel. Compound **161** was made by the same procedure as for **156** using **160** (0.500 g, 2.11 mmol), α-bromoacetophenone (0.419 g, 2.11 mmol) and K₂CO₃ (0.437 g, 3.16 mmol). Column chromatography on silica with a gradient

elution from 0-25 % EtOAc in pet. ether gave the product as a yellow oil (0.322 g, 0.906 mmol, 43 %). (Found (ESI): $M^+ + H$ 356.1859, $C_{20}H_{30}NOSi_2$ requires 356.1860); ν_{max} 2960, 1682, 1599, 1449, 1315, 1249, 1174, 1112, 1026, 986, 837, 757, 689 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.00-8.05 (2H, m, Ar), 7.53-7.60 (1H, m, Ar), 7.42-7.49 (2H, m, Ar), 4.06 (2H, s, COCH_2), 3.56 (4H, s, NCH_2C), 0.15 (18H, s, Si(CH_3)$_3$); δ_C (75 MHz, CDCl$_3$) 136.0, 133.3, 128.5, 128.2, 100.6, 90.7, 57.8, 44.1, -0.1; m/z (ESMS+) 356 [M + H]$^+$.

N-tert-Butoxycarbonyl-1,7-bis(*tert*-butyldimethylsilyl)dipropargylamine, **162**.
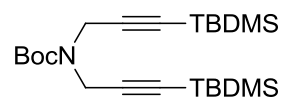
This compound is novel. Compound **162** was made by the same procedure as for **122** using **121** (1.495 g, 7.74 mmol), 1.6 M *N*-butyllithium in hexanes (10.2 cm^3, 16.3 mmol) and *tert*-butyldimethylsilyl chloride (2.565 g, 17.0 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-16 % EtOAc in pet. ether to give a yellow oil (2.394 g, 5.68 mmol, 73 %). (Found (ESI): $M^+ + Na$ 444.2726, $C_{23}H_{43}NaO_2Si_2$ requires 444.2725); ν_{max} 2953, 2928, 2857, 2176, 1706, 1461, 1391, 1366, 1248, 1161, 1006, 939, 824, 774, 681 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 4.17 (4H, broad s, CH_2), 1.46 (9H, s, CO$_2$C(CH_3)$_3$), 0.92 (18H, s, SiC(CH_3)$_3$), 0.09 (12H, s, Si(CH_3)$_2$); δ_C (75 MHz, CDCl$_3$) 154.4, 101.3, 80.8, 35.8, 28.3, 26.0, 16.5, -4.7; m/z (ESMS+) 444 [M + Na]$^+$.

1,7-Bis(*tert*-butyldimethylsilyl)dipropargylamine, **163**.
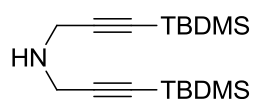
This compound is novel. Compound **163** was made by the same procedure as for **155** using **162** (2.394 g, 5.68 mmol) and TFA (4.35 cm^3, 56.8 mmol). The product was isolated as an orange oil (1.826 g, 5.68 mmol, 100 %). (Found (ESI): M$^+$ + H 322.2381, C$_{18}$H$_{36}$NSi$_2$ requires 322.2381); ν_{max} 2952, 2928, 2884, 2856, 2162, 1686, 1471, 1462, 1409, 1389, 1361, 1324, 1249, 1107, 1030, 988, 939, 824, 773, 681 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 3.54 (4H, s, CH_2), 1.51 (1H, broad s, NH), 0.93 (18H, s, SiC(CH_3)$_3$), 0.09 (12H, s, Si(CH_3)$_2$); δ_C (75 MHz, CDCl$_3$) 103.9, 86.6, 37.9, 26.0, 16.4, -4.6; m/z (ESMS+) 322 [M + H]$^+$.

N,N-Bis(3-(*tert*-butyldimethylsilyl)-2-propyne)-α-aminoacetophenone, **164**.
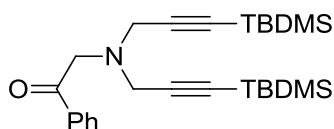
This compound is novel. Compound **164** was made by the same procedure as for **156** using **163** (1.826 g, 5.68 mmol), α-bromoacetophenone (1.130 g, 5.68 mmol) and K$_2$CO$_3$ (1.177 g, 8.52 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-16 % EtOAc in pet. ether to give an orange oil (1.836 g, 4.17 mmol, 74 %). (Found (ESI): M$^+$ + H 440.2799, C$_{26}$H$_{42}$NOSi$_2$ requires 440.2799); ν_{max} 2952, 2928, 2885, 2856, 2367, 2176, 1686, 1471, 1449, 1462, 1389, 1361, 1249, 1175, 1110, 1006, 938, 824, 774, 734, 711, 684 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.00-8.05 (2H, m, Ar), 7.54-7.60 (1H, m, Ar), 7.42-7.49 (2H, m, Ar), 4.07 (2H, s, C(O)CH_2), 3.59 (4H, s, NCH_2), 0.92 (18H, s, SiC(CH_3)$_3$), 0.09 (12H, s, Si(CH_3)$_2$); δ_C (75 MHz, CDCl$_3$) 135.9, 133.3, 128.5, 128.2, 101.1, 88.9, 58.1, 44.0, 26.1, 16.5, -4.6; m/z (ESMS+) 440 [M + H]$^+$.

(*S*)-*N*,*N*-Bis(3-(*tert*-butyldimethylsilyl)-2-propyne)-2-amino-1-phenylethanol, **(*S*)-165**.
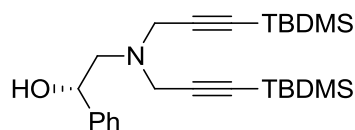
This compound is novel. Compound **(*S*)-165** was made by the same procedure as for **(*S*)-157** using **164** (0.719 g, 1.64 mmol) and **86** (5.0 mg, 8.10 μmol) with 5:2 FA/TEA (1.63 cm^3) and dry EtOAC (1.63 cm^3). The product was purified by column chromatography on silica with a gradient elution from 0-16 % EtOAc in pet. ether to give an orange oil (0.457 g, 1.03 mmol, 63 %). The e.e. for this compound could not be determined but could be indirectly assigned as 90 % based on **(*S*)-166**. $[\alpha]_D^{26}$ +55.6 (c 0.5 in CHCl$_3$) (*S*); (Found (ESI): M$^+$ + H 442.2956, C$_{26}$H$_{44}$NOSi$_2$ requires 442.2956); ν_{max} 2951, 2927, 2884, 2856, 2164, 1671, 1470, 1462, 1408, 1389, 1361, 1249, 1199, 1113, 1028, 1007, 985, 939, 824, 809, 774, 698, 683 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.28-7.40 (5H, m, Ar), 4.73 (1H, dd, *J* 3.4 10.6, C*H*), 3.56 (4H, s, NC*H*$_2$), 2.83 (1H, dd, *J* 3.4 12.8, CH(OH)C*H*H), 2.63 (1H, dd, *J* 10.6 12.8, CH(OH)CH*H*), 0.94 (18H, s, SiC(C*H*$_3$)$_3$), 0.11 (12H, s, Si(C*H*$_3$)$_2$); δ_C (75 MHz, CDCl$_3$) 141.8, 128.3, 127.6, 125.9, 101.0, 88.6, 69.5, 60.9, 43.6, 26.1, 16.5, -4.6; *m/z* (ESMS+) 442 [M + H]$^+$.

(*S*)-*N*,*N*-Bis(2-propyne)-2-amino-1-phenylethanol, **(*S*)-166**.
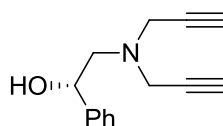
This compound is novel. 1 M TBAF in THF (4.58 cm^3, 4.58 mmol) was added to a solution of **(*S*)-165** (0.963 g, 2.18 mmol) in dry THF (5 cm^3) cooled to 0 °C. After stirring for 1 h, H$_2$O (10 cm^3) was added and the product was extracted into Et$_2$O (3

x 15 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. The product was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in pet. ether to give a yellow oil (0.292 g, 1.37 mmol, 64 %). $[\alpha]_D^{26}$ +80.6 (c 0.5 in CHCl$_3$) 90 % e.e. (*S*); (Found (ESI): M$^+$ + H 214.1224, C$_{14}$H$_{16}$NO requires 214.1226); ν_{max} 3419, 3287, 2829, 1603, 1493, 1449, 1328, 1249, 1198, 1116, 1062, 1027, 984, 913, 856, 755, 699 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.27-7.42 (5H, m, Ar), 4.75 (1H, dd, *J* 3.0 10.6, C*H*), 3.56 (4H, d, *J* 2.3, NC*H*$_2$), 2.86 (1H, dd, *J* 3.0 12.8, CH(OH)C*H*H), 2.62 (1H, dd, *J* 10.6 12.8, CH(OH)CH*H*), 2.27 (2H, t, *J* 2.3, CC*H*); δ_C (100 MHz, CDCl$_3$) 141.6, 128.4, 127.6, 125.9, 73.4, 69.7, 61.1, 42.5; *m/z* (ESMS+) 214 [M + H]$^+$. The e.e. was determined by chiral HPLC analysis (Chiralpak IC column, 4.6 mm x 250 mm, hexane:2-propanol 96:4, 0.6 cm^3/min, T = 28 °C, 210 nm UV, *R* isomer 16.0 mins, *S* isomer 17.8 mins). A racemic standard was prepared via the sodium borohydride reduction of **164** followed by deprotection with TBAF.

(*R,R*)-*N*-*tert*-Butoxycarbonyl-1,2-diaminocyclohexane, (***R,R***)-168.
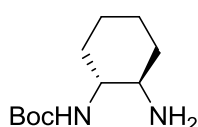
This compound is known and fully characterised.[230] 35 % Aqueous HCl solution (0.30 cm^3, 3.40 mmol) was added to MeOH (0.88 cm^3) at 0 °C to make a 3 M solution. The solution was added to a flask charged with (*R,R*)-diaminocyclohexane (0.400 g, 3.50 mmol) cooled to 0 °C. After stirring for 15 mins at room temperature H$_2$O (0.6 cm^3) was added and the solution was left to stir for a further 30 mins before the addition of *tert*-butoxycarbonyl anhydride (1.20 cm^3, 5.22 mmol). After 1 h H$_2$O (10 cm^3) was added and the mixture was washed with Et$_2$O (10 cm^3). To

the aqueous fraction a 2 M NaOH solution (15 cm^3) was added and the product was extracted into DCM (3 x 20 cm^3). The combined DCM fractions were dried over MgSO$_4$, filtered and the solvent was removed in vacuo. The product was purified by column chromatography on silica with 20 % MeOH in DCM to give the product as an off-white solid (0.369 g, 1.72 mmol, 49 %). $[\alpha]_D^{24}$ +2.1 (c 0.1 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 215.1752, C$_{11}$H$_{23}$N$_2$O$_2$ requires 215.1754); ν_{max} 3348, 3189, 2927, 2856, 1692, 1591, 1544, 1444, 1387, 1361, 1312, 1275, 1239, 1172, 1109, 1039, 1014, 963, 934, 897, 849, 759 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 4.52 (1H, broad s, N*H*Boc), 3.01-3.08 (1H, broad m, BocHNC*H*), 2.28 (1H, td, *J* 3.8 10.2, NH$_2$C*H*), 1.89-2.00 (2H, broad m, C*H*$_2$), 1.62-1.71 (2H, broad m, C*H*$_2$), 1.42 (9H, s, C(C*H*$_3$)$_3$), 1.36 (2H, broad s, N*H*$_2$), 0.99-1.31 (4H, broad m, C*H*$_2$); δ_C (75 MHz, CDCl$_3$) 156.1, 79.2, 57.6, 55.6, 35.2, 32.9, 28.3, 25.1, 25.0; *m/z* (ESMS+) 215 [M + H]$^+$.

(*R,R*)-*N,N*-Bis-propargyl-*N'*-*tert*-butoxycarbonyl-1,2-diaminocyclohexane, **(R,R)-169**.

(*R,R*)-*N*-Propargyl-*N'*-*tert*-butoxycarbonyl-1,2-diaminocyclohexane, **(R,R)-170**.
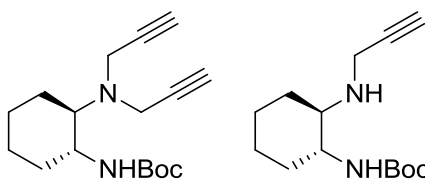
Compound **(R,R)-169** is novel. Compound **(R,R)-170** is known and fully characterised.[231] An 80 % Propargyl bromide solution in toluene (0.43 cm^3, 3.99 mmol) was added to a solution of **(R,R)-168** (0.409 g, 1.91 mmol) and K$_2$CO$_3$ (1.319 g, 9.54 mmol) in dry MeCN (15 cm^3) and heated at 80 °C for 24 h, after which the solvent was removed under reduced pressure. Following the addition of

H_2O (10 cm^3) the product was extracted into CHCl$_3$ (3 x 10 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Column chromatography on silica with a gradient elution from 0-60 % EtOAc in pet. ether gave two products. **(*R,R*)-169**, yellow oil (0.240 g, 0.826 mmol, 43 %). [α]$_D^{24}$ +34.9 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 261.2068, C$_{17}$H$_{27}$N$_2$O$_2$ requires 291.2067); ν_{max} 3297, 2975, 2929, 2857, 1697, 1485, 1450, 1390, 1364, 1316, 1235, 1166, 1128, 1042, 1022, 989, 954, 910, 864, 779 cm^{-1}; δ$_H$ (300 MHz, CDCl$_3$) 4.93 (1H, broad s, N*H*Boc), 3.51 (2H, dd, *J* 2.6 17.0, NC*H*H), 3.43 (2H, dd, *J* 2.6 17.0, NCH*H*), 3.23-3.36 (1H, broad m, BocHNC*H*), 2.60 (1H, td, *J* 3.4 10.6, (CH$_2$)$_2$NC*H*), 2.31-2.40 (1H, broad m, C*H*$_2$), 2.20 (2H, t, *J* 2.6, CC*H*), 1.96-2.04 (1H, broad m, C*H*$_2$), 1.71-1.79 (1H, broad m, C*H*$_2$), 1.60-1.68 (1H, broad m, C*H*$_2$), 1.43 (9H, s, C(C*H*$_3$)$_3$), 1.01-1.39 (4H, broad m, C*H*$_2$); δ$_C$ (75 MHz, CDCl$_3$) 156.1, 80.7, 78.9, 72.5, 64.4, 51.7, 38.6, 33.3, 28.4, 25.4, 25.3, 24.5; *m/z* (ESMS+) 291 [M + H]$^+$. **(*R,R*)-170**, off-white solid (0.243 g, 0.963 mmol, 50 %). Mp 120-121 °C; [α]$_D^{24}$ -13.9 (c 0.5 in CHCl$_3$) (*R,R*) (lit.[231] [α]$_D^{24}$ -18.3 (c 0.94 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 253.1907, C$_{14}$H$_{25}$N$_2$O$_2$ requires 253.1911); ν_{max} 3350, 3312, 3253, 2972, 2933, 2859, 1719, 1680, 1520, 1445, 1390, 1365, 1319, 1255, 1234, 1168, 1109, 1041, 1101, 926, 917, 879, 864, 847, 777, 743, 714, 689 cm^{-1}; δ$_H$ (300 MHz, CDCl$_3$) 4.46 (1H, broad s, N*H*Boc), 3.50 (1H, dd, *J* 2.6 17.3, NC*H*H), 3.36 (1H, dd, *J* 2.6 17.0, NCH*H*), 3.20-3.31 (1H, broad m, BocHNC*H*), 2.43 (1H, td, *J* 3.8 10.2, (CH$_2$)$_2$NC*H*), 2.18 (1H, t, *J* 2.6, CC*H*), 1.96-2.06 (2H, broad m, C*H*$_2$), 1.75 (1H, broad s, N*H*CH$_2$) 1.62-1.72 (2H, broad m, C*H*$_2$), 1.42 (9H, s, C(C*H*$_3$)$_3$), 0.99-1.32 (4H, broad m, C*H*$_2$); δ$_C$ (75 MHz, CDCl$_3$) 155.9, 82.5, 79.3, 71.1, 59.2, 54.3, 35.2, 32.9, 31.0, 28.3, 24.8, 24.3; *m/z* (ESMS+) 253 [M + H]$^+$.

(*R,R*)-*N,N*-Bis-(3-phenyl-2-propyne)-*N'*-*tert*-butoxycarbonyl-1,2-

diaminocyclohexane, (***R,R***)-171.
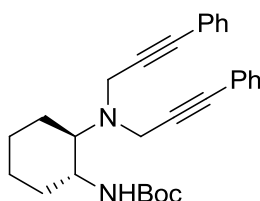
This compound is novel. Compound (***R,R***)-171 was made by the same procedure as

for **130c** using (***R,R***)-169 (98.0 mg, 0.338 mmol), iodobenzene (0.09 cm^3, 0.804

mmol), PdCl$_2$(PPh$_3$)$_2$ (10.0 mg, 14.3 μmol) and CuI (7.0 mg, 36.8 μmol). The

product was purified by column chromatography on silica with a gradient elution

from 0-20 % EtOAc in pet. ether to give a yellow oil (73.0 mg, 0.165 mmol, 49 %).

$[\alpha]_D^{24}$ +17.2 (c 0.13 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 443.2691, C$_{29}$H$_{35}$N$_2$O$_2$

requires 443.2693); ν_{max} 3370, 2974, 2929, 2857, 2362, 1701, 1597, 1489, 1443,

1390, 1364, 1336, 1316, 1236, 1166, 1126, 1098, 1070, 1042, 1022, 987, 953, 912,

864, 755, 737, 691 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.41-7.47 (4H, m, Ar), 7.28-7.33

(6H, m, Ar), 5.09-5.14 (1H, m, N*H*Boc), 3.80 (2H, d, *J* 17.3, NC*H*H), 3.73 (2H, d,

J 17.3, NCH*H*), 3.36-3.48 (1H, m, C*H*NHBoc), 2.75 (1H, td, *J* 3.4 11.7, C*H*NCH$_2$),

2.40-2.49 (1H, m, C*H$_2$*), 2.13-2.21 (1H, m, C*H$_2$*), 1.76-1.85 (1H, m, C*H$_2$*), 1.64-

1.73 (1H, m, C*H$_2$*), 1.46 (9H, s, C(C*H$_3$*)$_3$), 1.43-1.51 (1H, m, C*H$_2$*), 1.07-1.37 (3H,

m, C*H$_2$*); δ_C (75 MHz, CDCl$_3$) 156.2, 131.5, 128.2, 128.0, 123.2, 86.6, 84.5,78.9,

64.4, 51.9, 39.7, 33.3, 28.4, 25.6, 25.5, 24.5; *m/z* (ESMS+) 443 [M + H]$^+$.

4-Hydroxy-2,5-diphenylcyclopent-4-ene-1,3-dione, **173**.
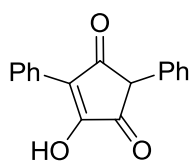
This compound is known but not fully characterised.[232, 233] Sodium (1.093 g, 47.5 mmol) was added to dry ethanol (30 cm^3) at 0 °C. After complete dissolution of the sodium a solution of 1,3-diphenyl-2-propanone (5.00 g, 23.8 mmol) and diethyloxalate (3.23 cm^3, 23.8 mmol) in dry ethanol (15 cm^3) was added and the mixture was left to stir for 3 h. The reaction was quenched with acetic acid (3 cm^3) followed by the addition of 2 M H_2SO_4 (15 cm^3) which precipitated a pale yellow solid which was isolated by filtration and washed with water (20 cm^3). After removal of the solvent under reduced pressure the residue was dissolved in acetone (10 cm^3) causing the precipitation of a white solid. Filtration and evaporation of the mother liquor gave the product as a yellow solid (3.979 g, 15.1 mmol, 63 %). Mp 194-196 °C; (Found (ESI): M$^+$ + Na 265.0860, $C_{17}H_{13}O_3$ requires 265.0859); ν_{max} 3262, 1735, 1668, 1628, 1492, 1378, 1267, 1223, 1191, 1130, 1076, 1026, 969, 936, 901, 813, 776, 734, 693 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.17-8.22 (2H, m, Ar), 7.22-7.53 (8H, m, Ar), 4.36 (1H, s, CH); δ_C (75 MHz, CDCl$_3$) 197.4, 165.8, 164.9, 135.3, 130.5, 130.2, 130.0, 129.7, 129.6, 129.1, 128.4, 56.7; m/z (ESMS+) 265 [M + H]$^+$.

(R,R)-1-Phenyl-(3,4-diphenyl)-diazaphospholidine, (***R***,***R***)-174.
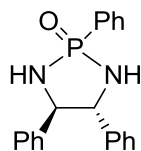
This compound is known and has been fully characterised.[202, 234] Phenylphosphonic dichloride (0.67 cm^3, 47.2 mmol) was added dropwise to a solution of (R,R)-DPEN (1.00 g, 4.71 mmol) and NEt$_3$ (1.31 cm^3, 9.40 mmol) in dry DCM (50 cm^3) cooled to 0 °C. After 18 h the reaction was quenched with H_2O (50 cm^3) and extracted into DCM (1 x 50 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in*

vacuo to give an off-white solid (1.535 g, 4.59 mmol, 98 %). $[\alpha]_D^{26}$ +89.0 (c 0.1 in CHCl$_3$) (*R,R*) (lit.[234] $[\alpha]_D^{20}$ +74.4 (c 1.0 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 335.1308, C$_{20}$H$_{20}$N$_2$OP requires 335.1308); ν_{max} 3185, 1496, 1456, 1438, 1396, 1293, 1275, 1169, 1122, 1091, 1051, 1028, 994, 898, 833, 785, 747, 718, 694 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 8.05-8.14 (2H, m, Ar), 7.49-7.58 (3H, m, Ar), 7.29-7.33 (8H, m, Ar), 7.18-7.23 (2H, m, Ar), 4.72 (1H, dd, *J* 8.7, 1.9, PhC*H*), 4.56 (1H, d, *J* 8.7, PhC*H*), 3.20 (1H, broad d, J 14.7, N*H*), 3.08 (1H, broad d, *J* 8.7, N*H*); δ_C (75 MHz, CDCl$_3$) 139.6 (*J* 11.0), 139.1 (*J* 7.1), 133.9 (*J* 160.3), 132.2, 132.0, 131.3 (*J* 2.7), 128.2, 128.1, 128.0, 127.9, 127.2, 126.8, 68.2 (*J* 3.8), 65.5 (*J* 4.4); δ_P (121 MHz, CDCl$_3$) 26.4; *m/z* (ESMS+) 335 [M + H]$^+$.

(*R,R*)-1-Phenyl-*N,N'*-dimethyl-(3,4-diphenyl)-diazaphospholidine, **(*R,R*)-175**.
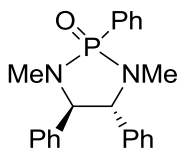
This compound is known and has been fully characterised.[202, 234] 1.6 M *N*-Butyllithium in hexanes (6.03 cm^3, 9.65 mmol) was added dropwise to a solution of **(*R,R*)-174** (1.535 g, 4.59 mmol) in dry THF (25 cm^3) cooled to 0 °C. Methyl iodide (0.63 cm^3, 10.1 mmol) was added after 1 h and the reaction mixture was left to stir for a further 2 h. The reaction was quenched with water (25 cm^3) and the THF was removed under reduced pressure. The product was extracted into DCM (3 x 25 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo* to give a yellow solid (1.643 g, 4.53 mmol, 99 %). $[\alpha]_D^{26}$ +23.6 (c 0.5 in CHCl$_3$), (*R,R*) (lit.[234] $[\alpha]_D^{20}$ +27.2 (c 1.0 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + Na 385.1439, C$_{22}$H$_{23}$N$_2$NaOP requires 385.1440); ν_{max} 3031, 2878, 2817, 1494, 1456, 1439, 1284, 1244, 1197, 1151, 1117, 1073, 992, 782, 740, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$)

7.86-7.97 (2H, m, Ar), 7.41-7.49 (3H, m, Ar), 7.08-7.24 (8H, m, Ar), 6.98-7.07 (2H, m, Ar), 4.16 (1H, d, J 8.7, PhCH), 4.02 (1H, d, J 8.7, PhCH), 2.33 (3H, d, J 10.6, CH_3), 2.09 (3H, d, J 9.8, CH_3); δ_C (75 MHz, CDCl$_3$) 137.4 (J 9.9), 136.8 (J 6.0), 132.5 (J 9.9), 131.4 (J 2.7), 130.7 (J 157.0), 128.3, 128.2, 128.1, 128.0, 127.9 (J 1.7), 127.6, 127.2, 73.0 (J 8.2), 71.5 (J 7.1), 29.6, 29.5 (J 9.3); δ_P (121 MHz, CDCl$_3$) 30.5; m/z (ESMS+) 363 [M + H]$^+$.

(R,R)-N,N'-Dimethyl-1,2-diphenylethylenediamine, **(R,R)-176**.
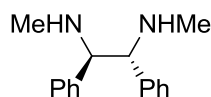
This compound is known and has been fully characterised.[202, 234] 1.25 M HCl in MeOH (2.11 cm^3, 2.64 mmol) was added to a flask charged with **(R,R)-175** (0.562 g, 1.55 mmol) and dry MeOH (4 cm^3) and heated at reflux for 24 h after which the solvent was removed under reduced pressure. Crystallisation from 2-propanol gave a white solid which was dissolved in a saturated K$_2$CO$_3$ solution (20 cm^3), extracted with DCM (3 x 20 cm^3), the organic fractions were dried over K$_2$CO$_3$, filtered and the solvent was removed *in vacuo* to give a white solid (0.227 g, 0.944 mmol, 61 %). Mp 47-48 °C; $[\alpha]_D^{26}$ +46.0 (c 0.1 in CHCl$_3$), (R,R) (lit.[234] $[\alpha]_D^{20}$ +19.3 (c 1.0 in CHCl$_3$) (R,R); (Found (ESI): M$^+$ + Na 241.1700, C$_{16}$H$_{21}$N$_2$ requires 241.1699); ν_{max} 3027, 2945, 2845, 2789, 1601, 1492, 1473, 1453, 1348, 1304, 1249, 1171, 1136, 1101, 1072, 1028, 913, 866, 844, 756, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.09-7.23 (6H, m, Ar), 7.00-7.06 (4H, m, Ar), 3.53 (2H, s, CH), 2.25 (6H, s, CH_3), 1.93 (2H, broad s, NH); δ_C (75 MHz, CDCl$_3$) 140.9, 127.9, 127.8, 126.8, 71.1, 34.6; m/z (ESMS+) 341 [M + H]$^+$.

(*S,S*)-*N,N'*-Bis((*S*)-1-phenylethyl)ethanediimine, **(*S,S*)-177**.
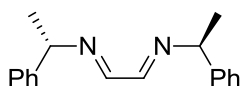
This compound is known but not fully characterised.[235, 236] (*S*)-α-Methylbenzylamine (0.250 g, 2.06 mmol), 40 % glyoxal in H_2O (0.12 cm^3, 1.05 mmol), $MgSO_4$ (5.00 g) and a catalytic amount of HCO_2H were stirred in DCM (10 cm^3) for 20 mins after which the mixture was filtered through celite and the solvent was removed under reduced pressure. The orange residue was dissolved in cyclohexane (15 cm^3), dried over Na_2SO_4, filtered and the solvent was removed *in vacuo* to give the diimine as a yellow oil (0.278 g, 1.05 mmol, 51 %). $[\alpha]_D^{25}$ -85.0 (c 0.05 in CHCl$_3$), (*S,S*) (lit.[236] $[\alpha]_D^{20}$ -114.1 (c 0.2 in CHCl$_3$) (*S,S*); (Found (ESI): M^+ + H 265.1696, $C_{18}H_{21}N_2$ requires 265.1699); ν_{max} 3028, 2973, 2929, 2869, 1661, 1493, 1451, 1372, 1267, 1205, 1143, 1083, 1028, 1011, 980, 910, 759, 696 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 8.06 (2H, s, NC*H*), 7.29-7.37 (10H, m, Ar), 4.51 (2H, q, *J* 6.5, C*H*Ph), 1.58 (6H, d, *J* 6.5, C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 160.7, 130.7, 128.6, 127.2, 126.7, 69.7, 24.0; *m/z* (ESMS+) 265 [M + H]$^+$.

(*S,S*)-*N,N'*-Bis((*S*)-1-phenylethyl)ethanediamine, **(*S,S*)-178**.
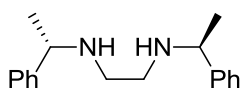
This compound is known but not fully characterised.[235, 236] (*S,S*)-N,N-Bis-1-phenylethylethylenediimine (0.253 g, 0.957 mmol) was dissolved in MeOH (10 cm^3) and cooled to 0 °C. Sodium borohydride (0.144 g, 3.81 mmol) was added portionwise and the mixture was left to stir. After tlc showed complete conversion (1 h) the reaction was quenched with a saturated NH_4Cl solution (10 cm^3) and the MeOH was removed under reduced pressure. The product was extracted into Et$_2$O

(3 x 15 cm^3), dried over MgSO$_4$, filtered and the solvent was removed *in vacuo* to give the product as a yellow oil (0.205 g, 0.764 mmol, 80 %). $[\alpha]_D^{25}$ -25.5 (c 0.1 in CHCl$_3$), (*S,S*) (lit.[236] $[\alpha]_D^{20}$ -70.0 (c 0.5 in CHCl$_3$) (*S,S*); (Found (ESI): M$^+$ + H 269.2012, C$_{18}$H$_{25}$N$_2$ requires 269.2012); ν_{max} 3027, 2970, 2823, 1669, 1602, 1492, 1451, 1370, 1305, 1204, 1120, 1074, 1027, 957, 912, 760, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.14-7.35 (10H, m, Ar), 3.61 (2H, q, *J* 6.4, C*H*), 2.49 (4H, s, C*H*$_2$), 1.31 (6H, d, *J* 6.5, C*H*$_3$); δ_C (75 MHz, CDCl$_3$) 133.8, 128.4, 126.9, 126.6, 58.1, 46.9, 24.2; *m/z* (ESMS+) 269 [M + H]$^+$.

Oxidation of 1-Phenylethanol using **126**.

Complex **126** (10.0 mg, 19.1 μmol) and 1-phenylethanol (23.0 mg, 0.188 mmol) were dissolved in acetone (1 cm^3) and heated at 60 °C in a sealed pressure tube for 4 days after which the solution was allowed to cool to room temperature and the solvent was removed under reduced pressure. The conversions were calculated from the integrations of the methyl peaks in the ^{1}H NMR spectra.

General Procedure for the Oxidation of Alcohols using Iron Catalysts and TMANO.

Complex **126** (10.0 mg, 19.1 μmol), trimethylamine-*N*-oxide (2.10 mg, 18.9 μmol) and 1-phenylethanol (23.0 mg, 0.188 mmol) were dissolved in acetone (1 cm^3) and heated at 60 °C for 24 h. The reaction was monitored over time by GC (BP20 PEG column, T = 130 °C, inj T = 220 °C, det T = 220 °C, 15 psi He carrier gas). R$_T$: Acetophenone: 4.7 minutes, 1-phenylethanol: 8.1 minutes.

General Procedure for the Oxidation of Alcohols using Iron Catalysts, TMANO and Aldehydes.

Complex **126** (10.0 mg, 19.1 μmol), trimethylamine-*N*-oxide (2.1 mg, 18.9 μmol), 1-phenylethanol (23 mg, 0.188 mmol) and paraformaldehyde (29.0 mg, 0.966 mmol) were dissolved in toluene (1 cm^3) and heated at 60 °C for 24 h. After 4 h more paraformaldehyde (29.0 mg, 0.966 mmol) was added. The reaction was monitored over time by GC (BP20 PEG column, T = 130 °C, inj T = 220 °C, det T = 220 °C, 15 psi He carrier gas). R$_T$: Acetophenone: 4.7 minutes, 1-phenylethyl formate: 5.0 minutes, 1-phenylethanol: 8.1 minutes.

General Procedure for the Reduction of Acetophenone using Iron Catalysts.

Complex **136** (7.80 mg, 19.0 μmol), trimethylamine-*N*-oxide (2.10 mg, 18.9 mmol) and acetophenone (23.0 mg, 0.191 mmol) were dissolved in 2-propanol (0.96 cm^3) or 5:2 FA/TEA (0.2 cm^3) and heated at 40 °C for 18 h. The conversion was determined by GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 130 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, acetophenone 13.4 mins, 1-phenylethylformate 15.1 (*S*), 15.5 (*R*) mins, 1-phenylethanol 17.4 (*R*), 18.0 (*S*) mins.

3.5 Procedures from Section 2.5.

Benzyl azide.
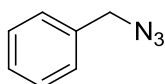
This compound is known and fully characterised.[237] Benzyl bromide (1.00 g, 5.85 mmol) in DMSO (10 cm^3) was added to a solution of sodium azide (0.418 g, 6.43 mmol) in DMSO (10 cm^3) and left to stir for 2 h. The reaction was quenched with H$_2$O (10 cm^3) and the product was extracted into Et$_2$O (3 x 20 cm^3), washed with brine (60 cm^3), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure to give a colourless oil (0.724 g, 5.44 mmol, 93 %). ν_{max} 3032, 2926, 2089, 1701, 1496, 1454, 1349, 1252, 1201, 1077, 1028, 875, 735, 696 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.30-7.45 (5H, m, Ar), 4.34 (2H, s, CH_2); δ_C (100 MHz, CDCl$_3$) 135.3, 128.8, 128.3, 128.2, 54.8. Caution should be taken in the isolation and storage of azides; many are reported to decompose explosively.

(*S*)-*N*,*N*-Bis(1-benzyl-4-methylene-1,2,3-triazole)-2-amino-1-phenylethanol,　(*S*)-**179**.
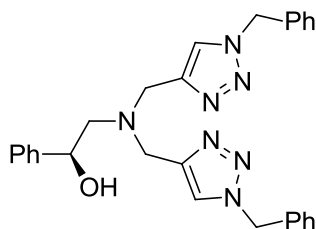
This compound is novel. Compound (*S*)-**166** (0.188 g, 0.890 mmol) in 1:1 ^{t}BuOH/H$_2$O (5 cm^3) was added to a solution of benzyl azide (0.296 g, 2.22 mmol), Cu(OAc)$_2$ (32.0 mg, 0.176 mmol) and sodium ascorbate (71.0 mg, 0.358 mmol) in 1:1 ^{t}BuOH/H$_2$O (17 cm^3). After stirring for 72 h the solution was diluted with EtOAc (40 cm^3) and washed with 35 % ammonia solution (20 cm^3) and brine (40 cm^3). The organic fraction was dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography on silica with a gradient elution from 0-5 % MeOH in DCM gave the product as an off-white solid (0.373 g, 0.777 mmol, 87 %). Mp 119-120 °C; $[\alpha]_D^{26}$ +55.8 (c 0.5 in CHCl$_3$) (*S*); (Found

(ESI): M$^+$ + H 480.2504, C$_{28}$H$_{30}$N$_7$O requires 480.2506); ν_{max} 3420, 3068, 2929, 2835, 2361, 1496, 1458, 1400, 1333, 1214, 1203, 1134, 1114, 1082, 1053, 1035, 990, 914, 897, 872, 851, 831, 803, 756, 723, 710, 696 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.55 (2H, s, N$_3$C*H*), 7.34-7.43 (6H, m, Ar), 7.21-7.33 (9H, m, Ar), 5.50 (4H, s, C*H*$_2$Ph), 4.81 (1H, dd, *J* 3.4 10.2, C*H*OH), 3.89 (2H, d, *J* 14.3, NC*H*HC), 3.84 (1H, broad s, O*H*), 3.80 (2H, d, *J* 14.3, NCH*H*C), 2.75 (1H, dd, *J* 3.4 13.2, CH(OH)C*H*H), 2.62 (1H, dd, *J* 10.2 13.2, CH(OH)CH*H*); δ_C (75 MHz, CDCl$_3$) 144.2, 142.0, 134.6, 129.0, 128.6, 128.1, 127.8, 127.2, 125.8, 123.0, 69.6, 61.5, 54.0, 47.8; *m/z* (ESMS+) 480 [M + H]$^+$.

(*R*,*R*)-*N*,*N*-Bis(1-benzyl-4-methylene-1,2,3-triazole)-*N*'-*tert*-butoxycarbonyl-1,2-diaminocyclohexane, (**R**,**R**)-**180**.
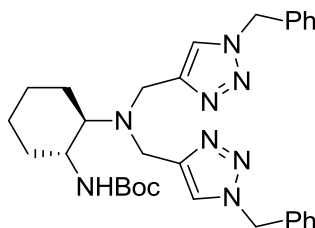
This compound is novel. Compound (**R**,**R**)-**180** was made by the same procedure as for (**S**)-**179** using (**R**,**R**)-**169** (76.0 mg, 0.262 mmol), benzyl azide (87.0 mg, 0.653 mmol), Cu(OAc)$_2$ (10.0 mg, 55.1 µmol) and sodium ascorbate (21.0 mg, 0.106 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-10 % MeOH in DCM to give an orange solid (0.136 g, 0.244 mmol, 93 %). Mp 147-149 °C; [α]$_D^{24}$ -10.0 (c 0.5 in CHCl$_3$) (*R*,*R*); (Found (ESI): M$^+$ + H 557.3346, C$_{31}$H$_{41}$N$_8$O$_2$ requires 557.3347); ν_{max} 3369, 2925, 2854, 1708, 1496, 1454, 1365, 1331, 1235, 1216, 1161, 1127, 1051, 1018, 987, 909, 815, 716 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.41 (2H, s, N$_3$C*H*), 7.29-7.34 (6H, m, Ar), 7.16-7.20 (4H, m, Ar), 5.48 (2H, d, *J* 14.7, PhC*H*H), 5.41 (2H, d, *J* 14.7, PhCH*H*), 5.06

(1H, broad s, N*H*Boc), 3.80 (2H, d, *J* 14.3, NC*H*H), 3.69 (2H, d, *J* 14.3, NCH*H*),

3.27-3.39 (1H, broad m, BocHNC*H*), 2.32 (1H, td, *J* 2.6 10.9, (CH$_2$)$_2$NC*H*), 2.17-

2.26 (1H, broad m, C*H*$_2$), 1.84-1.92 (1H, broad m, C*H*$_2$), 1.68-1.76 (1H, broad m,

C*H*$_2$), 1.57-1.65 (1H, broad m, C*H*$_2$), 1.37-1.45 (1H, broad m, C*H*$_2$), 1.31 (9H, s,

C(C*H*$_3$)$_3$), 0.86-1.25 (3H, broad m, C*H*$_2$); δ$_C$ (75 MHz, CDCl$_3$) 155.9, 147.2, 134.9,

129.0, 128.5, 127.7, 122.5, 78.4, 63.0, 54.0, 51.6, 44.6, 33.5, 28.5, 25.3, 24.7, 24.4;

m/z (ESMS+) 557 [M + H]$^+$.

(*R,R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N'*-*tert*-butoxycarbonyl-1,2-

diaminocyclohexane, (*R,R*)-181.
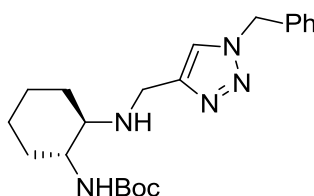
This compound is novel. Compound (*R,R*)-181 was made by the same procedure as

for (*S*)-179 using (*R,R*)-170 (0.212 g, 0.840 mmol), benzyl azide (0.134 g, 1.01

mmol), Cu(OAc)$_2$ (15.0 mg, 82.6 μmol) and sodium ascorbate (33.0 mg, 0.167

mmol). The product was purified by column chromatography on silica with a

gradient elution from 0-10 % MeOH in DCM to give an off-white solid (0.311 g,

0.807 mmol, 96 %). Mp 107-108 °C; [α]$_D^{24}$ -27.1 (c 0.5 in CHCl$_3$) (*R,R*); (Found

(ESI): M$^+$ + H 386.2549, C$_{21}$H$_{32}$N$_5$O$_2$ requires 386.2551); ν$_{max}$ 3354, 3073, 2927,

2854, 1681, 1509, 1455, 1364, 1315, 1254, 1230, 1166, 1045, 1018, 850, 709 cm^{-1};

δ$_H$ (300 MHz, CDCl$_3$) 7.37 (1H, s, N$_3$C*H*), 7.30-7.36 (3H, m, Ar), 7.21-7.26 (2H,

m, Ar), 5.48 (2H, s, PhC*H*$_2$), 4.58 (1H, broad s, N*H*Boc), 3.96 (1H, d, *J* 13.9,

NC*H*H), 3.79 (1H, d, *J* 13.9, NCH*H*), 3.20-3.34 (1H, broad m, BocHNC*H*), 2.28

(1H, td, *J* 3.8 9.8, (CH$_2$)$_2$NC*H*), 1.98-2.07 (2H, broad m, C*H*$_2$), 1.93 (1H, broad m,

NHCH$_2$), 1.58-1.71 (2H, broad m, CH_2), 1.38 (9H, s, C(CH_3)$_3$), 1.02-1.31 (4H, broad m, CH_2); δ_C (75 MHz, CDCl$_3$) 155.9, 147.9, 134.7, 129.0, 128.6, 128.0, 121.4, 79.1, 60.6, 54.4, 54.0, 41.9, 32.8, 31.5, 28.3, 24.7, 24.4; m/z (ESMS+) 386 [M + H]$^+$.

(*R,R*)-*N,N'*-Bis-propargyl-1,2-diphenylethylenediamine, **(*R,R*)-182**.
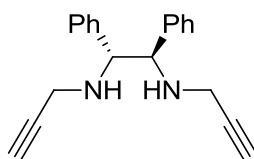
This compound is novel. Compound **(*R,R*)-182** was made by the same procedure as for **156** using (*R,R*)-DPEN (0.100 g, 0.471 mmol), 80 % propargyl bromide in toluene (0.10 cm^3, 0.928 mmol) and K$_2$CO$_3$ (0.195 g, 1.41 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in pet. ether to give a white solid (0.051 g, 0.177 mmol, 38 %). Mp 79-80 °C; [α]$_D^{25}$ -92.4 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 289.1704, C$_{20}$H$_{21}$N$_2$ requires 289.1699); ν_{max} 3340, 3117, 2912, 2856, 2358, 2089, 1492, 1453, 1441, 1333, 1276, 1202, 1154, 1113, 1098, 1072, 1062, 1026, 945, 919, 828, 796, 756, 732, 696 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.03-7.20 (10H, m, Ar), 3.89 (2H, s, CHNH), 3.38 (2H, dd, *J* 2.3 16.6, CHH), 3.10 (2H, dd, *J* 2.3 16.6, CHH), 2.29 (2H, broad s, NH), 2.18 (2H, t, *J* 2.3, CCH); δ_C (75 MHz, CDCl$_3$) 139.9, 128.0, 127.9, 127.2, 82.1, 71.2, 67.1, 35.9; m/z (ESMS+) 289 [M + H]$^+$.

(*R,R*)-*N*,*N*'-Bis-(1-benzyl-4-methylene-1,2,3-triazole)-1,2-diphenylethylenediamine, (***R,R***)-183.
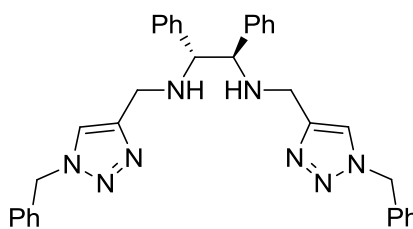
This compound is novel. Compound (***R,R***)-183 was made by the same procedure as for (***S***)-179 using (***R,R***)-182 (38.0 mg, 0.132 mmol), benzyl azide (42.0 mg, 0.315 mmol), Cu(OAc)$_2$ (4.8 mg, 26.4 μmol) and sodium ascorbate (10.0 mg, 50.5 μmol). The product was purified by column on silica with a gradient elution from 0-10 % MeOH in DCM to give a pale yellow solid (46.0 mg, 82.9 μmol, 63 %). Mp 124-126 °C; $[\alpha]_D^{26}$ +2.4 (c 0.1 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 555.2982, C$_{34}$H$_{35}$N$_8$ requires 555.2979); ν_{max} 3307, 3132, 3061, 3029, 2761, 2365, 1560, 1494, 1452, 1338, 1215, 1126, 1053, 1026, 987, 915, 870, 847, 820, 795, 750, 719, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.33-7.43 (6H, m, Ar), 7.22-7.31 (6H, m, Ar), 7.08-7.16 (6H, m, Ar), 6.95-7.04 (4H, m, Ar), 5.51 (2H, d, *J* 14.7, C*H*HPh), 5.45 (2H, d, *J* 14.7, CH*H*Ph), 3.74 (2H, d, *J* 13.9, NHC*H*$_2$), 3.68 (2H, s, C*H*), 3.62 (2H, d, *J* 13.9, NHC*H*$_2$), 2.51 (2H, broad s, N*H*); δ_C (75 MHz, CDCl$_3$) 147.4, 140.5, 134.8, 129.0, 128.5, 128.0, 127.9, 127.8, 126.9, 121.6, 68.3, 53.9, 42.5; *m/z* (ESMS+) 555 [M + H]$^+$. The triazole C*H* resonances are listed with the Ar resonances.

(*R*,*R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-1,2-diaminocyclohexane, **(*R*,*R*)-184**.
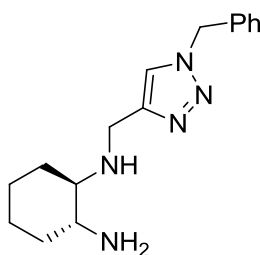
This compound is novel. Compound **(*R*,*R*)-184** was made by the same procedure as for **155** using **(*R*,*R*)-181** (98.0 g, 0.254 mmol) and TFA (0.19 cm^3, 2.48 mmol) to give the product as a yellow oil (58.0 mg, 0.203 mmol, 80 %). $[\alpha]_D^{29}$ -52.1 (c 0.4 in CHCl$_3$) (*R*,*R*); (Found (ESI): M$^+$ + H 286.2023, C$_{16}$H$_{24}$N$_5$ requires 286.2026); ν_{max} 2927, 2856, 1686, 1497, 1449, 1332, 1265, 1200, 1172, 1126, 1048, 1029, 825, 799, 731, 698 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.42 (1H, s, N$_3$C*H*), 7.27-7.34 (3H, m, Ar), 7.18-7.23 (2H, m, Ar), 5.43 (2H, s, C*H*$_2$Ph), 3.96 (1H, d, *J* 13.6, NHC*H*H), 3.73 (1H, d, *J* 13.6, NHCH*H*), 3.36 (3H, broad s, N*H*), 2.37-2.47 (1H, m, C*H*NH$_2$), 2.18 (1H, td, *J* 3.8 10.6, C*H*NHCH$_2$), 2.02-2.11 (1H, m, C*H*$_2$), 1.83-1.92 (1H, m, C*H*$_2$), 1.60-1.71 (2H, m, C*H*$_2$), 1.09-1.23 (3H, m, C*H*$_2$), 0.86-1.01 (1H, m, C*H*$_2$); δ_C (75 MHz, CDCl$_3$) 147.4, 134.6, 128.9, 128.5, 127.9, 121.6, 61.8, 55.0, 53.9, 41.8, 34.1, 31.0, 24.8, 24.7; *m*/*z* (ESMS+) 286 [M + H]$^+$.

(*R*,*R*)-*N*-Propargyl-*N*'-4-toluenesulphonyl-1,2-diaminocyclohexane, **(*R*,*R*)-188**.

This compound is novel. Compound **(*R*,*R*)-188** was made by the same procedure as for **(*R*,*R*)-170** using (*R*,*R*)-*N*-tosyldiaminocyclohexane (0.150 g, 0.559 mmol), 80

% propargyl bromide in toluene (0.09 cm^3, 0.835 mmol) and K$_2$CO$_3$ (0.116 g, 0.839 mmol). The product was purified by column chromatography on silica with a gradient elution from 20-80 % EtOAc in pet. ether to give a white solid (0.109 g, 0.356 mmol, 64 %). Mp 87-88 °C; [α]$_D^{26}$ -17.6 (c 0.4 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 307.1476, C$_{16}$H$_{23}$N$_2$O$_2$S requires 307.1475); ν$_{max}$ 3264, 2939, 2857, 2803, 1598, 1495, 1442, 1314, 1290, 1226, 1186, 1119, 1091, 1076, 1064, 1031, 982, 948, 897, 860, 840, 820, 771, 674 cm^{-1}; δ$_H$ (400 MHz, CDCl$_3$) 7.72-7.76 (2H, m, Ar), 7.24-7.28 (2H, m, Ar), 5.35 (1H, broad s, TsN*H*), 3.37 (1H, dd, *J* 2.5 17.1, NC*H$_2$*), 3.27 (1H, dd, *J* 2.5, 17.1, NC*H$_2$*), 2.68-2.77 (1H, broad m, C*H*NHTs), 2.35-2.42 (1H, m, C*H*NHCH$_2$), 2.37 (3H, s, C*H$_3$*), 2.17 (1H, t, *J* 2.5, CH$_2$CC*H*), 1.97-2.04 (1H, m, C*H$_2$*), 1.74-1.81 (1H, m, C*H$_2$*), 1.68 (1H, broad s, N*H*CH$_2$), 1.50-1.63 (2H, m, C*H$_2$*), 1.03-1.18 (3H, m, C*H$_2$*), 0.87-0.98 (1H, m, C*H$_2$*); δ$_C$ (100 MHz, CDCl$_3$) 143.2, 137.4, 129.5, 127.0, 82.1, 71.4, 58.9, 57.2, 34.9, 32.5, 30.6, 24.5, 24.0, 21.4; *m/z* (ESMS+) 307 [M + H]$^+$.

(*R,R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N'*-4-toluenesulphonyl-1,2-diaminocyclohexane, (***R,R***)-185.
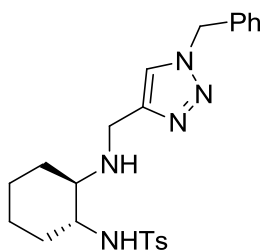
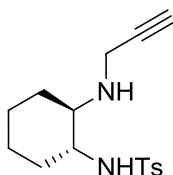

This compound is novel. Compound (***R,R***)-185 was made by the same procedure as for (***S***)-179 using (***R,R***)-188 (0.100 g, 0.326 mmol), benzyl azide (52.0 mg, 0.391 mmol), Cu(OAc)$_2$ (6.0 mg, 33.0 μmol) and sodium ascorbate (13.0 mg, 65.6 μmol). The product was purified by column on silica with a gradient elution from 0-10 %

MeOH in DCM to give a pale yellow oil (0.143 g, 0.325 mmol, quantitative). $[\alpha]_D^{28}$ -2.8 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 440.2127, C$_{23}$H$_{30}$N$_5$O$_2$S requires 440.2115); ν_{max} 3137, 2930, 2856, 2256, 1598, 1496, 1451, 1323, 1287, 1217, 1158, 1092, 1049, 976, 908, 838, 814, 725, 662 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.66-7.73 (2H, m, Ar), 7.33-7.41 (4H, m, Ar), 7.27-7.32 (2H, m, Ar), 7.15-7.20 (2H, m, Ar), 5.60 (1H, broad s, TsN*H*), 5.54 (1H, d, *J* 14.7, C*H*HPh), 5.48 (1H, d, *J* 14.7, CH*H*Ph), 3.85 (1H, d, *J* 13.9, NHC*H*H), 3.69 (1H, d, *J* 13.9, NHCH*H*), 2.61-2.70 (1H, m, C*H*NHTs), 2.36 (3H, s, C*H*$_3$), 2.27 (1H, td, *J* 3.8 10.1, C*H*NHCH$_2$), 1.94-2.11 (2H, m, C*H*$_2$), 1.61-1.69 (1H, broad s, N*H*CH$_2$), 1.53-1.61 (2H, m, C*H*$_2$), 1.07-1.19 (3H, m, C*H*$_2$), 0.89-1.03 (1H, m, C*H*$_2$); δ_C (75 MHz, CDCl$_3$) 147.4, 143.2, 137.2, 134.7, 129.5, 129.1, 128.7, 128.0, 127.1, 121.4, 59.8, 57.4, 54.1, 41.5, 32.6, 31.2, 24.5, 24.4, 21.5; *m/z* (ESMS+) 440 [M + H]$^+$. The triazole C*H* is listed with the Ar resonances.

(*R,R*)-*N*-Propargyl-*N*'-4-toluensulphonyl-1,2-diphenylethylenediamine, (***R,R***)-189.
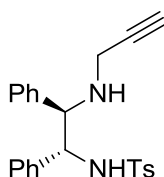
This compound is novel. Compound (***R,R***)-189 was made by the same procedure as for (***R,R***)-170 using (*R,R*)-TsDPEN (0.500 g, 1.36 mmol), 80 % propargyl bromide in toluene (0.22 cm^3, 2.04 mmol) and K$_2$CO$_3$ (0.283 g, 2.05 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-40 % EtOAc in pet. ether to give a white solid (0.367 g, 0.907 mmol, 67 %). Mp 127-128 °C; $[\alpha]_D^{27}$ -66.7 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 405.1639, C$_{24}$H$_{25}$N$_2$O$_2$S requires 405.1631); ν_{max} 3202, 3027, 2849, 2357, 1600, 1491, 1454,

1438, 1332, 1259, 1225, 1201, 1189, 1154, 1107, 1095, 1075, 1052, 1037, 1023, 912, 847, 809, 774, 757, 698, 671 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.34-7.39 (2H, m, Ar), 7.10-7.15 (3H, m, Ar), 6.91-7.07 (9H, m, Ar), 5.90 (1H, d, *J* 6.0, TsN*H*), 4.33-4.40 (1H, m, C*H*NHTs), 4.00 (1H, d, *J* 7.5, C*H*NHCH$_2$), 3.35 (1H, dd, *J* 2.3 17.0, C*H*$_2$), 3.03 (1H, dd, *J* 2.3 17.0, C*H*$_2$), 2.31 (3H, s, C*H*$_3$), 2.17 (1H, t, *J* 2.3, CH$_2$CC*H*), 1.84 (1H, broad s, N*H*CH$_2$); δ_C (75 MHz, CDCl$_3$) 142.7, 138.1, 138.0, 136.9, 129.1, 128.3, 128.0, 127.8, 127.6, 127.3, 127.2, 127.0, 81.3, 71.8, 65.8, 63.0, 35.6, 21.4; *m/z* (ESMS+) 405 [M + H]$^+$.

(*R,R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N*'-4-toluenesulphonyl-1,2-diphenylethylenediamine, (***R,R***)-186.
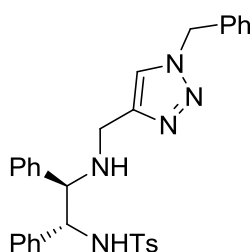
This compound is novel. Compound (***R,R***)-186 (0.235 g, 0.581 mmol) in 1:1 THF/H$_2$O (5 cm^3) was added to a solution of benzyl azide (93.0 mg, 0.699 mmol), Cu(OAc)$_2$ (11.0 mg, 60.6 μmol) and sodium ascorbate (23.0 mg, 0.116 mmol). in 1:1 THF/H$_2$O (10 cm^3). After stirring for 72 h the THF was removed under reduced pressure. The residue was dissolved in EtOAc (20 cm^3) and washed with 35 % ammonia solution (20 cm^3) and brine (20 cm^3). The organic fraction was dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography on silica with a gradient elution from 0-10 % MeOH in DCM gave the product as an off-white solid (0.274 g, 0.510 mmol, 88 %). Mp 192-194 °C; [α]$_D^{29}$ -21.3 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 538.2271, C$_{31}$H$_{32}$N$_5$O$_2$S

requires 538.2271); ν_{max} 3346, 3032, 2822, 1596, 1496, 1454, 1432, 1325, 1219, 1151, 1121, 1090, 1077, 1051, 983, 933, 910, 846, 834, 813, 769, 757, 745, 715, 695, 663 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.34-7.43 (5H, m, Ar), 7.27-7.32 (2H, m, Ar), 7.11-7.17 (4H, m, Ar), 6.96-7.06 (7H, m, Ar), 6.89-6.95 (2H, m, Ar), 6.28 (1H, TsN*H*), 5.53 (1H, d, *J* 14.7, C*H*HPh), 5.47 (1H, d, *J* 14.7, CH*H*Ph), 4.33 (1H, d, *J* 7.5, C*H*NHTs), 3.75-3.79 (1H, m, C*H*NHCH$_2$), 3.70-3.77 (1H, m, NHC*H*H), 3.59 (1H, d, *J* 14.3, NHCH*H*), 2.34 (3H, s, C*H*$_3$), 2.00 (1H, broad s, N*H*CH$_2$); δ_C (75 MHz, CDCl$_3$) 146.7, 142.7, 138.6, 138.1, 136.9, 134.7, 129.1, 128.7, 128.3, 128.0, 127.9, 127.6, 127.5, 127.4, 127.2, 127.0, 121.5, 67.0, 63.0, 54.0, 42.2, 21.4; *m/z* (ESMS+) 538 [M + H]$^+$. The triazole C*H* is listed with the Ar resonances.

(*R,R*)-*N*-Propargyl-1,2-diphenylethylenediamine, (***R,R***)-190.
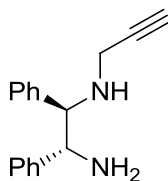
This compound is novel. A solution of 80 % propargyl bromide in toluene (0.11 cm^3, 1.02 mmol) was added to dry MeCN (10 cm^3) and the resultant mixture added dropwise to a vigorously stirred mixture of (*R,R*)-DPEN (0.200 g, 0.942 mmol) and K$_2$CO$_3$ (0.195 g, 1.41 mmol) in dry MeCN (20 cm^3). After stirring for 20 h the solvent was removed under reduced pressure. Water (10 cm^3) was added and the product was extracted into CHCl$_3$ (3 x 10 cm^3), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica with a gradient elution from 0-10 % MeOH in DCM to give an off-white solid (0.123 g, 0.491 mmol, 52 %). Mp 60-61 °C; $[\alpha]_D^{30}$ -51.0 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 251.1540, C$_{17}$H$_{19}$N$_2$ requires

251.1543); ν_{max} 3349, 3321, 3278, 3141, 3026, 2893, 2835, 2359, 2096, 1585, 1491, 1454, 1435, 1341, 1307, 1290, 1261, 1204, 1155, 1105, 1072, 1055, 1026, 1003, 986, 917, 855, 797, 758, 695 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.11-7.24 (10H, m, Ar), 3.98 (2H, s, CH), 3.38 (1H, dd, J 2.6 17.0, CHH), 3.07 (1H, dd, J 2.6 17.0, CHH), 2.17 (1H, t, J 2.6, CH$_2$CCH), 1.95 (3H, broad s, NH); δ_C (75 MHz, CDCl$_3$) 143.4, 140.0, 128.12, 128.11, 128.0, 127.2, 126.9, 126.8, 82.1, 71.2, 67.6, 61.5, 35.8; m/z (ESMS+) 251 [M + H]$^+$.

(R,R)-N-Propargyl-N'-tert-butoxycarbonyl-1,2-diphenylethylenediamine, **(R,R)-191**.
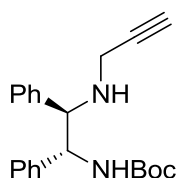
This compound is novel. Boc anhydride (0.05 cm^3, 0.218 mmol), was added to a solution of **(R,R)-190** (46.0 mg, 0.184 mmol) in dry Et$_2$O (3 cm^3) and left to stir for 3.5 h. The reaction was quenched with a 1 M NaOH solution (10 cm^3) and the product was extracted into Et$_2$O (3 x 10 cm^3), dried over MgSO$_4$, filtered and the solvent was removed under reduced pressure. The product was purified by column chromatography on silica with a gradient elution from 0-20 % EtOAc in pet. ether to give a white solid (55.0 mg, 0.157 mmol, 86 %). Mp 77-79 °C; $[\alpha]_D^{26}$ -25.1 (c 0.5 in CHCl$_3$) (R,R); (Found (ESI): M$^+$ + H 351.2066, C$_{22}$H$_{27}$N$_2$O$_2$ requires 351.2067); ν_{max} 3378, 3292, 3030, 2930, 2852, 2363, 1686, 1508, 1453, 1390, 1364, 1356, 1291, 1244, 1166, 1114, 1072, 1009, 914, 872, 849, 774, 756, 698 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.20-7.36 (10H, m, Ar), 5.56 (1H, broad s, NHBoc), 4.90 (1H, broad s, CHNHBoc), 4.23 (1H, broad s, CHNHCH$_2$), 3.32 (1H, dd, J 2.3 17.3,

C*H*H), 3.04 (1H, dd, *J* 2.3 17.3, CH*H*), 2.14 (1H, t, *J* 2.3, CH$_2$CC*H*), 1.67 (1H, broad s, N*H*CH$_2$), 1.11-1.42 (9H, broad s, C(C*H$_3$*)$_3$); δ_C (75 MHz, CDCl$_3$) 155.5, 140.2, 138.9, 128.4, 128.3, 128.0, 127.6, 127.2, 126.5, 81.5, 79.4, 71.5, 65.3, 59.5, 35.6, 28.2; *m/z* (ESMS+) 351 [M + H]$^+$.

(*R,R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N'*-*tert*-butoxycarbonyl-1,2-diphenylethylenediamine, **(*R,R*)-187**.
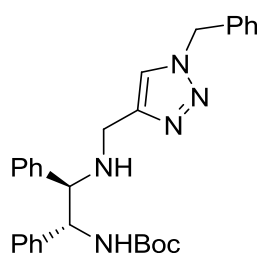
This compound is novel. Compound **(*R,R*)-187** was made by the same procedure as for **(*R,R*)-186** using **(*R,R*)-191** (55.0 mg, 0.157 mmol), benzyl azide (25.0 mg, 0.188 mmol), Cu(OAc)$_2$ (2.9 mg, 16.0 μmol) and sodium ascorbate (6.2 mg, 31.3 μmol). The product was purified by column on silica with a gradient elution from 0-10 % MeOH in DCM to give a white solid (61.0 mg, 0.126 mmol, 80 %). Mp 140-143 °C; [α]$_D^{26}$ +5.5 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 484.2707, C$_{29}$H$_{34}$N$_5$O$_2$ requires 484.2707); ν$_{max}$ 3380, 3061, 3031, 2929, 2837, 2362, 1685, 1507, 1453, 1389, 1364, 1354, 1294, 1246, 1165, 1122, 1073, 1052, 1028, 1011, 914, 871, 847, 753, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.34-7.40 (3H, m, Ar), 7.17-7.25 (10H, m, Ar), 7.10-7.15 (2H, m, Ar), 7.07 (1H, s, N$_3$C*H*), 5.63-5.69 (1H, m, N*H*Boc), 5.39-5.51 (2H, m, C*H$_2$*Ph), 4.80 (1H, broad s, C*H*NHBoc), 3.90-3.96 (1H, m, C*H*NHCH$_2$), 3.71 (1H, d, *J* 14.3, NHC*H*H), 3.54 (1H, d, *J* 14.3, NHCH*H*), 1.98 (1H, broad s, N*H*CH$_2$), 1.33 (9H, broad s, C*H$_3$*); δ_C (75 MHz, CDCl$_3$) 155.5, 146.8,

139.6, 134.7, 129.0, 128.6, 128.3, 128.2, 127.9, 127.8, 127.4, 127.1, 126.5, 121.3, 79.3, 66.5, 59.7, 53.9, 42.1, 28.2; *m/z* (ESMS+) 484 [M + H]$^+$.

R,R)-*N*-Benzyl-*N'-tert*-butoxylcarbonyl-1,2-diaminocyclohexane, (***R,R***)-**192**.
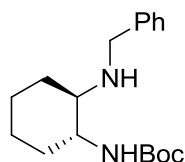
This compound is novel. Glacial acetic acid (3 drops) was added to a mixture of

(***R,R***)-**168** (51.0 mg, 0.238 mmol), benzaldehyde (29.0 μL, 0.285 mmol) and 4 Å

molecular sieves (0.5 g) in dry MeOH (5 cm^3). After stirring for 1 h 20 mins

NaBH$_3$CN (45.0 mg, 0.716 mmol) was added and the mixture was left to stir for a

further 18 h before filtration and removal of the solvent under reduced pressure.

The residue was dissolved in CHCl$_3$ (20 cm^3), washed with a saturated NaHCO$_3$

solution (20 cm^3), dried over MgSO$_4$, filtered, and the solvent was removed *in*

vacuo. The product was purified by column chromatography on silica with a

gradient elution from 0-80 % EtOAc in pet. ether to give a pale yellow solid (42.0

mg, 0.138 mmol, 58 %). Mp 99-100 °C; $[\alpha]_D^{29}$ -12.1 (c 0.5 in CHCl$_3$) (*R,R*); (Found

(ESI): M$^+$ + H 305.2222, C$_{18}$H$_{29}$N$_2$O$_2$ requires 305.2224); ν_{max} 3355, 2923, 2853,

2362, 2324, 1678, 1524, 1446, 1390, 1365, 1317, 1254, 1235, 1169, 1043, 1015,

911, 867, 849, 730, 697 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.13-7.28 (5H, m, Ar), 4.44

(1H, broad s, N*H*Boc), 3.84 (1H, d, *J* 12.8, C*H*H), 3.61 (1H, d, *J* 12.8, CH*H*), 3.19-

3.35 (1H, m, C*H*NHBoc), 2.20 (1H, td, *J* 3.8 10.2, C*H*NHCH$_2$), 1.97-2.09 (2H, m,

C*H*$_2$), 1.70 (1H, s, N*H*CH$_2$), 1.56-1.68 (2H, m, C*H*$_2$), 1.38 (9H, s, C(C*H*$_3$)$_3$), 0.97-

1.28 (4H, m, C*H*$_2$); δ_C (75 MHz, CDCl$_3$) 156.0, 140.9, 128.3, 128.0, 126.7, 79.1,

60.5, 54.2, 50.4, 32.9, 31.5, 28.4, 24.8, 24.6; *m/z* (ESMS+) 305 [M + H]$^+$.

(*R,R*)-*N*-Benzyl-*N'*-4-toluenesulphonyl-1,2-diphenylethylenediamine, **(*R,R*)-193**.
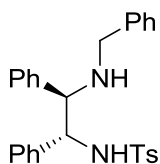
This compound is known and has been fully characterised.[196] Compound **(*R,R*)-193** was made by the same procedure as for **(*R,R*)-186** using (*R,R*)-TsDPEN (0.100 g, 0.273 mmol), glacial acetic acid (3 drops), benzaldehyde (33.0 μL, 0.325 mmol), 4 Å molecular sieves (0.7 g), and NaBH$_3$CN (51.0 mg, 0.812 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-100 % EtOAc in pet. ether to give a white solid (80.0 mg, 0.175 mmol, 64 %). Mp 130-131 °C; $[\alpha]_D^{30}$ -29.6 (c 0.5 in CHCl$_3$) (*R,R*) (lit.[196] $[\alpha]_D^{20}$ -33 (c 0.5 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 457.1945, C$_{28}$H$_{29}$N$_2$O$_2$S requires 457.1944); ν_{max} 3246, 3060, 3027, 2927, 2846, 2363, 1600, 1492, 1453, 1438, 1375, 1328, 1239, 1219, 1198, 1185, 1158, 1097, 1059, 1040, 1024, 975, 916, 840, 807, 761, 737, 697, 671 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.35-7.41 (2H, m, Ar), 7.25-7.32 (3H, m, Ar), 7.13-7.19 (5H, m, Ar), 6.90-7.08 (9H, m, Ar), 6.18 (1H, broad s, N*H*Ts), 4.32 (1H, d, *J* 7.5, C*H*H), 3.70 (1H, d, *J* 7.5, CH*H*), 3.63 (1H, d, *J* 13.2, C*H*NHTs), 3.42 (1H, d, *J* 13.2, C*H*NHBn), 2.32 (3H, s, CH$_3$), 1.73 (1H, broad s, N*H*Bn); δ_C (75 MHz, CDCl$_3$) 142.7, 139.3, 138.8, 138.2, 136.9, 129.0, 128.4, 128.4, 128.0, 127.9, 127.6, 127.5, 127.4, 127.2, 127.1, 127.0, 66.7, 63.1, 50.8, 21.4; *m/z* (ESMS+) 457 [M + H]$^+$.

(R,R)-N-Propargyl-N-methyl-N'-4-toluenesulphonyl-1,2-diphenylethylenediamine, (**R,R)-198**.
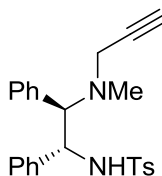
This compound is novel. Compound (**R,R)-198** was made by the same procedure as for (**R,R)-192** using (**R,R)-189** (0.251 g, 0.621 mmol), glacial acetic acid (3 drops), paraformaldehyde (37.0 mg, 1.23 mmol), 4 Å molecular sieves (0.6 g), and NaBH$_3$CN (0.117 g, 1.86 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-10 % EtOAc in pet. ether to give a white solid (59.0 mg, 0.141 mmol, 23 %). Mp 106-110 °C; $[\alpha]_D^{29}$ -18.1 (c 0.5 in CHCl$_3$) (R,R); (Found (ESI): M$^+$ + H 419.1803, C$_{25}$H$_{27}$N$_2$O$_2$S requires 419.1788); ν_{max} 3294, 3031, 2924, 2805, 2359, 1598, 1494, 1453, 1349, 1314, 1265, 1184, 1152, 1092, 1055, 1018, 972, 930, 851, 810, 760, 734, 698, 663 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.48-7.54 (2H, m, Ar), 7.13-7.22 (5H, m, Ar), 7.06-7.12 (2H, m, Ar), 6.91-7.03 (5H, m, Ar), 6.59 (1H, broad s, N*H*Ts), 4.66 (1H, d, *J* 10.9, C*H*NHTs), 4.00 (1H, d, *J* 10.9, C*H*NMe), 3.11 (1H, dd, *J* 2.3 16.2, C*H*H), 2.92 (1H, dd, *J* 2.3 16.2, CH*H*), 2.34 (3H, s, C$_6$H$_4$C*H*$_3$), 2.30 (1H, t, *J* 2.3, CC*H*), 2.09 (3H, s, NHC*H*$_3$); δ_C (75 MHz, CDCl$_3$) 142.7, 138.0, 137.0, 130.7, 129.7, 129.0, 128.4, 127.9, 127.8, 127.6, 127.3, 127.1, 79.6, 73.3, 70.0, 57.0, 43.3, 36.0, 21.4; *m/z* (ESMS+) 419 [M + H]$^+$.

(*R,R*)-*N*-Propargyl-*N*'-4-toluenesulphonyl-*N*'methyl-1,2-diphenylethylenediamine, **(R,R)-199**.
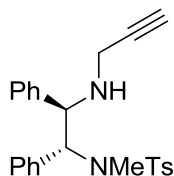
This compound is novel. Compound **(R,R)-199** was made by the same procedure as for **(R,R)-170** using **(R,R)-189** (0.200 g, 0.494 mmol), iodomethane (31.0 μL, 0.498 mmol) and K_2CO_3 (0.103 g, 0.745 mmol). The product was purified by column chromatography on silica with a gradient elution from 0-10 % EtOAc in pet. ether to give a white solid (0.115 g, 0.275 mmol, 56 %). Mp 128-131 °C; $[\alpha]_D^{32}$ -61.2 (c 1.0 in CHCl₃) (*R,R*); (Found (ESI): M⁺ + H 419.1783, $C_{25}H_{27}N_2O_2S$ requires 419.1788); ν_{max} 3318, 3201, 3028, 2917, 1598, 1493, 1444, 1333, 1304, 1269, 1209, 1193, 1157, 1110, 1087, 1073, 1044, 1029, 1017, 952, 924, 861, 837, 809, 775, 758, 696, 663 cm⁻¹; δ_H (300 MHz, CDCl₃) 7.68-7.74 (2H, m, Ar), 7.41-7.47 (2H, m, Ar), 7.27-7.35 (5H, m, Ar), 7.19-7.25 (5H, m, Ar), 5.48 (1H, d, *J* 10.6, C*H*NMeTs), 4.67 (1H, d, *J* 10.6, C*H*NHCH₂), 3.66 (1H, dd, *J* 2.3 17.7, C*H*H), 3.16 (1H, dd, *J* 2.3 17.7, CH*H*), 3.08 (3H, s, NC*H₃*), 2.53 (3H, s, C₆H₄C*H₃*), 2.46 (1H, t, *J* 2.3, CC*H*), 2.30 (1H, broad s, N*H*); δ_C (75 MHz, CDCl₃) 143.0, 138.7, 136.3, 134.9, 129.2, 129.1, 129.0, 128.1, 127.8, 127.6, 127.5, 127.4, 82.2, 71.5, 65.8, 59.4, 35.0, 29.3, 21.4; *m/z* (ESMS+) 419 [M + H]⁺.

(*R*,*R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N*-methyl-*N'*-4-toluenesulphonyl-1,2-diphenylethylenediamine, **(*R*,*R*)-196**.
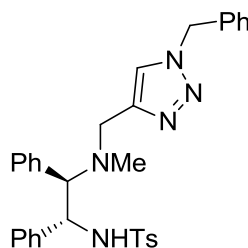

This compound is novel. Compound **(*R*,*R*)-196** was made by the same procedure as for **(*R*,*R*)-186** using **(*R*,*R*)-198** (55.0 mg, 0.131 mmol), benzyl azide (21.0 mg, 0.158 mmol), Cu(OAc)$_2$ (3.0 mg, 16.5 μmol) and sodium ascorbate (6.0 mg, 30.3 μmol). The product was purified by column on silica with a gradient elution from 0-6 % MeOH in DCM to give a white solid (67.0 mg, 0.121 mmol, 92 %). $[\alpha]_D^{26}$ +1.2 (c 0.5 in CHCl$_3$) (*R*,*R*); (Found (ESI): M$^+$ + H 552.2448, C$_{32}$H$_{34}$N$_5$O$_2$S requires 552.2428); ν_{max} 3031, 2938, 1598, 1495, 1453, 1323, 1266, 1184, 1152, 1093, 1048, 1028, 932, 812, 761, 732, 698, 664 cm^{-1}; δ_H (300 MHz, CDCl$_3$) 7.68 (1H, s, N$_3$C*H*), 7.29-7.42 (7H, m, Ar), 7.14-7.21 (3H, m, Ar), 6.96-7.04 (4H, m, Ar), 6.84-6.93 (5H, m, Ar), 5.56 (2H, s, C*H*$_2$Ph), 4.74 (1H, d, *J* 10.9, C*H*NH), 3.71 (1H, d, *J* 10.9, C*H*NMe), 3.65 (1H, d, *J* 13.9, C*H*H), 3.46 (1H, d, *J* 13.9, CH*H*), 2.30 (3H, s, C$_6$H$_4$C*H*$_3$), 2.07 (3H, s, NC*H*$_3$); δ_C (75 MHz, CDCl$_3$) 145.5, 142.7, 137.7, 137.0, 134.8, 131.0, 129.8, 129.0, 128.8, 128.6, 128.2, 127.9, 127.8, 127.5, 127.1, 127.0, 126.6, 122.7, 71.1, 57.1, 54.1, 48.1, 37.0, 21.3; *m*/*z* (ESMS+) 552 [M + H]$^+$.

(*R,R*)-*N*-(1-Benzyl-4-methylene-1,2,3-triazole)-*N'*-4-toluenesulphonyl-*N'*-methyl-1,2-diphenylethylenediamine, **(*R,R*)-197**.
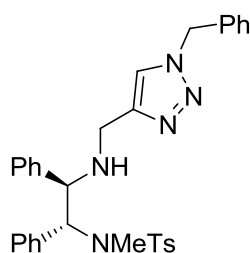

This compound is novel. Compound **(*R,R*)-197** was made by the same procedure as for **(*R,R*)-186** using **(*R,R*)-199** (0.104 g, 0.249 mmol), benzyl azide (40.0 mg, 0.300 mmol), Cu(OAc)$_2$ (5.0 mg, 27.5 µmol) and sodium ascorbate (10.0 mg, 50.5 µmol). The product was purified by column on silica with a gradient elution from 0-10 % MeOH in DCM to give a white solid (0.134 g, 0.243 mmol, 98 %). Mp 57-60 °C; $[\alpha]_D^{27}$ -6.6 (c 0.4 in CHCl$_3$) (*R,R*); (Found (ESI): M$^+$ + H 552.2425, C$_{32}$H$_{34}$N$_5$O$_2$S requires 552.2428); ν_{max} 3028, 2365, 1598, 1494, 1453, 1327, 1215, 1157, 1087, 1046, 1028, 943, 862, 838, 812, 750, 697, 662 cm^{-1}; δ_H (400 MHz, CDCl$_3$) 7.58-7.63 (2H, m, Ar), 7.41-7.47 (4H, m, Ar), 7.36-7.39 (2H, m, Ar), 7.27-7.31 (2H, m, Ar), 7.03-7.20 (9H, m, Ar), 6.96-6.99 (1H, m, N$_3$C*H*), 5.58 (2H, s, C*H*$_2$Ph), 5.38 (1H, d, *J* 10.5, C*H*NMeTs), 4.27 (1H, d, *J* 10.5, C*H*NH), 3.85 (1H, d, *J* 14.6, C*H*H), 3.70 (1H, d, *J* 14.6, CH*H*), 2.74 (3H, s, NC*H*$_3$), 2.48 (1H, broad s, N*H*), 2.39 (3H, s, C$_6$H$_4$C*H*$_3$); δ_C (100 MHz, CDCl$_3$) 147.3, 142.8, 139.4, 136.4, 136.1, 134.8, 129.7, 129.1, 128.9, 128.6, 128.4, 127.9, 127.8, 127.6, 127.4, 127.2, 127.1, 121.8, 65.7, 60.4, 53.8, 41.4, 29.1, 21.2; *m/z* (ESMS+) 552 [M + H]$^+$.

General Procedure for the Reduction of Ketones with 1,2,3-triazole ligands.

Dry 2-propanol (6 cm^3) was added to a vessel charged with Ru$_3$(CO)$_{12}$ (1.8 mg, 2.82 µmol) and **(R,R)-186** (4.6 mg, 8.56 µmol) and the mixture was heated at 80 °C. After 30 mins acetophenone (0.103 g, 0.857 mmol) in dry 2-propanol (2.5 cm^3) was added. The reaction was monitored by chiral GC.

(*R*)-1-Phenylethanol.
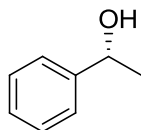
(*R*)-1-Phenylethanol. Colourless oil. $[\alpha]_D^{25}$ +49.4 (c 0.45 in CHCl$_3$) 92 % e.e (*R*) (lit.[131] $[\alpha]_D^{22}$ +49.0 (c 1.0 in CHCl$_3$) 98 % e.e. (*R*); δ_H (300 MHz, CDCl$_3$) 7.25-7.41 (5H, m, Ar), 4.90 (1H, q, *J* 6.4, C*H*), 1.82 (1H, broad s, O*H*), 1.50 (3H, d, *J* 6.4, C*H*$_3$). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 µm, T = 115 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, ketone 9.2 min, *R* isomer 14.0 min, *S* isomer 15.2 min.

(*R*)-1-(4-Trifluoromethylphenyl)ethanol.
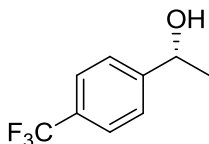
(*R*)-1-(4-Trifluoromethylphenyl)ethanol. Colourless oil. $[\alpha]_D^{25}$ +35.0 (c 0.3 in CHCl$_3$) 91 % e.e (*R*) (lit.[238] $[\alpha]_D^{22}$ +27.0 (c 0.4 in MeOH) 88 % e.e. (*R*); δ_H (300 MHz, CDCl$_3$) 7.58-7.63 (2H, m, Ar), 7.47-7.52 (2H, m, Ar), 4.97 (1H, q, *J* 6.4,

C*H*), 1.88 (1H, broad s, O*H*), 1.51 (3H, d, *J* 6.4, C*H*$_3$). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 130 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, ketone 6.4 min, *R* isomer 12.6 min, *S* isomer 13.8 min.

(*R*)-1-(4-Methoxyphenyl)ethanol.
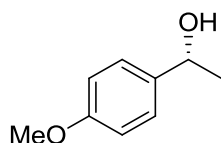
(*R*)-1-(4-Methoxyphenyl)ethanol. Colourless oil. $[\alpha]_D^{27}$ +46.7 (c 0.5 in CHCl$_3$) 89 % e.e (*R*) (lit.[239] $[\alpha]_D^{27}$ +32.3 (c 1.0 in CHCl$_3$) 90 % e.e. (*R*); δ$_H$ (300 MHz, CDCl$_3$) 7.58-7.63 (2H, m, Ar), 7.47-7.52 (2H, m, Ar), 4.97 (1H, q, *J* 6.4, C*H*), 1.88 (1H, broad s, O*H*), 1.51 (3H, d, *J* 6.4, C*H*$_3$). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 130 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, ketone 27.1 min, *R* isomer 29.3 min, *S* isomer 30.8 min.

(*R*)-1-(3-Methoxyphenyl)ethanol.

(*R*)-1-(3-Methoxyphenyl)ethanol. Colourless oil. $[\alpha]_D^{28}$ +41.0 (c 0.4 in CHCl$_3$) 93 % e.e (*R*) (lit.[132] $[\alpha]_D^{22}$ -30.9 (c 0.85 in MeOH) 94 % e.e. (*S*); δ$_H$ (300 MHz, CDCl$_3$) 7.17-7.24 (1H, m, Ar), 6.87-6.91 (2H, m, Ar), 6.73-6.78 (1H, m, Ar), 4.82 (1H, q, *J* 6.4, C*H*), 3.76 (3H, s, OC*H*$_3$), 1.82 (1H, broad s, O*H*), 1.43 (3H, d, *J* 6.4, C*H*$_3$). Conversion and enantiomeric excess were determined by chiral GC analysis:

(Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 130 °C, P = 15 psi H_2, det = FID 220 °C, inj = 220 °C, ketone 18.7 min, *R* isomer 30.1 min, *S* isomer 32.1 min.

(*R*)-1-(2-Methoxyphenyl)ethanol.
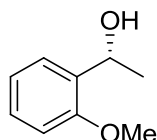
(*R*)-1-(2-Methoxyphenyl)ethanol. Colourless oil. $[\alpha]_D^{28}$ +21.1 (c 0.5 in $CHCl_3$) 85 % e.e (*R*) (lit.[240] $[\alpha]_D^{31}$ +38.7 (c 0.67 in $CHCl_3$) 71 % e.e. (*R*); δ_H (300 MHz, $CDCl_3$) 7.32-7.37 (1H, m, Ar), 7.22-7.28 (1H, m, Ar), 6.94-7.00 (1H, m, Ar), 6.87-6.91 (1H, m, Ar), 5.10 (1H, q, *J* 6.4, C*H*), 3.87 (3H, s, OC*H₃*), 2.67 (1H, broad s, O*H*), 1.52 (3H, d, *J* 6.4, C*H₃*). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 130 °C, P = 15 psi H_2, det = FID 220 °C, inj = 220 °C, ketone 18.1 min, *S* isomer 24.0 min, *R* isomer 24.9 min.

(*R*)-1-(2-Fluorophenyl)ethanol.
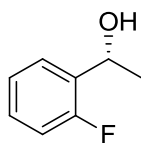
(*R*)-1-(2-Fluorophenyl)ethanol. Colourless oil. $[\alpha]_D^{28}$ +35.0 (c 0.6 in $CHCl_3$) 85 % e.e (*R*) (lit.[134] $[\alpha]_D^{20}$ +44.4 (c 1.0 in $CHCl_3$) 92 % e.e. (*R*); δ_H (300 MHz, $CDCl_3$) 7.46-7.52 (1H, m, Ar), 7.21-7.28 (1H, m, Ar), 7.12-7.18 (1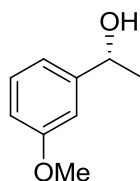H, m, Ar), 6.98-7.05 (1H, m, Ar), 5.20 (1H, q, *J* 6.4, C*H*), 1.97 (1H, broad s, O*H*), 1.52 (3H, d, *J* 6.4, C*H₃*). Conversion and enantiomeric excess were determined by chiral GC analysis:

(Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 120 °C, P = 15 psi H_2, det = FID 220 °C, inj = 220 °C, ketone 6.4 min, *R* isomer 12.6 min, *S* isomer 13.5 min.

(*R*)-1-(2-Chlorophenyl)ethanol.
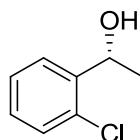
(*R*)-1-(2-Chlorophenyl)ethanol. Colourless oil. $[\alpha]_D^{28}$ +46.0 (c 0.55 in $CHCl_3$) 84 % e.e (*R*) (lit.[238] $[\alpha]_D^{24}$ +44.0 (c 0.4 in $CHCl_3$) 67 % e.e. (*R*); δ_H (300 MHz, $CDCl_3$) 7.52-7.57 (1H, m, Ar), 7.12-7.30 (3H, m, Ar), 5.25 (1H, q, *J* 6.4, C*H*), 1.96 (1H, broad s, O*H*), 1.44 (3H, d, *J* 6.4, C*H*₃). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 150 °C, P = 15 psi H_2, det = FID 220 °C, inj = 220 °C, ketone 6.8 min, *R* isomer 10.7 min, *S* isomer 11.9 min.

(*R*)-1-(2-Bromophenyl)ethanol.
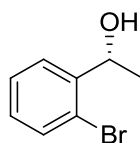
 (*R*)-1-(2-Bromophenyl)ethanol. Colourless oil. $[\alpha]_D^{29}$ +35.6 (c 0.60 in $CHCl_3$) 77 % e.e (*R*) (lit.[238] $[\alpha]_D^{24}$ +32.7 (c 0.8 in $CHCl_3$) 64 % e.e. (*R*); δ_H (300 MHz, $CDCl_3$) 7.57-7.62 (1H, m, Ar), 7.49-7.54 (1H, m, Ar), 7.31-7.38 (1H, m, Ar), 7.09-7.16 (1H, m Ar), 5.24 (1H, q, *J* 6.4, C*H*), 2.03 (1H, broad s, O*H*), 1.49 (3H, d, *J* 6.4, C*H*₃). Conversion and enantiomeric excess were determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 145 °C, P =

15 psi H$_2$, det = FID 220 °C, inj = 220 °C, ketone 11.0 min, *R* isomer 19.2 min, *S* isomer 23.3 min.

(*R*)-1-Cyclohexylethanol.
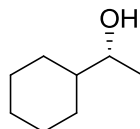
(*R*)-1-Cyclohexylethanol. Colourless oil. [α]$_D$ not measured due to low e.e. δ$_H$ (300 MHz, CDCl$_3$) 3.54 (1H, q, *J* 6.4, C*H*OH), 1.62-1.89 (5H, m, cyclohexyl), 1.42 (1H, broad s, O*H*), 1.10-1.31 (4H, m, cyclohexyl), 1.15 (3H, d, *J* 6.4, C*H*$_3$), 0.88-1.09 (2H, m, cyclohexyl). Conversion was determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 80 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, ketone 28.4 min, alcohol 57.1 min. Enantiomeric excess was determined by chiral GC analysis of the acetate derivative: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 115 °C, P = 15 psi H$_2$, det = FID 220 °C, inj = 220 °C, *S* isomer 12.1 min, *R* isomer 13.1 min. Preparation of derivative: Acetic anhydride (20 μL) was added to a solution of the reduction product (10 mg) and DMAP (3 crystals) in DCM (1 cm^3). After stirring overnight the solvent was removed under reduced pressure to give the acetate derivative.

(*R*)-1-Tetralol.
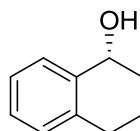
(*R*)-1-Tetralol. The compound was not isolated and the optical rotation was not measured due to low conversion. Conversion and enantiomeric excess were

determined by chiral GC analysis: (Chrompac cyclodextrin-β-236M-19 50 m x 0.25 mm x 0.25 μm, T = 120 °C, P = 15 psi H_2, det = FID 220 °C, inj = 220 °C, ketone 42.7 min, *S* isomer 58.4 min, *R* isomer 60.3 min.

4 References.

1. K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc*, 1946, 39-45.

2. J. C. Collins, W. W. Hess and F. J. Frank, *Tetrahedron Lett*, 1968, **9**, 3363-3366.

3. E. J. Corey and J. W. Suggs, *Tetrahedron Lett*, 1975, **16**, 2647-2650.

4. S. Ball, T. W. Goodwin and R. A. Morton, *Biochem. J*, 1948, **42**, 516.

5. K. Omura and D. Swern, *Tetrahedron*, 1978, **34**, 1651-1660.

6. K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc*, 1963, **85**, 3027-3028.

7. J. R. Parikh and W. v. E. Doering, *J. Am. Chem. Soc*, 1967, **89**, 5505-5507.

8. C. Liu, J. S. Ng, J. R. Behling, C. H. Yen, A. L. Campbell, K. S. Fuzail, E. E. Yonan and D. V. Mehrotra, *Org. Process Res. Dev*, 1997, **1**, 45-54.

9. M. Frigerio and M. Santagostino, *Tetrahedron Lett*, 1994, **35**, 8019-8022.

10. D. B. Dess and J. C. Martin, *J. Org. Chem*, 1983, **48**, 4155-4156.

11. P. Lucio Anelli, C. Biffi, F. Montanari and S. Quici, *J. Org. Chem*, 1987, **52**, 2559-2562.

12. C. Bilgrien, S. Davis and R. S. Drago, *J. Am. Chem. Soc*, 1987, **109**, 3786-3787.

13. J.-E. Bäckvall, R. L. Chowdhury and U. Karlsson, *J. Chem. Soc., Chem. Commun*, 1991, 473-475.

14. G.-Z. Wang, U. Andreasson and J.-E. Bäckvall, *J. Chem. Soc., Chem. Commun*, 1994, 1037-1038.

15. A. Hanyu, E. Takezawa, S. Sakaguchi and Y. Ishii, *Tetrahedron Lett*, 1998, **39**, 5557-5560.

16. P. Müller and J. Godoy, *Tetrahedron Lett*, 1981, **22**, 2361-2364.

17. K. B. Sharpless, K. Akashi and K. Oshima, *Tetrahedron Lett*, 1976, **17**, 2503-2506.

18. S. V. Ley, J. Norman, W. P. Griffith and S. P. Marsden, *Synthesis*, 1994, 639-666.

19. A. B. Jones, *J. Org. Chem*, 1992, **57**, 4361-4367.

20.   S. W. Chaikin and W. G. Brown, *J. Am. Chem. Soc*, 1949, **71**, 122-125.

21.   R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc*, 1947, **69**, 1197-1199.

22.   S. M. Capitosti, T. P. Hansen and M. L. Brown, *Bioorg. Med. Chem*, 2004, **12**, 327-336.

23.   M. M. Midland, D. C. McDowell, R. L. Hatch and A. Tramontano, *J. Am. Chem. Soc*, 1980, **102**, 867-869.

24.   M. M. Midland, S. Greer, A. Tramontano and S. A. Zderic, *J. Am. Chem. Soc*, 1979, **101**, 2352-2355.

25.   C. Byung Tae, *Tetrahedron*, 2006, **62**, 7621-7643.

26.   E. J. Corey, R. K. Bakshi, S. Shibata, C. P. Chen and V. K. Singh, *J. Am. Chem. Soc*, 1987, **109**, 7925-7926.

27.   T. Ohkuma, H. Ooka, S. Hashiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*, 1995, **117**, 2675-2676.

28.   T. Ohkuma, H. Ooka, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*, 1995, **117**, 10417-10418.

29.   H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya and R. Noyori, *Angew. Chem. Int. Ed*, 1998, **37**, 1703-1707.

30.   R. Noyori and H. Takaya, *Acc. Chem. Res*, 1990, **23**, 345-350.

31.   H. Meerwein and R. Schmidt, *Justus Liebigs Ann. Chem*, 1925, **444**, 221-238.

32.   W. Ponndorf, *Angew. Chem*, 1926, **39**, 138-143.

33.   M. Verley, *Bull. Soc. Chim. Fr*, 1925, **37**, 871-874.

34.   R. V. Oppenauer, *Recl. Trav. Chim. Pays-Bas*, 1937, **56**, 137-144.

35.   R. Kow, R. Nygren and M. W. Rathke, *J. Org. Chem*, 1977, **42**, 826-827.

36.   K. G. Akamanchi and V. R. Noorani, *Tetrahedron Lett*, 1995, **36**, 5085-5088.

37.   K. Konishi, K. Makita, T. Aida and S. Inoue, *J. Chem. Soc., Chem. Commun*, 1988, 643-645.

38.   Y.-C. Liu, B.-T. Ko, B.-H. Huang and C.-C. Lin, *Organometallics*, 2002, **21**, 2066-2069.

39.   T. Ooi, H. Ichikawa and K. Maruoka, *Angew. Chem. Int. Ed*, 2001, **40**, 3610-3612.

40. E. J. Campbell, H. Zhou and S. T. Nguyen, *Angew. Chem. Int. Ed*, 2002, **41**, 1020-1022.

41. D. A. Evans, S. G. Nelson, M. R. Gagne and A. R. Muci, *J. Am. Chem. Soc*, 1993, **115**, 9800-9801.

42. C. Djerassi, A. J. Manson and M. Gorman, *J. Am. Chem. Soc*, 1955, **77**, 4925-4926.

43. R. Uson, L. A. Oro, R. Sariego and M. A. Esteruelas, *J. Organomet. Chem*, 1981, **214**, 399-404.

44. R. L. Chowdhury and J.-E. Bäckvall, *J. Chem. Soc., Chem. Commun*, 1991, 1063-1064.

45. D. Morton and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun*, 1988, 1154-1156.

46. O. Pàmies and J.-E. Bäckvall, *Chem. Eur. J*, 2001, **7**, 5052-5058.

47. S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*, 1995, **117**, 7562-7563.

48. K.-J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya and R. Noyori, *Angew. Chem. Int. Ed*, 1997, **36**, 285-288.

49. R. Noyori, M. Yamakawa and S. Hashiguchi, *J. Org. Chem*, 2001, **66**, 7931-7944.

50. S. Chakraborty and H. Guan, *Dalton Trans*, 2010, **39**, 7427-7436.

51. G. Z. Wang and J.-E. Bäckvall, *J. Chem. Soc., Chem. Commun*, 1992, 337-339.

52. R. H. Meijer, G. B. W. L. Ligthart, J. Meuldijk, J. A. J. M. Vekemans and L. A. Hulshof, *J. Mol. Catal. A: Chem*, 2004, **218**, 29-40.

53. N. A. Abdelaziz, *Tetrahedron Lett*, 2001, **42**, 13-15.

54. K.-I. Fujita, S. Furukawa and R. Yamaguchi, *J. Organomet. Chem*, 2002, **649**, 289-292.

55. F. Hanasaka, K.-I. Fujita and R. Yamaguchi, *Organometallics*, 2004, **23**, 1490-1492.

56. F. Hanasaka, K.-I. Fujita and R. Yamaguchi, *Organometallics*, 2005, **24**, 3422-3433.

57. F. Hanasaka, K.-I. Fujita and R. Yamaguchi, *Organometallics*, 2006, **25**, 4643-4647.

58. D. Morales-Morales, R. O. Redón, Z. Wang, D. W. Lee, C. Yung, K. Magnuson and C. M. Jensen, *Can. J. Chem*, 2001, **79**, 823-829.

59. R. Levy, C. Azerraf, D. Gelman, K. Rueck-Braun and P. N. Kapoor, *Catal. Commun*, 2009, **11**, 298-301.

60. C. Azerraf and D. Gelman, *Chem. Eur. J*, 2008, **14**, 10364-10368.

61. T. Suzuki, K. Morita, M. Tsuchida and K. Hiroi, *J. Org. Chem*, 2003, **68**, 1601-1602.

62. Ana C. da Silva, H. Piotrowski, P. Mayer, K. Polborn and K. Severin, *Eur. J. Inorg. Chem*, 2001, **2001**, 685-691.

63. S. B. Gauthier, R. Scopelliti and K. Severin, *Organometallics*, 2004, **23**, 3769-3771.

64. J. A. Turner, *Science*, 2004, **305**, 972-974.

65. T. C. Johnson, D. J. Morris and M. Wills, *Chem. Soc. Rev*, 2010, **39**, 81-88.

66. A. Dobson and S. D. Robinson, *J. Organomet. Chem*, 1975, **87**, C52-C53.

67. A. Dobson and S. D. Robinson, *Inorg. Chem*, 1977, **16**, 137-142.

68. W. K. Rybak and J. J. Ziolkowski, *J. Mol. Catal*, 1981, **11**, 365-370.

69. C. W. Jung and P. E. Garrou, *Organometallics*, 1982, **1**, 658-666.

70. J. van Buijtenen, J. Meuldijk, J. A. J. M. Vekemans, L. A. Hulshof, H. Kooijman and A. L. Spek, *Organometallics*, 2006, **25**, 873-881.

71. H. Junge and M. Beller, *Tetrahedron Lett*, 2005, **46**, 1031-1034.

72. H. Junge, B. Loges and M. Beller, *Chem. Commun*, 2007, 522-524.

73. G. R. A. Adair and J. M. J. Williams, *Tetrahedron Lett*, 2005, **46**, 8233-8235.

74. A. Prades, E. Peris and M. Albrecht, *Organometallics*, 2011, **30**, 1162-1167.

75. K.-I. Fujita, N. Tanino and R. Yamaguchi, *Org. Lett*, 2006, **9**, 109-111.

76. R. Yamaguchi, C. Ikeda, Y. Takahashi and K.-I. Fujita, *J. Am. Chem. Soc*, 2009, **131**, 8410-8412.

77. A. M. Royer, T. B. Rauchfuss and D. L. Gray, *Organometallics*, 2010, **29**, 6763-6768.

78. H. Li, G. Lu, J. Jiang, F. Huang and Z.-X. Wang, *Organometallics*, 2011, **30**, 2349-2363.

79. K.-I. Fujita, T. Yoshida, Y. Imori and R. Yamaguchi, *Org. Lett*, 2011, **13**, 2278-2281.

80. A. M. Royer, T. B. Rauchfuss and S. R. Wilson, *Inorg. Chem*, 2007, **47**, 395-397.

81. W. Baratta, G. Bossi, E. Putignano and P. Rigo, *Chem. Eur. J*, 2011, **17**, 3474-3481.

82. J. Zhang, M. Gandelman, L. J. W. Shimon, H. Rozenberg and D. Milstein, *Organometallics*, 2004, **23**, 4026-4033.

83. J. Zhang, M. Gandelman, L. J. W. Shimon and D. Milstein, *Dalton Trans*, 2007, 107-113.

84. M. Nielsen, A. Kammer, D. Cozzula, H. Junge, S. Gladiali and M. Beller, *Angew. Chem. Int. Ed*, 2011, **50**, 9593-9597.

85. S. Musa, I. Shaposhnikov, S. Cohen and D. Gelman, *Angew. Chem. Int. Ed*, 2011, **50**, 3533-3537.

86. E. Delgado-Lieta, M. A. Luke, R. F. Jones and D. J. Cole-Hamilton, *Polyhedron*, 1982, **1**, 839-840.

87. D. Morton and D. J. Cole-Hamilton, *J. Chem. Soc., Chem. Commun*, 1987, 248-249.

88. D. Morton, D. J. Cole-Hamilton, I. D. Utuk, M. Paneque-Sosa and M. Lopez-Poveda, *J. Chem. Soc., Dalton Trans*, 1989, 489-495.

89. S. Shinoda, H. Moriyama, Y. Kise and Y. Saito, *J. Chem. Soc., Chem. Commun*, 1978, 348-349.

90. H. Moriyama, T. Aoki, S. Shinoda and Y. Saito, *J. Chem. Soc., Perkin Trans. 2*, 1982, 369-374.

91. T. Yamakawa, H. Miyake, H. Moriyama, S. Shinoda and Y. Saito, *J. Chem. Soc., Chem. Commun*, 1986, 326-327.

92. K. Nomura, Y. Saito and S. Shinda, *J. Mol. Catal*, 1989, **50**, 303-313.

93. H. Arakawa and Y. Sugi, *Chem. Lett*, 1981, 1323-1326.

94. C. G. Griggs and D. J. H. Smith, *J. Organomet. Chem*, 1984, **273**, 105-109.

95. H. Adkins, R. M. Elofson, A. G. Rossow and C. C. Robinson, *J. Am. Chem. Soc*, 1949, **71**, 3622-3629.

96. K. Wagner, *Angew. Chem. Int. Ed*, 1970, **9**, 50-54.

97. A. Fujii, S. Hashiguchi, N. Uematsu, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*, 1996, **118**, 2521-2522.

98. D. Müller, G. Umbricht, B. Weber and A. Pfaltz, *Helv. Chim. Acta*, 1991, **74**, 232-240.

99. Y. Jiang, Q. Jiang and X. Zhang, *J. Am. Chem. Soc*, 1998, **120**, 3817-3818.

100. Y. Jiang, Q. Jiang, G. Zhu and X. Zhang, *Tetrahedron Lett*, 1997, **38**, 215-218.

101. N. J. Lawrence and S. M. Bushell, *Tetrahedron Lett*, 2000, **41**, 4507-4512.

102. Y. Nishibayashi, I. Takei, S. Uemura and M. Hidai, *Organometallics*, 1999, **18**, 2291-2293.

103. A. Naik, T. Maji and O. Reiser, *Chem. Commun*, 2010, **46**, 4475-4477.

104. J.-B. Sortais, V. Ritleng, A. Voelklin, A. Holuigue, H. Smail, L. Barloy, C. Sirlin, G. K. M. Verzijl, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries and M. Pfeffer, *Org. Lett*, 2005, **7**, 1247-1250.

105. P. Gamez, F. Fache, P. Mangeney and M. Lamaire, *Tetrahedron Lett*, 1993, **34**, 6897-6898.

106. P. Gamez, F. Fache and M. Lemaire, *Tetrahedron: Asymmetry*, 1995, **6**, 705-718.

107. S.-I. Inoue, K. Nomura, S. Hashiguchi, R. Noyori and Y. Izawa, *Chem. Lett*, 1997, **26**, 957-958.

108. L. Schwink, T. Ireland, K. Püntener and P. Knochel, *Tetrahedron: Asymmetry*, 1998, **9**, 1143-1163.

109. M. Aitali, S. Allaoud, A. Karim, C. Meliet and A. Mortreux, *Tetrahedron: Asymmetry*, 2000, **11**, 1367-1374.

110. J.-X. Gao, T. Ikariya and R. Noyori, *Organometallics*, 1996, **15**, 1087-1089.

111. P. Krasik and H. Alper, *Tetrahedron*, 1994, **50**, 4347-4354.

112. N. Meyer, A. J. Lough and R. H. Morris, *Chem. Eur. J*, 2009, **15**, 5605-5610.

113. P. E. Sues, A. J. Lough and R. H. Morris, *Organometallics*, 2012, **30**, 4418-4431.

114. C. Sui-Seng, F. N. Haque, A. Hadzovic, A.-M. Pütz, V. Reuss, N. Meyer, A. J. Lough, M. Zimmer-De Iuliis and R. H. Morris, *Inorg. Chem*, 2008, **48**, 735-743.

115. J. Yutong, J. Qiongzhong, Z. Guoxin and Z. Xumu, *Tetrahedron Lett*, 1997, **38**, 6565-6568.

116. Q. Jiang, D. Van Plew, S. Murtuza and X. Zhang, *Tetrahedron Lett*, 1996, **37**, 797-800.

117. A. Bøgevig, I. M. Pastor and H. Adolfsson, *Chem. Eur. J*, 2004, **10**, 294-302.

118. A. B. Zaitsev and H. Adolfsson, *Org. Lett*, 2006, **8**, 5129-5132.

119. K. Ahlford, M. Livendahl and H. Adolfsson, *Tetrahedron Lett*, 2009, **50**, 6321-6324.

120. K. Ahlford, J. Ekström, A. B. Zaitsev, P. Ryberg, L. Eriksson and H. Adolfsson, *Chem. Eur. J*, 2009, **15**, 11197-11209.

121. H. Brunner, F. Henning and M. Weber, *Tetrahedron: Asymmetry*, 2002, **13**, 37-42.

122. M. T. Reetz and X. Li, *J. Am. Chem. Soc*, 2006, **128**, 1044-1045.

123. W. Baratta, G. Chelucci, E. Herdtweck, S. Magnolia, K. Siega and P. Rigo, *Angew. Chem. Int. Ed*, 2007, **46**, 7651-7654.

124. J. Takehara, S. Hashiguchi, A. Fujii, S.-I. Inoue, T. Ikariya and R. Noyori, *Chem. Commun*, 1996, 233-234.

125. M. Palmer, T. Walsgrove and M. Wills, *J. Org. Chem*, 1997, **62**, 5226-5228.

126. D. A. Alonso, D. Guijarro, P. Pinho, O. Temme and P. G. Andersson, *J. Org. Chem*, 1998, **63**, 2749-2751.

127. S. J. M. Nordin, P. Roth, T. Tarnai, D. A. Alonso, P. Brandt and P. G. Andersson, *Chem. Eur. J*, 2001, **7**, 1431-1436.

128. K. Matsumura, S. Hashiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*, 1997, **119**, 8738-8739.

129. K. Murata, K. Okano, M. Miyagi, H. Iwane, R. Noyori and T. Ikariya, *Org. Lett*, 1999, **1**, 1119-1121.

130. A. M. Hayes, D. J. Morris, G. J. Clarkson and M. Wills, *J. Am. Chem. Soc*, 2005, **127**, 7318-7319.

131. F. K. Cheung, C. Lin, F. Minissi, A. L. Crivillé, M. A. Graham, D. J. Fox and M. Wills, *Org. Lett*, 2007, **9**, 4659-4662.

132. D. J. Morris, A. M. Hayes and M. Wills, *J. Org. Chem*, 2006, **71**, 7035-7044.

133. V. Parekh, J. A. Ramsden and M. Wills, *Catal. Sci. Tech*, 2012, **2**, 406-414.

134. T. Touge, T. Hakamata, H. Nara, T. Kobayashi, N. Sayo, T. Saito, Y. Kayaki and T. Ikariya, *J. Am. Chem. Soc*, 2011, **133**, 14960-14963.

135. K. Mashima, T. Abe and K. Tani, *Chem. Lett*, 1998, 1199-1200.

136. K. Murata, T. Ikariya and R. Noyori, *J. Org. Chem*, 1999, **64**, 2186-2187.

137. D. S. Matharu, D. J. Morris, A. M. Kawamoto, G. J. Clarkson and M. Wills, *Org. Lett*, 2005, **7**, 5489-5491.

138. D. S. Matharu, D. J. Morris, G. J. Clarkson and M. Wills, *Chem. Commun*, 2006, 3232-3234.

139. B. L. Conley, M. K. Pennington-Boggio, E. Boz and T. J. Williams, *Chem. Rev*, 2010, **110**, 2294-2312.

140. Y. Blum, D. Reshef and Y. Shvo, *Tetrahedron Lett*, 1981, **22**, 1541-1544.

141. Y. Blum and Y. Shvo, *J. Organomet. Chem*, 1984, **263**, 93-107.

142. Y. Blum and Y. Shvo, *Isr. J. Chem*, 1984, **24**, 144.

143. Y. Blum and Y. Shvo, *J. Organomet. Chem*, 1985, **282**, C7-C10.

144. Y. Shvo, D. Czarkie, Y. Rahamim and D. F. Chodosh, *J. Am. Chem. Soc*, 1986, **108**, 7400-7402.

145. M. I. Bruce and J. R. Knight, *J. Organomet. Chem*, 1968, **12**, 411-413.

146. C. T. Sears Jr and F. G. A. Stone, *J. Organomet. Chem*, 1968, **11**, 644-646.

147. Y. Shvo and D. Czarkie, *J. Organomet. Chem*, 1986, **315**, C25-C28.

148. C. P. Casey, J. B. Johnson, S. W. Singer and Q. Cui, *J. Am. Chem. Soc*, 2005, **127**, 3100-3109.

149. C. P. Casey, S. W. Singer, D. R. Powell, R. K. Hayashi and M. Kavana, *J. Am. Chem. Soc*, 2001, **123**, 1090-1100.

150. J. B. Johnson and J.-E. Bäckvall, *J. Org. Chem*, 2003, **68**, 7681-7684.

151. A. Comas-Vives, G. Ujaque and A. Lledós, *Organometallics*, 2007, **26**, 4135-4144.

152. M. L. S. Almeida, M. Beller, G.-Z. Wang and J.-E. Bäckvall, *Chem. Eur. J*, 1996, **2**, 1533-1536.

153. M. L. S. Almeida, P. Kocovský and J.-E. Bäckvall, *J. Org. Chem*, 1996, **61**, 6587-6590.

154. U. Karlsson, G. Z. Wang and J. E. Bäckvall, *J. Org. Chem*, 1994, **59**, 1196-1198.

155. J. H. Choi, N. Kim, Y. J. Shin, J. H. Park and J. Park, *Tetrahedron Lett*, 2004, **45**, 4607-4610.

156. H. M. Jung, J. H. Choi, S. O. Lee, Y. H. Kim, J. H. Park and J. Park, *Organometallics*, 2002, **21**, 5674-5677.

157. N. Menashe, E. Salant and Y. Shvo, *J. Organomet. Chem*, 1996, **514**, 97-102.

158. Y. Blum, D. Czarkie, Y. Rahamim and Y. Shvo, *Organometallics*, 1985, **4**, 1459-1461.

159. C. P. Casey, N. A. Strotman, S. E. Beetner, J. B. Johnson, D. C. Priebe, T. E. Vos, B. Khodavandi and I. A. Guzei, *Organometallics*, 2006, **25**, 1230-1235.

160. C. P. Casey, N. A. Strotman, S. E. Beetner, J. B. Johnson, D. C. Priebe and I. A. Guzei, *Organometallics*, 2006, **25**, 1236-1244.

161. L. Koren-Selfridge, H. N. Londino, J. K. Vellucci, B. J. Simmons, C. P. Casey and T. B. Clark, *Organometallics*, 2009, **28**, 2085-2090.

162. A. L. E. Larsson, B. A. Persson and J.-E. Bäckvall, *Angew. Chem. Int. Ed*, 1997, **36**, 1211-1212.

163. B. A. Persson, A. L. E. Larsson, M. l. Le Ray and J.-E. Bäckvall, *J. Am. Chem. Soc*, 1999, **121**, 1645-1650.

164. H. M. Jung, J. H. Koh, M.-J. Kim and J. Park, *Org. Lett*, 2000, **2**, 409-411.

165. H. M. Jung, J. H. Koh, M.-J. Kim and J. Park, *Org. Lett*, 2000, **2**, 2487-2490.

166. J. H. Choi, Y. H. Kim, S. H. Nam, S. T. Shin, M.-J. Kim and J. Park, *Angew. Chem. Int. Ed*, 2002, **41**, 2373-2376.

167. J. H. Choi, Y. K. Choi, Y. H. Kim, E. S. Park, E. J. Kim, M.-J. Kim and J. Park, *J. Org. Chem*, 2004, **69**, 1972-1977.

168. C. P. Casey, T. E. Vos, S. W. Singer and I. A. Guzei, *Organometallics*, 2002, **21**, 5038-5046.

169. J. Washington, R. McDonald, J. Takats, N. Menashe, D. Reshef and Y. Shvo, *Organometallics*, 1995, **14**, 3996-4003.

170. C. P. Casey and H. Guan, *J. Am. Chem. Soc*, 2007, **129**, 5816-5817.

171. D. J. Morris, G. J. Clarkson and M. Wills, *Organometallics*, 2009, **28**, 4133-4140.

172. A. Majewski, D. J. Morris, K. Kendall and M. Wills, *ChemSusChem*, 2010, **3**, 431-434.

173. A. Wolfson, C. Dlugy, Y. Shotland and D. Tavor, *Tetrahedron Lett*, 2009, **50**, 5951-5953.

174.   E. Farnetti, J. Kaspar and C. Crotti, *Green Chem*, 2009, **11**, 704-709.

175.   A. J. Pearson, R. J. Shively and R. A. Dubbert, *Organometallics*, 1992, **11**, 4096-4104.

176.   M. R. Burke, T. Funk, J. Takats and V. W. Day, *Organometallics*, 1994, **13**, 2109-2112.

177.   M. K. Thorson, K. L. Klinkel, J. Wang and T. J. Williams, *Eur. J. Inorg. Chem*, 2009, 295-302.

178.   G. N. Schrauzer, *J. Am. Chem. Soc*, 1959, **81**, 5307-5310.

179.   H.-J. Knölker, E. Baum, H. Goesmann and R. Klauss, *Angew. Chem. Int. Ed*, 1999, **38**, 2064-2066.

180.   S. Ogoshi, T. Kato, M. Ohashi and H. Kurosawa, *Dalton Trans*, 2008, 2232-2234.

181.   C. P. Casey, M. W. Meszaros, S. M. Neumann, I. G. Cesa and K. J. Haller, *Organometallics*, 1985, **4**, 143-149.

182.   C. P. Casey and S. M. Neumann, *J. Am. Chem. Soc*, 1978, **100**, 2544-2545.

183.   D. A. Brown, W. K. Glass and M. T. Ubeid, *Inorg. Chim. Acta*, 1984, **89**, L47-L48.

184.   T.-Y. Luh, *Coord. Chem. Rev*, 1984, **60**, 255-276.

185.   N. A. Bailey, V. S. Jassal, R. Vefghi and C. White, *J. Chem. Soc., Dalton Trans*, 1987, 2815-2822.

186.   C. P. Casey and H. Guan, *J. Am. Chem. Soc*, 2009, **131**, 2499-2507.

187.   A. J. Pearson and R. J. Shively, *Organometallics*, 1994, **13**, 578-584.

188.   M. G. Coleman, A. N. Brown, B. A. Bolton and H. Guan, *Adv. Synth. Catal*, 2010, **352**, 967-970.

189.   S. A. Moyer and T. W. Funk, *Tetrahedron Lett*, 2010, **51**, 5430-5433.

190.   O. Saidi, M. J. Bamford, A. J. Blacker, J. Lynch, S. P. Marsden, P. Plucinski, R. J. Watson and J. M. J. Williams, *Tetrahedron Lett*, 2010, **51**, 5804-5806.

191.   A. Berkessel, S. Reichau, A. von der Höh, N. Leconte and J. R.-M. Neudörfl, *Organometallics*, 2011, **30**, 3880-3887.

192.   Y. Yamamoto, K. Yamashita and M. Nakamura, *Organometallics*, 2010, **29**, 1472-1478.

193.   C. J. Taylor, M. Motevalli and C. J. Richards, *Organometallics*, 2006, **25**, 2899-2902.

194.   J. N. Abrams, Q. Zhao, I. Ghiviriga and Minaruzzaman, *Tetrahedron*, 2012, **68**, 423-428.

195.   E. R. Graham and R. R. Tykwinski, *J. Org. Chem*, 2011, **76**, 6574-6583.

196.   J. E. D. Martins and M. Wills, *Tetrahedron: Asymmetry*, 2008, **19**, 1250-1255.

197.   T. L. Mindt, C. Schweinsberg, L. Brans, A. Hagenbach, U. Abram, D. Tourwé, E. Garcia-Garayoa and R. Schibli, *ChemMedChem*, 2009, **4**, 529-539.

198.   E. Haak, *Eur. J. Org. Chem*, 2007, 2815-2824.

199.   E. Haak, *Eur. J. Org. Chem*, 2008, 788-792.

200.   S. Berger and E. Haak, *Tetrahedron Lett*, 2010, **51**, 6630-6634.

201.   N. Thies, C. G. Hrib and E. Haak, *Chem. Eur. J*, 2012, **18**, 6302-6308.

202.   H. Tye, C. Eldred and M. Wills, *Tetrahedron Lett*, 2002, **43**, 155-158.

203.   H. Struthers, T. L. Mindt and R. Schibli, *Dalton Trans*, 2010, **39**, 675-696.

204.   V. O. Rodionov, S. I. Presolski, S. Gardinier, Y.-H. Lim and M. G. Finn, *J. Am. Chem. Soc*, 2007, **129**, 12696-12704.

205.   D. Liu, W. Gao, Q. Dai and X. Zhang, *Org. Lett*, 2005, **7**, 4907-4910.

206.   R. J. Detz, S. A. V. Heras, R. de Gelder, P. W. N. M. van Leeuwen, H. Hiemstra, J. N. H. Reek and J. H. van Maarseveen, *Org. Lett*, 2006, **8**, 3227-3230.

207.   F. Tinnis and H. Adolfsson, *Org. Biomol. Chem*, 2010, **8**, 4536-4539.

208.   X. C. Cambeiro and M. A. Pericàs, *Adv. Synth. Catal*, 2011, **353**, 113-124.

209.   H. Zhang, C.-B. Yang, Y.-Y. Li, Z.-R. Donga, J.-X. Gao, H. Nakamura, K. Murata and T. Ikariya, *Chem. Commun*, 2003, 142-143.

210.   E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cederbaum, D. R. Swanson and T. Takahashi, *J. Am. Chem. Soc*, 1989, **111**, 3336-3346.

211.   H.-J. Zhang, Z. Song, C. Wang, C. Bruneau and Z. Xi, *Tetrahedron Lett*, 2008, **49**, 624-627.

212.   Z. Xi and Q. Song, *J. Org. Chem*, 2000, **65**, 9157-9159.

213.   P. A. Wender, T. J. Paxton and T. J. Williams, *J. Am. Chem. Soc*, 2006, **128**, 14814-14815.

214. J. Wu, X.-L. Hou and L.-X. Dai, *J. Org. Chem*, 2000, **65**, 1344-1348.

215. J. Tan, W. Tang, Y. Sun, Z. Jiang, F. Chen, L. Xu, Q. Fan and J. Xiao, *Tetrahedron*, 2011, **67**, 6206-6213.

216. A. Dijksman, J. M. Elzinga, Y.-X. Li, I. W. C. E. Arends and R. A. Sheldon, *Tetrahedron: Asymmetry*, 2002, **13**, 879-884.

217. D. L. Boger, J. K. Lee, J. Goldberg and Q. Jin, *J. Org. Chem*, 2000, **65**, 1467-1474.

218. L. P. McDonnell Bushnell, E. R. Evitt and R. G. Bergman, *J. Organomet. Chem*, 1978, **157**, 445-456.

219. L. V. R. Bonaga, H.-C. Zhang and B. E. Maryanoff, *Chem. Commun*, 2004, 2394-2395.

220. J.-J. Lian, P.-C. Chen, Y.-P. Lin, H.-C. Ting and R.-S. Liu, *J. Am. Chem. Soc*, 2006, **128**, 11372-11373.

221. M. J. Mays, M. J. Morris, P. R. Raithby, Y. Shvo and D. Czarkie, *Organometallics*, 1989, **8**, 1162-1167.

222. K. Tamao, K. Kobayashi and Y. Ito, *J. Org. Chem*, 1989, **54**, 3517-3519.

223. K. Niknam, M. A. Zolfigol, D. Saberi and M. Khonbazi, *Chin. J. Chem*, 2009, **27**, 1548-1552.

224. M. Jereb, D. Vražič and M. Zupan, *Tetrahedron Lett*, 2009, **50**, 2347-2352.

225. H. Suezawa, T. Hashimoto, K. Tsuchinaga, T. Yoshida, T. Yuzuri, K. Sakakibara, M. Hirota and M. Nishio, *J. Chem. Soc., Perkin Trans. 2*, 2000, 1243-1249.

226. M. Schuler, F. Silva, C. Bobbio, A. Tessier and V. Gouverneur, *Angew. Chem. Int. Ed*, 2008, **47**, 7927-7930.

227. M. Algueró, J. Bosch, J. Castañer, J. Castellá, J. Castells, R. Mestres, J. Pascual and F. Serratosa, *Tetrahedron*, 1962, **18**, 1381-1394.

228. K. M. Erixon, C. L. Dabalos and F. J. Leeper, *Org. Biomol. Chem*, 2008, **6**, 3561-3572.

229. R. Luque and D. J. Macquarrie, *Org. Biomol. Chem*, 2009, **7**, 1627-1632.

230. N. A. Cortez, G. Aguirre, M. Parra-Hake and R. Somanathan, *Tetrahedron Lett*, 2009, **50**, 2228-2231.

231. K. Takasu, T. Azuma, I. Enkhtaivan and Y. Takemoto, *Molecules*, 2010, **15**, 8327-8348.

232. R. L. Edwards, G. C. Elsworthy and N. Kale, *J. Chem. Soc. C*, 1967, 405-409.

233. A. C. Campbell, M. S. Maidment, J. H. Pick and D. F. M. Stevenson, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1567-1576.

234. N. Duguet, A. Donaldson, S. M. Leckie, E. A. Kallstrom, C. D. Campbell, P. Shapland, T. B. Brown, A. M. Z. Slawin and A. D. Smith, *Tetrahedron: Asymmetry*, 2010, **21**, 601-616.

235. S. Roland, P. Mangeney and A. Alexakis, *Synthesis*, 1999, **2**, 228-230.

236. C. D. Campbell, C. Concellón and A. D. Smith, *Tetrahedron: Asymmetry*, 2011, **22**, 797-811.

237. H. Ankati and E. Biehl, *Tetrahedron Lett*, 2009, **50**, 4677-4682.

238. J. E. D. Martins, M. A. Contreras Redondo and M. Wills, *Tetrahedron: Asymmetry*, 2010, **21**, 2258-2264.

239. J. R. M. Hannedouche, G. J. Clarkson and M. Wills, *J. Am. Chem. Soc*, 2004, **126**, 986-987.

240. C. V. Manville, G. Docherty, R. Padda and M. Wills, *Eur. J. Org. Chem*, 2011, 6893-6901.

5 Appendix.

5.1 X-ray Crystallography of 133b.
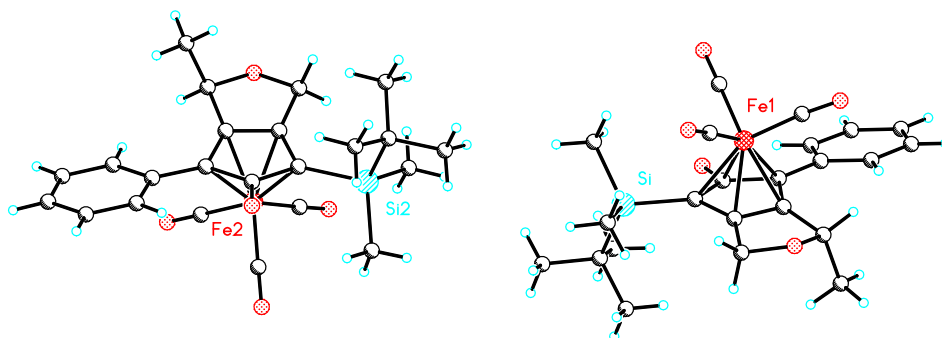
Picture showing the two crystallographically independent but chemically identical (enantiomers though) molecules in the solid state structure of **133b**.
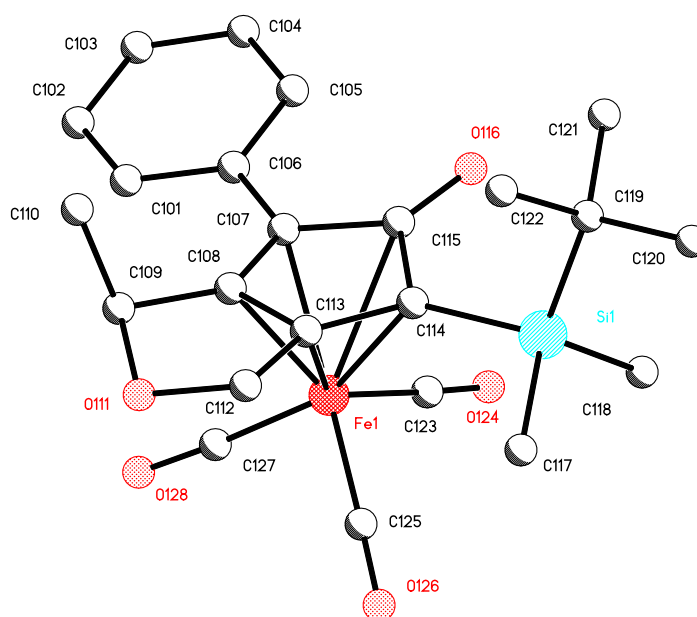
The Fe1 molecule in **133b** in close up showing atom labelling (which is the same in the Fe2 molecule only starting at 201).

The asymmetric unit contains two crystallographically independent but chemically identical complexes composed of a cyclopentadienone ether bound to an iron and three CO ligands. There are eight complexes in the unit cell.

Crystal Data.

C23 H26 Fe O5 Si, M = 466.38, Monoclinic, space group P2(1)/n

a = 23.8945(7), b = 7.1593(2), c = 27.4516(8) A,

alpha = 90 deg., beta = 106.380(3) deg., gamma = 90 deg.,

U = 4505.5(2) A^3 (by least squares refinement on 7326 reflection positions),

T =100(2)K, lambda = 0.71073 A, Z = 8,

D(cal) = 1.375 Mg/m^3, F(000) = 1952.

mu(MoK-alpha) = 0.753 mm^-1.

Crystal character:yellow block.

Crystal dimensions 0.25 x 0.08 x 0.04 mm.

Data Collection and Processing.

Oxford Diffraction Gemini four-circle system with Ruby CCD area detector.

The crystal was held at 100(2) K with the Oxford Cryosystem Cryostream Cobra.

Maximum theta was 29.35 deg.

The hkl ranges were -32/ 31, -9/ 9, -36/ 37.

44024 reflections measured, 11045 unique   [R(int) = 0.1002].

Absorption correction by Semi-empirical from equivalents;

Minimum and maximum transmission factors: 0.95, 1.00.

No crystal decay.

Structure Analysis and Refinement.

Systematic absences indicated space group.

P2(1)/n and shown to be correct by successful refinement.

The structure was solved by direct methods using SHELXS (Sheldrick, 1990) (TREF) with additional light atoms found by Fourier methods.

Hydrogen atoms were added at calculated positions and refined using a riding model with freely rotating methyl groups. Anisotropic displacement parameters were used for all non-H atoms; H-atoms were given isotropic displacement parameters equal to 1.2 (or 1.5 for methyl hydrogen atoms) times the equivalent isotropic displacement parameter of the atom to which the H-atom is attached.

The weighting scheme was calc $w=1/[\backslash s^2{}^\wedge(Fo^2{}^\wedge)+(0.0107P)^2{}^\wedge+0.0000P]$ where $P=(Fo^2{}^\wedge+2Fc^2{}^\wedge)/3$. Goodness-of-fit on F^2 was 0.745, R1[for 5020 reflections with I>2sigma(I)] = 0.0465, wR2 = 0.0582. Data / restraints / parameters 11045/ 108/ 552.

Largest difference Fourier peak and hole 0.992 and -0.561 e.A^-3.

Refinement used SHELXL 97 (Sheldrick, 1997).

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and the remaining bond lengths and angles.

The Oxford Diffraction Gemini XRD system was obtained through the Science City Advanced Materials project: Creating and Characterising Next Generation

Advanced Materials, with support from Advantage West Midlands (AWM) and part funded by the European Regional Development Fund (ERDF).

References.

For relevant information for the SHELXTL suite of programmes used to solve, refine and produce the files for this structure, please refer to "A Short History of Shelx, G. M. Sheldrick, Acta Cryst. 2008, 64, 112-122."

5.2 Ferrole Complexes.

During the synthesis of (cyclopentadienone)iron tricarbonyl complexes it was found that if the iron source, $Fe(CO)_5$, was substituted for $Fe_3(CO)_{12}$ then in most cases, the major product of the reaction ceased to be the expected cyclopentadienone complex but a bimetallic 'ferrole' complex was formed instead.
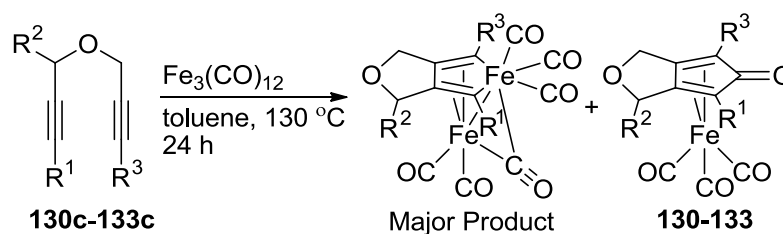
Ligand Precursor	Yield (%)	
	Ferrole	**Cyclopentadienone**
130c	39	18
131c	45	27
132c	42	25
133c	28	32

The ferrole complexes were formed as single diastereoisomers and could be isolated in impure form by column chromatography and one such complex derived from **132c** was recrystallised from an ether/2-propanol mixture and characterised by X-ray crystallography (section 5.2.1).

X = CH$_2$, NH, O
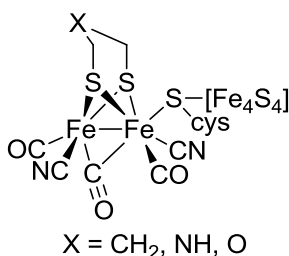
The active site of [FeFe]-hydrogenase enzymes. The identity of the X group has not been determined.

The structure shows some similarities with the structure of the active site of [FeFe]-hydrogenase enzymes which are known to catalyse the reduction of protons to dihydrogen. Many analogues of the [FeFe]-hydrogenase active site based on the dithiolate scaffold are known and have been demonstrated to catalyse proton reduction either photochemically with a photosensitiser and sacrificial electron donor or by electrolysis.

Studies on ferrole complexes by cyclic voltammetry were carried out by Dr. Massimo Peruffo and Professor Pat Unwin at the University of Warwick to evaluate their potential for the production of hydrogen from protons. It was found that a 2-electron reduction of the complex takes place and is irreversible; indicating decomposition. Studies under catalytic conditions in the presence of acid (acetic acid or trichloroacetic acid) showed a similar irreversible 2-electron reduction.

References.

For the structure of the active site of [FeFe]-hydrogenase enzymes see C. Tard and C.J. Pickett, *Chem. Rev.* 2009, **109**, 2245-2274.
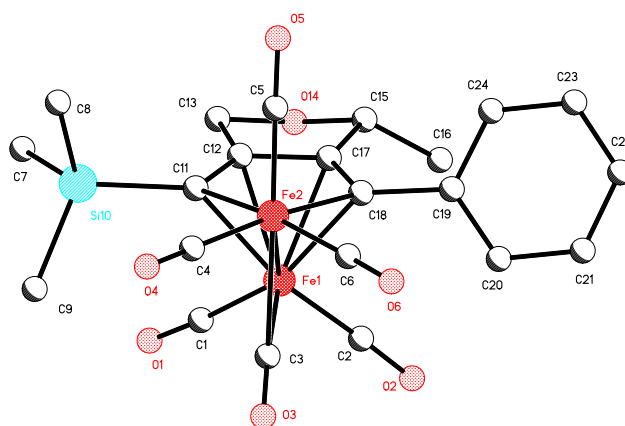
For catalysis with [FeFe]-hydrogenase analogues see:

Y. Na, J. Pan, M. Wang and L. Sun, *Inorg. Chem.* 2007, **46**, 3813-3815.

L.-C. Song, L.-X. Wang, M.-Y. Tang, C.-G. Li, H.-B. Song and Q.-M. Hu, *Organometallics* 2009, **28**, 3834-3841.

L.-C. Song, W. Gao, C.-P. Feng, D.-F. Wang and Q.-M. Hu, *Organometallics* 2009, **28**, 6121-6130.

5.2.1 X-ray Crystallography of a Ferrole Complex.

The X-ray crystal structure of a ferrole complex. Hydrogen atoms have been removed for clarity.

The asymmetric unit contains a diiron complex with a bridiging carbon monoxide. The sample is a racemic mixture containing both enantiomers. There is a warning for a close contact between the bridging CO oxygen and O5, the oxygen of a CO of

a neighbouring complex. The distance is 2.8172 (0.0023) Angstroms O3 - O5_$1

There is a short contact between the ether O14 and the CO (C1-O1) of a neghbouring complex 3.1258 (0.0027) Angstroms O14 - C1_$2.

Symmetry operators used to define atoms discussed in the above contact are

$1 1-x, 1-y, 1/2+z

$2 1/2-x, y, z-1/2

Crystal Data.

C22 H20 Fe2 O7 Si, M = 536.17, Orthorhombic, space group Pca2(1)

a = 16.5260(3), b = 10.3723(2), c = 13.1868(3) A,

alpha = 90 deg., beta = 90 deg., gamma = 90 deg.,

U = 2260.38(8) A^3 (by least squares refinement on 6298 reflection positions),

T =100(2)K, lambda = 0.71073 A, Z = 4,

D(cal) = 1.576 Mg/m^3, F(000) = 1096.

 mu(MoK-alpha) = 1.377 mm^-1.

 Crystal character:orange block.

 Crystal dimensions 0.30 x 0.18 x 0.18 mm,

Data Collection and Processing.

Oxford Diffraction Gemini four-circle system with Ruby CCD area detector.

The crystal was held at 100(2).

K with the Oxford Cryosystem Cryostream Cobra.

Maximum theta was 29.39 deg.

The hkl ranges were -22/ 16, -13/ 10, -13/ 16.

8814 reflections measured, 4737 unique   [R(int) = 0.0205].

Absorption correction by Semi-empirical from equivalents;

minimum and maximum transmission factors: 0.91; 1.00.

no crystal decay

Structure Analysis and Refinement.

Systematic absences indicated space group Pca2(1) or Pbcm.

The former was chosen on the basis of intensity statistics and shown to be correct

by successful refinement.

The structure was solved by direct methods using SHELXS (Sheldrick, 1990)

(TREF) with additional light atoms found by Fourier methods.

Hydrogen atoms were added at calculated positions and refined using a riding

model with freely rotating methyl groups. Anisotropic displacement parameters

were used for all non-H atoms; H-atoms were given isotropic displacement

parameters equal to 1.2 (or 1.5 for methyl hydrogen atoms) times the equivalent

isotropic displacement parameter of the atom to which the H-atom is attached.

The absolute structure of the individual crystal chosen was checked by refinement

of a delta-f" multiplier.

Absolute structure parameter x = 0.001(10).

Floating origin constraints were generated automatically.

The weighting scheme was calc w=1/[\s^2^(Fo^2^)+(0.0251P)^2^+0.0000P] where

P=(Fo^2^+2Fc^2^)/3.

Goodness-of-fit on F^2 was 0.958,

R1[for 4253 reflections with I>2sigma(I)] = 0.0242, wR2 = 0.0486.

Data / restraints / parameters 4737/ 1/ 293.

Largest difference Fourier peak and hole 0.379 and -0.280 e.A^-3.

Refinement used SHELXL 97 (Sheldrick, 1997).

Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom coordinates, thermal parameters and the remaining bond lengths and angles.

The Oxford Diffraction Gemini XRD system was obtained through the Science City Advanced Materials project: Creating and Characterising Next Generation Advanced Materials, with support from Advantage West Midlands (AWM) and part funded by the European Regional Development Fund (ERDF)

References.

For relevant information for the SHELXTL suite of programmes used to solve, refine and produce the files for this structure, please refer to "A Short History of Shelx, G. M. Sheldrick, Acta Cryst. 2008, 64, 112-122."