This thesis is submitted in part fulfilment for the degree award of

Doctor of Philosophy

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Loughborough University August 2010

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Abstract

Atropoisomerism of Nitrogen Based Ligands and Natural Products

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Key Words: Atropoisomerism, catalysis, palladium, amination, Buchwald-Hartwig, ligand, organocatalysis

This thesis details the attempt to design and synthesis a range of ligands and organocatalysts based on a common backbone design. Initial results were promising with a number of ligands being generated from our common C_2-symmetric backbone. Unfortunately none of the molecules synthesises gave promising results in test reactions. Variations on the initial design also failed to give any encouraging results.

More positively, work on phosphorus-nitrogen (P,N) ligands was successful, with a number of different ligands being synthesised and metal complexes prepared. Pleasingly we were able to obtain X-ray crystallography of one of these complexes indicating that the ligand was complexed to the metal *via* the phosphorus moiety.

Work using the Buchwald-Hartwig reaction for coupling aryl bromides to both 1,2,3,4-tetrahydroisoquinoline and 1,2,3,4-tetrahydroquinoline was successful, with methodology being developed which we believe can be applied to the synthesis of Ancistrocladinium A. In particular the coupling between 1,2,3,4-tetrahydroisoquinoline and 1-bromonaphthalene afforded us the full carbon skeleton of the ring system of the natural product in one step, from which we were able to generate the iminium salt. We also investigated an alternative route for the synthesis of Ancistrocladinium A achieving atropoisomerism.

Experimental data is provided in chapter three, and all X-ray crystallography structures reported in chapter two are provided in the appendix.

Acknowledgements

I would like to take this opportunity to thank both Dr Steve Christie and Professor Philip C. B. Page for giving me the opportunity to work within their groups and for their encouragement and guidance. I would also like to thank Dr Ben Buckley for the invaluable help and advice given over the last three years. A further thank you has to be extended to Dr Martin Smith for his considerable help with phosphorus chemistry.

I would also like to thank all the other members of the organic section who have given support and advice during my time at Loughborough, Dr Mark Elsegood for his help with X-ray crystallography, Dr Mark Edgar for his help with NMR, Al Daley for technical assistance, and to John Kershaw & Sheena Grainger for their assistance with Mass spectroscopy. A special mention has to go to Marion Dillon who has been my 'mum' of the chemistry department for the last 3 years.

Thanks also go to past and present members of F001 & F009, for the people who made day to day life in the lab fun, even when the chemistry wasn't working and for the F001 dance floor moments! For those who have to be named; first and foremost thank you to Laura for introducing me to the wonders of Ibsotck, for teaching me to be a good little chemist and for general entertainment value! Special thanks go to both Jess for living with me and making me smile, and to Hayley who despite 'borrowing' the majority of my glassware has been my friend for a very long time! To Stephen for never failing to answer the 'TEA!' summons, to my little French friend Céline merci beaucoup (is that some French?!) for being wonderful at chemistry and at being a friend and Rachel for providing fun times and far too much wine times! Beyond chemistry (if there is such a place) thank you to both Jennie & Heather for being the best friends I could ever ask for.

To my parents I would like to say thank you for their continued support and belief in me, even when I didn't believe in myself. I would not have succeeded without your love and support not just during my PhD but throughout my time at university. To my sisters Hayley & Lauren Rose; thank you for reminding me that there is more to life than chemistry and that life isn't to be taken too seriously. And finally to Carol & Dave my second parents, thank you for always being there for me.
This work has enjoyed the financial support of Loughborough University.

Abbreviations

Å	Ångström
Ac	acetyl
$[\alpha]_D$	specific optical rotation at the sodium D line
aq.	aqueous
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BINOL	1,1'-Bi-2-naphthol
Bn	benzyl
Boc	*tert*-butoxycarbonyl
bp	boiling point
bs	broad singlet
^{t}Bu	*tert*-butyl
°C	degrees Celsius
c	concentration
CIP	Chan, Ingold and Prelog
cm^{-1}	wavenumber
conc.	concentration
conv.	conversion
δ	chemical shift
d.	days
d	doublet
dd	doublet of doublets
dt	doublet of triplets
DABCO	1,4-diazabicyclo[2.2.2]octane
DMF	*N,N*-dimethylformamide
DMSO-d_6	dimethyl sulphoxide (deuteriated)
Δ	reflux
ee	enantiomeric excess
EI	electron impact
eq.	equivalent
ES	electrospray
Et	ethyl
FAB	fast atom bombardment

h	hour(s)
HEH	Hantzsch 1,4-dihydropyridine
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	hertz
g	gram(s)
IR	infra red
J	coupling constant
M	molar
m	multiplet
MAO	monoamine oxidase
MAP	2-dimethylamino-2'-diphenyl phosphine-1,1'-binaphthyl
Me	methyl
MHz	megahertz
min	minute(s)
mL	millilitres
mmol	millimole
mol	mole
m.p.	melting point
MS	molecular sieves
NADH	nicotinamide adenine dinucleotide
NBS	*N*-bromosuccinimide
NHC	*N*-heterocyclic carbene
nm	nanometers
NMR	nuclear magnetic resonance
nOe	nuclear Overhauser effect
Tf	trifluoromethanesulphonate
$pd_2(dba)_3$	tris(dibenzylideneacetone)dipalladium(0)
Ph	phenyl
ppm	parts per million
^{i}Pr	isopropyl
q	quartet
R	alkyl/acyl/aryl
R	Rictus

rt	room temperature
S	Sinister
s	singlet
sm	starting material
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilane
VT	variable temperature

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Appendix

1.0 Introduction

Catalysis is defined as the process in which the rate of a chemical reaction is increased by a substance, the catalyst, which itself is not affected during the reaction.[1] Generally, catalysts speed up a reaction by changing the reaction pathway to one with lower activation energy.

The development of methodologies for efficient asymmetric synthesis, that is the synthesis of compounds in which one enantiomer or diastereomer is favoured preferentially in the reaction, is one of the most important areas of synthetic organic chemistry.[2] Asymmetric synthesis has fundamental significance in biology and medicine; one of the main goals of organic chemists is the catalytic enantioselective formation of C-C and C-heteroatom bonds,[3] by the design of catalysts, which both speed up the rate of reaction and control the stereochemistry of the product formed.

Asymmetric synthesis can be described as a chemical reaction in which the product formed has a new element of chirality.[1] A molecule is described as being chiral if the mirror images of the molecule are non-superimposable; these different non-superimposable molecules are called enantiomers. If a molecule is superimposable on its mirror image then the molecule is described as achiral.

'Chirality is the geometric property of a rigid object (or spatial arrangement of points or atoms) being non-*superposable* on its mirror image; such an object has no symmetry elements of the second kind (a mirror plane, $\sigma = S_1$, a centre of inversion, $i = S_2$, a rotation-reflection axis, S_{2n}). If the object is superposable on its mirror image the object is described as being achiral.'[4]

Chan, Ingold and Prelog (CIP) developed a set of priority rules,[5] which allowed the absolute configuration at four coordinate and six coordinate stereogenic centres. The CIP priority rules are used to distinguish between enantiomers by assigning priority numbers to substituents around a chiral centre. A chiral centre is defined as:

'An atom holding a set of ligands in a spatial arrangement which is not superposable on its mirror image.'[4]

Molecules can be defined as *R* or *S* from use of CIP rules; R (Rectus) and S (Sinister), derived from the Latin for left and right, are used to distinguish between enantiomers (Figure 1, using σ-methylbenzylamine).

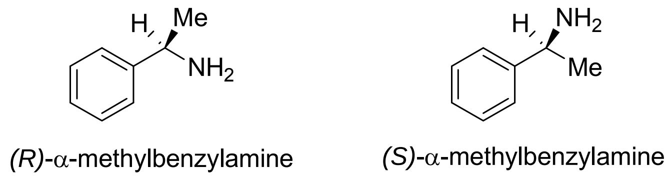


Figure 1

Enantiomers have the same physical properties, as well as the same NMR and IR spectra; however, they differ in optical rotation. Optical rotation is the ability of a material to rotate a plane of polarised light; if a molecule bends the light it is said to be optically active. Enantiomers which bend the light in a clockwise direction are called dextrorotary enantiomers and have the prefix (+); the opposite enantiomer is called the laevorotatory enantiomer and bends the light in an anti-clockwise direction, this is given the prefix (-).

Atropoisomerism is a chiral element, which is induced by lack of rotation around a single bond; this type of chirality is seen in molecules such as BINAP, which exists as atropoisomers (Figure 2).

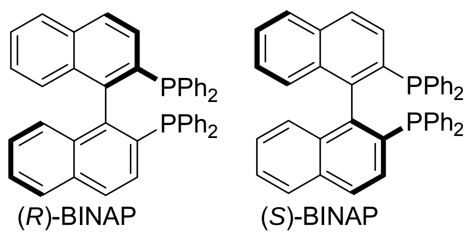


Figure 2

1.1 Phosphines

Phosphine ligands (PR_3 where R = alkyl, acyl or aryl) are omnipresent in the field of organometallic chemistry and have proved highly successful in both cross-coupling reactions as stabilising ligands and in nucleophilic catalysis. They are well known in such reactions as the Heck,[6] Stille-Suzuki,[7] and Buchwald-Hartwig,[8] and have proved to be very reactive and versatile ligands in these catalytic processes. In catalysis, phosphine ligands not only serve as simple ligands, being either monodentate or chelating, but can also be designed to carry functional groups that alter the properties of the catalyst. The phosphine ligand is a neutral two electron donor, which binds to transition metals through its lone pair.

Phosphine ligands are usually strong σ-donors and weak π-acceptors (Figure 3), σ-donor bonding can be increased by using electron-donating R- groups or π-acceptor backbonding increased by using electron-withdrawing R- groups.

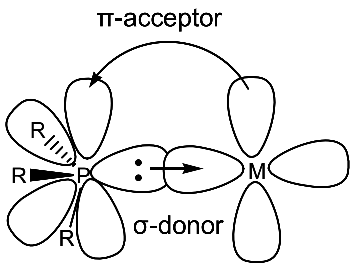


Figure 3

The ability to change functionality by changing R- groups is important for a class of ligands as it gives the ability to introduce a second weakly ligating atom and therefore provide a second coordination site; ligands which are able to do this are known as hemiliable ligands and are extremely useful.[9] The ability to use different R- groups also leads to the possibility of introducing chirality to the ligand. Most chiral phosphines are chiral in the carbon backbone and have two phosphorus atoms by which they bind to the metal (bidentate) e.g. BINAP.[9]

However, as a class of ligand, phosphines have one major limitation: when exposed to high temperatures and extreme conditions some ligands experience deactivation through a process called phosphine degradation.[10] This is where the phosphine ligand undergoes oxidation and deactivates the metal centre towards further catalysis. There have been a number of protection strategies devised for phosphine ligands including the use of BH_3 adducts or the use of the protonated form of the phosphine.[11,12]

Another method uses the oxidation of the trivalent phosphorus, however this requires the deprotection of the tertiary phosphine oxide, usually by the use of silane and although this method does create an air stable species, upon deprotection the phosphine is once again air sensitive, delaying the problem rather than solving it. Therefore, a search for a new class of ligand, which would be air stable and could be used in replace of phosphine ligands began.

1.2 – Carbenes

Carbenes $:CR_2$ (where R = alkyl, acyl, aryl, amine, etc) were first introduced into organic chemistry by Doering in the 1950s,[13] and into organometallic chemistry by Fischer in 1964.[14] Carbenes are a neutral but highly reactive species which are useful in introducing a single carbon atom into a molecule. The carbon of a carbene is divalent with only six electrons in its valance shell and can therefore be imagined in two distinct geometries: either with linear geometry or angular geometry. The linear geometry implies a sp-hybridised carbon centre with two non-bonding degenerate orbitals (p_x and p_y) whereas the bent geometry breaks this degeneracy allowing the carbon atom to adopt sp^2 type hybridisation, where the p_y orbital remains almost unchanged and is often referred to as p_π. The p_x orbital becomes stabilised due to its adopting s character and is often called σ. In most cases, the linear geometry is extreme and the carbene will adopt a bent structure.

The reactivity of the carbene comes from its electronic unsaturation i.e. a carbene carbon has four valence electrons, four valence orbitals and two valence bonds. Thus, a choice arises: either place one electron in each of the remaining orbitals (a triplet carbene) or put both into one orbital thus leaving one empty (a singlet carbene). Although there are two types of carbene, singlet and triplet, there are in fact four ways in which the electrons can be arranged, (Figure 4) three corresponding to the singlet carbene and one to the triplet. Two singlets arise from the two electrons being placed in either the sp^2 or p orbital (type 1 and 2) or one electron can sit in the p orbital and the other in the sp^2 orbital and can have parallel spin resulting in a triplet state (type 3) or have opposite spin thus giving an excited singlet (type 4).

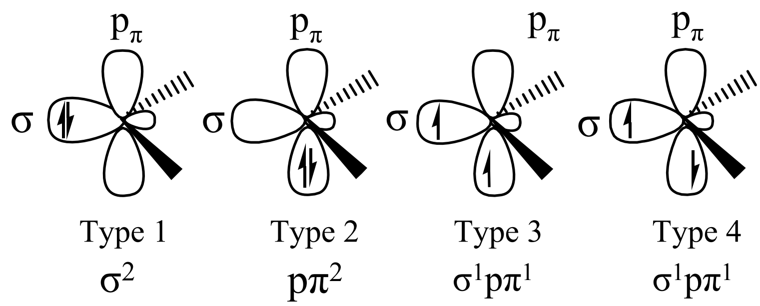


Figure 4

All carbenes can exist as either a singlet or a triplet, but for most the triplet is the most stable. The influence of the substituent electronegativities on the carbene multiplicity is well documented, and it is widely accepted that σ-electron withdrawing substituents favour the singlet state.[11] A good example of this was demonstrated by Harrison in 1971,[15] where the ground state of a carbene was changed from a triplet to a singlet by changing the substituent from an electropositive lithium to a proton and an electronegative fluorine. This effect was explained as:

"The σ-electron withdrawing substituents inductively stabilise the σ non-bonding orbital by increasing its s character and leave the p_π orbital unchanged. The σ-p_π gap is thus increased and the singlet state is favoured."[13]

For σ-electron donating substituents the opposite is true with the triplet state being favoured due to the substituents causing a small σ- p_π gap. As singlet carbenes feature both a filled and vacant orbital they exhibit ambiphilic character, showing both nucleophilic and electrophilic behaviour, whereas, triplets with two singularly occupied orbitals are more generally regarded as diradicals.[11]

Although synthetically useful, carbenes are highly reactive and non-isolable ligands, consequently, the main challenge is to synthesise a stable carbene that could be stored indefinitely without degrading. A stable carbene is defined as a carbene that is persistent at ambient temperature and can withstand temperatures as high as 200°C.[9] However, many "stable" carbenes are oxygen and moisture sensitive, with some being sensitive to chlorinated solvents.

Both Fischer and Shrock were able to generate carbenes which were stable within the coordination sphere of a transiting metal but both were unable to synthesise stable uncoordinated carbenes. A further attempt to isolate a stable carbene was by Wanzlick and was based on dihydroimidazole-2-ylidines which had been generated from 2-trichloromethyl dihydroimidazoles, (Figure 5).

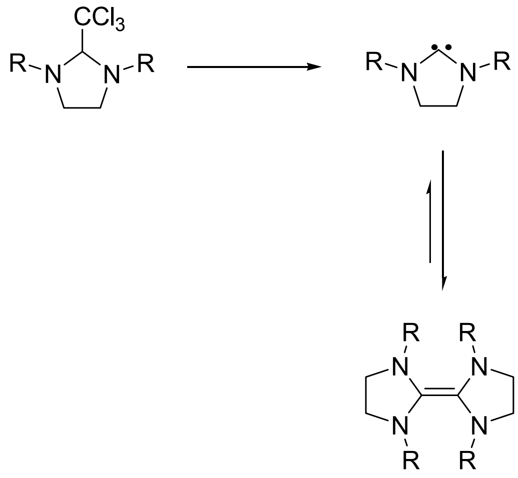


Figure 5

However, on preparation of these systems it was apparent that the carbenes existed in a state of equilibrium with the corresponding dimer;[16] this is known as the Wanzlick Equilibrium. Wanzlick also managed to synthesise bis[1,3-diphenyl-2-imidazolidinylidene] from the corresponding imidazoline (Figure 6) recognising that the aromatic resonance present in the five membered *N*-heterocyclic ring could help stabilise the carbene.

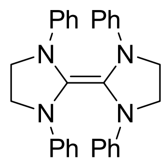
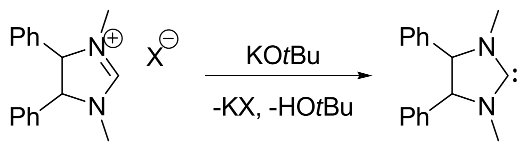


Figure 6

Although carbenes such as 1,3,4,5-tetraphenyl-2,3-diamino-1H-imidazole-2-ylidene (Scheme 1) were generated by the deprotonation of the corresponding imidazolium salt with potassium *tert*-butoxide, they were always reacted with isothiocyanates or metal precursors, resulting in a free carbene not being isolated until much later.[17]



Scheme 1

Upon isolation of the first stable *N*-heterocyclic carbene,[18] (NHCs), interest in these as ligands has grown rapidly. They were found to be much more electron-rich than phosphine ligands and when used in metal catalysis found to be more strongly bound.[9]

There are two main designs of NHC backbone. Type 1 has the carbene incorporated into an imidazole ring, whereas type 2 is the saturated counterpart, with the carbene integrated into an imidazoline ring, (Figure 7). Although many more subclasses of carbene have been developed most employ either of these common backbone types.

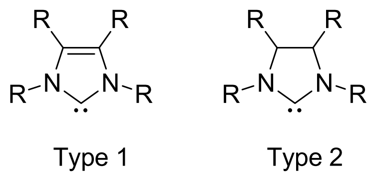
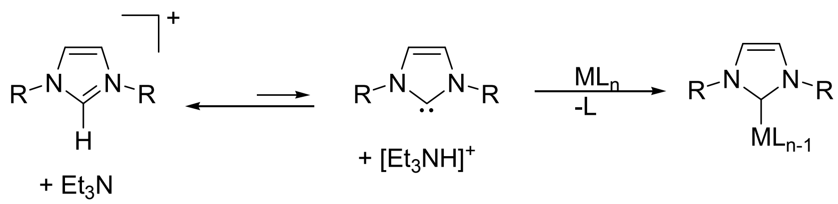


Figure 7

One of the major limitations in the synthesis of NHCs is the method for generating the carbene from the corresponding salt; as the hydrogen atom to be abstracted from the salt is not very acidic a strong base is often required. However, the use of a strong base can in some cases cause carbenes with additional acidic or electrophilic centres to undergo unwanted side reactions, leading to decomposition. In these cases it has been found that weaker bases such as triethylamine or caesium carbonate can be used to deprotonate the salt.[19] In all cases knowledge of the acidity/basicity of the salt and NHC is vital and much research has been undertaken on both the experimental and the theoretical pKa values of these.[19] The most basic carbene has a pKa value of 39.1 (in acetonitrile), whereas the least basic has a pKa value of 25.6 (N.B. pKa values in both cases refer to the acidity of the precursor salts).[19] With a pKa value of 25.6 the least basic NHC is more basic than the most basic phosphine ($Pt\text{-}Bu_3$ has a pKa of ~10), this indicates a higher proton affinity in carbenes. However, weak bases such as triethylamine, sodium acetate and caesium carbonate have all been used to generate carbene-metal complexes from the salt (Scheme 2). This is hard to explain using pKa values alone; a possible explanation is the suggestion that the stabilisation provided by the NHC-metal complex makes the overall reaction favourable.[19]



Scheme 2

It is the deprotonation by a base, which can limit the R- groups used. Any R- group used in the carbene synthesis must not be deprotonated in strongly basic conditions or risk decomposition of the NHC.

Many different NHC ligands can be synthesised by changing the R- groups attached to the nitrogens of the ring introducing π-electron donating groups (e.g. halogens, NR_2, PR_2, OR, SR etc.) which inductively stabilise the sp^2 non-bonding orbital; thus favouring the singlet state. On the other hand π-electron withdrawing substituents (e.g. COR, CN, CF_3, BR_2, PR_3^+ etc.) can be introduced having the opposite effect and therefore favour the triplet state.

The field of *N*-heterocyclic carbenes has grown rapidly in recent years with six distinct classes of ligand evolving. These classes are characterised by the position of chirality in the molecule relative to the carbene unit. The six classes that NHCs fall into are:

- *N*-heterocyclic carbenes with *N*-substituents containing a centre of chirality
- NHC ligands containing chiral elements within the *N*-heterocycle
- NHC ligands with an element of axial chirality
- Carbenes containing planar chirality
- Carbenes joined by a chiral *trans*-cyclohexanediamine ligand backbone
- Carbenes with oxazoline units present

1.2.1 - *N*-heterocyclic carbenes with *N*-substituents containing a centre of chirality

The class of *N*-heterocyclic carbenes with *N*-substituents containing a centre of chirality is based on the introduction of *N*-substituents with chirality present at positions 1 and 3 within the ring, (Figure 8).

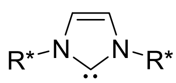


Figure 8

The first chiral NHCs were synthesised from enantiopure chiral amines by Herrmann and Enders in 1996,[20] (Figure 9), using the method developed by Arduengo.[18]

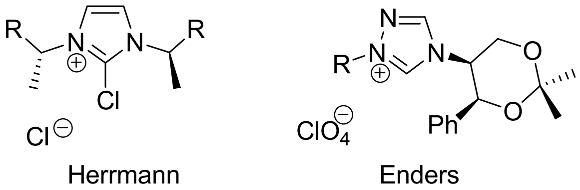
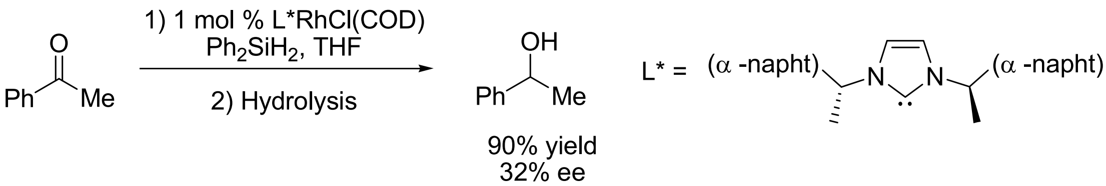


Figure 9

This class of NHC are often very efficient stereodirecting ligands, although this is only the case if the *N*-substituent is locked in a fixed conformation, or the *N*-substituent is of a sufficiently bulky nature as to cause steric limitations. Chiral induction of these ligands varies depending on how close the chirality situated on the *N*-substituent is to the reacting chiral centre; this type of chiral NHC can therefore often give moderate results in asymmetric catalysis, (Scheme 3).[20]



Scheme 3

1.2.2 - NHC ligands containing chiral elements within the *N*-heterocycle

NHC ligands containing chiral elements within the *N*-heterocycle are often referred to as imidazoinylidenes; they have sp^3 hybridised carbon atoms at both the 4- and 5- position of the N- heterocyclic ring. They have the general formula:

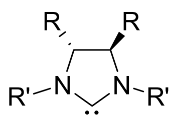
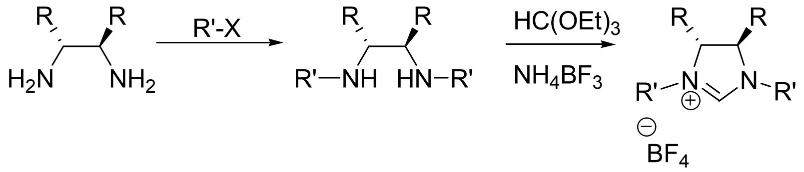


Figure 10

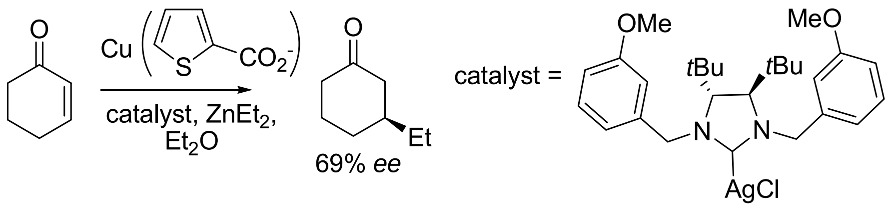
These types of NHC ligands are generally prepared from the imidazolium salt precursor, which has been synthesised using C_2-symmetric chiral vicinal diamines,[21] (Scheme 4).[22]



Scheme 4

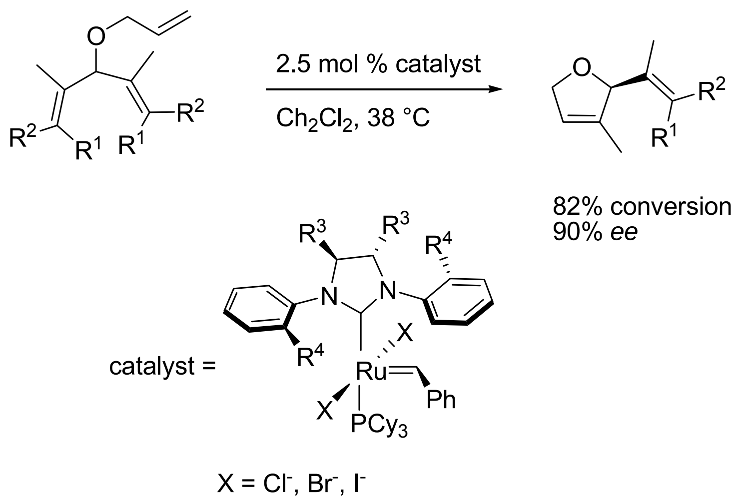
This type of ligand have been shown to be highly efficient stereodirecting ligands, which by careful selection of two (homo)chiral centres in the 4 and 5 positions, can by the means of steric repulsion induce chirality in the two R' substituents. These can then transmit this induced chirality to the reacting centre of the metal complex. The *N*-substituents themselves must have a certain steric bulk; it has been found that two methyls in these positions are ineffective at transferring chirality to the metal centre, however, when benzyl groups are used, the stereoselectivity is greatly increased.[20]

In the example (Scheme 5), the presence of a catalyst greatly increases the rate of reaction of the copper catalysed enantioselective addition of diethylzinc to cyclohexanone.[23]



Scheme 5

Chiral NHCs of this type have been widely used by Grubbs, particularly in the stereoselective ring closing metathesis of olefins.[20] When used in the desymmertisation of achiral trienes (Scheme 6) this type of ligand gave good to excellent enantiomeric excesses.[24]



Scheme 6

Further work on imidazolinylidenes by Hann has shown that they are widely versatile, with nonsymmetrical imidazolinylidenes (Figure 11) being prepared from secondary amines and imines.[25] These nonsymmetrical imidazolinylidenes have led to a wide range of novel NHC ligands.

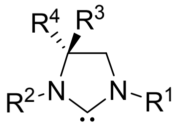


Figure 11

1.2.3 – NHC ligands containing an element of axial chiral

For NHC ligands containing an element of axial chiral the 1,1'-binaphthyl unit is one of the main backbones employed. Axial chirality is defined as:

'The term used to refer to stereoisomerism resulting from the non-planar arrangement of four groups in pairs around a chirality axis'[1]

Examples of which are atropoisomerism and depending on the substitution pattern, some allenes (Figure 12).

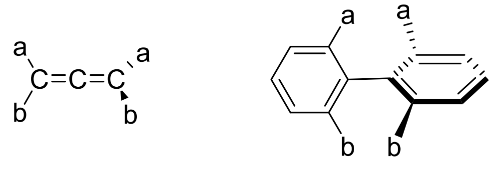


Figure 12[4]

The ligands derived from 1,1'-binaphthyl systems have been highly successful as catalysts and were first introduced into the field of asymmetric catalysis by Noyori, with BINAP and BINOL being the most widely used examples, (Figure 13).[26]

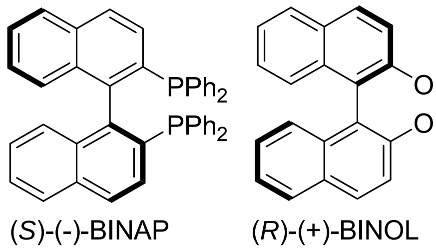
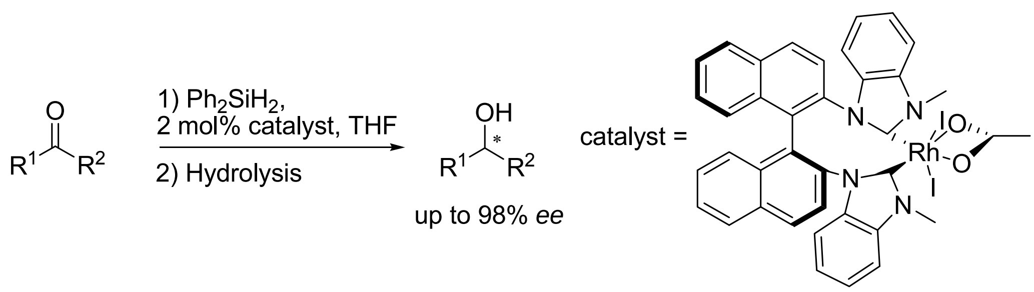


Figure 13

NHCs containing this type of backbone, exhibit axial chirality which is induced by the restricted rotation around the C-C axis which links the two naphthyl units. Rajanbabu published the synthesis of the first chiral NHC containing the 1,1'-binaphthyl unit and its coordination chemistry in 2000.[27] The enantiomeric excesses generated from using this type of NHC are often very high, (Scheme 7).



Scheme 7

1.2.4 – Carbenes containing planar chirality

The first planar chiral *N*-heterocyclic carbene was reported in 2002 by Bolm,[28] and was based on a ferrocene derivative, (Figure 14).

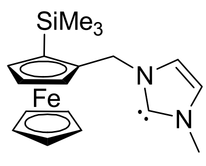


Figure 14

The development of this type of NHC ligand began when ferrocene derivatized ligands containing planar chirality proved excellent in the field of asymmetric catalysis. Josiphos and chiral DMAP developed by Togni and Fu respectively;[29] are typical examples of these types of ligands (Figure 15).

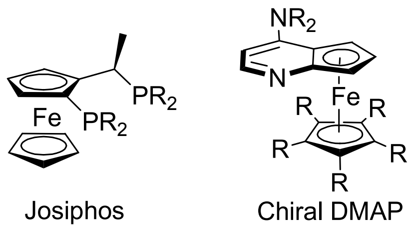
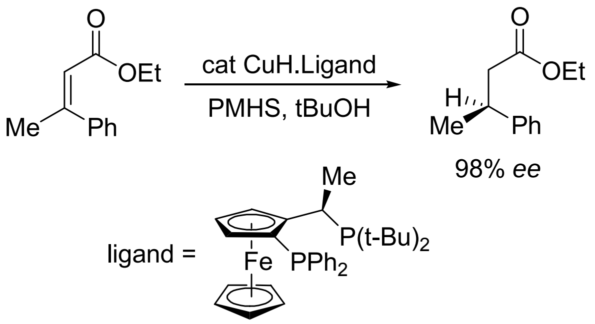


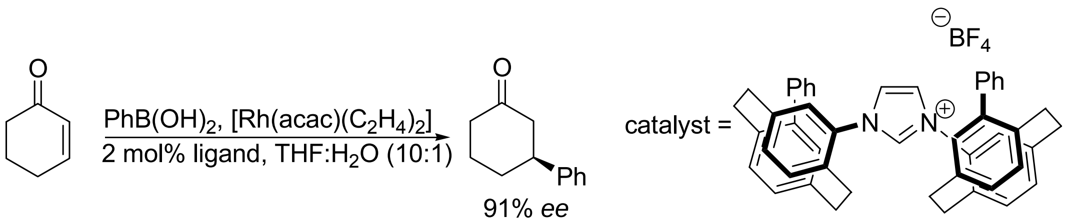
Figure 15

Josiphos has been utilised in the asymmetric 1,4-hydrosilylations of α,β-unsaturated esters with excellent results (Scheme 8).[30]



Scheme 8

Although ferrocene derivatized ligands have been successful in asymmetric catalysis, ferrocenyl substituted chiral carbenes have not yet given efficient results in this field. Recent results using chiral paracyclophane derivatives have proved more promising; supporting the theory that chiral *N*-substituents with larger bulkier groups tend to have greater chiral induction and therefore give better enantioselectivity than those with less bulky R groups, (Scheme 9).[20]



Scheme 9

1.2.5 – Carbenes joined by a chiral *trans*-cyclohexanediamine ligand backbone

Enantiomerically pure *trans*-1,2-diaminocyclohexane has been used in the design of many chiral ligands, and has more recently been used in NHC chemistry, creating a class of NHCs which all have a chiral *trans*-1,2-diaminocyclohexane backbone. The best known chiral ligand using this backbone is the Jacobsen epoxidation catalyst, (Figure 16).[31]

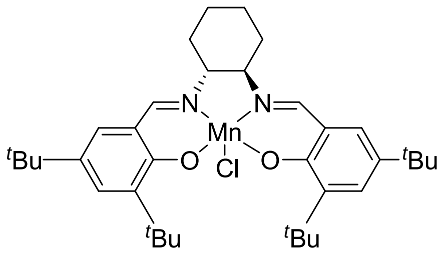
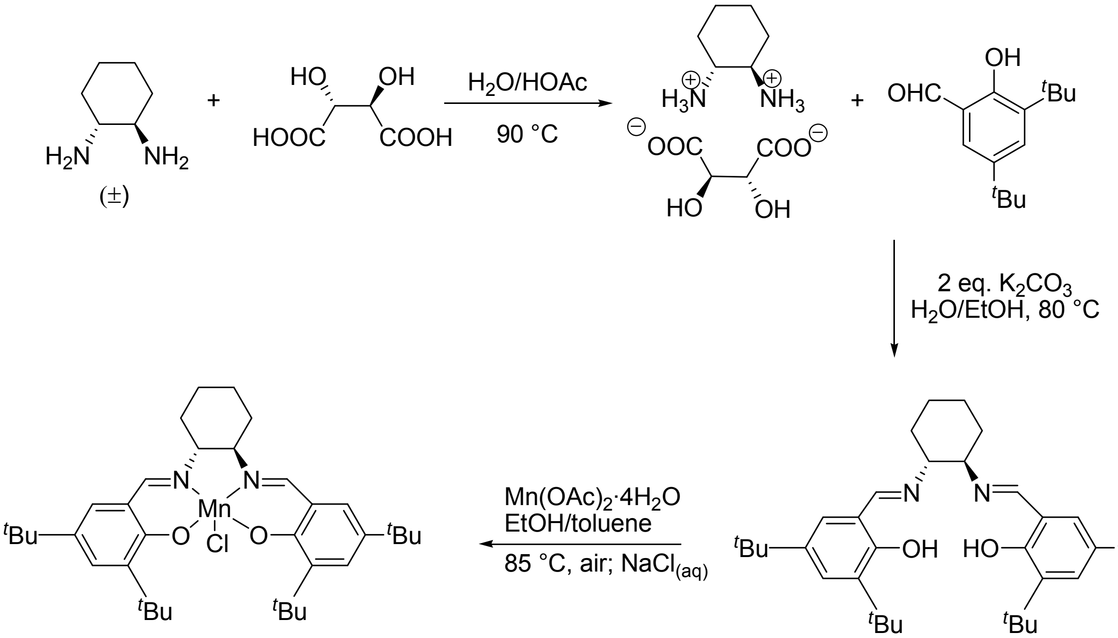


Figure 16

The Jacobsen catalyst is synthesised by the reaction of resolved 1,2-diaminocyclohexane with 3,5,-di-tert-butylsalicyaldehyde, synthesised using the Duff formylation,[32] to give a salen ligand. Reaction of this compound with manganese (II) acetate gives the manganese (III) complex that is isolated as the chloro compound. Synthesis of the (*R*,*R*) enantiomer of the Jacobsen epoxidation catalyst is shown below, (Scheme 10).[33]



Scheme 10

With ligands such as the Jacobsen epoxidation catalyst being highly successful in a wide range of enantioselective catalytic transformations, interest developed in using a similar backbone design for the synthesis of NHC ligands. The first ligand of this class was developed by Burgess in 2002, (Figure 17).[34]

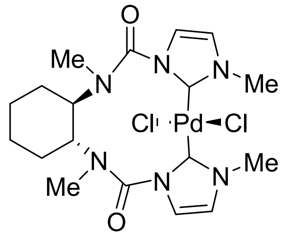
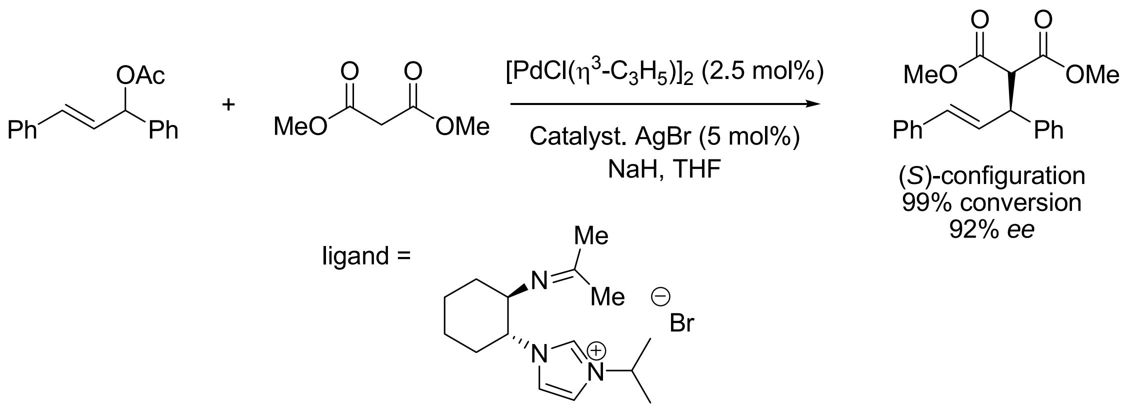


Figure 17

Further ligands of this class were developed by Douthwaite and exhibited high enantioselectivity,[35] however, relatively high catalyst loading (5 mol%) and elevated temperature were required to reach a high level of enantioselectivity, (Scheme 11).



Scheme 11

1.2.6 – Carbenes with oxazoline units present

The final class of NHC ligand incorporates an oxazoline unit. Oxazoline ligands and their related compounds have been widely used in catalysis due to the high enantioselectivities achieved in a large range of processes.[36] Oxazoline ligands used in asymmetric catalysis are typically polydentate ligands containing one or more of the oxazoline units. High enantioselectivities are achieved through the constrictions imposed upon coordination to the metal, as on complexation only one stereogenic centre lies close enough the to the coordination sphere to participate in the reaction giving high enantioselectivity.[36] Ligands which have oxazoline units tend to have rigidity and quasi-planarity, despite the two sp^3

hybridised carbons at positions 4 and 5 of the ring. Studies have suggested that there is delocalisation of the double bond (Figure 18) which contributes to the ring planarity,[37] this has been confirmed by studies of the torsion angles 5-1-2-3 and 4-3-2-1 which are 4.21 and 2.48° respectively and the bond angle 1-2-3 at 118.39° is close to the 120° expected for sp^2 hybridisation. Planar conformation is also the most energetically favourable configuration that the oxazoline can adopt.[37]

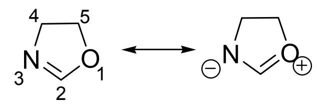


Figure 18

As a class of ligand, oxazolines are often stable towards nucleophiles, bases, radicals and even a number of acids; but can be sensitive to mineral and Lewis acids. One example of this class of ligand is that of JM Phos,[38] developed by Burgess and used in palladium mediated alkylation reactions (Figure 19).

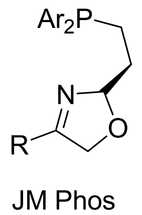


Figure 19

The first *N*-heterocyclic carbene containing an oxazoline unit was reported by Herrmann in 1998 (Figure 20) and when complexed to rhodium and used in the hydrosilation of ketones to alcohols gave moderate to good enantiomeric excesses, ranging from 70% to 90%.[39]

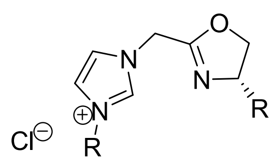
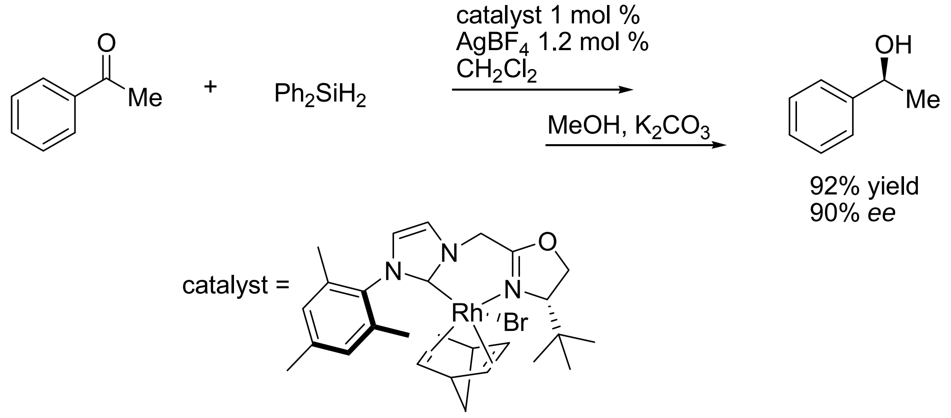


Figure 20

This type of ligand has different modes of action: upon coordination of the carbene to rhodium the ligand acts as a bidentate ligand coordinating not only through the carbene centre but also through the nitrogen present in the oxazoline ring, however, on coordination to palladium the ligand acts as a bridging ligand, (Scheme 12).[39]



Scheme 12

Work in this field by Burgess led to the development of a new kind of oxazoline-carbene ligand. Based on previous work with JM-Phos, Burgess developed a carbene ligand based on this framework, (Figure 21) which when coordinated to rhodium and used in the hydrosilation of ketones proved to be a highly enantioselective catalyst and gave enantiomeric excesses of up to 95%.

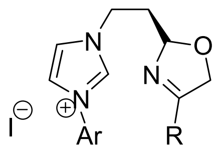


Figure 21

Over the last few years the use of NHCs has grown rapidly in the fields of coordination chemistry and catalysis and have begun to replace phosphines in many processes in which the ability of the ligand to transfer electron density to the metal centre gives the catalyst an advantage.[40] Additionally, they can easily be modified to introduce a second ligating group, which is often desirable in a catalyst. NHCs are particularly good spectator ligands as they do not undergo many of the side reactions associated with carbene ligands e.g. metathesis and cyclopropanation.[9,41] They also have higher thermal stability as they lack the sensitive P-C bond present in phosphine ligands which can be cleaved at high temperatures.

The main reactions in which NHCs are utilised can be limited to the reactions in which phosphine ligands were traditionally used, especially C-C coupling reactions such as the Heck, Suzuki, Sonogashira and other cross coupling reactions and olefin metathesis.

While the number of NHCs is rapidly increasing and widening to include many different R- groups and functionalities there is still a great interest in developing new chiral *N*-heterocyclic carbenes, as many chiral functionalised carbenes at present have little or no performance advantage over established bis-carbene and bis-phosphino complexes. In many cases for catalytic applications the performance of NHCs are either equal or inferior to that of other ligands.

1.3 – Phosphoramidites and Phosphordiamidites

A large number of chiral ligands which contain phosphorus and/or nitrogen atoms with either C_1- or C_2- symmetry have been developed in recent years. These are used in the catalytic enantioselective formation of carbon-carbon and carbon-heteroatom bonds. A molecule which falls into the C_1- symmetry point group, is one with no axis of chirality, (i.e. a molecule is achiral). The C_2- point group is applied to molecules which have one axis of chirality, (for example H_2O_2 is C_2- symmetric in one of its conformers). C_2-symmetry has been used in the design of many successful ligands used in asymmetric reactions. One suggestion for the success of ligands with this type of chirality is that a C_2-symmetric axis can dramatically reduce the number of competing diastereomeric transition states in a reaction.[42]

The use of phosphines as ligands is well known, with the limitations of these ligands being well documented.[10-12] Whilst various attempts to modify phosphine ligands have not successfully provided a solution to their tendency to undergo degradation when exposed to air, moisture or high temperatures, work in recent years by Feringa,[43] has brought phosphorus containing ligands back into the forefront of ligand design and catalysis. In 2000 Feringa reported the use of a ligand containing both phosphorus and nitrogen with C_2 – symmetry in enantioselective conjugate addition.

As a ligand type phosphoramidites have electron acceptor-donor properties similar to those of aryl phosphines.[43] In contrast to the wide use of phosphine and phosphite ligands, phosphoramidites have in the past, been largely ignored as a ligand type due to the assumption that they all have the sensitivity towards hydrolysis that some compounds of this class demonstrated.[43] Interest in this ligand type has now grown rapidly with these ligands proving popular and very effective in producing high enantiometric excesses.[44,45]

Phosphites, phosphoramidites and phosphordiamidites of the general structure below (Figure 22) are becoming much more widely used in a variety of different organic reactions with the development of air- and moisture-stable pentavalent phosphorus compounds.[46]

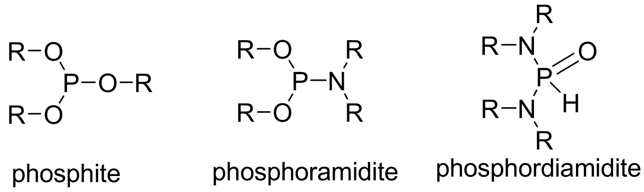


Figure 22

It is thought that phosphordiamidite compounds exist in a state of equilibrium between the pentavalent RR'P=OH and tautomeric trivalent RR'POH form, (Figure 23).[47] During equilibrium any stereochemical arrangement around the phosphorus is retained. At room temperature the pentavalent structure is predominant, this making the compound air and moisture stable. In the presence of a transition metal this tautomerisation from the pentavalent form to the trivalent acid form has to occur before any coordination is possible.[43]

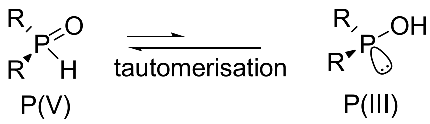
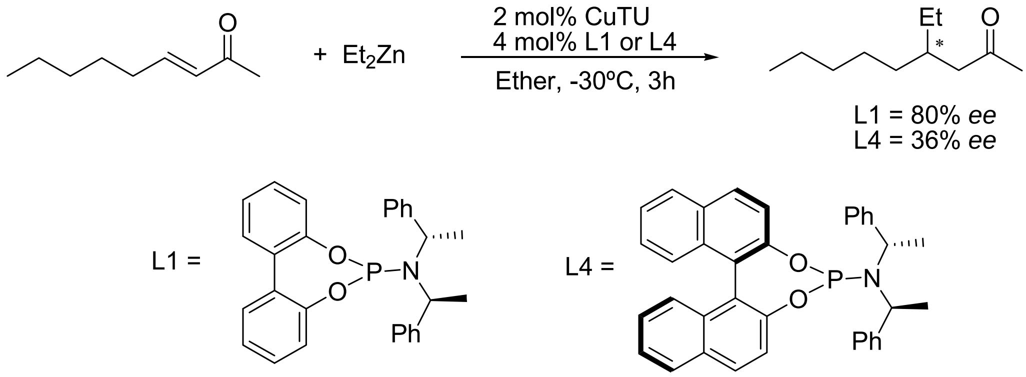


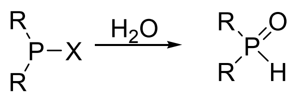
Figure 23

Phosphoramidite and phosphordiamidite ligands are strong π-accepting ligands that can be either monodentate or bidentate depending on the carbon backbone on which the ligand is based. The use of a rigid backbone was thought to be important in achieving high enantioselectivities,[48] therefore, many ligands were designed using 1,1'-Bi-2-naphthol (BINOL) as a starting material. Alexakis and co-workers challenged this idea by generating equal or greater enantiomeric excesses with a ligand based on the more flexible biphenol unit as the backbone (Scheme 13).[49,50]



Scheme 13

Chiral phosphoramidite ligands have become more important in the field of asymmetric catalysis due to their low cost, high resistance to hydrolysis and oxidation and their high synthetic availability.[51] The method of generating phosphoramidites or phosphordiamidites is relatively simple; the most employed method being the hydrolysis of the corresponding phosphine halide, most commonly the chloride generated by the reaction of the diol or diamine with PCl_3 (Scheme 14).[44]



Scheme 14

Other phosphoramidites have been synthesised from more complex starting materials such as the recently reported synthesis of a sugar-based diphosphoramidite ligand (Figure 24).[3]

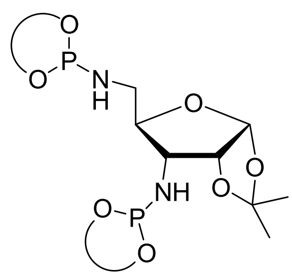
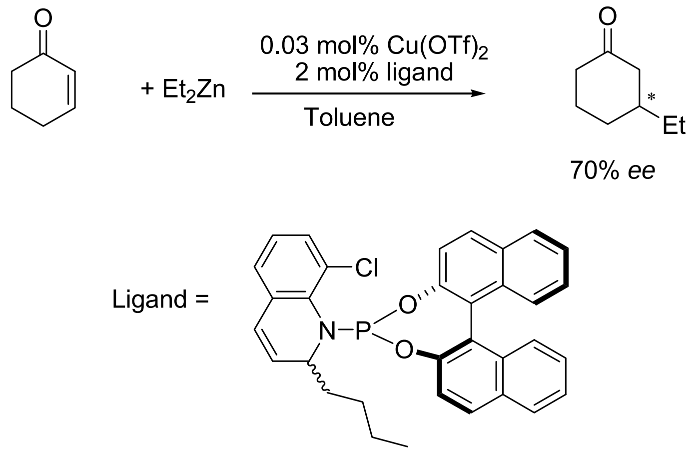


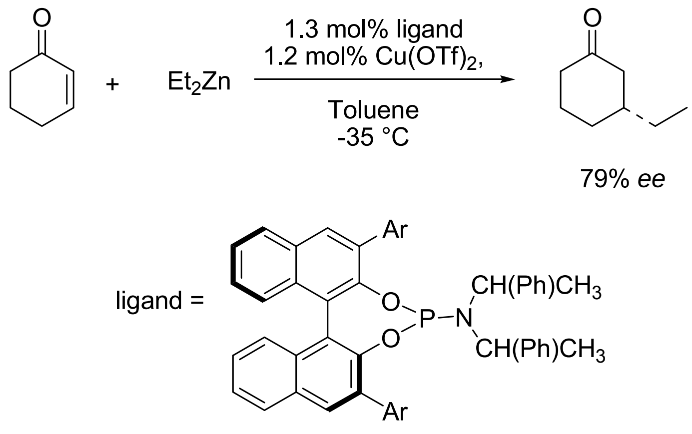
Figure 24

As early as 1994 de Vries and Feringa reported the use of a chiral phosphoramidite based on α-phenylethylamine as derivatizing agents for the determination of enantiomeric excesses in alcohols, amines and thiols.[52] In 1996 Faraone and co-workers reported the use of a chiral phosphoramidite based on 8-chloroquinoline (Scheme 15),[53] in a copper catalysed enantioselective Michael addition,[54] this brought phosphoramidite ligands back to the forefront at a time when there was rising interest in diphosphites and mixed phosphane/phosphite ligands.



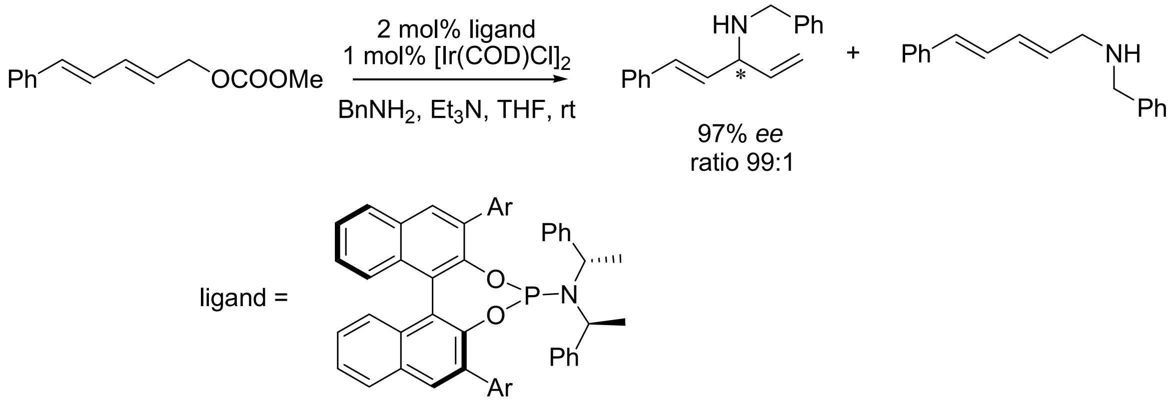
Scheme 15

It was not until 2000 that interest in this type of ligand was heightened by the publication by Feringa's Account of Chemical Research.[43] This account showed phosphoramidites to be excellent ligands in organocatalysis. Since then the development of phosphoramidites and phosphordiamidites has been widespread, with many different backbones being used in the design of such ligands. The use of these ligand types in a whole range of reactions continues to be of interest and more recently they have been shown to be excellent ligands for the copper catalysed 1,4-addition of R_2Zn to enones, (Scheme 16).[55]



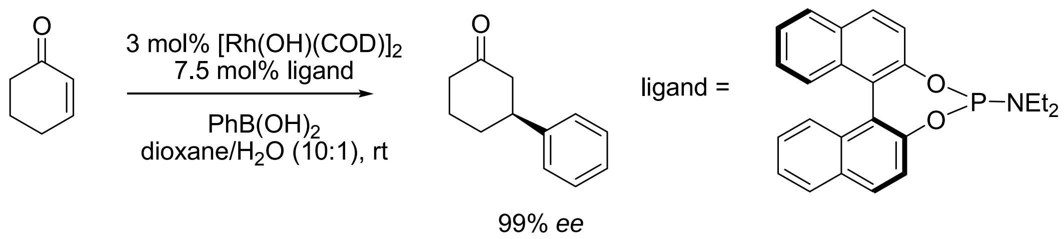
Scheme 16

Phosphoramidite ligands have also shown efficiency in iridium catalysed allylic amination reactions and allylic substitution of dienyl esters, (Scheme 17).[56,57]



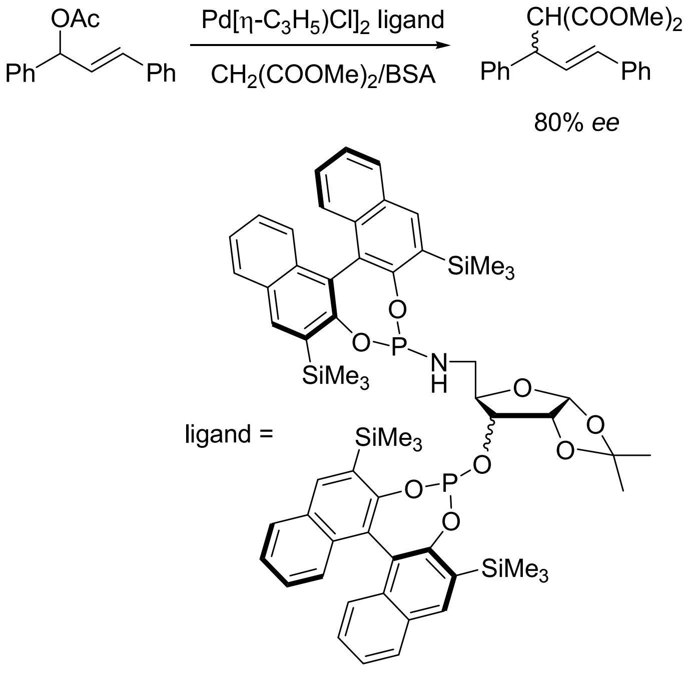
Scheme 17

Since the first successful applications by Feringa in 1994 and his use of this ligand type in catalysis in 2000,[43,52] phosphoramidites have continued to prove their potential as ligands in many different catalytic organic reactions; including the development of ligands for the use in copper- and rhodium-catalysed conjugated additions for both cyclic and acyclic 1,4-addition of arylboronic acids to enones, (Scheme 18).[58]



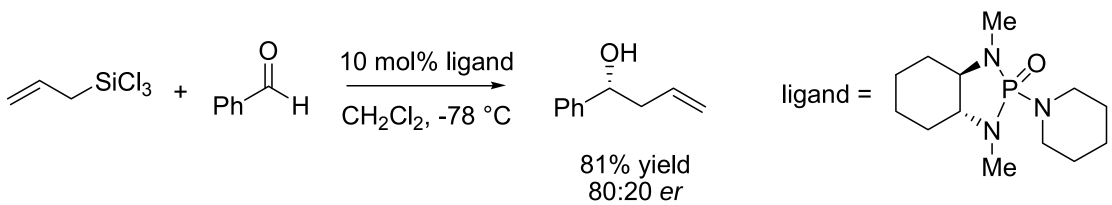
Scheme 18

Chiral bidentate phosphoramidite ligands have also been used successfully in asymmetric hydrogenation reactions.[59] Although biaryl and binaphthyl backbones are the more common backbones used in the synthesis of phosphoramidite ligands, other backbones have been developed from carbohydrate sources. One ligand, utilising D-xylose developed by Diéguez and co-workers gave good to excellent enantiomeric excesses when used in the palladium catalysed allylic substitution of many different substrates, (Scheme 19).[3]



Scheme 19

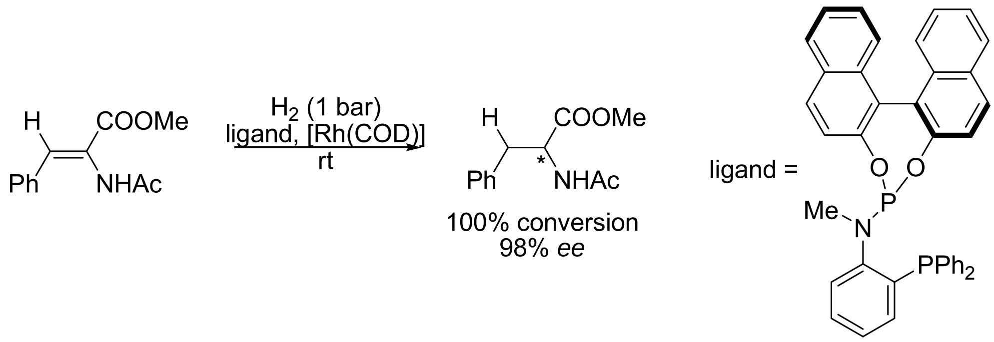
The versatility of phosphoramidites has been demonstrated by Denmark et al where their use as a Lewis base to activate the addition of allyltrichlorosilane to benzaldehyde to give the enantioenriched homoallylic alcohol proved highly successful, (Scheme 20).[60]



Scheme 20

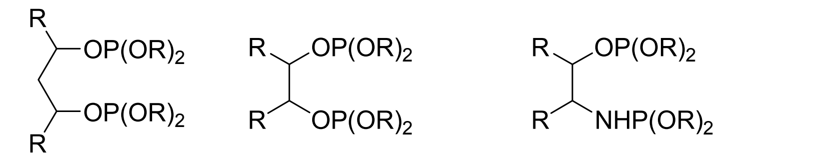
In comparison to traditional phosphines, chiral phosphoramidites tend to be more versatile as ligands. One attractive feature of this class of ligand is their versatility, the ease with which their structure can be modified in various ways is highly advantageous.[61] Phosphoramidites such as those developed by Feringa are the only types of ligand for which the monodentate form exhibits high enantioselectivity for a large number of asymmetric transformations thus increasing interest in the development of this type of ligand and others of similar design.[39,48]

Development of a new type of ligand containing both a phosphite and phosphoramidite moiety has also been successful. In 2006 Kostas and co-workers published the use of new chiral phosphine-phosphoramidite ligands in the asymmetric catalysis of olefin hydrogenation,[62] their ligands contain both a phosphine and a phosphoramidite moiety (Scheme 21) giving them different metal binding properties to that of the individual properties of phosphines or phosphoramidites.



Scheme 21

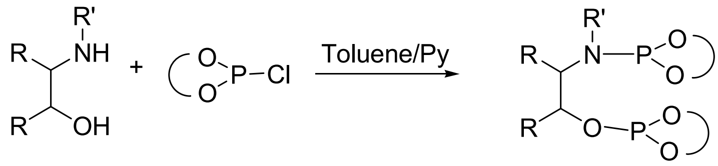
Subsequently De Viries along with Feringa and Minnaard published a paper highlighting the success of a large number of monodentate phosphoramidite ligands in asymmetric hydrogenation.[63] Other mixed ligands containing a phosphoramidite moiety combined with another phosphine-based group have been developed by Pamies and Diéguez and are based on the backbone of 1,2-diphosphites.[64] As a ligand type 1,2-diphosphites give lower enantioselectivities than the corresponding 1,3-diphosphites, leading to the development of the new mixed ligand, (Figure 25).[64]



1,3-diphosphite 1,2-diphosphite 1,2-phosphite-phosphoramidite

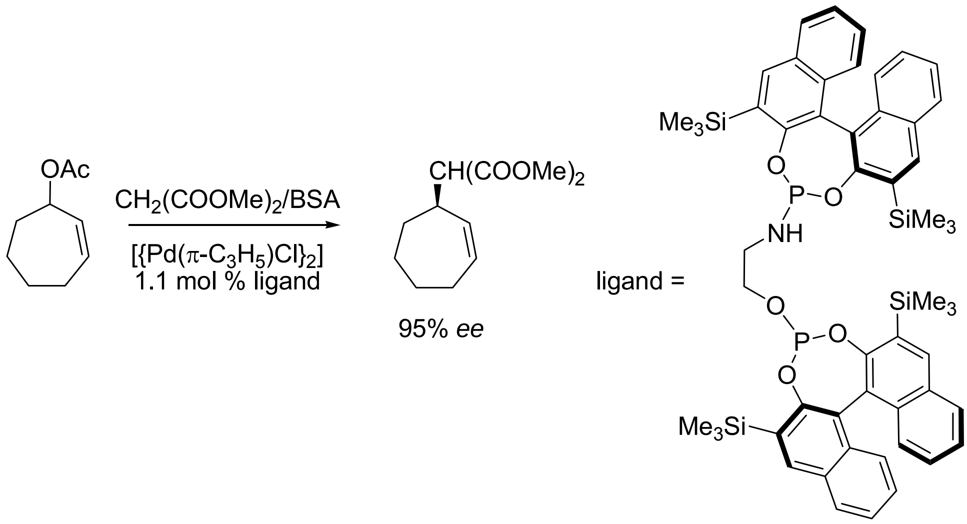
Figure 25

This new ligand design incorporates the phosphite and phosphoramidite moieties and offers a bidentate ligand with not only the benefit of the high activity phosphite ligand, but also the good π-acceptor character of the phosphoramidite ligand. Another advantage of this class of ligand is the ease by which they can be synthesised. The 1,2-phosphite-phosphoramidite ligand can be synthesised from the corresponding and commercially available chiral 1,2-amino alcohol and phosphorochloridite (Scheme 22).[6451]



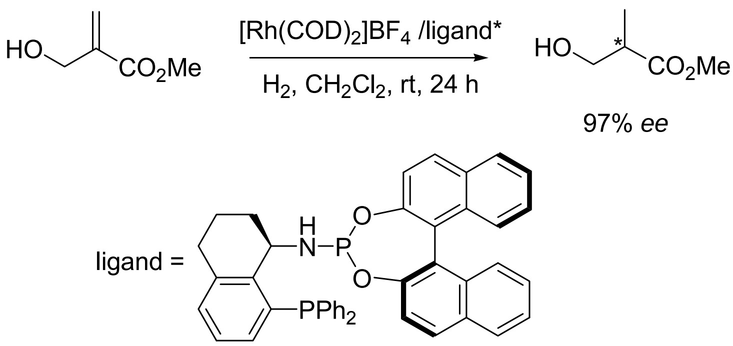
Scheme 22

This new type of ligand has three main advantages over phosphite ligands, as they are easily prepared in one-step; they have better π-acceptor character which increases reaction rate and their modular nature, allowing substituents of the backbone, the amino group and the biaryl moiety to be easily varied. They also often provide higher activity and enantioselectivity than their 1,2-diphosphite and phosphinite-aminophosphine analogues.[64] When used in the palladium catalysed allylic alkylation of cyclic substrates mixed phosphite-phosphoramidite ligands gave good to excellent enantiomeric excesses (Scheme 23).



Scheme 23

Further uses of mixed phosphine-phosphoramidite ligands have recently been highlighted by Hu and Zheng who utilised these ligands in the rhodium catalysed asymmetric hydrogenation of 2-hydroxymethylacrylates to generate the Roche ester in good to excellent enantiomeric excess, (Scheme 24) .[65]



Scheme 24

A more recent development in phosphoramidite chemistry has been the synthesis of a chiral phosphoramidite allenylidene complex by Bauer and co-workers, (Figure 26). Development of a chiral allenylidene complex with transfer of chirality to the metal centre is reported as being highly advantageous for use in catalysis and has been reported to have potential in metathesis reactions and in cyclization reactions or nucleophilic substitution reactions of propargylic alcohols.[66]

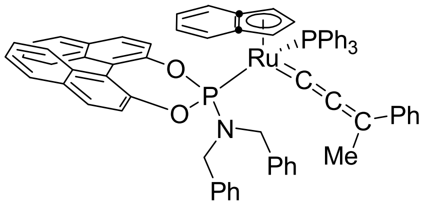
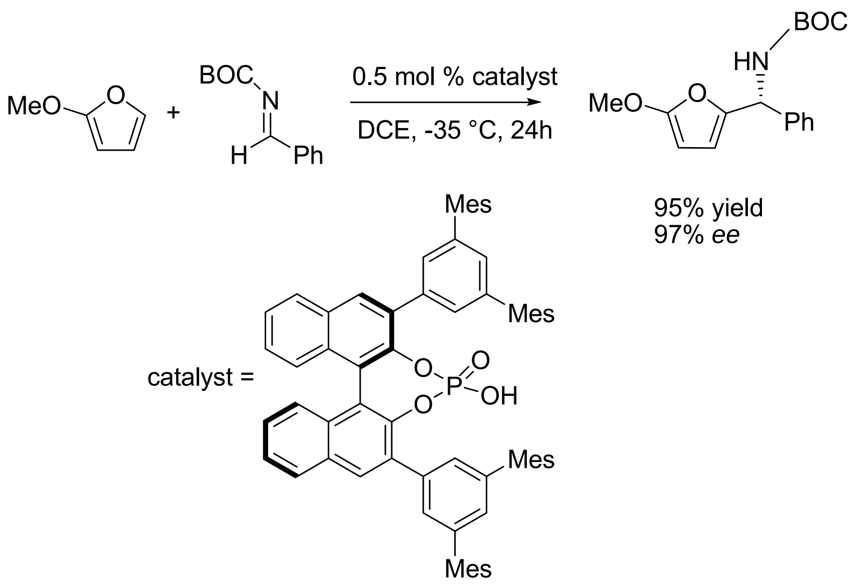


Figure 26

1.4 – Phosphoric Acids

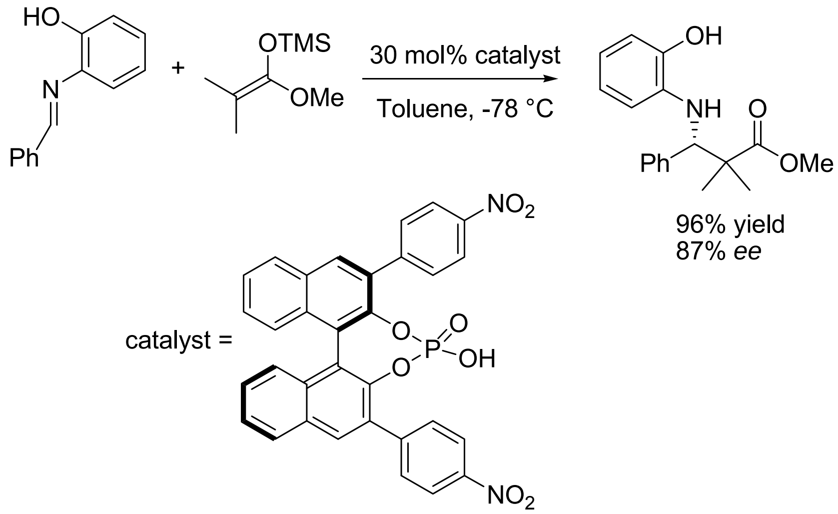
The development of chiral phosphoric acid catalysts for use in organocatalysis was initially slower than the corresponding phosphoramidites with far fewer examples of this class of ligand being reported. More recently interest in these type of compounds as catalysts has grown; initial work by two research groups first introduced phosphoric acids as catalysts into the field of organocatalysis, Terada and Akiyama independently reported the excellent catalytic activity of phosphoric acids.[67,68]

Terada reported the use of a binaphthol mono-phosphoric acid in the highly enantioselective 1,2-aza Friedel-Crafts reaction (Scheme 25), generating the product in an excellent enantiomeric excess.[67]



Scheme 25

Independently, Akiyama reported the use of a chiral phosphoric acid in the enantioselective Mannich-type reaction of ketene silyl acetal with aldimines; (Scheme 26) this was dependent on the R groups present in the 3,3’-positions of the BINOL scaffold, moderate to excellent enantiomeric excesses were achieved.[68]



Scheme 26

Many chiral phosphoric acids are based on 1,1’-binaphthol (BINOL) which gives easy access to the phosphoric acid by reaction of the diol with phosphoryl chloride in the presence of base, followed by aqueous work up. The phosphoric acid derived from (*R*)-BINOL can be used as a chiral resolving agent,[68] (Figure 27).

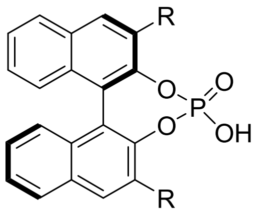
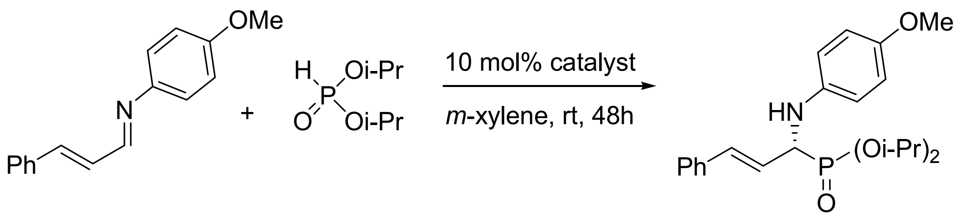
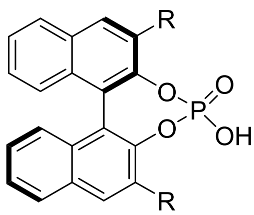


Figure 27

The 3,3'-substituents on the BINOL can be varied to change the properties of the catalyst. Recent studies on changing the substituents at the 3,3'- positions and the effect of these changes on the enantioselectivity achieved have been reported by Akiyama and co-workers.[69] A range of five phosphoric acids were tested in the hydrophosphorylation reaction of aldimines with diisopropyl phosphite. The results indicated that sterically bulky groups such as 3,5-$(CF_3)_2C_6H_3$ enhanced enantioselectivity, whereas less sterically demanding groups gave greatly diminished enantiomeric excesses, (Scheme 27).[69]



catalyst =

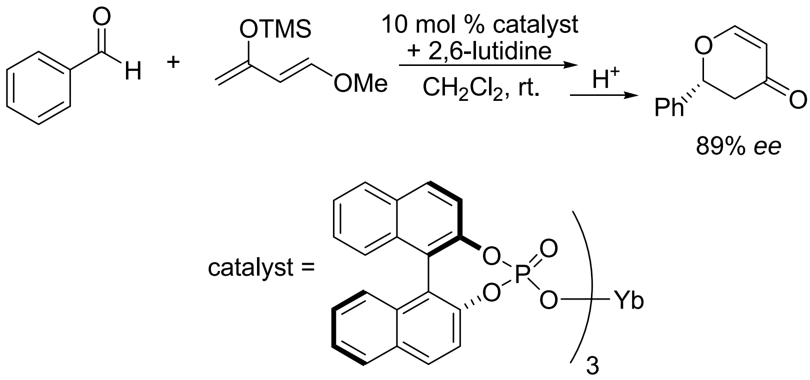


R group	*ee* (%)
H	11
Ph	30
4-$NO_2C_6H_4$	30
4-$CF_3C_6H_4$	33
3,5-$(CF_3)_2C_6H_3$	84

Scheme 27

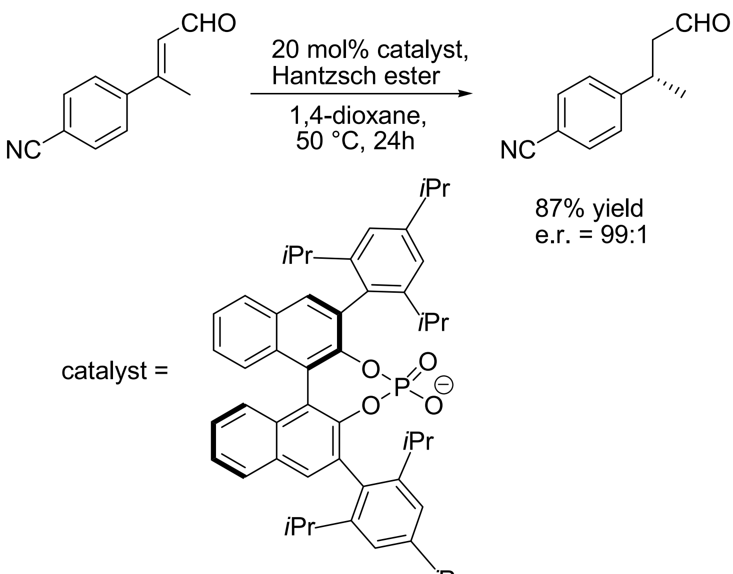
As a class of catalysts, phosphoric acids have only thus far been reported as organocatalysts, most commonly being used as hydrogen bonding catalysts for wide variety of reactions.[70]

Before the introduction of phosphoric acids into the field of organocatalysis in 2004, Inanaga utilised the lanthanide salt of the (*R*)-BINOL derivatized phosphoric acid as a catalyst for the hetero Diels-Alder reaction using Danishefsky's diene, (Scheme 28).[71]



Scheme 28

The reaction indicated that when used as an organocatalysts the BINOL derivatized phosphoric acid could give high enantioselectivity. The use of chiral phosphate salts as catalysts has also been demonstrated by List and co-workers who in 2006 published work using chiral phosphate salts in transfer hydrogenation reactions.[72] The catalyst consists of a chiral phosphate anion paired with an achiral ammonium cation and gave excellent enantioselectivities when used in the enantioselective transfer hydrogenation of α.β-unsaturated aldehydes, (Scheme 29). The phosphate salts were easily prepared by mixing a primary or secondary amine with the chiral binaphthol derived phosphoric acid.[72]



Scheme 29

The design of the phosphoric acid catalyst allows the molecule to act as a bifunctional catalyst with both a Brønsted acidic site and a Lewis basic site (Figure 28).[68]

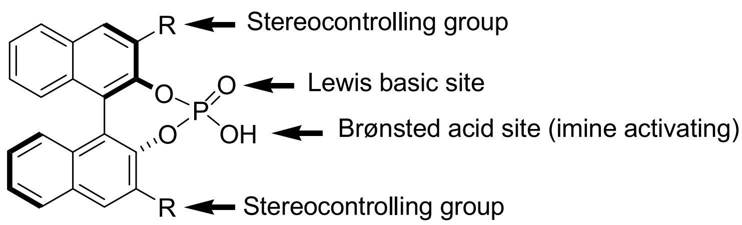
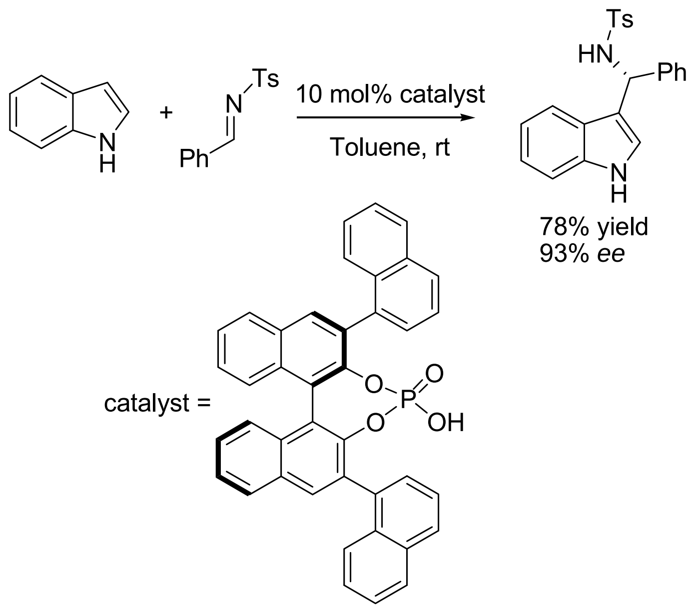


Figure 28

BINOL derived phosphoric acids are conformationally rigid with one proton which has high acidity,[73] (The pKa value of diethyl phosphate is 1.39)[74] with which to hydrogen bond, excluding any additional protons present in the R groups. Chiral substituents present at the 3,3'-positions transfer stereochemical information, and if chosen correctly can give excellent enantioselectivity. It is this presence of the Lewis basic phosphoryl moiety along with the Brønsted hydroxyl moiety that gives the catalyst its bifunctionality.

The range of reactions in which phosphoric acids have been used has grown rapidly since their introduction into organocatalysis and the discovery that their strong Brønsted acid properties gave high enantioselectivities. Initially used as hydrogen bonding catalysts for hydrogen transfer reactions they are now used in a wide range of reactions, such as the enantioselective hydrophosphonylation of aldimines,[69] and the aza Friedel-Crafts alkylation.[67]

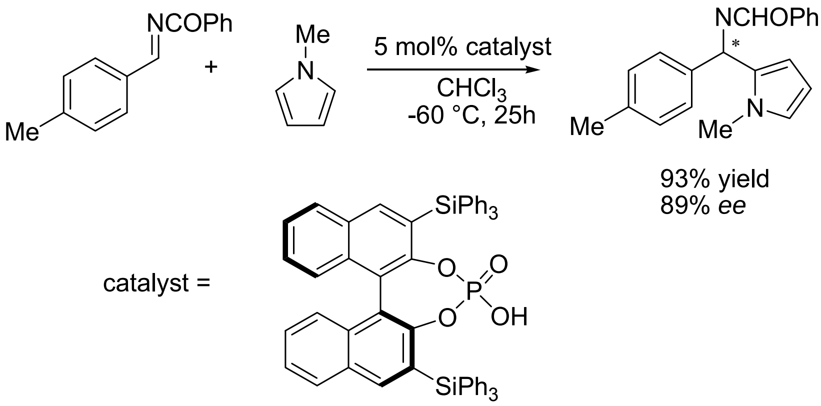
You and co-workers reported phosphoric acids to be excellent catalysts for the addition of indole to aldimines, (Scheme 30).[75]



Scheme 30

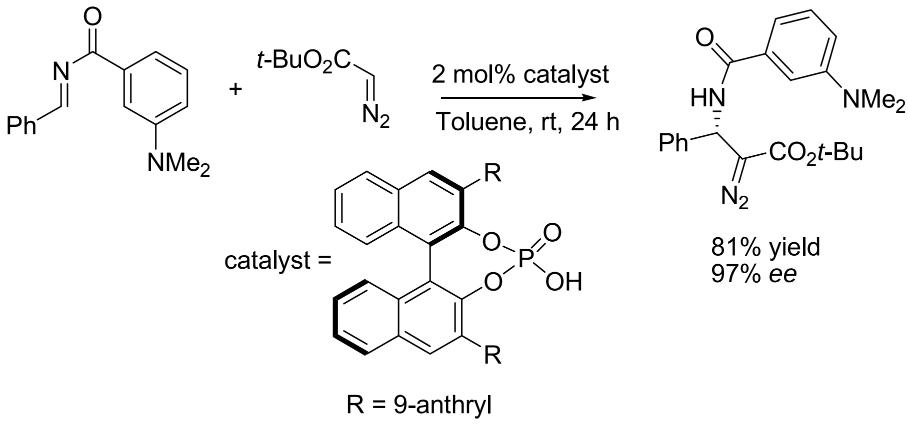
Other reactions in which phosphoric acids have been used successfully have been enantioselective Mannich-type reactions,[76] other aza Diels-Alder reactions[77] and the addition of other nucleophiles to imines,[78,79] to name just a few.

Antilla and co-workers reported the catalytic aza Friedel-Crafts reaction of *N*-benzoyl imines to pyrrole derivatives using three different phosphoric acid catalysts, generating moderate to excellent enantiomeric excesses, (Scheme 31). By changing the R groups present in the 3,3' positions to a triphenylsilyl moiety far higher enantiomeric excesses were achieved then those gained when 9-anthryl was present in these positions.[80]



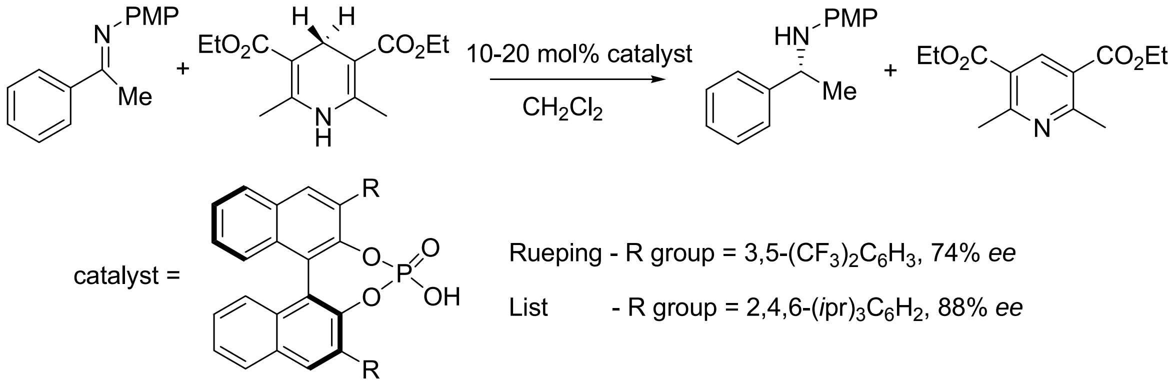
Scheme 31

Use of phosphoric acid catalysts has allowed the development of novel asymmetric reactions for the synthesis of chiral amine-based substrates.[73] Their potential in reactions in which no previous catalytic strategies were available is highlighted by Tereda, whose use of these catalysts in the reaction of *N*-acyl imine with an α-diazoester to generate a enantioenriched α-di-azo-β-amino acid derivative (Scheme 32).[81] In this reaction the bifunctionality of the phosphoric acid catalyst is used to prevent aziridination, which occurs without the presence of a base in the reaction.



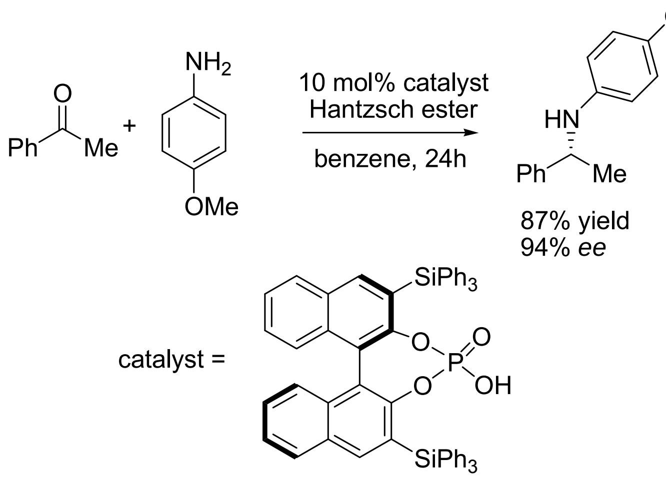
Scheme 32

Another important reaction using chiral phosphoric acids reported by three groups independently is the enantioselective reduction of imines and ketones. Rueping,[82] List and Macmillan all reported this transfer hydrogenation with excellent enantioselectivity, (Scheme 33).[70,83]



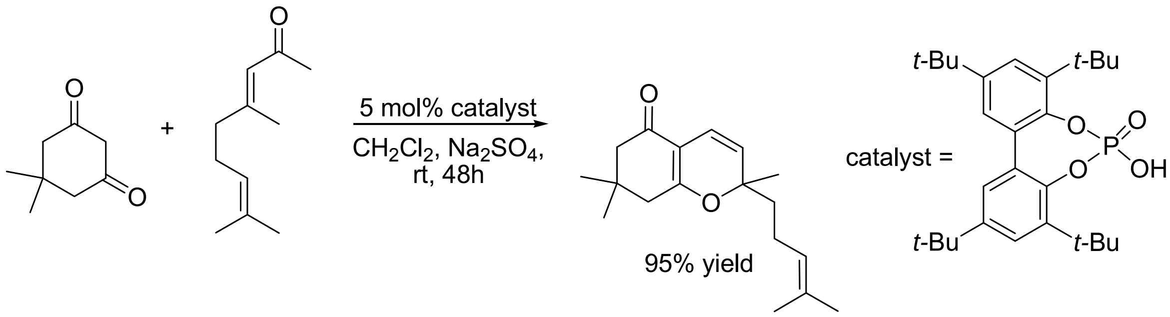
Scheme 33

The catalysts used by Rueping and List in the above reaction only differed in the R-groups present in the 3,3'-positions of the phosphoric acid catalyst, whereas Macmillan reported the reductive amination of a ketone using triphenylsilane groups at the 3,3'-position, (Scheme 34).



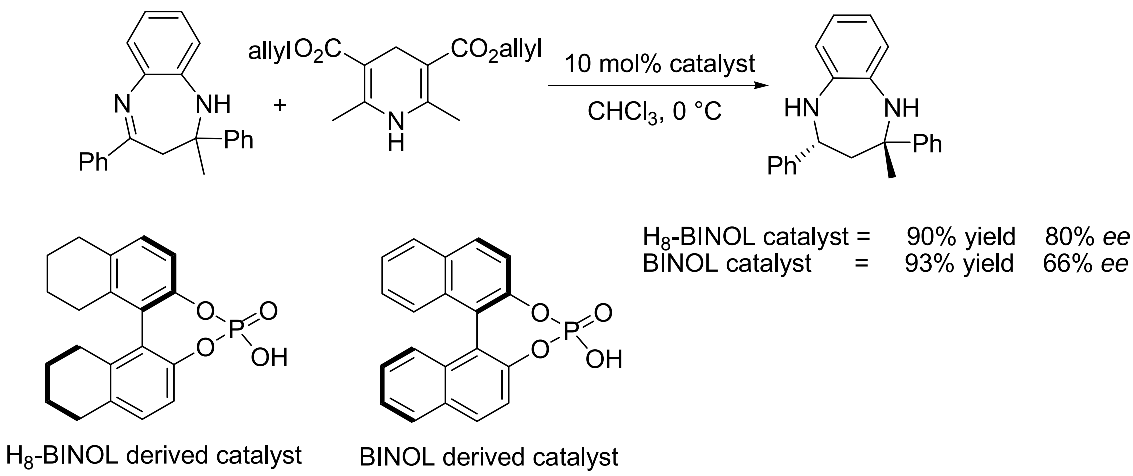
Scheme 34

In 2008 Renaud and co-workers reported the use of phosphoric acid catalysts in the synthesis of pyrans using a formal [3+3] cycloaddition. Although the catalyst used in this reaction was not the conventional BINOL derived phosphoric acid it gave good to excellent yields, (Scheme 35).[84]



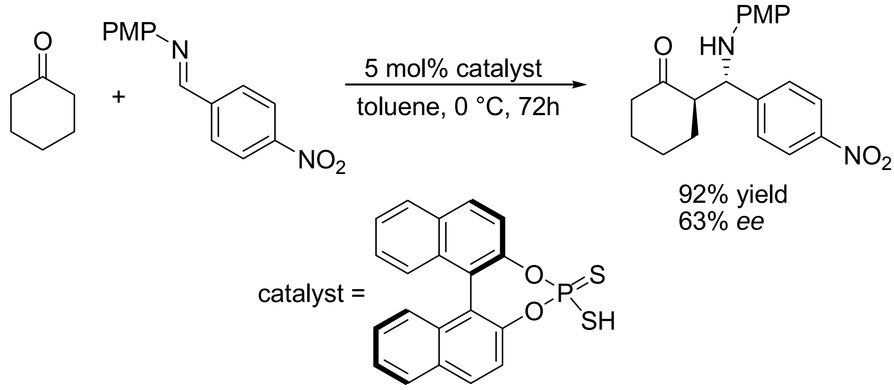
Scheme 35

Whilst the majority of phosphoric acid catalysts are synthesised using BINOL as a basis for the backbone other phosphoric acid catalysts have been developed using H_8-BINOL as an alternative backbone. Work by Gong and co-workers compared H_8-BINOL derived phosphoric acids with one derived from BINOL in an asymmetric hydrogen transfer reaction (Scheme 36).[85] For the same reaction the H_8-BINOL derived catalyst gave higher enantiomeric excesses, 80% compared to 66% for the conventional BINOL derived catalyst; although the reaction time for the H_8 reaction was significantly higher, 5.5 days compared to 2 days to get comparative yields.[85]



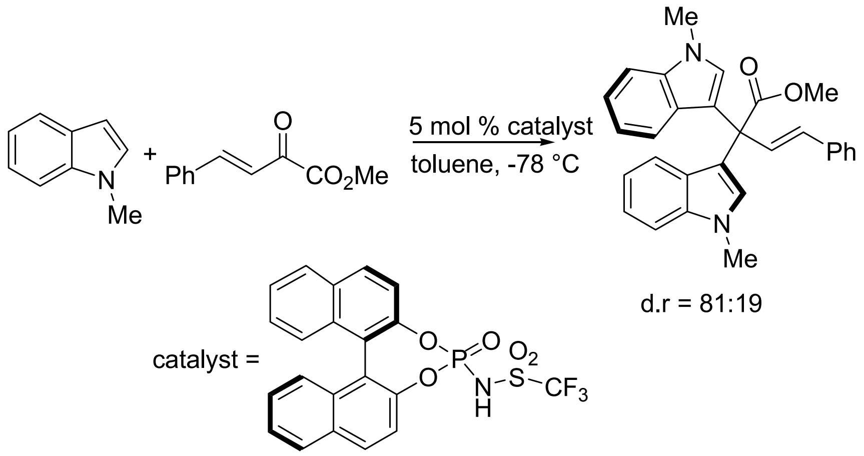
Scheme 36

Another variation of the group of chiral phosphoric acid based catalysts is the synthesis of phosphordithioic acid esters which are synthesised from H_8-BINOL. Treatment of the H_8-BINOL with P_4S_{10} gives the dithioic acids, which have been used by Blanchet and co-workers in a Mannich reaction between cyclohexanone and an electron poor aldimine giving moderate enantioselectivities (Scheme 37).[86]



Scheme 37

Another branch of phosphoric acid related compounds are the *N*-triflylphosphoramides, these have shown promise in work by Rueping on the addition of *N*-methylindole to β,γ-unsaturated α-ketoesters, (Scheme 38).[87] The resulting bisindole exhibits atropoisomerism and was obtained in an enantiomeric ratio of 81:19.



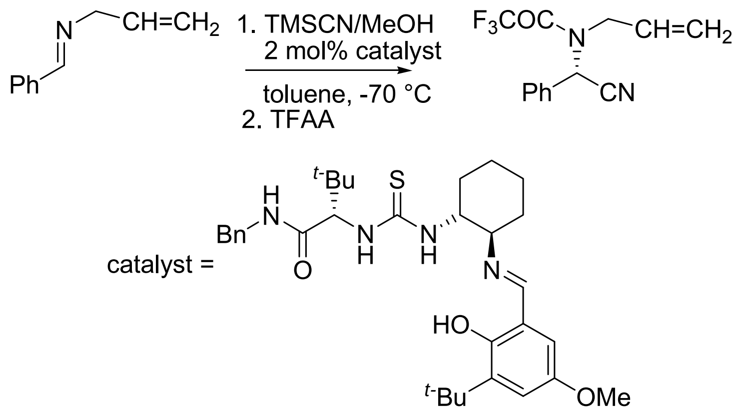
Scheme 38

Overall, the range of phosphoric acid catalysts and variants of these catalysts available and the reactions in which they are used has grown rapidly in recent years due to the high enantioselectivities achieved and the ease with which the R-groups on the backbone can be varied.

1.5 – Thioureas

Chiral thiourea and urea catalysts have been at the forefront of the drive to develop phosphine replacement ligands and catalysts. As a class of ligand, thioureas can be used in both organocatalysis and organometallic catalysis, and have been used as ligands in a large range of metal mediated reactions.

In 1998, the discovery that a Schiff base could catalyse the asymmetric hydrocyanation of a large number of imine substituents introduced chiral thioureas into the field of organocatalysis, (Scheme 39).[88]



Scheme 39

Originally ureas and thioureas had been used in the design of Schiff base catalysts which served as ligands for Lewis acids. However, when they were used without the Lewis acid present they gave high enantioselectivity, generating interest in this type of compound as catalyst in its own right. Upon discovery of their ability to catalyse reactions without the Lewis acid present, various techniques were used to investigate their mode of action including NMR studies, kinetic studies and computational studies. These concluded that the mode of action was that of a double hydrogen bonding catalyst, giving them the benefit of increased strength and directionability compared to that of single hydrogen bonding catalysts.[88] Hydrogen bonding interactions help provide an organised transition state in which greater stereocontrol can be achieved.[89] The above reaction (Scheme 39) works without the Lewis acid present as the thiourea forms two hydrogen bonds *via* the two acidic NH protons to the imine lone pair activating the imine towards nucleophilic attack.[88]

The general term thiourea refers to a wide range of compounds which have the general structure shown below, (Figure 29). Thioureas have the ability to donate two hydrogen bonds simultaneously for electrophilic activation, although the mode of action of thioureas can impose limitations on the substrates on which the catalysts work. Two point binding is also considered very useful in asymmetric catalysis with a metal centred Lewis acid.[90]

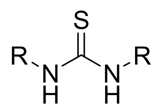
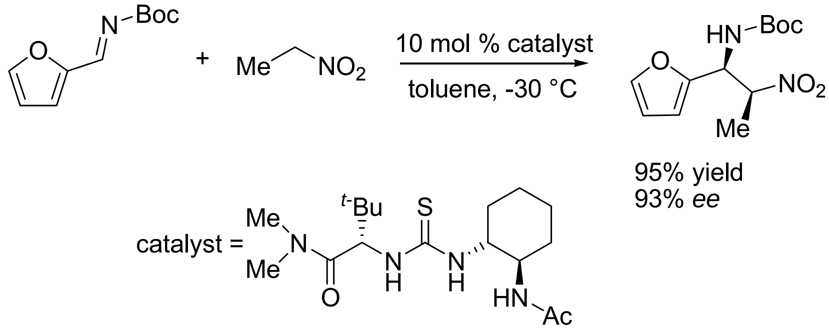


Figure 29

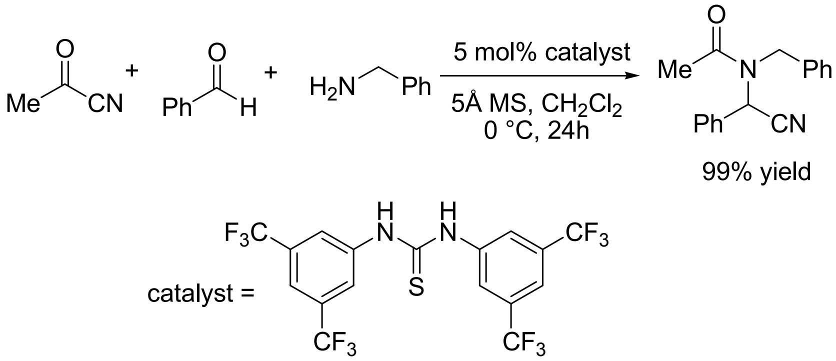
Curran and Schreiner independently published work indicating that achiral ureas and thioureas catalysed reactions.[91,92] Their work found that both achiral ureas and thioureas accelerated the rate of the reaction, especially when the R groups present on the nitrogens were phenyl groups with electron withdrawing groups present on the 3- and 5- positions. The presence of the electron withdrawing groups on the phenyl ring decreases the pK_a of the N-H protons and thus increased their ability to donate hydrogen bonds.[88]

Thioureas have been used in the reaction of various protected imines with nucleophiles due to their ability to activate imines which have been protected with many different protecting groups. This has proved very useful in the field of enantioselective carbon-carbon bond formation, for example their use in the diastereoselective nitro-Mannich reaction between nitroalkanes and *N*-Boc protected imines gave good to excellent enantiomeric excesses, (Scheme 40).[93]



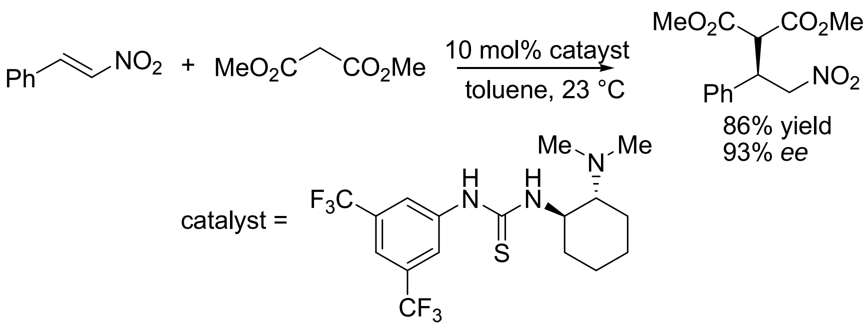
Scheme 40

List and co-workers have used a thiourea catalyst as a Brønsted acid catalyst in the one pot acyl-Strecker reaction of aldehydes, amines and acyl cyanides.[94] When used in this reaction the Schreiner thiourea catalyst gave good to excellent yields, (Scheme 41).



Scheme 41

The structure of thioureas allows the easy preparation of bifunctional catalysts, that is a catalyst with an additional acidic or basic group in addition to the thiourea moiety present. Synergistic activation by bifunctional catalysts has been shown to lead to effective activation of less reactive substrates.[95] Thioureas can easily be designed to have additional functionality due to the reliability and functional group tolerance of the isothiocyanate coupling used in their preparation.[88] The development of these catalysts were based on the idea that a thiourea moiety would, when coupled with a chiral Lewis base exert greater stereocontrol.[96] Bifunctional thioureas have been used in the catalysis of many enantioselective reactions with a wide range of substrates. Takemoto and co-workers reported the use of a bifunctional thiourea incorporating basic dimethylamino groups in the enantioselective Michael addition of malonates to nitroolefins, giving excellent enantiomeric excesses (Scheme 42).[97]



Scheme 42

The proposed mechanism for this reaction is that the thiourea activates the nucleophile by base catalysis and activates the electrophile by hydrogen bonding to the nitro group. Thioureas, which contain an acidic group for their second functionality, have also shown promise as catalysts.

Further thiourea catalysts developed by Jacobsen and co-workers have been used successfully in the Strecker reaction.[98] These catalysts differ structurally from other thiourea catalysts as they contain four distinct units, an α-amino acid unit, a urea or thiourea moiety, a *trans*-1,2-diamino cyclohexane unit and a salicylaldimine unit, (Figure 30). The optimal units were established by parallel screening, as were other factors such as substituents on the salicylaldimine unit.

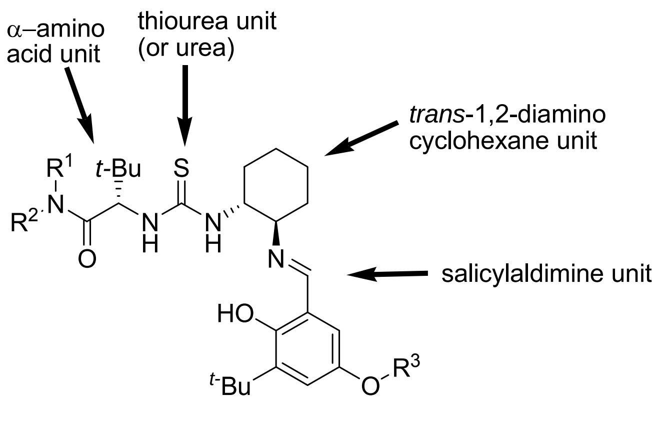
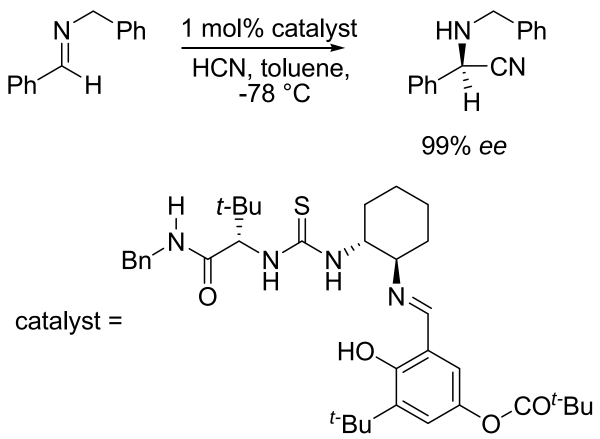


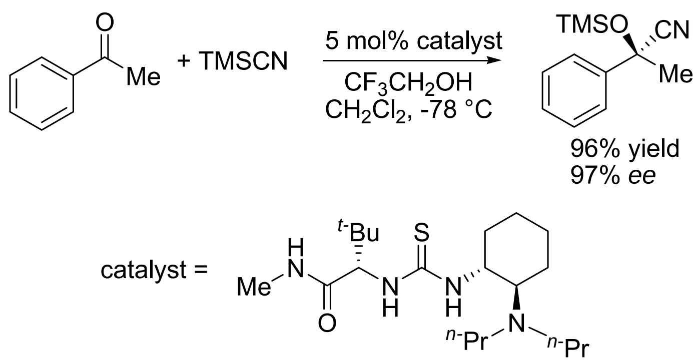
Figure 30

It has been demonstrated that even small seemingly minor changes at the amino acid amino group can have major effects on the stereoselectivity of the reaction.[96] When used in the hydrocyanation of imines the optimised catalysts gave higher enantiomeric excesses than the Schiff base on which they were originally based, (Scheme 43).[98]



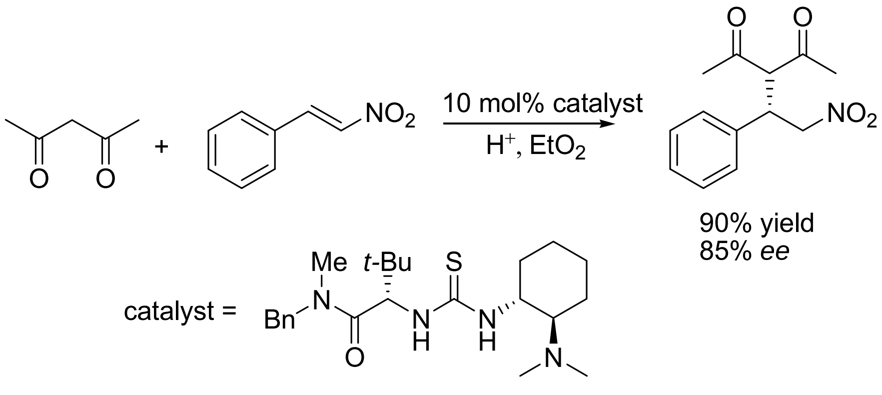
Scheme 43

Thioureas have also been applied to the asymmetric catalytic activation of carbonyl compounds with varying success. Jacobsen and co-workers developed their work further by the developing a catalyst for the cyanosilylation of ketones. They found that their previously developed catalyst (Scheme 43) gave no catalytic activity in this reaction, but by exchanging the salicylaldimine unit present for an amine substituent the new catalyst gave excellent enantiomeric excesses in the enantioselective cyanosilation of aldimines and ketones, (Scheme 44).[99] However, increasing the steric hindrance of the tertiary amine moiety on the catalyst can decrease enantioselectivity.[100]



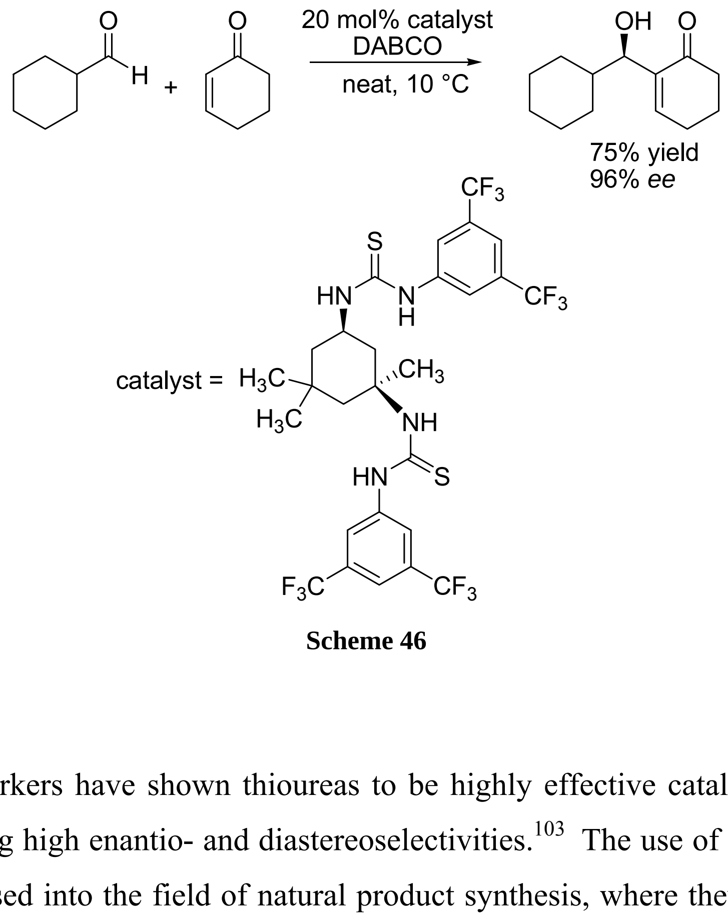
Scheme 44

Another use of bifunctional catalysts of similar design to the ones used by Jacobsen is their use in the reaction between *trans*-β-nitrostyrene and acetyl acetone to give moderate to good enantiomeric excesses (Scheme 45).



Scheme 45

Thioureas have also been utilised as catalysts in the Morita-Baylis-Hillman reaction This versatile carbon-carbon bond forming reaction is the reaction of an electron deficient alkene to an aldehyde, usually promoted by nucleophilic bases such as DABCO. The use of a bis-thiourea in this reaction by Nagasawa gave good to excellent yields and moderate to excellent enantiomeric excesses.[101] Another bis-thiourea was also in the Morita-Baylis-Hillman reaction by Berkessel and co-workers with similar results, (Scheme 46).[102]



Scheme 46

Deng and co-workers have shown thioureas to be highly effective catalysts for Mannich reactions showing high enantio- and diastereoselectivities.[103] The use of thiourea catalysts has also progressed into the field of natural product synthesis, where they have been used by Hatakeyama in the asymmetric synthesis of (+)-trachyspic.[104]

A variation in the design of thiourea catalysts has been the development of chiral phosphinothiourea catalysts by Wu and co-workers (Figure 31). Developed for use in the Morita-Baylis-Hillman reaction where tertiary phosphines and thioureas have both been proven as effective catalysts. The new catalysts are easily prepared by the condensation of (*R*,*R*)-2-amino-1-(diphenylphosphino)cyclohexane with an iso(thio)cyanate to give the phosphinothiourea.[105]

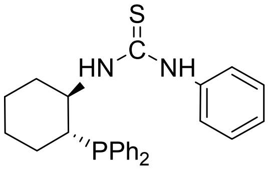
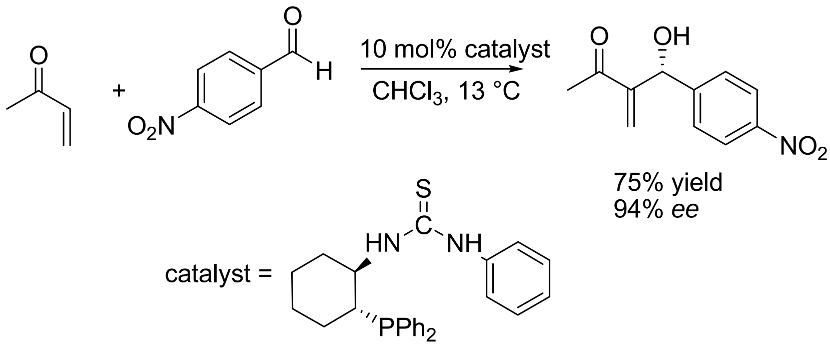


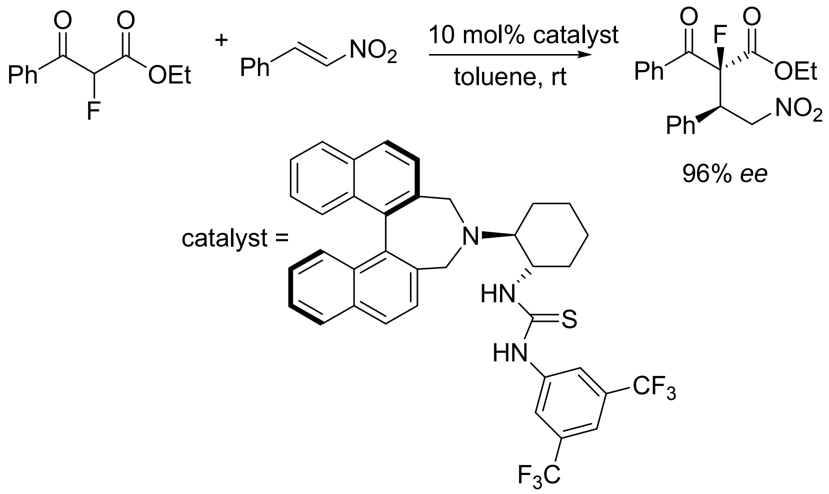
Figure 31

When used in the enantioselective Morita-Baylis-Hillman reaction between vinyl methyl ketone and aromatic aldehydes the new class of organocatalysts gave enantiomeric excesses up to 94% and good to excellent yields (Scheme 47).[105]



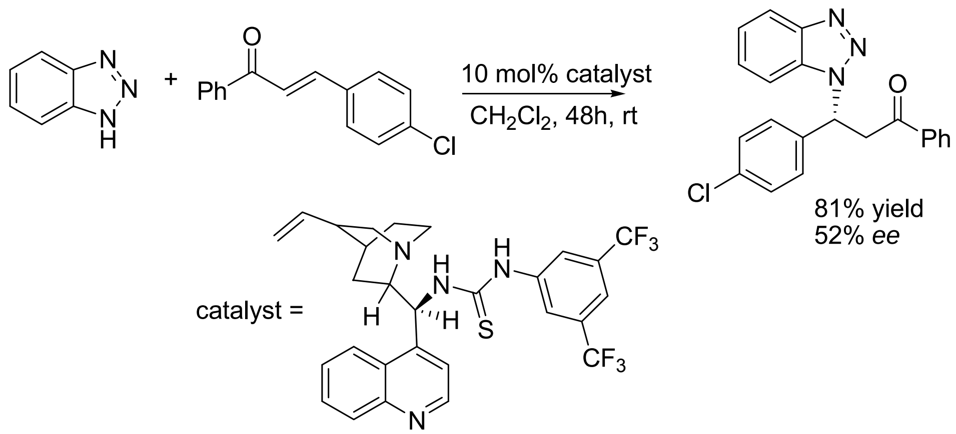
Scheme 47

Other more recent uses of thioureas catalysts has been in the field of fluoroorganic compound synthesis, where Kim and co-workers successfully used a bifunctional thiourea catalyst in the enantioselective conjugate addition of α-fluoro-β-ketoesters to nitroalkenes.[106] The thiourea catalyst containing a binaphthyl moiety in this reaction gave excellent enantiomeric excesses (Scheme 48).



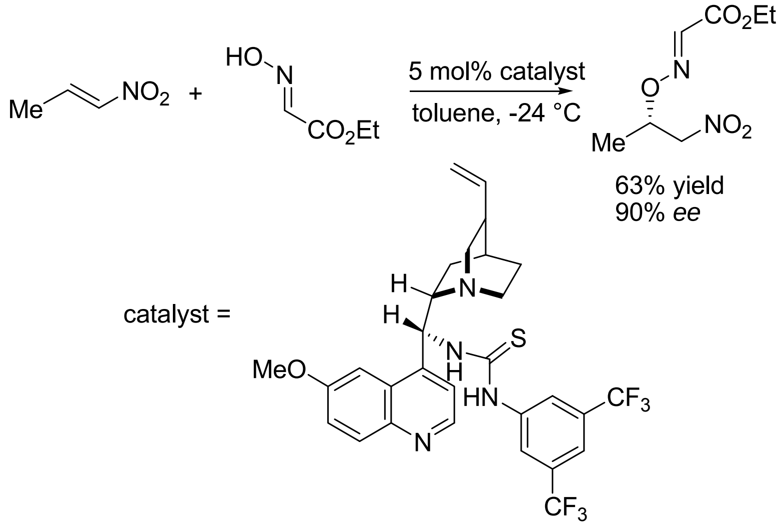
Scheme 48

Further designs of thiourea catalysts are those which are derived from cinchona alkaloids. These thioureas developed by Wang and co-workers gave good yields and moderate enantioselectivities when used as catalysts in the enantioselective conjugate addition of *N*-heterocycles to enones (Scheme 49); more specifically weakly nucleophilic and acidic *N*-heterocycles such as benzotriazole.[95]



Scheme 49

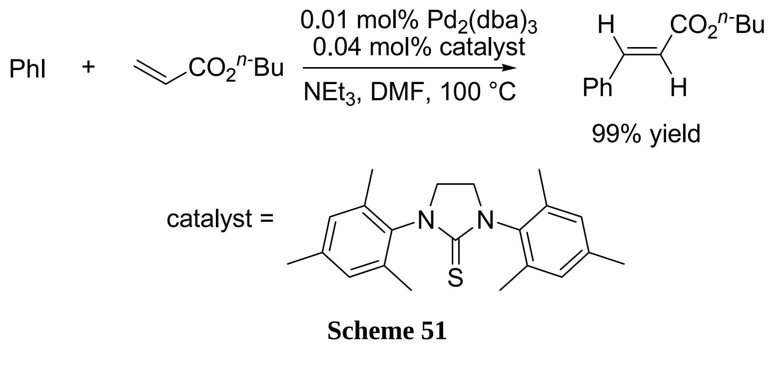
The use of cinchona alkaloid containing thioureas has also been reported by Jørgensen and co-workers in the enantioselective hydroxylation of nitroalkenes.[107] When used in this reaction the catalysts have the potential to activate the basic quinuclidine nitrogen atom by hydrogen bonding and by Lewis acid activation of the nitroalkene by the thiourea unit. The enantiomeric excesses achieved using alkaloid based thiourea catalysts in the stereoselective conjugate hydroxylation of nitroalkenes using oximes as the oxygen source were excellent, (Scheme 50). Cinchona alkaloids have also been shown to be effective catalysts for Mannich reactions.[107]



Scheme 50

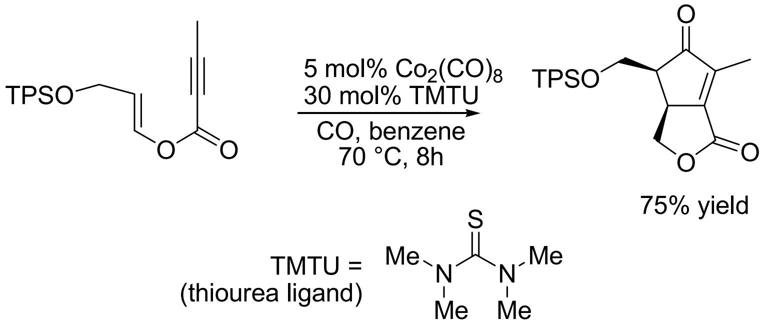
In organometallic catalysis, thiourea compounds have been at the forefront of the rush to develop phosphine-free ligands. Phosphine ligands are generally used to stabilise the reactive palladium intermediate in Heck and other carbon-carbon bond forming reactions and although, as ligands, phosphines give excellent results, their air sensitivity places limitations on their synthetic use.

Thioureas have proved to be air and moisture stable solids which can be employed as ligands in a large range of ruthenium-, rhodium- and palladium-catalysed reactions.[108,109] In 2004 Yang and co-workers reported the use of a thiourea as a ligand for the palladium catalysed Heck and Suzuki.[110] Yang and co-workers varied the structure of the thioureas to study the influence the structure of the catalyst had on catalyst efficiency.[108] They found that bulky *N,N'*-disubstituted cyclic thioureas gave much higher activity than acyclic or less sterically demanding groups when used in the palladium catalysed Heck reaction of aryl halides, (Scheme 51).

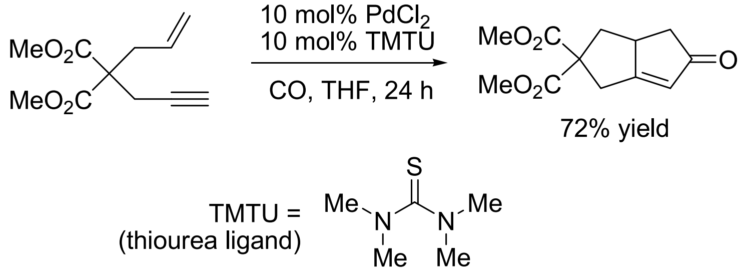


Scheme 51

Yang and co-workers reported further uses of thiourea ligands in the cobalt catalysed Pauson-Khand reaction,[111] (Scheme 52), and the palladium catalysed Pauson-Khand reaction, (Scheme 53).[112] In both cases, they report complexation between the thiourea and the metal significantly speeds up the reaction although the mechanism for this is unclear.

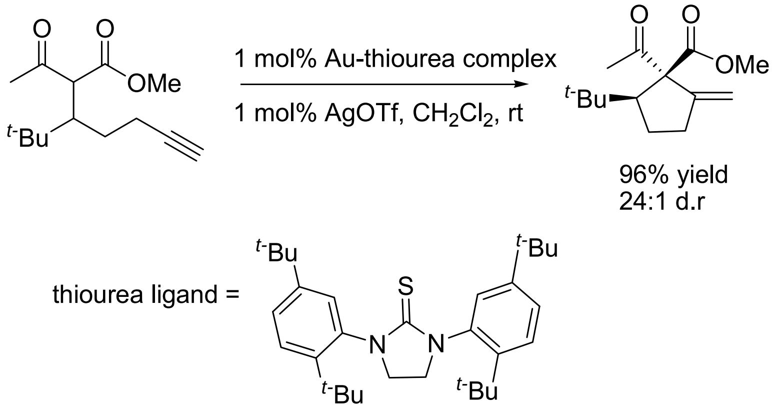


Scheme 52



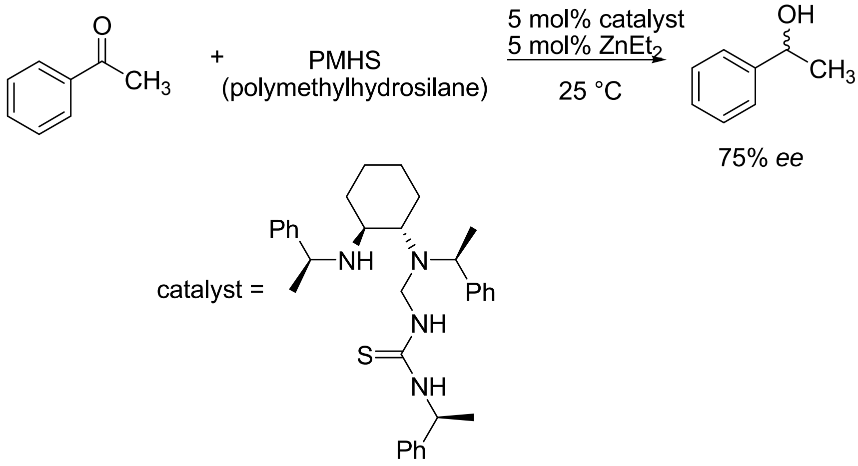
Scheme 53

Thioureas have shown promise in the field of gold catalysis, Yang and co-workers have utilised bulky *N,N'*-disubstituted thioureas as ligands for gold(I) catalysis. When used in the cyclization of acetylenic 1,3-dicarbonyl compounds with alkynes (the Conia-ene reaction) thioureas gave high yields with low catalyst loading and moderate diastereoselectivity, (Scheme 54).[113]



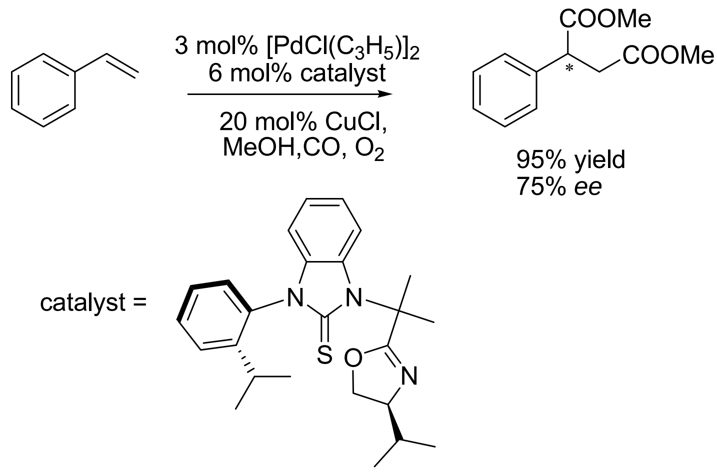
Scheme 54

Thioureas can be manipulated to contain other chiral functionalities as demonstrated in work by Anaya de Parrodi and co-workers who use thioureas with (*S*)-α-phenylethyl groups as chiral appendages as catalysts for the zinc mediated hydrosilation reaction of acetophenone with polymethylhydrosilane, achieving good enantiomeric excesses, (Scheme 55).[114]



Scheme 55

Use of bifunctional thiourea catalysts has also been demonstrated in the field of organometallic catalysts, where Liang and co-workers developed a thiourea containing an oxazoline unit.[115] This chiral S,N-heterobidentate thiourea oxazoline ligand was designed for use in the palladium catalysed asymmetric Bis(methoxycarbonylation) of terminal olefins, and it is the oxazoline which gives the reaction stereocontrol. This ligand gave high yields and moderate enantioselectivity when used in the enantioselective carbonylation of styrene, (Scheme 56).[115]



Scheme 56

Thioureas have proved in recent years to be excellent organometallic catalysts and highly useful as organocatalysts emerging as good catalysts, which do not require strictly controlled reaction conditions.[116] Their tuneability is highly advantageous, they can have their electronic and steric properties easily modified by changing the nitrogen substituents, thus altering the properties of the catalyst. They are structurally diverse molecules and are relatively easy to produce. When used comparatively in reactions thioureas have, in some cases proved superior to the urea catalyst; presumably due to stronger hydrogen bonding interactions.[105]

1.6 – Phosphorus-Nitrogen (P,N) Ligands

Phosphorus-Nitrogen ligands (P,N Ligands), that is ligands which contain a nitrogen unit, examples include pyridyl units, secondary or tertiary amines or imine moieties along with a phosphine unit, typically aryl phosphines have received high interest in the field of organometallic catalysis. In 1990 Budzelaar and co-workers described the synthesis of two P,N ligands (Figure 32) for the chelation to a metal centre which would form a strong chelation to the metal and therefore not fragment during chemical reactions, more specifically the anion which was capable of forming a N-bridged bis-chelate complex.[117]

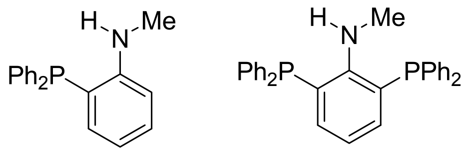


Figure 32

Budzelaar successfully accomplished complexation with $Mo(CO)_6$ and achieved a species which was stable to adverse reaction conditions, (Figure 33).

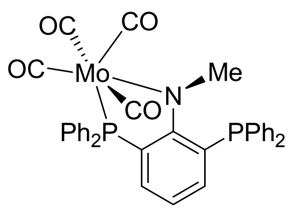


Figure 33

Many ligands for metal catalysis are based on a C_2- symmetrical structure, whereas most P,N ligands are unsymmetrical. Work by Lee and co-workers suggested that non-symmetrical ligands with two coordinating heteroatoms allow for higher stereocontrol than their C_2- symmetric counterparts.[118] However, Trost and co-workers reported a ligand derived from C_2-symmetrical *trans*-diamines to be effective catalysts in many enantioselective reactions (Figure 34), generating enantiomeric excesses of up to 80% in asymmetric allylic alkylation reactions for example.[119]

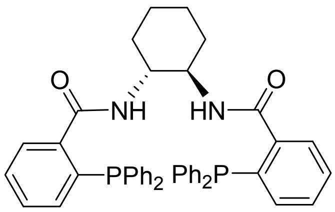


Figure 34

P,N ligands contain a hard donor, the nitrogen atom, and a soft donor, the phosphorus atom, thus a wider range of metal centres can be stabilised by the ligand than those containing two hard or soft donors.

Donor atoms can be defined as hard or soft depending on the properties of the atom. Hardness is associated with low polarizability and high electronegativity, whereas a soft donor is related to high polarizability and low electronegativity. [120] On the principle of Hard-Soft Acid-Base (HSAB) theory the presence of the two types of donor atom gives the ligand the ability to bind to both hard acids and soft acids;

'Hard acids prefer to bond to hard bases and soft acids prefer to bond to soft bases'[120]

Thus hard N/O donors can stabilise s and p and early d block metal cations whereas the softer P/S donors will show a preference for stabilising heavier p block and latter d block metals.[120] Therefore, a ligand with a hard and soft donor should be able to stabilise metal ions in low oxidation states by the π-accepting character of the phosphorus, whereas metals in higher oxidations states are stabilised by the hard character of the nitrogen donor giving the ligand a wide range of metals to which it can be successfully complexed.[121]

Using this theory and the knowledge that P,N ligands form stable complexes with metals Helmchem, Pflatz and Williams all independently synthesised a non-symmetric catalyst containing an oxazoline unit and a phosphine moiety generating phosphinooxazoline ligands such as the PHOX ligand, (Figure 35).[122,123,124]

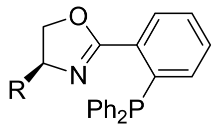
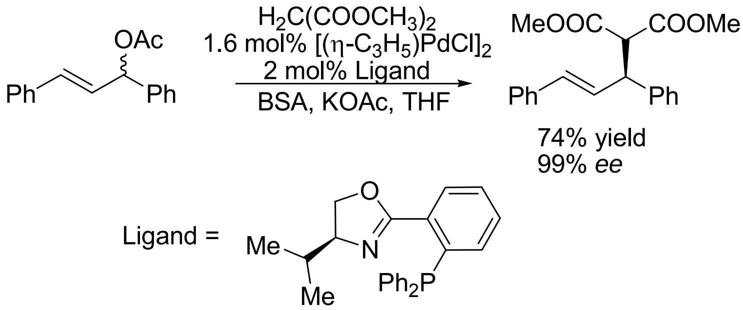


Figure 35

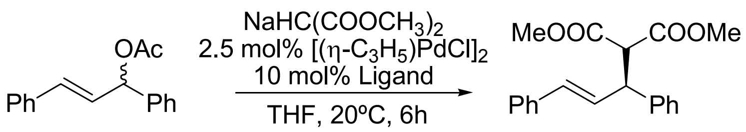
The phosphine moiety can be added either before of after the synthesis of the oxazoline ring and when used in allylic substitution reactions allowed 'electronic differentiation' of the two termini of the π-allyl complex due to the two ligating groups having different electronic properties.[118] Thus high enantiomeric excesses can be achieved, (Scheme 57).[122]

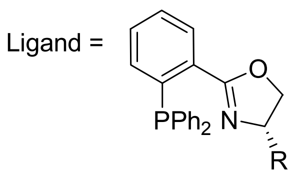


Scheme 57

With the high enantioselectivities achieved with phox ligands Helmchen and Pflatz investigated the palladium, tungsten, iridium and platinum complexes of phosphinooxazoline ligands in allylic substitution reactions, with varying results. The modular structure of the ligands allows easy manipulation of the ligand by allowing the oxazoline ring, the backbone and the phosphine moiety to all be easily changed.[45] The high enantioselectivities achieved by this type of ligands increased interest in P,N ligands with many new ligands based on phox ligands being reported. The allylic alkylation reaction in which Helmchen and Pflatz achieved such high enantiomeric excesses became one of the test reactions in which groups tested their new P,N ligands.

Williams and co-workers investigated the effect changing the R group present on the oxazoline ring on the enantiomeric excess achieved in an allylic alkylation reaction, (Scheme 58).[124]





R groups	*ee* (%)
Me	90
$PhCH_2$	92
iPr	94
Ph	92
tBu	90

Scheme 58

Williams and co-workers also reported the use of platinum complexes using the same type of ligands, however the enantiomeric excesses seen in these reactions were poor (ca. 20%), which they attributed to the P-Pt-N complex formed by the oxazoline lingand not being as stable in the presence of other ligands as the corresponding palladium complex.[125]

Increasing the chelate ring size from a five to six membered chelate ring or having a more rigid backbone between donor atoms can greatly affect the enantiomeric excesses achieved. Guiry and co-workers reported work utilising three different types of P,N ligands (Figure 36) with differing designs to highlight these affects.[126]

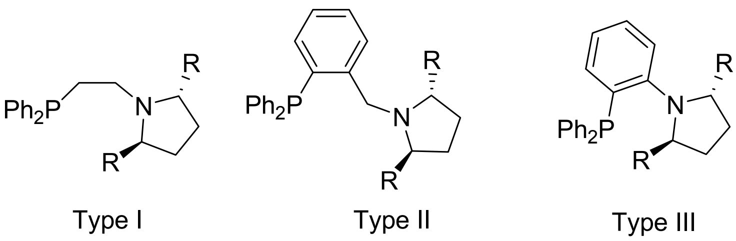


Figure 36

Ligands of Type I gave poor enantiomeric excesses of between 11-20% when used in palladium catalysed allylic alkylation, increasing the chelate ring from five to six, as in the case of Type II gave higher enantiomeric excesses, from 55-90% although this design of ligand could also have benefited from the more rigid phenyl backbone. Therefore a ligand was designed using the Type III scaffold, this ligand also give much lower enantiomeric excesses of between 10-34%. From this Guiry concluded that a six membered chelate ring and bulkier substituents were necessary in designing a ligand which would generate satisfactory enantioselectivity.[126]

Lee and co-workers reported the use of a bisphosphine-oxazoline ligand which is C_2-symmetric with a conformationally rigid bioxazole ring for use in enantioselective hydrosilation reactions (Figure 37).[127]

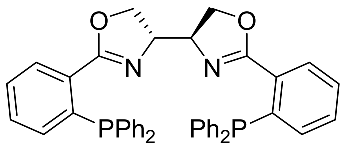
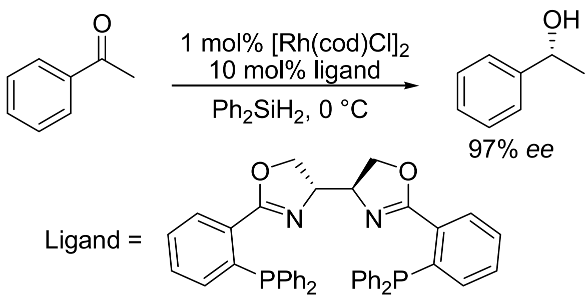


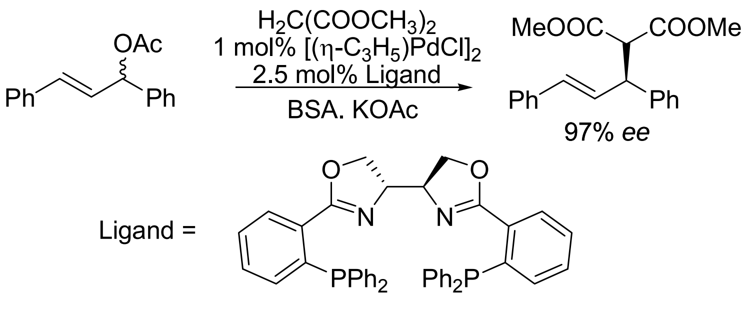
Figure 37

The design of this ligand transfers chirality to the phosphine *via* the backbone, which combined with the chelate ring, which creates a wide bite angle, generates a deep 'chiral pocket' for the metal to reside, giving greater stereocontrol. Lee and co-workers used this ligand design in the rhodium(I) catalysed enantioselective hydrosilation of acetophenone and its derivatives generating good to excellent enantiomeric excesses, (Scheme 59).[127]



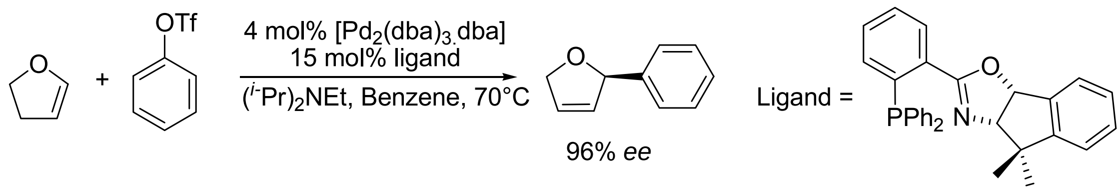
Scheme 59

Lee has also reported use of the same ligand in palladium catalysed enantioselective allylic substitution reactions generating enantiomeric excesses of up to 97%, (Scheme 60.)[118]



Scheme 60

Other reactions in which these phosphinooxazoline ligands have been successful includes the asymmetric Heck reaction, reported in 2000 by Hashimoto and co-workers use of a phox type ligand gave excellent enantiomeric excesses (Scheme 61).[128]



Scheme 61

In 2001 Gilbertson reported the use of a chiral P,N ligand based on ketopinic acid. This type of ligand still contains the oxazoline unit so common in P,N ligands but has a more rigid norbornyl backbone, (Figure 38).[129]

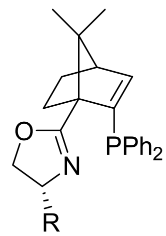
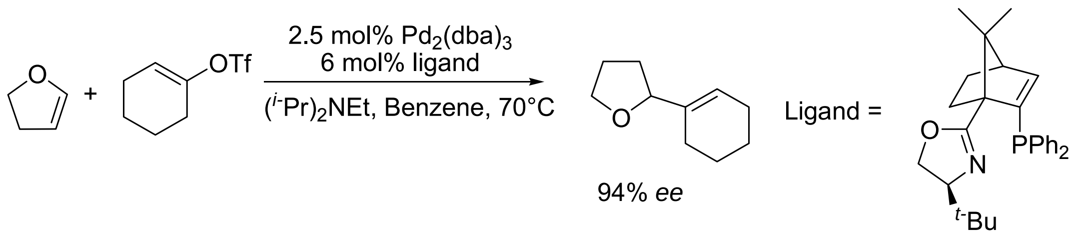


Figure 38

Gilbertson and co-workers used this ligand in the Heck reaction of cyclic and acyclic triflates with cyclic alkenes, generating excellent enantioselectivity, (Scheme 62).



Scheme 62

For comparison, a ligand not containing a norbornyl backbone was also synthesised and tested in the same reactions, (Figure 39). The enantioselectivity achieved with this ligand was much lower (only 6%) which was contributed to the lack or rigidity in the backbone.[129]

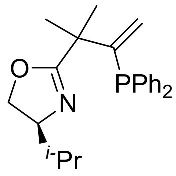


Figure 39

Further developments in backbone design of P,N ligands have been reported by Fu and co-workers by the synthesis of a phosphaferrocene-oxazoline ligand (Figure 40) which was tested in palladium catalysed allylic alkylations giving good enantiomeric excesses, (Scheme 63).[130]

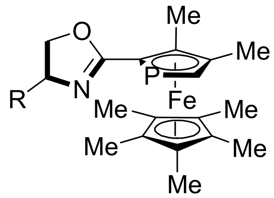
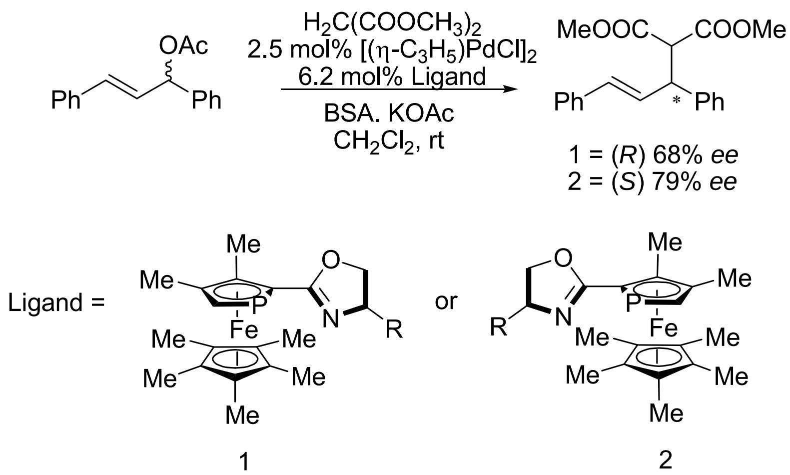


Figure 40

Fu investigated whether the phosphaferrocene or the oxazoline unit were responsible for the stereocontrol achieved in the reaction and found that the enantioselectivity is controlled not by the oxazoline unit as in other P,N ligands but by the phosphaferrocene. This was established by one enantiomer being favoured when one phosphaferrocene diastereomer was used as the ligand and the other enantiomer being favoured upon the opposite phosphaferrocene diastereomer being used.[130]



Scheme 63

Another class of P,N ligands are iminophosphines (Figure 41), these contain a weak π-accepting imine with the strong σ-donor phosphine. They have shown promise in a range of reactions, many palladium mediated, including the cross-coupling of organostannanes with aryl halides and the carbostannylation of arynes.[131,132]

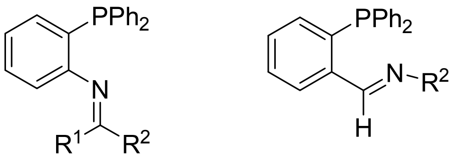
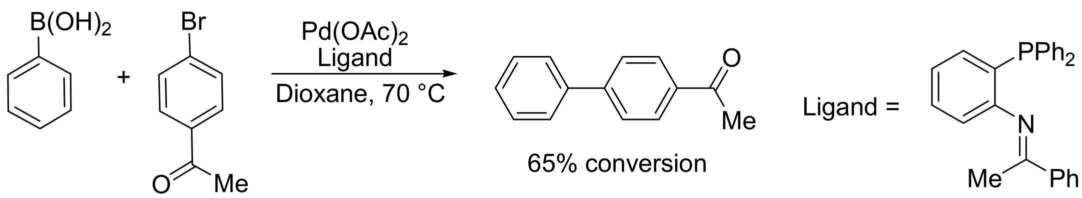


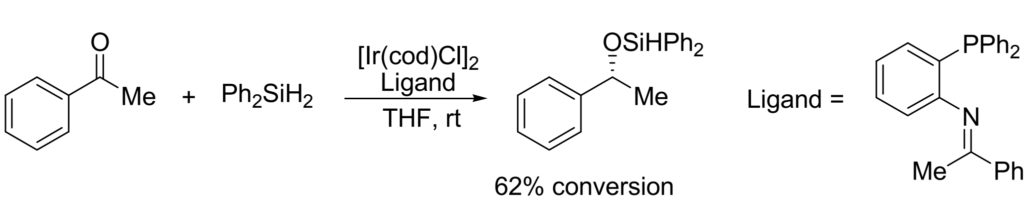
Figure 41

The steric bulk of the iminophosphine affects the rate of reaction and the regioselectivity, the more bulky the imino substituent the higher the yield and regioselectivity,[133] with some iminophosphines proving more efficient than their corresponding amino-phosphine counterparts. One highly attractive feature of iminophosphines is their relative ease of synthesis and therefore the ease at which the imine substituents can be varied. Of the different structures of iminophosphines available (Figure 41), one is synthesised by the condensation of 2-(diphenylphosphino)aniline with an aldehyde or ketone or to generate the second type, condensation of 2-(diphenylphosphino) benzaldehyde with an amine.[133]

When Doherty and co-workers used iminophosphine ligands in a palladium catalysed Suzuki cross-coupling reaction (Scheme 64) and the hydrosilation of ketones (Scheme 65) only moderate conversions were achieved.

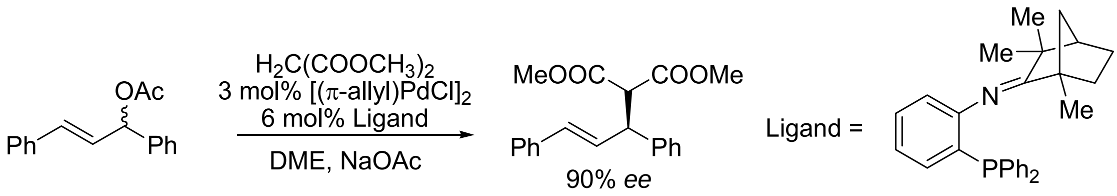


Scheme 64



Scheme 65

The iminophosphine functionality has planarity over five atoms (P-C-C-N=C) and this coupled with a chiral auxiliary is able to give good to excellent enantioselectivity in palladium mediated reactions. Horoi and co-workers demonstrate this by achieving excellent enantiomeric excesses in asymmetric alkylation reactions with a ligand of this design, (Scheme 66).[134]



Scheme 66

Ruffo and co-workers used the iminophosphine functionality as a basis for the design of P,N ligands which are derived from carbohydrates. Ligands which contained D-mannoside or D-glucoside residues (Figure 42) were used olefin hydroboration reactions and in the palladium mediated test reaction of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate but only poor enantioselectivity was seen; anenantiomeric excess of around 20% was obtained.[135]

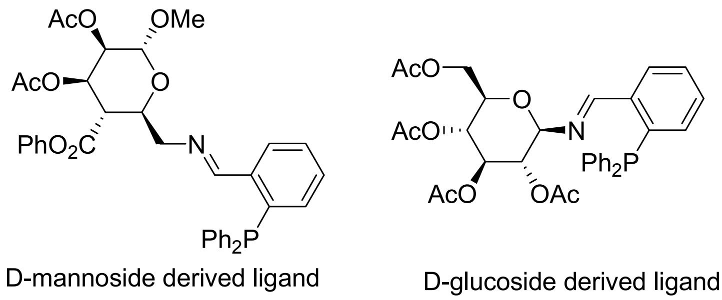


Figure 42

Whilst the number of P,N ligands has grown rapidly there have been far fewer reports of P,N ligands in which the nitrogen donor atom is contained within a pyridine ring. Chelucci and co-workers have reported such ligands derived from naturally occurring compounds (Figure 43), when used in the favoured test reaction of the enantioselective palladium catalysed allylic alkylation reaction of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate this type of ligand generated enantiomeric excesses of up to 70%.[136]

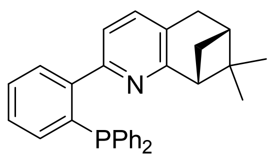
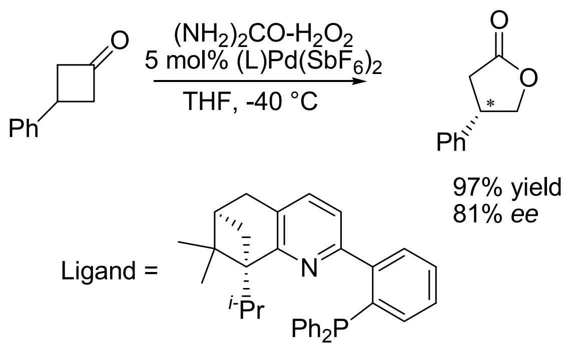


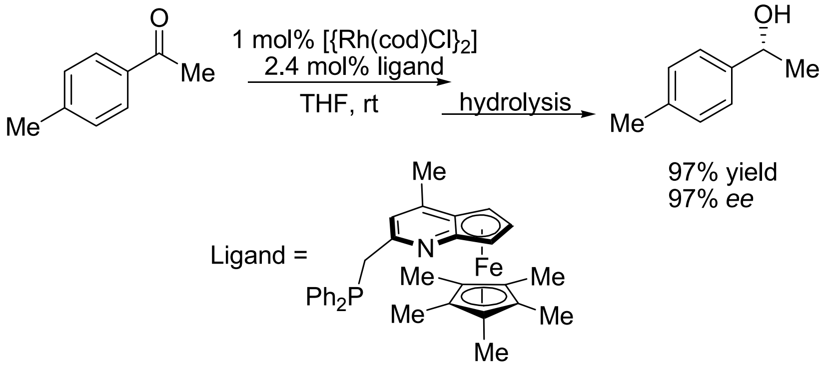
Figure 43

Malkov and Kočovský have reported the use of a terpene derived P,N ligand for use in the Baeyer-Villiger oxidation reaction, generating moderate to excellent enantiomeric excesses. The same group has also reported the use of these ligands in the asymmetric Heck and palladium catalysed allylic substitution reactions (Scheme 67).[137]



Scheme 67

Further developments of ligands containing the pyridyl functionality have been reported by Fu and co-workers. Based on their previous work with planar chiral phosphaferrocene oxazolines Fu developed a new type of planar chiral ligand containing the nitrogen donor within a pyridine ring. The use of this ligand in the rhodium catalysed asymmetric hydrosilation of various ketones including electronically varied and sterically demanding ketones all gave good to excellent enantiometric excesses (Scheme 68).[138]



Scheme 68

Another variation on the pyridyl derived P,N ligands has been the synthesis by Wilson and co-workers of an acetal prepared from 2-chloro-4-methyl-6,7-dihydro-5H-[1]-pyridine-7-one (Figure 44) generating a new class of ligand, which when used in the palladium test reaction of 1,3-diphenylprop-2-enyl acetate with dimethyl malonate gave good to excellent enantioselectivity.[139]

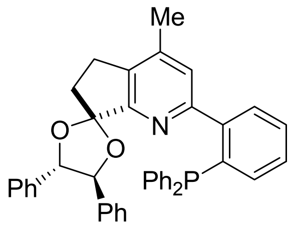


Figure 44

P,N ligands based on a binaphthyl backbone have shown promise in a wide range of reactions. 2-dimethylamino-2'-diphenylphosphino-1,1'-binaphthyl (MAP) was first synthesised in 1998 and is available in both the (*R*) and (*S*) enantiomers, (Figure 45).[26]

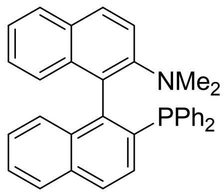
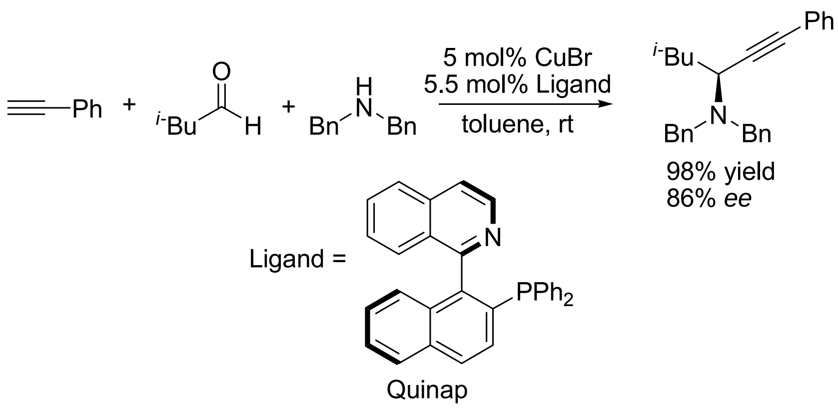


Figure 45

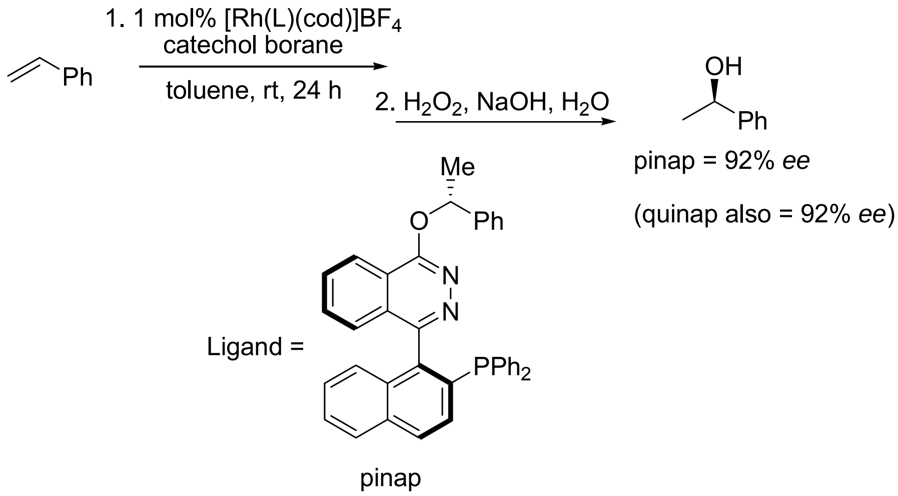
Since the discovery of MAP there have been various analogues of MAP synthesised, Buchwald has prepared a number of these, for example, the biphenyl version of MAP, many of which do not share the phosphorus and nitrogen donor atoms. The MAP ligand and analogues have been shown to accelerate both the Buchwald-Hartwig amination reaction and the Suzuki-Miyaura cross-coupling reaction.[26]

MAP is not the only binaphthyl based P,N ligand to have been used successfully, quinap has also proven highly successful in asymmetric in catalysis, and displays activity in many reactions, such as hydroboration and the copper (I) catalysed three component preparation of propargylamines (Scheme 69).[140]



Scheme 69

Pinap is also a readily available atropoisomeric P,N ligand which in some reactions proves to be superior to quinap. Designed by Carreira and co-workers, pinap has been used in the rhodium catalysed hydroboration of alkenes (Scheme 70) generating good to excellent enantiomeric excesses, although none reported were significantly higher than the ones achieved in the same reaction by quinap.[141]



Scheme 70

The same group has also used a different analogue of Pinap (Figure 46) successfully in the copper (I) catalysed three component preparation of propargylamines (Scheme 69), generating up to 90% enantiomeric excesses.[141]

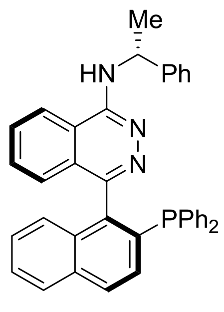


Figure 46

More recently other binaphthyl based P,N ligands have been used with varying success by Yuan and co-workers. The development of a chiral phosphine-Schiff base for the use in silver (I) catalysed asymmetric vinylogous Mannich reactions has generated a wide range of ligands of the general structure below, (Figure 47).[142]

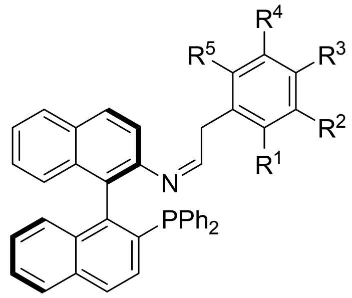
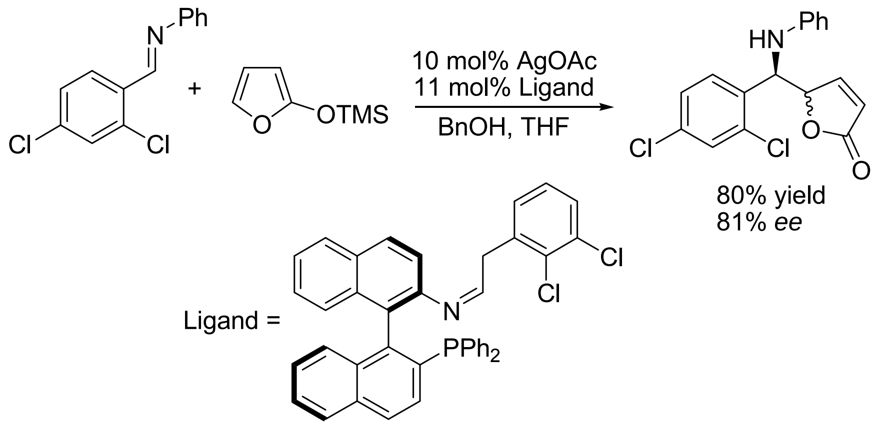


Figure 47

Yuan's work studied the effect of differing the R groups in the benzene ring when ligands were used in the asymmetric vinylogous Mannich reaction of an aldimine and siloxyfuran, (Scheme 71). They found that a benzene ring with an electron withdrawing or electron donating group in the R^2 position gave the best results.[142]



Scheme 71

A variation on the typical phosphine moiety present in P,N ligands has been reported by Willis and co-workers who varied the R groups on the phosphorus donor atom from the conventional two phenyl groups to cyclohexane or t-Butyl groups, (Figure 48).[143]

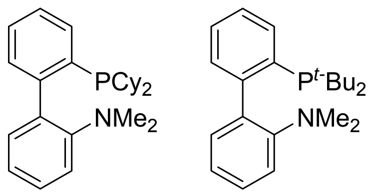


Figure 48

Both ligands proved ineffective in the coupling of enol triflates with amides, only giving up to 20% conversion in the case of the t-butyl substituted phosphorus and no conversion at all being seen with the cyclohexane substituted ligand.

P,N ligands have in more recent years found use in polymerisation and oligomerization reactions. Braunstein and co-workers reported the use of a P,N nickel chelate complexes in catalytic ethylene oligomerization reactions. Since this P,N ligands have had increased interest in the fields and have been used by Jin and co-workers, who found that simple P,N ligands (Figure 49) have very high activities in addition polymerisation.[144]

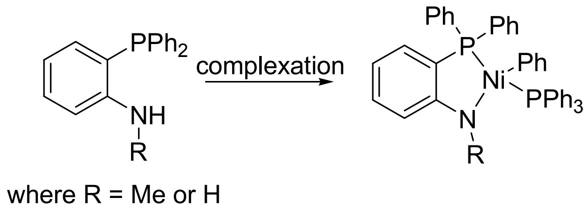


Figure 49

The mechanism by which this polymerisation works has been hypothesised as insertion of the norbornene into the Ni-C bond, thus having a more bulky group in the nitrogen, such as methyl, lowers the catalytic activity. These ligands can generate polymers of norbornene, after activation with MAO to give polynorbornene with high molecular weights of up to 3.07 x 10^{-6} g/mol^{-1}.[144]

In addition to the use of P,N ligands in the polymerisation of norbornene Cui and co-workers have reported the use of a P,N rare earth metal complex in ethylene polymerisation. The complexation of a soft phosphine donor with a rare earth metal is not widely explored as rare earth metals tend to flavoured hard donors such as nitrogen or oxygen donors. Cui and co-workers complexed their P,N ligands with yttrium, scandium, lutetium, ytterbium and thulium (Figure 50) and have used the scandium bis(alkyl) complex in the polymerisation of ethylene to liner polyethylene giving polymers with molecular weights of up to 0.592 x 10^{-6} g/mol^{-1}.[145]

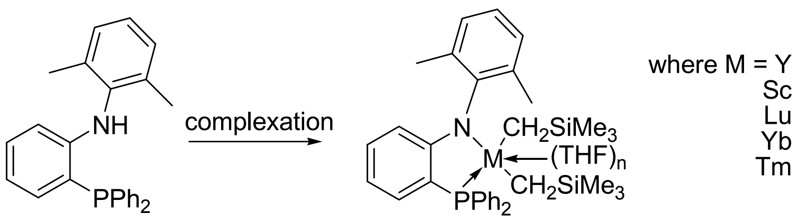


Figure 50

Ethylene oligomerization has also been investigated by Dyer and co-workers who took advantage of the hard/soft and electronic properties of the chelating P,N ligand for use in nickel (II) catalysed ethylene oligomerization. Dyer based his P,N ligand on a bicyclic guanidine skeleton, which gives the ligand and therefore the metal a very rigid structure, (Figure 51).[146]

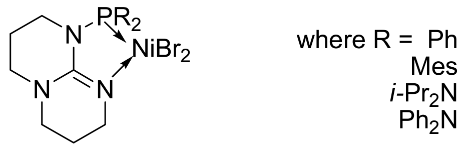
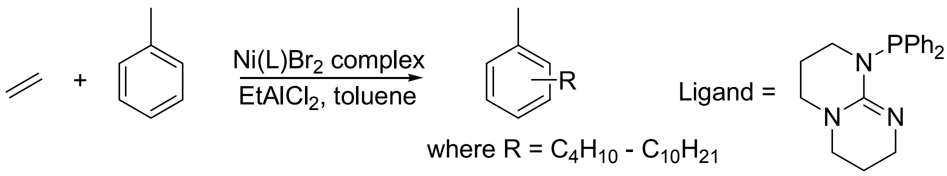


Figure 51

These ligands were active in ethylene oligomerization giving a mixture of butenes, hexenes and octenes depending on the R group present on the phosphorus donor. Surprisingly Dyer also reported that in the presence of the ligand where both R groups are phenyl that a Friedel-Crafts alkylation of the solvent occurs, (Scheme 72).[146]



Scheme 72

Phosphorus-nitrogen (P,N) ligands have been highly successful in field of organometallic catalysis, where the ease with which the R- groups can be modified is advantageous. Interest in this type of ligand and their metal complexes has grown in recent years as high enantioselectivities and good yields of high molecular weight polymers have been reported.

In conclusion, there are many successful ligand and organocatalyst systems already in place for a wide range of asymmetric reactions, most of which give excellent enantiomeric excesses and yields in their chosen reactions. Many are successful in reactions where it is advantageous to have a ligand or catalyst of modular structure allowing easy alterations in electronic and steric properties of the ligand. This allows for easy optimisation for the specific catalytic system in which it is to be used.

2.0 - Results and Discussion

2.1 – Research Aim

The primary aim was of this project to develop an effective new non-phosphine chiral ligand for use in organometallic chemistry and organocatalysis. Although there are many examples of non-phosphine ligands being used in a range of reactions, there are no reports of a common precursor being used to produce a range of ligands. This research therefore, aimed to design a common backbone from which four different ligand types: carbene, thiourea, phosphordiamidite and phosphoric acid are easily accessible.

Initial design focused on the synthesis of a C_2- symmetric diamine derived frim on 1,2-dibromobenzene, (Figure 52).

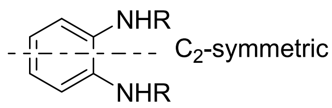
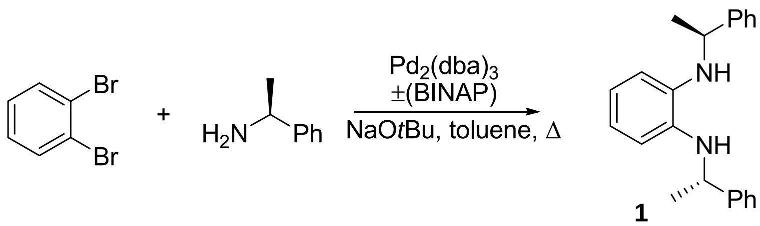


Figure 52

Different R groups could be introduced using chiral amines in the Buchwald-Hartwig reaction.[147]

Initially, the plan was to react 1,2-dibromobenzene with (*S*)-(-)-α-methylbenzylamine and *via* a double Buchwald-Hartwig reaction to generate the diamine, bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** (Scheme 73).



Scheme 73

This diamine could then be used to synthesise a range of ligands e.g. carbene, phosphordiamidite, thiourea and phosphoric acid, (Figure 53).

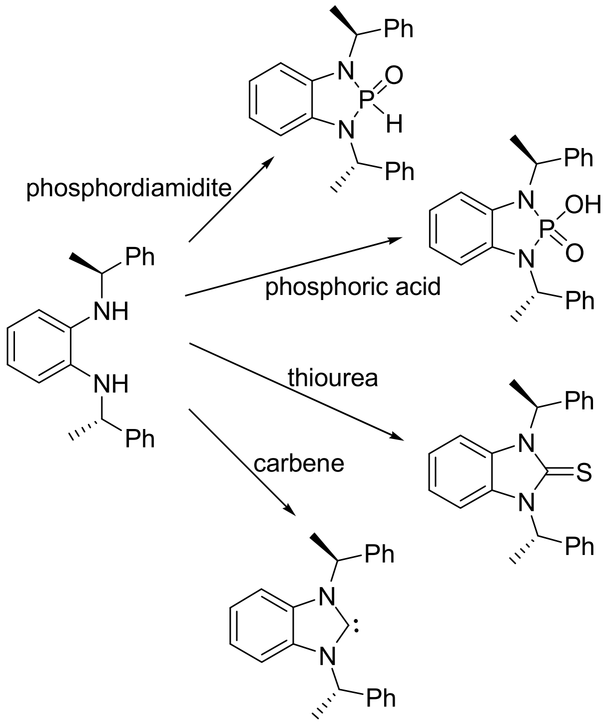


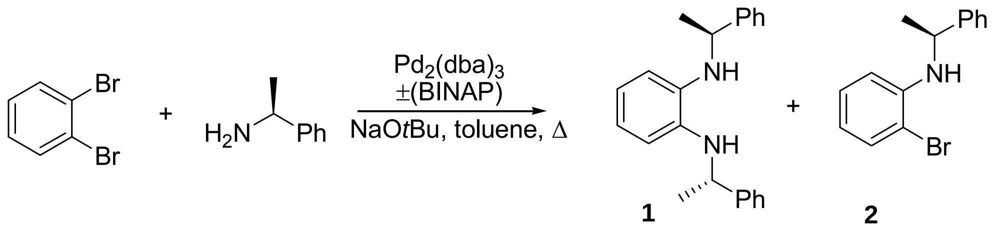
Figure 53

Once synthesised, these ligands would be tested in a range of different reactions. Other areas of research could include the use of the core backbone for the design and modification of a number of ligand types in the quest for both an organocatalysts and a ligand which can be used in organometallic chemistry.

2.2 – Ligand and Organocatalyst Synthesis

2.2.1 – Phosphordiamidite Synthesis

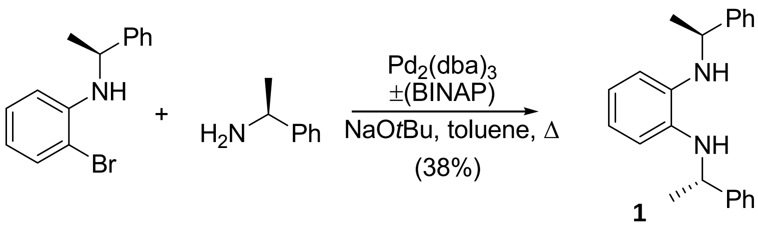
With the aim of this project being to synthesise a common backbone the first target, (**1** in Scheme 74) was synthesised by the reaction of 1,2-dibromobenzene with (*S*)-(-)-α-methylbenzylamine in toluene for 1.5 hours to generate both bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** and 2-bromo-((*S*)-1-phenylethyl) benzenamine **2**, in 22% and 54% yield respectively, using the Buchwald-Hartwig reaction.



1 22% **2** 54%

Scheme 74

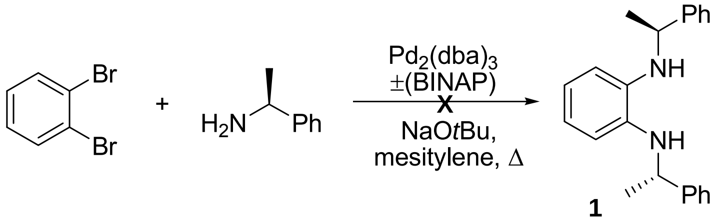
Previous preparations in the group synthesising diamine **1** had indicated that monoamine **2** was the highest yielding product in this reaction.[148] To generate more of diamine **1**, monoamine **2** was reacted with (*S*)-α-methylbenzylamine for a longer period of time, in a higher boiling solvent, mesitylene, to generate **1** in 38% yield (Scheme 75).



1

Scheme 75

As this reaction was also low yielding, optimisation of the reaction conditions was required. Primarily the original reaction was repeated for a longer time period (4 hours) in mesitylene, resulting in a complex mixture (Scheme 76).



Scheme 76

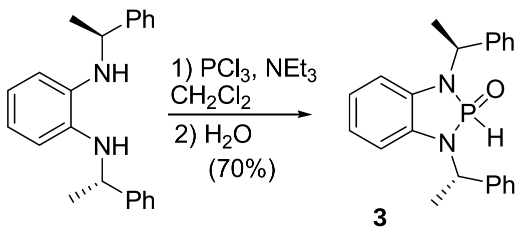
Further optimisation of the reaction can be seen in (Table 1) and overall the desired product **1**, was generated in 76% yield.

Table 1: Optimisation of reaction conditions

Entry	Solvent	Temperature	Time (h)	% yield of diamine (**1**)	yield of monoamine (**2**)
1	toluene	110°C	1.5	22	54
2	mesitylene	150°C	3	38	N/A
3	mesitylene	150°C	4	complex mixture	
5	toluene	110°C	4	60	21
8*	Toluene	110°C	4	76	0

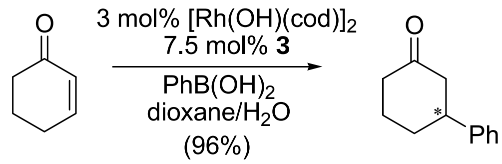
*new batch of tris(dibenzylideneacetone)dipalladium catalyst used

With the diamine in hand, an attempt to syntheses a ligand could be made. Initially it was decided that diamine **1** would be reacted with phosphorus trichloride in the presence of base, to generate the phosphordiamidite **3**; this reaction proceeded in 70% yield (Scheme 77).



Scheme 77

A test reaction reported by Feringa and co-workers was decided upon to determine the capabilities of phosphordiamidite **3**;[58] therefore the enantioselective conjugate addition of an arylboronic acid to an enone (in this case cyclohexanone) using a rhodium catalyst in the presence of a phosphoramidite ligand, was preformed. Cyclohexen-1-one was reacted with phenylboronic acid in the presence of 3 mol% $[Rh(OH)(cod)]_2$ and 7.5 mol% of ligand **3** to yield the desired product 3-phenylcyclohexanone **4** in a high 96% yield, (Scheme 78).

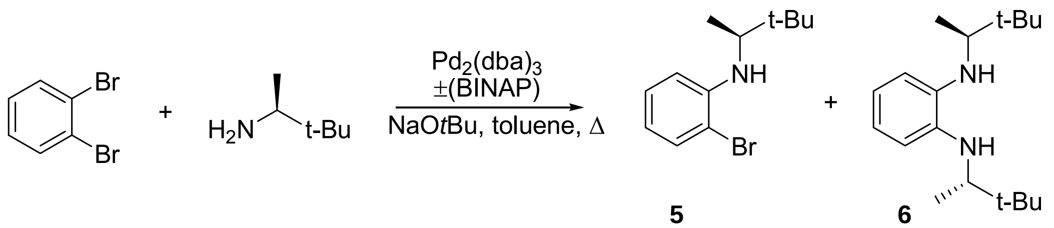


4

Scheme 78

For comparison the racemic product was generated from the reaction between cyclohexen-1-one and phenylmagnesium bromide in the presence of copper iodide in tetrahydrofuran, however, determination of the enantiomeric excess (%) using chiral HPLC gave 0% *ee*.

One explanation for this result is thought to be the design of the ligand **3**, where the presence of the phenyl rings on the nitrogen were allowed to freely rotate during the reaction, inhibiting any chiral induction. With this in mind it was suggested that a bulkier group, e.g. t-butyl, would be less inclined to rotate and therefore may afford higher enantioselectivity. Consequently a double Buchwald-Hartwig reaction was attempted using (*S*)-(+)-3,3-dimethyl-2-butylamine and 1,2-dibromobenzene under the optimised conditions to generate the mono 2-bromo-((*S*)-3,3-dimethylbutan-2-yl)benzenamine **5** (55% yield), and a second product which contained the desired bis-((*S*)-3,3-dimethylbutan-2-yl)benzene-1,2-diamine **6**, along with an undesired product (Scheme 79).

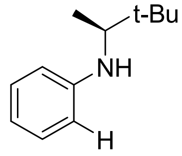


5 **6**

(up to 26%)

Scheme 79

Further analysis indicated the second product from the above reaction was a mixture of the diamine **6** and the reduced product **7** (Figure 54), which is formed in a competitive reaction in which the second bromine has undergone reduction.



7

Figure 54

As the reaction had only yielded the monoamine **5** in a good yield and not the desired diamine **6**, the reaction was attempted again, this time leaving the reaction heating under reflux for longer. The reaction gave the monoamine in a lower yield (42%) but did not generate a higher yield of the diamine, but a higher quantity of the reduced product **7** (30%). Therefore several different conditions were attempted to optimise the reaction for the synthesis of diamine **6**, including use of a higher boiling solvent, mesitylene, increasing the reaction time and the use of a different ligand, xantphos, details of optimisation are given in Table 2.

Table 2 – Optimisation of the reaction described in Scheme 79

Entry	Solvent	Ligand	Temperature	Time (h)	Yield **5** (%)	Yield **6** (%)	Yield **7** (%)
1	Toluene	(±) BINAP	110°C	4	55	5	20
2	Toluene	(±) BINAP	110°C	6	42	5	30
3	Toluene	(±) BINAP	110°C	Overnight	22	7	41
4*	Mesitylene	(±) BINAP	150°C	4	29	0	0
5	Mesitylene	(±) BINAP	150°C	Overnight	0	0	64
6	Toluene	Xantphos	110°C	Overnight	Complex mixture		
7	Mesitylene	Xantphos	150°C	Overnight	Complex mixture		
8	Toluene	(±) BINAP	Rt	4	starting material		
9	Toluene	(±) BINAP	110°C	4	48	26	15
10**	Toluene	(±) BINAP	110°C	4	4	0	0

* mono-product was reacted with further equivalents of amine
** 1,2-diiodbenzene was used instead of 1,2-dibromobenzene

Changes in temperature indicated that a higher boiling solvent such as mesitylene gave mainly the mono or reduced product depending on reaction time, and leaving the reaction at room temperature did not provide sufficient energy for any reaction to occur. Increasing the reaction time gave more of the reduced product the longer the reaction was left. Xantphos (Figure 55), which has a larger bite angle than BINAP, was used in place of (±) BINAP as a ligand for the palladium in case the bulky *t*-butyl was preventing the BINAP binding and thus the second Buchwald-Hartwig reaction taking place.

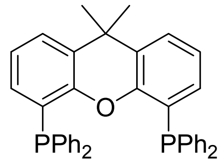
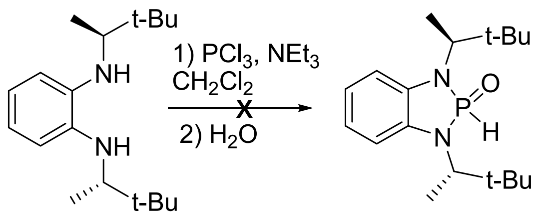


Figure 55

However, the reactions using Xantphos gave a complex mixture where neither the starting material nor any of the other products were seen. 1,2-Diiodobenzene was also suggested as it may be more willing to undergo the second Buchwald-Hartwig reaction and may give the diamine in a better yield. However, using 1,2-diiodobenzene gave only the mono product **5** in 4% yield and none of the diamine **6.**

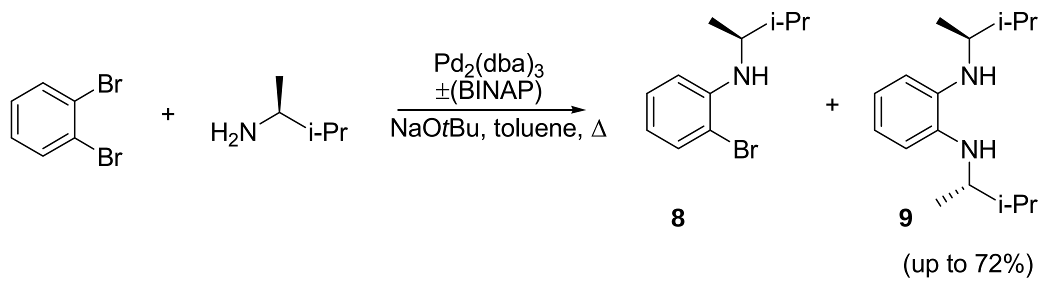
At this point there was a sufficient quantity of diamine **6** to attempt the synthesis of a phosphordiamidite from this backbone, using previous reaction conditions the bis-((*S)*-3,3-dimethylbutan-2-yl)benzene **6** was reacted with phosphorus trichloride in the presence of base, but after 4 days only starting material was recovered (Scheme 80).



Scheme 80

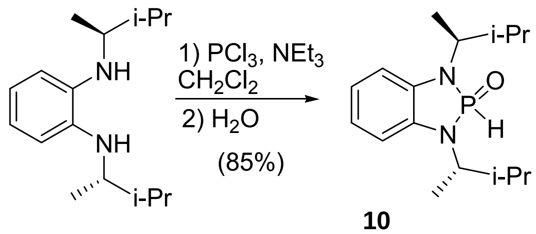
As attempts to synthesis a more bulky backbone using (*S*)-(+)-3,3-dimethy-2-butylamine were both low yielding and gave the reduced product **7** which was hard to separate from the desired diamine, it was suggested that the amine was changed for (*S*)-(+)-3-methybutylamine in the hope that the isopropyl group, being less bulky than the *t*-butyl, would allow the diamine to be formed, but, being more bulky than the phenyl ring present on (S)-(-)-α-methylbenzylamine, would stop any rotation.

Using our previous conditions for the Buchwald-Hartwig reaction, 1,2-dibromobenzene was reacted with (*S*)-(+)-3-methylbutylamine to yield the monoamine 2-bromo-((*S*)-3-methylbutan-2-yl)benzenamine **8** and the diamine bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** in 29% and 59% yield, respectively. Upon repetition of the reaction, **8** was produced in 12% yield with the desired diamine **9** being produced in 72% yield (Scheme 81).



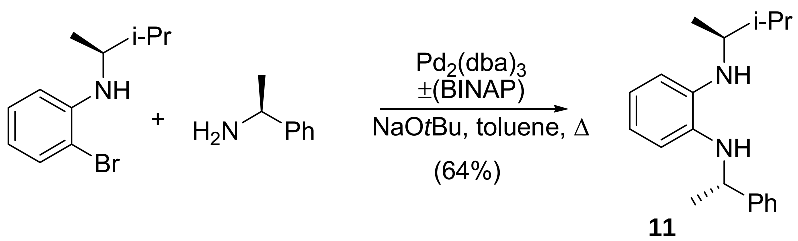
Scheme 81

Diamine **9** was then treated with phosphorus trichloride using the previous reaction conditions to generate the phosphordiamidite, **10**, in good yield (85%), (Scheme 82).



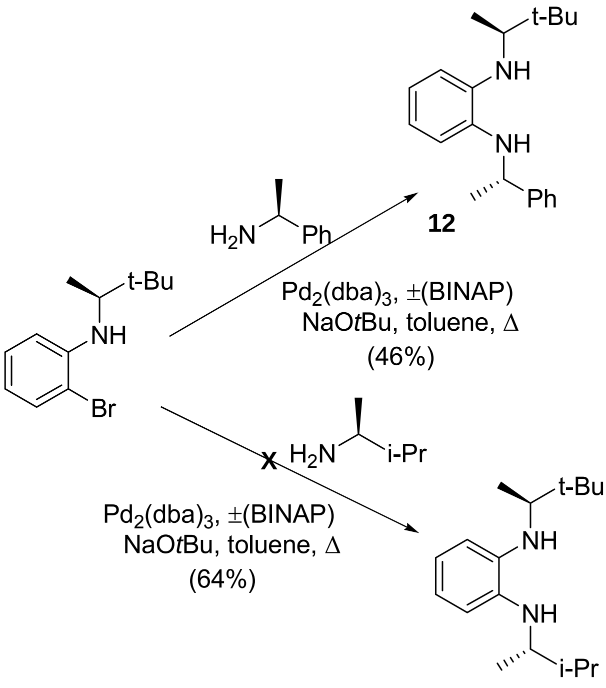
Scheme 82

The synthesis of a mixed backbone **11** was also envisaged stating from monoamine **8**, which was reacted using the previous reaction conditions with (*S*)-(-)-α-methylbenzylamine to yield ((*S*)-3-methylbutan-2-yl)-((*S*)-1-phenylethyl)benzene-1,2-diamine **11** in 64% yield, (Scheme 83).



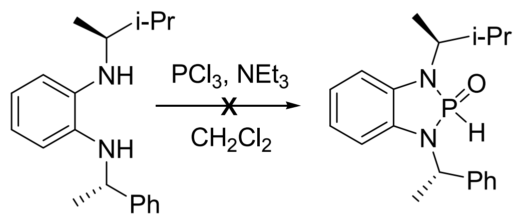
Scheme 83

Due to the success of the mixed diamine **11**, the synthesis of two other mixed products was attempted starting from 2-bromo-((*S*)-3,3-dimethylbutan-2-yl)benzenamine **5** using (*S*)-α-methylbenzylamine and (*S*)-(+)-3-methybutylamine, Scheme 84). Mixed diamine **12** was obtained in 46% yield, however attempts to synthesise the second mixed diamine were unsuccessful.



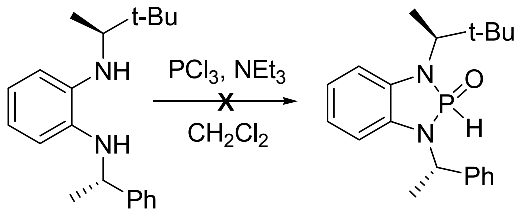
Scheme 84

Next, the synthesis of a phosphordiamidite from a mixed backbone was attempted, to begin with mixed diamine **11** was selected and using previous conditions reacted with phosphorus trichloride, Scheme 85). However, all attempts to synthesise the mixed phosphordiamidite were unsuccessful and the reaction resulted in a complex mixture with no starting material being seen by ^{1}H NMR or TLC. ^{1}H NMR spectroscopy of the reaction mixture did exhibit very small signals which indicated the potential presence of the desired compound, however any attempt to isolate this was futile.



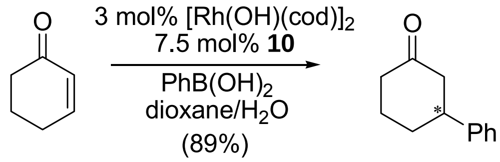
Scheme 85

As the first attempt to produce a mixed phosphordiamidite had failed, mixed diamine **12** was chosen and synthesis of the phosphordiamidite attempted (Scheme 86), this was also unsuccessful and a complex mixture was seen by both ^{1}H NMR spectroscopy and TLC of the crude reaction mixture.



Scheme 86

The test reaction which had previously been used to test the first synthesised phosphordiamidite ligand, **3**, was once again used to test the capabilities of phosphordiamidite **10**, however once again HPLC analysis of the product indicated that no stereocontrol had been achieved in the reaction with 0% *ee* being recorded (Scheme 87).

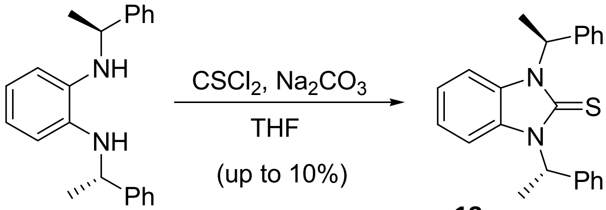


Scheme 87

As once again no enantiomeric excess had been achieved the attempt to synthesise a phosphordiamidite was abandoned.

2.2.2 – Thiourea Synthesis

Continuing in our attempts to synthesise a catalyst or ligand from our C_2-symmetric backbones we initiated attempts to synthesis a thiourea from diamine **1**. Using reaction conditions previously used by the group, and those reported by Yang,[108] diamine **1**, was treated with thiophosgene in the presence base (Na_2CO_3) in tetrahydrofuran overnight, followed by the addition of water, Scheme 88). The desired thiourea **13** was obtained as brown crystals in a very low 5% yield. A crystal structure of compound **13** was obtained (Figure 56) and confirmed the synthesis of the compound.



13

Scheme 88

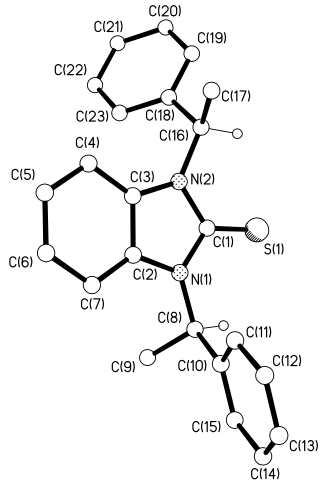
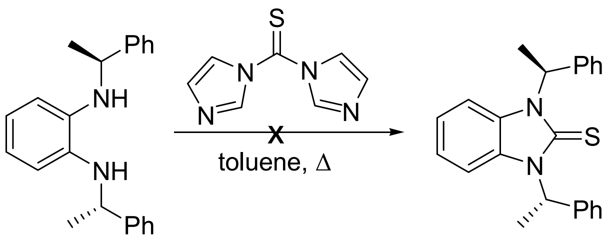


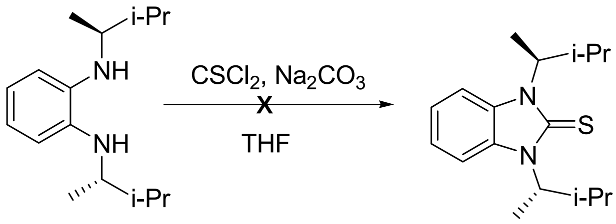
Figure 56

Owing to the low yield of thiourea **13** obtained, there was not a sufficient amount with which do any test reactions. Therefore an attempt to re-synthesise the thiourea in a higher yield using the same conditions was initiated, however the highest yield achieved was still poor, (10%). As the reaction was low yielding, the paper in which the initial method had been found was consulted and another method using 1,1-thiocarbonyldiimidazole was attempted (Scheme 89) but the reaction failed to produce any of the thiourea by TLC or ^{1}H NMR.



Scheme 89

As attempts to increase the yield obtained in the synthesis of thiourea **13** were unsuccessful, the initial method was used to try and synthesise the thiourea of the bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** (Scheme 90), however this also proved unsuccessful.



Scheme 90

Based on the suggestion the thiourea compounds may be acid sensitive and possibly decomposing during work up, crystallisation of the thiourea from the crude material without using an acid wash in the work up was attempted. This however was also unsuccessful at producing a higher yield of thiourea. With only a small amount of thiourea synthesised no test reactions were preformed on this compound, and due to the difficulty synthesising this type of catalyst, attempts to make thiourea compounds were abandoned.

2.2.3 – Carbene Synthesis

A paper by Gloruis reported the synthesis of pyridine derived *N*-heterocyclic carbenes using pyridine 2-carboxaldehyde as the starting material, from this a related carbene ligand derived from pyridine 2-carboxaldehyde and (*S*)-(-)-α-methylbenzylamine, (Figure 57) could be envisaged.[149]

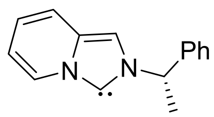
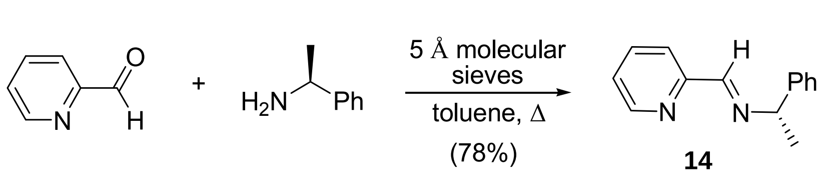


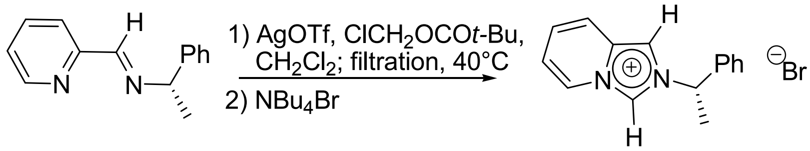
Figure 57

With this end product in mind, pyridine 2-carboxaldehyde was reacted with (*S*)-(-)-α-methylbenzylamine to generate the imine, **14** in a good 78% yield (Scheme 91).



Scheme 91

The imine **14** was then reacted with silver triflate in the presence of chloromethyl pivalate, to generate the triflate salt, followed by anion exchange with tetrabutylammonium bromide to generate the imidazolium salt **15**, (Scheme 92).



15

Scheme 92

The reaction produced the desired imidazolium salt **15**, shown to be present in the crude material by ^{1}H NMR spectroscopy, however, purification of the imidazolium salt **15**, proved highly difficult as the product could not be crystallised and purification by column chromatography proved impossible. In an attempt to induce crystallisation of the imidazolium salt a further anion exchange was attempted with a larger counter-ion; the crude material was dissolved in ethanol and tetrabutylammonium tetrafluoroborate in acetonitrile was added before the solution was left to stir overnight, however the resulting material was not crystalline and attempts to make the product crystallise proved unsuccessful. With only the crude material available no further work was attempted on the synthesis of the carbene.

2.2.4 – Phosphoric Acid Synthesis

In 2005 MacMillan reported that a BINOL derived phosphoric acid catalyst induced enantioselective reductive amination.[70] From this a phosphoric acid synthesised from the common backbone previously synthesised could be envisaged (Figure 58). First, the synthesis of a phosphoric acid was attempted using the bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1**.

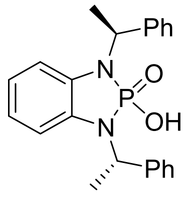
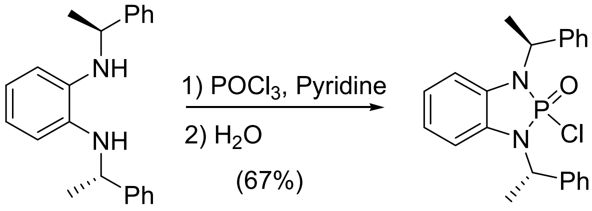


Figure 58

The diamine was dissolved in pyridine and reacted with phosphorus oxychloride overnight before water was added and the solution was allowed to stir for a further 30 minutes. The reaction was then worked up with HCl to remove the residual pyridine and purified by column chromatography to yield a white crystalline solid, which upon data obtained from mass spectrometry analysis and x-ray crystallography data (Figure 59) was discovered to be the phosphoryl chloride, **16** and not the desired phosphoric acid, (Scheme 93).



Scheme 93

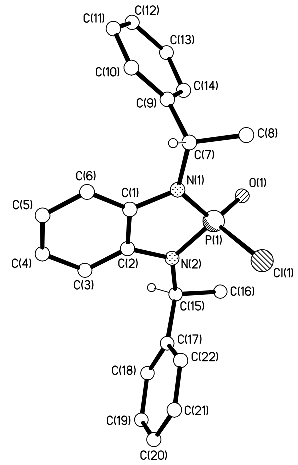


Figure 59

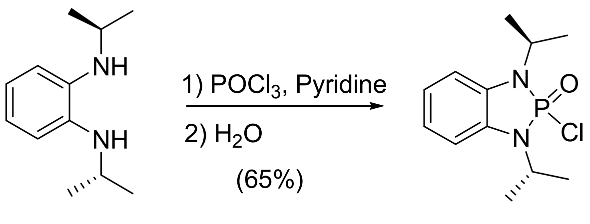
Initially the chloride was thought to be either reincorporated into the molecule from the work-up conditions (i.e. the HCl used to remove the residual pyridine was displacing the OH in the product), or wasn't being displaced in the work up conditions. Therefore H_2SO_4 was used as an alternative, as this should prevent displacement of the OH as SO_4^{2-} is a much weaker nucleophile than Cl^-. Consequently, a reaction was tried using the same method but using 1*N* H_2SO_4; however, the reaction gave the phosphoryl chloride. As another way of removing pyridine from a reaction mixture is the use of copper(II) salts this was also tried, but again the product isolated was the phosphoryl chloride **16**. Further work to displace the chloride also included leaving the reaction to stir over night with a large excess of water, however upon work-up the isolated compound was phosphoryl chloride **16**.

As the phosphoryl chloride was stable enough to be chromatographed on silica and withstood washing with 1*N* acids, this indicated that the phosphorus chlorine bond was stronger than first thought and that water was not a sufficiently strong nucleophile to displace the chloride. Thus a stronger nucleophile would be needed and it was suggested that dissolving the isolated phosphoryl chloride in a polar, non-protic solvent such as THF and mixing with 1M NaOH may yield the desired phosphoric acid. Another suggestion was to heat under reflux the phosphoryl chloride in an acetone:water mix for approximately 4 hours and then evaporate to dryness. Table 3 details attempts to produce the phosphoric acid from the phosphoryl chloride, none of which proved successful.

Table 3 - Attempts to generate phosphoric acid

Conditions	Time	% sm recovered
1M NaOH, THF, reflux	4 h	64
1M NaOH, THF, reflux	Overnight	79
Acetone: H_2O 2:1, reflux	4 h	100
Acetone: H_2O 2:1, reflux	Overnight	98
THF: H_2O 2:1, reflux	4 h	96
THF:H_2O 2:1, reflux	Overnight	98
NaOH pellets in THF:H_2O 2:1, reflux	6 h → Overnight	89
1M NaOH, MeOH, reflux	4 h	96
1M NaOH, MeOH, reflux	72 h	92

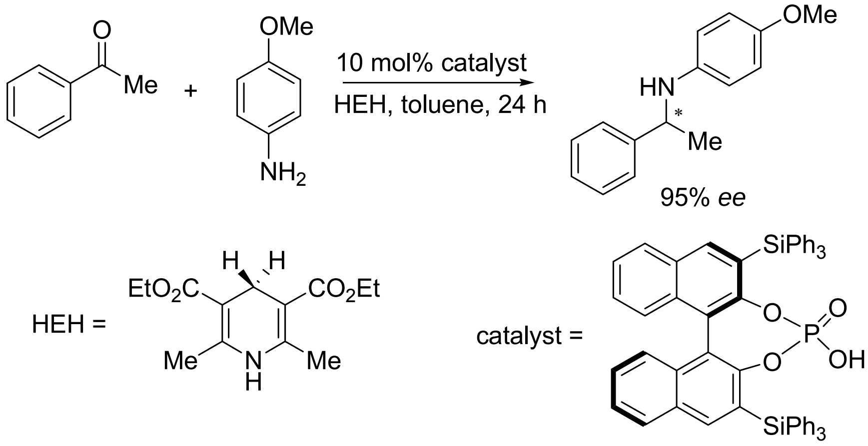
Since synthesising the phosphoric acid of bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** was proving problematic, the synthesis of the phosphoric acid derived from bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** was attempted to see if differing the R- group would allow us to isolate the phosphoric acid. Hence, bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** was reacted under the same conditions previously used, to generate not the phosphoric acid but again the phosphoryl chloride **17**, in 65% yield (Scheme 94).



17

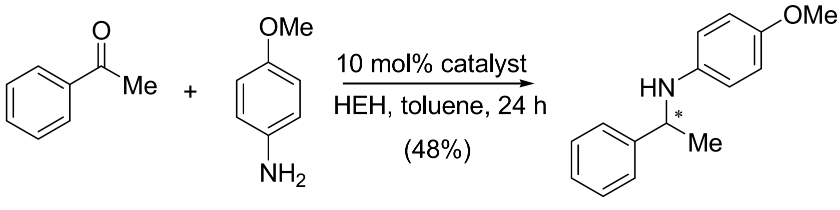
Scheme 94

As the phosphoryl chloride was already in hand a test reaction reported by MacMillan (Scheme 95) was used to test the liganc capabilities,[70] however as the phosphoryl chloride is unable to act as a hydrogen bonding catalyst we expected this reaction to fail. The reaction used by Macmillan was the enantioselective reductive amination of aromatic ketones, using an NADH analogue HEH (Hantzsch ester) alongside a hydrogen-bonding catalyst, in this case a phosphoric acid.



Scheme 95

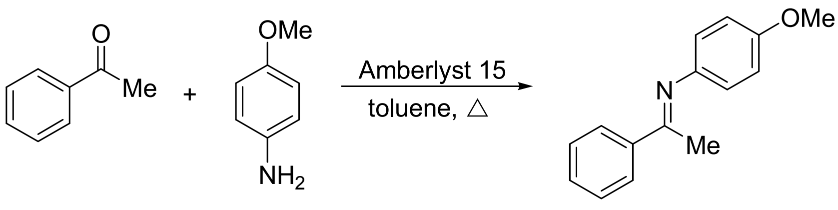
Using the same conditions as MacMillan (Scheme 95), acetophenone and *p*-anisidine were dissolved in toluene and the HEH and phosphoryl chloride added. The reaction gave the desired product **18**, in a moderate 48% yield (Scheme 96).



18

Scheme 96

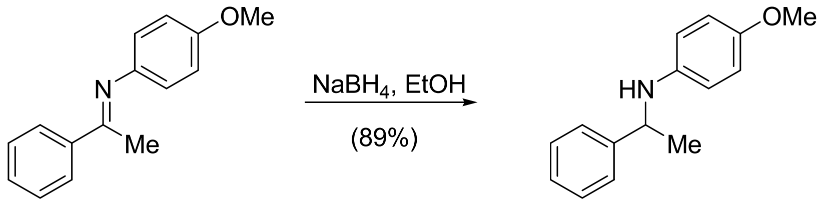
For comparison the racemic product was generated, by first reacting acetophenone with *p*-anisidine in the presence of Amberlyst 15, under reflux Dean Stark conditions for 4 hours (Scheme 97), following the formation of imine **19** by IR spectroscopy (peak at 1684 cm^{-1}), ^{1}H NMR spectroscopy also confirmed the formation of imine **19**.



19

Scheme 97

Imine **19** was then reacted with sodium borohydride in ethanol to give the desired product **18a** in 98% yield, (Scheme 98).



18a

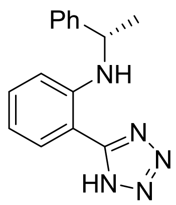
Scheme 98

Comparison by chiral HPLC gave 0% enantiomeric excess (*ee*) indicating that no chiral induction is observed during the reaction. This may be explained by either of two reasons, either the catalyst is not participating in the reaction but instead HCl liberated from the catalyst is causing the reaction to proceed. Alternatively, lack of hydrogen bonding the chloride can participate in prevents stereocontrol, a chiral phosphoric acid uses both the P=O functionality and the P-O-H moiety in which to direct the substrate and induce chirality.[68] As the phosphoryl chloride does not have the P-O-H with which to hydrogen bond to the substrate, just the P=O Lewis basic site, stereocontrol is not achieved.

2.2.5 – Organocatalyst Synthesis

As attempts to generate the phosphoric acid from the phosphoryl chloride were proving futile, and the phosphoryl chloride gave no stereocontrol in the test reaction it was decided to focus on the preparation and use of other ligands rather than continue work on this ligand.

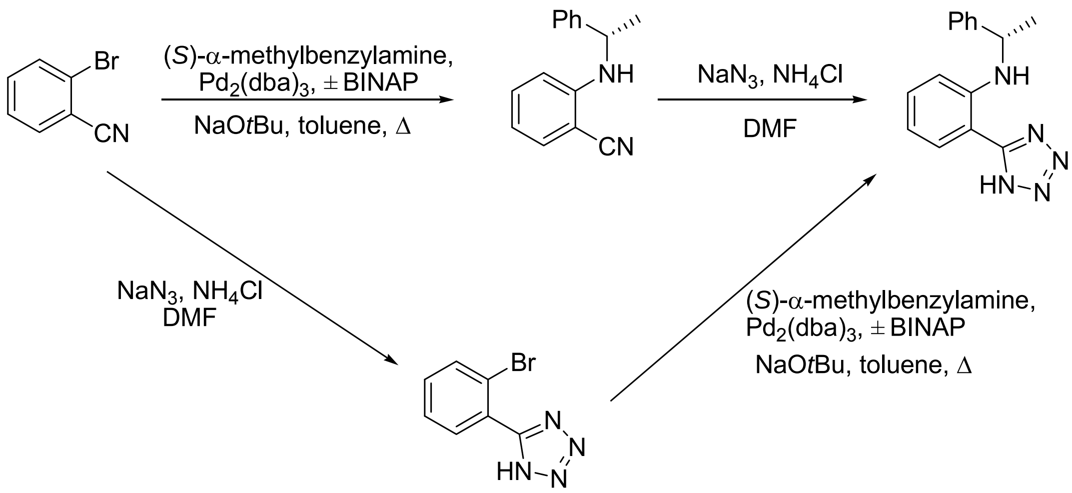
A search of literature brought to our attention a paper by Ley and co-workers utilising an organocatalyst with a tetrazole unit incorporated for the use in asymmetric Mannich, nitro-Michael and aldol reactions,[150] we believed that we could adapt this design, thus creating a tetrazole ligand which was based on our core backbone, (Figure 60).



20

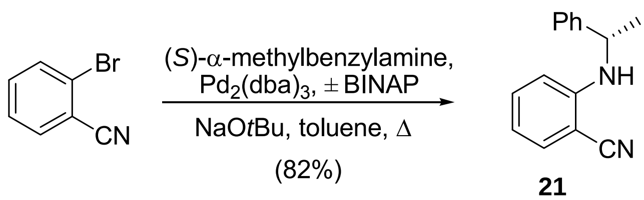
Figure 60

With this ligand in mind, two pathways in which to design the ligand were considered, both using 2-bromobenzonitrile as the starting material. First was the reaction of 2-bromobenzonitrile with (*S*)-α-methylbenzylamine using the Buchwald-Hartwig reaction to introduce the chiral amine into the molecule, and then using NaN_3 to add the tetrazole. The second pathway was to first introduce the tetrazole and then the (*S*)-α-methylbenzylamine, thus allowing us to diverge later in the synthesis, if the ligand proved to be successful, (Scheme 99).



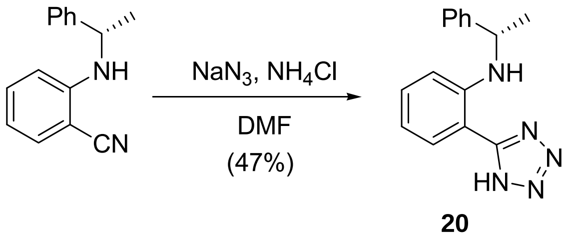
Scheme 99

(*S*)-α-methylbenzylamine was reacted with 2-bromobenzonitrile using the standard Buchwald-Hartwig reaction conditions previously used to yield the desired monoamine, 2-((*S)*-1-phenylethylamino)benzonitrile **21** in 73% yield, which upon optimization increased to 82% (Scheme 100).



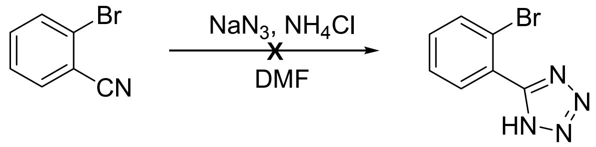
Scheme 100

With monoamine **21** in hand the tetrazole ring was incorporated into the molecule by reaction of **21**, with sodium azide in the presence of ammonium chloride, to yield the desired ((*S*))-1-phenylethyl)-2-(tetrazol-5-yl)benzenamine **20** in 47% yield (Scheme 101).



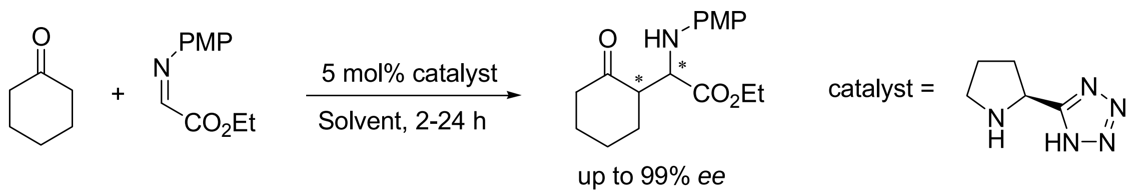
Scheme 101

In an attempt to increase the yield of the desired ligand **21** the second pathway was attempted. 2-Bromobenzonitrile was reacted with sodium azide in the presence of ammonium chloride for 48 hours (Scheme 102). Upon isolation of the crude reaction product none of the desired product was seen by either TLC or ^{1}H NMR spectroscopy and after purification 75% of the starting material was recovered.



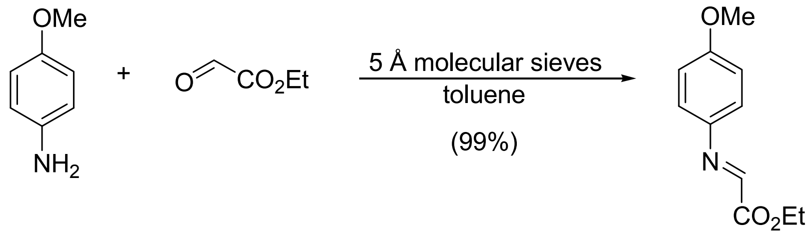
Scheme 102

As enough catalyst had been generated from both the first attempt to synthesis the catalyst and by a repeat of the first synthesis, we decided to choose a test reaction and after consulting the initial paper a reductive amination reaction (Scheme 103) was decided upon.



Scheme 103

First the imine was synthesised in 99% yield by the reaction of *p*-anisidine and ethyl glyoxyalate in the presence of molecular sieves, (Scheme 104).



23

Scheme 104

With imine **23** now in hand the test reaction was attempted using 5 mol% of catalyst **20**. Cyclohexanone was reacted with imine **23** in the presence of catalyst **20** in dry dichloromethane, and monitored by TLC. After 24 hours, no reaction was seen by TLC and so the reaction was left a further 24 hours before work up, but no product was seen by TLC or ^{1}H NMR spectroscopy, with only starting materials being present. A further attempt at the test reaction which was left for 72 hours gave a complex mixture by TLC. List and Houk suggested that for this type of reaction to proceed a rigid chiral environment is required,[151] this chiral environment created by the hydrogen bonding transition state between the catalyst and the imine. As a result we concluded that either our catalyst did not give a rigid enough transition state and therefore the reaction did not proceed, or that the catalyst did not hydrogen bond to the imine hence no transition state is present, and no reaction occurs.

2.2.6 – Chiral Diamine Synthesis

We also chose to investigate the use of chiral amines in magnesium mediated reactions. A paper by Kerr in 2004 used chiral diamines for magnesium mediated asymmetric deprotonation reactions with good results.[152] Once again this design could be modified to incorporate our basic backbone design, with modifications, as both a tertiary and secondary amine would need to be present. This could be envisaged by reaction of monoamine **2** with morpholine to generate a ligand (Figure 61) which could be tested in this type of reaction.

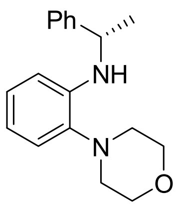
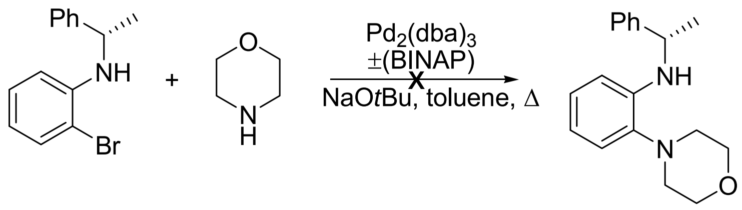


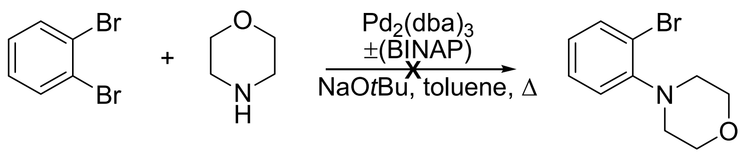
Figure 61

With this ligand design in mind, 1,2-dibromobenzene was reacted with (*S*)-α-methylbenzylamine using the previously investigated Buchwald-Hartwig reaction conditions to generate the monoamine, in a high 86% yield. A further Buchwald-Hartwig reaction was attempted between monoamine **2** and morpholine, however, the reaction proved unsuccessful (Scheme 105).



Scheme 105

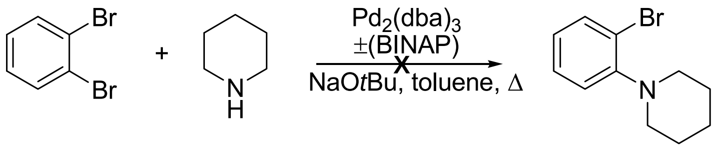
As the second coupling had failed, it may be possible that the morpholine could not react once the (*S*)-α-methylbenzylamine had been coupled, consequently an attempt to synthesise the desired molecule by first inserting the morpholine and sequentially adding (*S*)-α-methylbenzylamine began. Using Buchwald-Hartwig conditions 1,2-dibromobenzene was reacted with morpholine (Scheme 106), the reaction was monitored by TLC and after 18 hours since no reaction was visible, another 2 equivalents of morpholine were added and the reaction left overnight, resulting in a complex mixture.



Scheme 106

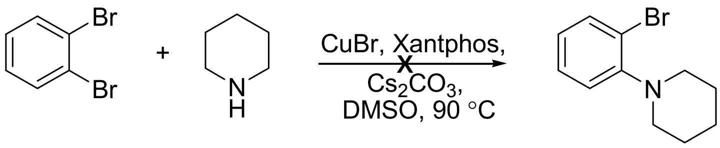
Since the coupling had been unsuccessful, a search of literature was conducted, and a paper found which indicated that morpholine gave significantly lower yields in coupling reactions compared to other amines.[153] Therefore piperidine was chosen as an alternative. Once again, initially, Buchwald-Hartwig reaction conditions would be used, but in case this approach proved futile other methods for inserting piperidine into a carbon-halide bond were sought.

Initially 1,2-dibromobenzene was reacted with piperidine using the standard Buchwald-Hartwig reaction conditions previously discussed, but this reaction did not generate the desired monoamine (Scheme 107).



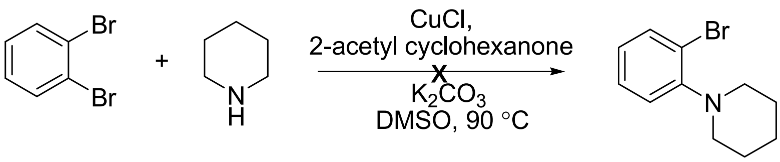
Scheme 107

As this attempt had not worked one of the researched methods was tried, this time using copper instead of palladium as the metal source.[154] First 1,2-dibromobenzene was reacted with piperidine in the presence of copper (I) bromide, Xantphos and caesium carbonate for 18 hours at 90 °C (Scheme 108), after work up and purification by column chromatography it was clear that the reaction had failed to yield the desired product.



Scheme 108

The second method utilised another copper (I) source, however instead of copper (I) bromide, copper (I) chloride was used with 2-acetylcyclohexanone as a co-catalyst, (Scheme 109).[153] Therefore a reaction between 1,2-dibromobenzene and piperidine using this method was attempted, however this also failed to yield the desired product.

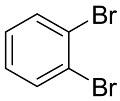
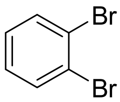
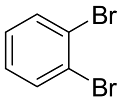
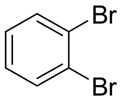
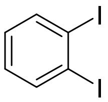
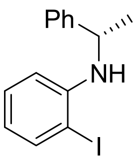
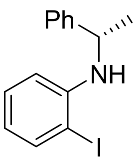
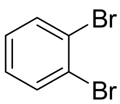
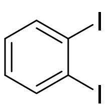
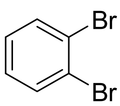


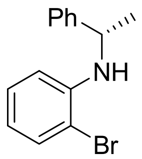
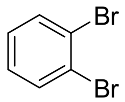
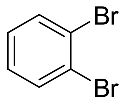
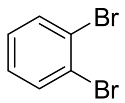
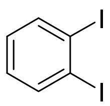
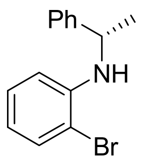
Scheme 109

Using the three different methods, and using the microwave, many attempts were made to try to insert piperidine into different aromatic halides with little success; attempts are detailed in

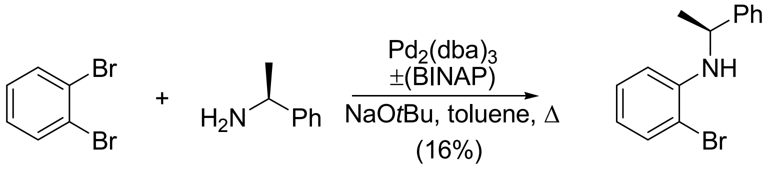
Table 4 below.

Table 4 – attempts to insert piperidine into aromatic halide

Starting Material	Conditions	Time (h)	Product obtained
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	4	sm
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	24	Complex mixture
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	48	Complex mixture
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	72	Complex mixture
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	24	sm
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	24	sm (96%)
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, Δ	24	sm (85%)
	CuBr, Xantphos, Cs_2CO_3, DMSO	18	Not product by NMR
	CuBr, Xantphos, Cs_2CO_3, DMSO	18	Not product by NMR
	CuCl (10 mol%), 2-acetylcyclohexanone,	18	Complex mixture

	K_2CO_3, DMSO		
	CuCl (10 mol%), 2-acetylcyclohexanone, K_2CO_3, DMSO	18	sm (87%)
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, microwave	0.25	Complex mixture
	CuBr, Xantphos, Cs_2CO_3, DMSO, microwave	0.25	Complex mixture
	CuCl (10 mol%), 2-acetylcyclohexanone, K_2CO_3, DMSO, microwave	0.25	Complex mixture
	$Pd_2(dba)_3$, (±) BINAP, NaO*t*Bu, toluene, microwave	0.25	Complex mixture
	CuBr, Xantphos, Cs_2CO_3, DMSO, microwave	0.25	Complex mixture

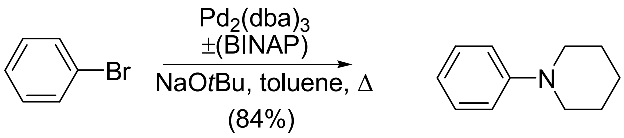
Since attempts to couple piperidine to the aromatic bromides had been futile it was decided that the coupling between bromobenzene and piperidine would be attempted, as literature had shown that this compound was easily synthesised in high yields (up to 95%). A test reaction was also preformed to check the palladium catalyst, the reaction between 1,2-dibromobenzene and (*S*)-α-methylbenzylamine was chosen as the test reaction as this had been preformed many times. However, this failed to give the results expected, giving only 16% of the monoamine **2**, with starting material being the main product isolated from the reaction, (Scheme 110).



2

Scheme 110

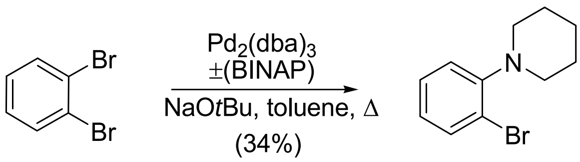
From this it was concluded that there may be a problem with our palladium catalyst and a new source of $Pd_2(dba)_3$ was purchased. Using the new palladium catalyst the reaction between bromobenzene and piperidine was carried out using Buchwald-Hartwig reaction conditions, and the desired product **23** was achieved in 84% yield (Scheme 111).



23

Scheme 111

With the knowledge that the reaction between bromobenzene and piperidine was successful, once again the reaction between 1,2-dibromobenzene and piperidine was attempted, this time the reaction proceeded generating the desired monoamine **24**, albeit in a low 34% yield (Scheme 112).



24

Scheme 112

The low 34% yield can in part be attributed to generation of the twice coupled product where the piperidine inserts twice rather than the desired once, (Figure 62). Evidence of this product was visible in both the ^{1}H NMR spectroscopy and by mass spectrometry.

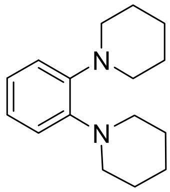
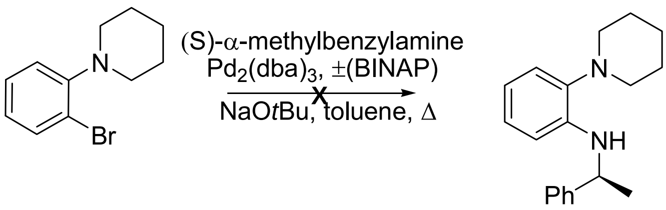


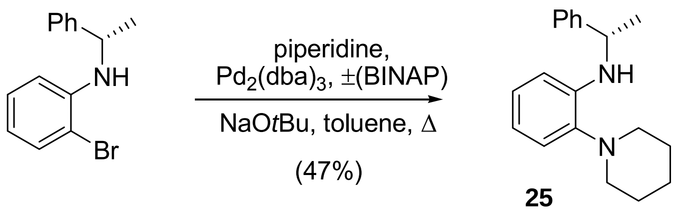
Figure 62

With the monoamine **24** now in hand the second step was to attempt the second coupling using (*S*)-α-methylbenzylamine to give the desired product which could then be co-ordinated to magnesium. Therefore using Buchwald-Hartwig conditions the second coupling was attempted between monoamine **24** and (*S*)-α-methylbenzylamine (Scheme 113), however the reaction resulted in a complex mixture by both TLC and ^{1}H NMR spectroscopy.



Scheme 113

As this route had failed to yield the desired product, it was decided that the piperidine coupling should be attempted after the (*S*)-α-methylbenzylamine had been inserted. First (*S*)-α-methylbenzylamine was reacted with 1,2-dibromobenzene to yield monoamine **2**, as previously described. The monoamine was then used in a further Buchwald-Hartwig reaction with piperidine. After more than one attempt at this reaction the desired product **25** was generated in a moderate 47% yield, (Scheme 114).



Scheme 114

A repeat of the previously mentioned reactions generated enough of compound **25** to complex to magnesium and test in a reaction. Following the procedure detailed by Chong,[155] the ligand can be converted to the organomagnesium compound (Figure 63) by addition of the ligand to a dialkylmagnesium species.

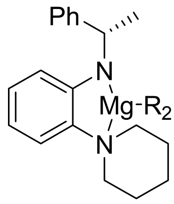
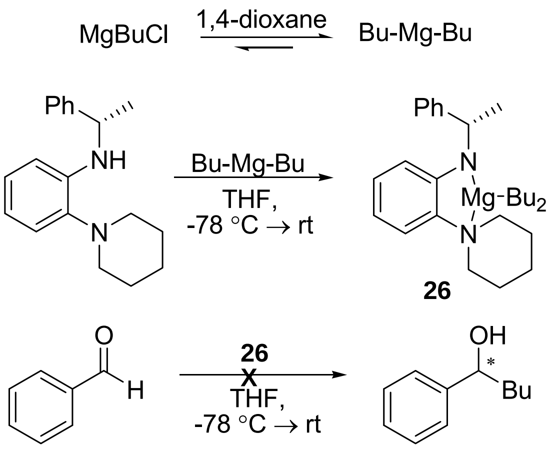


Figure 63

The dialkylmagnesium species was easily prepared following literature procedure,[155] by the slow addition of 1,4-dioxane to a stirred solution of butylmagnesium chloride, resulting in the precipitation of the magnesium salt, and the formation of the dialkylmagnesium species. It was this species which was added to the previously prepared ligand **25**, and following complexation benzaldehyde was added in one portion at -78 °C, (Scheme 115). Unfortunately the asymmetric Grignard reaction was unsuccessful, however the diamine was easily recovered from the reaction using a literature procedure.[156]



Scheme 115

No further attempts to usilise ligand **25** in an asymmetric Grignard reaction were attempted.

2.2.7 – P,N Ligand Synthesis

Instead focus shifted to the design of a new type of P-N ligand, using our core backbone structure. This design incorporated both a phosphorus and a nitrogen into the ligand motif, giving different electronic and donor properties to the ligand, (Figure 64).

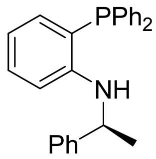


Figure 64

From this P-N ligand a P-N carbene (Figure 65) could be synthesised. This type of carbene have been reported as particularly difficult to synthesise.[157]

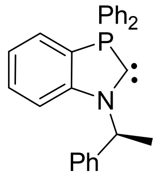
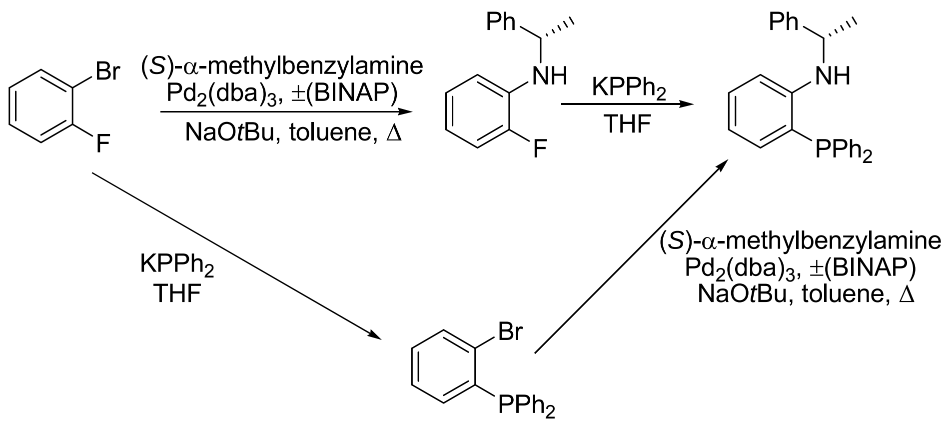


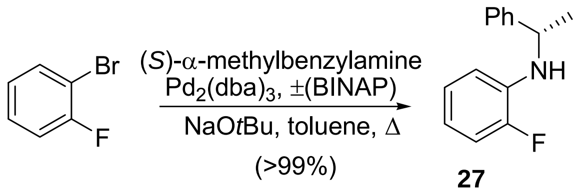
Figure 65

Consulting the literature a method was found, reported by both Hiroi and Stelzer,[158,159] in which use of a diphenylphosphide salt can substitute fluorine in a nucleophilic phosphination, giving tertiary phosphines in good yields. Therefore, with this method in mind 1-bromo-2-fluorobenzene was sourced. Two routes by which the backbone of the compound could be synthesised were proposed, one reacting 1-bromo-2-fluorobenzene with (*S*)-α-methylbenzylamine to give the monoamine and then proceed with the phosphorylation reaction, to introduce the PPh_2 into the molecule or by reverse addition (Scheme 116).



Scheme 116

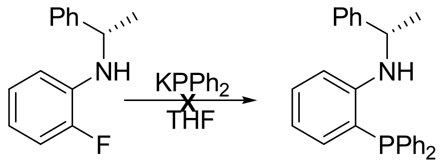
Following our first proposed route, (*S*)-α-methylbenzylamine was reacted with 1-bromo-2-fluorobenzene using standard Buchwald-Hartwig reaction conditions to yield the desired product, 2-fluoro-((*S*)-1-phenylethyl)benzenamine **27**, in 22% yield, upon optimisation quantitative yields were obtained (Scheme 117).



27

Scheme 117

The 2-fluoro-((*S*)-1-phenylethyl)benzenamine **27**, was reacted with potassium diphenylphosphide in THF, however this reaction did not yield the desired product. As only one equivalent of potassium diphenylphosphide had been used, a further reaction using 2 equivalents of the potassium diphenylphosphide was tried, due to deprotonation of the NH of the 2-fluoro-((*S*)-1-phenylethyl)benzenamine. This also failed to give the desired product (Scheme 118).

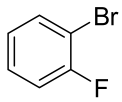


Scheme 118

It is possible that the nucleophilic phosphination reaction using the potassium diphenylphosphide salt may not have worked due to the electron donating abilities of the NH present on the amine, and therefore the second proposed route may prove to be more successful. The nucleophilic phosphination of 1-bromo-2-fluorobenzene was attempted using different solvents and time scales but none yielded the desired product,

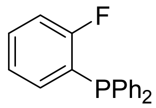
Table 5 details the reactions tried.

Table 5 –attempted nucleophilic phosphination reactions

Starting material	Conditions			Product obtained
	$KPPh_2$, THF	Rt	48 h	sm
	$KPPh_2$, THF	reflux	48 h	sm
	$KPPh_2$, THF	microwave	10 min	Complex mixture
	$KPPh_2$, 1,4-dioxane	microwave	10 min	sm
	$KPPh_2$, 1,4-dioxane	reflux	4 d	Compound **28***
	$KPPh_2$, 1,4-dioxane	microwave	30 min	Complex mixture

* see Figure 66

During the attempts at the nucleophilic phosphination reaction a report was found in which microwave irradiation could be used to speed up nucleophilic phosphination reactions,[160] which otherwise took 5 days. As our attempts to use microwave irradiation had generated complex mixtures, by both TLC and ^{1}H NMR spectroscopy, we used this proceedure as a guide and increased our reaction time to 4 days under reflux in 1,4-dioxane, after which a new spot was seen by TLC. Upon purification and characterisation by NMR spectroscopy, we discovered it was not the desired compound but instead (2-fluorophenyl)diphenylphosphine **28** (Figure 66).

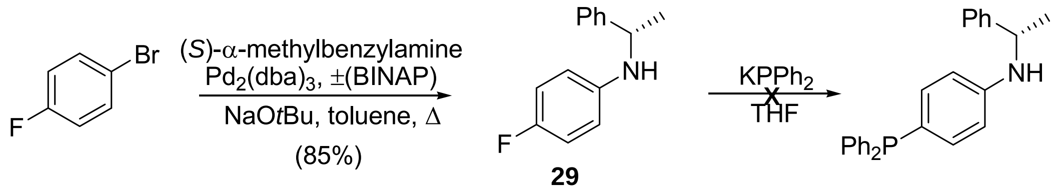


28

Figure 66

The compound was characterised by ^{1}H, ^{19}F and ^{31}P NMR spectroscopy, the use of ^{19}F NMR spectroscopy allowed us to quickly ascertain that the bromine had undergone nucleophilic phosphination preferentially over the flourine, and therefore another method by which to make the P-N ligand was to be researched.

As a test reaction the same reaction scheme using 1-bromo-4-fluorobenzene as an alternative to 1-bromo-2-fluorobenzene was tried. Although this would not generate our desired P-N ligand, if after the incorporation of (*S*)-α-methylbenzylamine *via* a Buchwald-Hartwig reaction, the nucleophilic phosphination could be achieved this would allow us to establish whether the secondary amine being *ortho* to the site of nucleophilic phosphination was creating the problem. Therefore 1-bromo-4-fluorobenzene was reacted with (S)-α-methylbenzylamine using standard Buchwald-Hartwig conditions to yield the desired product, 4-fluoro-((*S*)-1-phenylethyl)benzenamine **29** in 85% yield. Compound **29** was subject to previously used nucleophilic phosphination conditions (Scheme 119), but after 6 days no change was seen by TLC, and on purification only starting material **29**, was recovered (82%).

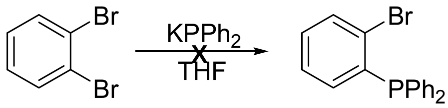


29

Scheme 119

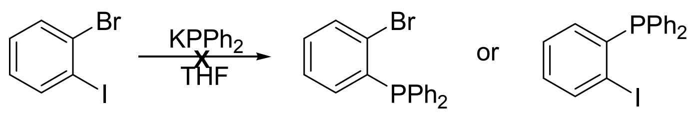
This confirmed to us that the nucleophilic phosphination conditions were not working as increasing the equivalents of the potassium diphenylphosphide salt to counteract the deprotonation of the NH and altering the position of the secondary amine, to either the *ortho* or *para* positions, did not affect the outcome of the reaction, therefore we conducted further research into nucleophilic phosphination conditions.

Whilst researching different nucleophilic phosphination conditions we thought it would be interesting to see what the product of the reaction would be if 1,2-dibromobenzene was used as the starting material instead of 1-bromo-2-fluorobenzene, however the reaction failed to generate the desired (2-bromophenyl)diphenylphosphine (Scheme 120).



Scheme 120

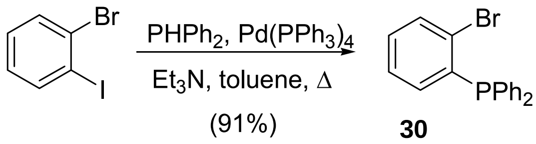
Further attempts at the nucleophilic phosphination also included use of 1-bromo-2-iodobenzene as the starting material, as either bromide or iodide elimination during the nucleophilic phosphination would give a compound with which the Buchwald-Hartwig reaction could be attempted. However all attempts at this reaction failed (Scheme 121).



Scheme 121

Research into other methods in which to insert the phosphorus into the starting material generated three different methods, two methods used palladium cross coupling reactions with either palladium-tetrakis(triphenylphosphine) or palladium acetate as the palladium source,[161,162] and a third using either a palladium or nickel catalyst and microwave irradiation for the cross-coupling reaction.[163]

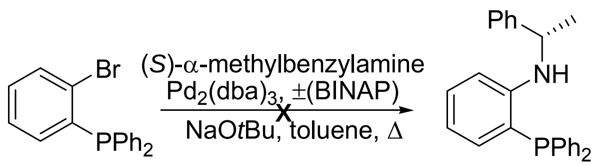
As a source of palladium-tetrakis(triphenylphosphine) was readily available and our experience with microwave irradiation in our previous attempts at the nucleophilic phosphination reaction were unsuccessful generating complex mixtures, it was decided to first test the method using palladium-tetrakis(triphenylphosphine) and diphenylphosphine. To first test that in our hands the reaction would work 1-bromo-2-iodobenzene was reacted with diphenylphosphine in the presence of base (Et_3N) and a catalytic amount of palladium-tetrakis(triphenylphosphine). The reaction proceeded in a high 91% yield (Scheme 122).



Scheme 122

This reaction could easily be monitored by ^{31}P NMR spectroscopy; diphenylphosphine has a chemical shift of -40 ppm in the ^{31}P NMR spectra.[164] Consulting the literature it was found compound **30** had a known chemical shift of -4.4 ppm,[165] and therefore during the reaction the appearance of a peak at -5.1 ppm enabled us to monitor when the reaction.

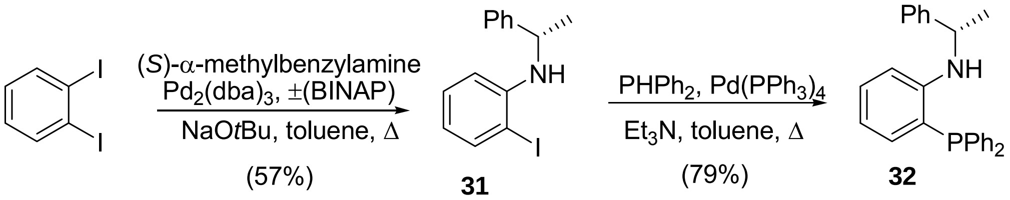
Compound **30** was subject to a Buchwald-Hartwig reaction (Scheme 123), which did not generate the desired compound, with only the starting material being recovered. This may be in part due to the steric bulk of the phosphine moiety preventing the palladium from inserting into the carbon-bromine bond.



Scheme 123

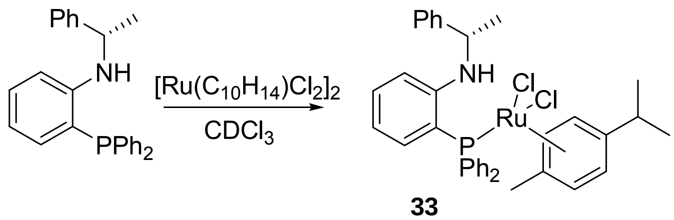
Therefore use of the reverse addition pathway to generate the desired P-N compound was proposed. 1,2-Diiodobenzene would have to be used for the Buchwald-Hartwig reaction as if 1-bromo-2-iodobenzene were used the palladium would insert at the carbon-iodine bond preferentially to the carbon-bromine bond, leaving a bromide with which to attempt the second cross-coupling reaction. Therefore the first reaction was the Buchwald-Hartwig reaction between 1,2-diiodobenzene and (*S*)-α-methylbenzylamine, which proceeded in

28% yield, to give compound **31**. Optimisation of the reaction increased the yield of compound **31** to 57%. With compound **31** in hand the palladium cross coupling reaction with diphenylphosphine was attempted using the previously described method and generated the desired compound **31** in 79% yield (Scheme 124).



Scheme 124

With our P-N ligand now in hand, complexation with a metal could be attempted. For this two metals were suggested; a ruthenium dimer $[Ru(C_{10}H_{14})Cl_2]_2$ and a rhodium dimer $[Rh(C_5H_{15})Cl_2]_2$. With only a small amount of material available for complexation we chose one metal, ruthenium, and added the dimer to a solution of compound **32** in $CDCl_3$ (Scheme 125). The orange solution was transferred immediately to an NMR tube and ^{1}H and ^{31}P NMR spectra obtained.

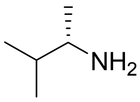
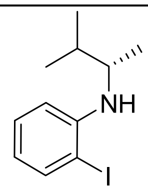
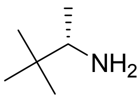
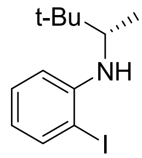
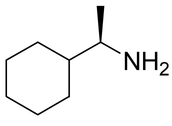
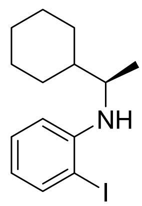
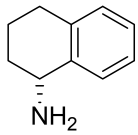
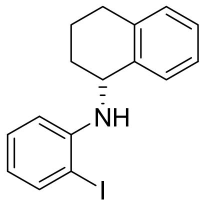
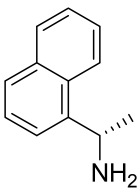
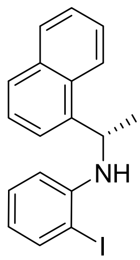
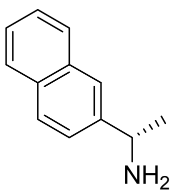
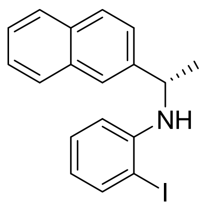


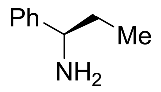
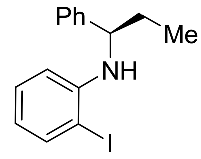
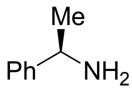
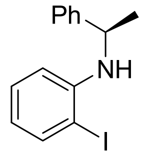
Scheme 125

There was a noticeable chemical shift in the ^{31}P spectrum from -20.07 ppm to 27.09 ppm, with a smaller lower intensity second peak at 24.21 ppm, indicating that complexation had occurred through the phosphorus to the ruthenium. To encourage co-ordination of the nitrogen to the ruthenium, triethylamine was added to the NMR tube and another ^{31}P NMR spectrum recorded, however no change in the chemical shift was observed. As there had been no change in the ^{31}P NMR spectrum methanol was also added to the NMR tube to encourage co-ordination of the nitrogen to the ruthenium, however again no change was seen in the ^{31}P NMR spectrum.

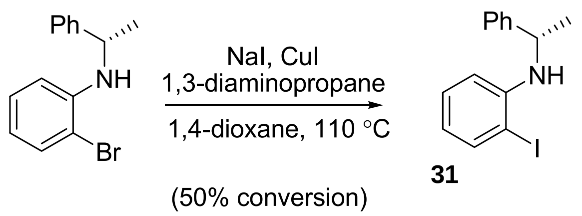
With the success of complexing our P-N ligand to a metal, if only through the phosphorus attention turned to synthesising a range of aromatic iodides from 1,2-diiodobenzene with different chiral amines in the 1- position. Therefore using the Buchwald-Hartwig reaction and a range of both aryl and alkyl chiral amines we prepared a range of monoamines in low to good yields, details shown in Table 6.

Table 6 – Monoamines synthesised

Amine	Product	Yield (%)
 (*S*)-3-methylbutan-2-amine	 **34**	57
 (*S*)-3,3-dimethylbutan-2-amine	 **35**	25
 (*R*)-1-cyclohexylethylamine	 **36**	48
 (*R*)-1,2,3,4-tetrahydronaphthylamine	 **37**	32
 (*S*)-1-(1-naphthyl)ethylamine	 **38**	32
 (*S*)-1-(2-naphthyl)ethylamine	 **39**	22

 (*R*)-1-phenylpropylamine	 **40**	54
 (*R*)-α-methylbenzylamine	 **41**	65

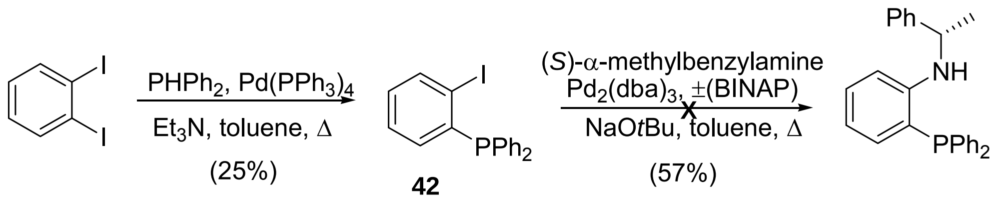
As the yields for the Buchwald-Hartwig reactions were only moderate at best, a method for displacing bromine and replacing this with an iodine was sought. This would allow use of 1,2-dibromobenzene in the Buchwald-Hartwig reactions, which in our experience gave higher yields than when 1,2-diiodobenzene is used. One such method reported by Buchwald is the copper catalysed aromatic halogen exchange reaction.[166] This method uses a catalytic amount of copper iodide and in the presence of sodium iodide and 1,3-diaminopropane in an aromatic Finkelstein reaction. Using the conditions reported by Buchwald bromo-monoamine **2** was reacted with sodium iodide in the presence a copper (I) catalyst, to yield the iodo-monoamine **31**. However the ^{1}H NMR spectrum indicated that the reaction had only given a 50% conversion, with the two compounds being inseparable by column chromatography.



Scheme 126

The 1:1 mixture was subjected to the same reaction conditions in an attempt to gain a higher conversion, however evidence of the starting material was still evident the ^{1}H NMR, with the conversion still being 50%. As the attempt to exchange the bromine with an iodine had resulted in a 1:1 mixture of product and starting material it was decided to continue using 1,2-diiodobenzene for the Buchwald-Hartwig reaction.

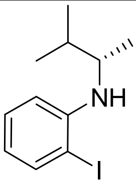
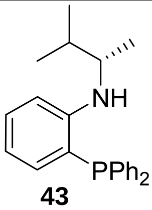
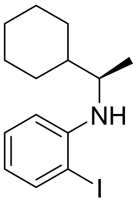
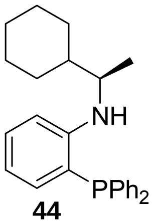
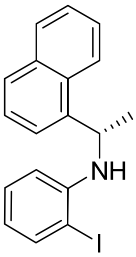
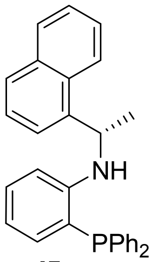
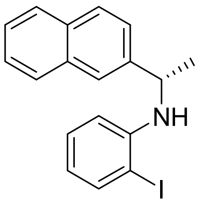
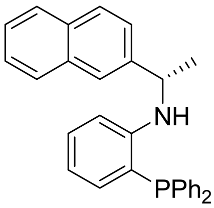
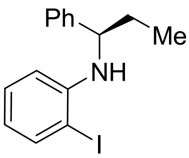
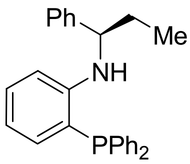
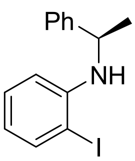
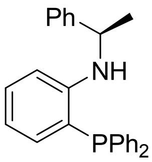
An attempt to diverge the synthesis later was also tried, where 1,2-diiodobenzene was reacted with diphenylphosphine to generate compound **42** in 25% yield (Scheme 127), which could then be used in a Buchwald-Hartwig reaction with a chiral amine to product the desired diphenylphosphine compound. However the second reaction did not prove successful with compound **42** being reisolated (Scheme 127).



Scheme 127

We next attempted the second palladium cross-coupling reaction on all monoamines available, results of which are shown in Table 7. We found however, the second palladium cross-coupling reaction was capricious, with not all the monoamines generating the desired phosphine compound in good yields. When investigated further we found the purity of the diphenylphosphine plays a large role in the outcome of the reaction, any air incorporated into the reaction can also cause the yields of the desired products to be much lower.

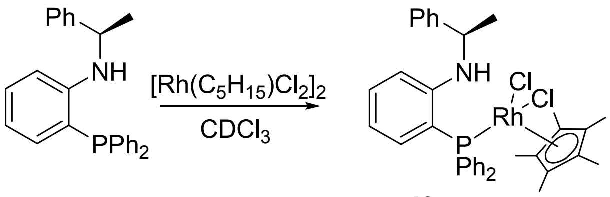
Table 7- Diphenylphosphino compounds synthesised

Monoamine	Product	% desired compound*
 **34**	 **43**	97
 **36**	 **44**	21
 **38**	 **45**	58
 **39**	 **46**	41
 **40**	 **47**	57
 **41**	 **48**	68

*determined using ^{31}P NMR spectroscopy

All monoamines except monoamines **35** and **37** generated the desired diphenylphosphino compounds in varying yields. The lower yielding reactions all had peaks in the ^{31}P NMR spectra which correlated to the diphenylphosphine oxide (~2.2 ppm).

We selected three compounds with which to attempt further complex to metals; we chose compound **43** as this was our highest yielding reaction with low levels of impurities, compound **45** as this has a large R' group present on the nitrogen and was one of the higher yielding reactions, and compound **48** as this was the opposite enantiomer to compound **32** which had previously been used to complex to ruthenium. For compound **32** we decided upon complexation with a rhodium dimer, $[Rh(C_5H_{15})Cl_2]_2$, and this complexation was carried out using the same procedure as before, again due to limited material (Scheme 128).



49

Scheme 128

Once again there was a significant change in the ^{31}P NMR spectrum; upon complexation we observed a chemical shift from one peak at -20.1 ppm to three doublets at 13.4 ppm, 27.3 ppm and 29.8 ppm. The presence of these doublets confirms that the phosphorus has complexed to the metal as rhodium is NMR active [^{103}Rh, I = ½, natural abundance = 100%]; however we were unable to explain why three doublets were seen in the NMR.

To help explain this we assumed that if one of the doublets present in the ^{31}P NMR spectrum corresponded to the compound with both the nitrogen and the phosphorus complexed (Figure 67) the addition of triethylamine to the NMR tube would cause an increase in the intensity of the corresponding signals.

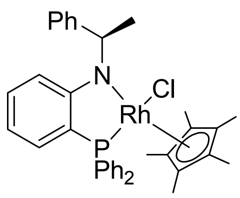
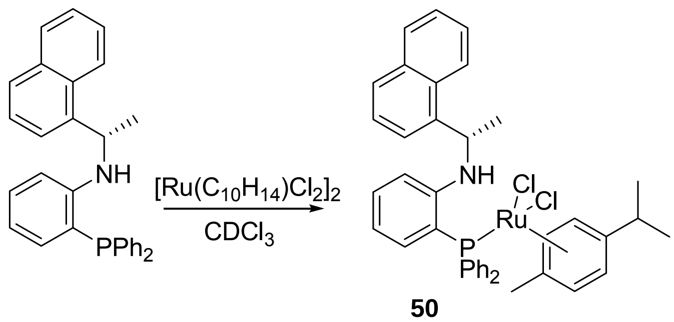


Figure 67

The addition of triethylamine did result in a drop in intensity of the doublet present at 13.4 ppm, and an increase in intensity of the doublet present at 29.8 ppm. However, no change was seen in the peak present at 27.3 ppm, which could be due to impurities in the starting material. To help confirm if the highest intensity peak was our desired compound we attempted to crystallise the sample, however this proved unsuccessful.

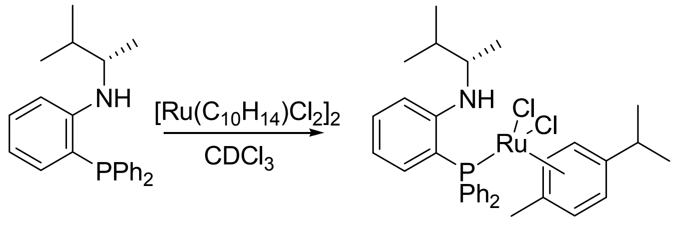
Compound **45** was complexed to the ruthenium dimer (Scheme 129), previously used with compound **32** and gave two peaks in the ^{31}P NMR spectrum, one at 24.2 ppm and the other at 26.9 ppm, both of equal intensity.



Scheme 129

Once again the addition of triethylamine, and then methanol had no effect on the ^{31}P NMR spectrum, with no change in chemical shift being seen.

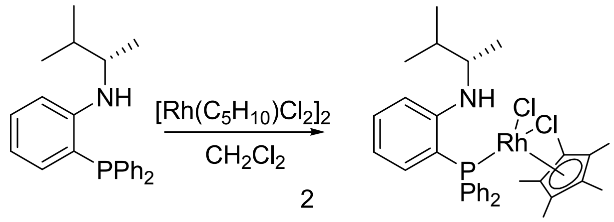
The compounds complexed to metals were thus far in small quantities and moderate purity, however compound **43** was both available in a larger quantity and of a higher purity. Therefore, this ligand was chosen for complexation to both the ruthenium and the rhodium dimers. Initially the same procedure was followed as with the previous examples with small amounts of the ligand being used and the ^{31}P NMR spectrum taken. First the ruthenium dimer was used to generate compound **51** (Scheme 130), which gave a chemical shift in the ^{31}P NMR spectrum of 27.2 ppm, a significant difference from the starting material (-20.3 ppm).



51

Scheme 130

The complexation of the ligand with the rhodium dimer gave better results. Therefore, using this as a guideline, compound **43** was allowed to stir with the rhodium dimer in dichloromethane. The desired compound **52** was obtained in 68 % yield (Scheme 131).



52

Scheme 131

Once again three doublets were apparent in the ^{31}P NMR spectrum, one at 28.6 ppm, with an intensity of 37%, a second at 28.9 ppm which was the major species in the ^{31}P NMR spectrum with an intensity of 58%, and a third of very low intensity at 30.0 ppm. We were not certain if the higher intensity peak corresponded to compound **51** or the compound with both the nitrogen and the phosphorus complexed to the metal (Figure 68).

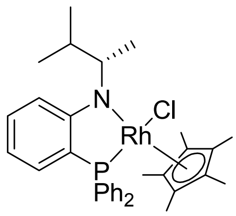


Figure 68

Therefore, we endeavoured to obtain a crystal which we could submit for X-ray crystallography. Once crystallography data was obtained (Figure 69) it confirmed that the ligand was complexed to the metal through the phosphorus, but not through the nitrogen.

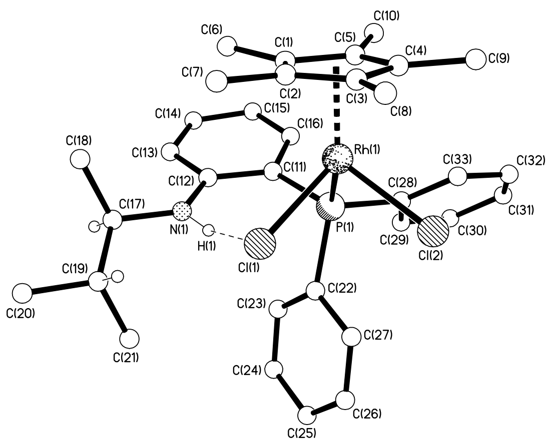


Figure 69

However, the crystal structure does show hydrogen bonding between the hydrogen of the NH of the ligand and one chlorine present on the rhodium. From this it can be concluded that the second complexation between the nitrogen and the rhodium should not be too problematic, as the nitrogen already has a partial negative charge, although further work upon this ligand and complex would be needed to confirm this.

2.3 – An aromatic amination approach towards natural products

The use of atropoisomerism in catalyst and ligand design has become common in organic chemistry; we ourselves have been interested in developing a new catalyst which exhibits this type of chirality. Therefore a range of naphthylisoquinoline alkaloids from the *Ancistrocladaceae* and *Dioncophyllaceae* families, were of significant interest to us as natural products which contained atropoisomerism. These natural products are secondary metabolites from topical lianas of the *Ancistrocladaceae* and *Dioncophyllaceae* families and not only contain a carbon-nitrogen bond, of which there are a numerous examples, but are some of only a few natural products which exhibit atropoisomerism due to restricted rotation around the carbon-nitrogen bond. These alkaloids (Figure 70) have been subject to increasing interest in recent years.[167]

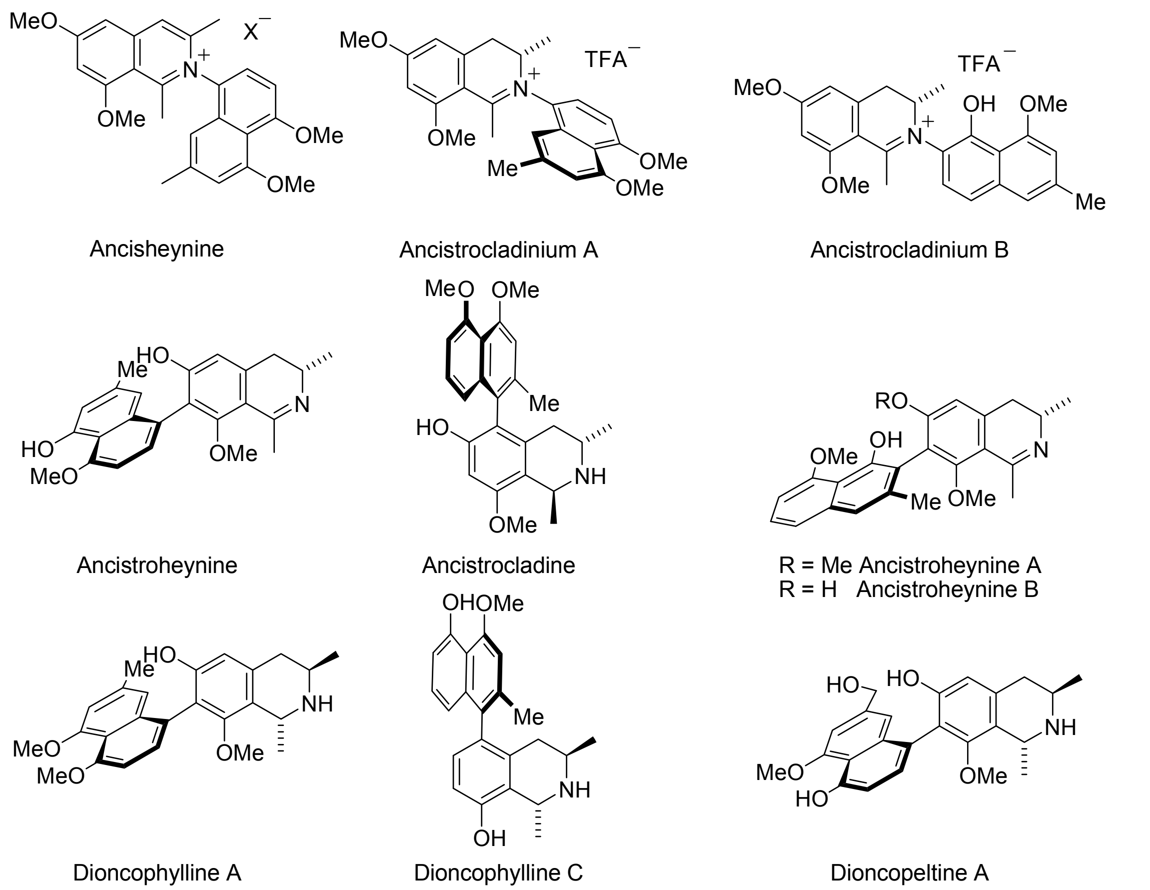


Figure 70

In these natural products a similar structure to that of our backbone usef got ligand and catalyst design can be distinguished (Figure 71) seen in blue, from this one could envisage synthesising the carbon nitrogen bond (Figure 71) seen in red *via* a Buchwald-Hartwig reaction, between an aryl bromide and an isoquinoline containing compound.

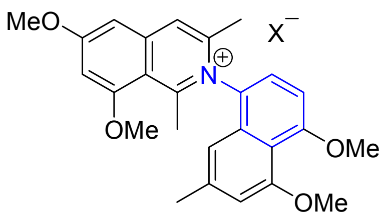
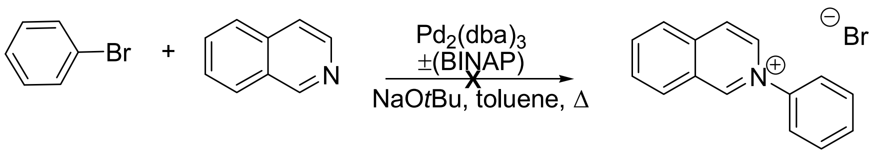


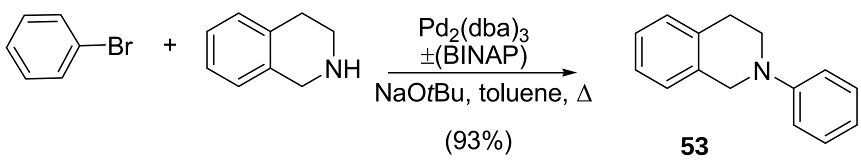
Figure 71

During this project many of the coupling reactions have been nitrogen-carbon bond formation, using the Buchwald-Hartwig reaction. Therefore our initial study was to be directed towards the synthesis of Ancisheynine (Figure 70) by direct amination of bromobenzene with an isoquinoline (Scheme 132), however only starting materials were recovered.



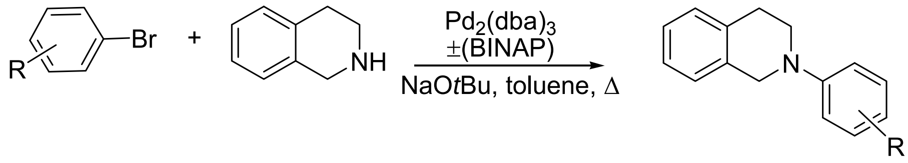
Scheme 132

As a consequence the same reaction using saturated 1,2,3,4-tetrahydroisoquinoline, in replace of isoquinoline was attempted. The reaction gave the product in an excellent yield (Scheme 133) and encouraged us to apply this methodology to a range of aryl bromides.



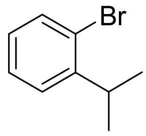
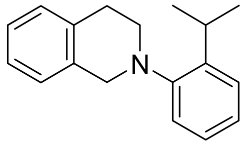
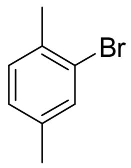
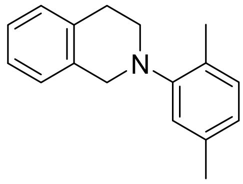
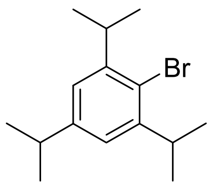
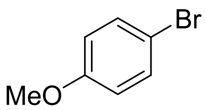
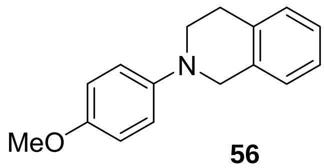
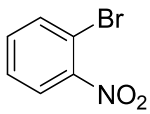
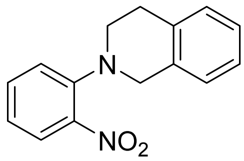
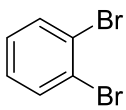
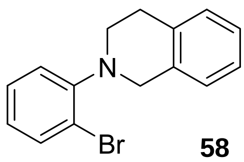
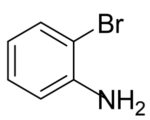
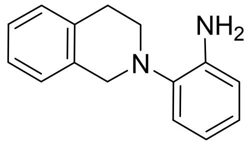
Scheme 133

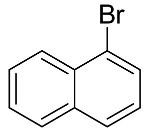
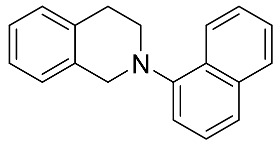
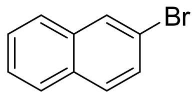
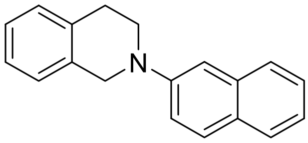
The amination of tetrahydroquinolines has previously been reported by Giorgi-Renault and co-workers,[168] however they only used a few aryl bromides and the product yields achieved were only moderate. A range of aryl bromides were sourced with which to attempt the coupling reaction, which gave the desired compounds in good to excellent yields (Scheme 134, Table 8), with only two exceptions.



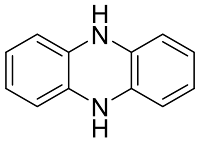
Scheme 134

Table 8 – Synthesis of aryl 1,2,3,4-tetrahyroisoquinolines

Bromide	Product	Yield (%)
	 **54**	86
	 **55**	89
	sm	
	 **56**	68
	 **57**	69
	 **58**	78
	 **59**	51

	 **60**	96
	 **61**	99

The only reactions which did not give satisfactory yields were the reaction between the bulky 2,4,6-triisopropyl phenyl bromide, presumably due to the steric bulk of the molecule interfering in the insertion of the palladium in the carbon-bromide bond, and the reaction using 2-bromoaniline. This was presumably due to dimerisation of the 2-bromoaniline, to prove if this was the case, the reaction was repeated and the secondary product analysed using ^{1}H NMR and ^{13}C NMR spectroscopy and mass spectrometry. Analysis established the presence of compound **62** (Figure 72) which confirmed that the lower yield in the reaction between 2-bromoaniline and 1,2,3,4-tetrahydroisoquinoline was due to dimerisation.



62

Figure 72

The structure of compound **57** was also confirmed by X-ray crystallography (Figure 73).

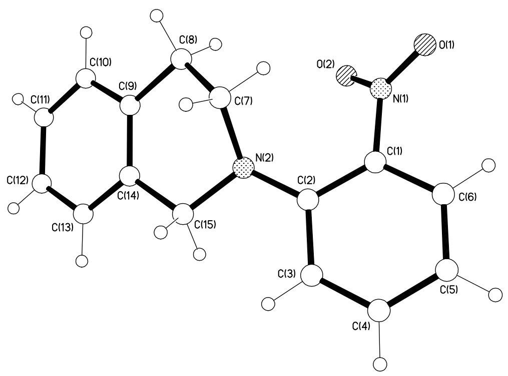


Figure 73

Particularly pleasing was the result of the reaction between 1-bromonaphthalene and 1,2,3,4-tetrahydroisoquinoline which in one step gave us the full carbon skeleton of the ring system of Ancistrocladinium A, compound **60** (Figure 74).

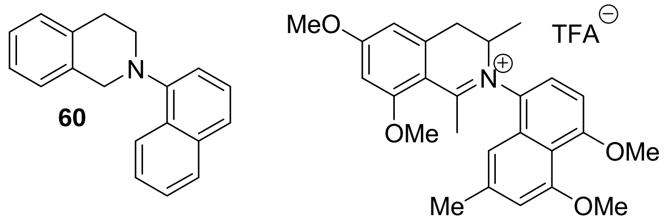
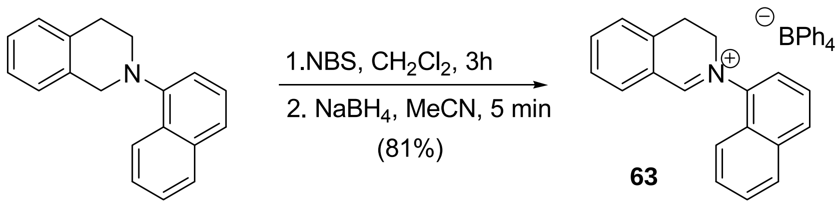


Figure 74

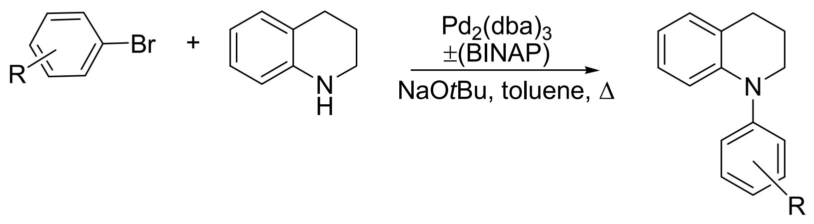
From compound **60** we knew from previous work in the group,[169] that the iminium bond could easily be installed by treatment with *N*-bromosuccinimide. Using this methodology compound **60** was heated under reflux in dichloromethane with *N*-bromosuccinimide to give the dihydroisoquinolinium salt in a good yield, (Scheme 135).



Scheme 135

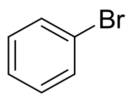
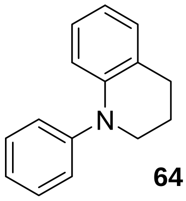
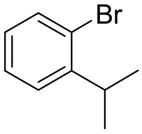
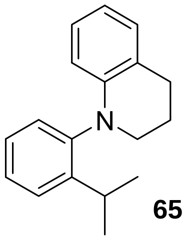
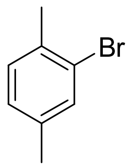
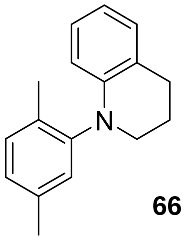
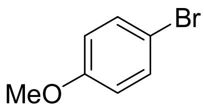
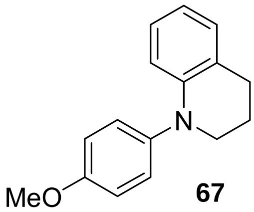
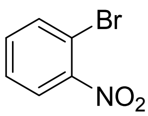
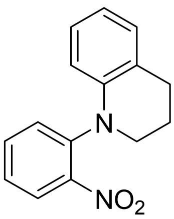
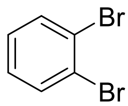
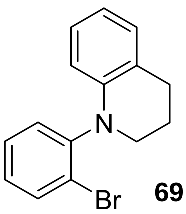
With the isolation of compound **63**, a methodology has been developed with which the carbon skeleton of the ring system Ancistrocladinium A can be prepared and the iminium bond inserted in just two high yielding steps. This is an encouraging result towards the total synthesis of Ancistrocladinium A, where using this methodology for the final two steps of the synthesis can be envisaged.

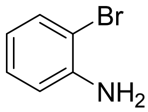
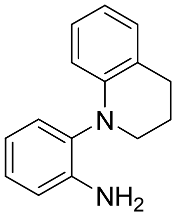
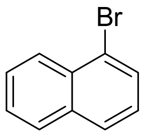
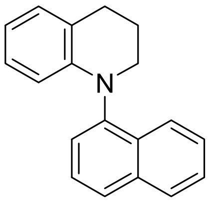
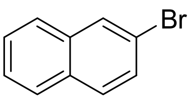
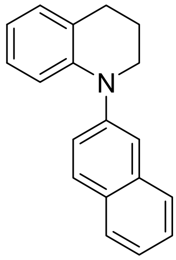
Following the success of the synthesis of aryl tertahydroisoquinolines the same range of aryl bromides were reacted with 1,2,3,4-tetrahydroquinoline, (Scheme 136) which again gave good to excellent yields, with the exception again being the reaction with 2-bromoaniline.



Scheme 136

Table 9 - Synthesis of aryl 1,2,3,4-tetrahyroquinolines

Bromide	Product	Yield (%)
	 **64**	94
	 **65**	89
	 **66**	87
	 **67**	64
	 **68**	69
	 **69**	56

	 **70**	51
	 **71**	94
	 **72**	87

The structure of compound **71** was also confirmed by X-ray crystallography (Figure 75), which shows slight distortion of the *N*-heterocycle.

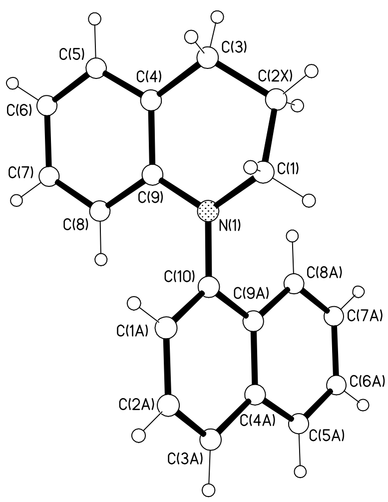


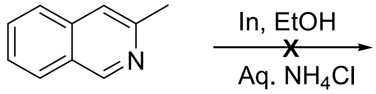
Figure 75

To further this work, and give us more of an indication that the coupling methodology would work for the penultimate step in the natural product synthesis it was decided that a coupling using 3-methyl-1,2,3,4-tetrahydroisoquinoline instead of 1,2,3,4-

tertrahydroisoquinoline would be attempted. The methyl in the 3' position is present in many of the natural products.

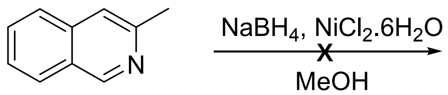
As 3-methyl-1,2,3,4-tetrahydroisoquinoline is not commercially available reduction of the unsaturated compound, 3-methylisoquinoline, using a method reported by Moody and co-workers was attempted.[170]

Our first attempt at reducing 3-methylisoquinoline was using an indium mediated reduction in aqueous ethanolic ammonium chloride as described in the literature, which yielded a yellow oil (Scheme 137). Neither the ^{1}H or ^{13}C NMR spectroscopy data were consistent with the reported data.



Scheme 137

As the indium reduction had proved futile another method to reduce 3-methylisoquinoline reported by Kudo using sodium borohydride in the presence of nickel (II) chloride hexahydrate was attempted (Scheme 138).[171] Once again attempts to reduce 3-methylisoquinoline were unsuccessful with only starting material being seen.



Scheme 138

With attempts to reduce 3-methylisoquinoline being unsuccessful another route with which to generate a tetrahydroisoquinoline with a group in the 3' position was investigated. A methodology developed in the Page group was chosen which should allow synthesis of 3-methyl-tetrahydroisoquionline, (Figure 76) or the corresponding methyl ester from phenylacetone, with which a coupling with an aryl bromide, using the Buchwald-Hartwig reaction could be tried.

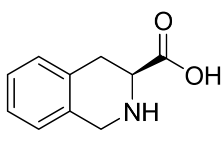
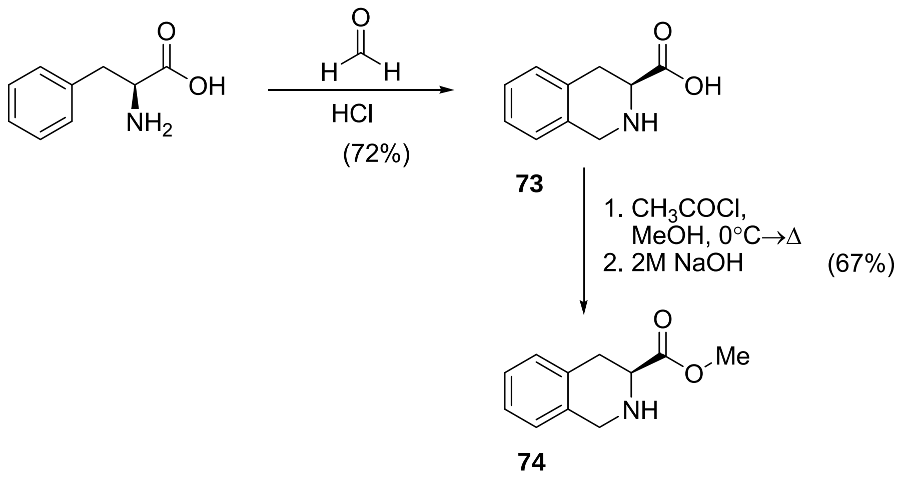


Figure 76

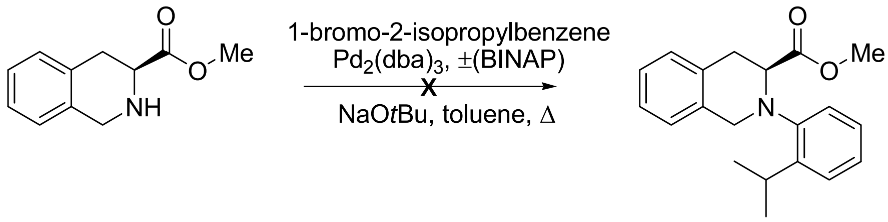
The starting material chosen for the proposed synthesis (Scheme 139) was *L*-phenylaniline, which is available commercially enantiomerically pure at a relatively low cost compared to the methyl ester which although available commercially is expensive.



Scheme 139

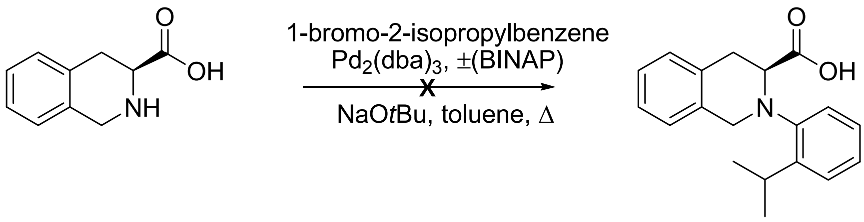
Initially the Pictet-Spengler reaction was used to form the six membered tetrahydroisoquinoline ring, by the insertion of formaldehyde to yield the tetrahydroisoquinoline-3-carboxylic acid **73** in a good yield of 72% (Scheme 139), followed by the conversion of the carboxylic acid into the methyl ester using acetyl chloride, in methanol. Upon neutralisation of the solution, the desired tetrahydroisoquinoline-3-carboxylic acid methyl ester **74** was isolated in a good 67% yield.

With both the tetrahydroisoquinoline-3-carboxylic acid **73** and tetrahydroisoquinoline-3-carboxylic acid methyl ester **74** in hand a palladium coupling could be attempted. First the Buchwald-Hartwig reaction using 1-bromo-2-isopropylbenzene with the tetrahydroisoquinoline-3-carboxylic acid methyl ester **74** (Scheme 140) was tried, as this has no free OH which could undergo a competitive coupling reaction and the isopropyl group present on the aryl bromide should result in atropoisomerism in the product. This reaction however failed to yield the desired compound, with a complex mixture being obtained.



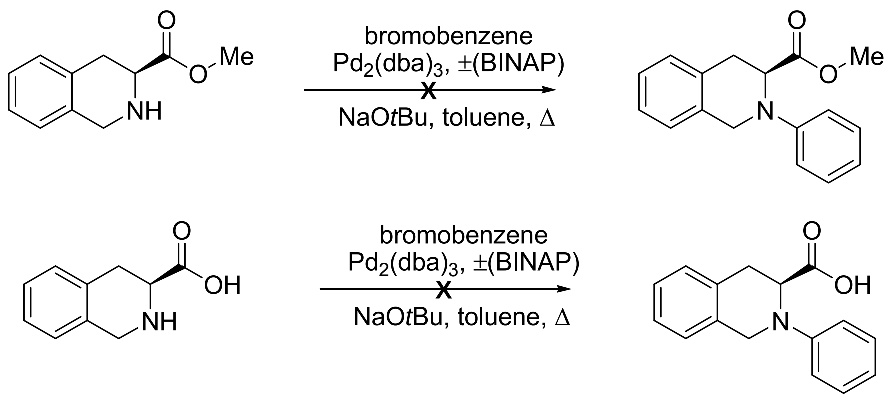
Scheme 140

As this reaction had failed, the same reaction using the tetrahydroisoquinoline-3-carboxylic acid **73** (Scheme 141) was attempted, with two equivalents of the aryl bromide, which also failed to give the desired compound.



Scheme 141

These reactions may have failed due to the steric bulk of the isopropyl group present on the aryl bromide, and therefore if this group was too bulky then using bromobenzene should allow the reaction to proceed. Therefore, the same reactions were attempted using bromobenzene (Scheme 142) in place of the 1-bromo-2-isopropylbenzene, however neither reaction was successful.

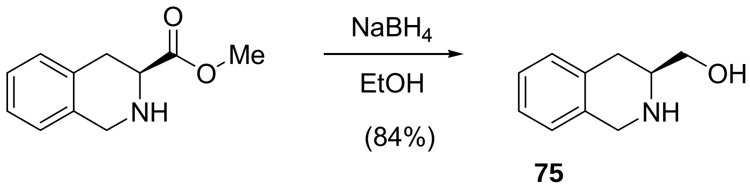


Scheme 142

As these reactions had failed, compound **73** and **74** were subjected to the reaction conditions without the aryl bromide present, to see if the reaction conditions were causing the material decompose and therefore unable to participate in the cross-coupling reaction. Tetrahydroisoquinoline-3-carboxylic acid methyl ester and tetrahydroisoquinoline-3-

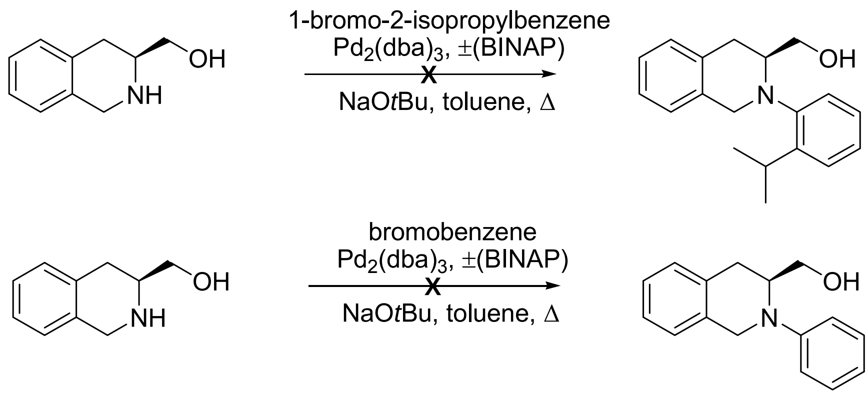
carboxylic acid were both refluxed in toluene in the presence of tris(dibenzylideneacetone)dipalladium, BINAP and sodium *tert*-butoxide for four hours. Interestingly the starting material was not present by TLC or ^{1}H NMR after the four hours, indicating that the material was not stable under the reaction conditions.

As a result, attention turned to reducing the tetrahydroisoquinoline-3-carboxylic acid methyl ester **74** to an alcohol, as it had also been suggested that the carbonyl moiety could be causing the nitrogen to have a lower electron density than tetrahydroisoquinoline, and this could contribute to the reaction to failing. Therefore the tetrahydroisoquinoline-3-carboxylic acid methyl ester **74** treated with sodium borohydride to generate hydroxymethyl-1,2,3,4-tetrahydroisoquinoline **75** in 84% yield (Scheme 143).



Scheme 143

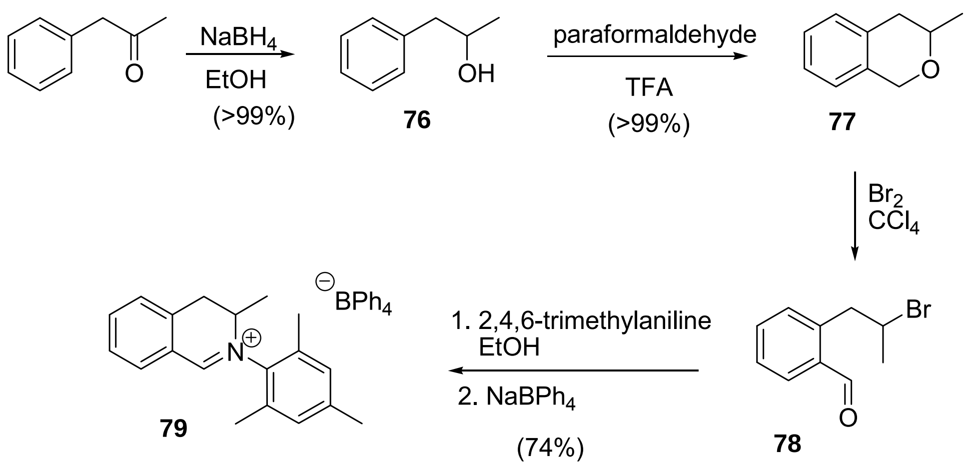
The resulting product **75** was subject to the Buchwald-Hartwig reaction with 1-bromo-2-isopropylbenzene (Scheme 144), however none of the coupled product was seen by ^{1}H NMR in the crude material. Once again, the reaction was repeated using bromobenzene in the place of 1-bromo-2-isoproylbenzene (Scheme 144), however none of the desired compound was seen to form during the reaction.



Scheme 144

Interestingly Bringmann and co-workers published the total synthesis of Ancistrocladinium A in which the one of the latter steps was a Buchwald-Hartwig coupling,[172] they however preformed the coupling on the secondary amine, followed by a Bischler-Napieralski ring closure reaction to install the tetrahydroisoquinoline ring.

During our work on the Buchwald-Hartwig reaction we simultaneously instigated a different route towards the same natural products. Initially we proposed to synthesise the desired product from the failed coupling reaction between 1,2,3,4-tetrahydroisoquinoline and 2,4,6-triisopropylbenzene.



Scheme 145

The first reaction was the reduction of phenylacetone with sodium borohydride in ethanol, which yielded the desired product 1-phenylpropan-2-ol, **76**, in a quantitative yield, (Scheme 145). This was followed by an Oxa-Pictet-Spengler reaction to generate the isochroman **77** in quantitative yield. The isochroman is then ring opened with molecular bromine, to give the secondary bromide **78**.

Initially the method followed called for the isochroman to be treated with molecular bromine, followed by reflux in HBr, however this gave a low conversion (by ^{1}H NMR) which we attributed either to a competing elimination reaction, or to decomposition, caused by refluxing the product in HBr. There was no evidence of the product from the elimination reaction (Figure 77) in the ^{1}HMR spectrum.

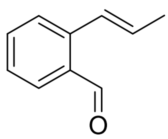


Figure 77

Therefore we concluded that the bromine may be inserting in the first step of the reaction, during the addition of Br_2 and thus we were getting decomposition during the second step of the reaction.

For this reason we chose to modify the method, only following the first step, which gave us a higher conversion. Attempts to purify compound **78** did not allow us to isolate the pure compound, however we found that Kügelrohr distillation gave us a compound of sufficient purity to allow the next step of the synthesis to be carried out.

Compound **78** was reacted with 2,4,6-trimethylaniline and upon addition of sodium tetraphenylborate the desired compound **79** was seen to precipitate from the reaction, and was obtained in 74% yield (Scheme 145).

Pleasingly we were able to obtain X-ray crystallography data for compound **79**, which is shown below (Figure 78) with the counter-ion, and with the counter-ion removed for clarity.

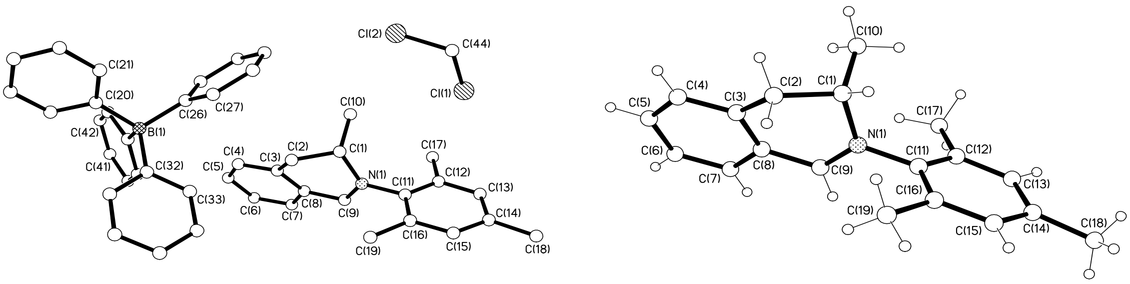
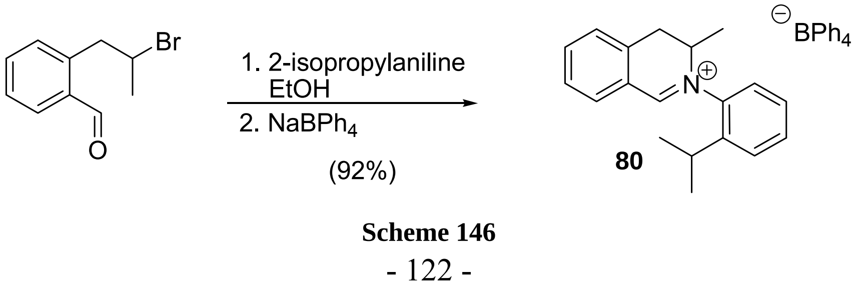


Figure 78

Encouraged by the success of this reaction we repeated the same scheme, this time using 2-isopropylaniline for the last step to generate compound **80**, in an excellent 92% yield (Scheme 146).



Scheme 146

A crystal structure allowed us to confirm the structure of compound **80** (Figure 79). Of particular interest to us is the position of the isopropyl moiety in the solid state, which is positioned away from the methyl present on the tetrahydroisoquinoline ring, from this we can conclude that atropoisomerism is present in the structure.

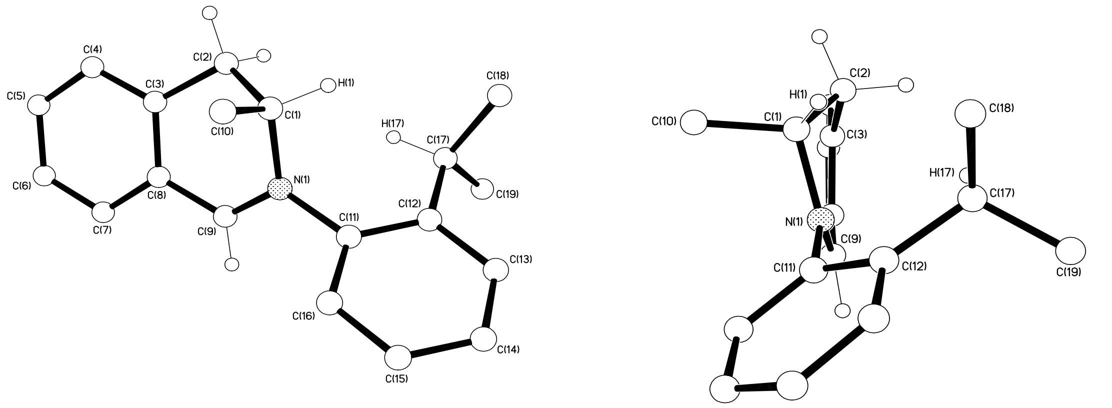


Figure 79

We were interested in the possibility that compound **80** exhibited atropoisomerism, which we thought maybe present due to the position of the isopropyl in the crystal structure. In the ^{1}H NMR there are two sets of peaks present, a major and minor peak, best demonstrated by the iminium peak at 9.54 ppm. Figure 80 shows the iminium peak for compound **80**, with major and minor peak apparent. As the majority of peaks in the ^{1}H NMR were broad, we proposed to investigate this with a VT study.

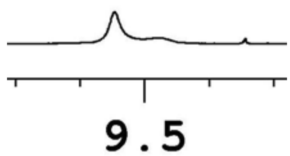


Figure 80

Compound **80** had better solubility in DMSO-d_6 so this was used as the solvents for the VT. Results from the VT were pleasing, as all the peaks are seen to sharpen and the minor peaks disappear on heating the compound (Figure 81). This is due to an increase in the energy of the system to above that of the rotational barrier, which results in free rotation around the carbon-nitrogen bond, resulting in the major and minor peaks becoming one.

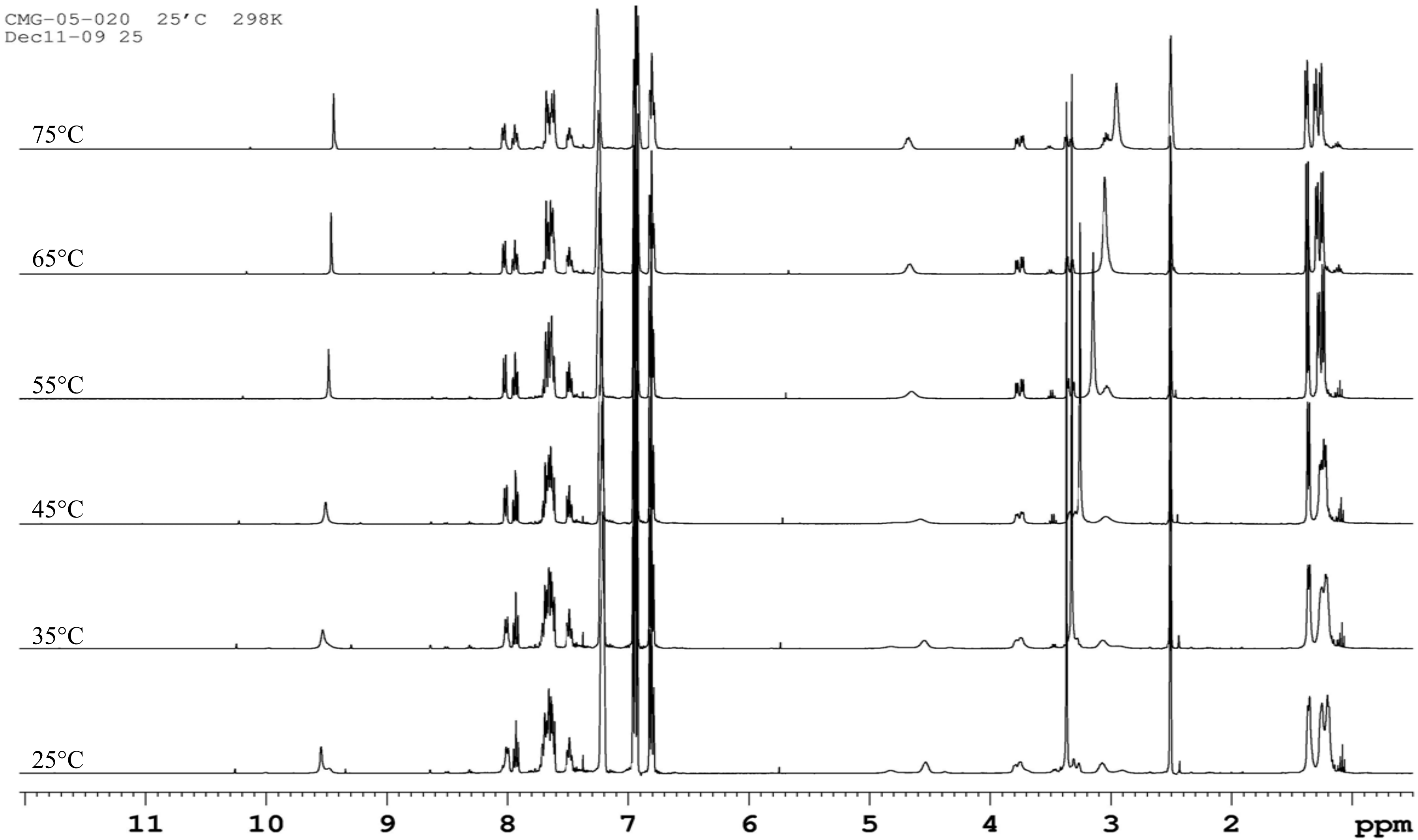

CMG-05-020 25'C 298K
Dec11-09 25
75°C
65°C
55°C
45°C
35°C
25°C
11
10
9
8
7
6
5
4
3
2
ppm

Figure 81

When the sample was allowed to cool, a further ^{1}H NMR spectrum was obtained and the two peaks of the major and minor compounds were once again present, in the same ratio.

These results were pleasing as not only could we demonstrate what we believed was another method which we could apply to our attempts to synthesise the natural products, but through NMR studies have shown that atropoisomerism can be achieved through this method, as there is restricted rotation around the carbon-nitrogen bond.

2.4 – Conclusion and Future Work

Initial results were promising with a C_2-symmetric backbone synthesised and more than one ligand type generated from this. Unfortunately none of the ligands synthesised from this backbone were successful in giving enantiomeric excess in test reactions, or in the case of the thiourea viable due to the low yields obtained. Alterations on this backbone design, by synthesising mixed diamines or the incorporation of a more bulky isopropyl group failed to give any positive results.

Investigation of different catalyst designs were also unsuccessful, we were unable to synthesise the carbene and the tetrazole containing catalysts failed to give any enantiomeric excess. Incorporation of a tertiary amine allowed us to use our ligand in an asymmetric Grignard reaction; however this reaction was not a success. As the ligand could be recovered from the reaction, further work could be to once again try asymmetric Grignard reaction and to use different secondary amines in the synthesis of the ligand. Future work could also explore different test reactions for the different ligands synthesised.

More positively, work on a new type of phosphorus-nitrogen (P,N) ligands was successful, with a number of different ligands being synthesised and some of these complexed to metals in NMR studies. Pleasingly this was easily transferred to a larger scale reaction, and X-ray crystallography confirmed the ligand was complexed to the metal *via* the phosphorus moiety. Further work on this would allow the complexation through the nitrogen to be achieved, and the metal complex to then be used in a test reaction. Using the different diphenylphosphino compounds synthesised and the method developed for complexing these to metals, we could then develop a range of metal complexes for testing in different reactions.

Work using the Buchwald-Hartwig reaction for coupling various aryl bromides to both 1,2,3,4-tetrahydroisoquinoline and 1,2,3,4-tetrahydroquinoline was for the most part successful, with methodology being developed which we believe can be applied to the synthesis of Ancistrocladinium A.

In particular the coupling between 1,2,3,4-tetrahydroisoquinoline and 1-bromonaphthalene afforded us the full carbon skeleton of the ring system of the natural product in one step, from which we were able to generate the iminium salt. Unfortunately, we were unable to synthesise a tetrahydroisoquinoline with a methyl in the 3' position, with which we could carry out further study towards the natural product. Future work would be to continue with attempts to produce a tetrahydroisoquinoline with a methyl in the three position and to successfully use this in a Buchwald-Hartiwig reaction.

Further research allowed us to investigate the feasibility of an alternative route for the synthesis of Ancistrocladinium A and we were particularly pleased when analysis of X-ray crystallography data indicated that atropoisomerism had been achieved.

3.0 - Experimental

3.1 - General Experimental

All solvents and reagents were purified by standard techniques as reported in Perrin. D.D.; Armarego, W. L. F., Purification of Laboratory Chemicals, 3rd edition. Pergamon Press, Oxford, 1998 or used as supplied from commercial sources as appropriate.

Reagent chemicals were purchased from Aldrich Chemical Company Ltd., Lancaster Chemical Synthesis Ltd. and Acros (Fisher) Chemicals Ltd. Commercially available reagents were used as supplied, without further purification unless otherwise stated. Air- and moisture-sensitive reactions were carried out using glassware that had been dried overnight in an oven at 240 ^{o}C.

Solvents where necessary, were dried and stored over 4Å molecular sieves prior to use. Molecular sieves were activated at 240°C over a period of 3 days. Light petroleum (P.E. 40-60) refers to the fraction of the light petroleum ether which boils between 40-60 °C.

Analytical thin layer chromatography (TLC) was conducted using aluminium or glass backed plates coated with 0.25 mm silica containing fluorescer. Plates were visualised by quenching of UV light (254 nm). Flash chromatography was conducted using Merck Kieslgel (70-230 Mesh ASTM) as the stationary phase unless otherwise stated. Samples were applied as saturated solutions in the appropriate solvent.

High Performance Liquid Chromatography (HPLC) was carried out on a Chrom Elite Automated HPLC system with a chiral reverse phase column. Samples were run at 0.5mL/min in a 99:1 solution of hexane:isopropyl alcohol.

Infra-red spectroscopy (IR) was conducted in the range of 4000-600 cm^{-1}, using a Perkin-Elmer Fourier Transform Paragon 1000 spectrophotometer (with internal calibration). Samples were dissolved in an appropriate solvent and applied as a thin film to NaCl plates, only the major absorbances have been reported.

Proton (^{1}H), carbon (^{13}C), phosphorus (^{31}P) and fluorine (^{19}F) magnetic resonance spectra were recorded at 400 MHz, 100 MHz, 162 MHz and 376 MHz respectively using a DPX-

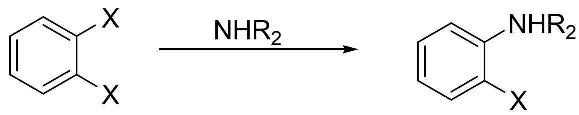
400 spectrometer, as solutions in deuterated $CDCl_3$ unless otherwise specified. Chemical shifts (δ) are quoted as parts per million (ppm) and proton and carbon spectra are referenced to tetramethylsilane (TMS) as the internal standard at 0 ppm. Phosphorus spectra are referenced to triphenylphosphate at 0 ppm and fluorine spectra referenced to hexafluorobenzene at 0 ppm. The following abbreviations are used; singlet (s), doublet (d), triplet (t), quartet (q) multiplet (m) and broad (b). Assignment of individual proton signals was assisted by analysis of ^1H COSY spectra and nOe data. Coupling constants (J values) are reported in hertz (Hz). Assignment of individual carbon signals was assisted by DEPT and HMQC data.

Mass spectra (high/low resolution) were recorded using a Fisons VG Quattro II SQ instrument, with modes of ionisation being indicated as electron impact (EI) and fast atom bombardment (FAB) and electrospray (ES) with only the molecular ion, molecular ion fragments and major peaks being reported. Accurate masses were recorded using a Jeol SX104 or obtained from the EPSRC National Mass Spectrometry Service Centre in Swansea.

Melting points where appropriate were determined using an electrical 9100 Thermal Melting point instrument and are uncorrected. Yields (unless otherwise stated) are quoted for isolated pure products.

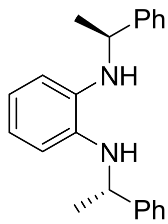
3.2 - Individual experimental procedures and characterisation

General procedure for Buchwald-Hartwig reactions:



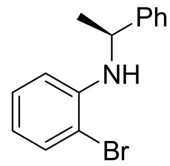
A dry flask was charged with $Pd_2(dba)_3$ (0.088 mmol), (±) BINAP (0.18 mmol) and toluene (6 mL). The resulting solution was degassed for 10 mins before being heated to 110 °C for 15 mins. The reaction mixture was allowed to cool to room temperature before sodium *tert*-butoxide (4.1 mmol), the aryl halide (2.2 mmol) and amine (4.4 mmol) were added. The resulting mixture was heated under reflux for 4-16 h, before being cooled to room temperature and filtered through a pad of Celite. Solvents were removed under reduced pressure and the coupled products purified by column chromatography typically eluting with light petroleum:ethyl acetate (99:1)

Bis-((*S*)-1-phenylethyl)benzene-1,2-diamine 1[173]



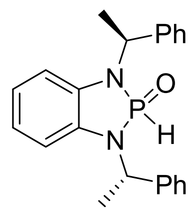
Yellow Oil, (0.52 g, 71%) Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3407,1598, 1507, 1255, 740; δ_H (400 MHz, $CDCl_3$) 1.59 (6 H, d, *J* 6.4 Hz, 2 C*H*$_3$), 3.71 (2 H, bs, 2 N*H*), 4.52 (2 H, q, *J* 6.8 Hz, 2 C*H*), 6.41-6.54 (2 H, m, Ar-*H*), 6.55-6.59 (2 H, m, Ar-*H*), 7.24-7.29 (2 H, m, Ar-*H*), 7.31-7.36 (4 H, m, Ar-*H*), 7.39-7.41 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.66 (2 *C*H$_3$), 55.86 (2 *C*H), 113.60 (2 Ar-*C*H), 119.13 (2 Ar-*C*H), 125.98 (2 Ar-*C*H*)*, 126.88 (4 Ar-*C*H*)*, 128.62 (4 Ar-*C*H), 136.27 (2 Ar-*C*), 145.24 (2 Ar-*C*). *m/z* (FAB^+) 317 (37), 316 (94), 211 (100), 105 (67). HRMS (ES) calcd for [$C_{22}H_{24}N_2$] 316.1939, found [M^+] 316.1939. $[\alpha]_D^{20}$ +176.7 [c = 0.90, $CHCl_3$], literature $[\alpha]_D$ +182.0 [c = 0.76, $CHCl_3$].

2-Bromo-((*S*)-1-phenylethyl)benzenamine 2[173]



Clear oil (0.13 g, 21%) Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3409, 1596, 1506, 1320, 1223, 741, 550; δ_H (400 MHz, $CDCl_3$) 1.57 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 4.54-4.47 (1 H, m, C*H*), 4.70 (1 H, bs, N*H*), 6.38 (1 H, d, *J* 5.6 Hz, Ar-*H*), 6.51 (1 H, t, *J* 6.4 Hz, Ar-*H*), 6.98 (1 H, t, *J* 6.8 Hz, Ar-*H*), 7.31-7.32 (5 H, m, Ar-*H*), 7.41 (1 H, d, *J* 6.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.14 (*C*H$_3$), 52.45 (*C*H), 108.52 (Ar-*C*), 111.56 (Ar-*C*H), 116.65 (Ar-*C*H), 124.64 (2 Ar-*C*H), 125.97 (Ar-*C*H), 127.23 (Ar-*C*H), 127.67 (2 Ar-*C*H), 131.17 (Ar-*C*H), 142.87 (Ar-*C*), 143.46 (Ar-*C*); *m/z* (FAB$^+$) 277 (40), 276 (30), 275 (40), 105 (100). HRMS (ES) calcd for [$C_{14}H_{14}N^{79}Br$] 275.0309, found [M^+] 275.0306. $[\alpha]_D^{20}$ +103.0 [c = 0.92, $CHCl_3$].

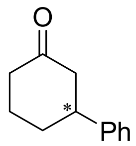
Synthesis of phosphordiamidite 3



Bis-(*S*)-1-phenylethyl)benzene-1,2-diamine (0.20 g, 0.63 mmol) was dissolved in dry CH_2Cl_2 (10 mL), triethylamine (0.7 mL, 4.7 mmol) added and the solution cooled to 0 °C. With rapid stirring PCl_3 (0.06 mL, 0.63 mmol) was added dropwise over 30 mins and the solution allowed to warm to ambient temperature. After stirring at ambient temperature for 1 hour the reaction was cooled to 0 °C before water (0.01 mL, 0.63 mmol) was added. The resulting solution was allowed to stir overnight at ambient temperature, filtered through Celite and concentrated under vacuum. The crude residue was purified using column chromatography (silica, light petroleum:ethyl acetate 1:4→0:1) to yield the desired product as a red solid (0.16 g, 70%).

υ_{max} (thin film)/cm^{-1} 2345, 1468, 1375, 1250, 1240, 732; δ_H (400 MHz, $CDCl_3$) 1.87 (3 H, d, *J* 7.2 Hz, C*H*$_3$), 1.94 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 4.95-4.89 (1 H, m, C*H*), 5.09-5.14 (1 H, m, C*H*), 6.42 (1 H, d, *J* 7.6 Hz, Ar-*H*), 6.58-6.72 (3 H, m, Ar-*H*), 7.22-7.25 (1 H, m, Ar-*H*), 7.30-7.42 (5 H, m, Ar-*H*), 7.46-7.48 (2 H, m, Ar-*H*), 7.55-7.57 (2 H, m, Ar-*H*), 8.65 (1 H, d, *J* 650.8 Hz, P-*H*); δ_C (100 MHz, $CDCl_3$) 14.10 (*C*H$_3$), 22.37 (*C*H$_3$), 53.46 (*C*H), 55.35 (*C*H), 108.82 (2 Ar-*C*H), 109.56 (2 Ar-*C*H), 119.75 (2 Ar-*C*), 126.31 (4 Ar-*C*H), 126.36 (4 Ar-*C*H), 127.48 (2 Ar-*C*), 128.04 (2 Ar-*C*H); δ_P (162 MHz, $CDCl_3$) 7.36 (s, 100 %); (100%); *m/z* (EI) 364 (24), 363 (M^+, 100%), 213 (25), 154 (22), 122 (40), 120 (48), 109 (41), 94 (29), 52 (32), 44 (30). HRMS (ES) calcd for $[C_{22}H_{24}N_2OP]^+$ 363.1621, found $[M^+H^+]$ 363.1621. $[\alpha]_D^{20}$ -108.1 [c = 0.64, $CHCl_3$]

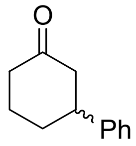
Synthesis of 3-phenylcyclohexanone 3[58]



$[RhCl(cod)]_2$ (0.005 g, 1.0 μmol) was dissolved in 1,4-dioxane (1 mL) and 1M KOH (0.3 mL) added, the solution was left to stir at 25 °C for 30 mins. After 30 mins the phosphordiamidite ligand, (0.02 g, 5.1 μmol) was added and the solution left stirring for a further 5 mins. Phenylboronic acid (0.09 g, 0.76 mmol) and cyclohexen-1-one (0.05 g, 0.51 mmol) were then added and the solution left to stir at 25 °C for 20 h before being quenched with $NaHCO_3$ and extracted with diethyl ether. The combined organic phase was dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude residue was purified using column chromatography (silica, light petroleum:ethyl acetate 9:1) to yield the desired product as a colourless oil (0.09g, 96%). Enantiomeric excess was determined using HPLC with a chiral reverse phase column, sample was run at 0.5ml/min in a 99:1 solution of hexane:isopropyl alcohol.

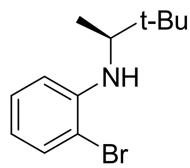
Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 1708, 1593, 1450, 1223, 756; δ_H (400 MHz, $CDCl_3$) 1.87-1.88 (2 H, m, C*H*$_2$), 2.07-2.19 (2 H, m, C*H*$_2$), 2.44-2.59 (4 H, m, 2 C*H*$_2$), 2.99-3.02 (1 H, m, C*H*), 7.22-7.32 (5 H, m, Ar-*H*) δ_C (100 MHz, $CDCl_3$), 25.52 (*C*H), 32.75 (*C*H$_2$), 41.17 (*C*H$_2$), 44.73 (*C*H$_2$), 48.93 (*C*H$_2$), 126.54 (Ar-*C*H), 126.67 (Ar-*C*H), 128.04 (2 Ar-*C*H), 128.66 (2 Ar-*C*H), 143.86 (Ar-*C*), 209.80 (C=O).

Synthesis of racemic 3-phenylcyclohexanone 3a



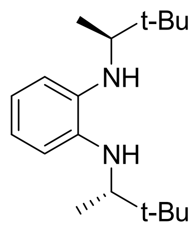
A solution of cyclohexen-1-one (1.0 g, 1.0 mmol) and copper iodide (0.2 g, 0.11 mmol) in THF (10 mL) was added to a stirred solution of 1.69 M PhMgBr in diethyl ether (1.2 g, 0.01 mol) over 30 mins. The solution was allowed to stir for 20 h before being quenched with aq. NH_4Cl, and the organic layer extracted into diethyl ether and dried over $MgSO_4$. Solvents were removed under vacuum and the crude product purified by column chromatography (silica, light petroleum:ethyl acetate 9:1) to give the desired product as a colourless oil (0.08 g, 84%). Enantiomeric excess was determined using HPLC with a chiral reverse phase column, sample was run at 0.5ml/min in a 99:1 solution of hexane:isopropyl alcohol.

2-Bromo-((*S*)-3,3-dimethylbutan-2-yl)benzenamine 5



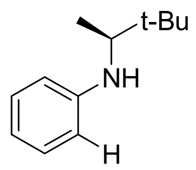
Clear Oil (0.26 g, 48%) υ_{max} (thin film)/cm^{-1} 3409, 2954, 1596, 1508, 1298, 736, 654; δ_H (400 MHz, $CDCl_3$) 0.98 (9 H, s, 3 $^{t-}$Bu C*H*$_3$), 1.12 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 3.24-2.28 (1 H, m, C*H*), 4.28 (1 H, bd, *J* 19 Hz, N*H*), 6.50 (1 H, t, *J* 7.2 Hz, Ar-*H*), 6.68 (1 H, d, *J* 8.0 Hz, Ar-*H*), 7.16 (1 H, t, *J* 8.4, Ar-*H*), 7.42 (1 H, d, *J* 8.0 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 15.54 (Me-*C*), 26.72 (3 *t*-Butyl Me-*C*), 34.76 (*t*-Butyl-*C*), 57.28 (*C*H), 110.04 (Ar-*C*), 111.46 (Ar-*C*H), 116.76 (Ar-*C*H), 128.47 (Ar-*C*H), 132.53 (Ar-*C*H), 144.98 (Ar-*C*). *m/z* (EI) 258 (31), 257 (48), 256 (36), 255 (47), 200 (96), 198 (M^+, 100%). HRMS (ES) calcd for [$C_{12}H_{19}$ $N^{79}Br$] 255.0623, found [M^+H^+] 255.0626. $[\alpha]_D^{20}$ +75.0 [c = 0.96, $CHCl_3$]

Bis-((*S*)-3,3-dimethylbutan-2-yl)benzene-1,2-diamine 6



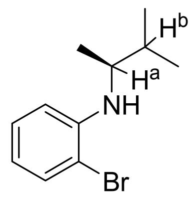
Yellow oil (0.16 g 26%) υ_{max} (thin film)/cm^{-1} 3350, 2956, 1599, 1510, 1210, 1151, 738; δ_H (400 MHz, $CDCl_3$) 0.99 (18 H, s, 6 $^{t-}$Bu C*H*$_3$), 1.09 (6 H, d, *J* 6.4, C*H*$_3$), 3.16-3.22 (2 H, m, 2 C*H*), 3.24 (2 H, bs, 2 N*H*), 6.60-6.71 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 15.39 (2 *C*H$_3$), 26.58 (6 $^{t-}$Bu *C*H$_3$), 34.65 (2 $^{t-}$Bu *C*), 57.05 (2 *C*H), 113.44 (2 Ar-*C*H), 129.70 (2 Ar-*C*H), 137.70 (2 Ar-*C*); *m/z* (EI) 276 (20), 219 (49), 135 (100). HRMS (ES) calcd for [$C_{18}H_{33}N_2$] 276.2569, found [M^+H^+] 276.2565. $[\alpha]_D^{18}$ +117.9 [c = 0.76, $CHCl_3$]

((S)-3,3-dimethylbutan-2-yl)benzenamine 7[174]



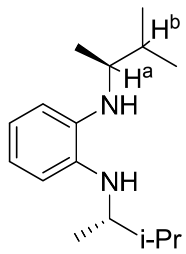
Yellow Oil, (only partial data available). Known compound, data is consistent with literature data. δ_H (400 MHz, $CDCl_3$) 0.95 (9 H, s, 3 $^{t-}$Bu C*H*$_3$), 1.07 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 3.23 (1 H q, *J* 6.4 Hz, C*H*), 3.38 (1 H, bs, N*H*), 6.57-6.64 (3 H, m, Ar-*H*), 7.12-7.16 (2H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 15.81 (*C*H$_3$), 26.51 (3 $^{t-}$Bu *C*H$_3$), 34.75 ($^{t-}$Bu *C*), 57.11 (*C*H), 112.94 (2 Ar-*C*H), 116.47 (Ar-*C*H), 129.24 (2 Ar-*C*H), 148.44 (Ar-*C*)

2-Bromo-((*S*)-3-methylbutan-2-yl)benzenamine 8



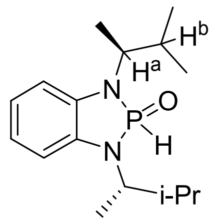
Clear oil (0.06 g, 12%) υ_{max} (thin film)/cm^{-1} 3408, 2959, 1595, 1507, 1322, 738, 667; δ_H (400 MHz, $CDCl_3$) 0.85 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr CH_3), 0.91 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr CH_3), 1.05 (3 H, d, *J* 6.8 Hz, CH_3), 1.78-1.83 (1 H, m, CH^b), 3.22-3.34 (1 H, m, CH^a), 4.16 (1 H, bs, N*H*), 6.42 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 6.53 (1 H, d, *J* 8.4 Hz, Ar-*H*), 7.06 (1 H, dt, *J* 1.6 Hz & 7.2 Hz, Ar-*H*), 7.39 (1 H, dd, *J* 1.2 Hz & 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.63 (*C*H_3), 17.67 ($^{i-}$Pr *C*H_3), 19.07 ($^{i-}$Pr *C*H_3), 32.26 ($^{i-}$Pr *C*H), 53.57 (*C*H), 109.89 (Ar-*C*), 111.68 (Ar-*C*H), 116.93 (Ar-*C*H), 128.42 (Ar-*C*H), 132.54 (Ar-*C*H), 144.49 (Ar-*C*); *m/z* (EI) 55 (35), 69 (22), 91 (21), 198 (100), 200 (99) 229 (29), 241 (48), 242 (20), 243 (46). HRMS (ES) calcd for [$C_{11}H_{17}$ $N^{79}Br$] 241.0469, found [M^+H^+] 241.0466. $[\alpha]_D^{18}$ +53.65 [c = 0.85, $CHCl_3$]

Bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine 9



Yellow Oil (0.4 g, 72%) υ_{max} (thin film)/cm^{-1} 3347, 2957, 1598, 1508, 1250, 1154, 737; δ_H (400 MHz, $CDCl_3$) 0.84 (6 H, d, *J* 6.8 Hz, 2 $^{i-}$Pr CH_3), 0.92 (6 H, d, *J* 6.8 Hz, 2 $^{i-}$Pr CH_3), 1.01 (6 H, d, *J* 6.8 Hz, 2 CH_3), 1.73-1.81 (2 H, m, 2 C-H^b), 3.07 (2 H, m, 2 N*H*), 3.16-3.24 (2 H, m, 2 C-H^a), 6.54-6.57 (2 H, m, Ar-*H*), 6.64-6.67 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.59 (2 $^{i-}$Pr *C*H_3), 17.54 (2 $^{i-}$Pr *C*H_3), 19.27 (2 *C*H_3), 32.27 (2 $^{i-}$Pr *C*H), 53.43 (2 *C*H), 113.99 (2 Ar-*C*H), 118.90 (2 Ar-*C*H), 137.21 (2 Ar-*C*); *m/z* (EI) 135 (25), 205 (47), 248 (100) 249 (43). HRMS (ES) calcd for [$C_{16}H_{29}N_2$] 248.2252, found [M^+H^+] 248.2252. $[\alpha]_D^{18}$ +95.79 [c = 0.38, $CHCl_3$]

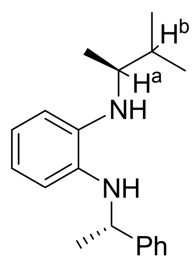
Synthesis of phosphordiamidite 10



Bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** (0.09 g, 0.36 mmol) was dissolved in dry CH_2Cl_2 (6 mL), triethylamine (0.4 mL, 2.70 mmol) added and the solution cooled to 0 °C. With rapid stirring PCl_3 (0.05 g, 0.36 mmol) was added dropwise over 15 mins and the solution allowed to warm to ambient temperature. After stirring at ambient temperature for 2 h the reaction was cooled to 0 °C before water (0.06 mL, 0.36 mmol) was added. The resulting solution was allowed to stir overnight at ambient temperature, filtered through Celite and concentrated under vacuum. The crude residue was purified using column chromatography (silica, light petroleum:ethyl acetate 1:4→0:1) to yield the desired product as a red oil (0.90 g, 85%).

υ_{max} (thin film)/cm^{-1} 2343, 1464, 1370, 1251, 1241, 733; δ_H (400 MHz, $CDCl_3$) 1.04 (12 H, m, 4 $^{i-}$Pr C*H*$_3$), 1.47 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 1.52 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 2.29-2.32 (2 H, m, 2 C*H*^{a}), 3.33-3.35 (2 H, m, 2 C*H*^{b}), 6.74-6.78 (4 H, m, Ar-*H*), 9.51 (1 H, d, *J* 639.6 Hz, P-*H*); δ_C (100 MHz, $CDCl_3$) 19.74 (2 $^{i-}$Pr *C*H$_3$), 20.74 (2, $^{i-}$Pr *C*H$_3$), 31.80 (2 *C*H$_3$), 56.52 (2 $^{i-}$Pr *C*H), 108.95 (2 *C*H), 119.24 (2 Ar-*C*H), (119.30 (2 Ar-*C*H), 131.78 (2 Ar-*C*); δ_P (162 MHz, $CDCl_3$) 10.01 (s, 91%); $[\alpha]_D^{18}$ +27.37 [c = 0.38, $CHCl_3$]

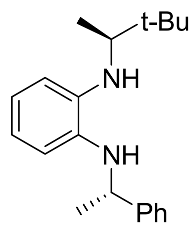
((*S*)-3-methylbutan-2-yl)-((*S*)-1-phenylethyl)benzene-1,2-diamine 11



Yellow oil (0.15 g, 64%) υ_{max} (thin film)/cm^{-1} 3412, 1595, 1509,1459, 1258, 750; δ_H (400 MHz, $CDCl_3$) 0.90 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr C*H*$_3$), 0,98 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr C*H*$_3$), 1.09 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 1.53 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 1.84-1.99 (1 H, m, C*H*^{b}), 3.28-3.34 (1 H, m, C*H*^{a}), 3.45 (1 H, m, N*H*), 4.44 (1 H, q, *J* 6.4 Hz, C*H*), 6.44 (1 H, d, *J* 7.2, Ar-*H*), 6.58-

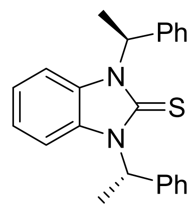
6.73 (3 H, m, Ar-*H*), 7.15-7.23 (5 H, m, Ar-*H*). δ_C (100 MHz, $CDCl_3$) 17.38 ($^{i-}$Pr CH_3), 17.48 ($^{i-}$Pr CH_3), 19.34 (CH_3), 25.04 (CH_3), 32.32 ($^{i-}$Pr *C*H), 50.90 (*C*H), 53.67 (*C*H), 113.29 (Ar-*C*H), 115.73 (Ar-*C*H), 125.84 (Ar-*C*H), 126.87 (Ar-*C*H), 127.07 (Ar-*C*H), 128.33 (Ar-*C*H), 128.59 (Ar-*C*H), 129.10 (Ar-*C*H), 130.44 (Ar-*C*H), 136.55 (Ar-*C*), 145.21 (Ar-*C*), 147.26 (Ar-*C*); HRMS (ES) calcd for [$C_{19}H_{26}N_2$] 281.2091, found [M^+] 281.005. $[\alpha]_D^{18}$ +101.54 [c = 0.13, $CHCl_3$]

((*S*)-3,3-dimethylbutan-2-yl)-((*S*)-1-phenylethyl)benzene-1,2-diamine 12



Yellow oil (0.16 g, 46%) υ_{max} (thin film)/cm^{-1} 3389, 1561, 1512, 1480, 1276, 761; δ_H (400 MHz, $CDCl_3$) 1.02 (9 H, s, 3 $^{t-}$Bu CH_3), 1.10 (3 H, d, *J* 6.4 Hz, CH_3), 1.52 (3 H, d, *J* 6.8 Hz, CH_3), 3.18 (1 H, q, *J* 6.4 Hz, C*H*), 3.42 (2 H, bs, 2 N*H*), 4.42 (1 H, q, *J* 6.8 Hz, C*H*), 6.48 (1 H, d, *J* 7.2 Hz, Ar-*H*), 6.69-6.71 (1 H, m, Ar-*H*), 6.72-6.74 (2 H, m, Ar-*H*), 7.37-7.41 (5 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.07 (CH_3), 25.03 (CH_3), 26.52 (3 $^{t-}$Bu CH_3), 34.64 ($^{t-}$Bu *C*), 53.94 (*C*H), 57.12 (*C*H), 116.47 (2 Ar-*C*H), 119.21 (2 Ar-*C*H), 125.87 (2 Ar-*C*H), 126.96 (Ar-*C*H), 128.40 (2 Ar-*C*H), 137.24 (2 Ar-*C*), 145.5 (Ar-*C*); *m/z* (EI) 296 (33), 254 (23), 240 (40), 239 (36), 191 (24), 135 (100), 105 (38); HRMS (ES) calcd for [$C_{20}H_{29}N_2$] 296.2258, found [M^+H^+] 296.2252. $[\alpha]_D^{18}$ +33.57 [c = 0.56, $CHCl_3$]

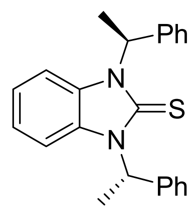
Synthesis of bis-((S)-1-phenylethyl)-benzoimidazole-2-thione 13



Bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** (0.5 g, 1.58 mmol) and Na_2CO_3 (0.3 g, 2.37 mmol) were dissolved in THF (6 mL) under nitrogen. Thiophosgene in THF (0.2 g, 1.90 mmol) was added dropwise with stirring over 15 mins, during addition the solution changed from yellow to dark green in colour. The reaction was left stirring overnight before water was added and the resulting solution washed with ethyl acetate. The organic layers were combined, washed with dilute HCl and brine and dried over $MgSO_4$ and the solvent removed under vacuum. The crude residue was recrystallised from 95% ethanol to yield the desired product as brown crystals (0.06 g, 10%).

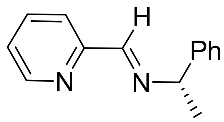
υ_{max} (thin film)/cm^{-1} 1545, 1484, 1388, 1242, 1069, 753, 737; δ_H (400 MHz, $CDCl_3$) 1.93 (6 H, d, *J* 7.2 Hz, 2 C*H*$_3$), 5.97 (1H, q, *J* 7.2 Hz, C*H*), 6.68-6.71 (1H, m, Ar-*H*), 6.77-6.79 (1 H, m, Ar-*H*), 6.82-6.84 (1 H, m, Ar-*H*), 6.87-6.90 (1 H, m, Ar-*H*), 7.00 (2 H, q, *J* 7.2 Hz, C*H*), 7.28-7.34 (10 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 17.35 (2 *C*H$_3$), 50.78 (2 *C*H), 109.76 (2 Ar-*C*H), 111.24 (2 Ar-*C*H), 126.79 (4 Ar-*C*H), 127.46 (2 Ar-*C*H), 128.69 (4 Ar-*C*H), 134.16 (2 Ar-*C*), 134.87 (2 Ar-*C*), 168.7 (C=S); *m/z* (EI) 358 (36), 342 (45), 150 (37), 134 (74), 105 (100); HRMS (ES) calcd for [$C_{22}H_{23}N_2S$] 358.1503, found [M^+H^+] 358.1507. $[\alpha]_D^{18}$ +8.3 [c = 0.87, $CHCl_3$]

Attempted synthesis of bis-((S)-1-phenylethyl)-benzoimidazole-2-thione



Bis-((*S*)-1-phenylethyl)benzene-1,2-diamine 1 (0.29 g, 0.91 mmol) was dissolved in dry toluene (15 mL) and 1,1'-thiocarbonyl diimidazole (0.20 g, 1.1 mmol) added. The solution was heated to reflux for 24 h, after this time a further portion of 1,1'-thiocarbonyl diimidazole (0.10 g , 0.5 mmol) was added and the reaction left for a further 24 h. The reaction was allowed to cool to ambient temperature before the solution was diluted with ethyl acetate (15 mL), washed with 1 M aq. HCl (2 x 15 mL) and brine (15 mL) before being dried over $MgSO_4$ and the solvent removed under reduced pressure.

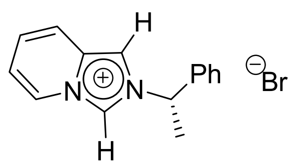
Synthesis of (*S*)-1-phenyl-((pyridin-2-yl)methylene)ethanamine 14[175]



2-Pyridine carboxaldehyde (3 mL, 31.5 mmol) and (*S*)-α-methylbenzylamine (3.8 g, 31.5 mmol) were dissolved in toluene (20 mL) and 5Å molecular sieves added (3 g). The reaction was heated under reflux for 4 h under nitrogen before being allowed to cool to ambient temperature and the solvent removed under vacuum. The crude product was purified using Kügelrohr distillation to yield the desired product as a yellow oil (5.17 g, 78%).

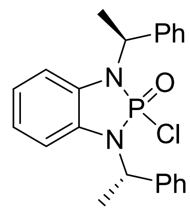
Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 1645, 1585, 1435, 1370, 762; δ_H (400 MHz, $CDCl_3$) 1.62 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 4.64 (1 H, q, *J* 6.4 Hz, C*H*), 7.22-7.27 (2 H, m, Ar-*H*), 7.28-7.36 (2 H, m, Ar-*H*), 7.42-7.45 (2H, m, Ar-*H*) 7.71 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 8.09 (1 H, d, *J* 7.2 Hz, Ar-*H*), 8.46 (1 H, s, N=C*H*), 8.61-8.63 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.36 (*C*H$_3$), 69.57 (*C*H), 121.45 (Ar-*C*H), 125.72 (Ar-*C*H), 126.68 (Ar-*C*H), 126.88 (2 Ar-*C*H), 128.47 (Ar-*C*H), 136.48 (2 Ar-*C*H), 144.53 (Ar-*C*), 149.31 (Ar-*C*H), 154.71 (Ar-*C*), 137.11 (N=*C*); *m/z* (EI) 210 (27) 195 (32), 194 (100), 103 (46). HRMS (ES) calcd for [$C_{14}H_{15}N_2$] 210.1157, found [M^+H^+] 210.1154. $[\alpha]_D^{18}$ +56.33 [c = 0.49, $CHCl_3$]

Attempted synthesis of imidazolium salt[175]



Silver triflate (4.4 g, 17.0 mmol) was suspended in dichloromethane (40 mL) and chloromethyl pivalate (2.6 g, 17.0 mmol) added. The resulting suspension was left stirring for 45 mins before being filtered through Celite. The filtrate was added to a flask containing (*S*)-1-phenyl-((pyridin-2-yl)methylene)ethanamine 14, and the solution left in the dark stirring for 24 h. Methanol (20 mL) was added and the solvents removed under reduced pressure to yield a brown oil.

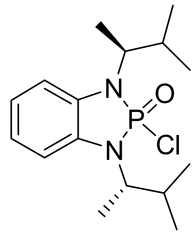
Synthesis of phosphoryl chloride 16



Bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** (0.3 g, 0.8 mmol) was dissolved in pyridine (1.1 mL) and phosphorous oxychloride (0.3 g, 1.6 mmol) added dropwise at room temperature with rapid stirring, and the solution left to stir overnight. Water (1 mL) was then added dropwise and the solution left stirring for one hour. The solution was then dissolved in CH_2Cl_2 and the residual pyridine extracted using 1M HCl. The combined organic phases were dried using Na_2SO_4 and the solvent removed under vacuum to yield the product as a white crystalline solid (0.22 g, 67%).

υ_{max} (thin film)/cm^{-1} 1599, 1484, 1380, 1265, 909, 737; δ_H (400 MHz, $CDCl_3$) 2.04 (6 H, dd, *J* 7.2 Hz & 8.8 Hz, C*H*$_3$), 5.18-5.20 (1 H, m, C*H*), 5.31-5.32 (1 H, m, C*H*), 6.63-6.66 (2 H, m, Ar-*H*), 6.45-6.49 (2 H, m, Ar-*H*), 7.28-7.34 (2 H, m, Ar-*H*), 7.37-7.43 (4 H, m, Ar-*H*), 7.49-7.54 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 18.97 (*C*H$_3$), 20.02 (*C*H$_3$), 53.14 (*C*H), 55.67 (*C*H), 110.14 (2 Ar-*C*H), 120.36 (2 Ar-*C*), 126.32 (4 Ar-*C*H), 126.81 (4 Ar-*C*H), 127.68 (2 Ar-*C*), 128.76 (4 Ar-*C*H); δ_P (162 MHz, $CDCl_3$) 19.81 (s, 100%); *m/z* (EI) 396 (47) 292 (41), 188 (55), 187 (28), 105 (100), 103 (23), 77 (30) 57 (24); HRMS (ES) calcd for [$C_{22}H_{23}ON_2{}^{35}ClP$] 397.1231, found [$M^+H^+$] 397.1227. $[\alpha]_D^{18}$ +98.3 [c = 0.46, $CHCl_3$]

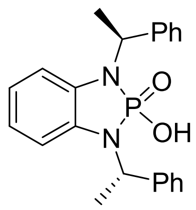
Synthesis of phosphoryl chloride 17



Bis-((*S*)-3-methylbutan-2-yl)benzene-1,2-diamine **9** (0.20 g, 0.9 mmol) was dissolved in pyridine (1.1 mL) and phosphorous oxychloride (0.28 g, 1.8 mmol) added dropwise with rapid stirring. The solution was then left to stir overnight. Water (1 mL) was then added dropwise and the solution left stirring for one hour. The solution was dissolved in CH_2Cl_2 and the residual pyridine extracted using 1M HCl. The combined organic phases were dried using Na_2SO_4 and the solvent removed under vacuum to yield the product as an off-white crystalline solid (0.19 g, 65%), (only partial data available)

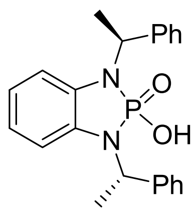
υ_{max} (thin film)/cm^{-1} 1598, 1454, 1379, 1264, 911, 738; δ_H (400 MHz, $CDCl_3$) 0.62 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 1.08 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 1.43-1.49 (12 H, m, 4 $^{i-}$Pr C*H*$_3$), 2.34-2.36 (2 H, m, 2C*H*), 7.08-7.10 (2 H, m, 2C*H*), 7.19-7.32 (4 H, m, Ar-*H*); δ_P 21.46 (s, 65%); $[\alpha]_D^{18}$ +22.22 [c = 0.63, $CHCl_3$]

Attempted synthesis of phosphoric acid



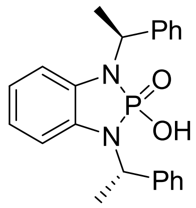
Phosphoryl chloride **16** (0.1 g, 0.25 mmol) was dissolved in THF (5 mL) and 1 M NaOH solution (5 mL) added, the solution was allowed to stir at reflux for 18 h, before removal of the solvent under reduced pressure. The residue was dissolved in dichloromethane, neutralised with 1 M aq. HCl and washed with brine. Solvents were removed under reduced pressure, to give the recovered starting material (64%)

Attempted synthesis of phosphoric acid



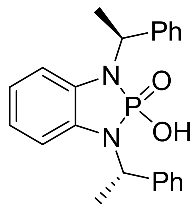
Phosphoryl chloride **16** (0.1 g, 0.25 mmol) was dissolved in acetone:water (2:1, 30 mL) the solution was heated to reflux for 4 h before the solvent removed under reduced pressure, starting material was obtained (98%)

Attempted synthesis of phosphoric acid



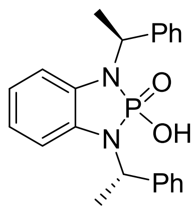
Phosphoryl chloride **16** (0.1 g, 0.25 mmol) was dissolved in THF:water (2:1, 30 mL) the solution was heated to reflux for 4 h before the solvent removed under reduced pressure, starting material obtained (79%)

Attempted synthesis of phosphoric acid



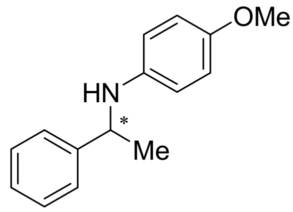
Phosphoryl chloride **16** (0.1 g, 0.25 mmol) was dissolved in THF:water (2:1, 30 mL) and NaOH pellets (1 g) added. The solution was heated to reflux for 4 h before the solvent removed under reduced pressure. The resulting residue was dissolved in dichloromethane, the solution neutralised with 1 M aq. HCl and washed with brine (15 mL). The solvent was removed under reduced pressure to yield the starting material obtained (89%)

Attempted synthesis of phosphoric acid



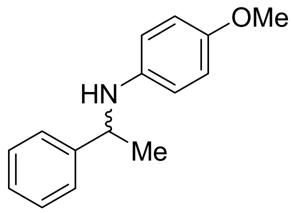
Bis-((*S*)-1-phenylethyl)benzene-1,2-diamine **1** (0.1 g, 0.32 mmol) was dissolved in pyridine (1.1 mL) and phosphorous oxychloride (0.1 g, 0.64 mmol) added dropwise at room temperature with rapid stirring and the solution left stirring overnight. Water (1 mL) was then added dropwise and the solution left stirring for one hour. The solution was then dissolved in CH_2Cl_2 and the residual pyridine extracted using $CuSO_4$. The combined organic phases were dried using $MgSO_4$ and the solvent removed under vacuum to yield phosphoryl chloride **16**.

Synthesis of 4-methoxy-1-phenylethylbenzenamine 18[70]



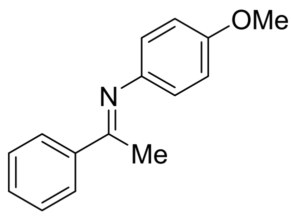
p-Anisidine (0.3 g, 2.43 mmol), phosphoryl chloride **16** (0.04 g, 0.1 mmol) and Hantzch ester (0.3 g, 0.97 mmol) were dissolved in toluene (10 mL) and 5Å molecular sieves (1.0 g) added. The reaction was set stirring under nitrogen and acetophenone (0.3 g, 2.43 mmol) added dropwise. The reaction mixture was heated to 50 °C and monitored by TLC. After 96 h, the reaction mixture was filtered through a plug of silica and eluted with diethyl ether to remove the molecular sieves and unreacted Hantzsch ester. The solvents were removed under vacuum and the crude material purified by column chromatography (silica, light petroleum:ethyl acetate 99:1→10:1) to yield the desired product as an orange oil (0.27 g, 48%). Enantiomeric excess was determined using HPLC with a chiral reverse phase column, sample was run at 0.5ml/min in a 99:1 solution of hexane:isopropyl alcohol. Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2980, 1680, 1562, 1508, 1452, 1301, 989, 762; δ_H (400 MHz, $CDCl_3$) 1.51 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 3.69 (3 H, s, OC*H*$_3$), 1.56 (1 H, s, N*H*), 4.42 (1 H, q, *J* 7.8 Hz, C*H*), 6.47-6.49 (2 H, m, Ar-*H*), 6.69-6.71 (2 H, m, Ar-*H*), 7.23-7.30 (5 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.15 (*C*H$_3$), 54.27 (*C*H), 55.47 (O *C*H$_3$), 114.54 (2 Ar-*C*H), 114.72 (Ar-*C*H), 125.85 (2 Ar-*C*H), 126.83 (2 Ar-*C*H), 128.62 (2 Ar-*C*H), 139.19 (Ar-*C*), 143.55 (Ar-*C*), 149.19 (Ar-*C*); $[\alpha]_D^{18}$ +0.17 [c = 0.56, $CHCl_3$]

Synthesis of racemic 4-methoxy-(1-phenylethyl)benzenamine 18a[70]



(E)-4-Methoxy-(1-phenylethylidene)benzenamine **19** (0.2 g, 0.81 mmol) was dissolved in ethanol (20 mL) and sodium borohydride (0.05 g, 1.22 mmol) added at room temperature. The reaction was allowed to stir for 2 h at room temperature before the reaction was quenched with water, extracted with ether (3 x 30 mL) and the combined organic layers dried over $MgSO_4$. The solvent was removed under reduced pressure to yield the desired product as an orange oil (0.16 g, 89%). Enantiomeric excess was determined using HPLC with a chiral reverse phase column, sample was run at 0.5ml/min in a 99:1 solution of hexane:isopropyl alcohol.

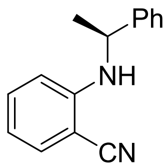
Synthesis of (*E*)-4-methoxy-(1-phenylethylidene)benzenamine 19[176]



Acetophenone (0.1 g, 0.81 mmol) and *p*-anisidine (0.1 g, 0.81 mmol) were dissolved in toluene (25 mL) and Amberlyst® 15 (0.5 g) added. The reaction was equipped with a Dean-Stark trap and heated under reflux for 4 h. Formation of the imine was followed by IR and after 4 h the solution was filtered through Celite and concentrated by vacuum. The IR indicated that the imine had been formed and the product was taken on to the next step without purification.

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 1684, 1598, 1448, 1266, 954, 759; δ_H (400 MHz, $CDCl_3$) 2.25 (3 H, s, CH_3), 3.82 (3 H, s, OCH_3), 6.74-6.90 (2 H, m, Ar-H), 6.92-6.98 (2 H, d, J 6.8 Hz, Ar-H), 7.48-7.57 (5 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 26.66 (CH$_3$), 55.49 (OCH$_3$), 114.79 (2 Ar-CH), 120.77 (2 Ar-CH), 128.36 (4 Ar-CH), 133.14 (Ar-CH), 137.11 (Ar-C), 145.51 (Ar-C), 155.92 (Ar-C), 198.25 (N=C)

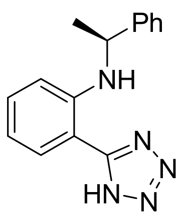
2-((*S*)-1-phenylethylamino)benzonitrile 21[177]



Compound prepared using the general Buchwald-Hartwig conditions, using 2-bromobenzonitrile as the arylbromide.

Waxy yellow solid (0.35 g, 82%). Known compound, data is consistent with literature data.υ_{max} (thin film)/cm^{-1} 3425, 2924, 2222, 1485, 756; δ_H (400 MHz, $CDCl_3$) 1.59 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 4.53-4.59 (1 H, m, C*H*), 4.90 (1 H, s, N*H*), 6.42 (1 H, d, *J* 8.8 Hz, Ar-*H*), 6.62 (1 H, t, *J* 7.6 Hz, Ar-*H*), 7.18-7.20 (1 H, m, Ar-*H*), 7.24-7.26 (1 H, m, Ar-*H*), 7.28-7.33 (4 H, m, Ar-*H*), 7.37-7.39 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.92 (*C*H$_3$), 53.28 (*C*H), 95.90 (Ar-*C*), 112.00 (Ar-*C*H), 116.71 (Ar-*C*H), 117.95 (Ar-*C*), 125.62 (2 Ar-*C*H), 127.34 (Ar-*C*H), 128.90 (2 Ar-*C*H), 132.63 (Ar-*C*H), 134.06 (Ar-*C*H), 143.71 (Ar-*C*), 149.27 (*C*=N); m.p. 47.2 °C *m/z* (EI) 223 (64), 222 (75), 221 (37), 207 (39), 206 (29), 145 (25), 135 (100), 69 (27), 57 (35), 55 (30). HRMS (ES) calcd for [$C_{15}H_{14}N_2$] 222.1157, found [M^+] 222.1159. $[\alpha]_D^{20}$ +58.8 [c = 0.81, $CHCl_3$]

Synthesis of ((*S*)-1-phenylethyl)-2-(1H-tetrazol-5-yl)benzenamine 20

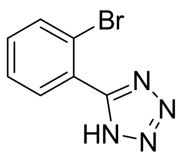


2-((S)-1-Phenylethylamino)benzonitrile **21** (0.4 g, 1.60 mmol) was dissolved in DMF (10 mL) and to the resulting solution sodium azide (0.1 g, 1.67 mmol) and ammonium chloride (0.09 g, 1.76 mmol) added with stirring. The resulting solution was fitted with a reflux condenser and the reaction heated to reflux for 6 h. After 6 h more sodium azide was added (0.1 g) and the reaction left stirring for 48 h at reflux. After this time the reaction was allowed to cool to ambient temperature before being acidified to pH 2 with 1M aq.

HCl and extracted with chloroform (3 x 25 mL). The combined organic layers were washed with saturated aqueous lithium chloride (50 mL) and dried over $MgSO_4$ before being filtered and the solvent removed under reduced pressure to yield the crude material as an off white solid. The crude material was purified by column chromatography (silica, 10:1 light petroleum:ethyl acetate) to give the desired product as a white solid (0.22 g, 47%).

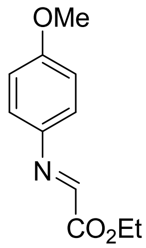
υ_{max} (thin film)/cm^{-1} 3200, 1721, 1613, 1590, 1155; δ_H (400 MHz, DMSO-d$_6$) 1.56 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 4.77 (1 H, q, *J* 6.4 Hz, C*H*), 6.68 (1 H, d, *J* 8.0 Hz, Ar-*H*), 6.72 (1 H, t, *J* 8.0 Hz, Ar-*H*), 7.21 (2 H, m, Ar-*H*), 7.31 (2 H, m, Ar-*H*), 7.36 (2 H, m, Ar-*H*), 7.81 (1 H, d, *J* 7.6 Hz, Ar-*H*), 8.16 (1 H, bs, N*H*) δ_C (100 MHz, DMSO-d$_6$) 24.81 (*C*H$_3$), 51.83 (*C*H), 105.20 (Ar-*C*), 105.44 (Ar-*C*), 112.76 (Ar-*C*H), 115.53 (Ar-*C*H), 125.67 (2 Ar-*C*H), 126.79 (Ar-*C*H), 128.31 (Ar-*C*H), 128.58 (2 Ar-*C*H), 132.10 (Ar-*C*H), 144.95 (Ar-*C*), 145.65 (*C*=N); m.p. 165.7 °C; *m/z* (EI) 266 (58), 265 (70), 250 (27), 136 (25), 105 (100). HRMS (ES) calcd for [$C_{15}H_{15}N_5$] 265.1327, found [M^+] 265.1324. $[\alpha]_D^{20}$ +200.0 [c = 0.51, $CHCl_3$]

Attempted synthesis of 5-(2-bromophenyl)-tetrazole[178]



2-Bromobenzonitrile (0.3 g, 1.4 mmol), was dissolved in DMF (10 mL) and to the resulting solution sodium azide (0.1 g, 1.4 mmol) and ammonium chloride (0.1 g, 1.5 mmol) added with stirring. The resulting solution was fitted with a reflux condenser and the reaction heated to reflux for 18 h. After this time the reaction was allowed to cool to ambient temperature before being acidified to pH 2 with 1M aq. HCl and extracted with chloroform (3 x 25 mL). The combined organic layers were washed with saturated aqueous lithium chloride (50 mL) and dried over $MgSO_4$ before being filtered and the solvent removed under reduced pressure to yield the starting material (75%).

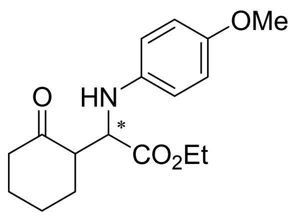
Synthesis of (*E*)-ethyl 2-(4-methoxyphenylimino)acetate 22[179]



p-Anisidine (1.2 g, 9.80 mmol) and ethyl glyoxylate (1.0 g, 9.80 mmol) were dissolved in dry toluene (10 mL) and 5Å molecular sieves (1g) added, the reaction was then allowed to stir under nitrogen for 4 h. After this time the reaction was heated to 80 °C for 24 h before being allowed to cool, filtered through Celite and the solvent removed under reduced pressure. No further purification was required and the desired product was obtained as a yellow oil (2.0 g, 99%).

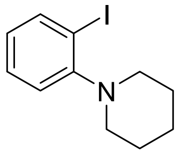
Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1}) 1782, 1643,1589, 1265, 740; δ_H (400 MHz, $CDCl_3$) 1.38 (3 H, t, *J* 7.2 Hz, CH_2-CH_3), 3.84 (3 H, s, OCH_3), 4.41 (2 H, q, *J* 7.2 Hz, CH_2-CH_3), 6.91-6.92 (2 H, m, Ar-*H*), 7.35-7.39 (2 H, m, Ar-*H*), 7.94 (1 H, s, N=C*H*); δ_C (100 MHz, $CDCl_3$) 14.25 (CH_2-*C*H_3), 55.53 (O*C*H_3), 61.95 (*C*H_2-CH_3), 114.54 (2 Ar-*C*H), 123.65 (2 Ar-*C*H), 141.39 (Ar-*C*), 148.03 (N=*C*H), 160.57 (Ar-*C*), 163.65 (*C*=O); *m/z* (FAB$^+$) 208 (76), 134 (100), 123 (25). HRMS (ES) calcd for $[C_{11}H_{14}O_3N]^+$ 208.0973, found [M^+H^+] 208.0986.

Attempted synthesis of ethyl 2-(4-methoxyphenylamino)-2-(-2-oxocyclohexyl)acetate[150]



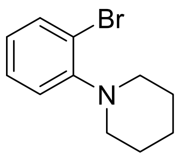
(*E*)-Ethyl-2-(4-methoxyphenylimino)acetate **23** (0.5 g, 2.4 mmol) was dissolved in dichloromethane and cyclohexanone (0.2 g, 2.4 mmol) added. To the resulting solution ((*S*)-1-phenylethyl)-2-(1H-tetrazol-5-yl)benzenamine **20** (0.03 g, 0.1 mmol) was added and the solution stirred at room temperature for 24 h. The reaction was then quenched with sat. ammonium chloride (10 mL) and extracted with ethyl acetate (2 x 25 mL). The combined organic phases were dried with $MgSO_4$ and the solvent removed under reduced pressure.

Attempted synthesis of 1-(2-iodophenyl)piperidine



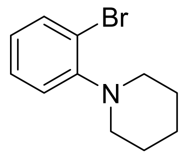
1,2-diiodobenzene (0.2 g, 0.5 mmol), piperidine (0.1 g, 0.8 mmol), caesium carbonate (0.3 g, 1.0 mmol), xantphos (0.03 g, 0.06 mmol), copper (I) bromide (0.007 g, 0.05 mmol) were placed into a round bottomed flask and DMSO (0.5 mL) added. The solution was heated to 55 °C and left to stir for 18 h. After the reaction had cooled to room temperature ethyl acetate (3 mL) and water (3 mL) were added and the organic phase separated. The aqueous phase was further extracted with ethyl acetate (4 x 5 mL), before the organic phases were combined and dried over $MgSO_4$.

Attempted synthesis of 1-(2-bromophenyl)piperidine



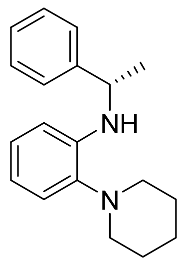
1,2-Dibromobenzene (0.2 g, 0.5 mmol), piperidine (0.1 g, 0.8 mmol), caesium carbonate (0.3 g, 1.0 mmol), xantphos (0.03 g, 0.06 mmol), copper (I) bromide (0.007 g, 0.05 mmol) were placed into a round bottomed flask and DMSO (0.5 mL) added. The solution was heated to 55 °C and left to stir for 18 h. After the reaction had cooled to room temperature ethyl acetate (3 mL) and water (3 mL) were added and the organic phase separated. The aqueous phase was further extracted with ethyl acetate (4 x 5 mL), before the organic phases were combined and dried over $MgSO_4$.

Attempted synthesis of 1-(2-bromophenyl)piperidine



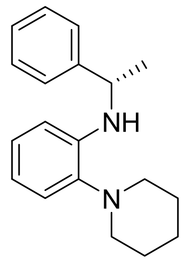
Potassium carbonate (0.1 g, 0.5 mmol), copper (I) chloride (0.005 g, 0.05 mmol) and DMSO (5 mL) were placed into a round bottomed flask and the solution flushed with nitrogen for 5 mins. To this solution 1,2-dibromobenzene (0.1 g, 0.5 mmol), piperidine (0.05 g, 0.6 mmol) and 2-acetylcyclohexanone (0.02 g, 0.1 mmol) were added. The reaction was heated to 130 °C for 20 h before being allowed to cool to room temperature. Dichloromethane (15 mL) and sat. aq. $NaHCO_3$ (15 mL) were added and the organic phase separated. The organic phase was washed with $NaHCO_3$ (3 x 15 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure.

Attempted synthesis of (*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine



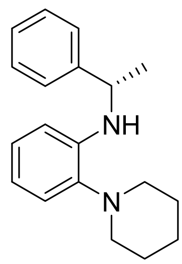
Potassium carbonate (0.1 g, 0.5 mmol), copper (I) chloride (0.005 g, 0.05 mmol) and DMSO (5 mL) were placed into a round bottomed flask and the solution flushed with nitrogen for 5 mins. To this solution 2-Bromo-((*S*)-1-phenylethyl)benzenamine 2 (0.1 g, 0.5 mmol), piperidine (0.05 g, 0.6 mmol) and 2-acetylcyclohexanone (0.02 g, 0.1 mmol) were added. The reaction was heated 130 °C for 20 h before being allowed to cool to room temperature. Dichloromethane (15 mL) and sat. aq. $NaHCO_3$ (15 mL) were added and the organic phase separated. The organic phase was washed with $NaHCO_3$ (3 x 15 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure to yield the starting material (87%).

Attempted synthesis of (*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine



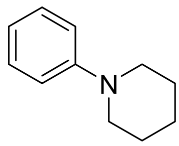
To a microwave tube potassium carbonate (0.1 g, 0.5 mmol), copper (I) chloride (0.005 g, 0.05 mmol), 2-Bromo-((*S*)-1-phenylethyl)benzenamine **2** (0.1 g, 0.5 mmol), piperidine (0.05 g, 0.6 mmol) and 2-acetylcyclohexanone (0.02 g, 0.1 mmol) and DMSO (5 mL) were added. The reaction was heated in the microwave at 130 °C for 10 mins before being diluted with dichloromethane (15 mL) and sat. aq. $NaHCO_3$ (15 mL) added. The organic phase was separated and washed with $NaHCO_3$ (3 x 15 mL), dried over $MgSO_4$ and the solvent removed under reduced pressure.

Attempted synthesis of (*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine



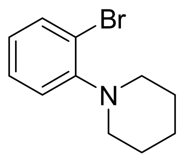
2-Bromo-((*S*)-1-phenylethyl)benzenamine **2** (0.2 g, 0.6 mmol), piperidine (0.1 g, 1.4 mmol), caesium carbonate (0.3 g, 1.0 mmol), xantphos (0.03 g, 0.06 mmol), copper (I) bromide (0.007 g, 0.05 mmol) were all placed into a microwave tube and DMSO (0.5 mL) added. The solution was heated in the microwave to 55 °C for 10 mins, and then ethyl acetate (3 mL) and water (3 mL) were added and the organic phase separated. The aqueous phase was further extracted with ethyl acetate (4 x 5 mL), before the organic phases were combined and dried over $MgSO_4$.

1-phenylpiperidine 23[180]



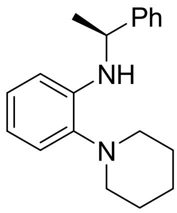
Yellow oil (0.30 g, 84%) Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2931, 1594, 1232, 918, 756; δ_H (400 MHz, $CDCl_3$) 1.55-1.59 (2 H, m, C*H*$_2$), 1.68-1.73 (4 H, m, 2 C*H*$_2$) 3.14 (4 H, t, *J* 5.6 Hz, 2 C*H*$_2$), 6.79-6.84 (1 H, m, Ar-*H*), 6.92-6.96 (2 H, m, Ar-*H*), 7.22-7.27 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.34 (*C*H$_2$), 26.06 (2 *C*H$_2$), 50.73 (2 *C*H$_2$), 116.58 (2 Ar-*C*H), 119.23 (Ar-*C*H), 129.02 (2 Ar-*C*H), 152.28 (Ar-*C*); *m/z* (FAB^+) 161 (100), 160 (55), 95 (35), 83 (40), 69 (57), 55 (78). HRMS (ES) calcd for [$C_{11}H_{15}N$] 161.1205, found [M+] 161.1209.

1-(2-bromophenyl)piperidine 24[181]



Yellow oil (0.18 g, 34%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3063, 1581, 1226, 756, 655; δ_H (400 MHz, $CDCl_3$) 1.50-1.60 (2 H, m, C*H*$_2$), 1.71-1.77 (4 H, m, 2 C*H*$_2$), 2.94-2.96 (4 H, m, 2 C*H*$_2$), 6.86 (1 H, dt, *J* 1.6 Hz & 7.2 Hz, Ar-*H*), 7.04 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*), 7.22-7.26 (1 H, m, Ar-*H*), 7.54 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.24 (*C*H$_2$), 26.26 (2 *C*H$_2$), 53.35 (2 *C*H$_2$), 120.15 (Ar-*C*), 120.97 (Ar-*C*H), 123.80 (Ar-*C*H), 128.12 (Ar-*C*H), 133.71 (Ar-*C*H), 151.98 (Ar-*C*); *m/z* (FAB^+) 241 (84), 240 (100), 239 (87), 160 (30), 91 (36), 81 (38), 79 (25), 69 (47). HRMS (ES) calcd for [$C_{11}H_{14}N^{79}Br$] 240.0305, found [M^+] 240.0309.

((*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine 25



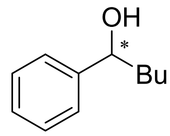
Waxy yellow solid (0.31 g, 47%) υ_{max} (thin film)/cm^{-1} 3363, 3060, 2931, 1597, 1505, 1240, 741; δ_H (400 MHz, $CDCl_3$) 1.45-1.49 (5 H, m, C*H*$_3$ & C*H*$_2$), 1.66 (4 H, bs, 2 C*H*$_2$), 2.90 (4 H, bs, 2 C*H*$_2$), 4.33-4.35 (1 H, m, C*H*) 5.08 (1 H, bs, N*H*), 6.25 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*), 6.54 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 6.75 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 6.90 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*), 7.12-7.14 (1 H, m, Ar-*H*), 7.23-7.30 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.43 (*C*H$_2$), 25.42 (*C*H$_3$) 27.10 (4 *C*H$_2$), 53.55 (*C*H), 111.05 (Ar-*C*H), 116.49 (Ar-*C*H), 119.31 (Ar-*C*H), 124.45 (Ar-*C*H), 125.80 (2 Ar-*C*H) 126.70 (Ar-*C*H), 128.57 (2 Ar-*C*H), 140.10 (Ar-C), 142.24 (Ar-*C*), 145.86 (Ar-*C*); *m/z* (FAB$^+$) 105 (22), 173 (28), 175 (60), 280 (100), 281 (34). HRMS (ES) calcd for [$C_{19}H_{24}N_2$] 280.1940, found [M$^+$] 280.1941; $[\alpha]_D^{18}$ +86.83 [c = 0.41, $CHCl_3$].

Synthesis of dibutylmagnesium solution and concentration calculation[155]

$$BuMgCl \rightarrow BuMgBu + MgCl_2$$

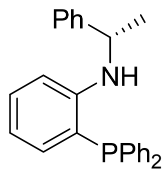
1,4-Dioxane (0.72 mL) was added slowly to a solution of 2 M butylmagnesium chloride (4 mL) and the resultant solution allowed to stir for 24 h. The suspension was then centrifuged and the supernatant containing the dialkylmagnesium transferred to a dry microwave tube. The concentration was determined by titration; the dialkylmagnesium was added dropwise to a stirred solution of accurately weighed salicylaldehyde phenylhydrazone (~ 0.5 mmol) in THF (5 mL) until the end point can be seen by a change from yellow to bright orange in colour. The exact amount of dialkylmagnesium solution was recorded and the concentration calculated to be 0.38 M using the following equation M = mmol of indicator / (2 x volume of R_2Mg in mL).

Attempted synthesis of 1-phenylpentan-1-ol



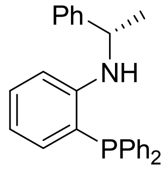
To a pre-cooled solution (- 78 °C) of (*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine 25 (0.2 g, 0.56 mmol) in diethyl ether (12 mL) the prepared solution of dibutylmagnesium (1.4 mL, 0.54 mmol) was added. The resulting solution was allowed to stir at room temperature for 30 mins before being cooled to - 78 °C and benzaldehyde (0.03 g, 0.25 mmol) added. The reaction was allowed to warm slowly to room temperature and left to stir for 16 h. The reaction was then quenched with sat. aq. NH_4Cl (5 mL) and the layers separated. The aqueous phase was extracted further with diethyl ether (3 x 10 mL) and the combined organic phase washed with 1 M HCl to removed the (*S*)-1-phenylethyl)-2-(piperidin-1-yl)benzenamine. The organic phase was then dried over Na_2SO_4 and the solvent removed under reduced pressure.

Attempted synthesis of ((*S*)-1-phenylethyl)-2-(diphenylphosphino)benzenamine



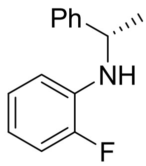
2-Fluoro-((*S*)-1-phenylethyl)benzenamine **27** (0.1 g, 0.47 mmol) was dissolved in THF (10 mL) and potassium diphenylphosphide (0.2 g, 0.94 mmol) added dropwise. The reaction was heated at reflux for 4 days. The solution was diluted with diethyl ether and filtered through Celite and the solvent removed under reduced pressure. Starting material (95%) was obtained.

Attempted synthesis of ((*S*)-1-phenylethyl)-2-(diphenylphosphino)benzenamine



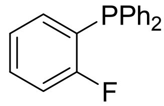
In a microwave tube 2-fluoro-((*S*)-1-phenylethyl)benzenamine **27** (0.4 g, 1.9 mmol) was dissolved in 1,4-dioxane (4 mL) and potassium diphenylphosphide (0.83 g, 3.7 mmol) added dropwise. The resulting orange solution was place in the microwave at 120 °C for 30 minutes. The reaction was quenched with water (5 mL) and the organics extracted with dichloromethane (2 x 15 mL) and filtered through a plug of silica. Solvents were removed under reduced pressure to yield a yellow oil, which was a inseperable mixture.

2-Fluoro-((*S*)-1-phenylethyl)benzenamine 27[182]



Clear oil (0.94 g, 99%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3255, 1566, 1265, 702; δ_H (400 MHz, $CDCl_3$) 1.53 (3 H, d, *J* 6.4 Hz, C*H*$_3$) 4.28 (1 H, s, N*H*), 4.47-4.49 (1 H, m, C*H*), 6.41 (1 H, dt, *J* 1.6 Hz & 9.2 Hz, Ar-*H*), 6.52-6.57 (1 H, m, Ar-*H*), 6.78-6.83 (1 H, m, Ar-*H*), 6.92-6.97 (1 H, m, Ar-*H*), 7.19-7.24 (1 H, m, Ar-*H*), 7.29-7.36 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.04 (*C*H$_3$), 53.29 (*C*H), 113.15 (Ar-*C*H), 113.18 (Ar-*C*H), 114.11 (Ar-*C*H), 114.30 (Ar-*C*H), 125.74 (2 Ar-*C*H), 127.01 (Ar-*C*H), 128.31 (2 Ar-*C*H), 144.78 (Ar-*C*), 150.18 (Ar-*C*), 152.54 (Ar-*C*); δ_F (376 MHz, $CDCl_3$) 25.58-25.51 (m, 100%) *m/z* (FAB$^+$) 215 (100), 200 (45), 138 (25), 111 (28), 105 (92). HRMS (ES) calcd for [$C_{14}H_{14}NF$] 215.1110, found [M^+] 215.1110; $[\alpha]_D^{18}$ +93.5 [c = 0.86, $CHCl_3$]

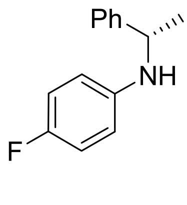
Synthesis of (2-fluorophenyl)diphenylphosphine 28[183]



1-Bromo-2-fluorobenzene (0.4 g, 2.2 mmol) was dissolved in 1,4-dioxane (2 mL) under nitrogen and potassium diphenylphosphide (4.9 g, 22.0 mmol) added dropwise at room temperature over 10 mins. The reaction was then heated to reflux for 5 days. The reaction was allowed to cool to ambient temperature before being quenched with water (15 mL) and extracted with dichloromethane (3 x 15 mL) and the combined organics dried over $MgSO_4$, before being filtered through a plug of silica. The crude material was purified using column chromatography (silica, 99:1 light petroleum:ethyl acetate) to yield the (2-fluorophenyl)diphenylphosphine as a white solid (0.41 g, 67%)

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3055, 1436, 1192, 722; δ_H (400 MHz, $CDCl_3$), 6.80-6.83 (1 H, m, Ar-*H*), 7.03-7.11 (2 H, m, Ar-*H*), 7.29-7.37 (11 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 126.88 (Ar-*C*H), 126.89 (Ar-*C*), 128.52 (4 Ar-*C*H), 128.58 (Ar-*C*H), 131.09 (Ar-*C*), 131.96 (Ar-*C*H), 132.06 (4 Ar-*C*H), 132.99 (Ar-*C*), 133.42 (Ar-*C*H), 133.50 (Ar-*C*), 134.86 (Ar-*C*H), 136.00 (Ar-*C*H); δ_P (162 MHz, $CDCl_3$) -18.89 (P-1, d, ^3J ^{31}P-^{19}F 53.4 Hz, 89%); δ_F (376 MHz, $CDCl_3$) 58.59 (F-1, d, ^3J ^{19}F-^{31}P 53.4 Hz), 58.49-58.55 (F-1, m, $^{3,4,5,6}J$ ^{19}F-^{1}H), 58.63-58.69 (F-1, m, ^{1-4}J ^{19}F-^{1}H); m.p. 45.8 °C; *m/z* (FAB$^+$) 281 (80), 280 (100), 221 (35), 207 (32), 183 (50), 147 (40), 73 (43). HRMS (ES) calcd for [$C_{18}H_{14}FP$] 280.0814, found [M$^+$] 280.0817.

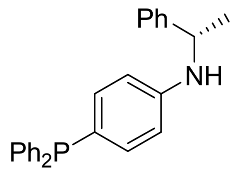
Synthesis of 4-fluoro-((*S*)-1-phenylethyl)benzenamine 29[184]



Clear oil (0.39 g, 83%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3025, 2970, 1589, 1280, 702; δ_H (400 MHz, $CDCl_3$) 1.49 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 3.91 (1 H, bs, N*H*), 4.40 (1 H, q, *J* 6.8 Hz, C*H*), 6.39-6.44 (2 H, m, Ar-*H*), 6.75-6.81 (2 H, m, Ar-*H*), 7.20-7.24 (1 H, m, Ar-*H*), 7.29-7.35 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.08 (*C*H$_3$), 54.05 (*C*H), 114.03 (Ar-*C*H), 114.10 (Ar-*C*H), 115.38 (Ar-*C*H), 115.60 (Ar-

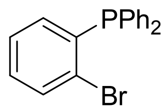
*C*H), 125.80 (2 Ar-*C*H), 126.95 (Ar-*C*H), 128.56 (2 Ar-*C*H), 145.00 (Ar-*C*), 154.47 (Ar-*C*), 156.80 (Ar-*C*); 33.83-33.91 (F-1, m, ^{1-4}J ^{19}F-^{1}H 25.97 Hz); *m/z* (FAB^{+}) 215 (100), 214 (29), 200 (56), 105 (86), 95 (28), 83 (28), 81 (27), 69 (47), 57 (56), 55 (74). HRMS (ES) calcd for [$C_{14}H_{14}NF$] 215.1110, found [M^{+}] 215.1112. $[\alpha]_D$ +100.51 [c = 0.78 in $CHCl_3$]

Attempted synthesis of ((*S*)-1-phenylethyl)-4-(diphenylphosphino)benzenamine



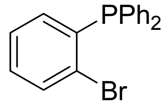
4-Fluoro-((*S*)-1-phenylethyl)benzenamine **29** (0.1 g, 0.4 mmol) was dissolved in 1,4-dioxane and potassium diphenylphosphide (0.6 g, 2.6 mmol) added dropwise. The resulting solution was heated under reflux for 16 h; the solvent was removed under reduced pressure, the residue quenched with water (6 mL) and extracted with dichloromethane (2 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered through a pad of silica and concentrated under reduced pressure. Starting material was obtained (85%).

Attempted synthesis of (2-bromophenyl)diphenylphosphine



1,2-Dibromobenzene (0.5 g, 2.2 mmol) was dissolved in 1,4-dioxane and potassium diphenylphosphide (1.2 g, 5.2 mmol) added dropwise. The resulting solution was heated under reflux for 48 h; the solvent was removed under reduced pressure, the residue was quenched with water (6 mL) and extracted with dichloromethane (2 x 15 mL). The combined organic phases were dried over $MgSO_4$, filtered through a pad of silica and concentrated under reduced pressure.

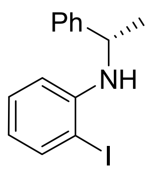
(2-bromophenyl)diphenylphosphine 30[165]



Under dry conditions 2-iodobenzene (1.0 g, 35.3 mmol), diphenylphosphine (0.7 g, 35.3 mmol), triethylamine (0.6 g, 60.0 mmol) and a catalytic amount of palladium-tetrakis(triphenylphosphine) (0.02 g, 0.18 mmol) were dissolved in toluene (10 mL) to give a clear yellow solution which upon stirring changed to orange in colour. The solution was heated to 80 °C for 16 h and resulted in the precipitation of triethylammonium iodide. The solvent was removed under reduced pressure, and the resulting residue dissolved in diethyl ether and filtered through a silica pad, which upon removal of the solvent under reduced pressure yielded a yellow solid. The yellow solid was dissolved in dichloromethane, filtered through silica and the solvent removed under reduced pressure to yield an off-white solid (1.02 g, 91%).

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3052, 1433, 1019, 746; δ_H (400 MHz, $CDCl_3$) 6.73-7.76 (1 H, m, Ar-*H*), 7.17-7.38 (12 H, m, Ar-*H*), 7.58-7.64 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 127.41 (Ar-*C*H), 128.39 (4 Ar-*C*H), 129.03 (2 Ar-*C*H), 129.73 (Ar-*C*), 130.14 (Ar-*C*H), 132.98 (Ar-*C*H), 133.93 (2 Ar-*C*H), 134.13 (2 Ar-*C*H), 134.46 (Ar-*C*H), 135.82 (Ar-*C*) 138.97 (Ar-*C*), 140.35 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) -5.06 (s, 91%) (Literature δ_P -4.4)[165]; m.p. 98.1 °C (Literature m.p. 113 °C)[185]; HRMS (ES) calcd for [$C_{18}H_{14}BrP$] 357.0089, found [M^+] 357.0028

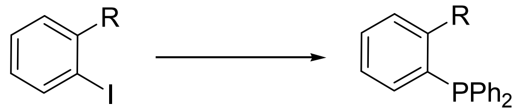
2-Iodo-((*S*)-1-phenylethyl)benzenamine 31[186]



Clear oil (0.41 g, 57%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3423, 1640, 1309, 1026, 743; δ_H (400 MHz, $CDCl_3$) 1.58 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 4.51 (1 H, q, *J* 6.8 Hz, C*H*), 4.58 (1 H, s, N*H*), 6.31 (1 H, dd, *J* 1.2 Hz & 8.0 Hz, Ar-*H*), 6.37 (1 H, dt, *J* 1.6 Hz & 7.2 Hz, Ar-*H*), 7.01 (1 H, dt, *J* 1.6 Hz & 7.2 Hz, Ar-*H*), 7.21-7.24 (1 H, m, Ar-*H*), 7.29-7.34 (4 H, m, Ar-*H*), 7.64 (1 H, dd, *J* 1.6 Hz & 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.21 (*C*H$_3$), 53.91 (*C*H), 85.48 (Ar-*C*H), 112.01 (Ar-*C*H), 118.64

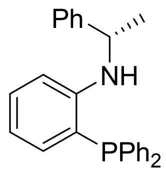
(Ar-*C*H), 125.74 (Ar-*C*H), 127.04 (2 Ar-*C*H), 128.74 (2 Ar-*C*H), 129.26 (Ar-*C*H), 138.88 (Ar-*C*), 145.45 (Ar-*C*), 146.19 (Ar-*C*); *m/z* (FAB^+) 105 (100), 246 (20), 308 (43), 322 (37), 323 (79), 324 (39); HRMS (ES) calcd for [$C_{14}H_{14}NI$] 323.0170 found [M^+] 323.0169; $[\alpha]_D^{18}$ +128.0 [c = 0.60, $CHCl_3$]

General Procedure for palladium cross-coupling reaction with dihphenylphosphine



The iodoamine compound, diphenylphosphine (1 eq.), triethylamine (1.7 eq.) and a catalytic amount of palladium-tetrakis(triphenylphosphine) (0.5 mol%) were dissolved in toluene (~10 mL) under nitrogen, to give a clear yellow solution which upon stirring changed to red in colour. The solution was heated under reflux for 16-24 h resulting in the precipitation of triethylammonium iodide. The solvent was removed under reduced pressure, and the resulting residue dissolved in dichloromethane and washed with water (3 x 10 mL), dried over $MgSO_4$ and filtered through a pad of silica and Celite, the solvent was removed under reduced pressure to yield the desired compounds.

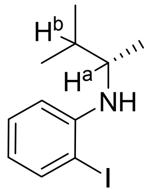
((*S*)-1-phenylethyl)-2-(diphenylphosphino)benzenamine 32[182]



Cloudy viscous oil (0.23 g, 79%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3380, 1586, 1311, 746; δ_H (400 MHz, $CDCl_3$) 1.32 (3 H, d, *J* 6.4 Hz, CH_3), 4.46 (1 H, q, *J* 6.4, C*H*), 4.98 (1 H, bs, N*H*), 6.38-6.51 (1 H, m, Ar-*H*), 6.55 (1 H, t, *J* 7.2 Hz, Ar-*H*), 6.81 (1 H, t, *J* 7.2 Hz, Ar-*H*), 7.03-7.08 (1 H, m, Ar-*H*), 7.12-7.23 (5 H, m, Ar-*H*), 7.29-7.37 (10 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.10 (CH_3), 53.46 (*C*H), 111.55 (Ar-*C*H), 117.13 (Ar-*C*H), 118.62 (Ar-*C*), 125.79 (4 Ar-*C*H), 126.81 (Ar-*C*H), 128.65 (4 Ar-*C*H), 128.88 (2 Ar-*C*H), 129.18 (Ar-*C*H), 130.63 (Ar-*C*H), 133.86 (2 Ar-*C*H), 134.12 (Ar-*C*H), 134.67 (Ar-*C*H), 135.58 (Ar-*C*), 145.18 (Ar-*C*), 149.71 (Ar-*C*), 149.87 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) -20.11 (s, 77%); HRMS (ES) calcd for

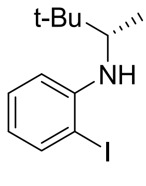
$[C_{26}H_{24}NPONa]$ 420.1441, found $[M^+]$ for $[C_{26}H_{24}NPONa]$ 420.1475; $[\alpha]_D^{20}$ +97.8 [c = 0.36, $CHCl_3$]

2-Iodo-((*S*)-3-methylbutan-2-yl)benzenamine 34



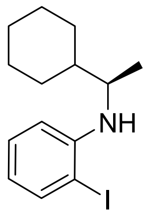
Clear oil (0.41 g, 57%) υ_{max} (thin film)/cm^{-1} 3392, 2960, 1588, 1505, 1318, 739; δ_H (400 MHz, $CDCl_3$) 0.98 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr CH_3), 0.99 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr CH_3), 1.14 (3 H, d, *J* 6.8 Hz, CH_3), 1.83-1.91 (1 H, m CH^b), 3.35-3.39 (1 H, m, CH^a), 4.10 (1 H, s, N*H*), 6.37 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 6.53 (1 H, dt, *J* 0.8 Hz & 8.0 Hz, Ar-*H*), 7.16 (1 H, dt, *J* 1.2 Hz & 7.2 Hz, Ar-*H*), 7.64 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.60 (CH_3), 17.74 ($^{i-}$Pr CH_3), 19.01 ($^{i-}$Pr CH_3), 32.24 ($^{i-}$Pr *C*H) 53.95 (*C*H), 85.91 (Ar-*C*), 111.001 (Ar-*C*H), 117.87 (Ar-*C*H), 129.06 (Ar-*C*H), 139.17 (Ar-*C*H), 146.71 (Ar-*C*); HRMS (ES) calcd for $[C_{11}H_{17}NI]^+$ 290.0405 found $[M^+H^+]$ 290.0405; $[\alpha]_D^{18}$ +53.6 [c = 0.85, $CHCl_3$]

2-Iodo-((*S*)-3,3-dimethylbutan-2-yl)benzenamine 35



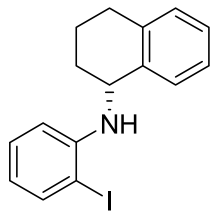
Clear oil (0.17 g, 25%) υ_{max} (thin film)/cm^{-1} 3496, 2962, 1587, 1507, 1318; δ_H (400 MHz, $CDCl_3$) 1.00 (9 H, s, 3 $^{t-}$Bu CH_3), 1.12 (3 H, d, *J* 6.4 Hz, CH_3), 3.26 (1 H, q, *J* 8.8 Hz, C*H*), 4.14 (1 H, d, *J* 9.2 Hz, N*H*), 6.38 (1 H, t, *J* 7.6 Hz, Ar-*H*), 6.56 (1 H, d, *J* 7.2 Hz, Ar-*H*), 7.15 (1 H, t, *J* 7.2 Hz, Ar-*H*), 7.63 (1 H, d, *J* 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 15.67 (CH_3), 26.50 (3 $^{t-}$Bu CH_3), 34.86 ($^{t-}$Bu *C*), 57.61 (*C*H), 86.04 (Ar-*C*), 110.68 (Ar-*C*H), 117.63 (Ar-*C*H), 128.72 (Ar-*C*H), 139.04 (Ar-*C*H), 147.04 (Ar-*C*); HRMS (ES) calcd for $[C_{12}H_{19}NI]^+$ 304.0561 found $[M^+H^+]$ 304.0561; $[\alpha]_D^{18}$ +51.0 [c = 0.51, $CHCl_3$]

((*R*)-1-cyclohexylethyl)-2-iodobenzenamine 36



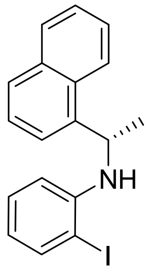
Clear oil (0.35 g, 48%) υ_{max} (thin film)/cm^{-1} 3393, 2923, 2850, 1580, 1505, 1319 739; δ_H (400 MHz, $CDCl_3$) 1.01-1.30 (5 H, m, C*H*$_2$), 1.15 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 1.44-1.52 (1 H, m, C*H*), 1.65-1.85 (5 H, m, C*H*$_2$), 3.32-3.38 (1 H, m, C*H*), 4.13 (1 H, bs, N*H*), 6.38 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 6.54 (1 H, dd, *J* 1.2 Hz & 8.4 Hz, Ar-*H*), 7.15-7.19 (1 H, m, Ar-*H*), 7.64 (1 H, dd, *J* 1.6 Hz & 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 17.33 (*C*H$_3$), 26.32 (*C*H$_2$), 26.45 (*C*H$_2$), 26.59 (*C*H$_2$), 28.51 (*C*H$_2$), 29.58 (*C*H$_2$), 42.79 (*C*H), 53.59 (*C*H), 85.86 (Ar-*C*), 110.96 (Ar-*C*H), 117.80 (Ar-*C*H), 129.32 (Ar-*C*H), 139.14 (Ar-*C*H), 146.70 (Ar-*C*); HRMS (ES) calcd for $[C_{14}H_{21}NI]^+$ 330.0710 found $[M^+H^+]$ 330.0711; $[\alpha]_D^{18}$ -46.1 [c = 0.66, $CHCl_3$]

(R)-1,2,3,4-tetrahydro-N-(2-iodophenyl)naphthalen-1-amine 37



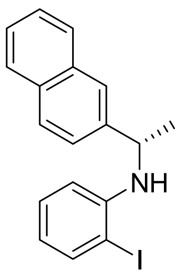
Clear oil (0.25 g, 32%) υ_{max} (thin film)/cm^{-1} 3063, 2923, 1289, 1020, 752; δ_H (400 MHz, $CDCl_3$) 1.89-2.03 (4 H, m, 2 C*H*$_2$), 2.76-2.90 (2 H, m, C*H*$_2$) 4.43 (1 H, s, N*H*), 4.66-4.67 (1 H, m, C*H*), 6.45 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 6.73 (1 H, d, *J* 7.6 Hz, Ar-*H*), 7.13-7.23 (4 H, m, Ar-*H*), 7.40 (1 H, d, *J* 6.8 Hz, Ar-*H*), 7.69 (1 H, d, *J* 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 19.63 (*C*H$_2$), 28.82 (*C*H$_2$), 29.92 (*C*H$_2$), 51.79 (*C*H), 85.70 (Ar-*C*), 110.94 (Ar-*C*H), 118.64 (Ar-*C*H), 126.24 (Ar-*C*H), 127.28 (Ar-*C*H), 128.96 (Ar-*C*H), 129.09 (Ar-*C*H), 129.42 (Ar-*C*H), 137.75 (Ar-*C*), 137.66 (Ar-*C*), 139.31 (Ar-*C*H), 146.61 (Ar-*C*); HRMS (ES) calcd for $[C_{16}H_{17}NI]$ 350.0403 found $[M^+H^+]$ 350.0404; $[\alpha]_D^{18}$ -60.7 [c = 0.27, $CHCl_3$]

2-Iodo-((*S*)-1-(naphthalen-1-yl)ethyl)benzenamine 38



Clear oil (0.26 g, 32%) υ_{max} (thin film)/cm^{-1} 3395, 1588, 1502, 1315, 777, 742; δ_H (400 MHz, $CDCl_3$) 1.73 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 4.72 (1 H, s, N*H*), 5.30-5.32 (1 H, m, C*H*), 6.15 (1 H, dd, *J* 1.2 Hz & 8.4 Hz, Ar-*H*), 6.36 (1 H, dt, *J* 1.6 Hz & 8.0 Hz, Ar-*H*), 6.89-6.93 (1 H, m, Ar-*H*), 7.40 (1 H, t, *J* 7.6 Hz, Ar-*H*), 7.52-7.60 (3 H, m, Ar-*H*), 7.65 (1 H, d, *J* 7.6 Hz, Ar-*H*), 7.75 (1 H, d, *J* 8.4 Hz, Ar-*H*), 7.91 (1 H, d, *J* 8.4 Hz, Ar-*H*), 8.15 (1 H, d, *J* 8.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 23.90 (*C*H$_3$), 50.04 (*C*H), 85.30 (Ar-*C*), 111.91 (Ar-*C*H), 118.62 (Ar-*C*H), 122.18 (Ar-*C*H), 122.34 (Ar-*C*H), 125.49 (Ar-*C*H), 125.95 (Ar-*C*H), 126.16 (Ar-*C*H), 127.57 (Ar-*C*H), 129.22 (Ar-*C*H), 129.30 (Ar-C*H*), 130.57 (Ar-*C*), 134.09 (Ar-*C*), 138.85 (Ar-C*H*), 139.20 (Ar-*C*), 145.98 (Ar-*C*); HRMS (ES) calcd for [$C_{18}H_{17}NI$] 374.0402 found [M^+H^+] 374.0403; $[\alpha]_D^{18}$ +288.0 [c = 0.10, $CHCl_3$]

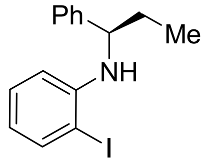
2-Iodo-((*S*)-1-(naphthalen-2-yl)ethyl)benzenamine 39



Clear oil (0.18 g, 22%) υ_{max} (thin film)/cm^{-1} 3385, 1586, 1502, 1312, 817, 742; δ_H (400 MHz, $CDCl_3$) 1.65 (3 H, d, *J* 6.0 Hz, C*H*$_3$) 4.72-4.67 (2 H, m, C*H* & N*H*), 6.34-6.38 (2 H, m, Ar-*H*), 6.94-6.99 (1 H, m, Ar-*H*), 7.41-7.48 (3 H, m, Ar-*H*), 7.64-7.66 (1 H, m, Ar-*H*), 7.77-7.83 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.18 (*C*H$_3$), 54.16 (*C*H), 85.50 (Ar-*C*), 112.06 (Ar-*C*H), 118.69 (Ar-*C*H), 124.13 (Ar-*C*H), 124.23 (Ar-*C*H), 125.60 (Ar-*C*H), 126.08 (Ar-*C*H), 127.67 (Ar-*C*H), 127.82 (Ar-*C*H), 128.62 (Ar-*C*H), 129.26 (Ar-C*H*), 132.76 (Ar-*C*), 133.53 (Ar-*C*), 138.85 (Ar-C*H*), 141.99 (Ar-*C*), 146.25 (Ar-*C*); HRMS

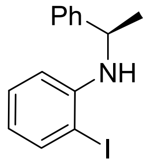
(ES) calcd for [$C_{18}H_{17}NI$] 374.0402 found [M^+H^+] 374.0400; $[\alpha]_D^{20}$ +216.6 [c = 0.24, $CHCl_3$]

2-Iodo-((*R*)-1-phenylpropyl)benzenamine 40[187]



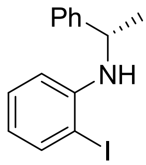
Clear oil (0.40 g, 54%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3396, 2962, 2870, 1587, 1503, 1316, 742; δ_H (400 MHz, $CDCl_3$) 1.01 (3 H, d, *J* 7.2 Hz, CH_3), 1.84-1.92 (2 H, m, CH_2), 4.27 (1 H, q, *J* 6.4 Hz, C*H*), 4.65 (1 H, bd, *J* 5.2 Hz, N*H*), 6.30 (1 H, d, *J* 8.4 Hz, Ar-*H*), 6.36 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 7.02 (1 H, dt, *J* 1.2 Hz & 8.4 Hz, Ar-*H*), 7.20-7.24 (1 H, m, Ar-*H*), 7.30-7.33 (4 H, m, Ar-*H*), 7.64 (1 H, dd, *J* 1.6 Hz & 8.0 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 10.85 (*C*H_3), 31.87 (*C*H_2) 60.05 (*C*H), 85.57 (Ar-*C*), 111.80 (Ar-*C*H), 118.45 (Ar-*C*H), 126.39 (2 Ar-*C*H), 127.00 (Ar-*C*H), 128.56 (2 Ar-*C*H), 129.22 (Ar-*C*H), 138.78 (Ar-*C*H), 143.20 (Ar-*C*), 146.33 (Ar-*C*); HRMS (ES) calcd for [$C_{15}H_{17}NI$] 338.0400 found [M^+H^+] 338.0392; $[\alpha]_D^{18}$ -122.2 [c = 0.38, $CHCl_3$]

2-Iodo-((*R*)-1-phenylethyl)benzenamine 41



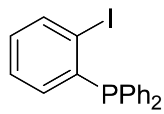
Clear oil (0.46 g, 65%) υ_{max} (thin film)/cm^{-1} 3445, 1587, 1313, 741, 699; δ_H (400 MHz, $CDCl_3$) 1.58 (3 H, d, *J* 6.8 Hz, CH_3), 4.05 (1 H, q, *J* 6.8 Hz, C*H*) 4.58 (1 H, bs, N*H*), 6.31 (1 H, d, *J* 8.0 Hz, Ar-*H*), 6.37 (1 H, t, *J* 7.6 Hz, Ar-*H*), 7.01 (1 H, t, *J* 8.4 Hz, Ar-*H*), 7.20-7.24 (1 H, m, Ar-*H*), 7.30-7.34 (4 H, m, Ar-*H*), 7.64 (1 H, dd, *J* 1.2 Hz & 7.6 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 25.17 (*C*H_3) 53.91 (*C*H), 85.46 (Ar-*C*), 112.01 (Ar-*C*H), 118.64 (Ar-*C*H), 125.72 (2 Ar-*C*H), 127.02 (Ar-*C*H), 128.72 (2 Ar-*C*H), 129.23 (Ar-*C*H), 138.85 (Ar-*C*H), 144.40 (Ar-*C*), 146.13 (Ar-*C*); HRMS (ES) calcd for [$C_{14}H_{15}NI$]$^+$ 324.0244 found [M^+H^+ 324.0237; $[\alpha]_D^{18}$ +143.6 [c = 0.49, $CHCl_3$]

Attempted synthesis of 2-Iodo-((S)-1-phenylethyl)benzenamine



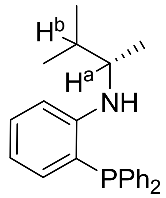
2-Bromo-((*S*)-1-phenylethyl)benzenamine **27** (0.2 g, 0.72 mmol), copper (I) iodide (0.01 g, 0.05 mmol), sodium iodide (0.2 g, 1.4 mmol) and 1,3-diaminopropane (0.005 g, 0.07 mmol) were dissolved in 1,4-dioxane (5 mL) and the flask flushed with nitrogen. The reaction was heated at reflux for 72 h and onced cooled to ambient temperature was diluted with aq. NH_3 (2 mL of 35% in 10 mL of water) and water (20 mL) added. The aqueous phase was extacted with dichloromethane (2 x 30 mL) and the combined organic phase dried over $MgSO_4$ and the solvent removed under reduced pressure. A 1:1 mixture of compound and the desired compound was obtained as an inseparable mixture.

(2-Iodophenyl)diphenylphosphine 42[165]



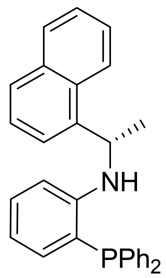
White solid (0.38 g, 25%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3052, 1426, 1020, 750, 697; δ_H (400 MHz, $CDCl_3$) 7.01-7.08 (5 H, m, Ar-*H*), 7.24-7.33 (2 H, m, Ar-*H*), 7.36-7.33 (2 H, m, Ar-*H*), 7.88-7.93 (5 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 107.87 (Ar-*C*), 128.27 (Ar-*C*H), 128.47 (Ar-*C*H), 128.54 (Ar-*C*H), 128.74 (4 Ar-*C*H), 130.15 (Ar-*C*H), 133.94 (Ar-*C*H), 134.13 (Ar-*C*H), 136.23 (Ar-*C*), 136.34 (Ar-*C*), 139.78 (4 Ar-*C*H), 142.21 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) 8.1 (s, 96%) (Literature δ_P 9.1)[165]m.p. 118.5 °C (Literature m.p. 119.1 °C)[165] HRMS (ES) calcd for [$C_{18}H_{14}PI$] 388.9953 found [M+] 388.9951

((S)-3-methylbutan-2-yl)-2-(diphenylphosphino)benzenamine 43



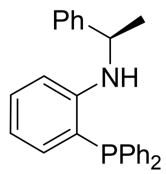
Cloudy viscous oil (0.29 g, 79%) υ_{max} (thin film)/cm^{-1} 3327, 2960, 1600, 1503, 1320, 745; δ_H (400 MHz, $CDCl_3$) 0.71 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr C*H*$_3$), 0.78 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr C*H*$_3$), 0.96 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 1.70-1.72 (1 H, m, C*H*^{b}), 3.31-3.40 (1 H, m, C*H*^{a}), 4.45 (1 H, m, N*H*), 6.53-6.40 (2 H, m, Ar-*H*), 7.16-7.20 (2 H, m, Ar-*H*), 7.32-7.37 (10 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 16.42 ($^{i-}$Pr *C*H$_3$), 17.76 ($^{i-}$Pr *C*H$_3$), 18.72 (*C*H$_3$), 32.26 ($^{i-}$Pr *C*H), 53.36 (*C*H), 85.88 (Ar-*C*), 110.39 (Ar-*C*H), 110.99 (Ar-*C*H), 116.21 (Ar-*C*H), 118.51 (Ar-*C*H), 128.55 (4 Ar-*C*H), 128.72 (Ar-*C*H), 129.32 (Ar-*C*H), 130.32 (Ar-*C*H), 133.64 (Ar-*C*H), 134.84 (Ar-*C*H), 134.90 (Ar-*C*), 139.16 (Ar-*C*H), 146.72 (Ar-*C*), 150.44 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) -20.25 (s, 97%); HRMS (ES) calcd for [$C_{23}H_{27}NP$] 348.1876, found [M^+H^+] for [$C_{23}H_{27}NPO$] 364.1813; $[\alpha]_D^{20}$ +34.5 [c = 0.51, $CHCl_3$]

((*S*)-1-(naphthalen-1-yl)ethyl)-2-(diphenylphosphino)benzenamine 45



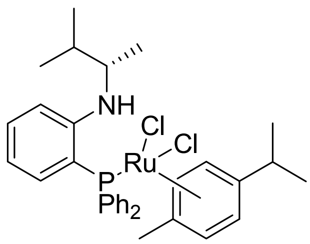
Cloudy viscous oil (0.18 g, 75%) υ_{max} (thin film)/cm^{-1} 3381, 3051, 2963, 1586, 1501, 1312, 799, 744, 696; δ_H (400 MHz, $CDCl_3$) 1.38 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 5.01-5.08 (1 H, m, N*H*), 5.14-5.20 (1 H, m, C*H*), 6.13 (1 H, dd, *J* 4.8 Hz & 7.6 Hz, Ar-*H*), 6.46 (1 H, t, *J* 7.2 Hz, Ar-*H*), 6.78 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 6.84-6.89 (1 H, m, Ar-*H*), 7.13-7.45 (14 H, m, Ar-*H*), 7.57-7.62 (1 H, m, Ar-*H*), 7.75-7.81 (1 H, m, Ar-*H*), 8.02 (1 H, d, *J* 8.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.56 (*C*H$_3$), 48.56 (*C*H), 110.31 (Ar-*C*H) 112.14 (Ar-*C*H), 116.05 (Ar-*C*H), 117.46 (Ar-*C*), 121.24 (Ar-*C*H), 121.56 (Ar-*C*H), 124.29 (Ar-*C*H), 124.83 (Ar-*C*H), 125.02 (Ar-*C*H), 126.23 (Ar-*C*H), 127.19 (Ar-*C*H), 127.42 (Ar-*C*H), 127.56 (Ar-*C*H), 127.63 (Ar-*C*H), 127.85 (Ar-*C*H), 128.09 (Ar-*C*H), 125.51 (Ar-*C*), 129.59 (Ar-*C*H), 132.60 (Ar-*C*H), 132.81 (Ar-*C*H), 132.96 (Ar-*C*H), 133.06 (Ar-*C*H), 133.60 (Ar-*C*H), 134.31 (Ar-*C*), 134.44 (Ar-*C*), 136.09 (Ar-*C*), 138.91 (Ar-*C*), 148.59 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) -19.98 (s, 58%); HRMS (ES) calcd for [$C_{30}H_{27}P$] 432.1797, found [M^+H^+] for [$C_{30}H_{27}NP$] 432.1864; $[\alpha]_D^{18}$ +150.0 [c = 0.40, $CHCl_3$]

((*R*)-1-phenylethyl)-2-(diphenylphosphino)benzenamine 48



Cloudy pale yellow oil (0.09 g, 49%) (only partial data available) υ_{max} (thin film)/cm^{-1} 3410, 2962, 2877, 1597, 1512, 1319, 1018, 740; δ_H (400 MHz, $CDCl_3$) 1.45 (3 H, d, *J* 6.4 Hz, C*H*$_3$), 4.41 (1 H, q, *J* 6.8 Hz, C*H*), 6.44-6.50 (2 H, m, Ar-*H*), 6.55-6.99 (1 H, m, Ar-*H*), 6.97-7.05 (3 H, m, Ar-*H*), 7.10-7.18 (3 H, m, Ar-*H*), 7.27-7.30 (10 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 23.91 (*C*H$_3$), 52.37 (*C*H), 112.38 (Ar-*C*H), 124.69 (Ar-*C*H), 124.85 (2 Ar-*C*H), 125.69 (Ar-*C*), 125.87 (Ar-*C*H), 127.43 (4 Ar-*C*H), 128.07 (4 Ar-*C*H), 132.62 (Ar-*C*H), 132.81 (Ar-*C*H), 136.02 (Ar-*C*); δ_P (162 MHz, $CDCl_3$) -20.07 (s, 68%); HRMS (ES) calcd for [$C_{26}H_{25}NP$] 382.1641, found [M+] for [$C_{26}H_{25}NP$]$^+$ 382.1707; $[\alpha]_D^{20}$ -82.5 [c = 0.63, $CHCl_3$]

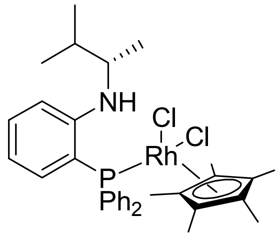
((S)-3-methylbutan-2-yl)-2-(diphenylphosphino)benzenamine ruthenium complex 51



((S)-3-Methylbutan-2-yl)-2-(diphenylphosphino)benzenamine **43** (0.02 g, 0.06 mmol) was dissolved in $CDCl_3$ and [$Ru(C_{10}H_{14})Cl_2]_2$ (0.02 g, 0.03 mmol) added in one portion. The solution was shaken and immediately transferred to a NMR tube. (Only partial data obtained)

δ_H (400 MHz, $CDCl_3$) 1.18-1.30 (15 H, m, 2 Ru ligand-C*H*$_3$, 2 $^{i-}$Pr C*H*$_3$ & C*H*$_3$), 2.08 (3 H, s, Ru ligand-C*H*$_3$), 2.81-2.86 (1 H, m, Ru ligand-$^{i-}$Pr C*H*), 3.02-3.10 (1 H, m, $^{i-}$Pr C*H*), 3.15-3.25 (1 H, m, C*H*), 4.91 (2 H, d, *J* 5.6 Hz, 2 Ru ligand Ar-*H*), 5.12 (1 H, d, *J* 5.6 Hz, Ru-ligand Ar-*H*), 6.51 (1 H, t, *J* 6.4 Hz, Ar-*H*), 6.63-6.65 (1 H, m, Ar-*H*), 6.90-6.93 (1 H, m, Ar-*H*), 7.16-7.30 (10 H, m, Ar-*H*), 7.75-7.76 (1 H, m, Ar-*H*); δ_P 27.16 (s, 82%)

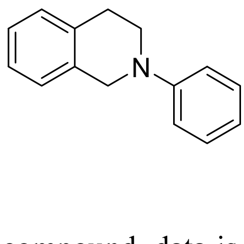
((S)-3-methylbutan-2-yl)-2-(diphenylphosphino)benzenamine rhodium complex 52



((S)-3-Methylbutan-2-yl)-2-(diphenylphosphino)benzenamine **43** (0.13 g, 0.37 mmol) and [Rh($C_{10}H_{15}$)Cl_3] (0.11 g, 0.33 mmol) were dissolved in distilled, dry dichloromethane (10 mL). The resulting dark red solution was allowed to stir at room temperature for 30 mins, before diethyl ether (20 mL) and light petroleum (10 mL) were added and the solution left stirring for a further 30 mins, resulting in crystallisation of the desired compound, which was dried under vacuum for 1 h. Orange crystalline solid (0.17 g, 68%) (only partial data obtained)

δ_H (400 MHz, $CDCl_3$) 0.47 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr CH_3), 0.53 (3 H, d, *J* 6.4 Hz, $^{i-}$Pr CH_3), 0.90 (3 H, d, *J* 6.8 Hz, CH_3), 1.43 (15 H, d, *J* 3.6 Hz, 5 CH_3 on Cp*), 3.12-3.23 (1 H, m, $^{i-}$Pr C*H*), 4.86 (1 H, bs, N*H*), 5.02-5.12 (1 H, m, C*H*), 6.53-6.67 (1 H, m Ar-*H*), 6.98-7.11 (1 H, m, Ar-*H*), 7.15-7.47 (10 H, m, Ar-*H*), 7.65-7.76 (1 H, m, Ar-*H*), 7.88-7.98 (1 H, m, Ar-*H*); δ_P 28.58 (d, ^1J ^{31}P-^{102}Rh 142.54, 37%), 28.93 (d, ^1J ^{31}P-^{102}Rh 142.54, 58%); $[\alpha]_D^{18}$ +86.4 [c = 0.25, $CHCl_3$]

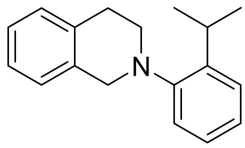
1,2,3,4-Tetrahydro-2-phenylisoquinoline 53[168]



Orange oil, (0.42 g, 93%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3058, 2852, 1599, 1382, 1234, 755 δ_H (400 MHz, $CDCl_3$) 2.98 (2 H, t, *J* 5.6 Hz, CH_2), 3.56 (2 H, t, *J* 6.0 Hz, CH_2), 4.41 (2 H, s, CH_2), 6.80-6.84 (1 H, m, Ar-*H*), 6.96-6.99 (2 H, m, Ar-*H*), 7.14-7.21 (4 H, m, Ar-*H*), 7.28-7.31 (2 H, m, Ar-*H*); δ_C (100

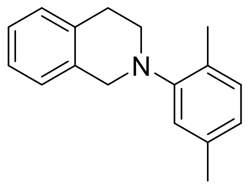
MHz, $CDCl_3$) 29.14 (*C*H_2), 46.55 (*C*H_2), 50.76 (*C*H_2), 114.96 (2 Ar-*C*H), 118.69 (Ar-*C*H), 126.05 (Ar-*C*H), 126.35 (Ar-*C*H), 126.56 (Ar-*C*H), 128.55 (Ar-*C*H), 129.02 (2 Ar-*C*H), 134.49 (Ar-*C*), 134.90 (Ar-*C*), 150.57 (Ar-*C*); *m/z* (FAB^+) 210 (42) 209 (100), 208 (81). HRMS (ES) calcd for [$C_{15}H_{15}N$] 209.1205, found [M^+] 209.1205.

1,2,3,4-Tetrahydro-2-(2-isopropylphenyl)isoquinoline 54[188]



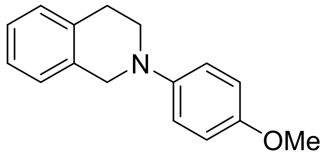
Off-white solid (0.47 g, 86%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2962, 1489,1211, 720; δ_H (400 MHz, $CDCl_3$) 1.20 (6 H, d, *J* 6.8 Hz, 2 $^{i-}$Pr C*H*$_3$), 3.02 (2 H, bs, C*H*$_2$), 3.19 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 3.56-3.59 (1 H, m, $^{i-}$Pr C*H*), 4.07 (2 H, s, C*H*$_2$), 7.05-7.07 (1 H, m, Ar-*H*), 7.11-7.22 (6 H, m, Ar-*H*), 7.29-7.31 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 24.13 (2 $^{i-}$Pr *C*H_3), 26.69 (*C*H), 30.00 (*C*H_2), 51.47 (*C*H_2), 56.02 (*C*H_2), 120.75 (Ar-*C*H), 124.62 (Ar-*C*H), 125.65 (Ar-*C*H), 126.17 (Ar-*C*H), 126.36 (Ar-*C*H), 126.42 (Ar-*C*H), 126.49 (Ar-*C*H), 128.96 (Ar-*C*H), 134.68 (Ar-*C*), 135.76 (Ar-*C*), 144.92 (Ar-*C*), 150.76 (Ar-*C*-N); *m/z* (FAB^+) 250 (100) HRMS (ES) calcd for [$C_{18}H_{20}N$]$^-$ 250.1595, found [M^+] 250.1592.

1,2,3,4-Tetrahydro-2-(2,5-dimethylphenyl)isoquinoline 55[188]



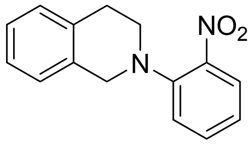
Yellow oil (0.44 g, 89%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3124, 1573, 1234, 810; δ_H (400 MHz, $CDCl_3$) 2.29 (3 H, s, C*H*$_3$), 2.33 (3 H, s, C*H*$_3$), 3.01 (2 H, t, *J* 6.0 Hz, C*H*$_2$), 3.19 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 4.10 (2 H, s, C*H*$_2$), 6.81-6.83 (1 H, m, Ar-*H*), 6.92 (1 H, s, Ar-*H*), 7.07-7.10 (2 H, m, Ar-*H*), 7.13-7.18 (3 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 17.68 (*C*H_3), 21.29 (*C*H_3), 29.90 (*C*H_2), 50.44 (*C*H_2), 54.21 (*C*H_2), 119.97 (Ar-*C*H), 123.86 (Ar-*C*H), 125.69 (Ar-*C*H), 126.20 (Ar-*C*H), 126.47 (Ar-*C*H), 128.96 (Ar-*C*H), 129.64 (Ar-*C*), 131.01 (Ar-*C*H), 134.66 (Ar-*C*), 135.58 (Ar-*C*), 136.25 (Ar-*C*), 151.44 (Ar-*C*-N); *m/z* (FAB$^+$) 236 (100) HRMS (ES) calcd for [$C_{17}H_{18}N$] 236.1439, found [M^+] 236.1438

1,2,3,4-Tetrahydro-2-(4-methoxyphenyl)isoquinoline 56[189]



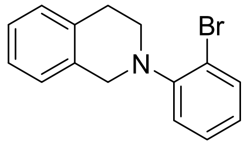
Viscous cloudy oil (0.36 g, 68%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2918, 1510, 1455, 1241, 1150, 1035, 755; δ_H (400 MHz, $CDCl_3$) 3.01 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 3.47 (2 H, t, *J* 6.0 Hz, C*H*$_2$), 3.80 (3 H, s, OC*H*$_3$), 4.32 (2 H, s, C*H*$_2$), 6.88-6.91 (2 H, m, Ar-*H*), 6.99-7.02 (2 H, m, Ar-*H*), 7.15-7.17 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 29.10 (*C*H$_2$), 48.41 (*C*H$_2$), 52.68 (*C*H$_2$), 55.64 (O*C*H$_3$), 114.58 (2 Ar-*C*H), 118.02 (Ar-*C*H), 120.09 (Ar-*C*), 125.90 (Ar-*C*H), 126.24 (Ar-*C*H), 126.50 (2 Ar-*C*H), 128.68 (Ar-*C*H), 134.61 (Ar-*C*), 144.21 (Ar-*C*), 145.92 (Ar-*C*); HRMS (ES) calcd for [$C_{16}H_{18}NO$] 240.1383, found [M^+] for [$C_{16}H_{18}NO$] 240.1377

1,2,3,4-Tetrahydro-2-(2-nitrophenyl)isoquinoline 57[190]



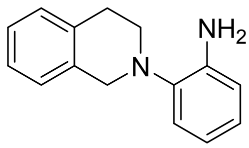
Orange solid (0.39 g, 69%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 1604, 1515, 1341, 1205, 753; δ_H (400 MHz, $CDCl_3$) 3.01 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 3.40 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 4.32 (2 H, s, C*H*$_2$), 6.96-6.99 (1 H, m, Ar-*H*), 7.09-7.15 (1 H, m, Ar-*H*), 7.17-7.22 (4 H, m, Ar-*H*), 7.70-7.73 (1 H, m, Ar-*H*), 7.82 (1 H, dd, *J* 1.6 Hz & 8.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 28.82 (*C*H$_2$), 50.09 (*C*H$_2$), 52.49 (*C*H$_2$), 120.24 (Ar-*C*H), 122.75 (Ar-*C*H), 124.56 (Ar-*C*H), 126.12 (Ar-*C*H), 128.78 (Ar-*C*H), 132.66 (Ar-*C*H), 133.48 (Ar-*C*H), 133.77 (Ar-*C*), 134.53 (Ar-*C*H), 144.08 (Ar-*C*), 145.52 (Ar-*C*), 146.37 (Ar-*C*); m.p. 102.7 °C; *m/z* (FAB$^+$) 206 (27) 221 (27), 237 (21), 254 (100), 255 (37). HRMS (ES) calcd for [$C_{15}H_{14}N_2O_2$] 254.1055, found [M^+] 254.1052

2-(2-Bromophenyl)-1,2,3,4-tetrahydroisoquinoline 58[188]



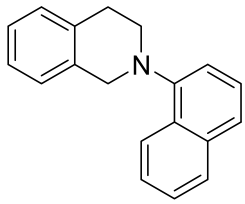
Pale yellow solid (0.49 g, 78%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2923, 1691, 1603, 1303, 1026, 750; δ_H (400 MHz, $CDCl_3$) 3.05 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 3.38 (2 H, t, *J* 6.0 Hz, C*H*$_2$), 4.26 (2 H, s, C*H*$_2$), 6.93 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 7.08-7.17 (5 H, m, Ar-*H*), 7.27-7.30 (1 H, m, Ar-*H*), 7.60 (1 H, dd, *J* 1.2 Hz & 8.0 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 29.18 (*C*H$_2$), 50.48 (*C*H$_2$), 53.57 (*C*H$_2$), 119.80 (Ar-*C*), 121.10 (Ar-*C*H), 124.28 (Ar-*C*H), 125.75 (Ar-*C*H), 126.31 (Ar-*C*H), 126.38 (Ar-*C*H), 128.19 (Ar-*C*H), 128.98 (Ar-*C*H), 133.94 (Ar-*C*H), 134.53 (Ar-*C*), 134.74 (Ar-*C*), 150.49 (Ar-*C*); m.p. 74.9 °C; HRMS (ES) calcd for [$C_{15}H_{14}N^{79}Br$] 286.0226, found [M+] 286.0223

1,2,3,4-Tetrahydro-1-(2-aminophenyl)isoquinoline 59[191]



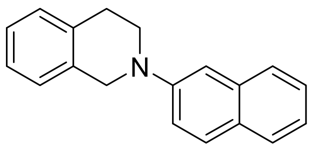
Brown oil, (0.22 g, 45%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3400, 1500, 750; δ_H (400 MHz, $CDCl_3$) 1.57 (2 H, bs, N*H*$_2$), 3.01 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 3.40 (2 H, t, *J* 5.6 Hz, C*H*$_2$), 4.31 (2 H, s, C*H*$_2$), 6.95-6.99 (1 H, m, Ar-*H*), 7.09-7.11 (1 H, m, Ar-*H*), 7.16-7.22 (4 H, m, Ar-*H*) 7.45-7.49 (1 H, m, Ar-*H*), 7.82 (1 H, dd, *J* 1.6 Hz & 8.4, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 28.85 (*C*H$_2$), 50.10 (*C*H$_2$), 52.49 (*C*H$_2$), 119.79 (Ar-*C*H), 120.21 (Ar-*C*H), 122.16 (Ar-*C*), 126.13 (Ar-*C*H), 126.30 (Ar-*C*H), 126.51 (Ar-*C*H), 126.65 (Ar-*C*H), 128.79 (Ar-*C*H), 133.49 (Ar-*C*H), 133.78 (Ar-*C*), 134.57 (Ar-*C*), 145.54 (Ar-*C*); HRMS (ES) calcd for [$C_{15}H_{16}N_2$] 225.1308, found [M+] for [$C_{15}H_{16}N_2$] 225.1380

1,2,3,4-Tetrahydro-2-(naphthalen-5-yl)isoquinoline 60



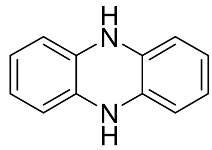
Off-white solid (0.55 g, 96%); υ_{max} (thin film)/cm^{-1} 1635, 1265, 740; δ_H (400 MHz, $CDCl_3$) 3.04 (2 H, s, C*H_2*), 3.64 (2 H, s, C*H_2*), 4.30 (2 H, s, C*H_2*), 7.08 (1 H, d, *J* 6.8 Hz, Ar-*H*), 7.14-7.22 (4 H, m, Ar-*H*), 7.38-7.48 (3 H, m, Ar-*H*), 7.56 (1 H, d, *J* 8.4 Hz, Ar-*H*), 7.81-7.85 (1 H, m, Ar-*H*), 8.22-8.26 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 29.74 (*C*H_2), 51.58 (*C*H_2), 55.41 (*C*H_2), 115.00 (Ar-*C*H), 123.59 (Ar-*C*H), 123.77 (Ar-*C*H), 125.49 (Ar-*C*H), 125.61 (Ar-*C*H), 125.83 (Ar-*C*H), 125.92 (Ar-*C*H), 126.39 (Ar-*C*H), 126.48 (Ar-*C*H), 128.43 (Ar-*C*H), 129.05 (Ar-*C*H), 129.17 (Ar-*C*), 134.59 (Ar-*C*), 134.81 (Ar-*C*), 135.36 (Ar-*C*), 149.66 (Ar-*C*); m.p. 108.7-109.4 °C; *m/z* (FAB$^+$) 259 (78), 258 (100), 69 (30), 55 (48). HRMS (ES) calcd for [$C_{19}H_{17}N$] 259.1361, found [M$^+$] 259.1366.

1,2,3,4-Tetrahydro-2-(naphthalen-6-yl)isoquinoline 61



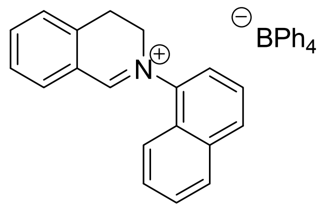
Off-white solid (0.56 g, 99%). υ_{max} (thin film)/cm^{-1} 1627, 1265, 740; δ_H (400 MHz, $CDCl_3$) 3.04 (2 H, t, *J* 5.6 Hz, C*H_2*), 3.67 (2 H, t, *J* 6.0 Hz, C*H_2*), 4.51 (2 H, s, C*H_2*), 7.17-7.21 (5 H, m, Ar-*H*), 7.26-7.28 (1 H, m, Ar-*H*), 7.33-7.36 (1 H, m, Ar-*H*), 7.39-7.41 (1 H, m, Ar-*H*), 7.76-7.68 (3 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 29.19 (*C*H_2), 47.18 (*C*H_2), 51.13 (*C*H_2), 109.37 (Ar-*C*H), 118.73 (Ar-*C*H), 123.01 (Ar-*C*H), 126.10 (Ar-*C*H), 126.29 (Ar-*C*H), 126.42 (Ar-*C*H), 126.58 (Ar-*C*H), 126.60 (Ar-*C*H), 127.46 (Ar-*C*H), 128.07 (Ar-*C*), 128.64 (Ar-*C*H), 128.84 (Ar-*C*H), 134.36 (Ar-*C*), 134.76 (2 Ar-*C*), 148.39 (Ar-*C*); m.p. 104.4 °C; *m/z* (FAB$^+$) 259 (100), 258 (64). HRMS (ES) calcd for [$C_{19}H_{17}N$] 259.1361, found [M$^+$] 259.1365.

5,10-Dihydrophenazine (by-product) 62[192]



Orange solid, known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3357, 1357, 745; δ_H (400 MHz, $CDCl_3$) 7.83-7.87 (4 H, m, Ar-*H*), 8.23-8.28 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 129.68 (4 Ar-*C*H), 130.53 (4 Ar-*C*H), 143.53 (4 Ar-*C*); HRMS (ES) calcd for [$C_{12}H_{10}N_2$] 181.0830, found [M+] for [$C_{12}H_{10}N_2$] 181.0758.

Synthesis of isoquinolium salt 63

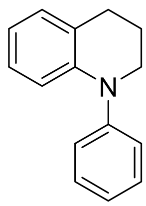


1,2,3,4-tetrahydro-2-(naphthalen-5-yl)isoquinoline **60** (0.26 g, 1 mmol) was dissolved in CH_2Cl_2 and *N*-bromosuccinimide (0.21 g, 1.2 mmol) and the reaction heated under reflux for 4 h, after which the reaction was allowed to cool to ambient temperature and the solvent removed under reduced pressure and the resulting residue was dissolved in ethanol. Sodium tetraphenylborate (0.38 g, 1.1 mmol) was dissolved in the minimum amount of acetonitrile and added to the solution, which was allowed to stir overnight. The precipitate was collected by vacuum filtration and dissolved in dichloromethane, washed with water (3 x 20 mL) and dried over $MgSO_4$, before the solvent was removed under reduced pressure to yield a yellow crystalline solid, (0.47 g, 81%)

υ_{max} (thin film)/cm^{-1} 1724, 1386, 1110; δ_H (400 MHz, DMSO-d$_6$) 3.43-3.65 (2 H, m, C*H*$_2$), 4.38-3.88 (2 H, m, C*H*$_2$), 6.83-6.86 (4 H, m, Ar-*H*), 6.98-7.01 (8 H, m, Ar-*H*), 7.27-7.29 (8 H, m, Ar-*H*), 7.62-7.67 (4 H, m, Ar-*H*), 7.83-8.00 (5 H, m, Ar-*H*), 8.07 (1 H, d, *J* 8.0 Hz, Ar-*H*), 8.47 (1 H, d, *J* 8.4 Ar-*H*), 9.02 (1 H, s, C*H*=N); δ_C (100 MHz, DMSO-d$_6$) 24.85 (*C*H$_2$), 53.07 (*C*H$_2$), 121.40 (8 Ar-*C*H) 121.86 (Ar-*C*H), 123.47 (Ar-*C*H), 124.76 (Ar-*C*), 125.21 (6 Ar-*C*H), 125.30 (Ar-*C*), 125.67 (Ar-*C*), 126.98 (Ar-*C*H), 128.49 (2 Ar-*C*H), 129.30 (Ar-*C*H), 129.34 (Ar-*C*H), 132.20 (Ar-*C*), 135.03 (Ar-*C*H), 135.39 (8 Ar-*C*H), 137.32 (Ar-*C*), 139.62 (Ar-*C*H), 162.69 (Ar-*C*), 163.18 (Ar-*C*), 163.67 (Ar-*C*), 164.16 (Ar-

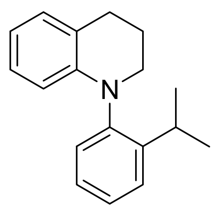
C), 170.49 (*C*H=N); m.p. 181.4 °C; HRMS (ES) calcd for [$C_{19}H_{16}N$] 258.1277, found [M^+] 258.1275

1,2,3,4-Tetrahydro-1-phenylquinoline 64[168]



Waxy yellow solid (0.94 g, 94%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3050, 2925, 1500, 1228, 754; δ_H (400 MHz, $CDCl_3$) 2.00-2.06 (2 H, m, C*H*$_2$), 2.84 (2 H, t, *J* 6.8 Hz, C*H*$_2$), 3.60-3.63 (2 H, m, C*H*$_2$), 6.67-6.75 (2 H, m, Ar-*H*), 6.89-6.93 (1 H, m, Ar-*H*), 7.02-7.09 (2 H, m, Ar-*H*), 7.21-7.24 (2 H, m, Ar-*H*), 7.29-7.35 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.76 (*C*H$_2$), 27.97 (*C*H$_2$), 50.84 (*C*H$_2$), 115.79 (Ar-*C*H), 118.33 (Ar-*C*H), 123.59 (Ar-*C*H), 124.66 (2 Ar-*C*H), 126.38 (Ar-*C*H), 129.40 (3 Ar-*C*H), 134.90 (Ar-*C*), 144.43 (Ar-*C*), 148.40 (Ar-*C*); *m/z* (FAB^+) 210 (45) 209 (100), 208 (47). HRMS (ES) calcd for [$C_{15}H_{15}N$] 209.1205, found [M^+] 209.1206.

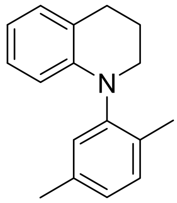
1,2,3,4-Tetrahydro-1-(2-isopropylphenyl)quinoline 65



Clear oil (0.49 g, 89%). υ_{max} (thin film)/cm^{-1} 3059, 2967, 1588, 1315, 1180, 742; δ_H (400 MHz, $CDCl_3$) 1.14 (3 H, d, *J* 6.8 Hz, $^{i-}$Pr C*H*$_3$), 1.19 (3 H, d, *J* 7.2 Hz, $^{i-}$Pr C*H*$_3$), 2.03-2.17 (2 H, m, C*H*$_2$), 2.83-3.00 (2 H, m, C*H*$_2$), 3.15 (1 H, m, $^{i-}$Pr C*H*) 3.39-3.64 (2 H, m, C*H*$_2$), 6.00 (1 H, d, *J* 8.4 Hz, Ar-*H*), 6.57 (1 H, dt, *J* 1.2 Hz & 7.6 Hz, Ar-*H*), 6.84 (1 H, dt, *J* 1.6 Hz & 1.6 Hz & 8.0 Hz, Ar-*H*) 7.02 (1 H, d, *J* 8.0 Hz, Ar-*H*), 7.19-7.22 (1 H, m, Ar-*H*), 7.24-7.31 (2 H, m, Ar-*H*), 7.38-7.41 (1 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.32 (*C*H$_2$), 23.59 (*C*H$_3$), 24.30 (*C*H$_3$), 27.56 (*C*H), 27..96 (*C*H$_2$), 51.36 (*C*H$_2$), 113.33 (Ar-*C*H), 116.24 (Ar-*C*H), 121.54 (Ar-*C*), 126.64 (Ar-*C*H), 126.92 (Ar-*C*H), 121.13 (Ar-*C*H), 127.49 (Ar-*C*H), 128.80 (Ar-*C*H), 129.12 (Ar-*C*H), 145.03 (Ar-*C*), 146.00 (Ar-*C*), 147.96 (Ar-*C*); *m/z*

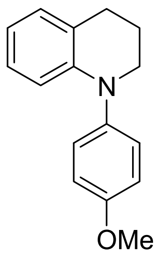
(FAB^+) 250 (33) 251 (100), 252 (27). HRMS (ES) calcd for [$C_{18}H_{21}N$] 251.1672, found [M^+] 251.1674.

1,2,3,4-Tetrahydro-1-(2,5-dimethylphenyl)quinoline 66



Yellow Oil (0.45 g, 87%). υ_{max} (thin film)/cm^{-1} 3019, 2800, 1607, 1235, 1026, 744; δ_H (400 MHz, $CDCl_3$) 2.06-2.11 (2 H, m, CH_2), 2.14 (3 H, s, CH_3), 2.30 (3H, s, CH_3), 2.89 (2 H, bs, CH_2), 3.49 (2 H, bs, CH_2), 6.04 (1 H, d, *J* 8.4 Hz, Ar-*H*), 6.57 (1 H, t, *J* 7.6 Hz, Ar-*H*), 6.85 (1 H, t, *J* 8.0 Hz, Ar-*H*), 6.99-7.01 (3 H, m, Ar-*H*), 7.18 (1 H, d, *J* 8.0 Ar-*H*); δ_C (100 MHz, $CDCl_3$) 17.35 (*C*H_3), 20.86 (*C*H_3), 22.46 (*C*H_2), 27.97 (*C*H_2), 50.49 (*C*H_2), 112.97 (Ar-*C*H), 116.20 (Ar-*C*H), 121.57 (Ar-*C*), 126.71 (Ar-*C*H), 127.16 (Ar-*C*H), 128.96 (Ar-*C*H), 129.14 (Ar-*C*H), 131.04 (Ar-*C*H), 133.61 (Ar-*C*), 137.23 (Ar-*C*), 145.15 (Ar-*C*), 145.77 (Ar-*C*); *m/z* (FAB^+) 236 (65) 237 (100), 238 (60). HRMS (ES) calcd for [$C_{17}H_{19}N$] 237.1517, found [M^+] 237.1517

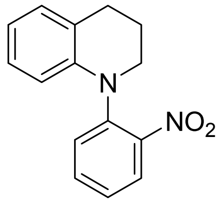
1,2,3,4-Tetrahydro-1-(4-methoxyphenyl)quinoline 67[168]



Viscous cloudy oil, (0.34 g, 64%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2936, 1584, 1488, 1247, 1072, 822; δ_H (400 MHz, $CDCl_3$) 2.03-2.09 (2 H, m, CH_2), 2.83-2.88 (2 H, m, CH_2), 3.55-3.64 (2 H, s, CH_2), 3.84 (3 H, s, OCH_3), 6.46 (1 H, dd, *J* 0.8 Hz & 7.2 Hz, Ar-*H*), 6.62 (1 H, dt, *J* 0.8 Hz & 7.2 Hz, Ar-*H*), 6.86-6.93 (3 H, m, Ar-*H*), 6.99-7.01 (1 H, m, Ar-*H*), 7.14-7.18 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.31 (*C*H_2), 27.76 (*C*H_2), 51.83 (*C*H_2), 55.48 (O*C*H_3), 114.68 (2 Ar-*C*H), 117.58 (Ar-*C*H), 122.06 (Ar-*C*), 124.62 (Ar-*C*H), 126.53 (Ar-*C*H), 127.57 (2 Ar-*C*H), 129.36 (Ar-

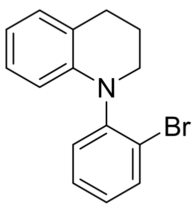
CH), 141.21 (Ar-C), 145.30 (Ar-C), 156.87 (Ar-C); HRMS (ES) calcd for [$C_{16}H_{17}NO$] 239.1305, found [M+] for $[C_{16}H_{18}NO]^+$ 240.1377

1,2,3,4-Tetrahydro-1-(2-nitrophenyl)quinoline 68[193]



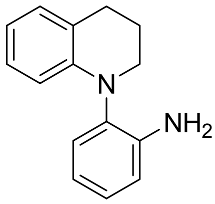
Orange solid (0.39 g, 69%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 2928, 1598, 1507, 1295, 1241, 747; δ_H (400 MHz, $CDCl_3$) 2.06-2.09 (2 H, m, C*H*$_2$), 2.88 (2 H, t, *J* 6.4 Hz, C*H*$_2$), 3.56-3.59 (2 H, m, C*H*$_2$), 6.34 (1 H, d, *J* 7.6 Hz, Ar-*H*), 6.71 (1 H, dt, *J* 1.2 Hz & 8.0 Hz, Ar-*H*), 6.88 (1 H, t, *J* 7.2 Hz, Ar-*H*), 7.05 (1 H, d, *J* 7.2 Hz, Ar-*H*), 7.28-7.31 (1 H, m, Ar-*H*) 7.42-7.44 (1 H, m, Ar-*H*) 7.55-7.57 (1 H, m, Ar-*H*), 7.88 (1 H, dd, *J* 1.6 Hz & 8.0, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.06 (*C*H$_2$), 27.44 (*C*H$_2$), 51.28 (*C*H$_2$), 114.44 (Ar-*C*H), 119.13 (Ar-*C*H), 124.18 (Ar-*C*), 125.33 (Ar-*C*H), 125.71 (Ar-*C*H), 126.67 (Ar-*C*H), 129.58 (Ar-*C*H), 130.08 (Ar-*C*H), 133.89 (Ar-*C*H), 141.74 (Ar-*C*), 143.39 (Ar-*C*), 146.79 (Ar-*C*); m.p. 112.3 °C; *m/z* (FAB^+) 136 (52), 137 (35), 154 (68) 206 (56) 221 (35), 237 (100), 253 (68), 254 (37), 255 (76). HRMS (ES) calcd for $[C_{15}H_{15}N_2O_2]^+$ 254.1133, found [M^+] 254.1131

1-(2-Bromophenyl)-1,2,3,4-tetrahydroquinoline 69



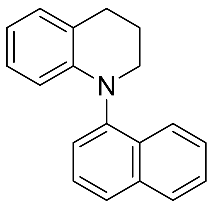
Pale yellow solid, (0.35 g, 56%) υ_{max} (thin film)/cm^{-1} 2924, 1662, 1474, 1327, 1026, 746; δ_H (400 MHz, $CDCl_3$) 2.10-2.17 (2 H, m, C*H*$_2$), 2.88-2.91 (2 H, m, C*H*$_2$), 3.54-3.56 (2 H, m, C*H*$_2$), 6.10 (1 H, d, *J* 8.0 Hz, Ar-*H*), 6.63 (1 H, t, *J* 7.2 Hz, Ar-*H*), 6.88 (1 H, t, *J* 6.4 Hz, Ar-*H*), 7.04 (1 H, d, *J* 7.6 Hz, Ar-*H*), 7.16 (1 H, dt, *J* 2.0 Hz & 8.0 Hz, Ar-*H*) 7.30-7.37 (2 H, m Ar-*H*), 7.68 (1 H, d, *J* 6.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.07 (*C*H$_2$), 27.84 (*C*H$_2$), 50.51 (*C*H$_2$), 113.63 (Ar-*C*H), 117.21 (Ar-*C*H), 122.20 (Ar-*C*), 124.50 (Ar-*C*), 126.64 (Ar-*C*H), 127.82 (Ar-*C*H), 129.03 (Ar-*C*H), 129.29 (Ar-*C*H), 130.73 (Ar-*C*H), 134.11 (Ar-*C*H), 144.37 (Ar-*C*), 146.18 (Ar-*C*); HRMS (ES) calcd for [$C_{15}H_{14}$ $N^{79}Br$] 288.0375, found [M+] 288.0386

1,2,3,4-Tetrahydro-1-(2-aminophenyl)quinoline 70[193]



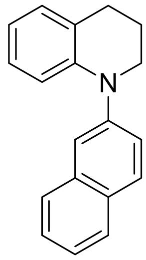
Brown oil, (0.25 g, 51%). Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3404, 2926, 1606, 1500, 1309, 1095, 746; δ_H (400 MHz, $CDCl_3$) 1.60 (2 H, bs, N*H*$_2$), 3.00-3.03 (2 H, m, C*H*$_2$), 3.23-3.26 (2 H, m, C*H*$_2$), 4.09-4.11 (2 H, m, C*H*$_2$), 6.78-6.81 (2 H, m, Ar-*H*), 7.08-7.19 (3 H, m, Ar-*H*), 7.18-7.20 (3 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 49.31 (*C*H$_2$), 53.82 (*C*H$_2$), 60.42 (*C*H$_2$), 110.24 (Ar-*C*), 115.29 (Ar-*C*H), 118.64 (Ar-*C*H), 120.20 (Ar-*C*H), 125.73 (Ar-*C*H), 126.30 (Ar-*C*H), 126.45 (Ar-*C*H), 128.35 (Ar-*C*H), 128.93 (Ar-*C*H), 134.30 (Ar-*C*), 141.78 (Ar-*C*), 143.15 (Ar-*C*); HRMS (ES) calcd for [$C_{15}H_{17}N_2$] 225.1308, found [M+] 225.1308

1,2,3,4-Tetrahydro-1-(naphthalen-5-yl)quinoline 71



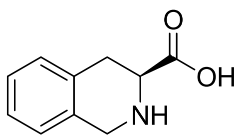
Off white solid (0.54 g, 94%); υ_{max} (thin film)/cm^{-1}1573, 1485, 740; δ_H (400 MHz, $CDCl_3$) 2.16-2.20 (2 H, m, C*H*$_2$), 2.97-3.03 (2 H, m, C*H*$_2$), 3.64-3.68 (2 H, m, C*H*$_2$), 6.02 (1 H, d, *J* 7.6 Hz, Ar-*H*), 6.60 (1 H, t, *J* 7.2 Hz, Ar-*H*), 6.76 (1H, t, *J* 7.6 Hz, Ar-*H*), 7.06 (1 H, d, *J* 6.4 Hz, Ar-*H*), 7.40-7.53 (4 H, m, Ar-*H*), 7.78 (1 H, d, *J* 8.4 Hz, Ar-*H*), 7.90 (1 H, d, *J* 8.0 Hz, Ar-*H*), 7.96 (1 H, d, *J* 8.4 Hz, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.62 (*C*H$_2$), 28.03 (*C*H$_2$), 51.58 (*C*H$_2$), 114.13 (Ar-*C*H), 116.78 (Ar-*C*H), 121.97 (Ar-*C*), 123.70 (Ar-*C*H), 125.46 (Ar-*C*H), 126.24 (Ar-*C*H), 126.31 (Ar-*C*H), 126.56 (Ar-*C*H), 126.59 (Ar-*C*H), 126.70 (Ar-*C*H), 128.49 (Ar-*C*H), 129.21 (Ar-*C*H), 131.28 (Ar-*C*), 135.12 (Ar-*C*), 144.68 (Ar-*C*), 146.09 (Ar-*C*); m.p. 132.7 °C; *m/z* (FAB^+) 259 (100), 258 (25). HRMS (ES) calcd for [$C_{19}H_{17}N$] 259.1361, found [M^+] 259.1363.

1,2,3,4-Tetrahydro-1-(naphthalen-6-yl)quinoline 72



Viscous yellow oil (0.39 g, 68%); υ_{max} (thin film)/cm^{-1} 1627, 1597, 1265, 702; δ_H (400 MHz, $CDCl_3$) 2.02-2.11 (2 H, m, CH_2), 2.86 (2 H, m, CH_2), 3.73 (2 H, m, CH_2), 6.72-6.76 (1 H, m, Ar-*H*), 6.82-6.85 (1 H, m, Ar-*H*), 6.92-6-96 (1 H, m, Ar-*H*), 7.07-7.10 (1 H, m, Ar-*H*), 7.33-7.45 (3 H, m, Ar-*H*), 7.54-7.55 (1 H, m, Ar-*H*), 7.72-7.70 (1 H, m, Ar-*H*), 7.78-7.75 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.86 (*C*H_2), 27.69 (*C*H_2), 50.82 (*C*H_2), 116.47 (Ar-*C*H), 119.07 (Ar-*C*H), 120.27 (Ar-*C*H), 124.41 (Ar-*C*H), 124.69 (Ar-*C*H), 125.53 (Ar-*C*), 126.25 (Ar-*C*H), 126.49 (Ar-*C*H), 127.10 (Ar-*C*H), 127.61 (Ar-*C*H), 128.85 (Ar-*C*H), 129.37 (Ar-*C*H), 130.42 (Ar-*C*), 134.56 (Ar-*C*), 144.01 (Ar-*C*), 145.81 (Ar-*C*); *m/z* (FAB^+) 259 (100), 258 (57). HRMS (ES) calcd for [$C_{19}H_{17}N$] 259.1361, found [M^+] 259.1364.

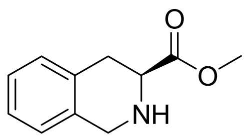
Synthesis of (*S*)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid 73[194]



Phenylaniline (10.0 g, 59.5 mmol) and aq. formaldehyde (32 mL of 37.8%) was dissolved in 100 mL of concentrated HCl (100 mL) and stirred under reflux for 3.5 h, the solution was cooled to room temperature and allowed to stir for 24 h. The product was collected by filtration, dissolved in MeOH (150 mL) and diethyl ether (100 mL) added. The solid was collected by vacuum filtration and allowed to dry under vacuum to give a white solid (7.63 g, 72%)

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3417, 2961, 1682, 1491, 1093, 823; δ_H (400 MHz, DMSO-d$_6$) 3.09-3.16 (1 H, m, 1 *H* of CH$_2$), 3.28-3.41 (1 H, m, 1 *H* of CH$_2$), 3.49 (1 H, bs, N*H*), 4.27-4.36 (2 H, m, C*H$_2$*), 4.37-4.41 (1 H, m, C*H*), 7.25-7.29 (4 H, m, Ar-*H*), 9.96 (1 H, bs, O*H*); δ_C (100 MHz, DMSO-d$_6$) 28.03 (*C*H$_2$), 43.71 (*C*H$_2$), 53.06 (*C*H), 126.48 (Ar-*C*H), 126.82 (Ar-*C*H), 127.45 (Ar-*C*H), 128.38 (Ar-*C*), 128.72 (Ar-*C*H), 130.77 (Ar-*C*), 169.88 (*C*=O); m.p. 302.7 °C (Literature m.p. >300 °C); *m/z* (EI) 132 (21), 136 (52), 137 (35), 154 (58), 176 (29), 177 (20), 178 (100); HRMS (ES) calcd for [$C_{10}H_{11}NO_2$] 178.0868, found [M+] for [$C_{10}H_{11}NO_2$] 178.0865; $[\alpha]_D^{18}$ -156.4 [c = 0.87, NaOH]; Literature $[\alpha]_D^{20}$ -163 [c = 1.00, NaOH][195]

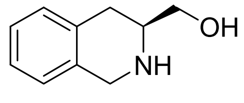
Synthesis of (*S*)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid methyl ester 71[196]



(*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid (6.25 g, 35.3 mmol) was added in one portion to an ice cooled solution of methanol (50 mL) and acetyl chloride (9 mL). The resulting solution was heated slowly to reflux and allowed to reflux for 4 h. Solvents were removed under reduced pressure and the residue dissolved in ethyl acetate (50 mL) and neutralised using 2M NaOH. The solution was extracted using ethyl acetate (3 x 20 mL), combined and dried over $MgSO_4$, before solvents removed under reduced pressure to yield the product as a yellow oil, (4.56 g, 67%)

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3338, 2948, 1739, 1435, 1306, 1202, 747; δ_H (400 MHz, CDCl$_3$) 2.94-3.01 (1 H, m, 1 *H* of CH$_2$), 3.08-3.13 (1 H, m, 1 *H* of CH$_2$), 3.40 (1 H, bs, N*H*), 3.76-3.80 (4 H, m, OC*H$_3$* & C*H*), 4.07-4.17 (2 H, m, C*H$_2$*), 7.03-7.05 (1 H, m, Ar-*H*), 7.10-7.12 (3 H, m, Ar-*H*); δ_C (100 MHz, CDCl$_3$) 31.49 (*C*H$_2$), 46.96 (*C*H$_2$), 52.25 (O*C*H$_3$), 55.60 (*C*H), 126.13 (Ar-*C*H), 126.29 (Ar-*C*H), 126.41 (Ar-*C*H), 129.13 (Ar-*C*H), 132.87 (Ar-*C*), 134.04 (Ar-*C*), 173.29 (*C*=O); *m/z* (EI) 130 (29), 132 (52), 190 (30), 192 (100); HRMS (ES) calcd for [$C_{11}H_{14}NO_2$] 192.1024, found [M^+H^+] for [$C_{11}H_{14}NO_2$] 192.1026; $[\alpha]_D^{18}$ -117.8 [c = 0.90, CH_2Cl_2]; Literature $[\alpha]_D^{20}$ -126 [c = 1.28, CH_2Cl_2][196]

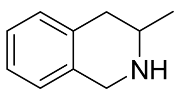
Synthesis of (*S*)-hydroxymethyl-1,2,3,4-tetrahydroisoquinoline 72



(*S*)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid methyl ester (3.0 g, 15.7 mmol), was dissolved in ethanol (100 mL) and sodium borohydride added in one portion (2.4 g, 62.8 mmol) and left to stir at room temperature for 24h. The resulting solution was cooled over ice and concentrated HCl (3 mL) added dropwise, immediately followed by the addition of water (12 mL). The ethanol was removed under reduced pressure and the solution extracted using ethyl acetate (3 x 50 mL) and concentrated under reduced pressure to yield the desired product as an yellow solid, (2.15 g, 84%)

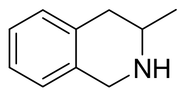
υ_{max} (thin film)/cm^{-1} 3269, 2971, 1451, 1358, 1084, 743; δ_H (400 MHz, $CDCl_3$) 2.57-2.79 (2 H, m, C*H*$_2$), 2.92 (2 H, bs, O*H* & N*H*), 2.03-3.08 (1 H, m, C*H*), 3.53-3.64 (1 H, m, 1 *H* of CH_2), 3.79-3.83 (1 H, m, 1 *H* of CH_2) 4.04 (2 H, bs, C*H*$_2$) 7.00-7.20 (4 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 30.68 (*C*H$_2$), 47.49 (*C*H$_2$), 55.14 (*C*H), 65.06 (*C*H$_2$), 126.06 (Ar-*C*H), 126.13 (Ar-*C*H), 126.46 (Ar-*C*H), 129.32 (Ar-*C*H), 133.72 (Ar-*C*), 152.11 (Ar-*C*); m.p. 84.3-84.9 °C (Literature m.p. 82-83 °C)[197]; HRMS (ES) calcd for [$C_{10}H_{14}NO$] 164.0992, found [M^+H^+] for [$C_{10}H_{14}NO$] 164.1067; $[\alpha]_D^{18}$ -61.2 [c = 0.66, MeOH]; Literatire $[\alpha]_D^{20}$ -84 [c = 1.10, CH_2Cl_2][197]

Attempted synthesis of 3-methyl-1,2,3,4-tetrahydroisoquinoline[170]



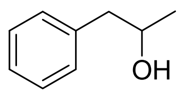
3-Methylisoquinoline (0.32 g, 2.2 mmol) was dissolved in ethanol, saturated aqueous ammonium chloride solution (3 mL) was added and in one portion indium powder (2 g). The reaction was then heated to reflux and monitored by TLC until complete. After 5 days the reaction was diluted with water (50 mL) and filtered through Celite. The filtrate was adjusted to pH 9 with 2 M sodium hydroxide and extracted with dichloromethane (3 x 25 mL). The combined organic fractions were dried over $MgSO_4$ before the solvent was removed under reduced pressure to yield the crude material as a brown oil. The crude product was purified using column chromatography (alumina, 5:1 light petroleum:ethyl acetate → 1:1 light petroleum:methanol) to yield a yellow oil.

Attempted synthesis of 1,2,3,4-tetrahydro-3-methylisoquinoline[171]



3-Methylisoquinoline (0.6 g, 4.0 mmol) and nickel (II) chloride hexahydrate (0.2 g, 0.7 mmol) were dissolved in methanol and cooled in an ice bath to 0 °C, before sodium borohydride (0.6 g, 16.0 mmol) was added in portions over 15 mins. During addition solution changed from light green to black, from the formation of Ni_2B. The resulting solution was allowed to stir at room temperature for 16 hours before the solvent was removed under reduced pressure. The black precipitate was dissolved in 1 M aq. HCl and the acidic solution basified by the addition of conc. ammonium hydroxide before being extracted into diethyl ether (3 x 25 mL). The organic phases were combined and dried over $MgSO_4$ before solvents were removed under reduced pressure.

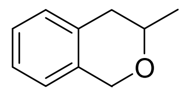
Synthesis of 1-phenylpropan-2-ol 73[198]



Phenylacetone (10.0 g, 74.5 mmol) was dissolved in ethanol (30 mL) and sodium borohydride (5.6 g, 149.0 mmol) added in one portion at room temperature. The reaction was allowed to stir for 2 h at room temperature before the reaction was quenched with water, extracted with ether (3 x 30 mL) and the combined organic layers dried over $MgSO_4$. The solvent was removed under reduced pressure to yield the product as a clear oil which required no further purification (10.41 g, >99%).

Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3371, 1598, 1327, 837, 743; δ_H (400 MHz, $CDCl_3$) 1.24 (3 H, d, *J* 6.0 Hz, C*H*$_3$), 1.66 (1 H, bs, O*H*), 2.68 (1 H, dd, *J* 8.0 Hz & *J* 13.6 Hz, 1 *H* of C*H*$_2$), 2.77 (1 H, dd, *J* 4.8 Hz & *J* 13.6 Hz, 1 *H* of C*H*$_2$), 3.98 - 4.02 (1 H, m, C*H*), 7.19-7.25 (3 H, m, Ar-*H*), 7.28-7.33 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 22.78 (Me-*C*), 45.78 (*C*H$_2$), 53.43 (*C*H), 125.87 (Ar-*C*H), 128.28 (2 Ar-*C*H), 129.40 (2 Ar-*C*H), 138.53 (Ar-*C*); *m/z* (FAB$^+$) 136 (48), 137 (50), 119 (100), 91 (64) HRMS (ES) calcd for [$C_9H_{13}O$] 137.0966, found [M^+H^+] 137.0968

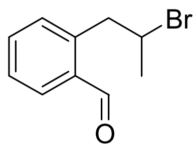
Synthesis of 3,4-dihydro-3-methyl-isochroman 74[199]



1-Phenylpropan-2-ol (10.0 g, 74.5 mmol), was dissolved in TFA (20 mL) and paraformaldehyde (3.8 g, 82.0 mmol) added in one portion at room temperature. The solution was allowed to stir for 30 mins before being diluted with ether and quenched with saturated aqueous $NaHCO_3$ and separated. The remaining aqueous layer was washed a further two times with ether (2 x 25 mL) and the organic layers combined and dried over $MgSO_4$ before solvents were removed under reduced pressure to yield the desired material as a light orange oil, no further purification was required, (11.70 g, >99%).

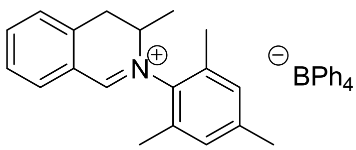
Known compound, data is consistent with literature data. υ_{max} (thin film)/cm^{-1} 3020, 1318, 742; δ_H (400 MHz, $CDCl_3$) 1.34 (3 H, d, *J* 6.0 Hz, C*H*$_3$), 1.68 (2 H, d, *J* 6.8 Hz, C*H*$_2$), 3.76-3.81 (1 H, m, C*H*), 4.81 (2 H, s, C*H*$_2$), 6.96-6.97 (1 H, m, Ar-*H*), 7.05-7.07 (1 H, m, Ar-*H*), 7.11-7.15 (2 H, m, Ar-*H*); δ_C (100 MHz, $CDCl_3$) 21.68 (C*H*$_3$), 35.83 (*C*H$_2$), 68.20 (*C*H$_2$), 71.00 (*C*H), 124.19 (Ar-*C*H), 125.98 (Ar-*C*H), 126.38 (Ar-*C*H), 128.77 (Ar-*C*H), 133.54 (Ar-*C*), 134.69 (Ar-*C*); *m/z* (FAB$^+$) 147 (100), 136 (42), 131 (28), 91 (25) HRMS (ES) calcd for $[C_{10}H_{11}O]^-$147.0809, found [M+] 147.080

Synthesis of 2-(2-bromopropyl)benzaldehyde 75



3,4-Dihydro-3-methyl-isochroman (5.1 g, 34.5 mmol) was dissolved in CCl_4 and the solution cooled to 0 °C in an ice bath. The flask was then fitted with a reflux condenser and molecular bromine (5.5 g, 34.5 mmol) added slowly over 5 mins down the condenser with vigorous stirring. Once the vigorous reaction had subsided the reaction was removed from the ice bath and placed on an already hot heating block (~100 °C) and an air condenser fitted to the reflux condenser. The reaction was allowed to reflux for 1 hour during which time the formation of HBr gas stopped and the reaction changed from dark red to light orange in colour. The reaction was allowed to cool before solvents were removed under reduced pressure to yield a dark orange oil. ^{1}H NMR of the crude material indicated that the required product had been formed and the material was purified using Kügelrohr distillation to yield the desired material, still not completely pure, as a yellow oil, (2.0 g, 25%). This product was carried on to the next step without further purification.

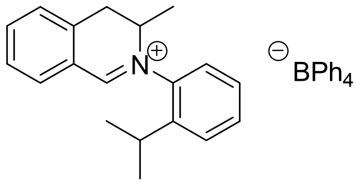
Synthesis of isoquinolium salt 76



2,4,6-Trimethylaniline (0.4 g, 2.75 mmol) was dissolved in ethanol (10 mL) and 2-(2-bromopropyl)benzaldehyde **75** (1.00 g, 4.4 mmol) added at room temperature. The reaction was allowed to stir for 18 h before sodium tetraphenylborate (1.0 g, 3.03 mmol) was added. The precipitate was collected via vacuum filtration and redissolved in dichloromethane (20 mL) before being washed with water (3 x 20 mL) and the organic layer dried with $MgSO_4$. The solvent was removed under reduced pressure to yield the desired material as a yellow crystalline solid (1.19 g, 74 %).

υ_{max} (thin film)/cm^{-1} 3055, 2114, 1627, 1566, 1473, 702; δ_H (400 MHz, DMSO-d$_6$) 1.19 (3 H, d, *J* 6.8 Hz, C*H*$_3$), 2.27 (3 H, s, C*H*$_3$), 2.34 (3 H, s, C*H*$_3$), 2.37 (3 H, s, C*H*$_3$), 3.32 (1 H, dd, *J* 6.4 Hz & *J* 16.8 Hz, 1 *H* of CH$_2$), 3.63 (1 H, dd, *J* 6.4 Hz & *J* 17.2 Hz, 1 *H* of CH$_2$), 4.69 (1 H, q, *J* 19.6 Hz, C*H*), 6.77-6.80 (4 H, m, Ar-*H*), 6.90-6.94 (8 H, m, Ar-*H*), 7.19-7.15 (10 H, m, Ar-*H*), 7.65 (2 H, m, Ar-*H*), 7.95 (1 H, dt, *J* 1.6 Hz & 7.6 Hz, Ar-*H*), 8.02 (1 H, dd, *J* 1.2 Hz & *J* 8.0 Hz, Ar-*H*), 9.46 (1 H, s, N=C-*H*); δ_C (100 MHz, DMSO-d$_6$) 15.83 (*C*H$_3$), 17.46 (*C*H$_3$), 17.62 (*C*H$_3$), 20.49 (*C*H$_3$), 31.71 (*C*H$_2$), 57.94 (*C*H), 121.48 (4 Ar-*C*H), 124.60 (Ar-*C*), 125.22 (4 Ar-*C*H), 125.28 (2 Ar-*C*H), 125.31 (2 Ar-*C*H), 128.43 (2 Ar-*C*H), 129.10 (2 Ar-*C*H), 130.91 (Ar-*C*), 132.55 (Ar-*C*), 134.72 (2 Ar-*C*H), 135.49 (6 Ar-*C*H), 136.50 (Ar-*C*), 137.37 (Ar-*C*), 139.08 (2 Ar-*C*H), 140.21 (Ar-*C*), 162.59 (Ar-*C*), 163.07 (Ar-*C*), 163.56 (Ar-*C*), 164.06 (Ar-*C*), 170.74 (*C*H=N); m.p. 180.2 °C; *m/z* (FAB$^+$) 264 (100) HRMS (ES) calcd for [$C_{19}H_{22}N$] 264.1752, found [M+] 264.1752

Synthesis of isoquinolium salt 77



2-Isopropylaniline (2.6 g, 18.9 mmol) was dissolved in ethanol (10 mL) and 2-(2-bromopropyl)benzaldehyde **75** (6.9 g, 30.3 mmol) added at room temperature. The reaction was allowed to stir for 18 h before sodium tetraphenylborate (7.11 g, 20.7 mmol) was added. The precipitate was collected via vacuum filtration and redissolved in dichloromethane (50 mL) before being washed with water (3 x 40 mL) and the organic layer dried with $MgSO_4$. The solvent was removed under reduced pressure to yield the desired material as a yellow crystalline solid (10.1 g, 92 %).

δ_H (400 MHz, DMSO-d_6) 1.18-1.24 (6 H, m, 2 i^-Pr C*H*$_3$), 1.35-1.36 (3 H, m, C*H*$_3$), 2.85-2.97 (1 H, m, C*H*), 3.02-3.13 (1 H, m, 1 *H* of CH_2), 3.25-3.35 (1 H, m, 1 *H* of CH_2), 3.66-3.83 (1 H, m, C*H*), 6.79-6.82 (4 H, m Ar-*H*), 6.92-6.96 (8 H, m, Ar-*H*), 7.19-7.22 (8 H, m, Ar-*H*), 7.45-7.48 (1 H, m, Ar-*H*), 7.61-7.71 (5 H, m, Ar-*H*), 7.89-7.96 (1 H, m, Ar-*H*), 7.97-8.03 (1 H, m, Ar-*H*), 9.54 (1 H, s, N=C-*H*); δ_C (100 MHz, DMSO-d_6) 15.96 (*C*H$_3$), 22.89 (*C*H$_3$), 24.70 (*C*H$_3$), 28.06 (*C*H), 31.46 (*C*H$_2$), 59.33 (*C*H), 121.51 (4 Ar-*C*H), 124.49 (Ar-*C*), 125.29 (8 Ar-*C*H), 126.62 (Ar-*C*H), 127.20 (Ar-*C*H), 127.85 (2 Ar-*C*H), 128.31 (Ar-*C*H), 129.23 (Ar-*C*H), 131.53 (Ar-*C*), 134.98 (Ar-*C*H), 135.53 (8 Ar-*C*H), 138.94 (Ar-*C*), 139.40 (Ar-*C*H), 143.16 (Ar-*C*), 162.61 (Ar-*C*), 163.10 (Ar-*C*), 163.59 (Ar-*C*), 164.08 (Ar-*C*), 169.72 (*C*H=N); m.p. 182.5 °C; HRMS (ES) calcd for [$C_{19}H_{22}N$] 264.1747, found [M+] 264.1737

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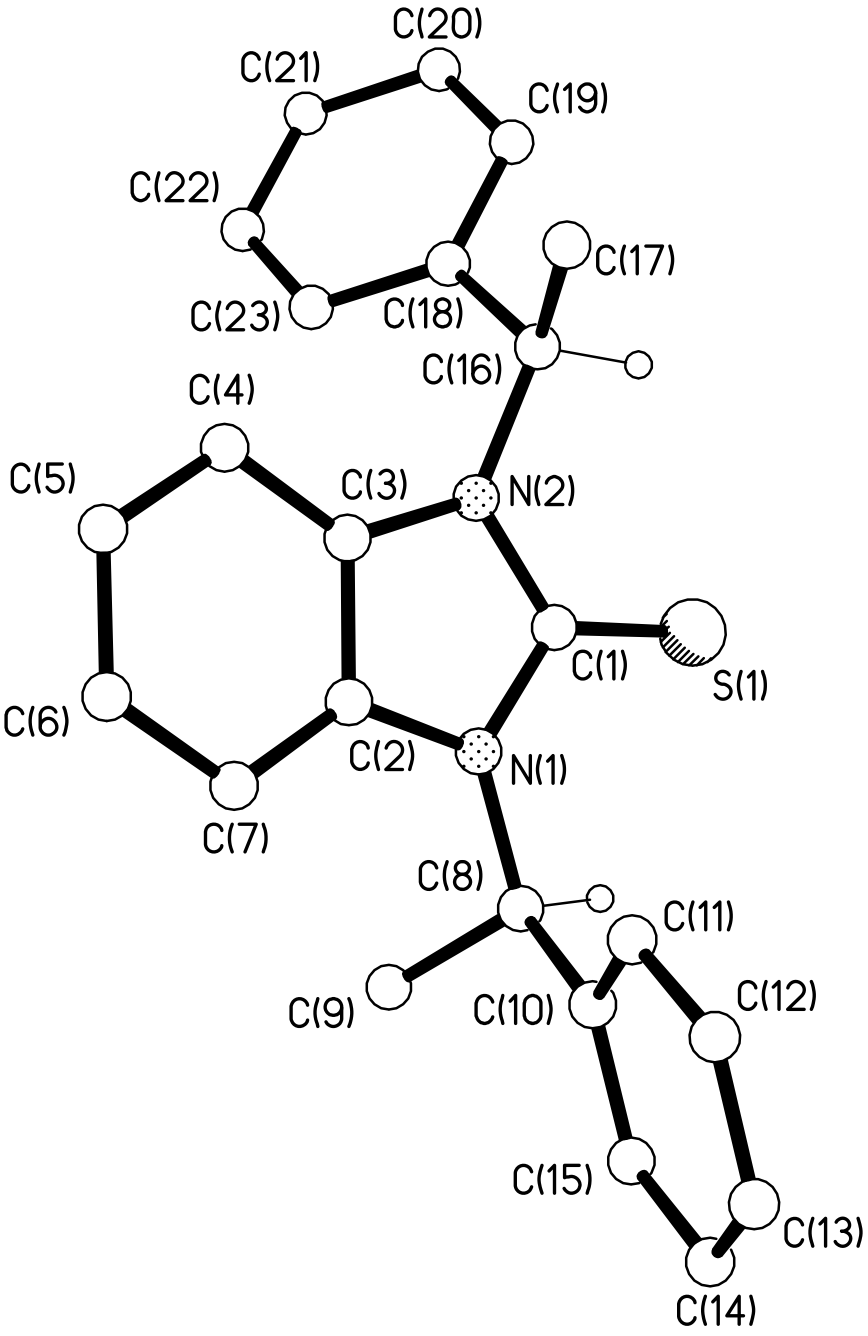
Appendix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C(11)
C(12)
C(9)
C(10)
C(15)
C(13)
C(14)

Table 1. Crystal data and structure refinement for sdrc16.

Identification code	sdrc16	
Chemical formula	$C_{23}H_{22}N_2S$	
Formula weight	358.49	
Temperature	150(2) K	
Radiation, wavelength	MoKα, 0.71073 Å	
Crystal system, space group	orthorhombic, $P2_12_12_1$	
Unit cell parameters	a = 8.4154(8) Å	α = 90°
	b = 10.2875(10) Å	β = 90°
	c = 20.961(2) Å	γ = 90°
Cell volume	1814.6(3) $Å^3$	
Z	4	
Calculated density	1.312 g/cm^3	
Absorption coefficient μ	0.187 mm^{-1}	
F(000)	760	
Crystal colour and size	pale yellow, 0.67 × 0.13 × 0.05 mm^3	
Reflections for cell refinement	6459 (θ range 2.20 to 26.21°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	2.21 to 26.46°	
Index ranges	h –10 to 10, k –12 to 12, l –26 to 26	
Completeness to θ = 26.46°	99.6 %	
Intensity decay	0%	
Reflections collected	16143	
Independent reflections	3746 (R_{int} = 0.0361)	
Reflections with $F^2>2\sigma$	3241	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.885 and 0.991	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.1149, 0.7007	
Data / restraints / parameters	3746 / 0 / 237	
Final R indices [$F^2>2\sigma$]	R1 = 0.0609, wR2 = 0.1728	
R indices (all data)	R1 = 0.0726, wR2 = 0.1835	
Goodness-of-fit on F^2	1.118	
Absolute structure parameter	0.13(18)	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.296 and –1.051 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc16. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
S(1)	0.02103(16)	0.59752(14)	0.23678(7)	0.0726(4)
C(1)	0.0686(3)	0.6022(3)	0.16718(14)	0.0251(6)
N(1)	0.1595(3)	0.6963(2)	0.13847(12)	0.0256(5)
N(2)	0.0279(3)	0.5131(2)	0.12121(11)	0.0256(5)
C(2)	0.1817(4)	0.6649(3)	0.07387(14)	0.0249(6)
C(3)	0.0980(4)	0.5494(3)	0.06299(14)	0.0246(6)
C(4)	0.0936(4)	0.4943(3)	0.00220(15)	0.0309(7)
C(5)	0.1767(4)	0.5576(3)	−0.04543(14)	0.0332(7)
C(6)	0.2627(4)	0.6694(3)	−0.03395(15)	0.0349(7)
C(7)	0.2685(4)	0.7250(3)	0.02646(14)	0.0295(7)
C(8)	0.2103(4)	0.8149(3)	0.17156(15)	0.0297(6)
C(9)	0.1510(6)	0.9358(3)	0.1366(2)	0.0536(11)
C(10)	0.3885(4)	0.8177(3)	0.18450(13)	0.0264(6)
C(11)	0.4869(4)	0.7121(3)	0.17210(14)	0.0299(7)
C(12)	0.6459(4)	0.7169(3)	0.18814(15)	0.0325(7)
C(13)	0.7108(4)	0.8266(3)	0.21572(15)	0.0361(7)
C(14)	0.6133(5)	0.9325(4)	0.22855(16)	0.0398(8)
C(15)	0.4528(4)	0.9278(3)	0.21286(15)	0.0346(7)
C(16)	−0.0502(4)	0.3905(3)	0.13738(15)	0.0272(6)
C(17)	0.0516(4)	0.2724(3)	0.1196(2)	0.0417(9)
C(18)	−0.2191(4)	0.3786(3)	0.11177(13)	0.0241(6)
C(19)	−0.3144(4)	0.2793(3)	0.13549(16)	0.0317(7)
C(20)	−0.4684(4)	0.2630(4)	0.11375(18)	0.0406(8)
C(21)	−0.5296(4)	0.3459(4)	0.06761(18)	0.0405(8)
C(22)	−0.4366(4)	0.4451(4)	0.04448(17)	0.0373(8)
C(23)	−0.2824(4)	0.4621(3)	0.06666(16)	0.0326(7)

Table 3. Bond lengths [Å] and angles [°] for sdrc16.

S(1)–C(1)	1.514(3)	C(1)–N(1)	1.372(4)
C(1)–N(2)	1.373(4)	N(1)–C(2)	1.404(4)
N(1)–C(8)	1.467(4)	N(2)–C(3)	1.406(4)
N(2)–C(16)	1.462(4)	C(2)–C(7)	1.379(4)
C(2)–C(3)	1.400(4)	C(3)–C(4)	1.395(4)
C(4)–C(5)	1.382(5)	C(5)–C(6)	1.380(5)
C(6)–C(7)	1.390(5)	C(8)–C(10)	1.524(4)
C(8)–C(9)	1.528(5)	C(10)–C(15)	1.389(4)
C(10)–C(11)	1.390(4)	C(11)–C(12)	1.381(5)
C(12)–C(13)	1.381(5)	C(13)–C(14)	1.389(5)
C(14)–C(15)	1.391(5)	C(16)–C(18)	1.524(4)
C(16)–C(17)	1.533(5)	C(18)–C(23)	1.384(4)
C(18)–C(19)	1.391(4)	C(19)–C(20)	1.384(5)
C(20)–C(21)	1.388(5)	C(21)–C(22)	1.375(5)
C(22)–C(23)	1.390(5)		
N(1)–C(1)–N(2)	107.6(2)	N(1)–C(1)–S(1)	126.3(2)
N(2)–C(1)–S(1)	126.1(2)	C(1)–N(1)–C(2)	109.6(2)
C(1)–N(1)–C(8)	122.8(2)	C(2)–N(1)–C(8)	127.4(3)
C(1)–N(2)–C(3)	109.1(2)	C(1)–N(2)–C(16)	121.7(2)
C(3)–N(2)–C(16)	128.3(3)	C(7)–C(2)–C(3)	121.9(3)

C(7)–C(2)–N(1)	131.5(3)	C(3)–C(2)–N(1)	106.5(2)
C(4)–C(3)–C(2)	120.5(3)	C(4)–C(3)–N(2)	132.3(3)
C(2)–C(3)–N(2)	107.2(2)	C(5)–C(4)–C(3)	117.1(3)
C(6)–C(5)–C(4)	122.1(3)	C(5)–C(6)–C(7)	121.4(3)
C(2)–C(7)–C(6)	117.0(3)	N(1)–C(8)–C(10)	112.8(2)
N(1)–C(8)–C(9)	110.8(3)	C(10)–C(8)–C(9)	113.0(3)
C(15)–C(10)–C(11)	119.0(3)	C(15)–C(10)–C(8)	118.4(3)
C(11)–C(10)–C(8)	122.5(3)	C(12)–C(11)–C(10)	120.3(3)
C(11)–C(12)–C(13)	120.9(3)	C(12)–C(13)–C(14)	119.2(3)
C(13)–C(14)–C(15)	120.0(3)	C(10)–C(15)–C(14)	120.5(3)
N(2)–C(16)–C(18)	114.0(2)	N(2)–C(16)–C(17)	112.1(3)
C(18)–C(16)–C(17)	111.8(3)	C(23)–C(18)–C(19)	118.6(3)
C(23)–C(18)–C(16)	123.3(3)	C(19)–C(18)–C(16)	118.1(3)
C(20)–C(19)–C(18)	120.8(3)	C(19)–C(20)–C(21)	120.1(3)
C(22)–C(21)–C(20)	119.4(3)	C(21)–C(22)–C(23)	120.5(3)
C(18)–C(23)–C(22)	120.7(3)		

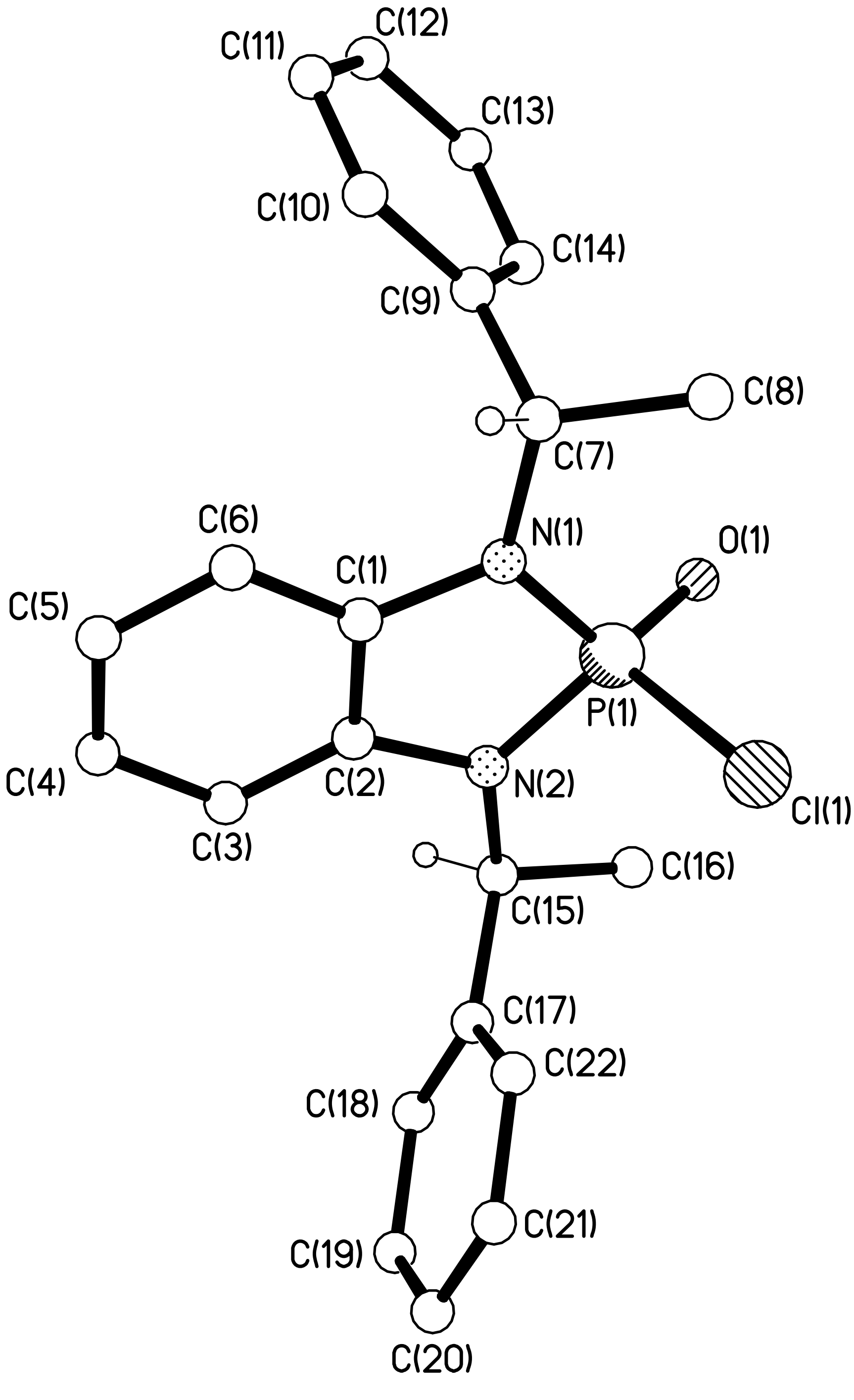
Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc16.

	x	y	z	U
H(4)	0.0360	0.4167	–0.0061	0.037
H(5)	0.1746	0.5229	–0.0874	0.040
H(6)	0.3190	0.7092	–0.0680	0.042
H(7)	0.3293	0.8009	0.0347	0.035
H(8)	0.1567	0.8143	0.2141	0.036
H(9A)	0.2105	0.9465	0.0968	0.080
H(9B)	0.1667	1.0124	0.1637	0.080
H(9C)	0.0376	0.9260	0.1270	0.080
H(11)	0.4445	0.6364	0.1525	0.036
H(12)	0.7116	0.6436	0.1801	0.039
H(13)	0.8208	0.8297	0.2258	0.043
H(14)	0.6563	1.0080	0.2480	0.048
H(15)	0.3867	1.0005	0.2216	0.041
H(16)	–0.0595	0.3893	0.1849	0.033
H(17A)	0.0671	0.2702	0.0733	0.062
H(17B)	–0.0022	0.1927	0.1333	0.062
H(17C)	0.1551	0.2787	0.1408	0.062
H(19)	–0.2733	0.2221	0.1670	0.038
H(20)	–0.5324	0.1949	0.1304	0.049
H(21)	–0.6347	0.3341	0.0522	0.049
H(22)	–0.4781	0.5025	0.0131	0.045
H(23)	–0.2197	0.5317	0.0507	0.039

Table 5. Torsion angles [°] for sdrc16.

N(2)–C(1)–N(1)–C(2)	–2.0(3)	S(1)–C(1)–N(1)–C(2)	178.3(2)
N(2)–C(1)–N(1)–C(8)	173.3(3)	S(1)–C(1)–N(1)–C(8)	–6.4(4)
N(1)–C(1)–N(2)–C(3)	1.8(3)	S(1)–C(1)–N(2)–C(3)	–178.5(2)
N(1)–C(1)–N(2)–C(16)	171.3(3)	S(1)–C(1)–N(2)–C(16)	–9.0(4)
C(1)–N(1)–C(2)–C(7)	–176.9(3)	C(8)–N(1)–C(2)–C(7)	8.1(5)
C(1)–N(1)–C(2)–C(3)	1.5(3)	C(8)–N(1)–C(2)–C(3)	–173.6(3)
C(7)–C(2)–C(3)–C(4)	–3.1(5)	N(1)–C(2)–C(3)–C(4)	178.4(3)
C(7)–C(2)–C(3)–N(2)	178.2(3)	N(1)–C(2)–C(3)–N(2)	–0.3(3)
C(1)–N(2)–C(3)–C(4)	–179.4(3)	C(16)–N(2)–C(3)–C(4)	12.0(5)
C(1)–N(2)–C(3)–C(2)	–0.9(3)	C(16)–N(2)–C(3)–C(2)	–169.5(3)
C(2)–C(3)–C(4)–C(5)	1.0(5)	N(2)–C(3)–C(4)–C(5)	179.3(3)
C(3)–C(4)–C(5)–C(6)	0.9(5)	C(4)–C(5)–C(6)–C(7)	–0.7(5)
C(3)–C(2)–C(7)–C(6)	3.2(5)	N(1)–C(2)–C(7)–C(6)	–178.7(3)
C(5)–C(6)–C(7)–C(2)	–1.4(5)	C(1)–N(1)–C(8)–C(10)	110.7(3)
C(2)–N(1)–C(8)–C(10)	–74.9(4)	C(1)–N(1)–C(8)–C(9)	–121.5(3)
C(2)–N(1)–C(8)–C(9)	52.9(4)	N(1)–C(8)–C(10)–C(15)	176.9(3)
C(9)–C(8)–C(10)–C(15)	50.3(4)	N(1)–C(8)–C(10)–C(11)	–6.5(4)
C(9)–C(8)–C(10)–C(11)	–133.2(3)	C(15)–C(10)–C(11)–C(12)	0.3(4)
C(8)–C(10)–C(11)–C(12)	–176.2(3)	C(10)–C(11)–C(12)–C(13)	–1.1(5)
C(11)–C(12)–C(13)–C(14)	1.3(5)	C(12)–C(13)–C(14)–C(15)	–0.9(5)
C(11)–C(10)–C(15)–C(14)	0.1(5)	C(8)–C(10)–C(15)–C(14)	176.8(3)
C(13)–C(14)–C(15)–C(10)	0.2(5)	C(1)–N(2)–C(16)–C(18)	114.3(3)
C(3)–N(2)–C(16)–C(18)	–78.4(4)	C(1)–N(2)–C(16)–C(17)	–117.4(3)
C(3)–N(2)–C(16)–C(17)	50.0(4)	N(2)–C(16)–C(18)–C(23)	12.8(4)
C(17)–C(16)–C(18)–C(23)	–115.7(3)	N(2)–C(16)–C(18)–C(19)	–166.7(3)
C(17)–C(16)–C(18)–C(19)	64.9(4)	C(23)–C(18)–C(19)–C(20)	1.0(5)
C(16)–C(18)–C(19)–C(20)	–179.5(3)	C(18)–C(19)–C(20)–C(21)	0.2(5)
C(19)–C(20)–C(21)–C(22)	–0.9(5)	C(20)–C(21)–C(22)–C(23)	0.4(5)
C(19)–C(18)–C(23)–C(22)	–1.5(5)	C(16)–C(18)–C(23)–C(22)	179.1(3)
C(21)–C(22)–C(23)–C(18)	0.8(5)		

sdrc18 fig.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C(20)

Table 1. Crystal data and structure refinement for sdrc18.

Identification code	sdrc18	
Chemical formula	$C_{22}H_{22}ClN_2OP$	
Formula weight	396.84	
Temperature	150(2) K	
Radiation, wavelength	MoKα, 0.71073 Å	
Crystal system, space group	monoclinic, $P2_1$	
Unit cell parameters	a = 9.3440(10) Å	α = 90°
	b = 11.2086(12) Å	β = 103.3773(15)°
	c = 9.6949(10) Å	γ = 90°
Cell volume	987.83(18) $Å^3$	
Z	2	
Calculated density	1.334 g/cm^3	
Absorption coefficient μ	0.289 mm^{-1}	
F(000)	416	
Crystal colour and size	colourless, 0.65 × 0.45 × 0.12 mm^3	
Reflections for cell refinement	5468 (θ range 2.24 to 30.49°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	2.16 to 30.56°	
Index ranges	h –13 to 13, k –15 to 15, l –13 to 13	
Completeness to θ = 29.00°	100.0 %	
Intensity decay	0%	
Reflections collected	11570	
Independent reflections	5819 (R_{int} = 0.0240)	
Reflections with $F^2>2\sigma$	5479	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.835 and 0.966	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0582, 0.0570	
Data / restraints / parameters	5819 / 1 / 246	
Final R indices [$F^2>2\sigma$]	R1 = 0.0355, wR2 = 0.0907	
R indices (all data)	R1 = 0.0381, wR2 = 0.0930	
Goodness-of-fit on F^2	1.030	
Absolute structure parameter	–0.01(4)	
Largest and mean shift/su	0.001 and 0.000	
Largest diff. peak and hole	0.553 and –0.193 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc18. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
P(1)	0.76060(4)	0.76927(3)	0.10516(4)	0.02120(8)
Cl(1)	0.66196(5)	0.63491(4)	0.19238(4)	0.03282(10)
O(1)	0.67657(12)	0.78148(13)	−0.04174(11)	0.0311(2)
N(1)	0.93833(13)	0.73865(11)	0.13654(13)	0.0213(2)
N(2)	0.78022(13)	0.88309(11)	0.21696(13)	0.0218(2)
C(1)	1.02006(16)	0.81703(13)	0.23873(15)	0.0211(3)
C(2)	0.92962(15)	0.90109(13)	0.28396(14)	0.0207(3)
C(3)	0.98848(18)	0.99123(15)	0.37712(17)	0.0273(3)
C(4)	1.14159(19)	0.99500(17)	0.42716(19)	0.0336(4)
C(5)	1.23057(18)	0.9109(2)	0.38430(17)	0.0340(4)
C(6)	1.17154(17)	0.82040(16)	0.28994(17)	0.0277(3)
C(7)	1.01136(17)	0.65070(14)	0.06203(16)	0.0247(3)
C(8)	0.9053(2)	0.55404(16)	−0.0117(2)	0.0356(4)
C(9)	1.08509(17)	0.71248(13)	−0.04338(16)	0.0237(3)
C(10)	1.23618(18)	0.70568(16)	−0.02835(18)	0.0295(3)
C(11)	1.30319(18)	0.75895(18)	−0.12724(19)	0.0336(4)
C(12)	1.2182(2)	0.81724(17)	−0.2426(2)	0.0353(4)
C(13)	1.0668(2)	0.82392(18)	−0.2598(2)	0.0355(4)
C(14)	1.00109(17)	0.77246(17)	−0.15972(17)	0.0298(3)
C(15)	0.66698(17)	0.96561(14)	0.24578(16)	0.0252(3)
C(16)	0.51869(19)	0.9485(2)	0.14151(18)	0.0377(4)
C(17)	0.65018(16)	0.95759(14)	0.39762(16)	0.0236(3)
C(18)	0.60981(19)	1.06097(15)	0.45890(19)	0.0302(3)
C(19)	0.58340(19)	1.05759(17)	0.5942(2)	0.0337(4)
C(20)	0.59904(19)	0.95208(19)	0.67072(18)	0.0332(4)
C(21)	0.64010(18)	0.84870(18)	0.61039(17)	0.0304(3)
C(22)	0.66627(17)	0.85196(15)	0.47433(16)	0.0262(3)

Table 3. Bond lengths [Å] and angles [°] for sdrc18.

P(1)–O(1)	1.4650(11)	P(1)–N(1)	1.6536(12)
P(1)–N(2)	1.6566(13)	P(1)–Cl(1)	2.0477(5)
N(1)–C(1)	1.4095(19)	N(1)–C(7)	1.4789(18)
N(2)–C(2)	1.4114(18)	N(2)–C(15)	1.4798(18)
C(1)–C(6)	1.388(2)	C(1)–C(2)	1.402(2)
C(2)–C(3)	1.382(2)	C(3)–C(4)	1.401(2)
C(4)–C(5)	1.383(3)	C(5)–C(6)	1.391(3)
C(7)–C(9)	1.525(2)	C(7)–C(8)	1.530(2)
C(9)–C(10)	1.387(2)	C(9)–C(14)	1.389(2)
C(10)–C(11)	1.395(2)	C(11)–C(12)	1.377(3)
C(12)–C(13)	1.387(3)	C(13)–C(14)	1.388(2)
C(15)–C(17)	1.519(2)	C(15)–C(16)	1.527(2)
C(17)–C(22)	1.388(2)	C(17)–C(18)	1.393(2)
C(18)–C(19)	1.390(3)	C(19)–C(20)	1.386(3)
C(20)–C(21)	1.391(3)	C(21)–C(22)	1.397(2)
O(1)–P(1)–N(1)	119.20(6)	O(1)–P(1)–N(2)	121.16(7)
N(1)–P(1)–N(2)	94.88(6)	O(1)–P(1)–Cl(1)	106.20(6)
N(1)–P(1)–Cl(1)	107.47(5)	N(2)–P(1)–Cl(1)	106.76(5)
C(1)–N(1)–C(7)	121.51(12)	C(1)–N(1)–P(1)	110.96(10)

C(7)–N(1)–P(1)	127.28(10)	C(2)–N(2)–C(15)	119.87(12)
C(2)–N(2)–P(1)	111.05(9)	C(15)–N(2)–P(1)	128.99(10)
C(6)–C(1)–C(2)	120.56(14)	C(6)–C(1)–N(1)	127.61(13)
C(2)–C(1)–N(1)	111.77(12)	C(3)–C(2)–C(1)	121.21(14)
C(3)–C(2)–N(2)	127.39(13)	C(1)–C(2)–N(2)	111.32(12)
C(2)–C(3)–C(4)	117.95(15)	C(5)–C(4)–C(3)	120.80(16)
C(4)–C(5)–C(6)	121.33(15)	C(1)–C(6)–C(5)	118.13(15)
N(1)–C(7)–C(9)	110.84(12)	N(1)–C(7)–C(8)	112.21(13)
C(9)–C(7)–C(8)	110.67(13)	C(10)–C(9)–C(14)	118.80(14)
C(10)–C(9)–C(7)	120.75(15)	C(14)–C(9)–C(7)	120.39(14)
C(9)–C(10)–C(11)	120.80(16)	C(12)–C(11)–C(10)	119.67(15)
C(11)–C(12)–C(13)	120.23(15)	C(12)–C(13)–C(14)	119.81(17)
C(13)–C(14)–C(9)	120.68(15)	N(2)–C(15)–C(17)	112.63(12)
N(2)–C(15)–C(16)	112.07(13)	C(17)–C(15)–C(16)	110.66(13)
C(22)–C(17)–C(18)	119.17(14)	C(22)–C(17)–C(15)	123.18(14)
C(18)–C(17)–C(15)	117.58(14)	C(19)–C(18)–C(17)	120.29(16)
C(20)–C(19)–C(18)	120.56(16)	C(19)–C(20)–C(21)	119.41(15)
C(20)–C(21)–C(22)	120.06(17)	C(17)–C(22)–C(21)	120.50(16)

Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc18.

	x	y	z	U
H(3)	0.9270	1.0489	0.4063	0.033
H(4)	1.1848	1.0561	0.4913	0.040
H(5)	1.3341	0.9149	0.4200	0.041
H(6)	1.2332	0.7626	0.2614	0.033
H(7)	1.0901	0.6106	0.1347	0.030
H(8A)	0.8624	0.5130	0.0584	0.053
H(8B)	0.9588	0.4964	–0.0569	0.053
H(8C)	0.8267	0.5908	–0.0839	0.053
H(10)	1.2947	0.6642	0.0502	0.035
H(11)	1.4069	0.7551	–0.1151	0.040
H(12)	1.2634	0.8530	–0.3106	0.042
H(13)	1.0083	0.8636	–0.3399	0.043
H(14)	0.8976	0.7783	–0.1709	0.036
H(15)	0.7007	1.0485	0.2318	0.030
H(16A)	0.5314	0.9557	0.0443	0.057
H(16B)	0.4497	1.0097	0.1583	0.057
H(16C)	0.4798	0.8693	0.1550	0.057
H(18)	0.6003	1.1341	0.4080	0.036
H(19)	0.5544	1.1282	0.6346	0.040
H(20)	0.5819	0.9503	0.7635	0.040
H(21)	0.6503	0.7758	0.6618	0.037
H(22)	0.6953	0.7813	0.4340	0.031

Table 5. Torsion angles [°] for sdrc18.

O(1)–P(1)–N(1)–C(1)	130.74(11)	N(2)–P(1)–N(1)–C(1)	0.75(11)
Cl(1)–P(1)–N(1)–C(1)	−108.54(9)	O(1)–P(1)–N(1)–C(7)	−43.49(15)
N(2)–P(1)–N(1)–C(7)	−173.47(12)	Cl(1)–P(1)–N(1)–C(7)	77.24(12)
O(1)–P(1)–N(2)–C(2)	−128.65(10)	N(1)–P(1)–N(2)–C(2)	−0.06(10)
Cl(1)–P(1)–N(2)–C(2)	109.84(9)	O(1)–P(1)–N(2)–C(15)	47.86(15)
N(1)–P(1)–N(2)–C(15)	176.45(12)	Cl(1)–P(1)–N(2)–C(15)	−73.64(13)
C(7)–N(1)–C(1)–C(6)	−4.0(2)	P(1)–N(1)–C(1)–C(6)	−178.64(13)
C(7)–N(1)–C(1)–C(2)	173.36(12)	P(1)–N(1)–C(1)–C(2)	−1.25(15)
C(6)–C(1)–C(2)–C(3)	1.8(2)	N(1)–C(1)–C(2)–C(3)	−175.75(13)
C(6)–C(1)–C(2)–N(2)	178.80(13)	N(1)–C(1)–C(2)–N(2)	1.21(16)
C(15)–N(2)–C(2)–C(3)	−0.8(2)	P(1)–N(2)–C(2)–C(3)	176.07(13)
C(15)–N(2)–C(2)–C(1)	−177.53(12)	P(1)–N(2)–C(2)–C(1)	−0.65(14)
C(1)–C(2)–C(3)–C(4)	−1.1(2)	N(2)–C(2)–C(3)–C(4)	−177.50(14)
C(2)–C(3)–C(4)–C(5)	0.0(3)	C(3)–C(4)–C(5)–C(6)	0.3(3)
C(2)–C(1)–C(6)–C(5)	−1.5(2)	N(1)–C(1)–C(6)–C(5)	175.71(15)
C(4)–C(5)–C(6)–C(1)	0.4(3)	C(1)–N(1)–C(7)–C(9)	−71.47(17)
P(1)–N(1)–C(7)–C(9)	102.21(14)	C(1)–N(1)–C(7)–C(8)	164.24(14)
P(1)–N(1)–C(7)–C(8)	−22.08(19)	N(1)–C(7)–C(9)–C(10)	117.97(16)
C(8)–C(7)–C(9)–C(10)	−116.87(16)	N(1)–C(7)–C(9)–C(14)	−64.75(19)
C(8)–C(7)–C(9)–C(14)	60.4(2)	C(14)–C(9)–C(10)–C(11)	0.6(2)
C(7)–C(9)–C(10)–C(11)	177.94(16)	C(9)–C(10)–C(11)–C(12)	−1.2(3)
C(10)–C(11)–C(12)–C(13)	0.6(3)	C(11)–C(12)–C(13)–C(14)	0.5(3)
C(12)–C(13)–C(14)–C(9)	−1.1(3)	C(10)–C(9)–C(14)–C(13)	0.5(3)
C(7)–C(9)–C(14)–C(13)	−176.84(16)	C(2)–N(2)–C(15)–C(17)	−66.73(17)
P(1)–N(2)–C(15)–C(17)	117.02(14)	C(2)–N(2)–C(15)–C(16)	167.71(14)
P(1)–N(2)–C(15)–C(16)	−8.54(19)	N(2)–C(15)–C(17)–C(22)	−34.6(2)
C(16)–C(15)–C(17)–C(22)	91.76(18)	N(2)–C(15)–C(17)–C(18)	148.56(14)
C(16)–C(15)–C(17)–C(18)	−85.12(19)	C(22)–C(17)–C(18)–C(19)	−1.2(2)
C(15)–C(17)–C(18)–C(19)	175.83(15)	C(17)–C(18)–C(19)–C(20)	1.0(3)
C(18)–C(19)–C(20)–C(21)	−0.7(3)	C(19)–C(20)–C(21)–C(22)	0.5(3)
C(18)–C(17)–C(22)–C(21)	1.0(2)	C(15)–C(17)–C(22)–C(21)	−175.82(15)
C(20)–C(21)–C(22)–C(17)	−0.7(2)		

SDRC30 Fig

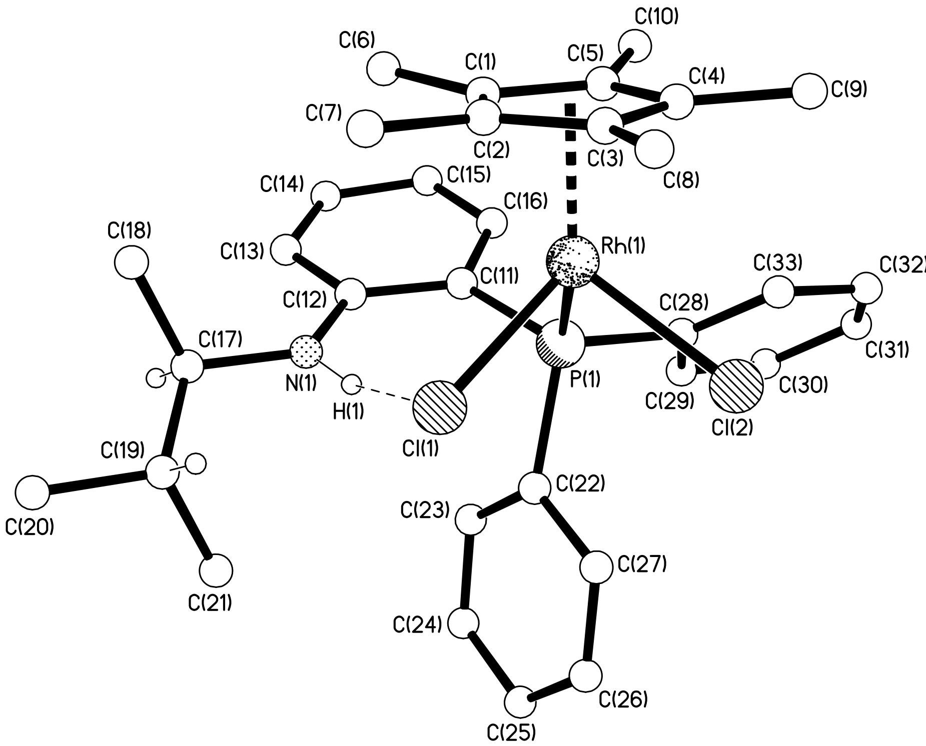

C(10)
C(6)
C(1)
C(5)
C(4)
C(9)
C(7)
C(2)
C(3)
C(8)
C(14)
C(15)
C(16)
C(18)
C(13)
Rh(1)
C(33)
C(32)
C(12)
C(11)
C(28)
C(17)
N(1)
P(1)
C(31)
H(1)
C(29)
Cl(2)
C(30)
Cl(1)
C(19)
C(22)
C(23)
C(20)
C(27)
C(21)
C(24)
C(26)
C(25)

Table 1. Crystal data and structure refinement for sdrc30.

Identification code	sdrc30	
Chemical formula	$C_{37}H_{51}Cl_2NOPRh$	
Formula weight	730.57	
Temperature	150(2) K	
Radiation, wavelength	MoKα, 0.71073 Å	
Crystal system, space group	monoclinic, $P2_1$	
Unit cell parameters	a = 10.494(2) Å	α = 90°
	b = 9.0286(17) Å	β = 91.685(4)°
	c = 18.950(4) Å	γ = 90°
Cell volume	1794.6(6) $Å^3$	
Z	2	
Calculated density	1.352 g/cm^3	
Absorption coefficient μ	0.698 mm^{-1}	
F(000)	764	
Crystal colour and size	red, 0.13 × 0.11 × 0.03 mm^3	
Reflections for cell refinement	1233 (θ range 2.15 to 16.61°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	1.94 to 26.45°	
Index ranges	h −13 to 13, k 0 to 11, l 0 to 23	
Completeness to θ = 26.45°	99.9 %	
Intensity decay	0%	
Reflections collected	31884	
Independent reflections	3951 (R_{int} = 0.1891)	
Reflections with F^2>2σ	2769	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.915 and 0.979	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0373, 0.0000	
Data / restraints / parameters	3951 / 1 / 398	
Final R indices [F^2>2σ]	R1 = 0.0552, wR2 = 0.0905	
R indices (all data)	R1 = 0.0862, wR2 = 0.1007	
Goodness-of-fit on F^2	0.960	
Largest and mean shift/su	0.001 and 0.000	
Largest diff. peak and hole	0.573 and −0.613 e $Å^{-3}$	

Absolute structure unreliable due to twinning. Friedel pairs merged. Enantiomer set from known chiral centre in the ligand.

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc30. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
Rh(1)	0.02452(5)	0.28266(7)	0.15822(3)	0.02326(16)
Cl(1)	0.0981(2)	0.0431(3)	0.12545(13)	0.0325(6)
Cl(2)	−0.1667(2)	0.1671(3)	0.19885(13)	0.0360(6)
C(1)	0.1305(8)	0.4558(9)	0.1023(4)	0.022(2)
C(2)	0.0596(8)	0.3682(9)	0.0511(4)	0.027(2)
C(3)	−0.0715(8)	0.3769(10)	0.0636(5)	0.034(2)
C(4)	−0.0851(8)	0.4766(10)	0.1221(5)	0.028(2)
C(5)	0.0360(9)	0.5255(10)	0.1462(4)	0.029(2)
C(6)	0.2687(8)	0.4884(10)	0.1024(5)	0.036(2)
C(7)	0.1194(8)	0.2820(15)	−0.0093(4)	0.042(2)
C(8)	−0.1773(8)	0.3057(14)	0.0224(5)	0.050(3)
C(9)	−0.2102(9)	0.5271(12)	0.1486(6)	0.053(3)
C(10)	0.0657(10)	0.6428(10)	0.1986(5)	0.045(3)
P(1)	0.13000(19)	0.2611(3)	0.26871(11)	0.0226(6)
C(11)	0.2890(7)	0.3414(9)	0.2721(4)	0.0228(19)
C(12)	0.3909(6)	0.2783(13)	0.2337(4)	0.0229(16)
C(13)	0.5111(8)	0.3439(10)	0.2397(4)	0.032(2)
C(14)	0.5305(9)	0.4708(10)	0.2791(5)	0.033(2)
C(15)	0.4303(9)	0.5381(10)	0.3121(5)	0.036(2)
C(16)	0.3134(8)	0.4715(10)	0.3076(4)	0.026(2)
N(1)	0.3748(7)	0.1535(8)	0.1929(4)	0.0342(19)
C(17)	0.4735(8)	0.0832(9)	0.1512(5)	0.027(2)
C(18)	0.4975(9)	0.1690(12)	0.0839(5)	0.051(3)
C(19)	0.4391(9)	−0.0784(10)	0.1360(5)	0.037(2)
C(20)	0.5425(10)	−0.1552(12)	0.0940(6)	0.065(4)
C(21)	0.4182(12)	−0.1620(11)	0.2032(6)	0.066(4)
C(22)	0.1548(8)	0.0780(9)	0.3088(4)	0.026(2)
C(23)	0.2676(9)	0.0443(10)	0.3451(4)	0.032(2)
C(24)	0.2807(8)	−0.0856(10)	0.3839(5)	0.035(2)
C(25)	0.1773(9)	−0.1845(10)	0.3861(4)	0.036(3)
C(26)	0.0660(10)	−0.1510(9)	0.3496(4)	0.035(2)
C(27)	0.0507(8)	−0.0211(9)	0.3111(4)	0.029(2)
C(28)	0.0497(8)	0.3517(9)	0.3415(4)	0.024(2)
C(29)	0.1038(9)	0.3523(10)	0.4103(5)	0.039(2)
C(30)	0.0428(11)	0.4203(12)	0.4654(5)	0.049(3)
C(31)	−0.0759(10)	0.4846(11)	0.4530(5)	0.048(3)
C(32)	−0.1319(9)	0.4828(11)	0.3868(5)	0.039(2)
C(33)	−0.0698(8)	0.4174(10)	0.3311(5)	0.031(2)
C(34)	0.7035(11)	−0.1150(14)	0.3484(6)	0.070(4)
C(35)	0.6762(12)	0.0459(15)	0.3621(7)	0.077(4)
O(1)	0.5947(7)	0.0536(9)	0.4202(4)	0.065(2)
C(36)	0.5687(11)	0.2064(13)	0.4405(6)	0.058(3)
C(37)	0.4703(13)	0.1983(15)	0.4975(7)	0.080(4)

Table 3. Bond lengths [Å] and angles [°] for sdrc30.

Rh(1)–C(4)	2.194(8)	Rh(1)–C(3)	2.201(9)
Rh(1)–C(1)	2.207(8)	Rh(1)–C(5)	2.208(9)
Rh(1)–C(2)	2.213(8)	Rh(1)–P(1)	2.347(2)
Rh(1)–Cl(1)	2.385(2)	Rh(1)–Cl(2)	2.408(2)
C(1)–C(2)	1.442(11)	C(1)–C(5)	1.455(11)
C(1)–C(6)	1.480(11)	C(2)–C(3)	1.405(11)
C(2)–C(7)	1.534(12)	C(3)–C(4)	1.437(12)
C(3)–C(8)	1.485(11)	C(4)–C(5)	1.409(12)
C(4)–C(9)	1.491(11)	C(5)–C(10)	1.480(12)
P(1)–C(11)	1.819(8)	P(1)–C(28)	1.830(8)
P(1)–C(22)	1.835(9)	C(11)–C(16)	1.375(11)
C(11)–C(12)	1.429(10)	C(12)–N(1)	1.374(12)
C(12)–C(13)	1.395(11)	C(13)–C(14)	1.380(11)
C(14)–C(15)	1.380(12)	C(15)–C(16)	1.366(11)
N(1)–C(17)	1.465(10)	C(17)–C(18)	1.520(12)
C(17)–C(19)	1.528(12)	C(19)–C(21)	1.504(13)
C(19)–C(20)	1.529(13)	C(22)–C(23)	1.385(11)
C(22)–C(27)	1.413(11)	C(23)–C(24)	1.388(12)
C(24)–C(25)	1.406(12)	C(25)–C(26)	1.374(12)
C(26)–C(27)	1.388(11)	C(28)–C(33)	1.396(11)
C(28)–C(29)	1.406(11)	C(29)–C(30)	1.383(12)
C(30)–C(31)	1.389(13)	C(31)–C(32)	1.370(13)
C(32)–C(33)	1.389(11)	C(34)–C(35)	1.504(15)
C(35)–O(1)	1.416(12)	O(1)–C(36)	1.460(12)
C(36)–C(37)	1.517(16)		

C(4)–Rh(1)–C(3)	38.2(3)	C(4)–Rh(1)–C(1)	63.4(3)
C(3)–Rh(1)–C(1)	63.9(3)	C(4)–Rh(1)–C(5)	37.3(3)
C(3)–Rh(1)–C(5)	63.7(3)	C(1)–Rh(1)–C(5)	38.5(3)
C(4)–Rh(1)–C(2)	62.3(3)	C(3)–Rh(1)–C(2)	37.1(3)
C(1)–Rh(1)–C(2)	38.1(3)	C(5)–Rh(1)–C(2)	63.1(3)
C(4)–Rh(1)–P(1)	125.0(3)	C(3)–Rh(1)–P(1)	162.0(2)
C(1)–Rh(1)–P(1)	104.8(2)	C(5)–Rh(1)–P(1)	98.6(2)
C(2)–Rh(1)–P(1)	139.5(2)	C(4)–Rh(1)–Cl(1)	144.4(3)
C(3)–Rh(1)–Cl(1)	106.4(2)	C(1)–Rh(1)–Cl(1)	110.2(3)
C(5)–Rh(1)–Cl(1)	148.7(3)	C(2)–Rh(1)–Cl(1)	90.8(2)
P(1)–Rh(1)–Cl(1)	90.53(9)	C(4)–Rh(1)–Cl(2)	90.7(2)
C(3)–Rh(1)–Cl(2)	93.6(2)	C(1)–Rh(1)–Cl(2)	153.7(2)
C(5)–Rh(1)–Cl(2)	120.8(2)	C(2)–Rh(1)–Cl(2)	127.4(2)
P(1)–Rh(1)–Cl(2)	93.11(8)	Cl(1)–Rh(1)–Cl(2)	88.24(9)
C(2)–C(1)–C(5)	105.9(7)	C(2)–C(1)–C(6)	126.6(8)
C(5)–C(1)–C(6)	126.7(8)	C(2)–C(1)–Rh(1)	71.2(5)
C(5)–C(1)–Rh(1)	70.8(5)	C(6)–C(1)–Rh(1)	130.3(6)
C(3)–C(2)–C(1)	110.1(7)	C(3)–C(2)–C(7)	125.4(8)
C(1)–C(2)–C(7)	124.5(8)	C(3)–C(2)–Rh(1)	71.0(5)
C(1)–C(2)–Rh(1)	70.8(4)	C(7)–C(2)–Rh(1)	126.2(6)
C(2)–C(3)–C(4)	106.6(8)	C(2)–C(3)–C(8)	127.4(9)
C(4)–C(3)–C(8)	125.9(8)	C(2)–C(3)–Rh(1)	71.9(5)
C(4)–C(3)–Rh(1)	70.6(5)	C(8)–C(3)–Rh(1)	125.3(7)
C(5)–C(4)–C(3)	109.7(8)	C(5)–C(4)–C(9)	126.1(9)
C(3)–C(4)–C(9)	124.0(9)	C(5)–C(4)–Rh(1)	71.9(5)
C(3)–C(4)–Rh(1)	71.2(5)	C(9)–C(4)–Rh(1)	126.7(6)
C(4)–C(5)–C(1)	107.6(8)	C(4)–C(5)–C(10)	127.8(9)
C(1)–C(5)–C(10)	124.0(9)	C(4)–C(5)–Rh(1)	70.8(5)

C(1)–C(5)–Rh(1)	70.7(5)	C(10)–C(5)–Rh(1)	130.7(6)
C(11)–P(1)–C(28)	103.7(4)	C(11)–P(1)–C(22)	103.0(4)
C(28)–P(1)–C(22)	98.8(4)	C(11)–P(1)–Rh(1)	114.0(3)
C(28)–P(1)–Rh(1)	114.8(3)	C(22)–P(1)–Rh(1)	120.1(3)
C(16)–C(11)–C(12)	117.3(8)	C(16)–C(11)–P(1)	121.0(6)
C(12)–C(11)–P(1)	121.5(6)	N(1)–C(12)–C(13)	119.3(8)
N(1)–C(12)–C(11)	122.1(7)	C(13)–C(12)–C(11)	118.5(9)
C(14)–C(13)–C(12)	121.0(9)	C(13)–C(14)–C(15)	120.5(9)
C(16)–C(15)–C(14)	118.3(9)	C(15)–C(16)–C(11)	124.0(8)
C(12)–N(1)–C(17)	125.6(7)	N(1)–C(17)–C(18)	111.6(7)
N(1)–C(17)–C(19)	110.4(7)	C(18)–C(17)–C(19)	111.8(7)
C(21)–C(19)–C(17)	111.0(8)	C(21)–C(19)–C(20)	109.7(8)
C(17)–C(19)–C(20)	111.3(8)	C(23)–C(22)–C(27)	119.7(8)
C(23)–C(22)–P(1)	120.8(7)	C(27)–C(22)–P(1)	118.8(7)
C(22)–C(23)–C(24)	121.2(9)	C(23)–C(24)–C(25)	119.2(8)
C(26)–C(25)–C(24)	119.3(8)	C(25)–C(26)–C(27)	122.3(9)
C(26)–C(27)–C(22)	118.3(9)	C(33)–C(28)–C(29)	117.7(8)
C(33)–C(28)–P(1)	121.0(6)	C(29)–C(28)–P(1)	121.2(6)
C(30)–C(29)–C(28)	121.2(9)	C(29)–C(30)–C(31)	119.4(10)
C(32)–C(31)–C(30)	120.5(9)	C(31)–C(32)–C(33)	120.2(9)
C(32)–C(33)–C(28)	120.9(9)	O(1)–C(35)–C(34)	107.7(10)
C(35)–O(1)–C(36)	112.0(9)	O(1)–C(36)–C(37)	106.2(10)

Table 4 Hydrogen bonds for sdrc30 [Å and °].

D–H...A	d(D–H)	d(H...A)	d(D...A)	<(DHA)
N(1)–H(1)...Cl(1)	0.88	2.50	3.293(8)	150.2

Table 5 Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc30.

	x	y	z	U
H(6A)	0.2834	0.5780	0.0746	0.054
H(6B)	0.3140	0.4048	0.0816	0.054
H(6C)	0.3002	0.5039	0.1510	0.054
H(7A)	0.0924	0.1782	–0.0075	0.064
H(7B)	0.2125	0.2874	–0.0045	0.064
H(7C)	0.0916	0.3253	–0.0546	0.064
H(8A)	–0.2266	0.3818	–0.0033	0.075
H(8B)	–0.2330	0.2530	0.0546	0.075
H(8C)	–0.1422	0.2354	–0.0113	0.075
H(9A)	–0.1968	0.5782	0.1938	0.079
H(9B)	–0.2658	0.4413	0.1551	0.079
H(9C)	–0.2503	0.5951	0.1143	0.079
H(10A)	0.0709	0.7387	0.1746	0.068
H(10B)	0.1475	0.6211	0.2227	0.068
H(10C)	–0.0017	0.6465	0.2334	0.068
H(13)	0.5807	0.3005	0.2163	0.039
H(14)	0.6136	0.5123	0.2836	0.039
H(15)	0.4422	0.6283	0.3372	0.043
H(16)	0.2447	0.5180	0.3305	0.031
H(1)	0.2988	0.1123	0.1918	0.041
H(17)	0.5545	0.0838	0.1804	0.033

H(18A)	0.4206	0.1667	0.0533	0.077
H(18B)	0.5685	0.1236	0.0593	0.077
H(18C)	0.5188	0.2719	0.0958	0.077
H(19)	0.3579	–0.0803	0.1070	0.044
H(20A)	0.6247	–0.1463	0.1196	0.097
H(20B)	0.5481	–0.1083	0.0476	0.097
H(20C)	0.5209	–0.2601	0.0880	0.097
H(21A)	0.4935	–0.1520	0.2347	0.099
H(21B)	0.4038	–0.2669	0.1924	0.099
H(21C)	0.3436	–0.1217	0.2265	0.099
H(23)	0.3373	0.1113	0.3435	0.038
H(24)	0.3585	–0.1074	0.4086	0.042
H(25)	0.1845	–0.2736	0.4126	0.043
H(26)	–0.0029	–0.2192	0.3507	0.042
H(27)	–0.0276	0.0007	0.2869	0.034
H(29)	0.1836	0.3053	0.4191	0.047
H(30)	0.0819	0.4229	0.5112	0.059
H(31)	–0.1187	0.5303	0.4908	0.058
H(32)	–0.2135	0.5263	0.3790	0.047
H(33)	–0.1091	0.4174	0.2853	0.037
H(34A)	0.7422	–0.1598	0.3910	0.105
H(34B)	0.7624	–0.1236	0.3094	0.105
H(34C)	0.6237	–0.1664	0.3360	0.105
H(35A)	0.7566	0.0997	0.3729	0.092
H(35B)	0.6345	0.0915	0.3199	0.092
H(36A)	0.5351	0.2636	0.3995	0.070
H(36B)	0.6475	0.2549	0.4589	0.070
H(37A)	0.3884	0.1665	0.4766	0.120
H(37B)	0.4607	0.2963	0.5190	0.120
H(37C)	0.4984	0.1271	0.5337	0.120

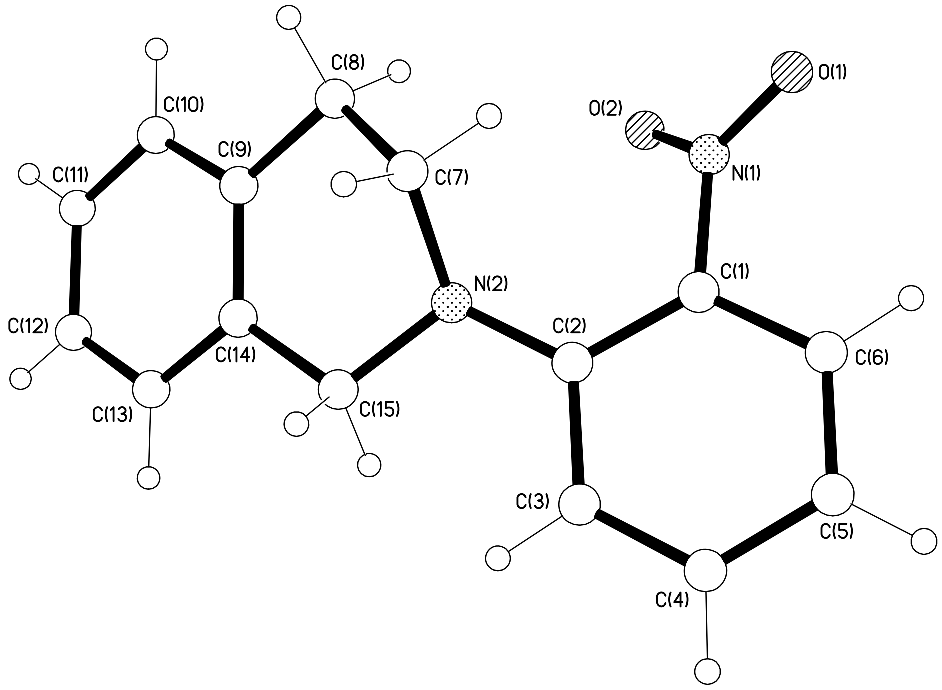
Table 6 Torsion angles [°] for sdrc30.

C(4)–Rh(1)–C(1)–C(2)	–78.2(5)	C(3)–Rh(1)–C(1)–C(2)	–35.4(5)
C(5)–Rh(1)–C(1)–C(2)	–115.2(7)	P(1)–Rh(1)–C(1)–C(2)	159.7(4)
Cl(1)–Rh(1)–C(1)–C(2)	63.5(5)	Cl(2)–Rh(1)–C(1)–C(2)	–68.8(7)
C(4)–Rh(1)–C(1)–C(5)	37.0(5)	C(3)–Rh(1)–C(1)–C(5)	79.8(5)
C(2)–Rh(1)–C(1)–C(5)	115.2(7)	P(1)–Rh(1)–C(1)–C(5)	–85.1(5)
Cl(1)–Rh(1)–C(1)–C(5)	178.7(4)	Cl(2)–Rh(1)–C(1)–C(5)	46.4(8)
C(4)–Rh(1)–C(1)–C(6)	159.3(9)	C(3)–Rh(1)–C(1)–C(6)	–157.9(9)
C(5)–Rh(1)–C(1)–C(6)	122.3(10)	C(2)–Rh(1)–C(1)–C(6)	–122.5(10)
P(1)–Rh(1)–C(1)–C(6)	37.2(8)	Cl(1)–Rh(1)–C(1)–C(6)	–59.0(8)
Cl(2)–Rh(1)–C(1)–C(6)	168.7(5)	C(5)–C(1)–C(2)–C(3)	–2.3(10)
C(6)–C(1)–C(2)–C(3)	–172.9(8)	Rh(1)–C(1)–C(2)–C(3)	60.3(6)
C(5)–C(1)–C(2)–C(7)	176.1(8)	C(6)–C(1)–C(2)–C(7)	5.5(14)
Rh(1)–C(1)–C(2)–C(7)	–121.3(9)	C(5)–C(1)–C(2)–Rh(1)	–62.6(6)
C(6)–C(1)–C(2)–Rh(1)	126.8(9)	C(4)–Rh(1)–C(2)–C(3)	–39.0(5)
C(1)–Rh(1)–C(2)–C(3)	–120.4(7)	C(5)–Rh(1)–C(2)–C(3)	–81.2(5)
P(1)–Rh(1)–C(2)–C(3)	–151.5(4)	Cl(1)–Rh(1)–C(2)–C(3)	116.7(5)
Cl(2)–Rh(1)–C(2)–C(3)	28.3(6)	C(4)–Rh(1)–C(2)–C(1)	81.4(5)
C(3)–Rh(1)–C(2)–C(1)	120.4(7)	C(5)–Rh(1)–C(2)–C(1)	39.1(5)
P(1)–Rh(1)–C(2)–C(1)	–31.2(6)	Cl(1)–Rh(1)–C(2)–C(1)	–122.9(5)
Cl(2)–Rh(1)–C(2)–C(1)	148.7(4)	C(4)–Rh(1)–C(2)–C(7)	–159.4(9)
C(3)–Rh(1)–C(2)–C(7)	–120.4(10)	C(1)–Rh(1)–C(2)–C(7)	119.2(10)

C(5)–Rh(1)–C(2)–C(7)	158.3(9)	P(1)–Rh(1)–C(2)–C(7)	88.0(8)
Cl(1)–Rh(1)–C(2)–C(7)	–3.7(7)	Cl(2)–Rh(1)–C(2)–C(7)	–92.1(7)
C(1)–C(2)–C(3)–C(4)	2.4(10)	C(7)–C(2)–C(3)–C(4)	–176.0(8)
Rh(1)–C(2)–C(3)–C(4)	62.5(6)	C(1)–C(2)–C(3)–C(8)	178.7(9)
C(7)–C(2)–C(3)–C(8)	0.3(15)	Rh(1)–C(2)–C(3)–C(8)	–121.1(10)
C(1)–C(2)–C(3)–Rh(1)	–60.2(6)	C(7)–C(2)–C(3)–Rh(1)	121.4(9)
C(4)–Rh(1)–C(3)–C(2)	115.6(7)	C(1)–Rh(1)–C(3)–C(2)	36.3(5)
C(5)–Rh(1)–C(3)–C(2)	79.4(5)	P(1)–Rh(1)–C(3)–C(2)	90.7(9)
Cl(1)–Rh(1)–C(3)–C(2)	–68.6(5)	Cl(2)–Rh(1)–C(3)–C(2)	–157.8(5)
C(1)–Rh(1)–C(3)–C(4)	–79.3(5)	C(5)–Rh(1)–C(3)–C(4)	–36.2(5)
C(2)–Rh(1)–C(3)–C(4)	–115.6(7)	P(1)–Rh(1)–C(3)–C(4)	–24.9(10)
Cl(1)–Rh(1)–C(3)–C(4)	175.8(4)	Cl(2)–Rh(1)–C(3)–C(4)	86.5(5)
C(4)–Rh(1)–C(3)–C(8)	–120.9(10)	C(1)–Rh(1)–C(3)–C(8)	159.8(9)
C(5)–Rh(1)–C(3)–C(8)	–157.1(9)	C(2)–Rh(1)–C(3)–C(8)	123.5(10)
P(1)–Rh(1)–C(3)–C(8)	–145.8(7)	Cl(1)–Rh(1)–C(3)–C(8)	54.9(8)
Cl(2)–Rh(1)–C(3)–C(8)	–34.3(8)	C(2)–C(3)–C(4)–C(5)	–1.5(10)
C(8)–C(3)–C(4)–C(5)	–177.9(9)	Rh(1)–C(3)–C(4)–C(5)	61.9(6)
C(2)–C(3)–C(4)–C(9)	174.5(8)	C(8)–C(3)–C(4)–C(9)	–1.9(15)
Rh(1)–C(3)–C(4)–C(9)	–122.1(8)	C(2)–C(3)–C(4)–Rh(1)	–63.4(6)
C(8)–C(3)–C(4)–Rh(1)	120.2(9)	C(3)–Rh(1)–C(4)–C(5)	–119.1(7)
C(1)–Rh(1)–C(4)–C(5)	–38.2(5)	C(2)–Rh(1)–C(4)–C(5)	–81.2(5)
P(1)–Rh(1)–C(4)–C(5)	51.7(6)	Cl(1)–Rh(1)–C(4)–C(5)	–126.1(5)
Cl(2)–Rh(1)–C(4)–C(5)	146.0(5)	C(1)–Rh(1)–C(4)–C(3)	80.9(5)
C(5)–Rh(1)–C(4)–C(3)	119.1(7)	C(2)–Rh(1)–C(4)–C(3)	37.9(5)
P(1)–Rh(1)–C(4)–C(3)	170.8(4)	Cl(1)–Rh(1)–C(4)–C(3)	–7.0(7)
Cl(2)–Rh(1)–C(4)–C(3)	–94.9(5)	C(3)–Rh(1)–C(4)–C(9)	118.9(11)
C(1)–Rh(1)–C(4)–C(9)	–160.2(10)	C(5)–Rh(1)–C(4)–C(9)	–122.0(11)
C(2)–Rh(1)–C(4)–C(9)	156.8(10)	P(1)–Rh(1)–C(4)–C(9)	–70.3(9)
Cl(1)–Rh(1)–C(4)–C(9)	111.9(8)	Cl(2)–Rh(1)–C(4)–C(9)	24.0(9)
C(3)–C(4)–C(5)–C(1)	0.1(10)	C(9)–C(4)–C(5)–C(1)	–175.8(8)
Rh(1)–C(4)–C(5)–C(1)	61.5(6)	C(3)–C(4)–C(5)–C(10)	171.4(8)
C(9)–C(4)–C(5)–C(10)	–4.5(15)	Rh(1)–C(4)–C(5)–C(10)	–127.2(9)
C(3)–C(4)–C(5)–Rh(1)	–61.5(6)	C(9)–C(4)–C(5)–Rh(1)	122.7(9)
C(2)–C(1)–C(5)–C(4)	1.4(9)	C(6)–C(1)–C(5)–C(4)	171.9(8)
Rh(1)–C(1)–C(5)–C(4)	–61.6(6)	C(2)–C(1)–C(5)–C(10)	–170.4(8)
C(6)–C(1)–C(5)–C(10)	0.2(14)	Rh(1)–C(1)–C(5)–C(10)	126.7(8)
C(2)–C(1)–C(5)–Rh(1)	62.9(5)	C(6)–C(1)–C(5)–Rh(1)	–126.5(9)
C(3)–Rh(1)–C(5)–C(4)	37.0(5)	C(1)–Rh(1)–C(5)–C(4)	117.5(7)
C(2)–Rh(1)–C(5)–C(4)	78.7(5)	P(1)–Rh(1)–C(5)–C(4)	–139.4(5)
Cl(1)–Rh(1)–C(5)–C(4)	115.1(6)	Cl(2)–Rh(1)–C(5)–C(4)	–40.6(6)
C(4)–Rh(1)–C(5)–C(1)	–117.5(7)	C(3)–Rh(1)–C(5)–C(1)	–80.4(5)
C(2)–Rh(1)–C(5)–C(1)	–38.7(5)	P(1)–Rh(1)–C(5)–C(1)	103.1(5)
Cl(1)–Rh(1)–C(5)–C(1)	–2.3(8)	Cl(2)–Rh(1)–C(5)–C(1)	–158.1(4)
C(4)–Rh(1)–C(5)–C(10)	123.8(11)	C(3)–Rh(1)–C(5)–C(10)	160.8(10)
C(1)–Rh(1)–C(5)–C(10)	–118.8(11)	C(2)–Rh(1)–C(5)–C(10)	–157.5(10)
P(1)–Rh(1)–C(5)–C(10)	–15.7(9)	Cl(1)–Rh(1)–C(5)–C(10)	–121.1(8)
Cl(2)–Rh(1)–C(5)–C(10)	83.2(9)	C(4)–Rh(1)–P(1)–C(11)	–84.8(4)
C(3)–Rh(1)–P(1)–C(11)	–66.2(8)	C(1)–Rh(1)–P(1)–C(11)	–17.2(4)
C(5)–Rh(1)–P(1)–C(11)	–56.0(4)	C(2)–Rh(1)–P(1)–C(11)	2.1(5)
Cl(1)–Rh(1)–P(1)–C(11)	94.0(3)	Cl(2)–Rh(1)–P(1)–C(11)	–177.8(3)
C(4)–Rh(1)–P(1)–C(28)	34.7(4)	C(3)–Rh(1)–P(1)–C(28)	53.3(8)
C(1)–Rh(1)–P(1)–C(28)	102.3(4)	C(5)–Rh(1)–P(1)–C(28)	63.5(4)
C(2)–Rh(1)–P(1)–C(28)	121.6(4)	Cl(1)–Rh(1)–P(1)–C(28)	–146.5(3)

Cl(2)–Rh(1)–P(1)–C(28)	−58.3(3)	C(4)–Rh(1)–P(1)–C(22)	152.3(4)
C(3)–Rh(1)–P(1)–C(22)	170.9(8)	C(1)–Rh(1)–P(1)–C(22)	−140.1(4)
C(5)–Rh(1)–P(1)–C(22)	−178.9(4)	C(2)–Rh(1)–P(1)–C(22)	−120.8(5)
Cl(1)–Rh(1)–P(1)–C(22)	−29.0(3)	Cl(2)–Rh(1)–P(1)–C(22)	59.3(3)
C(28)–P(1)–C(11)–C(16)	−18.3(8)	C(22)–P(1)–C(11)–C(16)	−120.9(7)
Rh(1)–P(1)–C(11)–C(16)	107.3(7)	C(28)–P(1)–C(11)–C(12)	166.6(7)
C(22)–P(1)–C(11)–C(12)	63.9(8)	Rh(1)–P(1)–C(11)–C(12)	−67.9(7)
C(16)–C(11)–C(12)–N(1)	−176.1(8)	P(1)–C(11)–C(12)–N(1)	−0.7(12)
C(16)–C(11)–C(12)–C(13)	5.9(12)	P(1)–C(11)–C(12)–C(13)	−178.8(6)
N(1)–C(12)–C(13)–C(14)	178.8(8)	C(11)–C(12)–C(13)–C(14)	−3.0(13)
C(12)–C(13)–C(14)–C(15)	−1.7(13)	C(13)–C(14)–C(15)–C(16)	3.3(14)
C(14)–C(15)–C(16)–C(11)	−0.2(14)	C(12)–C(11)–C(16)–C(15)	−4.4(13)
P(1)–C(11)–C(16)–C(15)	−179.8(7)	C(13)–C(12)–N(1)–C(17)	−2.8(13)
C(11)–C(12)–N(1)–C(17)	179.1(8)	C(12)–N(1)–C(17)–C(18)	−76.1(11)
C(12)–N(1)–C(17)–C(19)	158.8(8)	N(1)–C(17)–C(19)–C(21)	−56.1(10)
C(18)–C(17)–C(19)–C(21)	178.9(8)	N(1)–C(17)–C(19)–C(20)	−178.6(8)
C(18)–C(17)–C(19)–C(20)	56.5(10)	C(11)–P(1)–C(22)–C(23)	13.0(8)
C(28)–P(1)–C(22)–C(23)	−93.4(7)	Rh(1)–P(1)–C(22)–C(23)	141.1(6)
C(11)–P(1)–C(22)–C(27)	−176.1(7)	C(28)–P(1)–C(22)–C(27)	77.5(7)
Rh(1)–P(1)–C(22)–C(27)	−48.0(7)	C(27)–C(22)–C(23)–C(24)	0.1(13)
P(1)–C(22)–C(23)–C(24)	170.9(7)	C(22)–C(23)–C(24)–C(25)	0.0(13)
C(23)–C(24)–C(25)–C(26)	0.4(13)	C(24)–C(25)–C(26)–C(27)	−1.0(13)
C(25)–C(26)–C(27)–C(22)	1.1(13)	C(23)–C(22)–C(27)–C(26)	−0.7(12)
P(1)–C(22)–C(27)–C(26)	−171.7(6)	C(11)–P(1)–C(28)–C(33)	129.7(7)
C(22)–P(1)–C(28)–C(33)	−124.4(7)	Rh(1)–P(1)–C(28)–C(33)	4.7(7)
C(11)–P(1)–C(28)–C(29)	−52.8(8)	C(22)–P(1)–C(28)–C(29)	53.1(8)
Rh(1)–P(1)–C(28)–C(29)	−177.8(6)	C(33)–C(28)–C(29)–C(30)	−2.2(13)
P(1)–C(28)–C(29)–C(30)	−179.7(7)	C(28)–C(29)–C(30)–C(31)	2.2(14)
C(29)–C(30)–C(31)–C(32)	−0.8(15)	C(30)–C(31)–C(32)–C(33)	−0.6(15)
C(31)–C(32)–C(33)–C(28)	0.5(14)	C(29)–C(28)–C(33)–C(32)	0.8(12)
P(1)–C(28)–C(33)–C(32)	178.4(7)	C(34)–C(35)–O(1)–C(36)	176.5(10)
C(35)–O(1)–C(36)–C(37)	174.2(10)		

SDRC33 figures.



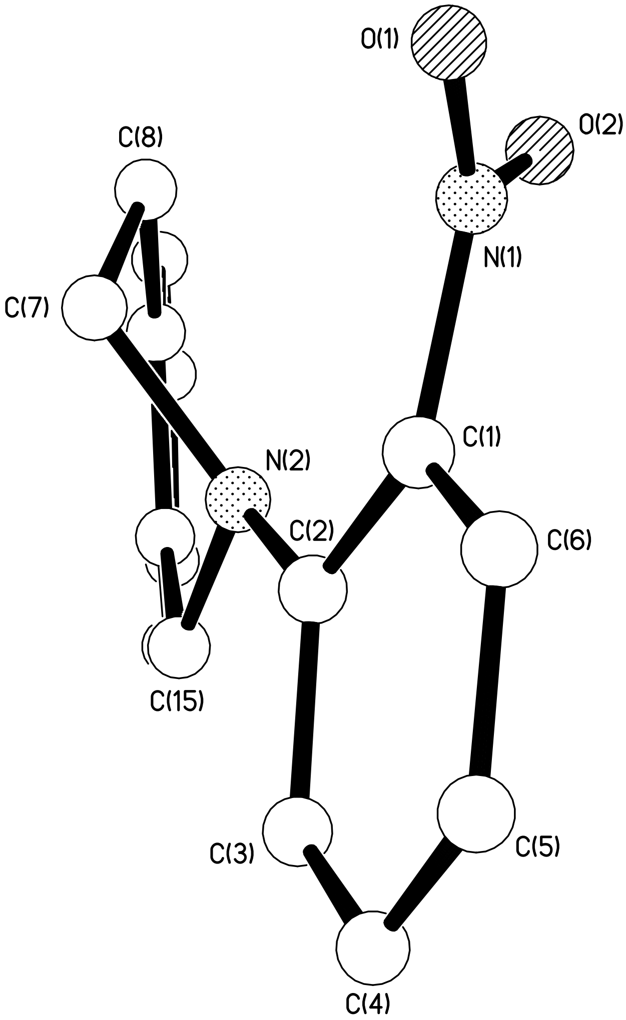

O(1)
O(2)
C(8)
N(1)
C(7)
C(1)
N(2)
C(2)
C(6)
C(15)
C(3)
C(5)
C(4)

Table 1. Crystal data and structure refinement for sdrc33.

Identification code	sdrc33	
Chemical formula	$C_{15}H_{14}N_2O_2$	
Formula weight	254.28	
Temperature	150(2) K	
Radiation, wavelength	synchrotron, 0.7749 Å	
Crystal system, space group	monoclinic, $P2_1/n$	
Unit cell parameters	a = 12.3796(12) Å	α = 90°
	b = 7.3766(7) Å	β = 111.6648(12)°
	c = 14.5036(14) Å	γ = 90°
Cell volume	1230.9(2) $Å^3$	
Z	4	
Calculated density	1.372 g/cm^3	
Absorption coefficient μ	0.093 mm^{-1}	
F(000)	536	
Crystal colour and size	orange, 0.17 × 0.16 × 0.07 mm^3	
Reflections for cell refinement	5515 (θ range 3.30 to 33.60°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	3.30 to 33.61°	
Index ranges	h –17 to 17, k –10 to 10, l –20 to 20	
Completeness to θ = 33.61°	98.6 %	
Intensity decay	0%	
Reflections collected	16842	
Independent reflections	3713 (R_{int} = 0.0580)	
Reflections with $F^2>2\sigma$	3122	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.984 and 0.994	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0901, 0.1348	
Data / restraints / parameters	3713 / 0 / 172	
Final R indices [$F^2>2\sigma$]	R1 = 0.0498, wR2 = 0.1444	
R indices (all data)	R1 = 0.0565, wR2 = 0.1510	
Goodness-of-fit on F^2	1.047	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.404 and –0.195 e $Å^{-3}$	

Acknowledgement: The Advanced Light Source is supported by the Director, Office of Science, Office of Basic Energy Sciences, of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231.

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc33. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
N(1)	0.55080(8)	0.77766(13)	0.01234(7)	0.0287(2)
O(1)	0.45692(8)	0.73063(15)	–0.05070(7)	0.0433(3)
O(2)	0.61627(8)	0.88917(13)	–0.00315(6)	0.0365(2)
C(1)	0.58232(9)	0.70146(14)	0.11225(8)	0.0233(2)
C(2)	0.69791(8)	0.65480(13)	0.17093(7)	0.0211(2)
C(3)	0.71642(9)	0.60281(14)	0.26932(8)	0.0243(2)
C(4)	0.62599(10)	0.59214(15)	0.30343(9)	0.0290(2)
C(5)	0.51201(10)	0.63071(16)	0.24209(10)	0.0316(3)
C(6)	0.49088(9)	0.68624(16)	0.14598(9)	0.0292(2)
N(2)	0.78870(7)	0.65938(12)	0.13630(6)	0.02164(19)
C(7)	0.77488(9)	0.57156(14)	0.04154(7)	0.0239(2)
C(8)	0.84467(9)	0.67563(16)	–0.00813(8)	0.0268(2)
C(9)	0.96666(9)	0.71312(14)	0.06379(8)	0.0243(2)
C(10)	1.05190(10)	0.77691(16)	0.02963(9)	0.0311(3)
C(11)	1.16404(10)	0.81351(18)	0.09491(11)	0.0350(3)
C(12)	1.19384(10)	0.78359(18)	0.19587(10)	0.0361(3)
C(13)	1.11012(9)	0.72092(17)	0.23092(9)	0.0314(3)
C(14)	0.99601(9)	0.68820(14)	0.16571(8)	0.0242(2)
C(15)	0.90649(8)	0.63396(15)	0.20878(8)	0.0245(2)

Table 3. Bond lengths [Å] and angles [°] for sdrc33.

N(1)–O(2)	1.2323(14)	N(1)–O(1)	1.2339(13)
N(1)–C(1)	1.4664(14)	C(1)–C(6)	1.3936(15)
C(1)–C(2)	1.4110(13)	C(2)–N(2)	1.3905(13)
C(2)–C(3)	1.4122(14)	C(3)–C(4)	1.3832(15)
C(4)–C(5)	1.3916(17)	C(5)–C(6)	1.3822(17)
N(2)–C(15)	1.4610(12)	N(2)–C(7)	1.4711(12)
C(7)–C(8)	1.5213(15)	C(8)–C(9)	1.5106(15)
C(9)–C(14)	1.3981(14)	C(9)–C(10)	1.4023(15)
C(10)–C(11)	1.3878(17)	C(11)–C(12)	1.3893(19)
C(12)–C(13)	1.3912(17)	C(13)–C(14)	1.4006(15)
C(14)–C(15)	1.5131(15)		

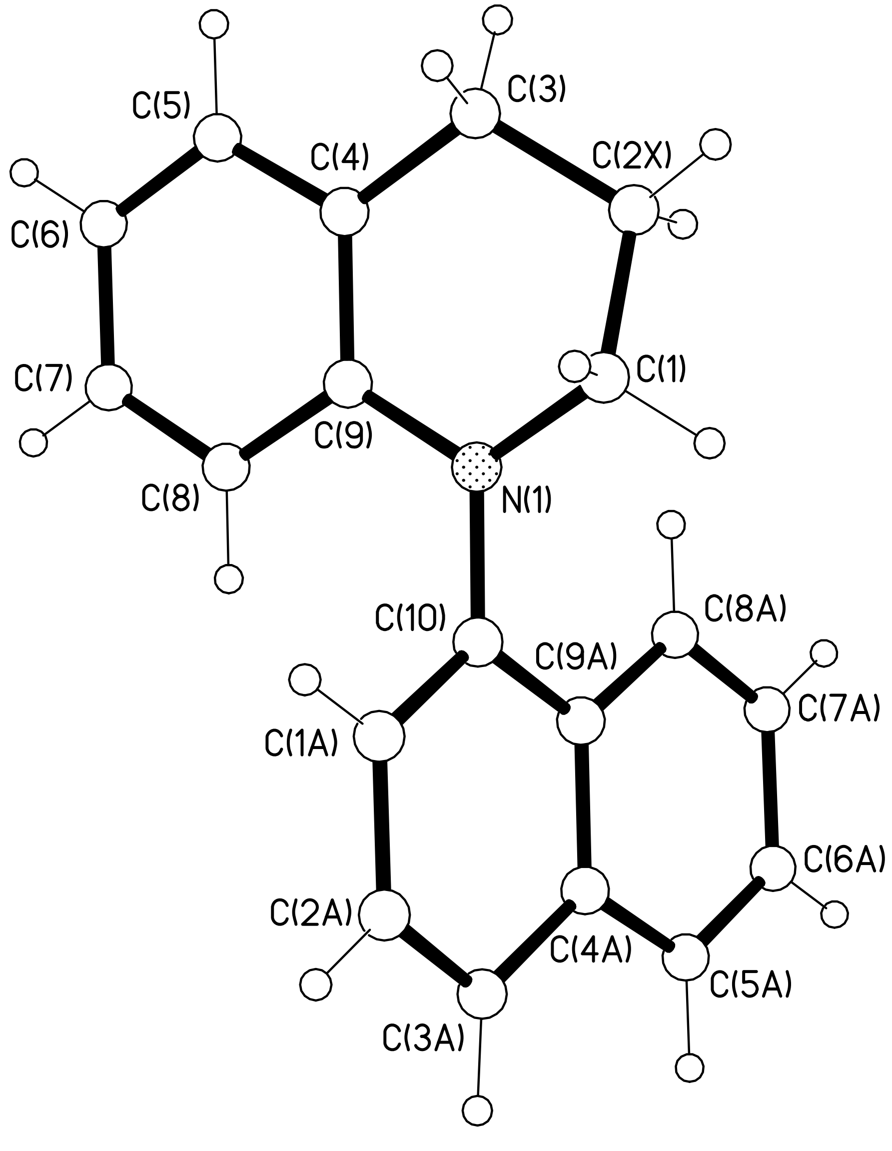
O(2)–N(1)–O(1)	123.75(10)	O(2)–N(1)–C(1)	118.89(9)
O(1)–N(1)–C(1)	117.31(10)	C(6)–C(1)–C(2)	122.88(10)
C(6)–C(1)–N(1)	115.05(9)	C(2)–C(1)–N(1)	122.02(9)
N(2)–C(2)–C(1)	123.45(9)	N(2)–C(2)–C(3)	121.35(9)
C(1)–C(2)–C(3)	115.20(9)	C(4)–C(3)–C(2)	121.74(10)
C(3)–C(4)–C(5)	121.55(11)	C(6)–C(5)–C(4)	118.37(10)
C(5)–C(6)–C(1)	120.13(10)	C(2)–N(2)–C(15)	117.53(8)
C(2)–N(2)–C(7)	119.73(8)	C(15)–N(2)–C(7)	110.89(8)
N(2)–C(7)–C(8)	109.25(8)	C(9)–C(8)–C(7)	111.29(9)
C(14)–C(9)–C(10)	118.81(10)	C(14)–C(9)–C(8)	120.62(9)
C(10)–C(9)–C(8)	120.55(10)	C(11)–C(10)–C(9)	121.20(11)
C(10)–C(11)–C(12)	119.84(11)	C(11)–C(12)–C(13)	119.62(11)
C(12)–C(13)–C(14)	120.81(11)	C(9)–C(14)–C(13)	119.67(10)
C(9)–C(14)–C(15)	121.81(9)	C(13)–C(14)–C(15)	118.47(10)
N(2)–C(15)–C(14)	110.96(8)		

Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc33.

	x	y	z	U
H(3)	0.7930	0.5744	0.3132	0.029
H(4)	0.6421	0.5577	0.3703	0.035
H(5)	0.4502	0.6191	0.2657	0.038
H(6)	0.4139	0.7141	0.1028	0.035
H(7A)	0.6917	0.5701	–0.0023	0.029
H(7B)	0.8026	0.4447	0.0535	0.029
H(8A)	0.8482	0.6044	–0.0648	0.032
H(8B)	0.8052	0.7918	–0.0342	0.032
H(10)	1.0325	0.7954	–0.0394	0.037
H(11)	1.2203	0.8589	0.0706	0.042
H(12)	1.2709	0.8058	0.2407	0.043
H(13)	1.1306	0.7001	0.2999	0.038
H(15A)	0.9179	0.5052	0.2293	0.029
H(15B)	0.9171	0.7081	0.2684	0.029

Table 5. Torsion angles [°] for sdrc33.

O(2)–N(1)–C(1)–C(6)	137.78(10)	O(1)–N(1)–C(1)–C(6)	–39.44(13)
O(2)–N(1)–C(1)–C(2)	–39.60(14)	O(1)–N(1)–C(1)–C(2)	143.18(11)
C(6)–C(1)–C(2)–N(2)	176.15(10)	N(1)–C(1)–C(2)–N(2)	–6.68(15)
C(6)–C(1)–C(2)–C(3)	–4.14(14)	N(1)–C(1)–C(2)–C(3)	173.03(9)
N(2)–C(2)–C(3)–C(4)	–177.84(9)	C(1)–C(2)–C(3)–C(4)	2.44(15)
C(2)–C(3)–C(4)–C(5)	0.56(17)	C(3)–C(4)–C(5)–C(6)	–2.05(17)
C(4)–C(5)–C(6)–C(1)	0.40(17)	C(2)–C(1)–C(6)–C(5)	2.83(16)
N(1)–C(1)–C(6)–C(5)	–174.52(10)	C(1)–C(2)–N(2)–C(15)	171.09(9)
C(3)–C(2)–N(2)–C(15)	–8.60(14)	C(1)–C(2)–N(2)–C(7)	–49.37(14)
C(3)–C(2)–N(2)–C(7)	130.94(10)	C(2)–N(2)–C(7)–C(8)	148.09(9)
C(15)–N(2)–C(7)–C(8)	–69.94(10)	N(2)–C(7)–C(8)–C(9)	48.11(11)
C(7)–C(8)–C(9)–C(14)	–13.17(14)	C(7)–C(8)–C(9)–C(10)	168.07(10)
C(14)–C(9)–C(10)–C(11)	0.62(17)	C(8)–C(9)–C(10)–C(11)	179.41(11)
C(9)–C(10)–C(11)–C(12)	1.24(19)	C(10)–C(11)–C(12)–C(13)	–1.43(19)
C(11)–C(12)–C(13)–C(14)	–0.22(19)	C(10)–C(9)–C(14)–C(13)	–2.26(16)
C(8)–C(9)–C(14)–C(13)	178.96(10)	C(10)–C(9)–C(14)–C(15)	175.13(10)
C(8)–C(9)–C(14)–C(15)	–3.65(16)	C(12)–C(13)–C(14)–C(9)	2.09(17)
C(12)–C(13)–C(14)–C(15)	–175.39(11)	C(2)–N(2)–C(15)–C(14)	–165.88(9)
C(7)–N(2)–C(15)–C(14)	51.22(11)	C(9)–C(14)–C(15)–N(2)	–14.88(14)
C(13)–C(14)–C(15)–N(2)	162.54(10)		


C(3)
C(5)
C(4)
C(2X)
C(6)
C(7)
C(1)
C(9)
C(8)
N(1)
C(10)
C(8A)
C(9A)
C(7A)
C(1A)
C(6A)
C(2A)
C(4A)
C(5A)
C(3A)

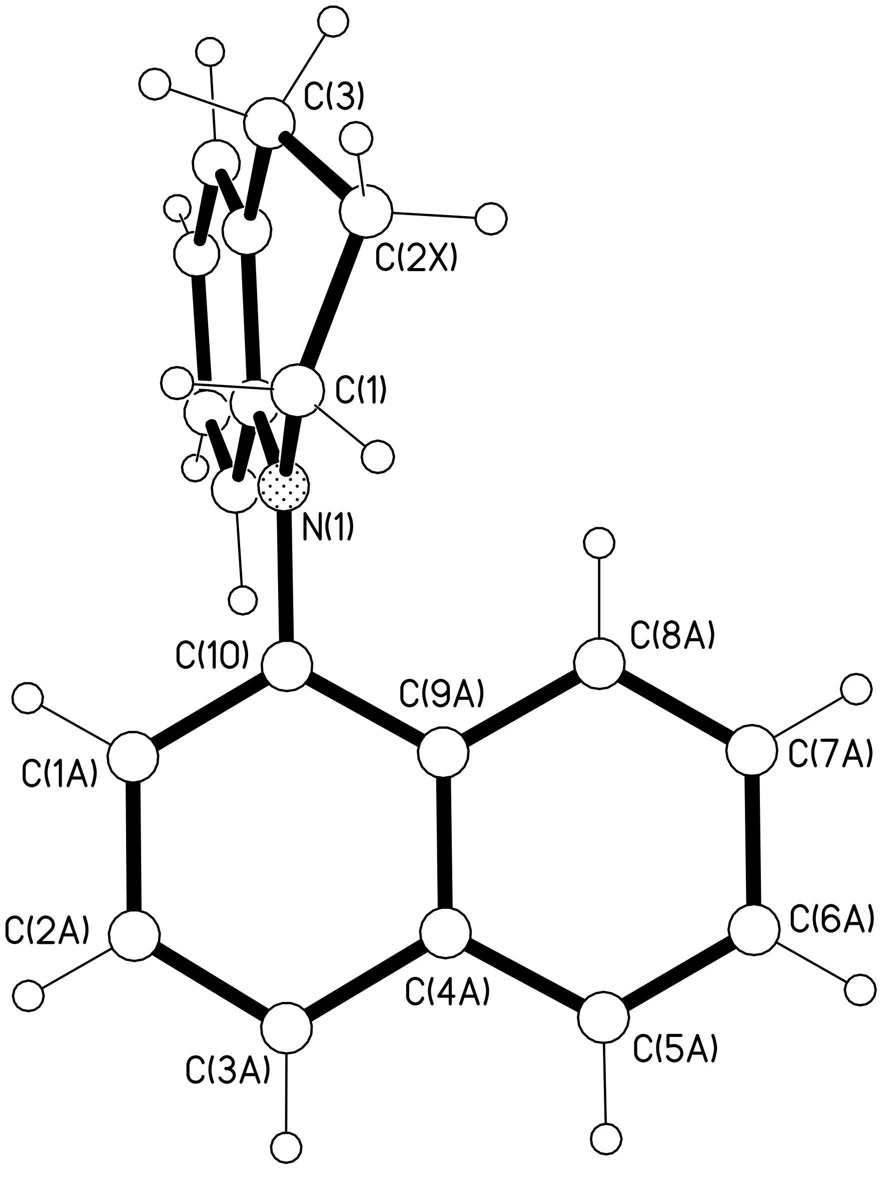

C(3)
C(2X)
C(1)
N(1)
C(10)
C(9A)
C(8A)
C(7A)
C(1A)
C(2A)
C(6A)
C(4A)
C(3A)
C(5A)

Table 1. Crystal data and structure refinement for sdrc23.

Identification code	sdrc23	
Chemical formula	$C_{19}H_{17}N$	
Formula weight	259.34	
Temperature	150(2) K	
Radiation, wavelength	MoKα, 0.71073 Å	
Crystal system, space group	tetragonal, $P4_32_12$	
Unit cell parameters	a = 7.0515(8) Å	α = 90°
	b = 7.0515(8) Å	β = 90°
	c = 28.297(3) Å	γ = 90°
Cell volume	1407.0(3) $Å^3$	
Z	4	
Calculated density	1.224 g/cm^3	
Absorption coefficient μ	0.071 mm^{-1}	
F(000)	552	
Crystal colour and size	pale yellow, 1.04 × 0.47 × 0.25 mm^3	
Reflections for cell refinement	4032 (θ range 2.88 to 27.15°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	2.88 to 29.67°	
Index ranges	h –9 to 8, k –9 to 9, l –39 to 39	
Completeness to θ = 29.67°	99.9 %	
Intensity decay	0%	
Reflections collected	13580	
Independent reflections	1247 (R_{int} = 0.0757)	
Reflections with $F^2>2\sigma$	1134	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.930 and 0.983	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0560, 0.3726	
Data / restraints / parameters	1247 / 39 / 100	
Final R indices [$F^2>2\sigma$]	R1 = 0.0489, wR2 = 0.1250	
R indices (all data)	R1 = 0.0532, wR2 = 0.1278	
Goodness-of-fit on F^2	1.094	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.243 and –0.229 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc23. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
N(1)	0.9956(3)	0.1307(3)	0.00769(5)	0.0293(4)
C(10)	0.9956(3)	0.1307(3)	0.00769(5)	0.0293(4)
C(1)	0.9843(3)	0.3078(3)	–0.01512(7)	0.0362(5)
C(2)	0.8564(8)	0.4452(9)	0.0009(2)	0.0413(13)
C(2X)	0.8002(8)	0.4032(8)	–0.01164(18)	0.0352(11)
C(3)	0.7324(3)	0.4111(3)	0.03871(7)	0.0352(5)
C(4)	0.7530(3)	0.2316(3)	0.06395(6)	0.0272(4)
C(5)	0.6467(3)	0.1936(3)	0.10487(7)	0.0356(5)
C(6)	0.6658(3)	0.0268(4)	0.12915(8)	0.0413(6)
C(7)	0.7926(3)	–0.1117(3)	0.11286(7)	0.0372(5)
C(8)	0.8993(3)	–0.0795(3)	0.07288(6)	0.0289(4)
C(9)	0.8836(3)	0.0936(3)	0.04791(6)	0.0241(4)

Table 3. Bond lengths [Å] and angles [°] for sdrc23.

N(1)–C(1)	1.408(3)	N(1)–C(9)	1.409(2)
N(1)–N(1')	1.416(4)	C(1)–C(2)	1.399(7)
C(1)–C(2X)	1.465(6)	C(2)–C(3)	1.403(7)
C(2X)–C(3)	1.504(6)	C(3)–C(4)	1.461(3)
C(4)–C(5)	1.405(3)	C(4)–C(9)	1.415(2)
C(5)–C(6)	1.369(3)	C(6)–C(7)	1.402(3)
C(7)–C(8)	1.378(3)	C(8)–C(9)	1.415(2)
C(1)–N(1)–C(9)	120.21(17)	C(1)–N(1)–N(1')	119.60(15)
C(9)–N(1)–N(1')	120.01(17)	C(2)–C(1)–N(1)	120.1(3)
C(2)–C(1)–C(2X)	24.4(2)	N(1)–C(1)–C(2X)	115.2(3)
C(1)–C(2)–C(3)	122.0(5)	C(1)–C(2X)–C(3)	111.3(3)
C(2)–C(3)–C(4)	117.4(3)	C(2)–C(3)–C(2X)	23.9(2)
C(4)–C(3)–C(2X)	113.5(3)	C(5)–C(4)–C(9)	118.69(18)
C(5)–C(4)–C(3)	121.04(18)	C(9)–C(4)–C(3)	120.26(17)
C(6)–C(5)–C(4)	121.7(2)	C(5)–C(6)–C(7)	119.75(19)
C(8)–C(7)–C(6)	120.3(2)	C(7)–C(8)–C(9)	120.62(18)
N(1)–C(9)–C(8)	121.31(16)	N(1)–C(9)–C(4)	119.73(17)
C(8)–C(9)–C(4)	118.96(17)		

Symmetry operations for equivalent atoms
' y+1,x–1,–z

Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc23.

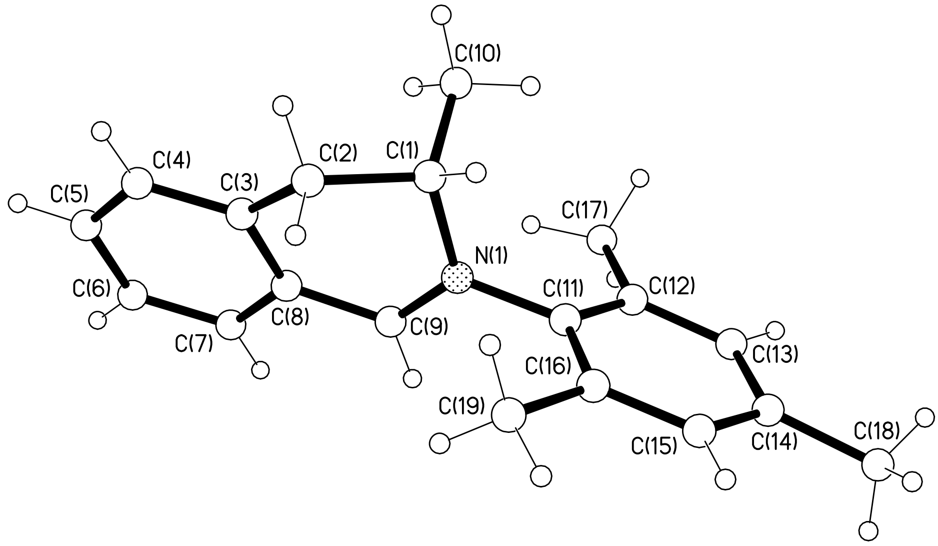
	x	y	z	U
H(1)	1.0636	0.3340	–0.0415	0.043
H(1A)	1.0147	0.2896	–0.0490	0.043
H(1B)	1.0823	0.3923	–0.0016	0.043
H(2)	0.8536	0.5654	–0.0143	0.050
H(2X1)	0.7060	0.3343	–0.0311	0.042
H(2X2)	0.8114	0.5337	–0.0242	0.042
H(3)	0.6387	0.5012	0.0475	0.042
H(3A)	0.8046	0.5103	0.0557	0.042
H(3B)	0.5970	0.4486	0.0390	0.042
H(5)	0.5594	0.2860	0.1160	0.043
H(6)	0.5934	0.0049	0.1569	0.050
H(7)	0.8049	–0.2281	0.1294	0.045
H(8)	0.9843	–0.1745	0.0620	0.035

Table 5. Torsion angles [°] for sdrc23.

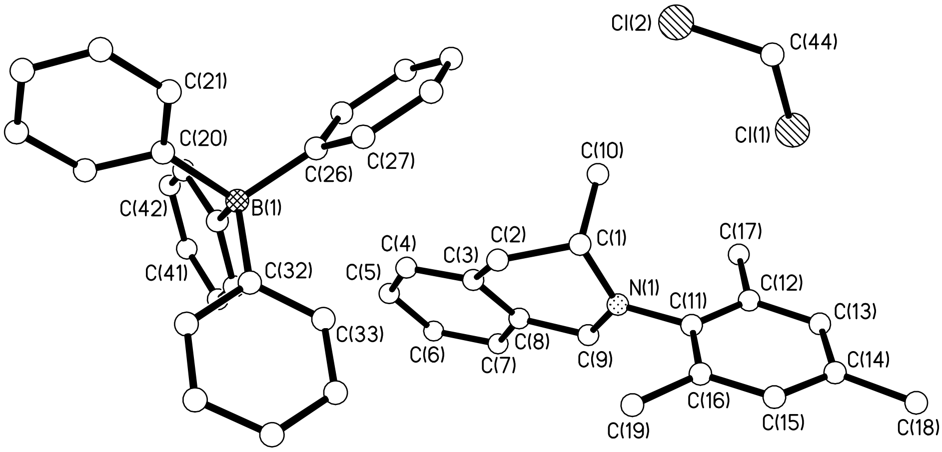
C(9)–N(1)–C(1)–C(2)	–2.48(16)	N(1')–N(1)–C(1)–C(2)	–177.52(17)
C(9)–N(1)–C(1)–C(2X)	–29.6(3)	N(1')–N(1)–C(1)–C(2X)	155.4(3)
N(1)–C(1)–C(2)–C(3)	–2.0(2)	C(2X)–C(1)–C(2)–C(3)	83.0(10)
C(2)–C(1)–C(2X)–C(3)	–57.4(9)	N(1)–C(1)–C(2X)–C(3)	50.4(4)
C(1)–C(2)–C(3)–C(4)	5.5(3)	C(1)–C(2)–C(3)–C(2X)	–81.1(10)
C(1)–C(2X)–C(3)–C(2)	59.1(9)	C(1)–C(2X)–C(3)–C(4)	–45.6(4)
C(2)–C(3)–C(4)–C(5)	174.0(2)	C(2X)–C(3)–C(4)–C(5)	–159.8(3)
C(2)–C(3)–C(4)–C(9)	–4.9(3)	C(2X)–C(3)–C(4)–C(9)	21.3(3)
C(9)–C(4)–C(5)–C(6)	–0.5(3)	C(3)–C(4)–C(5)–C(6)	–179.4(2)
C(4)–C(5)–C(6)–C(7)	–0.7(3)	C(5)–C(6)–C(7)–C(8)	0.7(3)
C(6)–C(7)–C(8)–C(9)	0.4(3)	C(1)–N(1)–C(9)–C(8)	–176.77(16)
N(1')–N(1)–C(9)–C(8)	–1.7(2)	C(1)–N(1)–C(9)–C(4)	3.1(2)
N(1')–N(1)–C(9)–C(4)	178.08(15)	C(7)–C(8)–C(9)–N(1)	178.26(18)
C(7)–C(8)–C(9)–C(4)	–1.6(3)	C(5)–C(4)–C(9)–N(1)	–178.26(17)
C(3)–C(4)–C(9)–N(1)	0.7(3)	C(5)–C(4)–C(9)–C(8)	1.6(3)
C(3)–C(4)–C(9)–C(8)	–179.51(17)		

Symmetry operations for equivalent atoms
' y+1,x–1,–z

sdrc24 figs



C(10)
C(4)
C(2)
C(1)
C(5)
C(3)
C(17)
N(1)
C(6)
C(11)
C(12)
C(8)
C(7)
C(9)
C(13)
C(16)
C(19)
C(18)
C(15)
C(14)



Cl(2)
C(44)
C(21)
Cl(1)
C(20)
C(10)
C(26)
C(27)
C(42)
B(1)
C(17)
C(1)
C(4)
C(2)
C(3)
C(12)
C(41)
C(5)
C(32)
N(1)
C(11)
C(13)
C(33)
C(6)
C(8)
C(7)
C(9)
C(14)
C(16)
C(15)
C(19)
C(18)

Table 1. Crystal data and structure refinement for sdrc24.

Identification code	sdrc24	
Chemical formula	$C_{44}H_{44}BCl_2N$	
Formula weight	668.51	
Temperature	150(2) K	
Radiation, wavelength	MoKα, 0.71073 Å	
Crystal system, space group	triclinic, P $\bar{1}$	
Unit cell parameters	a = 9.8921(19) Å	α = 75.011(3)°
	b = 13.383(3) Å	β = 75.523(3)°
	c = 14.556(3) Å	γ = 87.250(3)°
Cell volume	1802.1(6) $Å^3$	
Z	2	
Calculated density	1.232 g/cm^3	
Absorption coefficient μ	0.213 mm^{-1}	
F(000)	708	
Crystal colour and size	yellow, 0.60 × 0.33 × 0.09 mm^3	
Reflections for cell refinement	4865 (θ range 2.43 to 27.76°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	1.58 to 27.50°	
Index ranges	h –12 to 12, k –16 to 17, l 0 to 18	
Completeness to θ = 27.50°	98.4 %	
Intensity decay	0%	
Reflections collected	12940	
Independent reflections	8142 (R_{int} = 0.0684)	
Reflections with F^2>2σ	5871	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.883 and 0.981	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0792, 1.2228	
Data / restraints / parameters	8142 / 0 / 438	
Final R indices [F^2>2σ]	R1 = 0.0639, wR2 = 0.1586	
R indices (all data)	R1 = 0.0925, wR2 = 0.1781	
Goodness-of-fit on F^2	1.029	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.784 and –0.555 e $Å^{-3}$	

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc24. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
N(1)	0.2393(2)	0.41422(17)	0.23239(16)	0.0304(5)
C(1)	0.3918(3)	0.4084(2)	0.2325(3)	0.0433(7)
C(2)	0.4449(3)	0.5165(2)	0.2235(3)	0.0469(8)
C(3)	0.4028(3)	0.5971(2)	0.1422(2)	0.0384(7)
C(4)	0.4789(3)	0.6874(2)	0.0909(3)	0.0515(8)
C(5)	0.4253(3)	0.7628(3)	0.0256(3)	0.0537(9)
C(6)	0.2946(3)	0.7522(2)	0.0103(2)	0.0479(8)
C(7)	0.2168(3)	0.6623(2)	0.0606(2)	0.0389(6)
C(8)	0.2713(3)	0.5854(2)	0.12447(19)	0.0311(6)
C(9)	0.1888(3)	0.4944(2)	0.18152(18)	0.0291(5)
C(10)	0.4710(3)	0.3619(3)	0.1536(3)	0.0576(9)
C(11)	0.1499(3)	0.3251(2)	0.29051(19)	0.0300(5)
C(12)	0.1115(3)	0.2566(2)	0.24361(19)	0.0322(6)
C(13)	0.0217(3)	0.1745(2)	0.3027(2)	0.0345(6)
C(14)	−0.0293(3)	0.1624(2)	0.4028(2)	0.0368(6)
C(15)	0.0142(3)	0.2329(2)	0.4456(2)	0.0369(6)
C(16)	0.1028(3)	0.3155(2)	0.39120(19)	0.0327(6)
C(17)	0.1579(3)	0.2686(3)	0.1340(2)	0.0444(7)
C(18)	−0.1334(3)	0.0765(2)	0.4635(2)	0.0477(8)
C(19)	0.1416(3)	0.3941(2)	0.4387(2)	0.0409(7)
B(1)	0.8189(3)	0.7333(2)	0.2543(2)	0.0264(6)
C(20)	0.9712(2)	0.7619(2)	0.26875(17)	0.0270(5)
C(21)	1.0645(3)	0.6886(2)	0.30151(18)	0.0309(6)
C(22)	1.1906(3)	0.7145(2)	0.3175(2)	0.0392(7)
C(23)	1.2273(3)	0.8170(2)	0.3005(2)	0.0395(7)
C(24)	1.1379(3)	0.8926(2)	0.26865(19)	0.0365(6)
C(25)	1.0131(3)	0.8651(2)	0.25344(19)	0.0326(6)
C(26)	0.8234(2)	0.61869(19)	0.23048(18)	0.0267(5)
C(27)	0.8150(3)	0.5258(2)	0.30446(19)	0.0316(6)
C(28)	0.8194(3)	0.4286(2)	0.2861(2)	0.0367(6)
C(29)	0.8327(3)	0.4202(2)	0.1914(2)	0.0373(6)
C(30)	0.8414(3)	0.5095(2)	0.1163(2)	0.0340(6)
C(31)	0.8368(2)	0.6058(2)	0.13611(18)	0.0284(5)
C(32)	0.6981(3)	0.7340(2)	0.35567(18)	0.0287(5)
C(33)	0.5764(3)	0.6723(3)	0.3871(2)	0.0454(8)
C(34)	0.4732(3)	0.6747(3)	0.4715(2)	0.0569(9)
C(35)	0.4866(3)	0.7398(3)	0.5280(2)	0.0510(8)
C(36)	0.6047(3)	0.8031(2)	0.4991(2)	0.0461(7)
C(37)	0.7077(3)	0.7990(2)	0.4146(2)	0.0356(6)
C(38)	0.7821(3)	0.82146(19)	0.16228(18)	0.0273(5)
C(39)	0.6499(3)	0.8622(2)	0.1624(2)	0.0363(6)
C(40)	0.6208(3)	0.9368(2)	0.0834(2)	0.0456(7)
C(41)	0.7247(3)	0.9721(2)	−0.0006(2)	0.0417(7)
C(42)	0.8571(3)	0.9340(2)	−0.0051(2)	0.0363(6)
C(43)	0.8854(3)	0.8607(2)	0.07473(18)	0.0311(6)
C(44)	0.5623(4)	0.0331(3)	0.3129(3)	0.0700(11)
Cl(1)	0.40179(11)	0.06956(9)	0.28578(9)	0.0751(3)
Cl(2)	0.69111(11)	0.12947(10)	0.25631(8)	0.0793(3)

Table 3. Bond lengths [Å] and angles [°] for sdrc24.

N(1)–C(9)	1.294(3)	N(1)–C(11)	1.458(3)
N(1)–C(1)	1.507(3)	C(1)–C(10)	1.481(5)
C(1)–C(2)	1.524(4)	C(2)–C(3)	1.511(5)
C(3)–C(4)	1.388(4)	C(3)–C(8)	1.411(4)
C(4)–C(5)	1.381(5)	C(5)–C(6)	1.385(5)
C(6)–C(7)	1.389(4)	C(7)–C(8)	1.384(4)
C(8)–C(9)	1.439(3)	C(11)–C(12)	1.392(4)
C(11)–C(16)	1.396(4)	C(12)–C(13)	1.399(4)
C(12)–C(17)	1.514(4)	C(13)–C(14)	1.387(4)
C(14)–C(15)	1.393(4)	C(14)–C(18)	1.515(4)
C(15)–C(16)	1.382(4)	C(16)–C(19)	1.510(4)
B(1)–C(38)	1.643(4)	B(1)–C(20)	1.649(4)
B(1)–C(32)	1.652(4)	B(1)–C(26)	1.654(4)
C(20)–C(21)	1.390(4)	C(20)–C(25)	1.407(4)
C(21)–C(22)	1.400(4)	C(22)–C(23)	1.379(4)
C(23)–C(24)	1.377(4)	C(24)–C(25)	1.389(4)
C(26)–C(31)	1.401(4)	C(26)–C(27)	1.409(3)
C(27)–C(28)	1.390(4)	C(28)–C(29)	1.386(4)
C(29)–C(30)	1.384(4)	C(30)–C(31)	1.388(4)
C(32)–C(37)	1.392(4)	C(32)–C(33)	1.402(4)
C(33)–C(34)	1.394(4)	C(34)–C(35)	1.374(5)
C(35)–C(36)	1.387(5)	C(36)–C(37)	1.399(4)
C(38)–C(39)	1.392(4)	C(38)–C(43)	1.414(3)
C(39)–C(40)	1.395(4)	C(40)–C(41)	1.377(4)
C(41)–C(42)	1.375(4)	C(42)–C(43)	1.392(4)
C(44)–Cl(2)	1.746(4)	C(44)–Cl(1)	1.747(5)

C(9)–N(1)–C(11)	120.6(2)	C(9)–N(1)–C(1)	121.7(2)
C(11)–N(1)–C(1)	117.7(2)	C(10)–C(1)–N(1)	110.2(3)
C(10)–C(1)–C(2)	113.1(3)	N(1)–C(1)–C(2)	108.7(2)
C(3)–C(2)–C(1)	112.3(3)	C(4)–C(3)–C(8)	117.8(3)
C(4)–C(3)–C(2)	123.8(3)	C(8)–C(3)–C(2)	118.0(2)
C(5)–C(4)–C(3)	120.2(3)	C(4)–C(5)–C(6)	121.8(3)
C(5)–C(6)–C(7)	119.0(3)	C(8)–C(7)–C(6)	119.5(3)
C(7)–C(8)–C(3)	121.7(2)	C(7)–C(8)–C(9)	120.2(2)
C(3)–C(8)–C(9)	117.9(3)	N(1)–C(9)–C(8)	123.0(2)
C(12)–C(11)–C(16)	123.3(2)	C(12)–C(11)–N(1)	119.3(2)
C(16)–C(11)–N(1)	117.3(2)	C(11)–C(12)–C(13)	116.8(2)
C(11)–C(12)–C(17)	123.6(2)	C(13)–C(12)–C(17)	119.6(2)
C(14)–C(13)–C(12)	122.1(3)	C(13)–C(14)–C(15)	118.4(3)
C(13)–C(14)–C(18)	120.7(3)	C(15)–C(14)–C(18)	120.9(3)
C(16)–C(15)–C(14)	122.2(3)	C(15)–C(16)–C(11)	117.2(2)
C(15)–C(16)–C(19)	121.0(2)	C(11)–C(16)–C(19)	121.8(2)
C(38)–B(1)–C(20)	109.2(2)	C(38)–B(1)–C(32)	109.1(2)
C(20)–B(1)–C(32)	108.6(2)	C(38)–B(1)–C(26)	109.1(2)
C(20)–B(1)–C(26)	110.3(2)	C(32)–B(1)–C(26)	110.5(2)
C(21)–C(20)–C(25)	114.5(2)	C(21)–C(20)–B(1)	124.1(2)
C(25)–C(20)–B(1)	121.3(2)	C(20)–C(21)–C(22)	123.2(3)
C(23)–C(22)–C(21)	119.9(3)	C(24)–C(23)–C(22)	119.1(3)
C(23)–C(24)–C(25)	120.0(3)	C(24)–C(25)–C(20)	123.2(3)
C(31)–C(26)–C(27)	114.7(2)	C(31)–C(26)–B(1)	123.2(2)
C(27)–C(26)–B(1)	122.1(2)	C(28)–C(27)–C(26)	123.1(3)
C(29)–C(28)–C(27)	119.9(3)	C(30)–C(29)–C(28)	119.0(3)
C(29)–C(30)–C(31)	120.3(3)	C(30)–C(31)–C(26)	123.1(2)

C(37)–C(32)–C(33)	114.9(2)	C(37)–C(32)–B(1)	122.2(2)
C(33)–C(32)–B(1)	122.9(2)	C(34)–C(33)–C(32)	122.8(3)
C(35)–C(34)–C(33)	120.6(3)	C(34)–C(35)–C(36)	118.6(3)
C(35)–C(36)–C(37)	120.0(3)	C(32)–C(37)–C(36)	123.1(3)
C(39)–C(38)–C(43)	114.7(2)	C(39)–C(38)–B(1)	124.1(2)
C(43)–C(38)–B(1)	121.3(2)	C(38)–C(39)–C(40)	123.2(3)
C(41)–C(40)–C(39)	120.0(3)	C(42)–C(41)–C(40)	119.3(3)
C(41)–C(42)–C(43)	120.2(3)	C(42)–C(43)–C(38)	122.7(3)
Cl(2)–C(44)–Cl(1)	112.6(2)		

Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc24.

	x	y	z	U
H(1)	0.4008	0.3628	0.2969	0.052
H(2A)	0.4074	0.5352	0.2865	0.056
H(2B)	0.5480	0.5160	0.2107	0.056
H(4)	0.5682	0.6974	0.1007	0.062
H(5)	0.4795	0.8236	–0.0098	0.064
H(6)	0.2588	0.8056	–0.0340	0.057
H(7)	0.1269	0.6535	0.0512	0.047
H(9)	0.0927	0.4932	0.1818	0.035
H(10A)	0.4314	0.2934	0.1624	0.086
H(10B)	0.5691	0.3553	0.1565	0.086
H(10C)	0.4650	0.4064	0.0897	0.086
H(13)	–0.0052	0.1256	0.2732	0.041
H(15)	–0.0180	0.2238	0.5144	0.044
H(17A)	0.2073	0.3351	0.1022	0.067
H(17B)	0.0760	0.2664	0.1081	0.067
H(17C)	0.2204	0.2123	0.1206	0.067
H(18A)	–0.1235	0.0568	0.5312	0.072
H(18B)	–0.1156	0.0164	0.4357	0.072
H(18C)	–0.2283	0.1006	0.4630	0.072
H(19A)	0.2417	0.3904	0.4357	0.061
H(19B)	0.0885	0.3793	0.5075	0.061
H(19C)	0.1198	0.4636	0.4039	0.061
H(21)	1.0415	0.6175	0.3136	0.037
H(22)	1.2509	0.6615	0.3400	0.047
H(23)	1.3131	0.8352	0.3107	0.047
H(24)	1.1616	0.9635	0.2571	0.044
H(25)	0.9531	0.9187	0.2316	0.039
H(27)	0.8059	0.5297	0.3700	0.038
H(28)	0.8134	0.3681	0.3385	0.044
H(29)	0.8357	0.3541	0.1781	0.045
H(30)	0.8507	0.5048	0.0510	0.041
H(31)	0.8430	0.6658	0.0832	0.034
H(33)	0.5638	0.6269	0.3493	0.055
H(34)	0.3928	0.6310	0.4901	0.068
H(35)	0.4165	0.7414	0.5856	0.061
H(36)	0.6155	0.8493	0.5367	0.055
H(37)	0.7880	0.8427	0.3966	0.043
H(39)	0.5760	0.8380	0.2191	0.044
H(40)	0.5292	0.9633	0.0877	0.055
H(41)	0.7052	1.0223	–0.0550	0.050

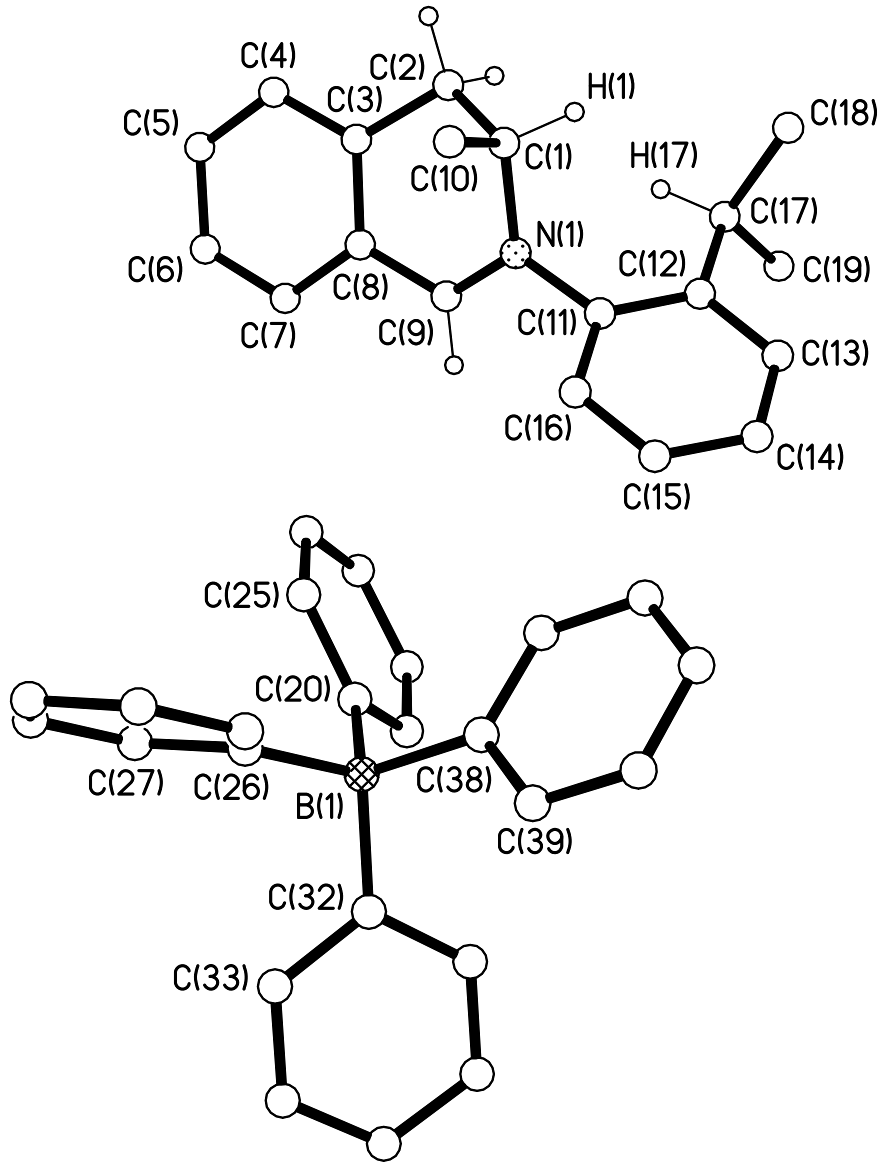
H(42)	0.9295	0.9577	–0.0628	0.044
H(43)	0.9779	0.8360	0.0702	0.037
H(44A)	0.5501	0.0167	0.3849	0.084
H(44B)	0.5933	–0.0304	0.2913	0.084

Table 5. Torsion angles [°] for sdrc24.

C(9)–N(1)–C(1)–C(10)	–90.3(3)	C(11)–N(1)–C(1)–C(10)	88.6(3)
C(9)–N(1)–C(1)–C(2)	34.1(4)	C(11)–N(1)–C(1)–C(2)	–147.0(3)
C(10)–C(1)–C(2)–C(3)	74.6(3)	N(1)–C(1)–C(2)–C(3)	–48.0(3)
C(1)–C(2)–C(3)–C(4)	–151.9(3)	C(1)–C(2)–C(3)–C(8)	35.2(4)
C(8)–C(3)–C(4)–C(5)	0.6(5)	C(2)–C(3)–C(4)–C(5)	–172.4(3)
C(3)–C(4)–C(5)–C(6)	1.1(5)	C(4)–C(5)–C(6)–C(7)	–1.3(5)
C(5)–C(6)–C(7)–C(8)	–0.2(5)	C(6)–C(7)–C(8)–C(3)	1.9(4)
C(6)–C(7)–C(8)–C(9)	176.3(3)	C(4)–C(3)–C(8)–C(7)	–2.1(4)
C(2)–C(3)–C(8)–C(7)	171.3(3)	C(4)–C(3)–C(8)–C(9)	–176.6(3)
C(2)–C(3)–C(8)–C(9)	–3.2(4)	C(11)–N(1)–C(9)–C(8)	178.7(2)
C(1)–N(1)–C(9)–C(8)	–2.4(4)	C(7)–C(8)–C(9)–N(1)	170.6(3)
C(3)–C(8)–C(9)–N(1)	–14.8(4)	C(9)–N(1)–C(11)–C(12)	77.0(3)
C(1)–N(1)–C(11)–C(12)	–101.9(3)	C(9)–N(1)–C(11)–C(16)	–100.6(3)
C(1)–N(1)–C(11)–C(16)	80.5(3)	C(16)–C(11)–C(12)–C(13)	–0.4(4)
N(1)–C(11)–C(12)–C(13)	–177.8(2)	C(16)–C(11)–C(12)–C(17)	177.6(3)
N(1)–C(11)–C(12)–C(17)	0.2(4)	C(11)–C(12)–C(13)–C(14)	1.2(4)
C(17)–C(12)–C(13)–C(14)	–176.9(3)	C(12)–C(13)–C(14)–C(15)	–1.9(4)
C(12)–C(13)–C(14)–C(18)	176.2(3)	C(13)–C(14)–C(15)–C(16)	1.9(4)
C(18)–C(14)–C(15)–C(16)	–176.2(3)	C(14)–C(15)–C(16)–C(11)	–1.2(4)
C(14)–C(15)–C(16)–C(19)	176.5(3)	C(12)–C(11)–C(16)–C(15)	0.4(4)
N(1)–C(11)–C(16)–C(15)	177.9(2)	C(12)–C(11)–C(16)–C(19)	–177.2(3)
N(1)–C(11)–C(16)–C(19)	0.2(4)	C(38)–B(1)–C(20)–C(21)	–147.5(2)
C(32)–B(1)–C(20)–C(21)	93.7(3)	C(26)–B(1)–C(20)–C(21)	–27.5(3)
C(38)–B(1)–C(20)–C(25)	36.1(3)	C(32)–B(1)–C(20)–C(25)	–82.7(3)
C(26)–B(1)–C(20)–C(25)	156.1(2)	C(25)–C(20)–C(21)–C(22)	–0.5(4)
B(1)–C(20)–C(21)–C(22)	–177.1(2)	C(20)–C(21)–C(22)–C(23)	–0.1(4)
C(21)–C(22)–C(23)–C(24)	0.5(4)	C(22)–C(23)–C(24)–C(25)	–0.4(4)
C(23)–C(24)–C(25)–C(20)	–0.2(4)	C(21)–C(20)–C(25)–C(24)	0.6(4)
B(1)–C(20)–C(25)–C(24)	177.3(2)	C(38)–B(1)–C(26)–C(31)	17.9(3)
C(20)–B(1)–C(26)–C(31)	–102.1(3)	C(32)–B(1)–C(26)–C(31)	137.8(2)
C(38)–B(1)–C(26)–C(27)	–162.6(2)	C(20)–B(1)–C(26)–C(27)	77.3(3)
C(32)–B(1)–C(26)–C(27)	–42.7(3)	C(31)–C(26)–C(27)–C(28)	–0.1(4)
B(1)–C(26)–C(27)–C(28)	–179.6(2)	C(26)–C(27)–C(28)–C(29)	0.0(4)
C(27)–C(28)–C(29)–C(30)	0.1(4)	C(28)–C(29)–C(30)–C(31)	–0.1(4)
C(29)–C(30)–C(31)–C(26)	0.0(4)	C(27)–C(26)–C(31)–C(30)	0.1(4)
B(1)–C(26)–C(31)–C(30)	179.6(2)	C(38)–B(1)–C(32)–C(37)	–87.5(3)
C(20)–B(1)–C(32)–C(37)	31.5(3)	C(26)–B(1)–C(32)–C(37)	152.6(2)
C(38)–B(1)–C(32)–C(33)	90.2(3)	C(20)–B(1)–C(32)–C(33)	–150.8(3)
C(26)–B(1)–C(32)–C(33)	–29.7(3)	C(37)–C(32)–C(33)–C(34)	–0.6(5)
B(1)–C(32)–C(33)–C(34)	–178.5(3)	C(32)–C(33)–C(34)–C(35)	0.5(6)
C(33)–C(34)–C(35)–C(36)	0.2(6)	C(34)–C(35)–C(36)–C(37)	–0.7(5)
C(33)–C(32)–C(37)–C(36)	0.1(4)	B(1)–C(32)–C(37)–C(36)	178.0(3)
C(35)–C(36)–C(37)–C(32)	0.6(5)	C(20)–B(1)–C(38)–C(39)	–139.3(2)
C(32)–B(1)–C(38)–C(39)	–20.8(3)	C(26)–B(1)–C(38)–C(39)	100.0(3)
C(20)–B(1)–C(38)–C(43)	41.7(3)	C(32)–B(1)–C(38)–C(43)	160.2(2)
C(26)–B(1)–C(38)–C(43)	–79.0(3)	C(43)–C(38)–C(39)–C(40)	–0.8(4)

B(1)–C(38)–C(39)–C(40)	−179.8(3)	C(38)–C(39)–C(40)–C(41)	1.3(5)
C(39)–C(40)–C(41)–C(42)	–0.8(5)	C(40)–C(41)–C(42)–C(43)	–0.2(4)
C(41)–C(42)–C(43)–C(38)	0.7(4)	C(39)–C(38)–C(43)–C(42)	–0.2(4)
B(1)–C(38)–C(43)–C(42)	178.9(2)		

Sdrc32 figs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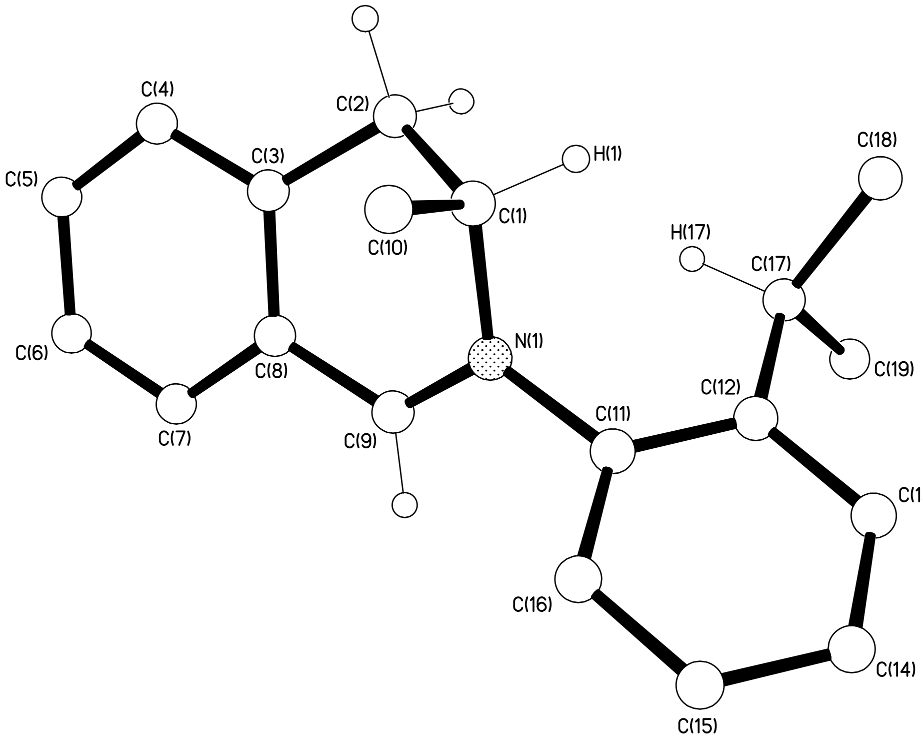
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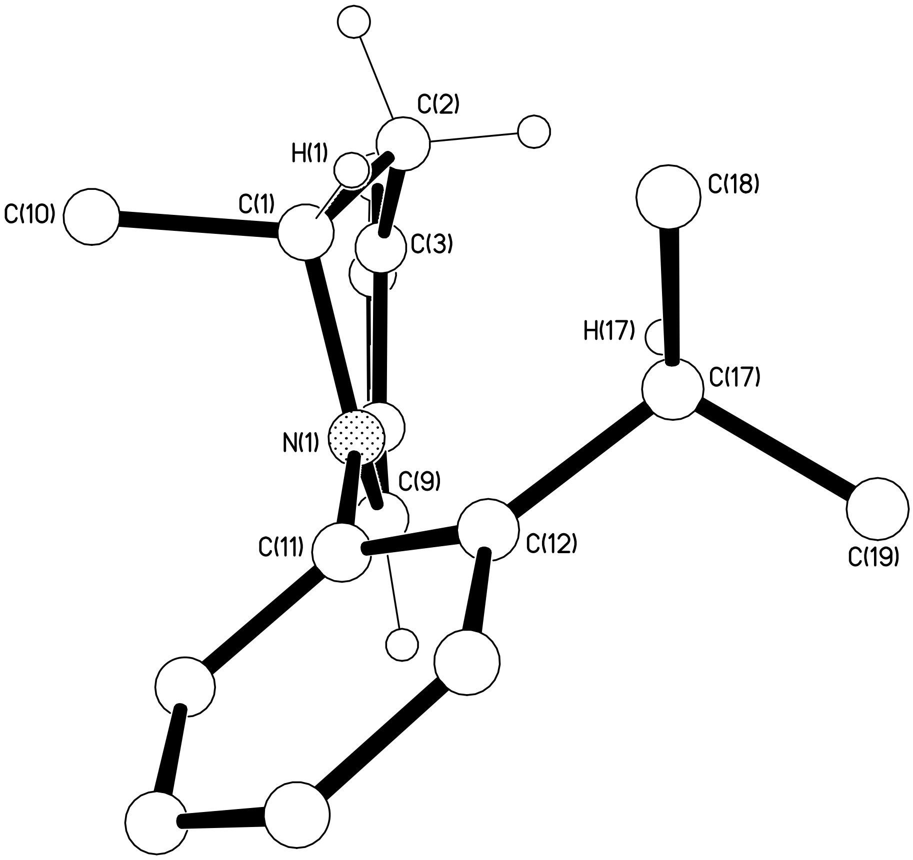
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C(19)

Table 1. Crystal data and structure refinement for sdrc32.

Identification code	sdrc32	
Chemical formula	$C_{43}H_{42}BN$	
Formula weight	583.59	
Temperature	150(2) K	
Radiation, wavelength	synchrotron, 0.7749 Å	
Crystal system, space group	monoclinic, $P2_1/n$	
Unit cell parameters	a = 9.7322(4) Å	α = 90°
	b = 34.0209(15) Å	β = 100.048(3)°
	c = 10.2636(4) Å	γ = 90°
Cell volume	3346.1(2) $Å^3$	
Z	4	
Calculated density	1.158 g/cm^3	
Absorption coefficient μ	0.065 mm^{-1}	
F(000)	1248	
Crystal colour and size	colourless, 0.22 × 0.02 × 0.01 mm^3	
Reflections for cell refinement	9977 (θ range 2.29 to 27.45°)	
Data collection method	Bruker APEX 2 CCD diffractometer	
	ω rotation with narrow frames	
θ range for data collection	2.29 to 27.96°	
Index ranges	h –11 to 11, k –41 to 41, l –12 to 12	
Completeness to θ = 27.96°	99.6 %	
Intensity decay	0%	
Reflections collected	46723	
Independent reflections	6190 (R_{int} = 0.0455)	
Reflections with F^2>2σ	4575	
Absorption correction	semi-empirical from equivalents	
Min. and max. transmission	0.986 and 0.999	
Structure solution	direct methods	
Refinement method	Full-matrix least-squares on F^2	
Weighting parameters a, b	0.0431, 0.8983	
Data / restraints / parameters	6190 / 0 / 410	
Final R indices [F^2>2σ]	R1 = 0.0408, wR2 = 0.0931	
R indices (all data)	R1 = 0.0624, wR2 = 0.1028	
Goodness-of-fit on F^2	1.015	
Extinction coefficient	0.0033(5)	
Largest and mean shift/su	0.000 and 0.000	
Largest diff. peak and hole	0.204 and –0.161 e $Å^{-3}$	

Acknowledgement: The Advanced Light Source is supported by the Director, Office of Science, Office of Basic Energy Sciences, of the U.S. Department of Energy under Contract No. DE-AC02-05CH11231.

Table 2. Atomic coordinates and equivalent isotropic displacement parameters (Å^2) for sdrc32. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U_{eq}
N(1)	0.97051(12)	0.13258(4)	0.16573(12)	0.0303(3)
C(1)	0.91609(16)	0.11537(5)	0.03173(15)	0.0351(4)
C(2)	1.03114(17)	0.09154(5)	–0.01354(15)	0.0393(4)
C(3)	1.10191(15)	0.06392(5)	0.09141(16)	0.0364(4)
C(4)	1.16017(17)	0.02830(5)	0.0658(2)	0.0481(4)
C(5)	1.23387(18)	0.00639(5)	0.1681(2)	0.0531(5)
C(6)	1.25373(18)	0.01951(5)	0.2981(2)	0.0509(5)
C(7)	1.19712(16)	0.05498(5)	0.32633(17)	0.0400(4)
C(8)	1.11996(15)	0.07673(4)	0.22356(15)	0.0319(3)
C(9)	1.05896(15)	0.11346(4)	0.25174(15)	0.0313(3)
C(10)	0.78507(17)	0.09216(5)	0.04136(17)	0.0424(4)
C(11)	0.90279(15)	0.16787(4)	0.20416(14)	0.0306(3)
C(12)	0.92519(15)	0.20403(4)	0.14701(14)	0.0330(3)
C(13)	0.85616(16)	0.23618(5)	0.18967(15)	0.0381(4)
C(14)	0.77306(17)	0.23241(5)	0.28552(16)	0.0414(4)
C(15)	0.75481(17)	0.19632(5)	0.34113(16)	0.0407(4)
C(16)	0.81898(16)	0.16357(5)	0.29895(15)	0.0358(4)
C(17)	1.02425(17)	0.20983(5)	0.04987(15)	0.0380(4)
C(18)	0.9426(2)	0.22084(6)	–0.08698(16)	0.0476(4)
C(19)	1.13352(19)	0.24117(6)	0.09940(18)	0.0487(4)
B(1)	0.38826(18)	0.11153(5)	0.73419(18)	0.0342(4)
C(20)	0.53979(15)	0.10660(5)	0.68410(15)	0.0358(4)
C(21)	0.65356(17)	0.13106(6)	0.72704(17)	0.0497(5)
C(22)	0.77715(19)	0.12867(7)	0.67592(19)	0.0632(6)
C(23)	0.79092(18)	0.10200(7)	0.5800(2)	0.0590(6)
C(24)	0.6815(2)	0.07733(6)	0.5338(2)	0.0569(5)
C(25)	0.55873(18)	0.07974(5)	0.58552(19)	0.0474(4)
C(26)	0.30556(15)	0.06899(5)	0.72211(15)	0.0340(3)
C(27)	0.37539(17)	0.03384(5)	0.76360(19)	0.0476(4)
C(28)	0.3102(2)	–0.00246(5)	0.7549(2)	0.0544(5)
C(29)	0.16950(19)	–0.00536(5)	0.70322(18)	0.0479(4)
C(30)	0.09589(18)	0.02824(5)	0.66368(17)	0.0435(4)
C(31)	0.16293(16)	0.06450(5)	0.67367(15)	0.0363(4)
C(32)	0.41065(15)	0.12727(5)	0.88790(16)	0.0374(4)
C(33)	0.40686(16)	0.10276(6)	0.99635(17)	0.0491(5)
C(34)	0.42900(19)	0.11649(8)	1.12608(19)	0.0651(6)
C(35)	0.4563(2)	0.15542(9)	1.1530(2)	0.0699(7)
C(36)	0.4618(2)	0.18077(7)	1.0496(2)	0.0683(6)
C(37)	0.4388(2)	0.16696(6)	0.92051(19)	0.0531(5)
C(38)	0.29640(15)	0.14430(4)	0.63715(15)	0.0316(3)
C(39)	0.17673(15)	0.16218(5)	0.67060(15)	0.0356(4)
C(40)	0.09607(16)	0.18920(5)	0.59007(16)	0.0373(4)
C(41)	0.13265(16)	0.20032(5)	0.47138(15)	0.0368(4)
C(42)	0.24907(17)	0.18337(5)	0.43412(15)	0.0369(4)
C(43)	0.32840(16)	0.15601(4)	0.51538(15)	0.0338(3)

Table 3. Bond lengths [Å] and angles [°] for sdrc32.

N(1)–C(9)	1.2954(18)	N(1)–C(11)	1.4568(18)
N(1)–C(1)	1.5035(18)	C(1)–C(10)	1.518(2)
C(1)–C(2)	1.519(2)	C(2)–C(3)	1.503(2)
C(3)–C(4)	1.383(2)	C(3)–C(8)	1.406(2)
C(4)–C(5)	1.382(3)	C(5)–C(6)	1.388(3)
C(6)–C(7)	1.378(2)	C(7)–C(8)	1.396(2)
C(8)–C(9)	1.435(2)	C(11)–C(16)	1.382(2)
C(11)–C(12)	1.396(2)	C(12)–C(13)	1.393(2)
C(12)–C(17)	1.516(2)	C(13)–C(14)	1.384(2)
C(14)–C(15)	1.378(2)	C(15)–C(16)	1.383(2)
C(17)–C(19)	1.529(2)	C(17)–C(18)	1.534(2)
B(1)–C(32)	1.644(2)	B(1)–C(26)	1.650(2)
B(1)–C(38)	1.650(2)	B(1)–C(20)	1.653(2)
C(20)–C(21)	1.394(2)	C(20)–C(25)	1.399(2)
C(21)–C(22)	1.396(3)	C(22)–C(23)	1.362(3)
C(23)–C(24)	1.374(3)	C(24)–C(25)	1.392(2)
C(26)–C(31)	1.399(2)	C(26)–C(27)	1.404(2)
C(27)–C(28)	1.384(2)	C(28)–C(29)	1.383(3)
C(29)–C(30)	1.372(3)	C(30)–C(31)	1.391(2)
C(32)–C(33)	1.396(2)	C(32)–C(37)	1.406(3)
C(33)–C(34)	1.392(3)	C(34)–C(35)	1.369(3)
C(35)–C(36)	1.375(3)	C(36)–C(37)	1.387(3)
C(38)–C(43)	1.398(2)	C(38)–C(39)	1.408(2)
C(39)–C(40)	1.385(2)	C(40)–C(41)	1.380(2)
C(41)–C(42)	1.383(2)	C(42)–C(43)	1.390(2)
C(9)–N(1)–C(11)	120.50(12)	C(9)–N(1)–C(1)	120.93(13)
C(11)–N(1)–C(1)	117.70(11)	N(1)–C(1)–C(10)	108.00(12)
N(1)–C(1)–C(2)	109.08(12)	C(10)–C(1)–C(2)	114.49(14)
C(3)–C(2)–C(1)	112.61(13)	C(4)–C(3)–C(8)	117.97(16)
C(4)–C(3)–C(2)	124.29(15)	C(8)–C(3)–C(2)	117.52(14)
C(5)–C(4)–C(3)	120.24(17)	C(4)–C(5)–C(6)	121.59(16)
C(7)–C(6)–C(5)	119.33(17)	C(6)–C(7)–C(8)	119.17(16)
C(7)–C(8)–C(3)	121.66(15)	C(7)–C(8)–C(9)	119.77(14)
C(3)–C(8)–C(9)	118.56(14)	N(1)–C(9)–C(8)	123.31(14)
C(16)–C(11)–C(12)	122.92(14)	C(16)–C(11)–N(1)	116.99(13)
C(12)–C(11)–N(1)	120.09(13)	C(13)–C(12)–C(11)	116.12(14)
C(13)–C(12)–C(17)	120.10(14)	C(11)–C(12)–C(17)	123.69(13)
C(14)–C(13)–C(12)	121.61(15)	C(15)–C(14)–C(13)	120.69(15)
C(14)–C(15)–C(16)	119.34(15)	C(11)–C(16)–C(15)	119.30(15)
C(12)–C(17)–C(19)	110.93(13)	C(12)–C(17)–C(18)	110.29(13)
C(19)–C(17)–C(18)	110.67(14)	C(32)–B(1)–C(26)	109.82(13)
C(32)–B(1)–C(38)	109.04(13)	C(26)–B(1)–C(38)	109.96(12)
C(32)–B(1)–C(20)	110.82(12)	C(26)–B(1)–C(20)	109.73(13)
C(38)–B(1)–C(20)	107.44(12)	C(21)–C(20)–C(25)	114.90(15)
C(21)–C(20)–B(1)	122.94(15)	C(25)–C(20)–B(1)	121.90(14)
C(20)–C(21)–C(22)	122.37(19)	C(23)–C(22)–C(21)	120.67(19)
C(22)–C(23)–C(24)	119.24(17)	C(23)–C(24)–C(25)	119.82(19)
C(24)–C(25)–C(20)	123.00(18)	C(31)–C(26)–C(27)	114.37(14)
C(31)–C(26)–B(1)	124.28(14)	C(27)–C(26)–B(1)	121.34(14)
C(28)–C(27)–C(26)	123.23(16)	C(29)–C(28)–C(27)	120.02(17)
C(30)–C(29)–C(28)	119.01(16)	C(29)–C(30)–C(31)	120.20(16)
C(30)–C(31)–C(26)	123.14(16)	C(33)–C(32)–C(37)	114.50(16)
C(33)–C(32)–B(1)	123.57(16)	C(37)–C(32)–B(1)	121.92(15)

C(34)–C(33)–C(32)	122.8(2)	C(35)–C(34)–C(33)	120.7(2)
C(34)–C(35)–C(36)	118.88(19)	C(35)–C(36)–C(37)	120.2(2)
C(36)–C(37)–C(32)	123.0(2)	C(43)–C(38)–C(39)	114.68(14)
C(43)–C(38)–B(1)	123.40(13)	C(39)–C(38)–B(1)	121.91(13)
C(40)–C(39)–C(38)	123.22(14)	C(41)–C(40)–C(39)	120.13(15)
C(40)–C(41)–C(42)	118.65(15)	C(41)–C(42)–C(43)	120.60(15)
C(42)–C(43)–C(38)	122.69(14)		

Table 4. Hydrogen coordinates and isotropic displacement parameters (Å^2) for sdrc32.

	x	y	z	U
H(1)	0.8902	0.1375	–0.0321	0.042
H(2A)	0.9909	0.0762	–0.0930	0.047
H(2B)	1.1015	0.1097	–0.0388	0.047
H(4)	1.1495	0.0188	–0.0225	0.058
H(5)	1.2719	–0.0182	0.1490	0.064
H(6)	1.3058	0.0042	0.3669	0.061
H(7)	1.2105	0.0645	0.4146	0.048
H(9)	1.0847	0.1243	0.3378	0.038
H(10A)	0.8099	0.0689	0.0968	0.064
H(10B)	0.7400	0.0839	–0.0473	0.064
H(10C)	0.7207	0.1087	0.0809	0.064
H(13)	0.8664	0.2613	0.1521	0.046
H(14)	0.7281	0.2549	0.3133	0.050
H(15)	0.6987	0.1940	0.4078	0.049
H(16)	0.8056	0.1384	0.3347	0.043
H(17)	1.0737	0.1844	0.0416	0.046
H(18A)	0.8707	0.2010	–0.1155	0.071
H(18B)	1.0067	0.2220	–0.1507	0.071
H(18C)	0.8984	0.2466	–0.0821	0.071
H(19A)	1.0879	0.2669	0.0994	0.073
H(19B)	1.2031	0.2421	0.0410	0.073
H(19C)	1.1795	0.2347	0.1895	0.073
H(21)	0.6468	0.1501	0.7935	0.060
H(22)	0.8524	0.1458	0.7083	0.076
H(23)	0.8752	0.1005	0.5455	0.071
H(24)	0.6895	0.0587	0.4667	0.068
H(25)	0.4844	0.0624	0.5524	0.057
H(27)	0.4721	0.0350	0.7994	0.057
H(28)	0.3621	–0.0254	0.7844	0.065
H(29)	0.1245	–0.0302	0.6952	0.057
H(30)	–0.0011	0.0267	0.6294	0.052
H(31)	0.1093	0.0873	0.6463	0.044
H(33)	0.3884	0.0756	0.9809	0.059
H(34)	0.4251	0.0987	1.1966	0.078
H(35)	0.4713	0.1648	1.2416	0.084
H(36)	0.4813	0.2078	1.0667	0.082
H(37)	0.4423	0.1851	0.8509	0.064
H(39)	0.1500	0.1554	0.7524	0.043
H(40)	0.0154	0.2001	0.6166	0.045
H(41)	0.0790	0.2192	0.4164	0.044
H(42)	0.2751	0.1905	0.3523	0.044
H(43)	0.4076	0.1448	0.4870	0.041

Table 5. Torsion angles [°] for sdrc32.

C(9)–N(1)–C(1)–C(10)	90.12(16)	C(11)–N(1)–C(1)–C(10)	–79.24(16)
C(9)–N(1)–C(1)–C(2)	–34.88(18)	C(11)–N(1)–C(1)–C(2)	155.77(13)
N(1)–C(1)–C(2)–C(3)	48.15(17)	C(10)–C(1)–C(2)–C(3)	–72.96(17)
C(1)–C(2)–C(3)–C(4)	149.62(15)	C(1)–C(2)–C(3)–C(8)	–35.88(19)
C(8)–C(3)–C(4)–C(5)	–0.2(2)	C(2)–C(3)–C(4)–C(5)	174.31(16)
C(3)–C(4)–C(5)–C(6)	–1.1(3)	C(4)–C(5)–C(6)–C(7)	0.9(3)
C(5)–C(6)–C(7)–C(8)	0.6(2)	C(6)–C(7)–C(8)–C(3)	–1.9(2)
C(6)–C(7)–C(8)–C(9)	179.22(14)	C(4)–C(3)–C(8)–C(7)	1.6(2)
C(2)–C(3)–C(8)–C(7)	–173.20(14)	C(4)–C(3)–C(8)–C(9)	–179.43(14)
C(2)–C(3)–C(8)–C(9)	5.7(2)	C(11)–N(1)–C(9)–C(8)	174.35(13)
C(1)–N(1)–C(9)–C(8)	5.3(2)	C(7)–C(8)–C(9)–N(1)	–170.06(14)
C(3)–C(8)–C(9)–N(1)	11.0(2)	C(9)–N(1)–C(11)–C(16)	–62.08(18)
C(1)–N(1)–C(11)–C(16)	107.31(15)	C(9)–N(1)–C(11)–C(12)	117.15(16)
C(1)–N(1)–C(11)–C(12)	–73.45(17)	C(16)–C(11)–C(12)–C(13)	–0.8(2)
N(1)–C(11)–C(12)–C(13)	179.98(13)	C(16)–C(11)–C(12)–C(17)	175.72(14)
N(1)–C(11)–C(12)–C(17)	–3.5(2)	C(11)–C(12)–C(13)–C(14)	1.5(2)
C(17)–C(12)–C(13)–C(14)	–175.18(15)	C(12)–C(13)–C(14)–C(15)	–0.7(2)
C(13)–C(14)–C(15)–C(16)	–0.9(2)	C(12)–C(11)–C(16)–C(15)	–0.7(2)
N(1)–C(11)–C(16)–C(15)	178.54(13)	C(14)–C(15)–C(16)–C(11)	1.5(2)
C(13)–C(12)–C(17)–C(19)	53.08(19)	C(11)–C(12)–C(17)–C(19)	–123.34(16)
C(13)–C(12)–C(17)–C(18)	–69.89(19)	C(11)–C(12)–C(17)–C(18)	113.68(17)
C(32)–B(1)–C(20)–C(21)	–33.2(2)	C(26)–B(1)–C(20)–C(21)	–154.68(15)
C(38)–B(1)–C(20)–C(21)	85.80(18)	C(32)–B(1)–C(20)–C(25)	152.93(15)
C(26)–B(1)–C(20)–C(25)	31.5(2)	C(38)–B(1)–C(20)–C(25)	–88.04(18)
C(25)–C(20)–C(21)–C(22)	–0.4(3)	B(1)–C(20)–C(21)–C(22)	–174.64(17)
C(20)–C(21)–C(22)–C(23)	0.4(3)	C(21)–C(22)–C(23)–C(24)	0.0(3)
C(22)–C(23)–C(24)–C(25)	–0.3(3)	C(23)–C(24)–C(25)–C(20)	0.2(3)
C(21)–C(20)–C(25)–C(24)	0.1(3)	B(1)–C(20)–C(25)–C(24)	174.43(16)
C(32)–B(1)–C(26)–C(31)	100.59(17)	C(38)–B(1)–C(26)–C(31)	–19.4(2)
C(20)–B(1)–C(26)–C(31)	–137.36(15)	C(32)–B(1)–C(26)–C(27)	–78.07(18)
C(38)–B(1)–C(26)–C(27)	161.94(15)	C(20)–B(1)–C(26)–C(27)	44.0(2)
C(31)–C(26)–C(27)–C(28)	1.4(3)	B(1)–C(26)–C(27)–C(28)	–179.79(17)
C(26)–C(27)–C(28)–C(29)	0.0(3)	C(27)–C(28)–C(29)–C(30)	–1.3(3)
C(28)–C(29)–C(30)–C(31)	1.0(3)	C(29)–C(30)–C(31)–C(26)	0.5(3)
C(27)–C(26)–C(31)–C(30)	–1.7(2)	B(1)–C(26)–C(31)–C(30)	179.56(15)
C(26)–B(1)–C(32)–C(33)	21.0(2)	C(38)–B(1)–C(32)–C(33)	141.59(15)
C(20)–B(1)–C(32)–C(33)	–100.35(17)	C(26)–B(1)–C(32)–C(37)	–160.53(14)
C(38)–B(1)–C(32)–C(37)	–39.98(19)	C(20)–B(1)–C(32)–C(37)	78.08(18)
C(37)–C(32)–C(33)–C(34)	0.1(2)	B(1)–C(32)–C(33)–C(34)	178.60(15)
C(32)–C(33)–C(34)–C(35)	–0.2(3)	C(33)–C(34)–C(35)–C(36)	–0.1(3)
C(34)–C(35)–C(36)–C(37)	0.5(3)	C(35)–C(36)–C(37)–C(32)	–0.6(3)
C(33)–C(32)–C(37)–C(36)	0.3(3)	B(1)–C(32)–C(37)–C(36)	–178.23(17)
C(32)–B(1)–C(38)–C(43)	136.52(14)	C(26)–B(1)–C(38)–C(43)	–103.02(16)
C(20)–B(1)–C(38)–C(43)	16.4(2)	C(32)–B(1)–C(38)–C(39)	–44.72(19)
C(26)–B(1)–C(38)–C(39)	75.74(18)	C(20)–B(1)–C(38)–C(39)	–164.88(14)
C(43)–C(38)–C(39)–C(40)	0.1(2)	B(1)–C(38)–C(39)–C(40)	–178.73(14)
C(38)–C(39)–C(40)–C(41)	–1.0(2)	C(39)–C(40)–C(41)–C(42)	1.3(2)
C(40)–C(41)–C(42)–C(43)	–0.7(2)	C(41)–C(42)–C(43)–C(38)	–0.2(2)
C(39)–C(38)–C(43)–C(42)	0.5(2)	B(1)–C(38)–C(43)–C(42)	179.32(14)