Synthesis and application of novel boronates containing intramolecular N-B interactions

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Submitted by Andrew Martin Kelly

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Acknowledgements

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'Do you not know? Have you not heard? The LORD is the everlasting God, the Creator of the ends of the earth. He will not grow tired or weary and his understanding no one can fathom. He gives strength to the weary and increases the power of the weak. Even youths grow tired and weary, and young men stumble and fall; but those who hope in the LORD will renew their strength. They will soar on wings like eagles, they will run and not grow weary. They will walk and not be faint.'

Isaiah 40:28-31

"Salvation is found in no-one else, for there is no other name under heaven given to men by which we must be saved."

The Acts of the Apostles 4:11

"Now this is eternal life: that they may know you, the only true God, and Jesus Christ, whom you have sent."

John 17:3

"Now all has been heard;
here is the conclusion of the matter:
Fear God and keep his commandments,
for this is the whole duty of man.
For God will bring every deed into judgment,
including every hidden thing,
whether it is good or evil."

Ecclesiastes 12:13,14

Abbreviations

Å	Angstrom
abs	absolute
app	apparent
aq.	aqueous
Ar	Aromatic
BINOL	1,1'-bi-2-naphthol
Boc	*tert*-butyloxycarbonyl
Bn	benzyl
br	broad
Bu	butyl
^{i}Bu	*iso*-butyl
^{n}Bu	*normal*-butyl
^{t}Bu	*tert*-butyl
^{o}C	degrees celsius
cat.	catalytic quantity
CBS	Corey-Bakshi-Shibata catalyst
CH_2Cl_2	dichloromethane
$CHCl_3$	chloroform
$CDCl_3$	deuterated chloroform
CDA	chiral derivatising agent
CI	chemical ionisation
conc.	concentrated
CSA	chiral solvating agent
CSR	chiral shift reagent
cy	cyclohexyl
δ	chemical shift in parts per million
Δ	difference in value (of chemical shift)
d	doublet
DCM	dichloromethane
dd	doublet of doublets
de	diastereomeric excess

dec.	decomposed
dil.	diluted
dt	doublet of triplets
ee	enantiomeric excess
EI	electron impact
eq.	equivalent(s)
ES	electrospray
Et	ethyl
Et_3N	triethylamine
EtOH	ethanol
g	gram
h	hour
HPLC	High Performance Liquid Chromatography
HRMS	High Resolution Mass Spectrometry
Hz	Hertz
ICT	Internal Charge Transfer
$IPcBH_2$	monoisopinocampheylborane
IPc_2BH	diisopinocampheylborane
IR	infrared
J	coupling constant
LA	Lewis acid
m	meta
m	multiplet
M	molar
Me	methyl
MeOD	methanol-d_4
mg	milligram
MHz	mega Hertz
mmol	millimole
min	minute(s)
mL	millilitre
mp	melting point
MS	molecular sieves, mass spectrometry

MTPA	α-methoxy-α-trifluoromethylphenylacetic acid (Mosher's reagent)
MW	molecular weight
m/z	mass to charge ratio
nm	nanometre
NMR	nuclear magnetic resonance
o	ortho
o	octet
p	para
PET	Photoinduced Electron Transfer
Ph	phenyl
ppm	parts per million
Pr	propyl
^{i}Pr	*iso*-propyl
^{n}Pr	*normal*-propyl
q	quartet
quin	quintet
R	generic substituent
rt	room temperature
s	singlet
sat.	saturated
sol.	solution
sxt	sextet
t	triplet
td	triplet of doublets
TBDMS	*tert*-butyldimethylsilyl
TBDMSCl	*tert*-butyldimethylsilylchloride
TICT	Twisted Internal Charge Transfer
TLC	thin layer chromatography
TMS	trimethylsilyl, tetramethylsilane
Tol	Toluene
v	wavenumber

Abstract

This thesis describes the investigations towards developing facile protocols for the determination of the enantiomeric excesses of three classes of compounds - chiral diols, diamines and amino alcohols - employing tandem imine and boronate ester condensation of pairs of enantiomers to afford corresponding pairs of diastereoisomeric iminoboronate esters or imidazolidine boronate esters from which the enantiomeric excess of the parent compound may be determined using ^{1}H NMR analysis.

The first chapter begins with a brief overview of boron chemistry before considering some examples of intermolecular N→B coordinate bonding. We then go on to focus on the nature and use of the intramolecular N→B interaction in a variety of synthetic methodologies.

The second chapter introduces our previous work toward the development of a novel protocol for the determination of the enantiopurity of chiral primary amines. We then consider different spectroscopic approaches for determination of *ee* before detailing individual studies to expand this methodology for the determination of the enantiopurity of chiral diols, diamines and amino alcohols.

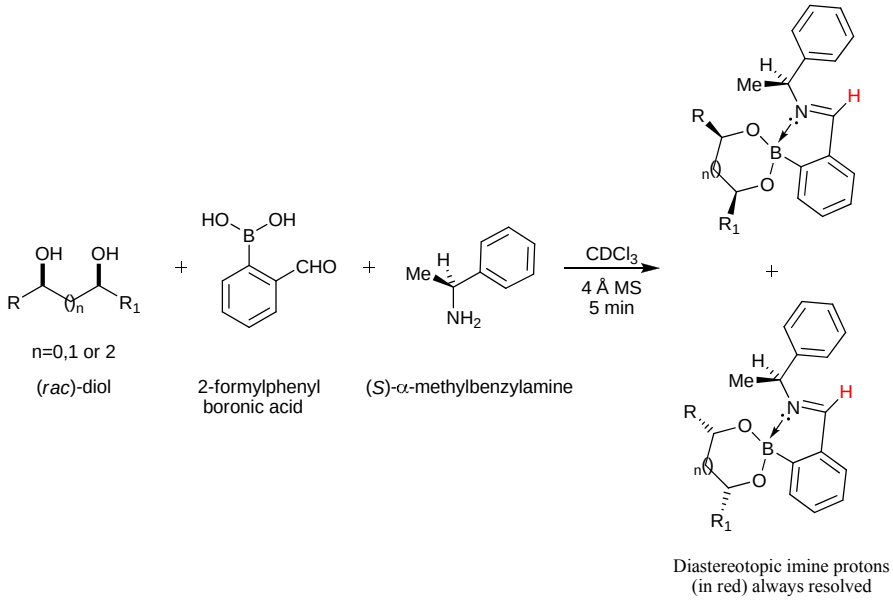


Figure 1 Three-component protocol for determination of the enantiomeric excess of a chiral diol.

For chiral diols, the approach involved a 3-component coupling of 2-formylphenylboronic acid with enantiopure (*S*)-α-methylbenzylamine and the diol

under investigation to afford a pair of iminoboronate esters which show baseline resolution of pairs of proton resonances by ^{1}H NMR spectroscopy (Figure 1).

For chiral diamines, two approaches were conceived. Three-component coupling of 1,2-diphenylethane-1,2-diamine with 2-formylphenylboronic acid and the enantiopure diol hydrobenzoin afforded pairs of imidazolidine boronate esters whose resonances were again distinct by ^{1}H NMR analysis. However, the general applicability of this protocol has not been established, in which case an alternative *mono*-Boc protection strategy was developed followed by iminoboronate ester formation with an enantiopure diol as before.

Attempted 3-component oxazolidine boronate ester formation for the determination of the enantiopurity of chiral amino alcohols proved unsuccessful. We therefore employed an *O*-protection approach before forming diastereomeric iminoboronate esters to determine their *ee*. The synthesis of a range novel chiral oxygen-bridged *di*-boron species, initially formed as *in situ* products in our early investigations with amino alcohols is then described (Figure 2).

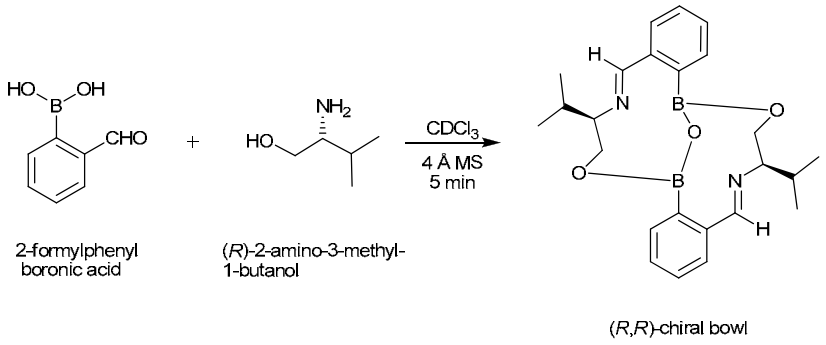


Figure 2 Synthesis of oxygen-bridged *di*-boron species.

Contents

1.1 General Introduction

In this short review, we will first consider some of the characteristic chemistry involving boron-containing compounds. We will then follow this with a brief overview of literature reporting intermolecular boron-nitrogen coordinate bonding before focusing in greater depth on the employment of intramolecular N→B bonding in a wide range of methodologies.

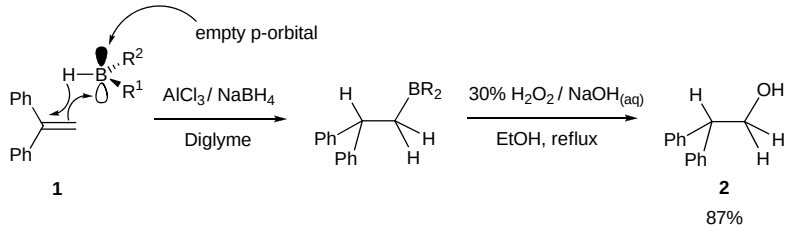
1.2 Boron-Nitrogen Bonds and Their Applications in Synthesis

There has been a significant amount of interest in the field of asymmetric synthesis in recent years, due in part to the increasing demand for enantiomerically pure compounds from the pharmaceutical industry.[1] Synthesising such compounds has been achieved using a variety of methodologies. These range from using 'chiral pool' substrates as enantioselective reagents,[2-4] chiral auxiliaries[5] and chiral reagents,[6, 7] through to kinetic resolution[8-10] and asymmetric catalysis.[5, 11, 12]

1.2.1 Hydroboration and the Origins of Boron in Asymmetric Synthesis

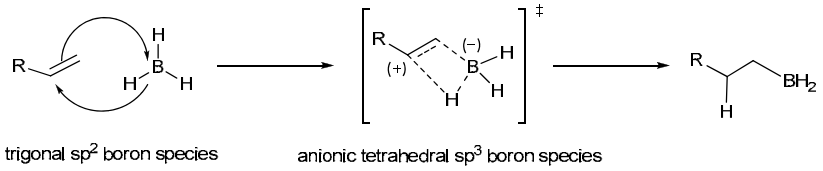
There has been growing interest in the application of electron-deficient boron species for asymmetric synthesis.[13-15] The proliferation of boron-based synthesis dates back to 1956 with seminal work published by Herbert C. Brown *et al.* for which he later received the Nobel Prize.[16†] In this paper, a novel technique for the conversion of olefins into trialkylboranes and through to their corresponding alcohols was described (Scheme 1).

[†] The 1979 Nobel Prize was awarded jointly to H. C. Brown and G. Wittig for their development of Boron and Phosphorous-containing compounds respectively into significant reagents for organic synthesis.



Scheme 1 The first reported hydroboration reaction of 1,1-diphenylethene **1** to 2,2-diphenylethanol **2** by H. C. Brown *et al.*

Of particular note was the apparent anti-Markovnikov regioselectivity of the B-H bond across the alkene.[17] This can be reasoned due to steric and electronic factors. Boron has an electronegativity (2.0) comparable, but importantly more electropositive than carbon (2.5) and hydrogen (2.2). As a consequence of this, the more electronegative hydrogen adds to the more substituted carbon atom (Scheme 2).



Scheme 2 Concerted addition of the B-H bond across an alkene.

The hydroboration step is considered to be concerted, although C-B bond formation occurs slightly more rapidly than the C-H bond, giving a more substituted carbocation. Hence, the mechanism proceeds *via* a 4-membered transition state with an anionic sp^3 boron species. It is this Lewis-acidic nature - due to the vacant 2p orbital - which characterises the chemistry of boron.[18,19]

H. C. Brown *et al.* expanded on this work with the synthesis of chiral organoborane reagents which can be used in asymmetric hydroboration reactions to afford chiral compounds.[20-23] Some of the most widely used chiral boranes are derived from inexpensive terpenes, such as monoisopinocampheylborane **3** and diisopinocampheylborane **4** (represented as $IpcBH_2$ and Ipc_2BH respectively) (Figure 1).[23-26]

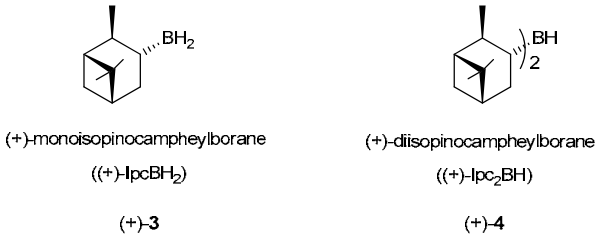
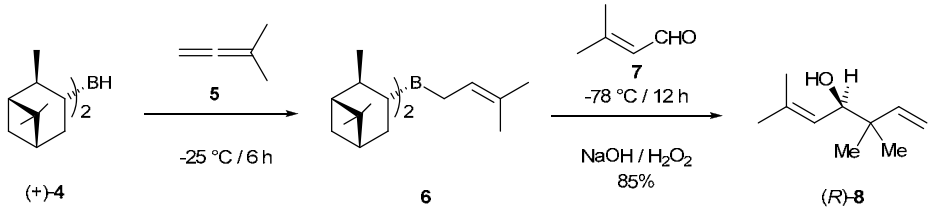


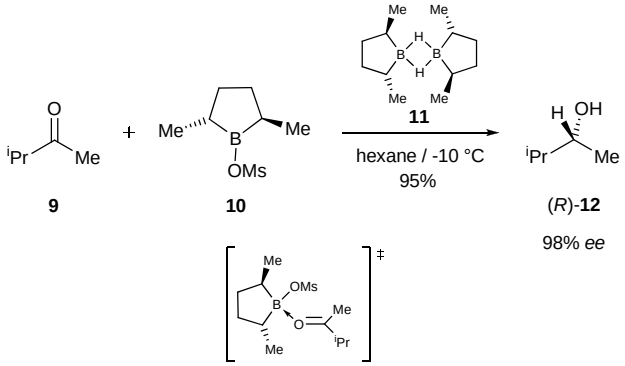
Figure 1 Commonly used chiral boranes in asymmetric hydroboration.

One such example, shown below, was reported by Brown *et al.* in 1984 (Scheme 3). They used (+)-diisopinocampheylborane (+)-**4** to effect a highly stereoselective asymmetric allylation reaction of 3-methylbuten-2-al **7** to (+)-artemisia alcohol **8** in 96% *ee*, 85% isolated yield.[7]



Scheme 3 Asymmetric allylation using chiral borane reagent (+)-**4**.

Following the pioneering work by H. C. Brown, organoboranes have been shown to undergo a wide range of chemical transformations utilising the electron deficient nature of the boron atom.[21, 23, 27-30] One such example is the work reported by Imai *et al*. in 1986.[6, 31] They employed a stoichiometric quantity of C_2-symmetric dimethylborolane reagent **10** to asymmetrically reduce prochiral ketones to their corresponding secondary alcohols with very high enantioselectivity (up to 98%). Chirality is induced into the alcohol in the diastereomeric transition state which directs the asymmetric reduction to afford one predominant enantiomer (Scheme 4).



Scheme 4 Asymmetric reduction of prochiral ketones using a C_2-symmetric chiral boron reagent.

A general feature which characterises the mechanism of many reactions of organoboranes (boron species which contain alkyl substituents) is that when the nucleophile bears a good leaving group (or a group capable of accepting electrons) adds to an sp^2 boron, affording an sp^3 tetrahedral conformation, 1,2-migration of an alkyl group can occur from the boron to the atom bearing the leaving group.

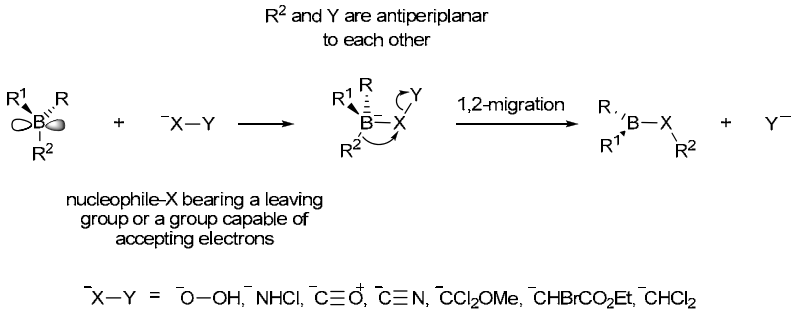


Figure 2 Addition-migration pathway which characterises much of the chemistry of boron.

Importantly, these migrations are stereoselective, with the migrating alkyl group and the leaving group aligning antiperiplanar to one another prior to the migration and with any stereocentres in the migrating group being conserved.[32, 33]

The full scope of organoborane reactions are beyond this review. More relevant is the use of boron-complexes as chiral Lewis acids in mediating reactions and generating high levels of enantioselectivity which we will now go on to consider.

1.2.2 Covalent Interactions between Boronic Acids and Diols

Phenylboronic acid was first synthesised in 1880 by Michaelis and Becker,[34, 35] some 20 years after the first reported synthesis of ethylboronic acid by Frankland in 1860.[36] The route documented by Michaelis and Becker involved treatment of boron trichloride and diphenyl mercury to form dichlorophenylboronate which was then hydrolysed and recrystallised to afford the boronic acid. This strategy was refined in 1909 when the classical route to boronic acids through Grignard reagents and trialkyl borates was established.[37]

The first binding study between phenylboronic acid and diols was not published until much later, with seminal work by Kuivila *et al*. in 1954 reporting the solvation of mixtures of phenylboronic acid and several different classes of diol. This included polyols and saccharides with the group suggesting that cyclic boronate esters were formed.[38, 39]

This was expanded in 1959 by Lorand and Edwards who reported a potentiometric investigation into the binding interaction between phenylboronic acid and different saccharides.[40] They first proposed the tetrahedral geometry of the phenylboronic acid anion although this structure is still disputed (Figure 3).[41]

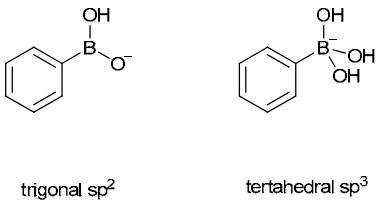
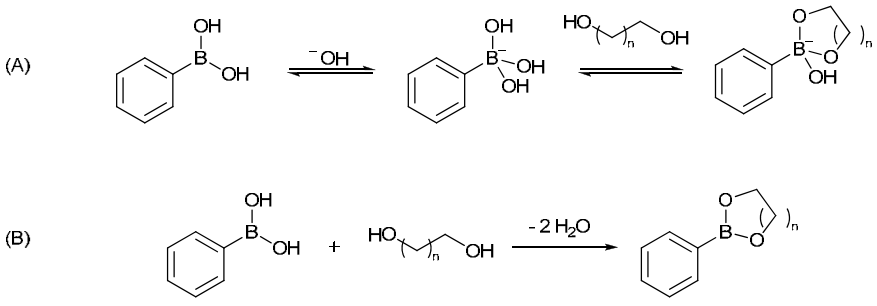


Figure 3 First reported investigation into the sp^2 *versus* sp^3 nature of the boronate anion was in 1959.

It is now known that boronic acids react rapidly and reversibly with diols to afford cyclic boronate esters in non-aqueous or basic aqueous conditions.[42-44] It has also been widely reported that boronic acids show good binding affinity with other nucleophiles such as dicarboxylic acids[42-47] and α-hydroxy-carboxylic acids.[46-48] The most common interactions involve *cis*-1,2- or 1,3-diols which afford 5 or 6-membered boronate ester rings respectively (Scheme 5).[49, 50]

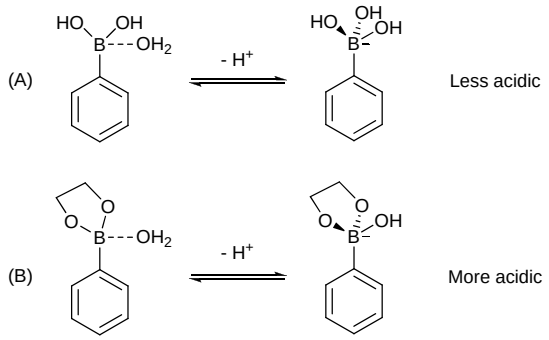


Scheme 5 Reversible formation in basic aqueous media (A) and irreversible cyclic boronate ester formation in aprotic solvent (B).

The formation of the cyclic boronate ring has a large impact on the hybridisation at the boron centre. The free boronic acid adopts a trigonal planar, sp^2 hybridised, geometry

(with a bond angle of 120°). When the boronic acid condenses with a diol the bond angle reduces to approximately 113° which is closer to the ideal bond angle of 109° for sp^3 hybridised systems. The addition of the diol therefore changes the hybridisation at the boron centre from sp^2 towards an sp^3 tetrahedral geometry.

Addition of a diol also changes the Lewis acidity of the boron atom. This change in acidity is often ascribed to the contraction of the oxygen-boron-oxygen (O-B-O) bond angle on complexation. Controlling the geometry around the boron centre through diol condensation can assist addition of a nucleophile such as a water molecule (Scheme 6).



Scheme 6 Lewis base addition assisted by cyclic boronate ester (B) rendering the boron centre more acidic.

The formation of an sp^3 hybridised boronic acid was reported by Wulff *et al.* in 1982.[51] They showed that incorporation of an adjacent amine would allow for N→B coordinate interaction with the boron atom adopting a tetrahedral conformation (Figure 4). This will be considered further, later in the chapter.

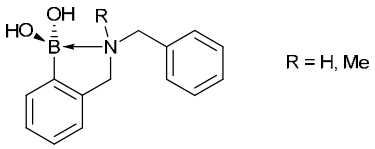


Figure 4 Intramolecular N→B interaction allows for a tetrahedral boron atom without need for a coordinating diol.

1.2.3 Chiral and Achiral Boron Lewis Acids

There has been a plethora of examples of chiral boron reagents used as Lewis acids in enantioselective reactions in the literature in recent years.[15, 52] Boron chemistry is characterised by the formation of three, two-centre-two-electron bonds leaving the boron centre sp^2 hybridised with bond angles of 120°.[53] This results in an electron deficient boron atom with an empty 2p orbital which is available to accept electrons from anions or electron-rich nucleophiles. This empty p-orbital is responsible for boron acting as a Lewis acid and as such it readily forms complexes with Lewis basic compounds to afford neutral tetrahedral species. Alternatively, reaction with an anionic nucleophile results in the formation of an "ate" anionic species (Figure 5).[29]

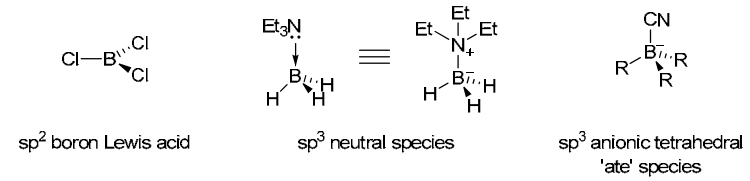


Figure 5 Trigonal sp^2 and tetrahedral sp^3 boron species.

Boron trigonal species can then be considered as neutral equivalents of carbocations, and tetrahedral boron species as mimics of sp^3 carbon compounds. The most commonly used boron Lewis acids contain electronegative ligands and are of the general structure BX_3, RBX_2 and R_2BX where X = F, Cl, Br, I and OTf.

We will now consider a couple of boron-ligand complexes employed in achiral and enantioselective reactions. We will then look at examples of boron-nitrogen, Lewis acid-base bonding in asymmetric synthesis before focusing on intramolecular boron-nitrogen bonds and their applications. For a more extensive appraisal, particularly of asymmetric reductions of ketones and reactions of boron enolates, see the review by Deloux *et al*.[32]

In the late 1980s, Yamamoto and co-workers developed a series of chiral catalysts prepared from monoacyl tartaric acids and borane, called CAB (chiral(acyloxy)borane) catalysts (Figure 6).[54, 55]

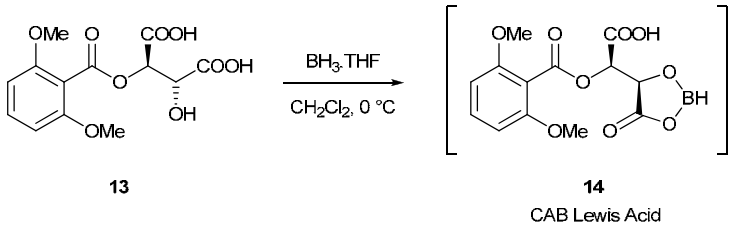
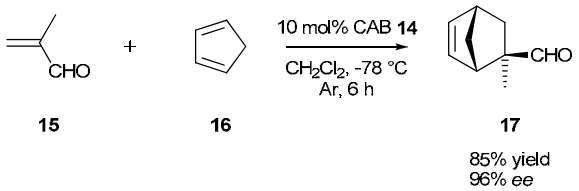


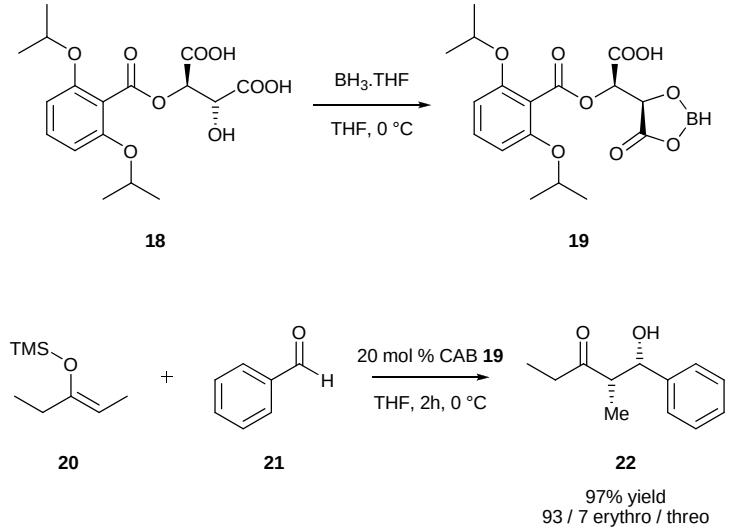
Figure 6 Formation of a CAB catalyst **14**.

Their use was reported in the asymmetric Diels-Alder reaction of an α,β-unsaturated aldehyde, such as methylacrylaldehyde **15**, with a variety of dienes, inferring a good level of asymmetric induction, with *ee*s of up to 96% and endo / exo ratios in the order of 9 / 1.[54]



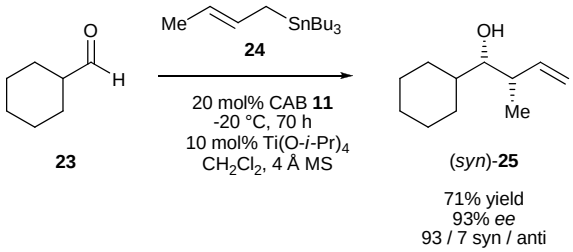
Scheme 7 Asymmetric Diels-Alder reaction catalysed by CAB catalyst **14**.

The use of these CAB catalysts was expanded on by the Yamamoto group, who, in 1991, reported their use in the asymmetric Mukaiyama aldol condensation of silyl enol ethers and aldehydes.[56] Sub-stoichiometric quantities of the CAB catalyst were used (20 mol%) while still retaining high stereocontrol of up to 96% *ee* (Scheme 8).



Scheme 8 CAB catalysed Mukaiyama aldol condensation.

More recently, work by Marshall *et al.* has demonstrated the excellent versatility of this class of chiral boron catalyst using the same CAB catalyst **14** (Figure 6) to catalyse addition of allylic stannanes such as (*E*)-but-2-enyltributylstannane **24** to achiral aldehydes, affording syn alcohols as major products with *ee*s of 55 - 96% (Scheme 9).[57]



Scheme 9 Asymmetric addition of organotin reagents to aldehydes.

1.2.4 Boron Lewis Acids with Inter-Molecular N→B Bonds

The use of boron as a Lewis acid extends to formation of coordinate bonds with a wide variety of hetero-atoms including oxygen, sulfur,[58] phosphorus[59] and nitrogen.[60] Such compounds have widespread use in organic synthesis (Figure 7).[20]

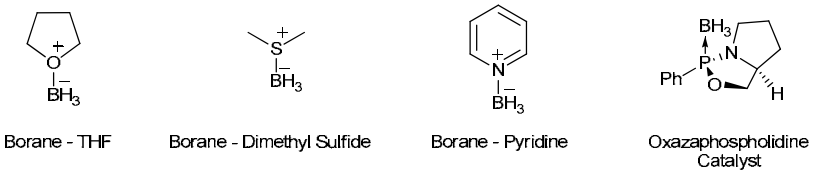
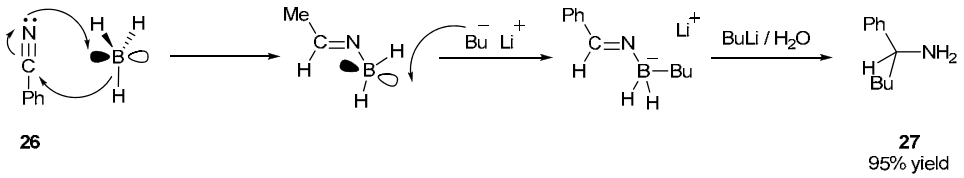


Figure 7 Some typical boron reagents incorporating heteroatom coordination.

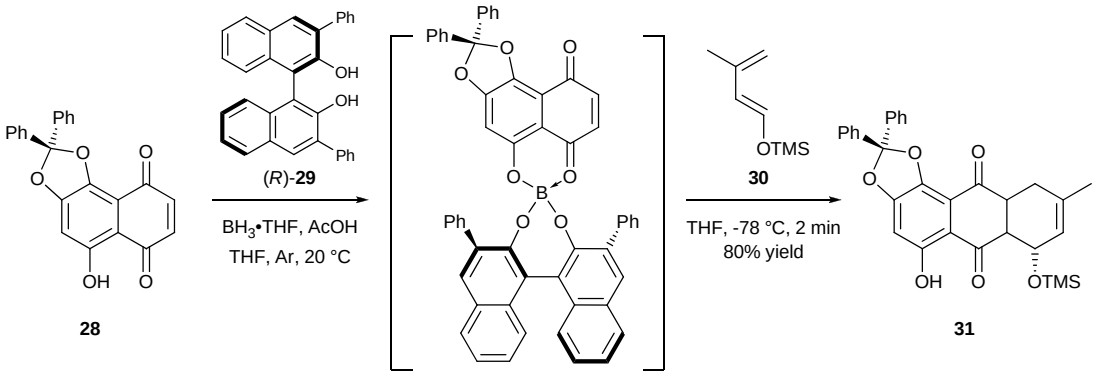
In 1991, Itsuno *et al.* reported the preparation of secondary amines from nitriles such as benzonitrile **26** in the first example of a reaction between an *N*-boryl imine and an organometallic compound.[61] Borane-tetrahydrofuran was used to form *N*-boryl imines from their respective nitrile substrates, followed by alkylation with various alkyl- or aryl-lithium reagents to afford their corresponding secondary amines (Scheme 14). The formation of the *N*-boryl imine occurs *in situ*, *via* a hydroboration-type pathway, involving borane addition across the nitrile bond.



Scheme 10 Reaction mechanism for the one-pot generation of secondary carbinamines from nitriles.

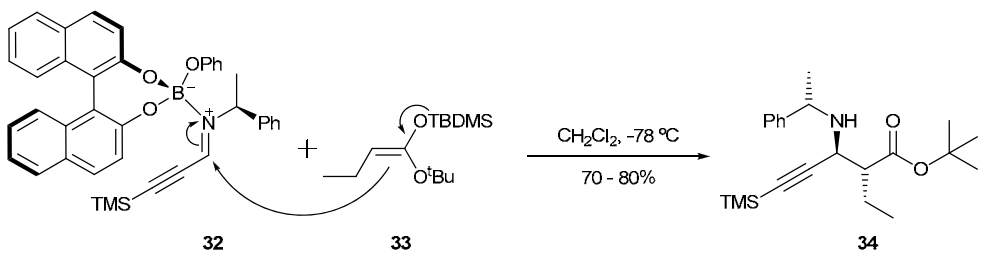
Nucleophilic-addition of the organometallic reagent is assisted by the presence of the *N*-boryl group, reducing the electron density around the nitrogen atom and hence increasing the imine carbon's electrophilicity. This was observed as the reaction proceeded rapidly with good-to-excellent yields at -80 ºC.

The first example of a boron complex with binaphthol ligands was reported by Kelly and co-workers in the mid 1980s.[62] They documented the use of *peri*-hydroxyquinones as substrates in the asymmetric Diels-Alder reaction with (*E*)-trimethyl(3-methylbuta-1,3-dienyloxy)silane **30** mediated by boron-BINOL complexes formed from substituted BINOL ligands such as (*R*)-3,3′-diphenyl-1,1′-binaphthyl-2,2′-diol (*R*)-**29**. Diels-Alder reactions carried out with these complexes afforded cycloaddition products with excellent enantioselectivities of up to >98% *ee*. The authors commented on the convenience of using *peri*-hydroxyquinones as substrates, as the phenolic hydroxyl group could act as a second ligand donor to the Lewis acid, thus forming a highly rigid complex (Scheme 11).



Scheme 11 Diels-Alder reaction of *peri*-hydroxyquinones.

In 1993, Hattori *et al.* reported the use of *N*-boryl BINOL complexes for the transformation of imines into β-amino esters in good to excellent *de*s of 74 - 94% (Scheme 12).[63]



Scheme 12 Boron-assisted diastereoselective reaction between a Lewis-acid coordinated imine and a silyl ketene acetal.

The diastereoselectivity arises from the intermolecular coordination of the imine with the chiral BINOL-boron Lewis acid (*R*)-**35** in the *N*-boryl complex transition state. The Lewis acid blocks the *si*-face of the imine, promoting preferential nucleophilic attack on the *re*-face (Figure 9).

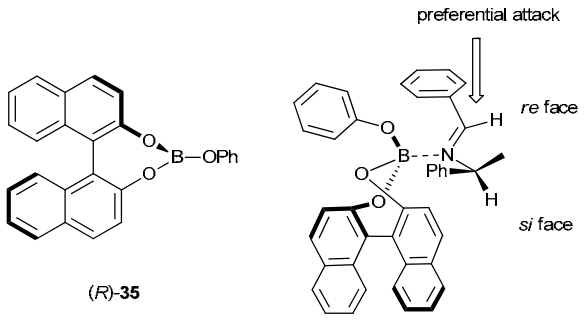
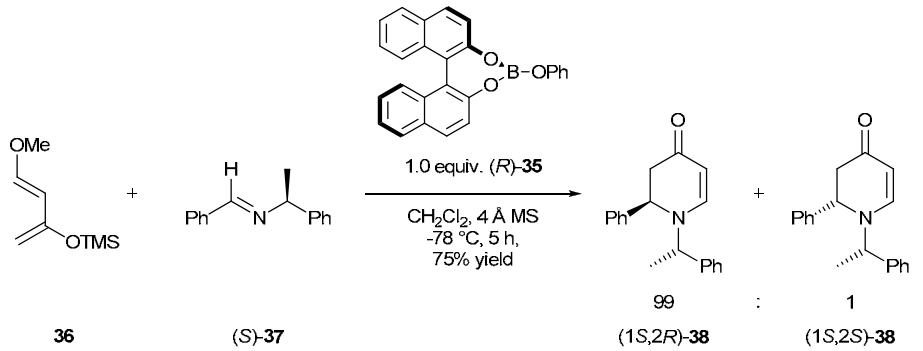


Figure 8 Intermolecular N→B coordination induces facial selective addition to the imine.

Lewis acid systems using a chiral biaryl backbone have since been employed in inducing stereoselectivity into a variety of reactions. Yamamoto *et al.* successfully applied this system to the aza-Diels-Alder reactions of an imine (*S*)-**37** with Danishefsky's diene **36**, reporting a high degree of selectivity (Scheme 13).[64, 65]

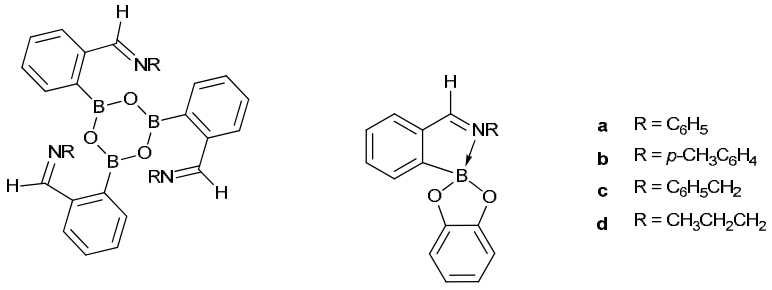


Scheme 13 Aza-Diels-Alder reaction mediated by a boron-BINOL Lewis acid (*R*)-**35**.

1.2.5 Boron Lewis Acids with Intramolecular N→B Bonds

There are few examples in the literature of compounds exploiting intramolecular boron-nitrogen bonds in organic synthesis. The use of such compounds has so far been restricted to the development of boronic acid-based sensors for saccharides such as glucose,[66] and in studies of the trigonal vs. tetrahedral nature of the boron centre.[67]

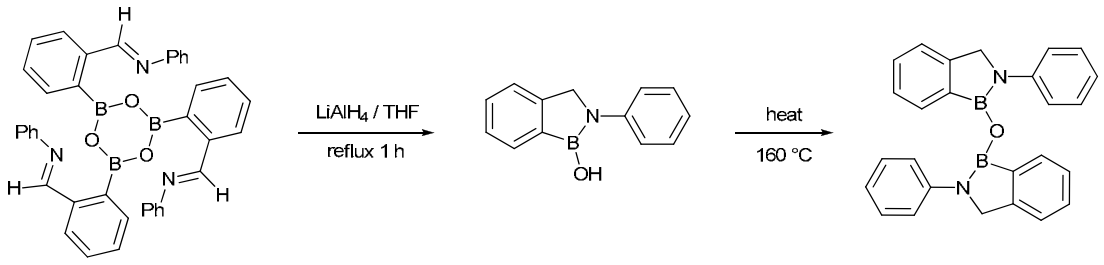
One of the earliest examples of a compound containing an intramolecular N→B bond was reported in 1968 by Dunn *et al*.[68] They reported the synthesis of trimeric boronic anhydride Schiff bases **39a-d** from condensation of the trimeric anhydride of 2-formylphenylboronic acid with primary aromatic / aliphatic amines (Figure 9). This was confirmed by the presence of infra-red absorbances in the region 1622-1648 cm^{-1} corresponding to the C=N stretch. Absence of absorptions due to OH or NH functionalities confirmed the trimeric anhydride structure. On addition of catechol, absorption was observed at 1220 cm^{-1} which the authors postulated to be an N-B stretch. This stretch was not seen in the spectra of **39a-d**, and it was concluded that this dative interaction was more prominent in catechol esters than in the trimeric anhydrides.



39 40

Figure 9 Dunn *et al.* reported examples of Schiff bases incorporating intramolecular N→B bonding.

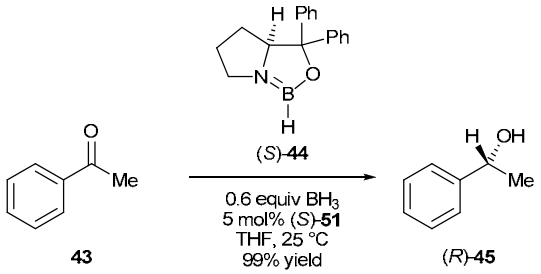
Of particular note is the application of these Schiff bases as intermediates for the formation of aminoboronic acids (Scheme 14). Lithium aluminium hydride reduction of **39a** gave *N*-phenylboronophthalimidine **41** which was subsequently further dehydrated to afford dimeric anhydride **42**. Importantly, the authors noted the difficulty of isolating the mono-aminoboronic acid.



39a **41** **42**

Scheme 14 Reduction of anhydride **39a** to aminoboronic acid **41a** which dimerised on heating.

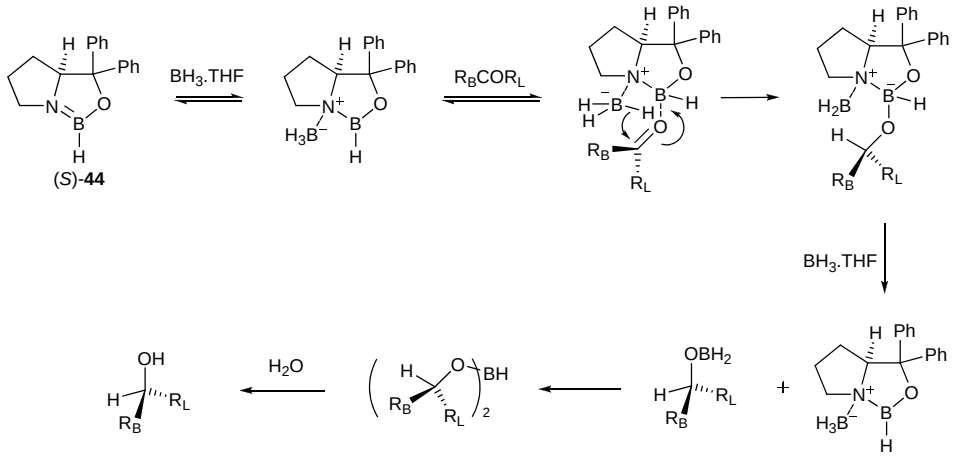
A range of chiral boron Lewis acids have been developed over the last 20 years which take advantage of the intramolecular N→B interaction. Perhaps the most well known example, the CBS (Corey-Bakshi-Shibata) catalyst, (*S*)-**44** was first reported by Corey in the late 1980s for the asymmetric reduction of prochiral ketones to their corresponding alcohols (Scheme 15).[69]



43 (*R*)-**45**

Scheme 15 CBS reduction of acetophenone.

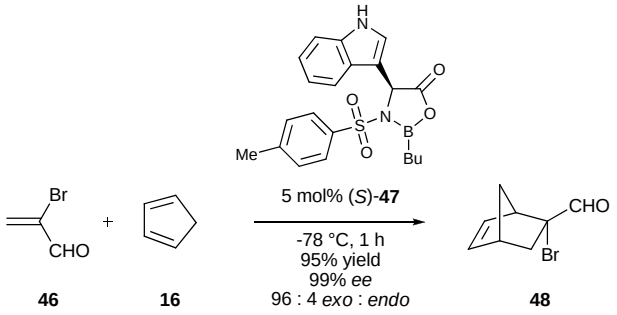
They employed an oxazaborolidine catalyst, prepared from treatment of an enantiopure α-amino acid (or their corresponding alcohol) with borane to induce excellent enantioselectivities of up to 97%. This work is particularly worthy of note since it advantageously uses both inter and intramolecular N→B bonding, with the nitrogen atom coordinating to the adjacent boron centre and an incoming BH_3 molecule, which is then activated to act as a hydride source for the reduction of the carbonyl group (Scheme 16).



Scheme 16 Inter and intramolecular N→B coordination involved in the CBS reduction mechanism.

The catalytically active species forms *via* the rapid and reversible coordination of a BH_3 molecule to the Lewis basic nitrogen on the α-face of the oxazaborolidine bicycle, affording a *cis*-oxazaborolidine.borane complex. Donation of the *N*-lone pair into the vacant 2p orbital of the boron atom activates this centre and allows the hydride transfer to occur.

This class of oxazaborolidine catalysts have since proven particularly versatile, with further published work by Corey *et al.* applying CBS catalysts to a variety of transformations, including the asymmetric Diels-Alder reaction between 2-bromoacrylaldehyde **46** and cyclopentadiene **16** (Scheme 17).[70]



Scheme 17 Asymmetric Diels-Alder transformation catalysed by a CBS catalyst (*S*)-**47**.

They reported excellent enantiomeric excesses of up to 99% and exo / endo-selectivity of up to 96 / 4. *N*-tosyl protection of the nitrogen interrupted the N→B interaction, delocalising the amine lone pair onto the sulphonyl moiety. This rendered the boron centre more electron deficient, and thus afforded a more potent Lewis acid.

This catalyst, (*S*)-tryptophan-derived (*S*)-**47**, has been used to prepare chiral building blocks for the asymmetric synthesis of natural products such as the potent antiulcer substance cassinol **49** and plant growth regulator gibberellic acid **50** (Figure 10).[71]

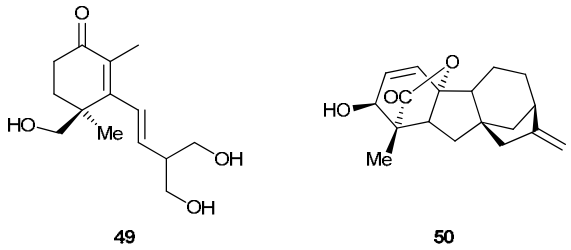
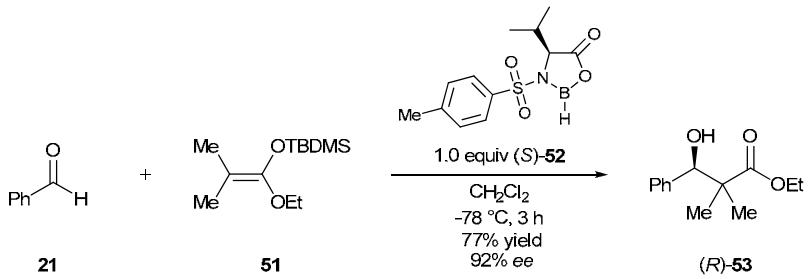


Figure 10 Two natural products synthesised using CBS methodology.

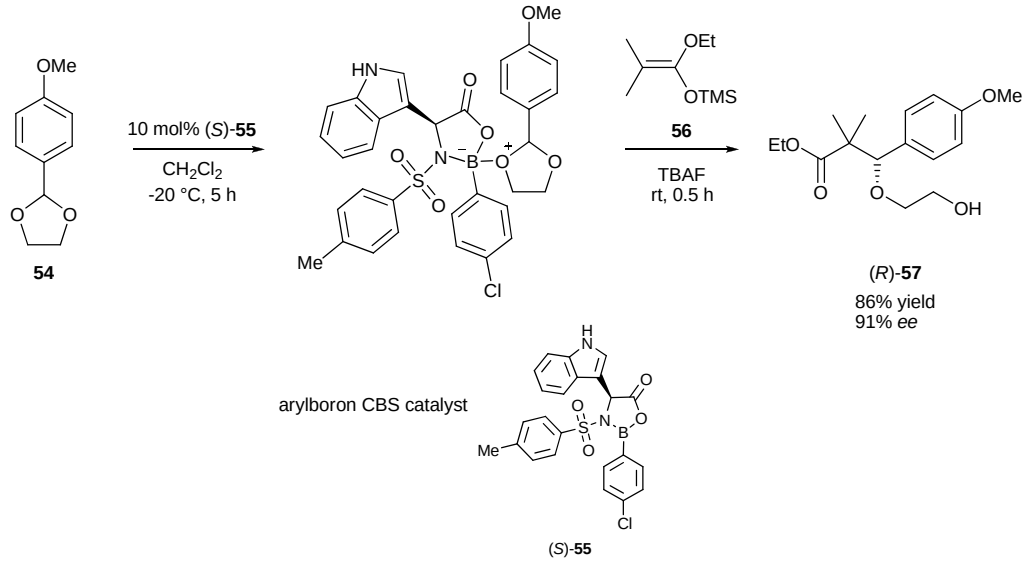
The CBS series has also been used in the Mukaiyama aldol reactions of silyl ketene acetals and aldehydes, as reported in 1991 by Kiyooka and co-workers.[72] They used an enantiopure (*S*)-valine-derived oxazaborolidine catalyst (*S*)-**52** as a stoichiometric Lewis acid to affect the chiral addition with *ee*s of up to 98% (Scheme 18).



Scheme 18 (*S*)-valine-derived CBS reagent used to effect chiral additions to aldehydes.

They reported chiral addition to simple aldehydes, such as benzaldehyde **21**, with good to excellent enantiomeric excesses (45 - 98% *ee*) and good yields (77 - 86%).

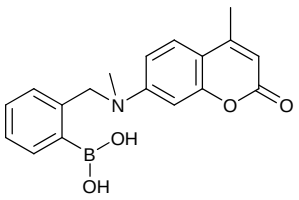
Kinugasa *et al.* reported the first example where an arylboron CBS catalyst (*S*)-**55** was used to catalyse the formal aldol reaction of a silyl enol ether with a 1,3-dioxolane substrate (Scheme 19).[73] Initial complexation of the catalyst to the dioxolane afforded an *in situ* oxonium intermediate which was then trapped *via* reaction with silyl ketene acetal **56** to generate the *O*-protected ether (*R*)-**57**.



Scheme 19 *N*-protected chiral boron CBS reagent used in enantioselective ring cleavage reactions.

These few examples have shown how powerful a synthetic tool the CBS oxazaborolidine series is in effecting stereoselective induction in a wide range of chemical transformations.

Perhaps the field in which the N→B interaction has been most widely exploited is in the design of novel sugar sensors.[74-78] Systems based on aniline-type nitrogens were reported by Sandanayake *et al*. in 1995,[79, 80] who prepared a fluorescent ICT (Internal Charge Transfer) sensor **58** which coupled donor nitrogen and acceptor boronic acid fragments based around a coumarin backbone (Figure 11).

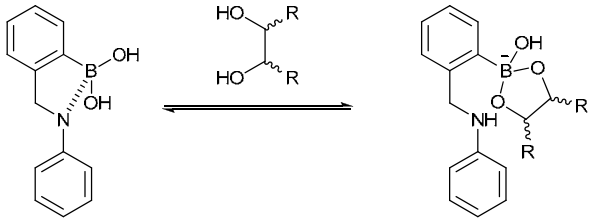


58

Figure 11 An ICT sensor containing an intramolecular N→B interaction.

Bosch *et al*. reported the synthesis of several novel aniline-based sensors including **59** (Figure 12).[81-83] They showed that following saccharide binding, the emission wavelength of the sensor was significantly altered. In aqueous solution, buffered at pH 8.21, the addition of D-fructose caused a blue-shifting of the emission maximum of **59**

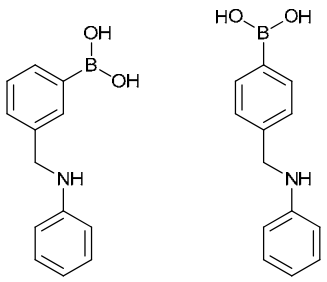
by 42 nm. This was ascribed to a change from TICT (or Twisted Internal Charge Transfer) in the boronic acid to LE (Locally Excited) fluorescence in boronate **60**.



59 **60**

Figure 12 Saccharide binding significantly affects emission wavelength.

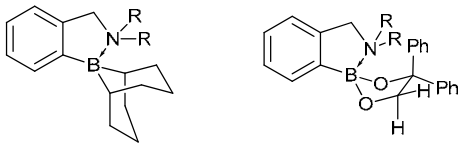
TICT arises in **59** due to a N→B interaction, confirmed by X-ray crystallography, which lies perpendicular to the π-system of the aniline. This stabilisation of the excited state is lost in the anionic boronate which shows no N→B interaction. No TICT stabilisation was observed when *meta*-**61** and *para*-**62** were used (Figure 13).



meta-**61** *para*-**62**

Figure 13 No TICT stabilisation for *meta*-**61** and *para*-**62**.

Further to this, an investigation by Toyota and Oki suggested a mathematical determination of the degree of N→B interaction in a molecule (their proposed formula will be discussed in Chapter 2). They found that the level of coordination between the nitrogen and boron atoms was subtly influenced by a number of factors including substituent and solvent effects (Figure 14). They compared the energy barrier for dissociation of the intramolecular N→B bond of three examples (**63a**, **63b** and **64**) and suggested that the Lewis basicity of the nitrogen lone pair was inversely affected by the size of the *N*-substituents, with larger R-groups reducing the energy barrier for dissociation.



63

a) R = Me
b) R = Et

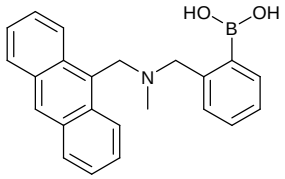
64

R = Me

Figure 14 Several factors influence the strength of the N→B interaction.

The Lewis acidity of the boron atom was also found to influence the strength of the interaction, with electron donating oxygen atoms reducing the Lewis acidity of boronates compared to the corresponding alkylboranes.

James *et al.* reported a novel design for a PET (Photoinduced Electron Transfer) sensor (boronic acid **65**, Figure 15) incorporating the N→B motif with a more Lewis basic nitrogen.[51,84, 85] They prepared an *N*-methyl-*o*-(aminomethyl)phenylboronic acid core structure modified with an additional anthracene fluorophore to facilitate PET, which responded with a large fluorescence increase on addition of saccharide.

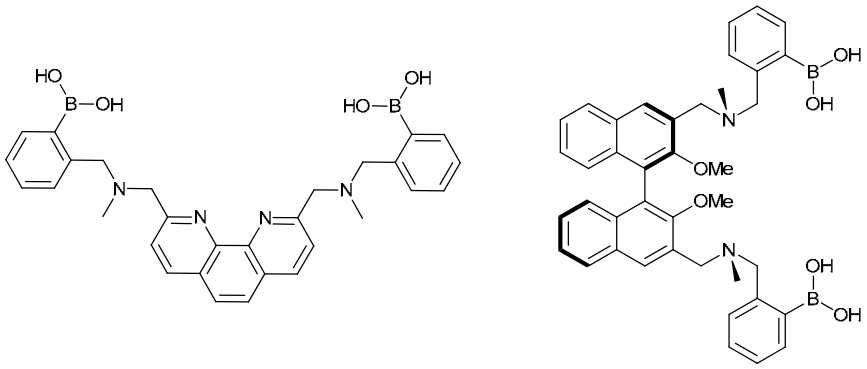


65

Figure 15 Anthracene PET sensor with the N→B 'on-off' switch controlled by saccharide binding.

PET is interrupted in the unbound sensor by a N→B coordinate interaction. Contraction of the O-B-O bond angle of the boronic acid on complexation with the saccharide (and the associated increase in the acidity at the boron centre) augments the N→B interaction, and hence disrupts PET.

Following this initial success, a wide range of boronic acid sensors bearing the same *N*-methyl-*o*-(aminomethyl)phenylboronic acid backbone have been reported, often involving more than one boronic acid moiety for multi-point binding to a saccharide, with a variety of linker motifs which affect the inter-boronic acid distance (Figure 16).[85-87]

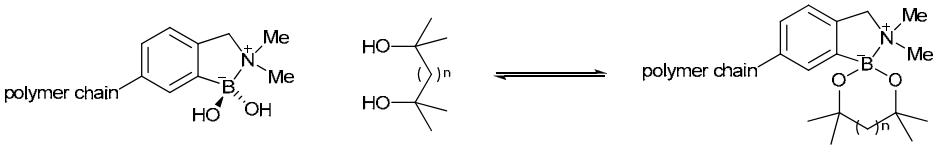


66 (*R*)-**67**

Figure 16 Two published saccharide sensor designs incorporating the aminoboronic acid moiety.

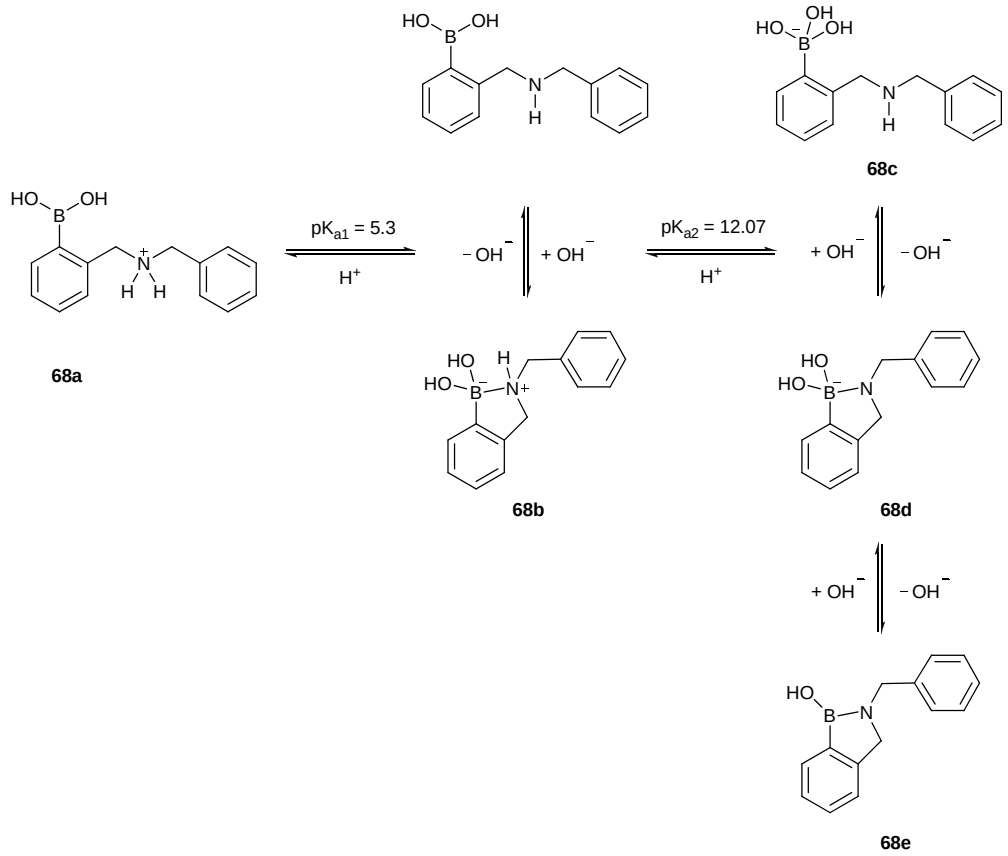
In 1982, Wulff and co-workers were considering novel techniques to improve a chromatographic procedure initially introduced in 1970 by Gilham *et al.* to separate diols from their impurities by binding the diols to boronic acids attached to a polymer chain.[51] It was observed that diol binding was several orders of magnitude faster when the reaction was conducted in aqueous alkaline solution than when a neutral organic solvent was used. They rationalised this by considering that in alkaline solution the boron centre adopted an sp^3 geometry with an extra hydroxyl group affiliated with the boron centre.

Wulff showed that altering the boron centre, such that it adopted a tetrahedral geometry by means of an intramolecular N→B coordinate bond, would have the same effect on the efficiency of diol binding (under neutral organic conditions) as in aqueous alkaline solution. The intramolecular bond is formed by the incorporation of an amine adjacent to the boronic acid (Scheme 20).



Scheme 20 N→B coordination improves the efficiency of diol binding.

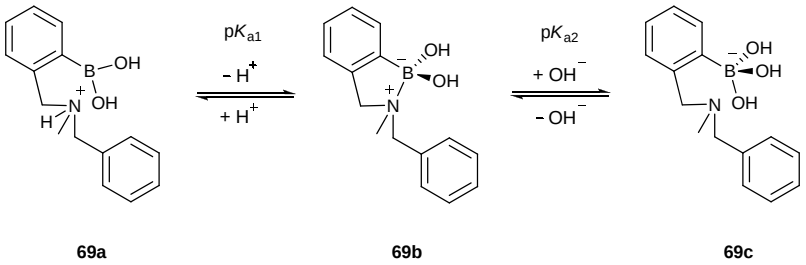
In 2001, Wiskur *et al.* reported a study on the pK_a values of secondary and tertiary amines adjacent to boronic acids.[67] They showed that secondary ammonium salts have comparable pK_a values with their analogous tertiary ammonium salts (Scheme 21).



Scheme 21 Equilibria involved in potential N→B intramolecular interaction.

This system was studied at a range of pHs. Initially, deprotonation of the ammonium ion (pK_{a1}) affords **68b**. This then allowed two deprotonation pathways (pK_{a2}) to afford either free amine (**68c**) or coordinated amine (**68d**). The hybridisation at boron remains sp^3 after either pathway, so ^{11}B NMR spectroscopy cannot be used to differentiate these alternative pathways. However, further elimination of hydroxide from species **68d** would be observable by ^{11}B NMR since the boron centre in **68e** would now be sp^2 hybridised. If this occurred, the effectiveness of this system for binding diols at high pH would be severely hampered.

This system was studied in comparison with the analogous tertiary amine system, where only one deprotonation of the amine functionality is possible, which indicated that the second pK_{a2} observed was a result of coordination of the hydroxyl group to the boron atom (Scheme 22).

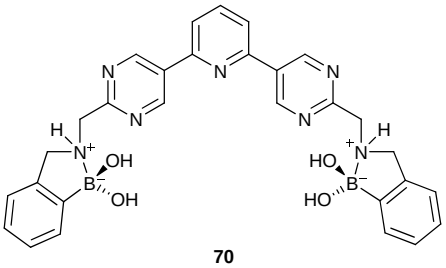


69a **69b** **69c**

Scheme 22 Analogous system involving a tertiary amine.

Potentiometric titrations of **68a** and **69a** showed comparable pK_{a1} values (5.3 and 5.2 respectively). ^{11}B NMR spectra were recorded as a function of pH and both systems showed upfield shifts at comparable pK_{a1} values to the pH titrations. This shift corresponds to a change of hybridisation around the boron from sp^2 to sp^3. Deprotonation at pK_{a1} precedes formation of a dative bond with the boron, which becomes tetrahedral in character. At neutral pH, the ^{11}B NMR shifts showed good correlation for both species.

The author therefore postulated that at neutral pH, species **69b** predominated (Scheme 22) which was supported by X-ray crystallographic data published in 2002 by Norrild *et al*. of a related secondary amine complex **70** (Figure 17). The X-ray crystallography data of this compound confirmed the favoured formation of N→B bonding which was predicted to preclude strong sugar binding at neutral pH.



70

Figure 17 Intramolecular N→B interaction in the solid state.

The authors noted the potential application of incorporating secondary ammonium groups adjacent to the boronic acid functionality in assisting boronic ester formation with 1,2- and 1,3-diols for saccharide sensors.[88, 89]

The energy of the N—B bond has been calculated from stepwise formation constants measured using potentiometric titrations.[83] It was calculated that the lower and upper

limits of the N—B interaction must be between approximately 15 and 25 kJ mol^{-1} in 2-((benzyl(methyl)amino)methyl)phenylboronic acid. This value is in good agreement with computational data which estimated the N—B interaction to be ≤ 13 kJ mol^{-1} in the absence of solvent. To qualify this in terms of familiar bonding motifs, the energy of the N—B interaction is approximately equivalent to that of a hydrogen bond.

Intramolecular N→B bonding has also been the subject of interest in the synthesis of novel metal ligands. In 1997, Ashe *et al.* reported the synthesis of novel aminoboratabenzene ligands **71a**, which were shown to form metal complexes and act as alternative 6-π-electron ligands to cyclopentadienyl ligands.[90] Such ligands, unlike their cyclopentadienyl counterparts, can interact with exo-cyclic substituents and thus change the properties of the ligand and hence the complex.

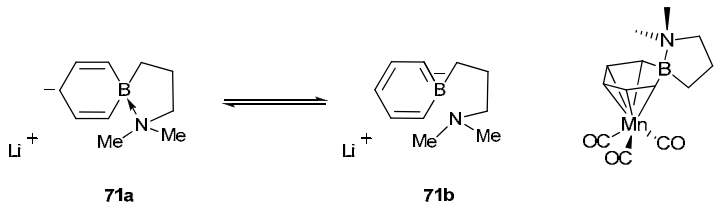
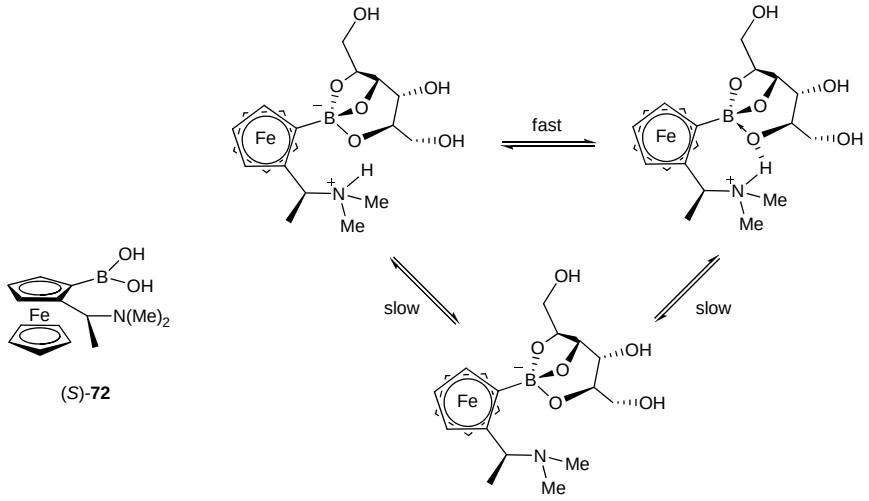


Figure 18 Ashe *et al's* aminoboratabenzene ligand, and complexed to manganese.

In previous work within the group,[90] they observed that the degree of N→B π-bonding was quite small in the uncomplexed aminoboratabenzenes. However, when metal derivatives were synthesised, the strength of the π-bonding increased. This was due to the electron withdrawing nature of the metal centre removing electron density from the boratabenzene ring. η^5 Coordination of the ring was confirmed by X-ray crystallography and is characteristic of a highly stable N→B bond. The Lewis acidity of the boron atom increases as electron density is removed, corresponding to an increased N→B bond strength.

However, despite these many examples of N→B interactions, it has been reported that having the correct alignment for N→B bonding does not necessarily preclude an interaction occurring, even at neutral pH.[91] For example, Norrild reported on a chiral ferroceneboronic acid which was published by Shinkai as an electrochemical carbohydrate sensor (*S*)-**72** (Scheme 23).[92] It was suggested by Norrild that no N→B interaction exists within this complex.



Scheme 23 Shinkai's novel electrochemical boronic acid sensor to polyol sorbitol.

Support for this hypothesis came from considering the bond lengths and angles in the ferroceneboronic acid. The potential N-B bond length was measured to be approximately 2.5 Å, with intramolecular N-B bonding requiring a bond length of approximately 1.6 – 1.7 Å. Such a disparity was too large to suggest such an interaction was present, although it was observed that complex (*S*)-**72** showed good binding properties with a polyol in solution. The 2,3,5-bound sorbitol complex contained a 'bridging' hydroxyl group between the boron and the nitrogen (Scheme 23). Therefore, it appears that it is crucial that care is taken in designing future carbohydrate sensors to maximize the 'tetrahedral effect' of co-ordinately bonded nitrogen.

From this short overview, it is clear that while boron has been widely used in many aspects of organic synthesis, applications of boron that contain an N→B functionality are limited. In particular, intramolecular boron-nitrogen coordinate bonds, increasingly found in novel saccharide sensors, and used with great success in early CBS oxazaborolidine catalysts for asymmetric reduction protocols have yet to be fully exploited in organic synthesis.

1.3 References

1. Wynn, R. L.; Blake, D. A., *Teratology* **1970,** 3, 211-214.
2. Blaser, H. U., *Chem. Rev.* **1992**, (92), 935-952.
3. Nicolaou, K. C.; Yang, Z.; Liu, J. J.; Ueno, H.; Nantermet, P. G.; Guy, R. K.; Clairborne, C. F.; Renaud, J.; Couladouros, E. A.; Paulvannan, K.; Sorensen, E. J., *Nature* **1994,** 367, 630-634.
4. Sheehan, J. C.; Henery-Logan, K. R., *J. Am. Chem. Soc.* **1959,** 81, 3089-3094.
5. Evans, D. A.; Ennis, M. D.; Mathre, D. J., *J. Am. Chem. Soc.* **1982,** 104, 1737-1739.
6. Imai, T.; Tamura, T.; Yamamuro, A.; Sato, T.; Wollmann, T. A.; Kennedy, R. M.; Masamune, S., *J. Am. Chem. Soc.* **1986,** 108, 7402-7404.
7. Brown, H. C.; Jadhav, P. K., *Tetrahedron Lett.* **1984,** 25, 1215-1218.
8. Keil, O.; Schneider, M. P.; Rasor, J. P., *Tetrahedron-Asymmetry* **1995,** 6, (6), 1257-1260.
9. Keil, O.; Schneider, M. P.; Rasor, J. P., *Tetrahedron-Asymmetry* **1995,** 6, 1257-1260.
10. Noyori, R.; Ikeda, T.; Ohkuma, T.; Widhalm, M.; Kitamura, M.; Takaya, H.; Akutagawa, S.; Sayo, N.; Saito, T.; Taketomi, T.; Kumobayashi, H., *J. Am. Chem. Soc.* **1989,** 111, 9134-9135.
11. Takamura, M.; Hamashima, Y.; Usuda, H.; Kanai, M.; Shibasaki, M., *Angew. Chem. Int. Ed.* **2000,** 39, 1650-1652.
12. Dalko, P. I.; Moisan, L., *Angew. Chem., Int. Ed.* **2001,** 40, 3726-3748.
13. Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M., *Advanced Inorganic Chemistry*. John Wiley and Sons: New York, 1999; p 131-174.
14. Greenwood, N. N.; Earnshaw, A., *Chemistry of the Elements*. Butterworth-Heinemann: Oxford, 1997; p 139-215.
15. Ishihara, K.; Yamamoto, H., *Eur. J. Org. Chem.* **1999**, (3), 527-538.
16. Brown, H. C.; Subba Rao, B. C., *J. Am. Chem. Soc.* **1956,** 78, 5694-5695.
17. Smith, K.; Pelter, A., *Comprehensive Organic Synthesis*. Pergamon Press: Oxford, 1991; Vol. 8, p 703-731.

18. Ishihara, K., Lewis Acids in Organic Synthesis. In Yamamoto, H., Ed. Wiley-VCH: Weinheim, 2000; Vol. Vol. 1, pp pp. 89-133.
19. Ishihara, K., Lewis Acids in Organic Synthesis. In Yamamoto, H., Ed. Wiley-VCH: Weinheim, 2000; Vol. Vol. 1, pp pp. 135-190.
20. Pelter, A.; Smith, K.; Brown, H. C., *Borane Reagents*. Academic Press Limited: London, 1988.
21. Matteson, D. S., *Stereodirected Synthesis with Organoboranes*. Springer-Verlag: Berlin, 1995.
22. Brown, H. C.; Jadhav, P. K., *Asymmetric Synthesis*. Academic Press: New York, 1983; Vol. Vol. 2, p pp. 1-43.
23. Brown, H. C.; Ramachandran, P. V., *Pure Appl. Chem.* **1994,** 66, 201.
24. Kalinin, A. V.; Scherer, S.; Snieckus, V., *Angew. Chem. Int. Ed.* **2003,** 42, 3399.
25. Bhat, N. G.; Garza, A., *Tetrahedron Lett.* **2003,** 44, 6833.
26. Crudden, C. M.; Edwards, D., *Eur. J. Org. Chem.* **2003**, 4695.
27. Matteson, D. S., *Chem. Rev.* **1989,** 89, 1535.
28. Pelter, A.; Smith, K.; Brown, H. C., *Borane Reagents*. Academic Press Limited: London, 1988.
29. Thomas, S. E., *Organic Synthesis: The Roles of Boron and Silicon*. Oxford University Press: Oxford, 1991.
30. Mori, Y.; Kobayashi, J.; Manabe, K.; Kobayashi, S., *Tetrahedron* **2002,** 58, 8263.
31. Masamune, S.; Kennedy, R. M.; Petersen, J. S., *J. Am. Chem. Soc.* **1986,** 108, 7404.
32. Deloux, L.; Srebnik, M., *Chem. Rev.* **1993,** 93, 763.
33. Ishihara, K., *Lewis Acids in Organic Synthesis*. Wiley-VCH: Weinheim, 2000; Vol. 1.
34. Michaelis, A.; Becker, P., *Ber. Dtsch. Chem. Ges.* **1880,** 13, 58.
35. Michaelis, A.; Becker, P., *Ber. Dtsch. Chem. Ges.* **1882,** 15, 180-185.
36. Frankland, E.; Duppa, B. F., *Justus Liebigs Ann. Chem.* **1860,** 115, 319-322.
37. Khotinsky, E.; Melamed, M., *Ber. Dtsch. Chem. Ges.* **1909,** 42, 3090.
38. Kuivila, H. G.; Keough, A. H.; Soboczenski, E. J., *J. Org. Chem.* **1954,** 19, 780.
39. Sugihara, J. M.; Bowman, C. M., *J. Am. Chem. Soc.* **1958,** 80, 2443.
40. Lorand, J. P.; Edwards, J. O., *J. Org. Chem.* **1959,** 24, 769.

41. Bielecki, M.; Eggert, H.; Norrild, J. C., *J. Chem. Soc., Perkin Trans. 2* **1999**, 449.
42. Lappert, M. F., *Chem. Rev.* **1956,** 56, 959-1064.
43. Torssel, K., *Arkiv. Kemi.* **1957,** 10, 473.
44. Wolfrom, M. I.; Solms, J., *J. Org. Chem.* **1956,** 21, 815-816.
45. DiCesare, N.; Lakowicz, J. R., *Anal. Biochem.* **2001,** 294, 154-160.
46. Friedman, S.; Pizer, R., *J. Am. Chem. Soc.* **1975,** 97, 6059-6062.
47. Pizer, R.; Selzer, R., *Inorg. Chem. Commun.* **1983,** 23, 3023.
48. Babcock, L.; Pizer, R., *Inorg. Chem. Commun.* **1980,** 19, 56-61.
49. James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S., *Angew. Chem. Int. Ed.* **1996,** 35, (17), 1911-1922.
50. Ferrier, R. J., *Adv. Carbohydr. Chem. Biochem.* **1978,** 35, 31-80.
51. Wulff, G., *Pure Appl. Chem.* **1982,** 54, 2093.
52. Ishihara, K.; Yamamoto, H., *Eur. J. Org. Chem.* **1999**, 527-538.
53. Flemming, I., *Frontier Orbitals and Organic Chemical Reactions*. John Wiley and Sons: London, 1978; p 161-164.
54. Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H., *J. Org. Chem.* **1989,** 54, 1481-1483.
55. Ishihara, K.; Gao, Q. Z.; Yamamoto, H., *J. Am. Chem. Soc.* **1993,** 115, 10412-10413.
56. Furuta, K.; Maruyama, T.; Yamamoto, H., *J. Am. Chem. Soc.* **1991,** 113, 1041-1042.
57. Marshall, J. M.; Palovich, M. R., *J. Org. Chem.* **1998,** 63, 4381-4384.
58. Brown, H. C.; Vara Prasad, J. V. N.; Zee, S.-H., *J. Org. Chem.* **1986,** 51, 439.
59. Itsuno, S.; Nakano, M.; Miyazaki, K.; Msauda, H.; Ito, K.; Hirao, A.; Nakahama, S., *J. Chem. Soc., Perkin Trans. 1* **1985**, 2039.
60. Pelter, A.; Rosser, R. M.; Mills, S., *J. Chem. Soc., Perkin Trans. 1* **1984**, 717.
61. Itsuno, S.; Hachisuka, C.; Ito, K., *J. Chem. Soc., Perkin Trans. 1* **1991**, 1767.
62. Kelly, T. R.; Whiting, A.; Chandrakumar, N. S., *J. Am. Chem. Soc.* **1986,** 108, (12), 3510-3512.
63. Hattori, K.; Mayumi, M.; Yamamoto, H., *J. Am. Chem. Soc.* **1993,** 115, 1151-1152.
64. Hattori, K.; Yamamoto, H., *J. Org. Chem.* **1992,** 57, (12), 3264-3265.

65. Hattori, K.; Yamamoto, H., *Tetrahedron* **1993,** 49, (9), 1749-1760.
66. Norrild, J. C.; Søtofte, I., *J. Chem. Soc., Perkin Trans. 2* **2002**, 303-311.
67. Wiskur, S. L.; Lavigne, J. J.; Ait-Haddou, H.; Lynch, V.; Chiu, Y. H.; Canary, J. W.; Anslyn, E. V., *Org. Lett.* **2001,** 3, 1311.
68. Dunn, H. E.; Catlin, J. C.; Snyder, H. R., *J. Org. Chem.* **1968,** 33, (12), 4483.
69. Corey, E. J.; Bakshi, R. K.; Shibata, S., *J. Am. Chem. Soc.* **1987,** 109, 5551-5553.
70. Corey, E. J.; Loh, T. P., *J. Am. Chem. Soc.* **1991,** 113, 8966-8967.
71. Corey, E. J.; Guzmanperez, A.; Loh, T. P., *J. Am. Chem. Soc.* **1994,** 116, 3611-3612.
72. Kiyooka, S.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M., *J. Org. Chem.* **1991,** 56, 2276-2278.
73. Kinugasa, M.; Harada, T.; Oku, A., *J. Org. Chem.* **1996,** 61, 6672-6673.
74. de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E., *Chem. Rev.* **1997,** 97, 1515.
75. Hartley, J. H.; James, T. D.; Ward, C. J., *Journal of the Chemical Society-Perkin Transactions 1* **2000**, (19), 3155-3184.
76. James, T. D.; Shinkai, S., *Host-Guest Chemistry* **2002,** 218, 159-200.
77. Striegler, S., *Curr. Org. Chem.* **2003,** 7, 81.
78. Wang, W.; Gao, X.; Wang, B., *Curr. Org. Chem.* **2002,** 6, 1285.
79. Sandanayake, K. R. A. S.; Imazu, S.; James, T. D.; Mikami, M.; Shinkai, S., *Chem. Lett.* **1995**, (2), 139-140.
80. Sandanayake, K. R. A. S.; James, T. D.; Shinkai, S., *Chem. Lett.* **1995**, (7), 503-504.
81. Arimori, S.; Bosch, L. I.; Ward, C. J.; James, T. D., *Tetrahedron Lett.* **2001,** 42, (27), 4553-4555.
82. Bosch, L. I.; Mahon, M. F.; James, T. D., *Tetrahedron Lett.* **2004,** 45, (13), 2859-2862.
83. Bosch, L. I.; Fyles, T. M.; James, T. D., *Tetrahedron* **2004,** 60, (49), 11175-11190.
84. James, T. D.; Sandanayake, K. R. A. S.; Iguchi, R.; Shinkai, S., *J. Am. Chem. Soc.* **1995,** 117, (35), 8982-8987.

85. James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S., *Chem. Commun.* **994**, (4), 477-478.

86. Gray, C. W.; Houston, T. A., *J. Org. Chem.* **2002,** 67, 5426-5428.

87. Zhao, J. Z.; Fyles, T. M.; James, T. D., *Angew. Chem. Int. Ed.* **2004,** 43, (26), 3461-3464.

88. Yoon, J.; Czarnik, A. W., *J. Am. Chem. Soc.* **1992,** 114, 5874.

89. James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S., *Chem. Commun.* **1994**, 477-478.

90. Ashe, A. J., III; Fang, X.; Hokky, A.; Kampf, J. W., *Organometallics* **2004,** 23, (9), 2197-2200.

91. Norrlid, J. C., *J. Chem. Soc., Perkin Trans. 2* **2001**, 719-726.

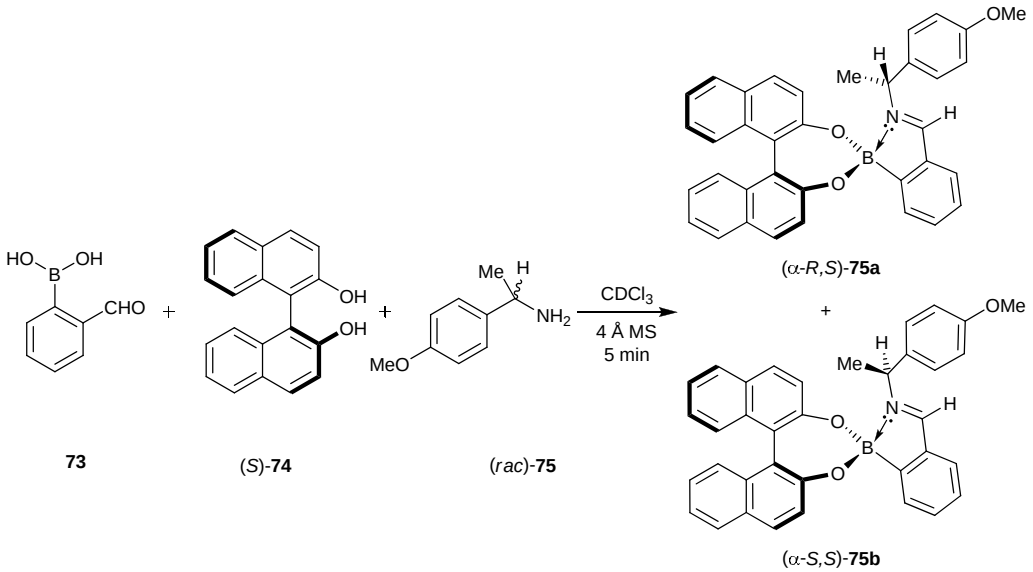
92. Yamakawa, M.; Noyori, R., *J. Am. Chem. Soc.* **1995,** 117, (23), 6327-6335.

2 The Synthesis of Stable Boronates with an Intramolecular Imino N→B Coordinate Bond and their Use as Novel Chiral Derivatising Agents

2.1 Introduction

This chapter describes the successful synthesis and applications of a variety of stable boronate esters containing either an imino or amino intramolecular N→B coordinate bond.

Previous work within the group had reported that this intramolecular coordinate bonding interaction can be advantageously applied to the one-pot construction of pairs of diastereomerically distinct imino-boronate esters whose ^{1}H NMR spectrum may be used to determine the enantiomeric excess of the parent primary amine.[1, 2] Therefore, 1.0 equivalent of 2-formylphenylboronic acid **73** was stirred with 1.1 equivalent of enantiopure (*S*)-BINOL (*S*)-**74** and 1.0 equivalent of (*rac*)-4-methoxy-α-methylbenzylamine (*rac*)-**75** in $CDCl_3$ in the presence of 4 Å molecular sieves (Scheme 1). The ^{1}H NMR spectra of an aliquot of the resultant solution was acquired after 5 minutes.



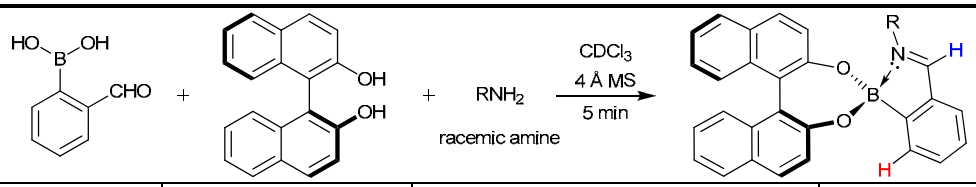
73 (*S*)-74 (*rac*)-75

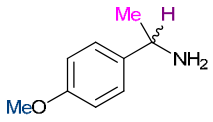
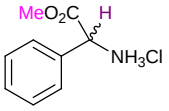
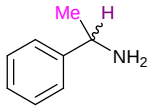
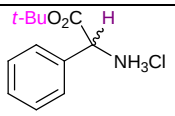
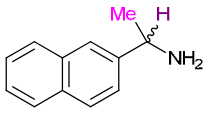
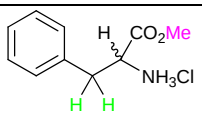
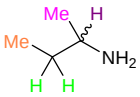
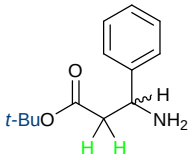
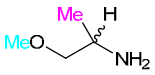
Scheme 1 Determination of the enantiomeric excess of primary amines.

The resultant ^{1}H NMR spectrum revealed that a 50 : 50 mixture of two diastereoisomeric complexes (α-*R*,*S*)-**75a** and (α-*S*,*S*)-**75b** had been formed in quantitative yield, whose respective imine, α-methine, α-methyl and *p*-methoxy resonances were all well resolved. This was highly promising because it meant that comparison of the relative intensities of four different sets of integrals could potentially be used to accurately confirm the enantiopurity of a scalemic sample of this amine by ^{1}H NMR spectroscopy.

To investigate the scope and limitation of this chiral derivatisation protocol, a range of eight additional racemic amines containing stereogenic centres at their α-positions were then derivatised. The diagnostic differences in their chemical shifts are summarized below (Table 1). Analysis of the 300 MHz ^{1}H NMR spectra of the resultant 50 : 50 mixture of diastereoisomeric imino-boronate esters revealed that baseline resolution was achieved for at least three sets of resonances in all cases (Table 1).[3]

Table 1 Chemical shift differences (Δδ) in the 300 MHz $CDCl_3$ ^1H NMR spectra of 50 : 50 mixtures of (*S*,*R*)-**93-101a** and (*S*,*S*)-**93-101b** derived from racemic primary amines that contain α-stereogenic centres.



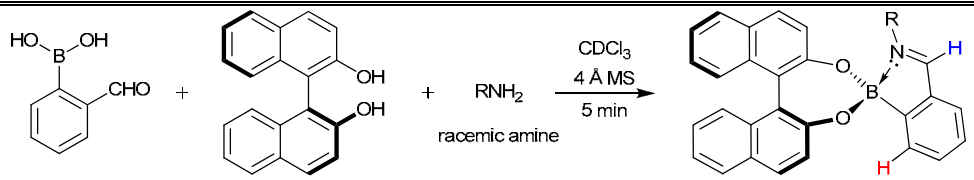
Amine	Δδ (ppm)	Amine	Δδ (ppm)
 **75**	0.21 -0.11 0.21 -0.15	 **80**	-0.05[c] -0.52 -0.02
 **76**	-0.17 -0.10[a] 0.21	 **81**	-0.43[c] 0.10 -0.67 -0.05
 **77**	0.17 -0.09[b] 0.20	 **82**	0.39[c] -0.34 0.13 0.19
 **78**	0.11 0.15 -0.19 -0.13 -0.22	 **83**	0.38 -0.12 -0.21 0.20 0.19
 **79**	-0.09 0.09 0.14 -0.20		

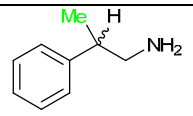
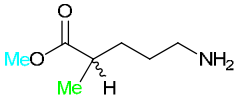
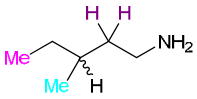
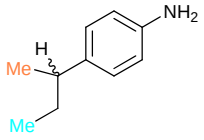
A negative value indicates that the resonance corresponding to the (*S*,*S*)-diastereoisomer is more deshielded than the (*S*,*R*)-diastereoisomer. [a] The quartet corresponding to the methine proton of the (*S*,*S*)-diastereoisomer partially overlaps with the resonance of phenolic protons of residual (*S*)-BINOL; these signals no longer overlap on addition of 5 mol% of *d*6-acetone to the NMR tube. [b] The quartet corresponding to the methine proton of (*S*,*R*)-**77a** partially overlaps with the resonance of phenolic protons of residual (*S*)-BINOL. [c] 1.1 equivalents of cesium carbonate were added to liberate the free amine, with excess cesium carbonate being removed by filtration, through a small plug of celite prior to ^1H NMR spectroscopic analysis.

Therefore, these results clearly demonstrated that this derivatisation approach appeared to be well suited for determining the enantiopurity of a wide range of chiral primary amines, including, α-arylethylamines, α-methylalkylamines, β-amino ethers, α-amino esters and β-amino esters.

We then considered whether these types of complexes could be used to determine the enantiopurity of primary amines that contain remote stereogenic centres (Table 2). It was found that treatment of racemic amines **84** - **87** with 2-formylphenylboronic acid and enantiopure (*S*)-BINOL under standard conditions afforded pairs of diastereoisomeric complexes whose stereogenic methyl groups were all baseline resolved in their ^{1}H NMR spectra.

Table 2 Chemical shift differences (Δδ) in the 300 MHz $CDCl_3$ ^{1}H NMR spectra of 50 : 50 mixtures of (*S*,*R*)-**84-87a** and (*S*,*S*)-**84-87b** derived from racemic primary amines that contain remote stereogenic centres.



Amine	Δδ (ppm)	Amine	Δδ (ppm)
 **84**	-0.22	 **86**	0.04[a,b] 0.02[b]
 **85**	-0.08 -0.31 0.30 -0.11 0.40	 **87**	0.02[a,b] 0.02[b] 0.03[b]

[a] ^{1}H NMR run in *d*6-acetone. [b] Unable to assign a sign to the Δδ values of these resonances because an enantiopure sample of the parent amines were not available.

Therefore, this derivatisation approach is also capable of determining the enantiomeric excesses of amines **84** - **87** that contain stereogenic centres at positions up to five bonds away from the amine functionality.

The detection limits of this method were determined by derivatising three samples of (*R*)-α-methylbenzylamine (*R*)-**76** of 80%, 90% and 98% *ee*, respectively, using enantiopure (*S*)-BINOL as the chiral diol. Analysis of the ^{1}H NMR spectrum of each sample revealed that the calculated diastereoisomeric excesses (de's) for the resultant mixture of (*S*,*R*)-**76a** and (*S*,*S*)-**76b** were in excellent agreement with the known enantiomeric purity of the starting α-methylbenzylamine. Thus, the ^{1}H NMR integrals measured for formation of (*S*,*R*)-**76a** of 80%, 90% and 97% *de* correlated well with the

known enantiopurity of the starting (*R*)-amine **76** of 80%, 90% and 98% *ee*, respectively, thus indicating that little or no kinetic resolution had occurred.

Following this success, we envisaged that this protocol could be extended to determination of the enantiomeric excess of a wider range of classes of organic compounds. This chapter, therefore, details the investigation into utilising these boronate compounds for determination of the enantiomeric excess of chiral 1,2- 1,3- and 1,4-diols.

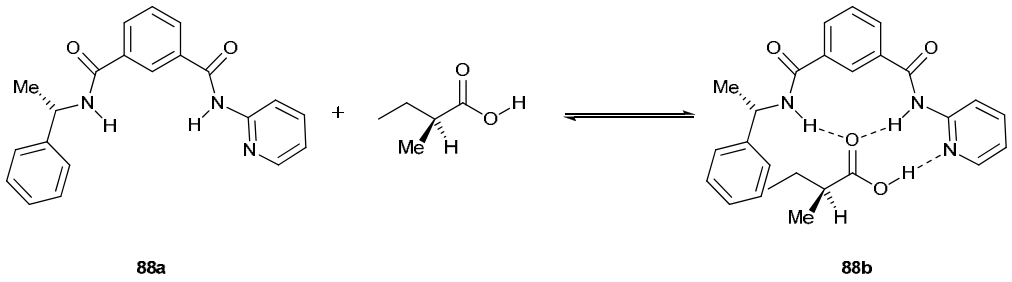
2.1.1 Determination of Enantiomeric Excess by NMR Spectroscopy

The rapid emergence of the field of asymmetric synthesis has led to the development of several methods to determine the enantiomeric excess of chiral compounds.[4] One, long-standing technique for determination of the enantiomeric excess of a chiral molecule has been by obtaining the specific rotation of the sample using a polarimeter. This is a highly sensitive technique and depends greatly on temperature, solvent, concentration at a given wavelength and purity. However, several examples have been reported where this method breaks down, either through inaccurate optical rotations published in the literature or through the non-linear relationship between specific rotation and enantiopurity.[5, 6]

More recently, methods based around NMR spectroscopy have attracted great interest due to the ease of use and general availability of NMR spectrometers.[7] These methods rely on transformation of a mixture of enantiomers into diastereomers which then show non-equivalency in their NMR spectra. If these resonances are suitably resolved, their relative integration would reveal their diastereomeric ratio and hence, if no kinetic resolution has occurred, the enantiomeric composition of the original substrate. In recent years, this has been achieved using a variety of methodologies, including chiral solvating agents, chiral shift reagents and chiral derivatising agents. This affords the potential for developing a database of NMR protocols for determining the enantiomeric purity and absolute configuration of different classes of chiral compound.

2.1.1.1 Chiral Solvating Agents

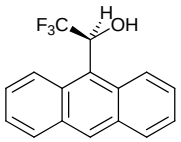
Chiral solvating agents (CSAs), like chiral shift reagents, form *in situ*, reversible diastereomeric complexes with enantiomers through non-covalent bonding interactions. One such example is the host-guest complex **88a**, which binds through three hydrogen bonds to a carboxylic acid moiety (Scheme 2).[8] Such diastereomeric complexes are in rapid equilibrium in solution with the uncomplexed enantiomeric mixture. Here, determination of the *ee* of a chiral acid arises from non-equivalent diastereomeric signals of the complexed substrates in its ^{1}H NMR spectrum.



Scheme 2 Host-guest intermolecular hydrogen bonding interaction in chiral solvating agents.

The simplicity of this method is its main advantage. Racemisation of the substrates is unlikely as is kinetic resolution. The main drawback of this approach is that the chemical shift differences (Δδ) between the diastereoisomeric complexes are often small, with only nuclei that are close to the stereogenic centre likely to show non-equivalency and even these peaks may not be resolved enough to permit accurate determination of the enantiopurity of the mixture. Another limitation of this method is the limited range of co-solvents which can be used. Non-polar solvents such as $CDCl_3$ and C_6D_6 tend to show better resolution for diastereomeric complexes, while more polar solvents can preferentially solvate the enantiomeric mixture over the CSA, causing (Δδ) to fall to zero.

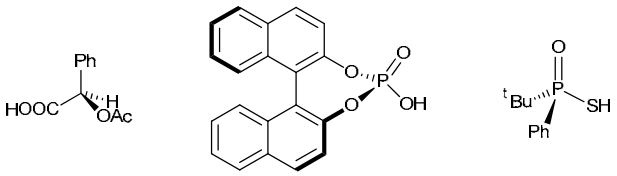
The best known example of a chiral solvating agent was published in 1966 by Pirkle who reported the use of (*S*)-2,2,2-trifluoro-1-phenyl ethanol (*S*)-TFAE **89** as a CSA to determine the enantiomeric excess of chiral primary amines by ^{19}F NMR analysis (Figure 1).[9]



(*S*)-TFAE **89**

Figure 1 Chiral solvating agent reported by Pirkle *et al*.

Other examples of chiral solvating agents include acids (*R*)-**90**[7] and (*S*)-**91**[10] which have been used to determine the enantiomeric purity of chiral amines and amino acids, and the highly versatile (-)-(*S*)-*t*-butylphenylphosphinothioic acid (*S*)-**92** used in the determination of *ee*s of alcohols, diols, thiols, mercaptoalcohols and amines (Figure 2).[11-14]

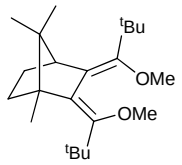
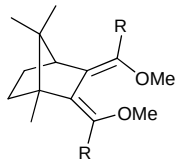
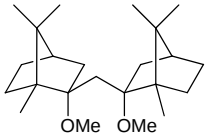


(*R*)-**90** (*S*)-**91** (*S*)-**92**

Figure 2 A selection of compounds used as chiral solvating agents.

2.1.1.2 Lanthanide Chiral Shift Complexes

Chiral shift reagents (CSRs) form transient diastereomeric complexes from reaction of a metal ion (most commonly from the Lanthanide series such as Eu^{3+}, Pr^{3+} and Yb^{3+}) with a large variety of organic compounds containing electron-donating functionalities (Figure 3). Lanthanide ions form weak addition complexes which are in rapid equilibrium with the uncomplexed substrate mixture. This method is more advantageous than chiral solvating agents in that a more pronounced chemical shift difference is observed. However, the size of this shift diminishes as the separation between the stereocentre and the metal centre increases. This upfield or downfield shift is associated with an increase in peak broadening, and in cases where a large shift is observed, the fine-coupling can be lost. This is due to the paramagnetism of the metal centre and is of particular significance at higher magnetic fields.

Ligands		Lanthanide	Abbreviation
		Eu	$Eu[pvc]_3$
	$R=CF_3$	Eu	$Eu[tfc]_3$
		Pr	$Pr[tfc]_3$
		Yb	$Yb[tfc]_3$
	$R=C_3F_7$	Eu	$Eu[hfc]_3$
		Pr	$Pr[hfc]_3$
		Yb	$Yb[hfc]_3$
		Eu	$Eu[dcm]_3$

pvc: pivaloyl-*d*-camphorato
tfc: trifluorohydroxymethylene-*d*-camphorato
hfc: heptafluorohydroxymethylene-*d*-camphorato
dcm: dicamphoyl-*d*-methanato

Figure 3 Examples of common chiral shift reagent lanthanide complexes.[7, 15]

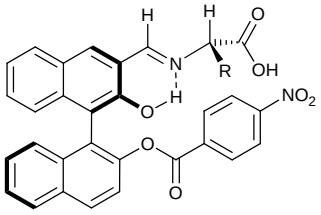
2.1.1.3 Chiral Derivatising Agents

Where chiral solvating agents and chiral shift reagents utilise *in situ* formation of diastereomeric complexes, chiral derivatising agents (CDAs) form long-lived diastereomeric complexes through covalent derivatisation of the substrate with an enantiomerically pure reagent. Such diastereoisomeric complexes generally show much greater chemical shift differences than both chiral solvating agents and chiral shift reagents. Indeed, using chiral derivatising agents, it is easier to develop models to account for the observed chemical shift patterns which have been used to predict the absolute configuration of the substrate under analysis.

Limitations to this approach include the need to use enantiomerically pure derivatising agents and the possibility of kinetic resolution due to differing reaction rates of the substrate enantiomers. Despite these limitations, this approach continues to be the most widely used NMR method for determining enantiomeric excess.

A common characteristic of chiral derivatising agents is the utilisation of the anisotropic effect of an aromatic ring in the CDA to induce a difference between the chemical shift differences (ΔΔδ) of enantiomeric substrates following derivatisation with the CDA.

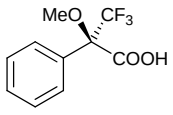
In 2004, Chin *et al.* reported the synthesis of a novel chiral derivatising agent for determining the enantiomeric excess of amino-acids using resonance-assisted hydrogen bonded imines derived from a chiral aldehyde CDA (Figure 4).[16] This involves hydrogen bonding between the BINOL hydroxyl group and a conjugated imine (in this case with the bi-naphthyl rings of (*R*)-BINOL). In this case the imine proton shows a marked downfield shift, appearing at ≈ δ 13.5 ppm.



(*R*)-**93**

Figure 4 A chiral derivatising agent complex reported by Chin and co-workers.

The most commonly used chiral derivatising agent, Mosher's reagent (MTPA, α-methoxy-α-trifluoromethyl-phenylacetic acid), (*R*)-**94**, was introduced in 1969 as a novel CDA for determining the enantiomeric excess of chiral amines and alcohols (Figure 5).[17, 18]

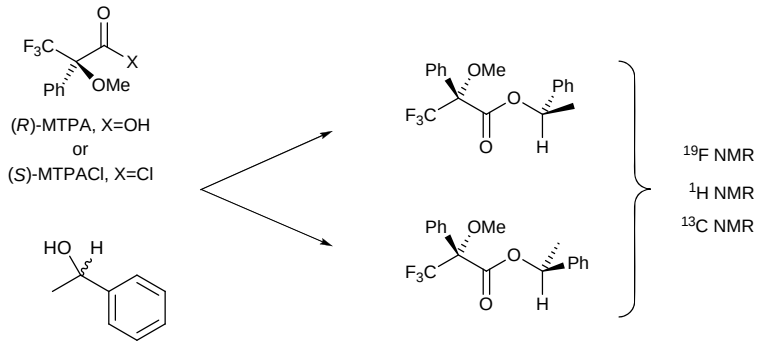


(*R*)-**94**
(*R*)-MTPA

Figure 5 Mosher's reagent was first reported in 1969.

MTPA succeeded MPA (α-methoxyphenylacetic acid) because epimerisation of the stereogenic centre was observed during ester formation with more hindered secondary carbinols. MTPA is stable to epimerisation due to the absence of hydrogens α to the

carboxyl moiety. Determination of the absolute configuration of secondary alcohols using this CDA is well reported and is deduced by interpretation of the signs of the Δδ values using empirical models.[19, 20] Mosher's reagent also has the potential for determining the enantiopurity of an alcohol or amine substrate by ^{19}F NMR spectroscopy (Scheme 3).



Scheme 3 Derivatisation of a secondary alcohol using Mosher's acid or acid chloride.

However, there have been several examples where Mosher's reagent has proven unsuccessful in the accurate determination of enantiomeric excess.[21] This can be due either to poor reactivity towards more sterically demanding substrates, resulting in kinetic resolution or incomplete derivatisation, or a negligible chemical shift difference for pairs of diastereoisomeric resonances. This has proven to be a particular problem for substrates with remote stereocentres. As such, this is an area which has yet to be fully exploited and in which great advances can still be made.[22]

2.2 A Novel Chiral Derivatising Agent for Determination of the Enantiomeric Excess of 1,2- 1,3- and 1,4-Diols

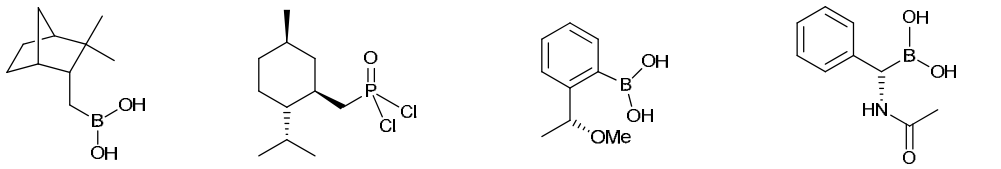
Following on from previous work within the group that developed a novel protocol for the chiral derivatisation of primary amines, we envisaged that this approach might also be suitable for determination of the enantiopurity of chiral diol fragments.

2.2.1 Chiral Derivatising Agents for Chiral Diols

The prevalence of chiral diols as synthetic intermediates[23] and as fragments of biologically active compounds[24] has led to a great demand for reliable techniques to accurately determine the enantiopurity of this class of compound. Therefore, the development of an inexpensive chiral derivatisation protocol that enables their enantiomeric excess to be simply determined by ^{1}H NMR spectroscopic analysis is currently of great interest to the synthetic community.

The use of chiral derivatisation agents (CDAs)[7] to determine the enantiomeric excess of diols is well established,[19, 25-27] with many having been derivatised to afford either MTPA (Mosher)[18] or MPA (Trost)[28] esters. The main drawback of using this type of approach is the potential for the two diol moieties of the parent diol to react at different rates, which can give rise to possible kinetic resolution of the diastereomers, severely impeding the application of this CDA for accurate determination of the *ee* of diols.[29]

When Mosher's acid is employed for a chiral diol, two equivalents of MTPA are required. This increases the potential for kinetic resolution of the parent enantiomers. Derivatisation of chiral diols with alternative CDAs that contain either a boronic acid,[30-33] dichlorophosphine,[34] dichlorophosphate,[35] or an aldehyde[36] moiety avoid such limitations since a single chiral derivatisation agent reacts with both alcohol functionalities of the diol substrate (Figure 6).

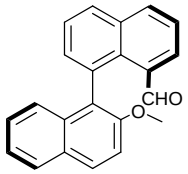


95 **96** (*R*)-**97** (*S*)-**98**

((1*R*,2*R*,4*S*)-3,3-dimethylbicyclo[2.2.1] heptan-2-yl)methylboronic acid | menthyldichlorophosphate | (*R*)-2-(1-methoxyethyl)-phenyl boronic acid | (*S*)-acetamido(phenyl)methyl boronic acid

Figure 6 Limited examples of chiral derivatising agents for diols in the literature.

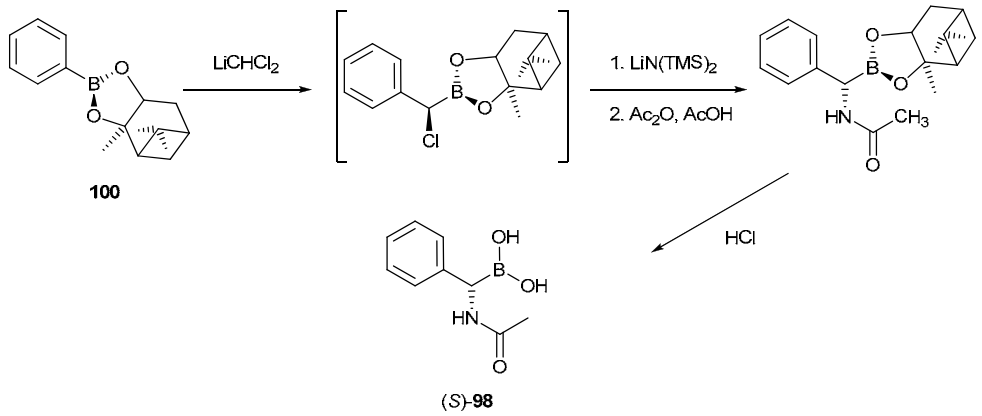
The dichlorophosphate system **96** is only suitable for determining the enantiomeric excess of *C*2-symmetric diols,[35] while other CDAs of this type afford diastereoisomers that only show nonequivalence in their ^{13}C or ^{31}P NMR spectra.[33-35] Furthermore, while the aldehyde system **99** (Figure 7) has been used to determine the absolute configuration of diols using NOE experiments, the observed ^{1}H NMR chemical shift differences of the resultant diastereoisomeric acetonides were not reported.[36]



99

Figure 7 Chiral aldehyde CDA.

The chemical shift differences observed by Burgess *et al*. for diastereoisomeric boronate esters prepared *via* treatment of diols with enantiopure (*R*)-2-(1-methoxyethyl)-phenylboronic acid (*R*)-**97** were also low in the range of Δδ 0.005-0.020 ppm.[30] Prior to my studies, diol derivatisation approaches based on the use of (*S*)-acetamido(phenyl)methylboronic acid (*S*)-**98** and derivatives appear to be the most effective for determining the enantiopurity of chiral diols, affording a resolution of Δδ 0.060-0.360 ppm for the resultant diastereoisomeric boronate esters. However, a complex multi-step synthesis is required with low overall yields (20 - 30%) and rigorous purification was required including column chromatography of the protected boronate (Scheme 4).[37]

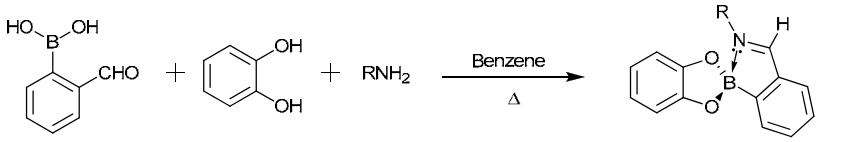


Scheme 4 Synthesis of chiral derivatising agent (*S*)-acetamido(phenyl)methylboronic acid ((*S*)-**98**).

All boronic acid CDAs reported to date form derivatisation complexes that contain a trigonal sp^2 hybridised boron atom. If the boron atom can adopt an sp^3 geometry then condensation with a diol is known to proceed much more rapidly. Furthermore, an sp^3 boron would generally afford a more rigid structure which then is more likely to give better shielding / deshielding for the diastereomeric complexes.

2.2.2 Determination of the Enantiomeric Excess of Chiral 1,2- 1,3- and 1,4- Diols

Dunn *et al.* first reported the 3-component synthesis of stable imino-boronate esters in 1968 from a refluxing mixture of 2-formylphenylboronic acid, catechol and a series of achiral primary amines (Scheme 5).[38] They noted the formation of trimeric boronic anhydride Schiff bases from the condensation of the trimeric anhydride of *o*-formylphenylboronic acid with a series of primary amines. On addition of catechol, an infra-red absorption was observed at 1220 cm^{-1} which was postulated as a B-N stretch, consistent with formation of imino-boronate esters **101a-d**.

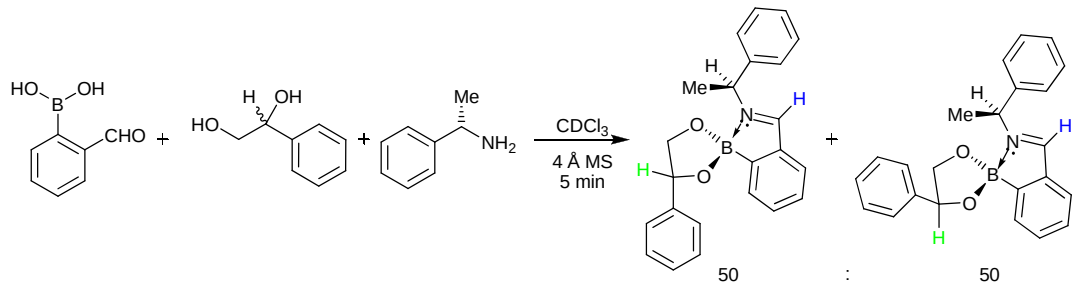


101a R = Ph
101b R = *p*-Me-C_6H_6
101c R = Bn
101d R = *n*-Pr

Scheme 5 Synthesis of imino-boronate esters from the one-pot reaction of 2-formyphenylboronic acid, catechol and an achiral primary amine.

As discussed earlier, previous work within the group reported a 3-component coupling protocol employing (*S*)-BINOL and 2-formylphenylboronic acid for determination of the enantiopurity of a wide range of primary amines by ^{1}H NMR analysis, including amines that contain remote stereocentres (Scheme 1).

It was postulated that such a system utilising a primary amine with an α-stereogenic centre could also be applied to determination of the enantiopurity of chiral diols. Therefore, 1.0 equivalent of a bifunctional aryl template, 2-formylphenylboronic acid **73**, 1.0 equivalent of (*S*)-α-methylbenzylamine (*S*)-**76** and 1.0 equivalent of (*rac*)-1-phenylethane-1,2-diol (*rac*)-**102** were stirred in $CDCl_3$ (Scheme 6) and the ^{1}H NMR spectra of an aliquot acquired after 5 minutes. Two discreet sets of signals were observed as a 50 : 50 mixture in the ^{1}H NMR spectrum, indicating that diastereomeric imino-boronate esters (α-*S*,*R*)-**102a** and (α-*S*,*S*)-**102b** have been formed in quantitative yield.



73 (*rac*)-**102** (*S*)-**76** (α-*S*,*R*)-**102a** (α-*S*,*S*)-**102b**

Scheme 6 Multi-component coupling reaction to afford diastereomeric imino-boronate esters (α-*S*,*R*)-**102a** and (α-*S*,*S*)-**102b**.

Analysis of the ^{1}H NMR spectroscopy in acetone-d_6 showed distinct resonances for the imine and benzylic diol protons (Figure 8). Baseline resolution of these signals allows for accurate determination of the relative integration of the two diastereoisomers. This

value directly reflects the enantiopurity of the parent diol, the reliability of which can be corroborated by comparison with other pairs of discreet diastereoisomeric resonances in the ^{1}H NMR spectrum. In this way, comparison of the relative intensities of a series of different sets of integrals could potentially be used to accurately confirm the enantiomeric composition of a scalemic sample of chiral 1,2- 1,3- or 1,4- diols by ^{1}H NMR spectroscopy.[39, 40]

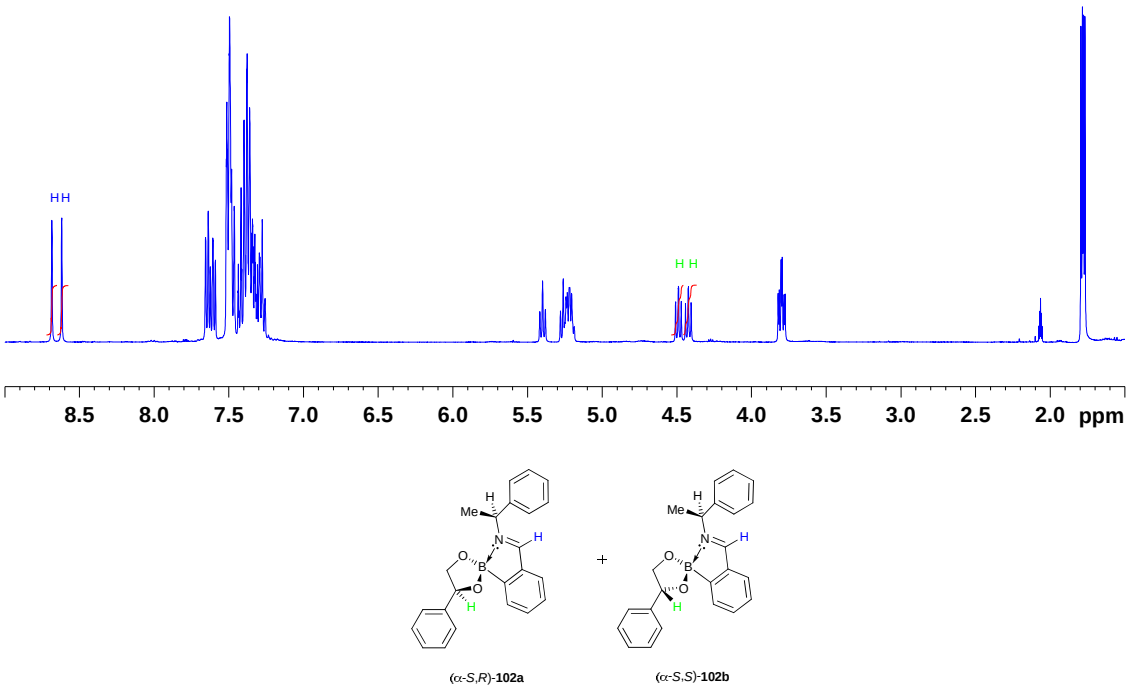
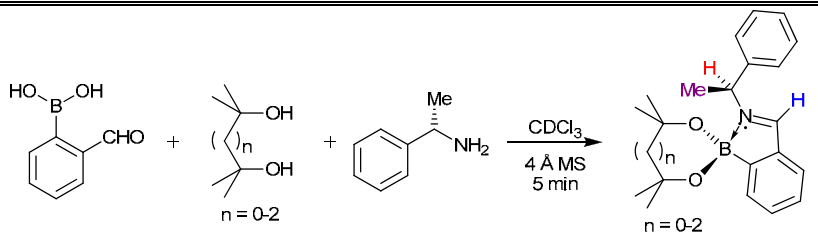
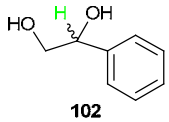
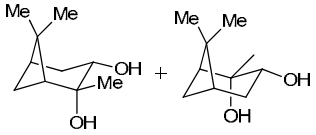
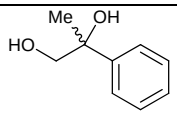
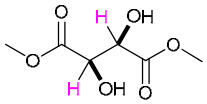
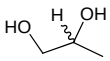
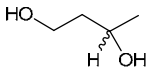
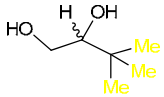
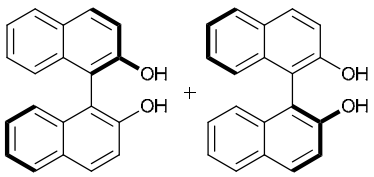
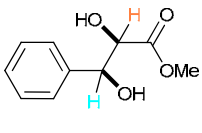


Figure 8 d_6-acetone 400 MHz ^{1}H NMR spectrum showing two distinct sets of resonances corresponding to the diastereomeric iminoboronate esters of (*rac*)-1-phenylethane-1,2-diol.

In order to investigate the scope and limitation of this chiral derivatisation protocol, a series of eight further racemic diols – bearing primary, secondary and tertiary hydroxyl moieties – were then derivatised to afford diastereoisomeric iminoboronate esters with diagnostic differences in their chemical shifts summarised in Table 3 below.

Table 3 Chemical shift differences (Δδ) in the 300 MHz $CDCl_3$ ^1H NMR spectra of 50 : 50 mixtures of **102-110a** and **102-110b**.



Diol	Δδ (ppm)	Diol	Δδ (ppm)
 **102**	-0.066[a] -0.066	 **107**	0.029[d]
 **103**	+/- 0.073[b]	 **108**	-0.310[e] 0.115 0.282
 **104**	-0.030[a]	 **109**	-0.017[a]
 **105**	+/- 0.070[b] +/- 0.044	 **110**	0.178 -0.108 0.205
 **106**	-0.297[c] 0.097 0.510 0.120		

[a] ^1H NMR spectra run in acetone-d_6 [b] Enantiopure samples of diols **103** and **105** were unavailable for derivatisation. Therefore, individual assignment of resonances to each diastereomer could not be performed. [c] The values for Δδ were obtained from deducting the resonances for (α-*S*,4*R*,5*S*)-**106b** from (α-*S*,4*S*,5*R*)-**106a** [d] The values for Δδ were obtained from deducting the resonances for (α-*S*,3a*S*,7a*S*,10*S*,11*R*)-**107b** from (α-*S*,3a*R*,7a*R*,10*R*,11*S*)-**107a** [e] The values for Δδ were obtained from deducting the resonances for (α-*S*,4*S*,5*S*)- **108b** from (α-*S*,4*R*,5*R*)- **108a**.

Derivatisation of the racemic parent diols was carried out by stirring 1.0 equivalent of diol **102-110** with 1.0 equivalent of (*S*)-α-methylbenzylamine and 1.0 equivalent of 2-formylphenylboronic acid in $CDCl_3$ in the presence of 4 Å molecular sieves, before an aliquot was taken for ^1H NMR analysis after 5 minutes.

Analysis of the ^{1}H NMR spectra of the resultant 50 : 50 mixture of diastereomeric iminoboronate esters **102-110a** and **102-110b** revealed that baseline resolution was achieved for at least 1 set of signals in all cases, with up to four distinct resonances observed in some instances (Figure 9). It was therefore reasoned that this approach would be suitable for accurate determination of the enantiopurity of a wide range of scalemic chiral diols.

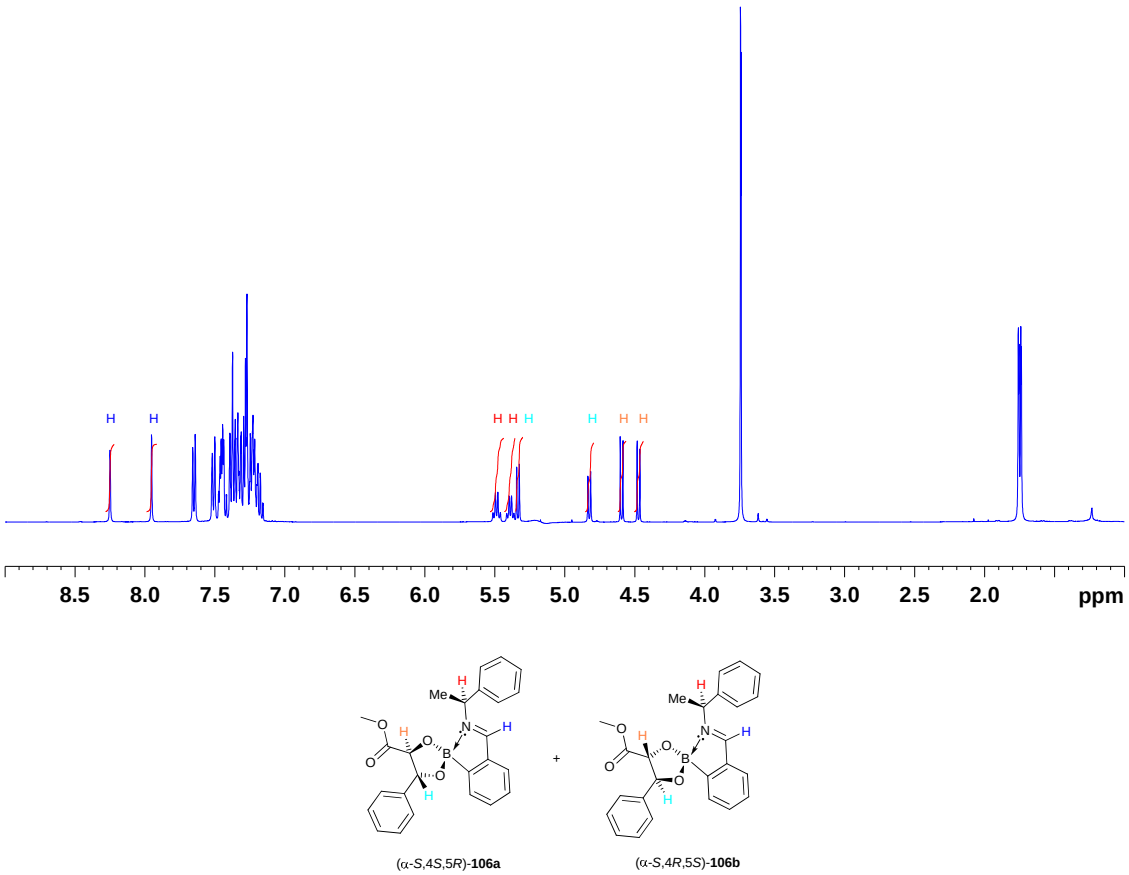


Figure 9 400MHz $CDCl_3$ ^{1}H NMR spectrum of a 50 : 50 mixture of imino-boronate esters (α-*S*,4*S*,5*R*)-**106a** and (α-*S*,4*R*,5*S*)- **106b**.

For example, analysis of the 400 MHz ^{1}H NMR spectra of a 50 : 50 mixture of imino-boronate esters derived from (*rac*)-methyl-2,3-dihydroxy-3-phenylpropionate (α-*S*,4*S*,5*R*)-**106a** and (α-*S*,4*R*,5*S*)-**106b** revealed that baseline resolution was achieved for four distinct sets of resonances with Δδ values of up to 0.510 ppm for the benzylic proton (Figure 9).

The individual resonances corresponding to each pair of diastereomers were assigned by comparison with the ^{1}H NMR spectra of diastereomerically pure iminoboronate

esters **102-110a** and **102-110b** prepared individually *via* reaction of enantiopure diols **102-110** with enantiomerically pure (*S*)-α-methylbenzylamine (*S*)-**76**. Complete derivatisation occurred for both diastereomers in all cases. Therefore, no kinetic resolution was occurring in the condensation of each diol with the boronic acid.

Interestingly, the rate of complexation of this derivatisation reaction appears to agree with work by Wulff *et al.* who reported a kinetic study on the reversible formation of boronate esters.[41] It has been shown that formation of a boronate ester complex occurs much more rapidly when the boron atom sits in an sp^3 tetrahedral environment rather than a trigonal planar sp^2 environment. Considering the rapid formation of these iminoboronate esters, whose condensation is complete in 5 minutes, one might postulate that the three-component formation of the imine and the cyclic boronate ester functionality is facilitated by N→B coordination that affords partial tetrahedral character to the boron centre.

The detection limits of this new derivatisation method were then determined by derivatisation of three samples of (2*S*,3*R*)-**106a** of 80%, 90%, and 98% *ee* respectively, using enantiopure (*S*)-α-methylbenzylamine (*S*)-**76** for complex formation. Analysis of the $CDCl_3$ ^1H NMR spectrum of each sample revealed that the calculated diastereomeric excess (*de*) for the resultant mixture of (α-*S*,2*S*,3*R*)-**106a** and (α-*S*,2*R*,3*S*)-**106b** were in excellent agreement with the known enantiomeric purity of their respective starting diols (2*S*,3*R*)-**106**. Therefore, the ^1H NMR integrals measured for formation of (α-*S*,2*S*,3*R*)-**106a** of 81%, 89%, and 98% *de* correlated well with the known enantiopurity of the starting (2*S*,3*R*)-diol of 80%, 90%, and 98% *ee* respectively, thus indicating that little or no kinetic resolution had occurred (Figure 10). These values are well within the accepted 5% error limit normally accepted for CDA analysis with NMR spectroscopy.[42, 43]

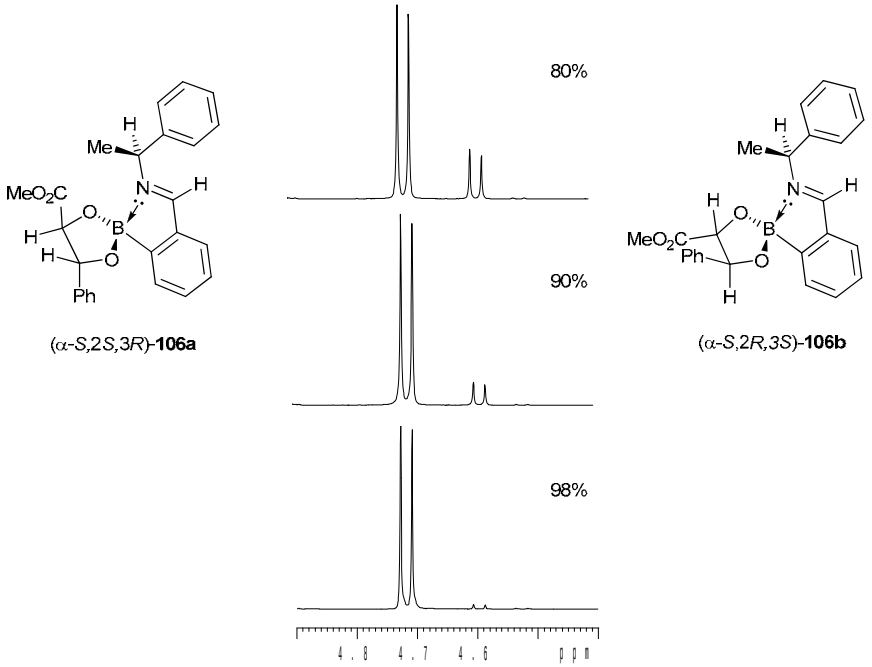


Figure 10 Expansion of the 400 MHz $CDCl_3$ ^1H NMR spectra of a mixture of iminoboronate esters (α-*S*,2*S*,3*R*)-**106a** and (α-*S*,2*R*,3*S*)-**106b** prepared from diol (2*S*,3*R*)-**106** of 80%, 90%, and 98% *ee*.

With this novel chiral derivatising protocol in hand, we decided to further test its discriminatory abilities for determining the *ee* of two further chiral 1,2-diols; butane-2,3-diol **111** and 1,2-diphenylethane-1,2-diol **112** which are commercially available in their enantiopure (1*R*,2*R*), (1*S*,2*S*) and (*meso*) forms. Therefore, 1.0 equivalent of butane-2,3-diol **111**, 1.0 equivalent of 2-formylphenylboronic acid **73** and 1.0 equivalent of (*S*)-α-methylbenzylamine, (*S*)-**76** were stirred in $CDCl_3$ for 5 minutes before an aliquot was removed and its ^1H NMR was obtained. The spectrum is shown below (Figure 11).

We found that the imine signal for all 3 diastereomers were individually baseline resolved sufficient for accurate integration to be performed, thus inferring the relative composition of the parent diol. This is particularly impressive since the substituents of the boronate ester fragment are sterically non-demanding methyl groups.

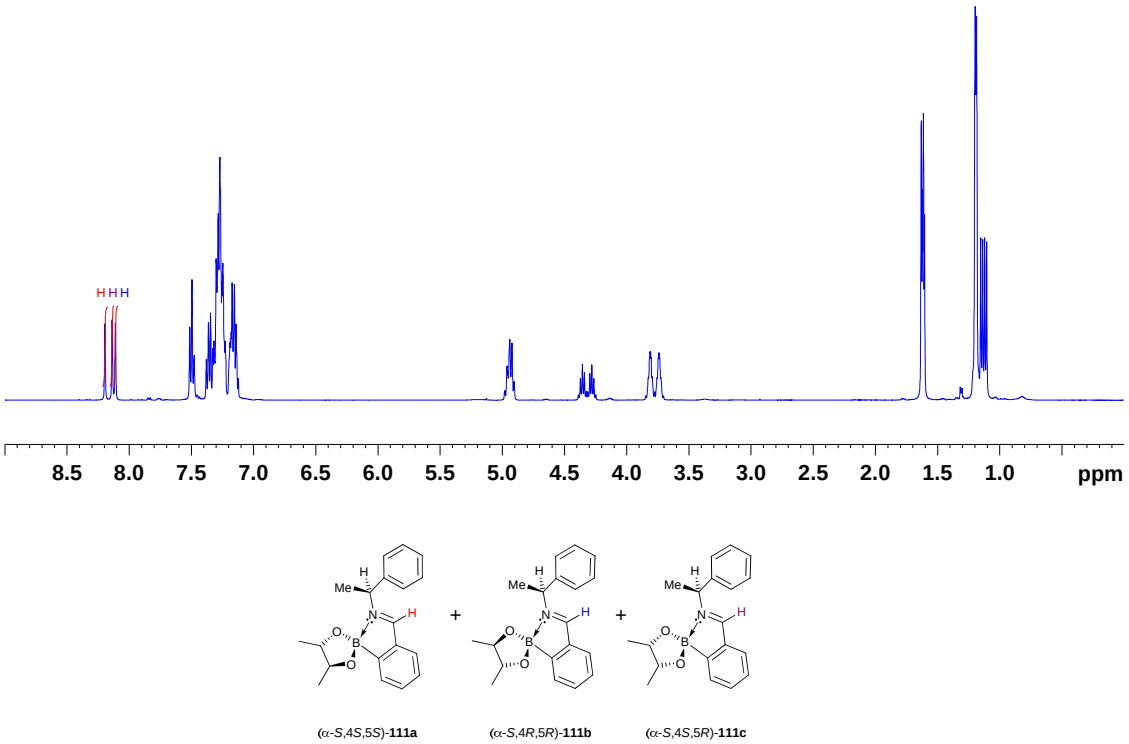


Figure 11 400 MHz $CDCl_3$ ^1H NMR splitting of three sets of imine signals for iminoboronate esters derived from a 1 : 1 : 1 mixture of (1*R*,2*R*), (1*S*,2*S*) and (*meso*)-butane-2,3-diol **111**.

Such discrimination was also observed for the three possible stereoisomers of 1,2-diphenylethane-1,2-diol **112**, a 1 : 1 : 1 mixture of which was derivatised in a similar manner (Figure 12).

Again, splitting of the three imino signals is observed in the ^1H NMR spectrum. This further demonstrates that this protocol is a powerful tool for determination of the enantiopurity of a wide range of chiral 1,2- 1,3- and 1,4-diols. Furthermore, the boronate ring protons may be used in the determination of the enantiomeric excess of a mixture of (1*S*,2*S*) and (1*R*,2*R*)-1,2-diphenylethane-1,2-diol appearing as sharp 2H singlets at 5.03 and 4.90 ppm respectively.

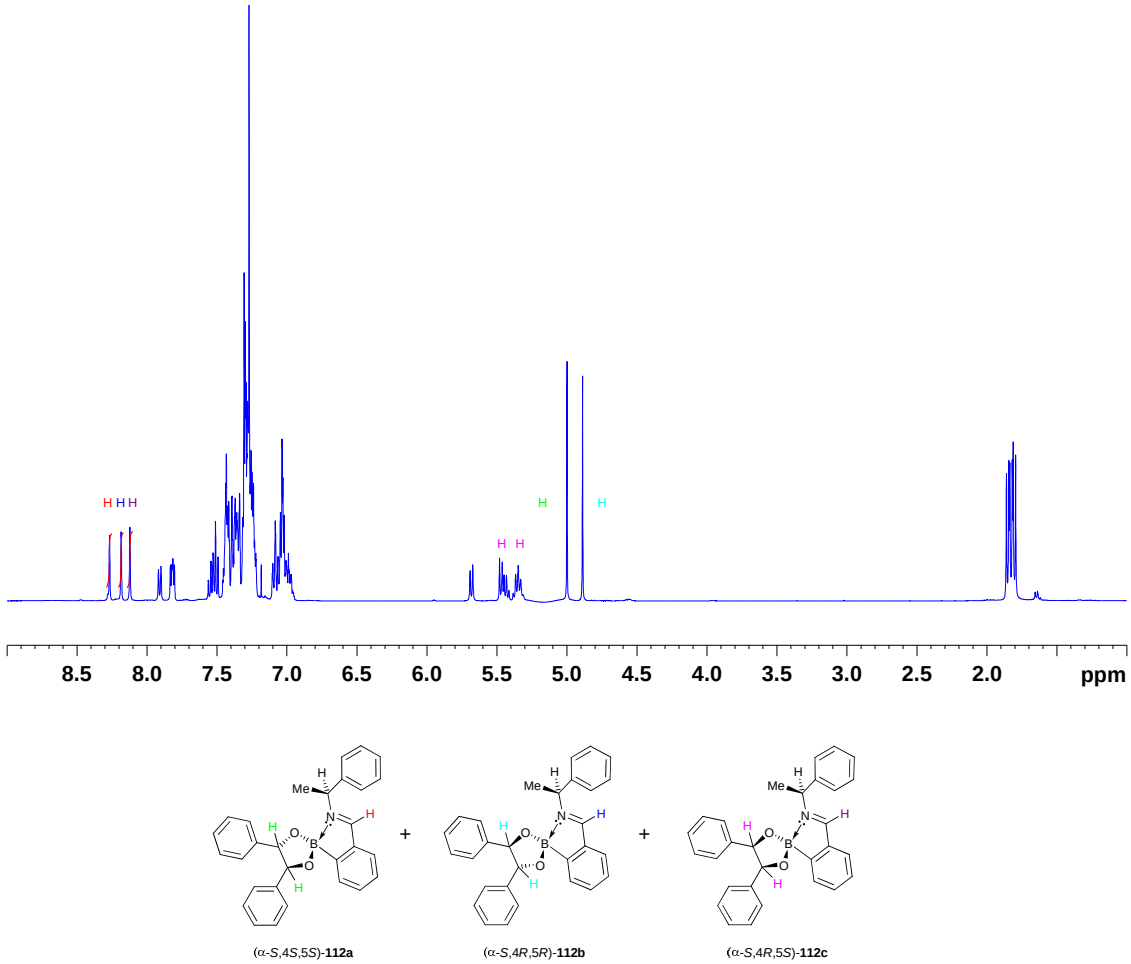


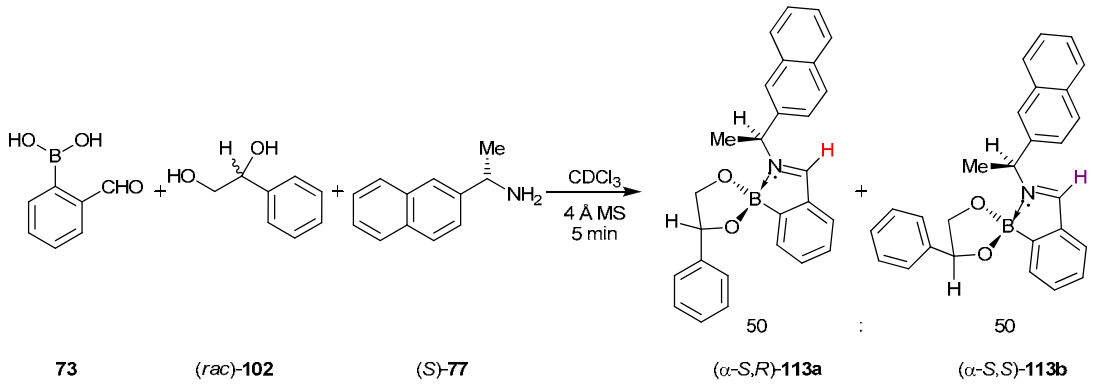
Figure 12 400 MHz $CDCl_3$ ^1H NMR resolution of three sets of resonances for the imine signals for imino-boronate esters derived from (1*R*,2*R*) (1*S*,2*S*) and (*meso*)-1,2-diphenylethane-1,2-diol **112**.

2.2.3 Influence of the Parent Amine on the Resolution of Diastereomeric Iminoboronate Esters

Following the highly successful resolution of pairs of diastereomeric iminoboronate ester resonances using enantiopure (*S*)-α-methylbenzylamine in the three-component chiral derivatisation protocol, our attention turned to changing the nature of the chiral amine in an effort to improve this resolution in their ^1H NMR spectra.

In order to investigate this, a new three-component coupling protocol was employed using (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** as the parent amine which we hoped would lead to improved anisotropic shielding / deshielding of its resultant iminoboronate ester diastereoisomers. Therefore, 1.0 equivalent of (*rac*)-1-phenyl-1,2-

ethanediol **102** was stirred in $CDCl_3$ with 1.0 equivalent of (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** and 1.0 equivalent of 2-formylphenylboronic acid **73** at room temperature with an aliquot removed after 5 minutes (Scheme 7).



Scheme 7 Three-component coupling using chiral amine (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77**.

The resulting ^{1}H NMR spectrum again showed two sets of signals in a 50 : 50 ratio corresponding to two diastereomeric iminoboronate esters **113a** and **113b** (Figure 13). Again, complete derivatisation was observed for both diastereomers indicating that no kinetic resolution had occurred.

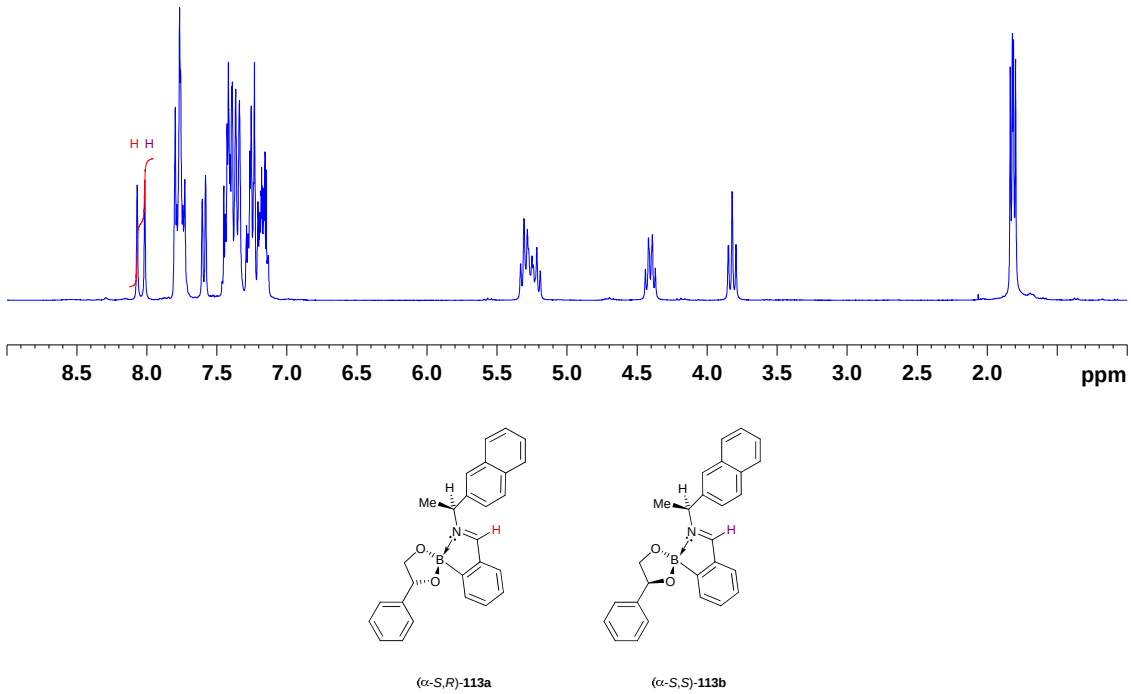
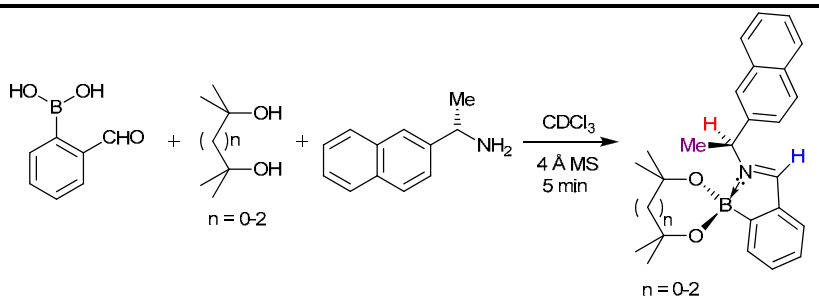
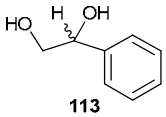
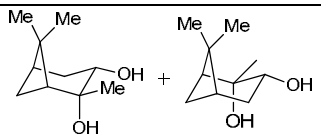
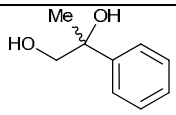
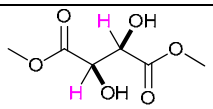
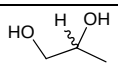
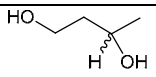
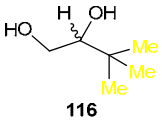
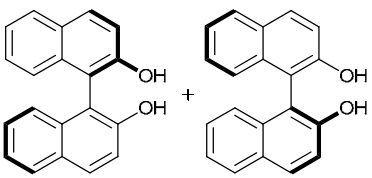
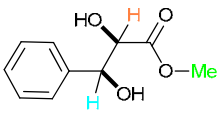


Figure 13 400 MHz $CDCl_3$ ^{1}H NMR resolution of diastereomers of 1-phenylethane-1,2-diol using (*S*)-(-)-1-(naphthalen-3-yl)ethanamine.

Splitting of the imine signal was again observed with a Δδ value of +/- 0.055. Surprisingly, in comparison with the equivalent spectrum for (*S*)-(-)-α-methylbenzylamine, poorer splitting was observed for this chiral amine with only the imine signals splitting in both cases, indicating that the greater potential anisotropic shielding effect of the naphthyl ring had minimal influence on the discrimination of the diastereomers. Despite this poor splitting, (*S*)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** was screened as a chiral auxiliary for three-component derivatisation of the range of diols considered previously.

Table 4: Chemical shift differences (Δδ) in the 400 MHz $CDCl_3$ ^1H NMR spectra of 50 : 50 mixtures of **113-121a** and **113-121b**.



Diol	Δδ (ppm)	Diol	Δδ (ppm)
 **113**	0.055	 **118**	0.020
 **114**	+/- 0.097	 **119**	-0.274 0.136 0.222
 **115**	-0.035	 **120**	-0.017
 **116**	+/- 0.077 +/-0.050	 **121**	0.165 -0.092 0.202
 **117**	-0.255 0.141 0.398 0.107 -0.029		

It may be concluded that the original rationale for the splitting of diastereoisomeric resonances through anisotropic effects appears largely unfounded. Although some sets of iminoboronate esters showed improved splitting ((α-*S*,4*S*,5*R*)-**117a** and (α-*S*,4*R*,5*S*)-**117b** (derived from parent diol (*rac*)-**106**) displayed resolution of five sets of signals compared to the four distinct sets previously observed for (*S*)-α-methylbenzylamine (*S*)-**76** (Figure 14), the improved resolution was not consistent and largely constituted of a small increase in Δδ of peaks that had already been split using (*S*)-α-methylbenzylamine.

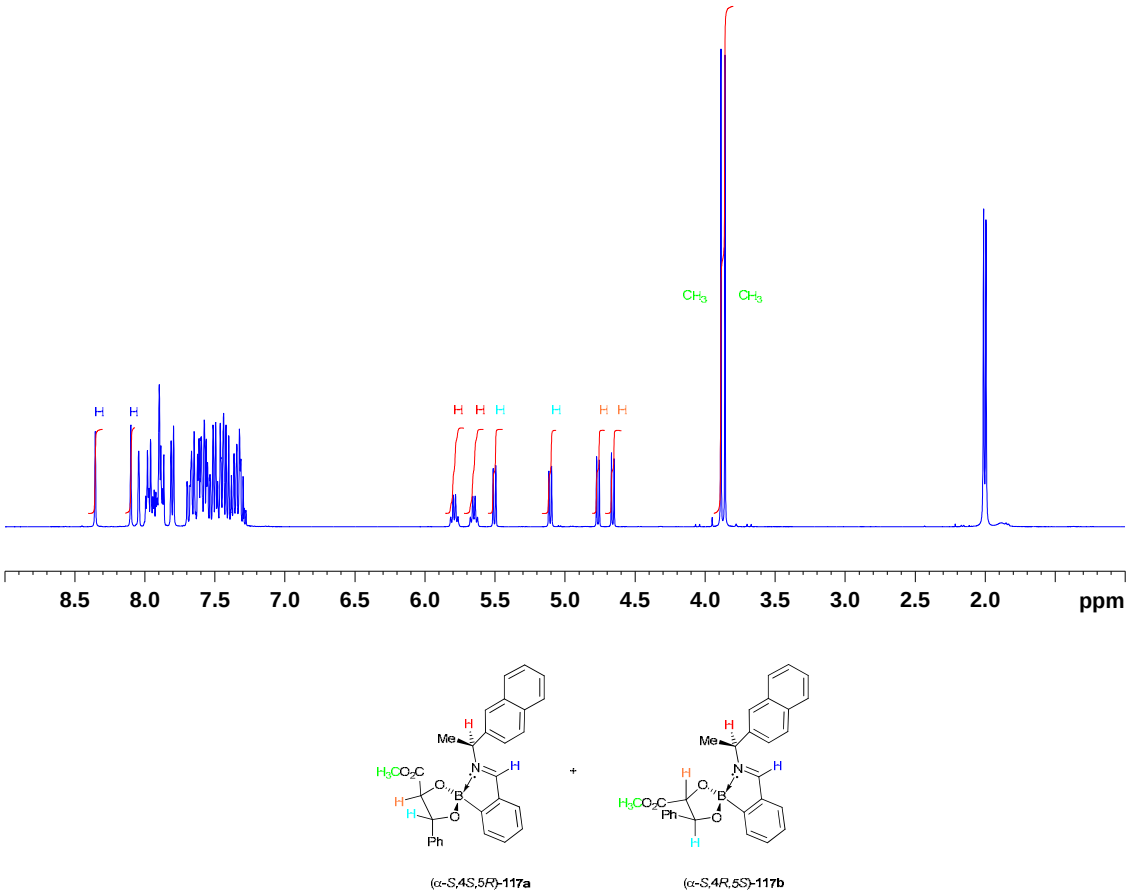


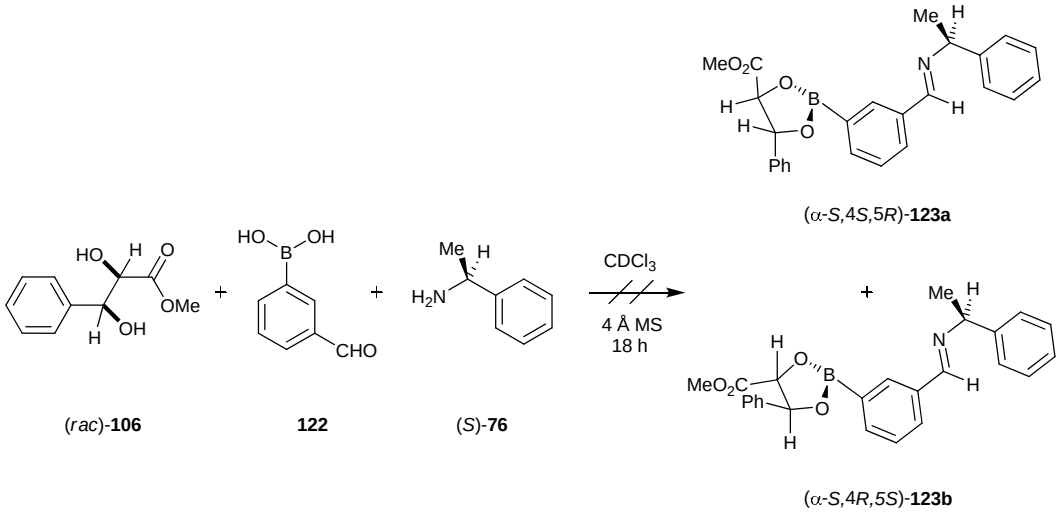
Figure 14 Slightly improved resolution observed in the 400 MHz $CDCl_3$ ^1H NMR when naphthyl CDA is used for (α-*S*,4*S*,5*R*)-**117a** and (α-*S*,4*R*,5*S*)-**117b**.

2.2.4 Influence of the Parent Boronic Acid on Resolution of Diastereomers

Continuing our work towards determining the cause of the resolution of the iminoboronate esters, our attention then turned to investigating the boronic acid

component of the coupling protocol. The potential for forming an intramolecular N→B coordinate bond was considered essential both for catalysing Lewis-acid assisted imine formation and for improved resolution of the diastereomers through anisotropic effects. Therefore, movement of the *ortho*-formyl group around the ring to the *meta*- and *para*-positions, thereby breaking the intramolecular N→B bond might be predicted to destroy any resolution of diastereoisomeric signals observed in the ^{1}H NMR spectrum of its resultant iminoboronate esters.

Therefore 1.0 equivalent of 3-formylphenylboronic acid **122**, 1.0 equivalent of (*S*)-(-)-α-methylbenzylamine (*S*)-**76** and 1.0 equivalent of (*rac*)-methyl-2,3-dihydroxy-3-phenylpropionate (*rac*)-**106** was stirred in $CDCl_3$ for 18 h in the presence of 4 Å molecular sieves (Scheme 8) before an aliquot was removed and a ^{1}H NMR spectrum acquired of the resulting mixture.



Scheme 8 3-component coupling using 3-formylphenylboronic acid **122**.

Whilst imine formation again proceeded quantitatively, potentially due to intermolecular Lewis-acid catalysis, the 1,2-diol did not condense with the boronic acid under such mild conditions, thus suggesting that N→B interaction appears to be a pre-requisite for the efficient three-component complexation to occur.

4-formylphenylboronic acid was then considered and again, since no N→B coordinate bonding was present, no complexation of the chiral diol unit to the boronic acid was observed.

2.2.5 References

1. Perez-Fuertes, Y.; Kelly, A. M.; Fossey, J. S.; Powell, M. E.; Bull, S. D.; James, T. D., *Nat Protoc* **2008,** 3, (2), 210-214.
2. Perez-Fuertes, Y.; Kelly, A. M.; Johnson, A. L.; Arimori, S.; Bull, S. D.; James, T. D., *Org. Lett.* **2006,** 8, (4), 609-612.
3. Shan, Z. X.; Xiong, Y.; Li, W. Z.; Zhao, D. J., *Tetrahedron-Asymmetry* **1998,** 9, (22), 3985-3989.
4. Finn, M. G., *Chirality* **2002,** 14, 534.
5. Demuth, M.; Ritterskamp, P.; Weigt, E.; Schaffner, K., *J. Am. Chem. Soc.* **1986,** 108, (14), 4149-4154.
6. Horeau, A.; Guette, J. P., *Tetrahedron* **1974,** 30, (13), 1923-1931.
7. Parker, D., *Chem. Rev.* **1991,** 91, (7), 1441-1457.
8. Bilz, A.; Stork, T.; Helmchen, G., *Tetrahedron-Asymmetry* **1997,** 8, (24), 3999-4002.
9. Pirkle, W. H., *J. Am. Chem. Soc.* **1966,** 88, 1837.
10. Burns, C. T.; Stelck, D. S.; Shapiro, P. J.; Vij, A.; Kunz, K.; Kehr, G.; Concolino, T.; Rheingold, A. L., *Organometallics* **1999,** 18, (26), 5432-5434.
11. Omelanczuk, J.; Mikolajczyk, M., *Tetrahedron-Asymmetry* **1996,** 7, (9), 2687-2694.
12. Bentrude, W. G.; Moriyama, M.; Mueller, H. D.; Sopchik, A. E., *J. Am. Chem. Soc.* **1983,** 105, (19), 6053-6061.
13. Drabowicz, J.; Dudzinski, B.; Mikolajczyk, M., *Tetrahedron-Asymmetry* **1992,** 3, (10), 1231-1234.
14. Drabowicz, J.; Dudzinski, B.; Mikolajczyk, M.; Colonna, S.; Gaggero, N., *Tetrahedron-Asymmetry* **1997,** 8, (13), 2267-2270.
15. Ghosh, I.; Kishi, Y.; Tomoda, H.; Omura, S., *Org. Lett.* **2004,** 6, (25), 4719-4722.
16. Chin, J.; Kim, D. C.; Kim, H.-J.; Panosyan, F.; Kim, K. M., *Org. Lett.* **2004,** 6, (15), 2591-2593.
17. Dale, J. A.; Dull, D. L.; Mosher, H. S., *J. Org. Chem.* **1969,** 34, 2543.
18. Dale, J. A.; Mosher, H. S., *J. Am. Chem. Soc.* **1973,** 95, (2), 512-519.

19. Seco, J. M.; Martino, M.; Quinoa, E.; Riguera, R., *Org. Lett.* **2000,** 2, (21), 3261-3264.
20. Seco, J. M.; Quinoa, E.; Riguera, R., *Chem. Rev.* **2004,** 104, (1), 17-117.
21. Takeuchi, Y.; Itoh, N.; Satoh, T.; Koizumi, T.; Yamaguchi, K., *J. Org. Chem.* **1993,** 58, (7), 1812-1820.
22. Perez-Fuertes, Y., *Thesis* University of Bath **2005**.
23. Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B., *Chem. Rev.* **1994,** 94, (8), 2483-2547.
24. Hanessian, S.; Delorme, D.; Beaudoin, S.; Leblanc, Y., *J. Am. Chem. Soc.* **1984,** 106, 5754.
25. Freire, F.; Seco, J. M.; Quinoa, E.; Riguera, R., *Org. Lett.* **2005,** 7, (22), 4855-4858.
26. Freire, F.; Seco, J. M.; Quinoa, E.; Riguera, R., *J. Org. Chem.* **2005,** 70, (10), 3778-3790.
27. Kouda, K.; Ooi, T.; Kusumi, T., *Tetrahedron Lett.* **1999,** 40, (15), 3005-3008.
28. Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P., *J. Org. Chem.* **1986,** 51, (12), 2370-2374.
29. Joshi, B. S.; Pelletier, S. W., *Heterocycles* **1999,** 51, (1), 183-184.
30. Burgess, K.; Porte, A. M., *Angew. Chem., Int. Ed.* **1994,** 33, (11), 1182-1184.
31. Caselli, E.; Danieli, C.; Morandi, S.; Bonfiglio, B.; Forni, A.; Prati, F., *Org. Lett.* **2003,** 5, (25), 4863-4866.
32. Resnick, S. M.; Torok, D. S.; Gibson, D. T., *J. Org. Chem.* **1995,** 60, (11), 3546-3549.
33. Tokles, M.; Snyder, J. K., *Tetrahedron Lett.* **1988,** 29, (47), 6063-6066.
34. Brunel, J. M.; Faure, B., *Tetrahedron-Asymmetry* **1995,** 6, (9), 2353-2356.
35. Garner, C. M.; McWhorter, C.; Goerke, A. R., *Tetrahedron Lett.* **1997,** 38, (44), 7717-7720.
36. Fukui, H.; Fukushi, Y.; Tahara, S., *Tetrahedron Lett.* **2003,** 44, (21), 4063-4065.
37. Morandi, S.; Caselli, E.; Forni, A.; Bucciarelli, M.; Torre, G.; Prati, F., *Tetrahedron-Asymmetry* **2005,** 16, (17), 2918-2926.
38. Dunn, H. E., *J. Org. Chem.* **1968,** 33, 4483.

39. Kelly, A. M.; Perez-Fuertes, Y.; Arimori, S.; Bull, S. D.; James, T. D., *Org. Lett.* **2006,** 8, (10), 1971-1974.

40. Kelly, A. M.; Perez-Fuertes, Y.; Fossey, J. S.; Yeste, S. L.; Bull, S. D.; James, T. D., *Nat Protoc* **2008,** 3, (2), 215-219.

41. Wulff, G., *Pure Appl. Chem.* **1982,** 54, 2093.

42. Kolodiazhnyi, O. I.; Demchuk, O. M.; Gerschkovich, A. A., *Tetrahedron-Asymmetry* **1999,** 10, (9), 1729-1732.

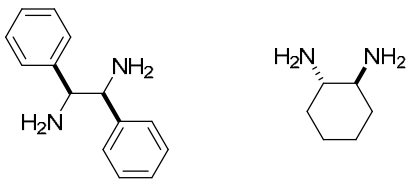
43. Hulst, R.; Zijlstra, R. W. J.; Devries, N. K.; Feringa, B. L., *Tetrahedron-Asymmetry* **1994,** 5, (9), 1701-1710.

2.3 A Novel Chiral Derivatising Agent for Determination of the Enantiomeric Excess of 1,2-Diphenylethane-1,2-diamine and Cyclohexane-1,2-diamine

2.3.1 Chiral Derivatising Agents for Diamines

Enantiopure diamines have proven to be highly effective components in a wide range of catalysts designed to induce enantioselectivity in a variety of asymmetric synthetic transformations. C_2-symmetric diamines 1,2-diphenylethane-1,2-diamine **124** and cyclohexane-1,2-diamine **125** have proven to be popular chiral building blocks for the synthesis of chiral auxiliaries and chiral reagents,[1,2] chiral sensors[3-5] and chiral derivatising or solvating agents.[6-12] They have also been widely used as chiral ligands for preparing transition metal complexes for asymmetric catalysis, and have recently been used for the preparation of highly enantioselective organocatalysts.[13-15]

Whilst a range of different strategies have been developed for their asymmetric synthesis, these C_2-symmetric amines are most commonly prepared in enantiopure form *via* resolution protocols.[16-19] This most often involves treatment of their respective racemic amines with either tartaric or mandelic acid, affording mixtures of diastereoisomeric salts that are then separated and individually decomplexed to afford both enantiomers of the parent diamine.[20-22] Since these chiral C_2-symmetric amines are normally used in chiral environments,[23] it is essential that their enantiopurity is determined accurately and, consequently, we envisaged extending our successful protocol for the determination of the enantiomeric excesses of primary amines and diols to diamines.[24]



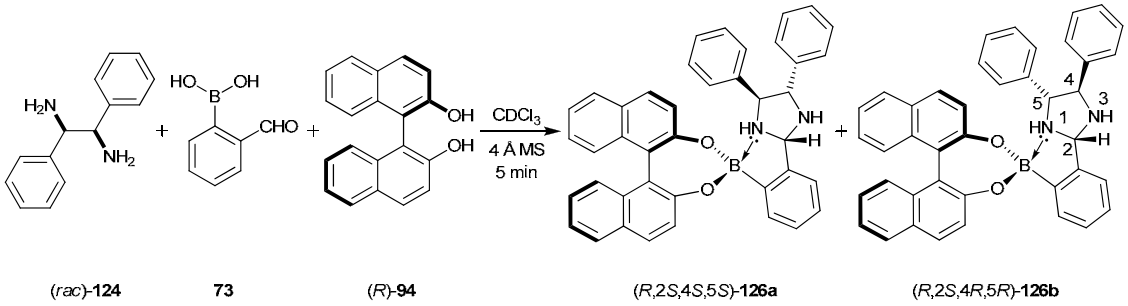
124 **125**

Figure 1 Two common diamines used in asymmetric transformations.

2.3.2 Determination of the Enantiomeric Excess of 1,2-Diphenylethane-1,2-diamine

Following our successful development of a 3-component strategy for determining the enantiopurity of chiral primary amines and diols, we reasoned that this type of NMR derivatisation protocol might also be useful for analysing the enantiopurity of chiral vicinal diamines such as 1,2-diphenylethane-1,2-diamine or cyclohexane-1,2-diamine.

Therefore, (*rac*)-diamine **124** was treated with one equivalent of 2-formylphenylboronic acid **73** and one equivalent of enantiopure (*R*)-BINOL (*R*)-**74** in $CDCl_3$ in the presence of 4 Å molecular sieves (Scheme 1) and its ^{1}H NMR spectrum acquired after five minutes. This ^{1}H NMR spectrum revealed that an efficient complexation reaction had occurred to afford a 50 : 50 mixture of two diastereoisomeric imidazolidine complexes (*R*,2*S*,4*S*,5*S*)-**126a** and (*R*,2*S*,4*R*,5*R*)-**126b** in quantitative yield.[25]



Scheme 1 Derivatisation protocol to afford a mixture of imidazolidine boronate esters.

The individual resonances of each diastereoisomer were assigned by comparison with the ^{1}H NMR spectra of authentic samples of (*R*,2*S*,4*S*,5*S*)-**126a** and (*R*,2*S*,4*R*,5*R*)-**126b** prepared independently *via* reaction of the individual (1*R*,2*R*)-**124** and (1*S*,2*S*)-**124** enantiomers of 1,2-diphenyl-1,2-ethanediamine with 2-formylphenylboronic acid **73** and (*R*)-BINOL (*R*)-**74**.

Analysis of the ^{1}H NMR spectra of (*R*,2*S*,4*S*,5*S*)-**126a** and (*R*,2*S*,4*R*,5*R*)-**126b** revealed structures consistent with formation of complexes containing an imidazolidine ring system. For example, resonances corresponding to the two N*H* protons of (*R*,2*S*,4*S*,5*S*)-

126a were assigned using a standard D_2O exchange experiment which revealed that one of its nitrogen atoms NH_A was coordinated to the central boron atom in an intramolecular manner. This was evident from the non-equivalence of the N*H* resonances of the imidazolidine ring system of (*R*,2*S*,4*S*,5*S*)-**126a** with the deshielded NH_A proton coordinated to the boron atom appearing downfield at δ 5.02, the uncoordinated NH_B proton appeared upfield at δ 2.80 (Figure 2).

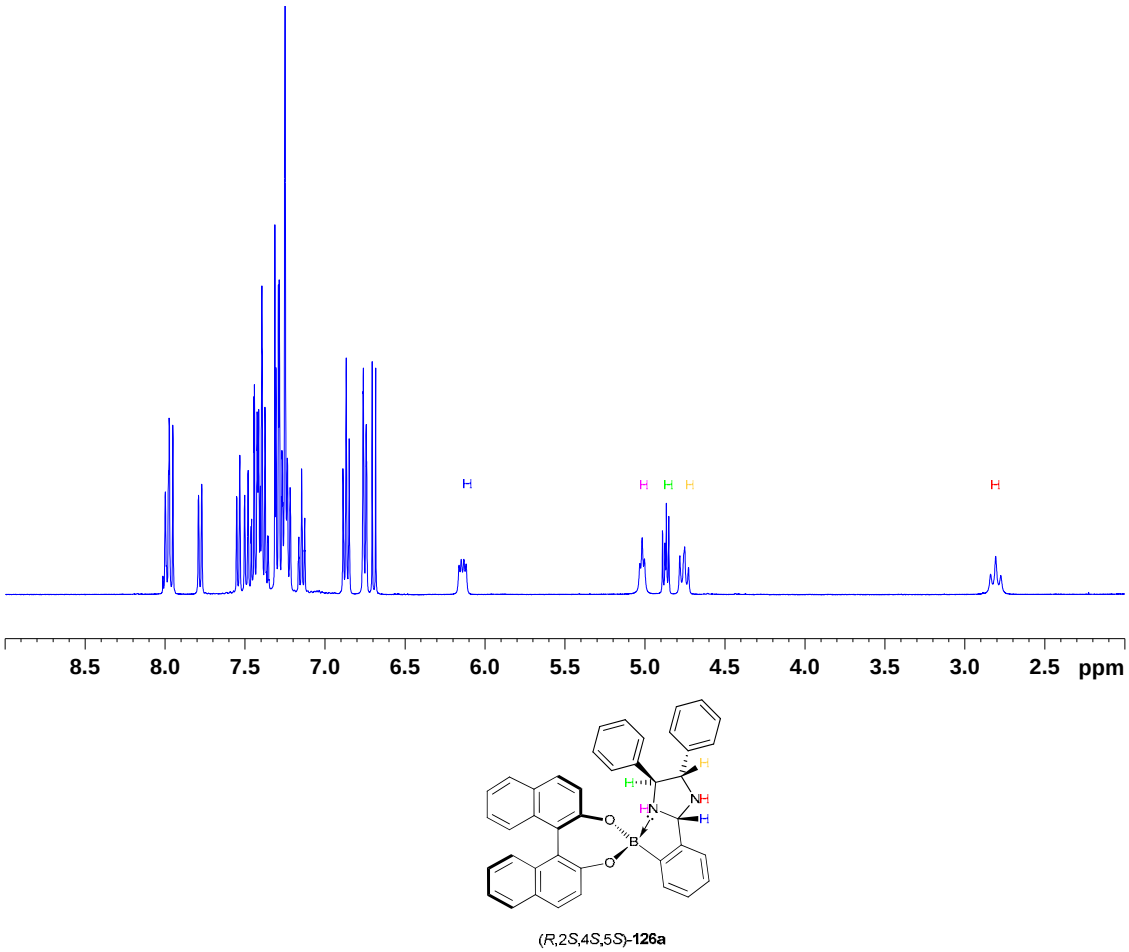
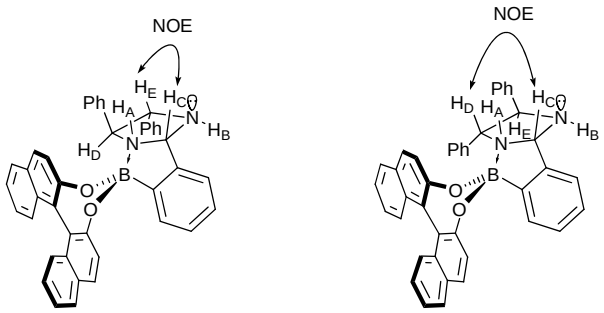


Figure 2 500 MHz $CDCl_3$ ^{1}H NMR spectrum showing imidazolidine boronate ester (*R*,2*S*,4*S*,5*S*)-**126a** formed in quantitative yield with complete stereocontrol over the new imidazolidine stereocentre.

The imidazolidine proton H_C appears as a doublet of doublets at δ 6.14, with a large *syn*-diaxial coupling constant $J_{(AC)}$ = 12.3 Hz and a small axial-equatorial coupling constant $J_{(BC)}$ = 5.8 Hz. NOESY experiments revealed cross-peaks between the imidazolidine H_C proton and the benzylic proton H_E that was vicinal to H_B, consistent with the imidazolidine ring structure of (*R*,2*S*,4*S*,5*S*)-**126a** (Figure 3).



(*R*,2*S*,4*S*,5*S*)-**126a** (*R*,2*S*,4*R*,5*R*)-**126b**

Figure 3 NOESY coupling to determine the absolute stereochemistry at the imidazolidine stereocentre.

The diastereoisomeric complexes (*R*,2*S*,4*S*,5*S*)-**126a** and (*R*,2*S*,4*R*,5*R*)-**126b** were sufficiently stable to allow for deuterium exchange of both their N*H* protons on shaking their NMR samples with D_2O which resulted in both diastereoisomers exhibiting much simplified ^{1}H NMR spectra, with their imidazolidine H_C protons collapsing from a quartet to a singlet and both pairs of benzylic H_D / H_E protons simplifying to doublets (Figure 4).

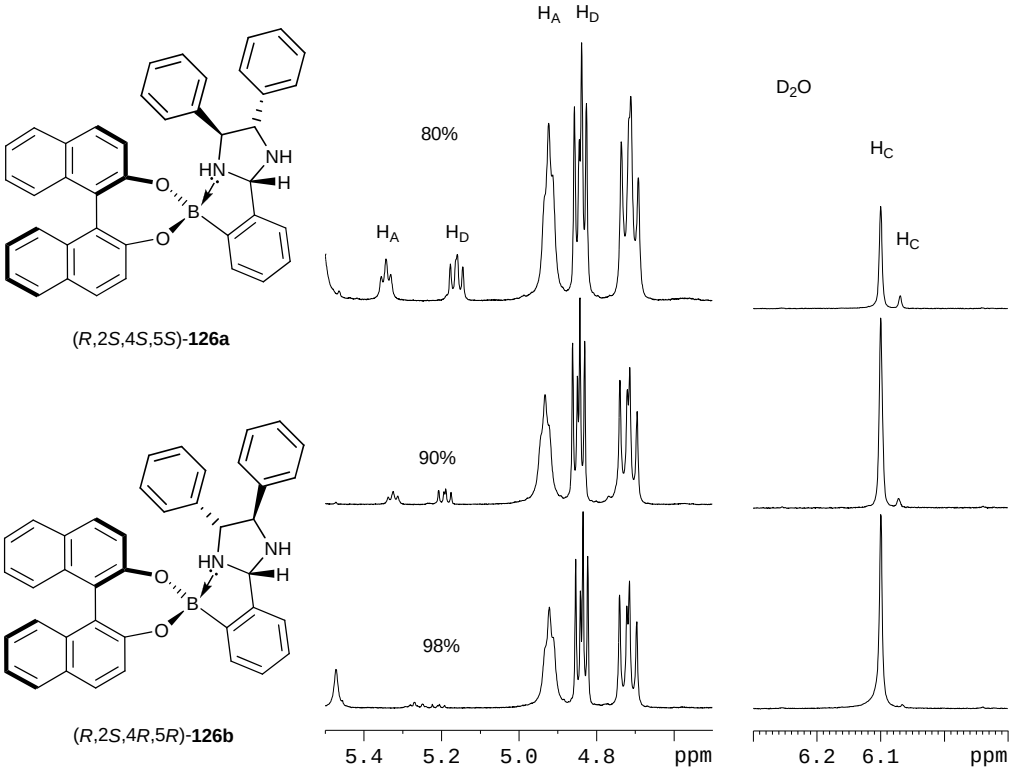


Figure 4 Simplification of the imidazolidine signals using a D_2O shake (500 MHz, $CDCl_3$).

Close examination of the ^{1}H NMR spectrum of the 50 : 50 mixture of complexes (*R*,2*S*,4*S*,5*S*)-**126a** and (*R*,2*S*,4*R*,5*R*)-**126b** revealed baseline resolution of a number of

complementary pairs of diastereoisomeric resonances. Most notably, two sets of resonances corresponding to their H_A protons ($\Delta\partial$ 0.42 ppm) and H_D protons ($\Delta\partial$, 0.32 ppm) were baseline resolved which allowed them to be integrated to accurately determine the diastereoisomeric ratio of the sample.

The detection limits of this method were determined by derivatisation of three samples of scalemic (1*S*,2*S*)-1,2-diphenyl-1,2-ethanediamine (1*S*,2*S*)-**124** of 80%, 90% and 98% *ee* respectively. Comparison of the relative intensities of the integrals for the diastereoisomeric pairs of H_A and H_D protons in the 500 MHz ^{1}H NMR spectrum of these mixtures revealed calculated diastereomeric excesses of 81%, 90% and 99% of (*R*,2*S*,4*S*,5*S*)-**126a**. These values were in excellent agreement with the known enantiomeric purity of their corresponding starting diamine (1*S*,2*S*)-**124**, thus indicating that little or no kinetic resolution had occurred in the derivatisation process.

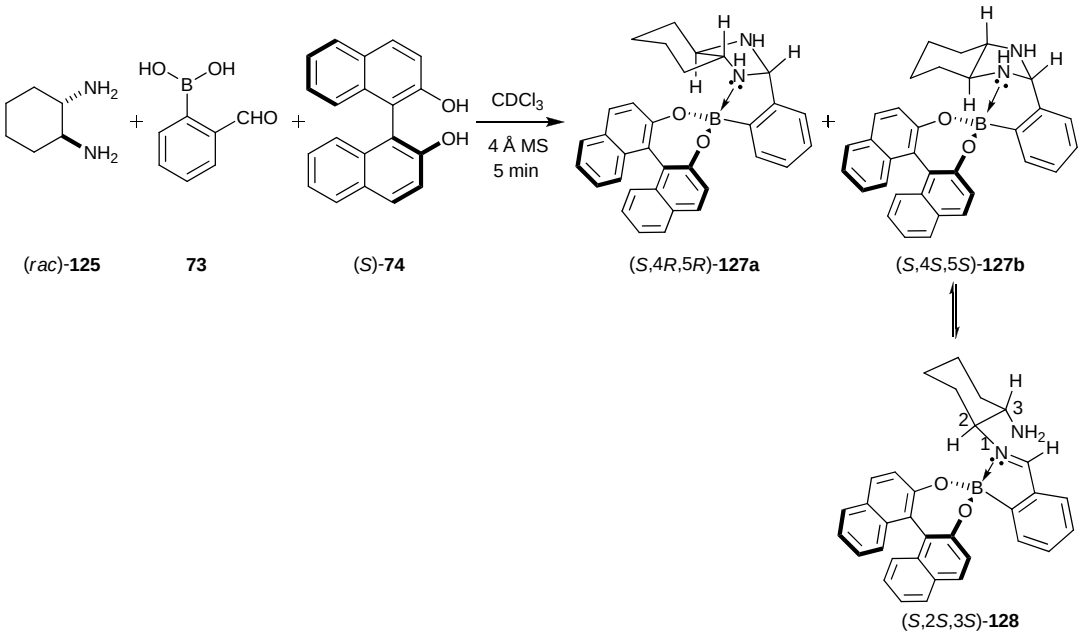
We can therefore conclude that the standard three-component protocol can be successfully translated to the formation of imidazolidine boronate esters for determination of the enantiomeric excess of 1,2-diphenylethane-1,2-diamine.

2.3.3 Determination of the Enantiomeric Excess of Cyclohexane-1,2-diamine

Following the successful application of the 3-component coupling strategy for formation of a pair of imidazolidine boronates under standard conditions for 1,2-diphenylethane-1,2-diamine, this approach was extended to cyclohexane-1,2-diamine **125**.

Derivatisation of the (1*R*,*2R*)-enantiomer with 2-formylphenylboronic acid and (*S*)-BINOL proceeded in quantitative yield to afford its corresponding imidazolidine (*S*,4*R*,5*R*)-**127a**. However, derivatisation of the (1*S*,2*S*)-enantiomer afforded a 50 : 50 mixture of its imidazolidine (*S*,4*S*,5*S*)-**127b** and its corresponding imine (*S*,2*S*,3*S*)-**128**. The failure of the (1*S*,2*S*)-enantiomer of **125** to undergo clean ring-closure reaction under these conditions is presumably due to the added strain involved in forming a

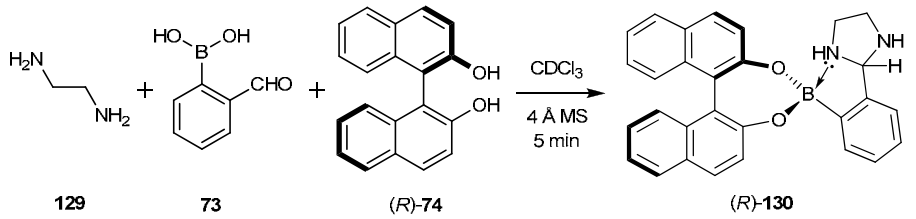
tricyclic imidazolidine ring system caused by unfavourable interactions between the methylene backbone of the cyclohexane ring system and the proximal aryl ring of the binaphthyl fragment (Scheme 2).



Scheme 2 Derivatisation of (*rac*)-diamine (*rac*)-**125** affords a mixture of imidazolidines (*S*,4*R*,5*R*)-**127a** and (*S*,4*S*,5*S*)-**127b** and imine (*S*,2*S*,3*S*)-**128**.

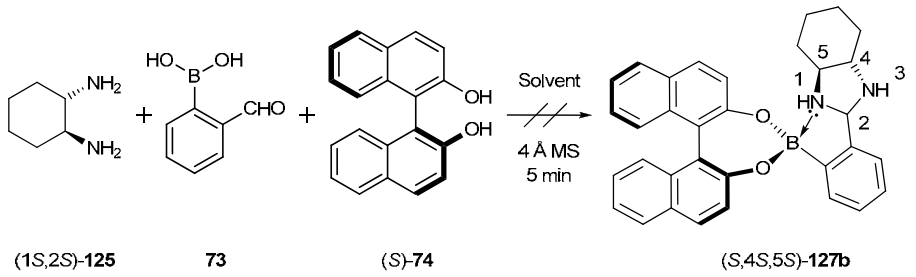
This clearly meant that the imidazolidine derivatisation protocol employed for 1,2-diphenylethane-1,2-diamine was unsuited to determining the enantiomeric excess of cyclohexane-1,2-diamine.

Indeed, a similar story was found with other chiral diamines that were tested. All diamines tested using BINOL as a chiral auxiliary displayed either broad spectra or incomplete reaction. We thought that the broad spectra were caused by free rotation of the imidazolidine fragment in solution, for example in the derivatisation of achiral ethane-1,2-diamine **129** (Scheme 3).



Scheme 3 Formation of an imidazolidine boronate ester using achiral ethane-1,2-diamine.

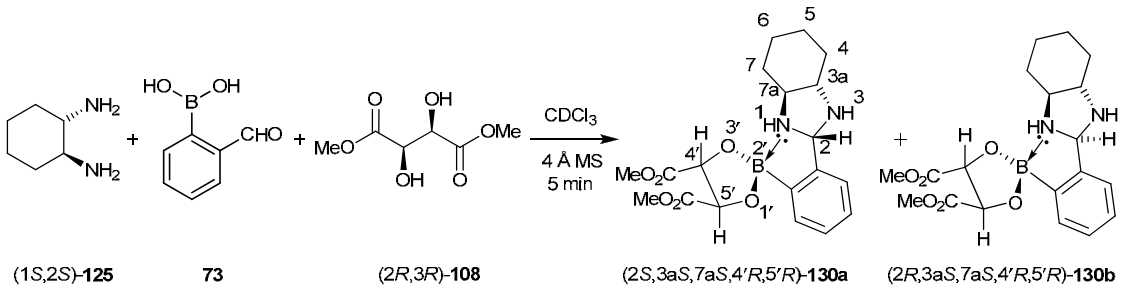
A short solvent screen was run for reaction of (1*S*,2*S*)-cyclohexane-1,2-diamine (1*S*,2*S*)-**125** with 2-formylphenylboronic acid **73** and (*S*)-BINOL (*S*)-**74** in an attempt to drive the equilibrium to the tricyclic ring-closed imidazolidine species (Scheme 4).



Scheme 4 Attempted ring closure to afford an imidazolidine in different solvents.

Best results were obtained with THF-d_8 which showed some imidazolidine formation although as with $CDCl_3$ and CD_2Cl_2 some ring-opened imine signals were observed. In most instances, aside from sterically undemanding diamines such as ethane-1,2-diamine **129** where signal broadening was more problematic, the steric bulk of the newly cyclised ring presented the main barrier to cyclisation. We therefore decided to look towards substituting BINOL for a different chiral diol moiety in the protocol which would allow a more facile imidazolidine ring formation to occur.

Dimethyl-L-tartrate was selected since it is commercially available in both enantiopure forms and is far less sterically demanding than BINOL. Therefore, 1.0 equivalent of dimethyl-L-tartrate **108** was stirred with 1.0 equivalent of 2-formylphenylboronic acid **73** and 1.0 equivalent of (1*S*,2*S*)-cyclohexane-1,2-diamine (1*S*,2*S*)-**125** in $CDCl_3$ in the presence of 4 Å molecular sieves for 5 minutes (Scheme 5) before an aliquot (0.7 mL) was removed and its ^{1}H NMR spectrum acquired.



Scheme 5 Incomplete stereoselectivity at the new chiral centre with dimethyl-L-tartrate.

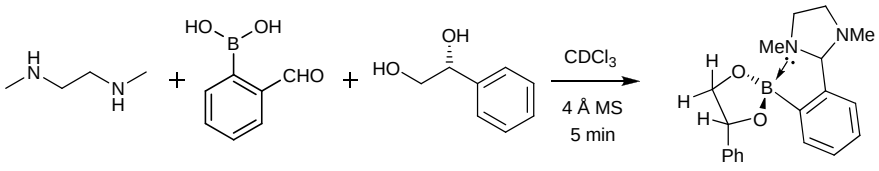
Whilst the switch to less sterically demanding dimethyl-L-tartrate proved highly successful in forcing complete cyclisation to the corresponding imidazolidine, a corresponding loss of stereoselectivity at the newly formed chiral centre was observed in all diamines tested, including 1,2-diphenylethane-1,2-diamine **124**. This was confirmed by the presence of two distinct sets of signals in its ^{1}H NMR spectrum. Whilst no imine resonances were observed, indicating complete imidazolidine boronate ester formation, two imidazolidine proton resonances were observed at δ 5.88 and 5.71 ppm.

We presumed that this was due to the steric influence being so greatly reduced so as to bring the energy gap between the two diastereomers (with differing stereochemistry at the new imidazolidine chiral centre) much closer together such that, despite the complex being in dynamic equilibrium in solution, it resulted in one ring form no longer predominating.

2.3.4 Diol Screen Using a Secondary Diamine

We therefore required a diol which would both promote quantitative cyclisation whilst still exerting complete control over the configuration at the new stereocentre. In order to test this, we used *N*,*N'*-dimethylethylamine as our parent diamine in a diol screen using the diols from our previous work to look for complete stereoselectivity at the new stereocentre.

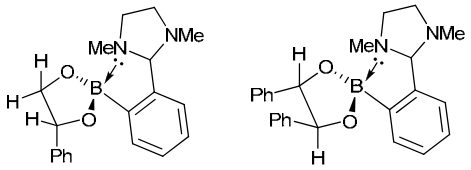
Therefore, 1.0 equivalent of *N*,*N'*-dimethylethylamine **131** was stirred with 1.0 equivalent of 2-formylphenylboronic acid **73** and 1.0 equivalent of (*R*)-1-phenylethane-1,2-diol (*R*)-**102** was stirred in $CDCl_3$ in the presence of 4 Å molecular sieves for 5 minutes (Scheme 6) before its ^{1}H NMR spectrum was acquired.



131 **73** (*R*)-**102** (*R*)-**132**

Scheme 6 Formation of imidazolidine boronate ester (*R*)-**132** *via* cyclisation onto an activated iminium intermediate.

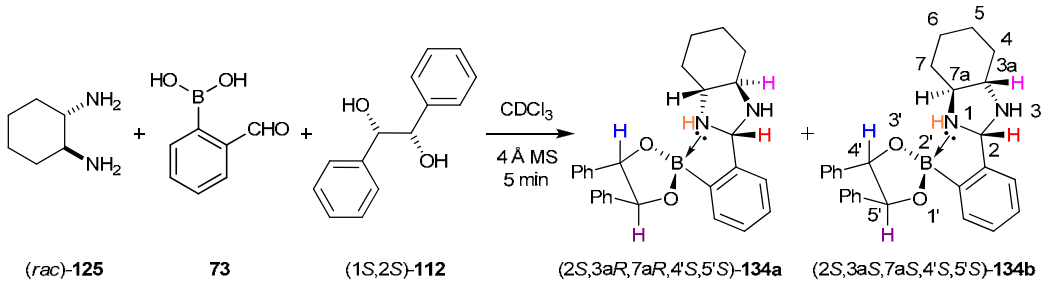
Of the diols tested, only (*R*)-1-phenylethane-1,2-diol (*R*)-**102** and (1*S*,2*S*)-hydrobenzoin (1*S*,2*S*)-**112** showed complete cyclisation combined with 100% stereocontrol at their newly-formed imidazolidine centres (Figure 5). These diols were then tested with (*rac*)-cyclohexane-1,2-diamine (*rac*)-**125** as before.



(*R*)-**132** (1*S*,2*S*)-**133**

Figure 5 Successful formation of a single diastereoisomer was observed with two diols.

^{1}H NMR analysis of the crude samples revealed that the diol (1*S*,2*S*)-hydrobenzoin (1*S*,2*S*)-**112** showed quantitative formation of a pair of cyclised imidazolidine boronate esters with complete stereoselectivity at their new imidazolidine stereocentres. Furthermore, resolution of a number of individual pairs of resonances was observed sufficient for baseline integration to be accurately performed (Scheme 7).



(*rac*)-**125** **73** (1*S*,2*S*)-**112** (2*S*,3a*R*,7a*R*,4'*S*,5'*S*)-**134a** (2*S*,3a*S*,7a*S*,4'*S*,5'*S*)-**134b**

Scheme 7 Successful formation of a 50 : 50 mixture of diastereoisomeric imidazolidine boronate esters.

The ^{1}H NMR spectrum showed resolution for several pairs of diastereoisomeric resonances which were individually resolved allowing for accurate integration of the individual signals (Figure 6). Although broadening of the individual peaks made

absolute assignment of the imidazolidine chiral centre impossible by consideration of the ^{1}H NMR spectrum alone, NOESY coupling again allowed for their configuration to be determined with the same assignment made in both cases as with 1,2-diphenylethane-1,2-diamine previously.

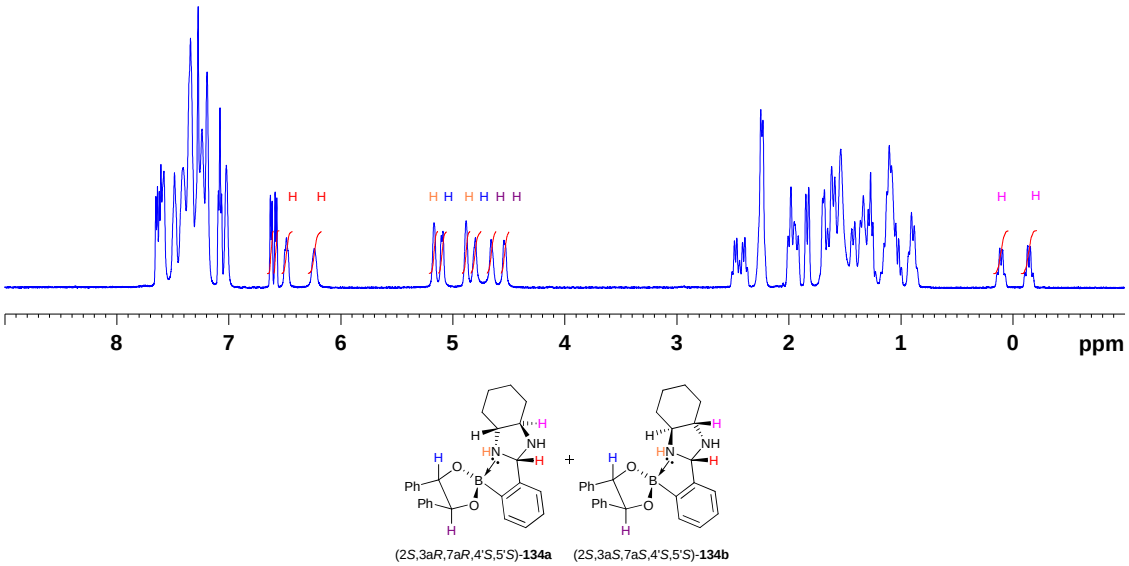


Figure 6 500 MHz $CDCl_3$ ^{1}H NMR spectrum of a 50:50 mixture of imidazolidineboronate esters from parent diamine (*rac*)-**125**.

Splitting was observed between pairs of resonances for protons on the boronate ester ring with the two C*H*(Ph)O doublets showing resolution of Δδ 0.32 and 0.13. Furthermore, resonances for the imidazolidine protons (Δδ 0.25) and the coordinating amine proton (Δδ 0.29) were also distinct enough to be able to accurately determine their diastereoisomeric excess. Indeed, additional sets of signals corresponding to a pair of highly shielded aromatic and cyclohexane ring protons show baseline resolution sufficient to make this a particularly powerful tool for directly determining the enantiopurity of cyclohexane-1,2-diamine.

Detection limits for this technique were then determined by derivatisation of three samples of (1*R*,2*R*)-cyclohexane-1,2-diamine (1*R*,2*R*)-**125** of 80% *ee*, 90% *ee* and 98% *ee* (Figure 7). Analysis of the ^{1}H NMR spectrum of each sample revealed that the calculated diastereomeric excess (*de*) for the resultant mixtures of (2*S*,3a*R*,7a*R*,4′*S*,5′*S*)-**134a** and (2*S*,3a*S*,7a*S*,4′*S*,5′*S*)-**134b** were in excellent agreement with the known enantiomeric purity of the starting diamine. Baseline integration of four pairs of resonances revealed that (2*S*,3a*R*,7a*R*,4′*S*,5′*S*)-**134a** had been formed in 83%, 92% and

97% *de* which correlated well with the known enantiopurities of the starting (1*R*,2*R*)-diamine (1*R*,2*R*)-**125** thus indicating that no kinetic resolution had occurred and, importantly, the imidazolidine rings formed both quantitatively and in an enantiopure fashion.

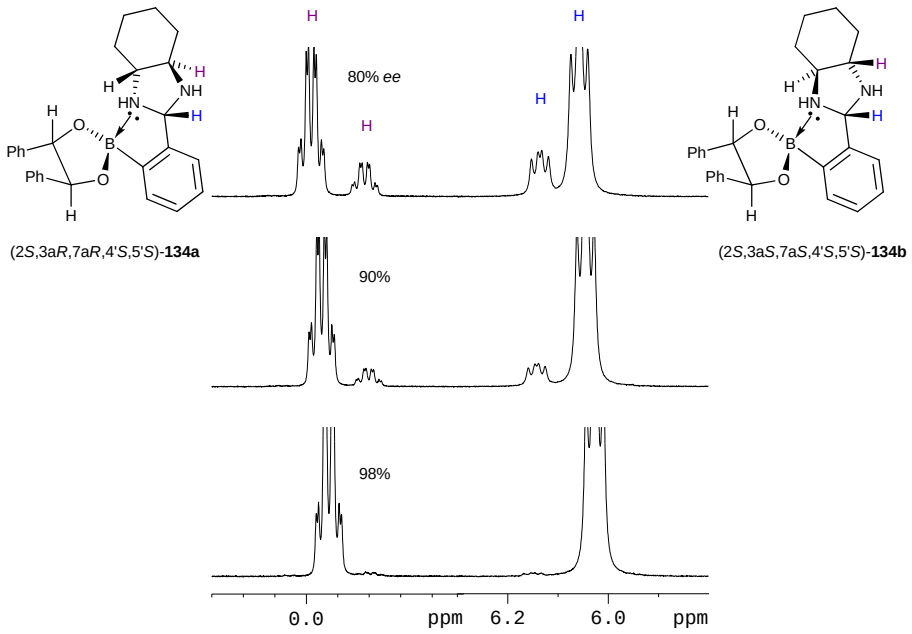
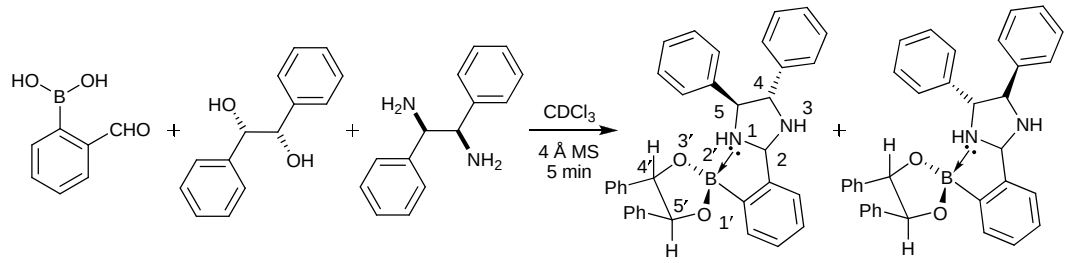


Figure 7 Two independent sets of signals used in the calculation of the *ee* of cyclohexane-1,2-diamine (500 MHz, $CDCl_3$).

Having successfully found a protocol for the derivatisation of cyclohexane-1,2-diamine, we then returned to 1,2-diphenylethane-1,2-diamine to test if this diol could be applied to that compound making this protocol more generally useful for chiral diamines (Scheme 8).

Therefore, 1.0 equivalent of (*rac*)-1,2-diphenylethane-1,2-diamine (*rac*)-**124** was stirred with 1.0 equivalent of (1*S*,2*S*)-hydrobenzoin (1*S*,2*S*)-**112** and 1.0 equivalent of 2-formylphenylboronic acid **73** in $CDCl_3$ in the presence of 4 Å molecular sieves. An aliquot was removed after 5 minutes for ^{1}H NMR analysis.



Scheme 8 Derivatisation of (*rac*)-1,2-diphenylethane-1,2-diamine (*rac*)-**124** with (1*S*,2*S*)-hydrobenzoin (1*S*,2*S*)-**112**.

Although ^{1}H NMR analysis showed complete formation of a pair of imidazolidine boronate esters with apparent total stereocontrol over the new imidazolidine centre, their resonances were significantly broadened with most signals appearing as broad multiplets with loss of fine coupling (Figure 8).

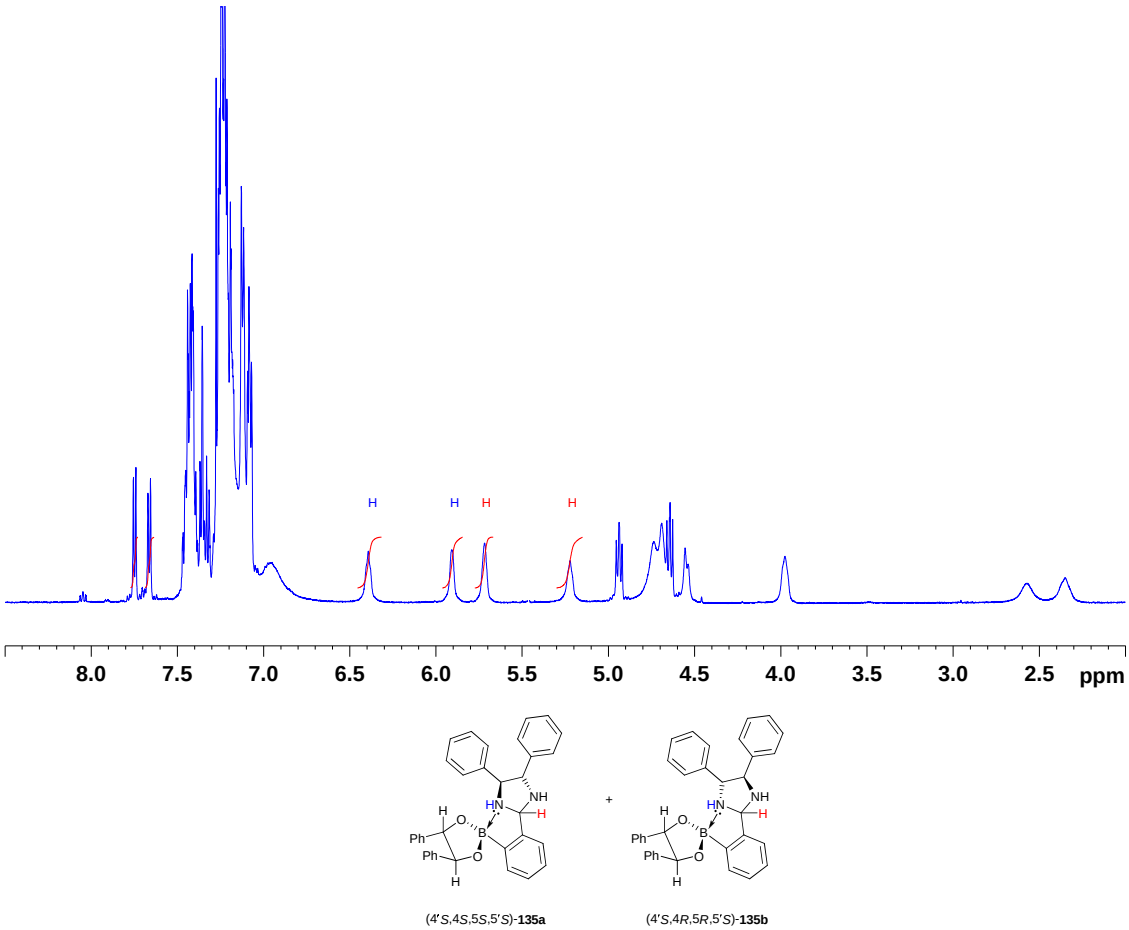


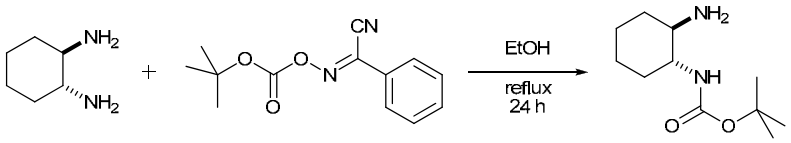
Figure 8 ^{1}H NMR of a racemic mixture of (4′*S*,4*S*,5*S*,5′*S*)-**135a** and (4′*S*,4*R*,5*R*,5′*S*)-**135b** in $CDCl_3$ (500 MHz, $CDCl_3$).

As a result, the significant broadening of the signals renders accurate integration of the diastereoisomers more difficult, which infers less accuracy in determination of enantiomeric excess. Nevertheless, three independent pairs of protons were available for baseline integration. This demonstrates that the diol used in the derivatisation protocol may be advantageously tuned to the chiral diamine whose enantiopurity is under investigation.

2.3.5 *mono*-Boc Protection Strategy for the General Determination of the Enantiopurity of Chiral Diamines

However, despite our confidence that such a protocol could be utilised successfully in the determination of the enatiomeric excess of any chiral diamine, it was decided to investigate whether a *mono*-protection strategy could be devised to enable an iminoboronate ester approach to be employed.

For this investigation, we again used troublesome cyclohexane-1,2-diamine as our test compound since this would present many of the difficulties that would arise with other types of chiral diamine. Consequently, an alternative approach was conceived involving *mono*-*N*-Boc protection of one of the amino functionalities of (*rac*)-cyclohexane-1,2-diamine (*rac*)-**125** using 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile **136** to afford (*rac*)-*N*-Boc-amine (*rac*)-**137** (Scheme 9) whose free amino functionality could then be derivatised using our previously reported procedure.[26]

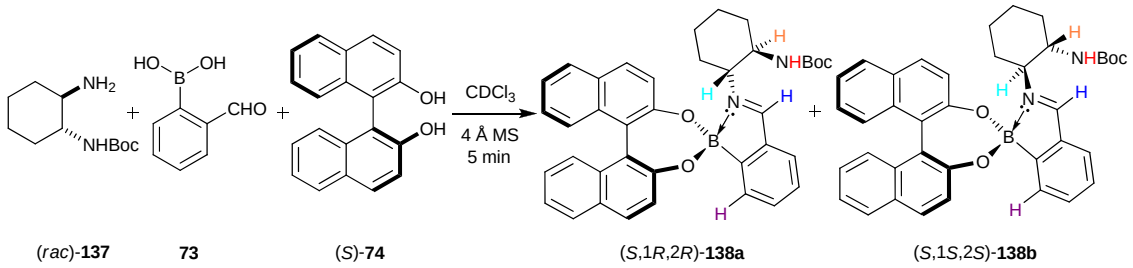


(*rac*)-**125** **136** (*rac*)-**137**

Scheme 9 *mono*-*N*-Boc-protection of cyclohexane-1,2-diamine (*rac*)-**125**.

Therefore, 1.0 equivalent of (*rac*)-*N*-Boc-carbamate (*rac*)-**137** was treated with 1.0 equivalent of 2-formylphenylboronic acid **73** and 1.0 equivalent of (*S*)-BINOL (*S*)-**74**

in $CDCl_3$ in the presence of 4 Å molecular sieves (Scheme 10) and the ^1H NMR spectrum of an aliquot acquired after 5 minutes.



Scheme 10 *mono*-Boc protection followed by derivatisation to afford a mixture of diastereomeric iminoboronate esters.

The resultant ^1H NMR spectrum revealed, as expected, a mixture of two diastereomeric imino-boronate ester complexes (*S*,1*R*,2*R*)-**138a** and (*S*,1*S*,2*S*)-**138b** that had been formed in a 50 : 50 ratio in quantitative yield with baseline resolution of five pairs of diastereoisomeric signals (Figure 9).

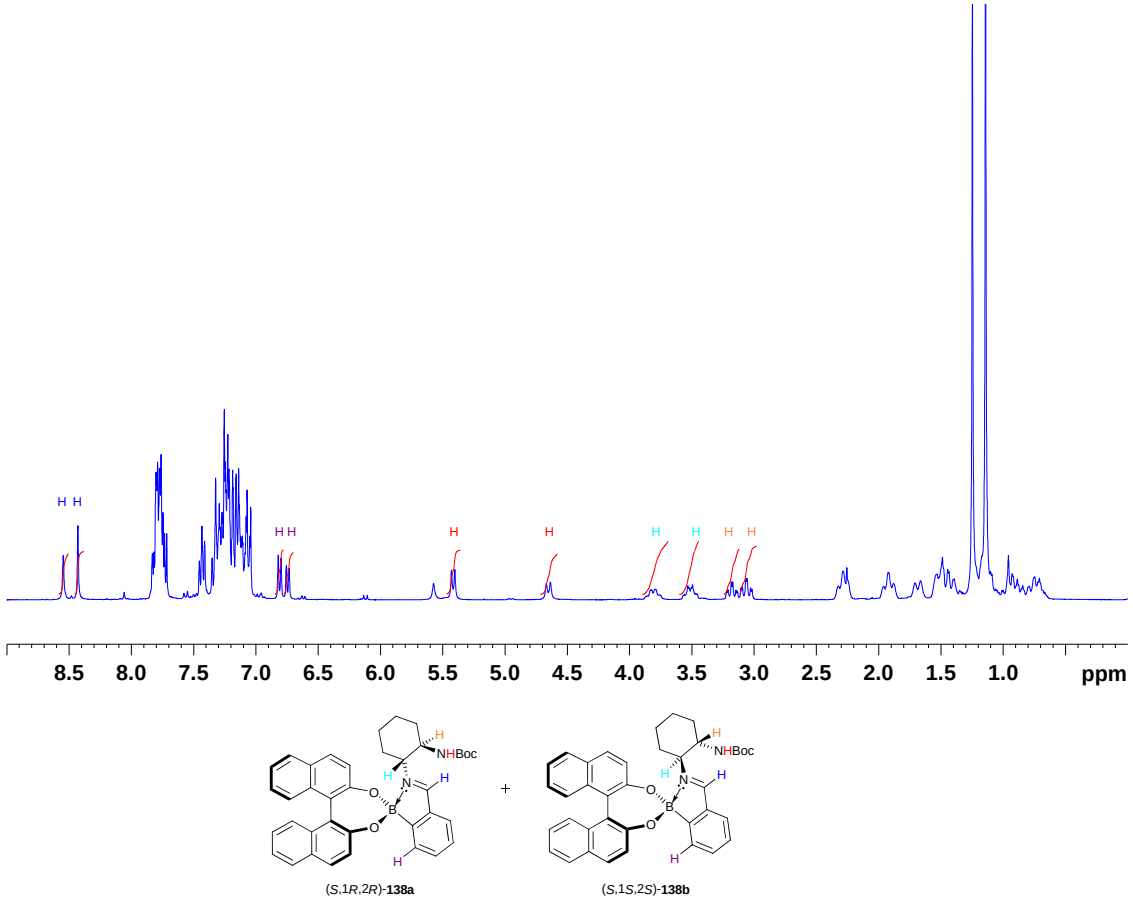


Figure 9 300 MHz $CDCl_3$ ^1H NMR spectrum of a pair of *mono*-Boc protected iminoboronate esters derived from parent (*rac*)-cyclohexane-1,2-diamine.

Significant splitting of the imine resonances (Δδ = 0.125 ppm) and the N*H*Boc protons (Δδ = 0.767 ppm) allowed for accurate determination and reliable confirmation of the enantiopurity of a scalemic sample of cyclohexane-1,2-diamine.

The detection limits of this method were determined by derivatisation of three samples of (1*S*,2*S*)-*tert*-butyl 2-aminocyclohexylcarbamate of 60% *ee*, 80% *ee* and 96% *ee*.

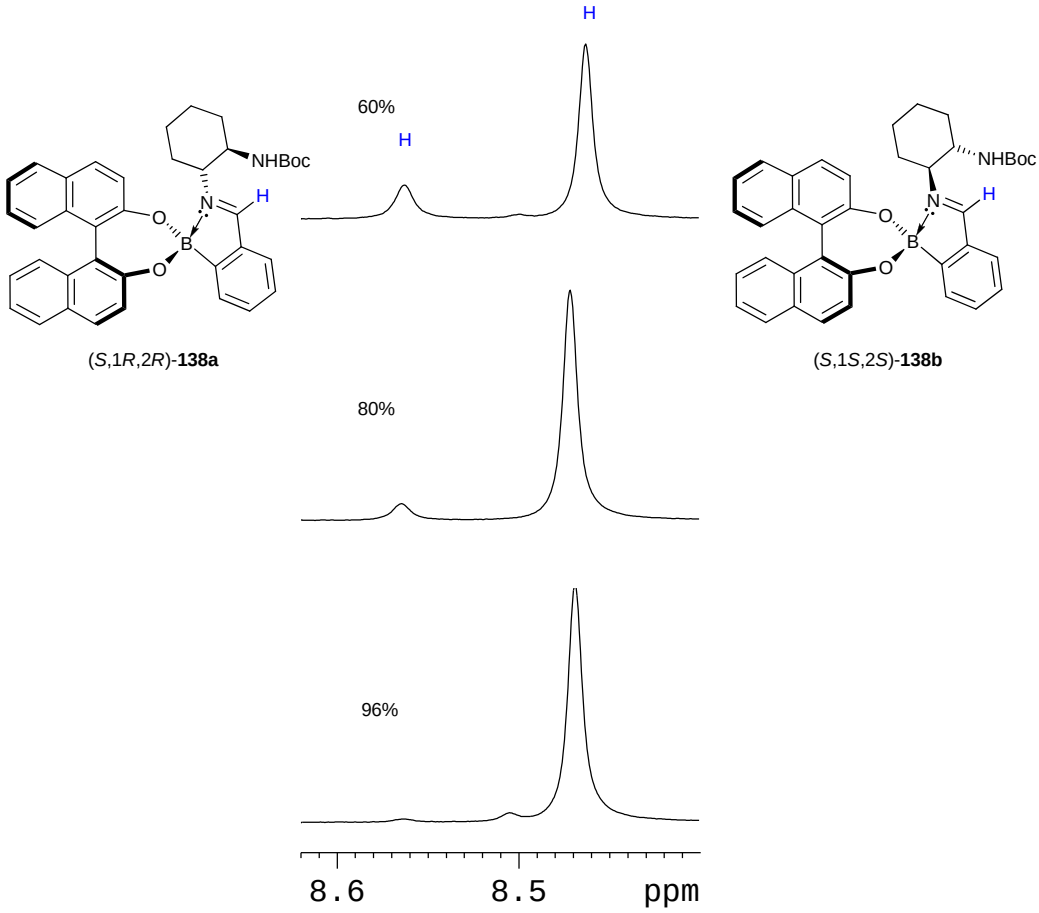


Figure 10 Expansion of the 300 MHz ^{1}H NMR spectrum of a mixture of (*S*,1*R*,2*R*)-**138a** and (*S*,1*S*,2*S*)-**138b** prepared from (1*S*,2*S*)-**125** of 60%, 80%, and 96% *ee*.

Analysis of the ^{1}H NMR spectrum of each sample revealed that the calculated *de* for the resultant mixtures of (*S*,1*R*,2*R*)-**138a** and (*S*,1*S*,2*S*)-**138b** were in excellent agreement with the known enantiomeric purity of the starting diamine. Therefore, the integrals measured for their imine resonances revealed that (*S*,1*S*,2*S*)-**138b** had been formed in 60%, 84% and 98% *de* which correlated well with the known enantiopurities of their starting (1*S*,2*S*)-diamine, thus indicating that no kinetic resolution had occurred.

We have therefore developed two novel protocols for determination of the enantiomeric excesses of 1,2-diphenylethane-1,2-diamine and cyclohexane-1,2-diamine. The first approach employs our original three-component protocol employed for the formation of iminoboronate esters for determination of the *ee* of primary amines and diols to form a pair of diastereoisomeric imidazolidine boronate esters, which display diastereoisomeric resonances that are distinct under ^{1}H NMR analysis. However, this protocol proved unsuccessful when applied to some more sterically demanding diamines so a novel *mono*-Boc protection-iminoboronate ester formation strategy was conceived, which again led to significant resolution of a series of diastereoisomeric sets of signals in the ^{1}H NMR spectrum for the corresponding diastereoisomeric iminoboronate esters. We expect that such a protocol will prove to be useful for other chiral diamines, such is the ease of the *mono*-Boc protection step and the reliability of iminoboronate ester formation.

2.3.6 References

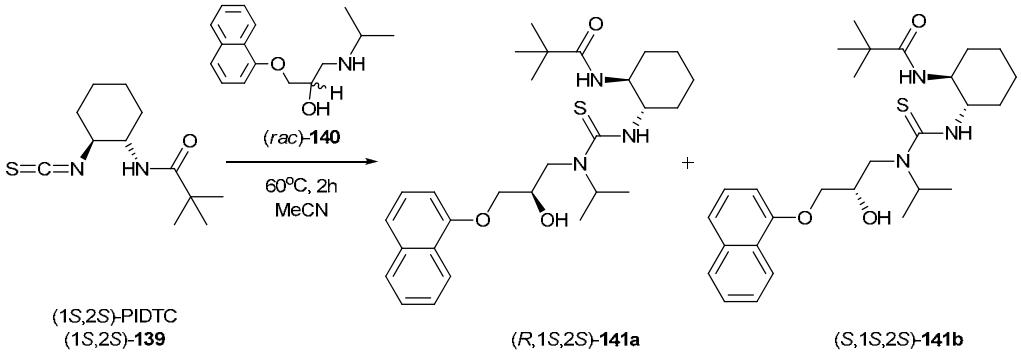
1. Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P.-W.; Connell, R. D., *J. Am. Chem. Soc.* **1989,** 111, 9243.
2. Davies, S. G.; Mortlock, A. A., *Tetrahedron* **1993,** 49, 4419.
3. Gasparrini, F.; Misiti, D.; Pierini, M.; Villani, C., *Org. Lett.* **2002,** 4, 3993.
4. Mizuno, T.; Takeuchi, M.; Shinaki, S., *Tetrahedron* **1999,** 55, 9455.
5. Rossi, S.; Kyne, G. M.; Turner, D. L.; Wells, N. J.; Kilburn, J. D., *Angew. Chem., Int. Ed.* **2002,** 41, 4233.
6. Rajamoorthi, K.; Stockton, G. W., *Spectrosc. Lett.* **2001,** 34, 255.
7. Staubach, B.; Buddrus, J., *Angew. Chem., Int. Ed.* **1996,** 35, 1344.
8. Yang, X.; Wang, G.; Zhong, C.; Wu, X.; Fu, E., *Tetrahedron-Asymmetry* **2006,** 17, 916.
9. Yoo, S.; Kim, S., *Bull. Korean Chem. Soc.* **1996,** 17, 673.
10. Alexakis, A.; Mutti, S.; Mangeney, P., *J. Org. Chem.* **1992,** 57, 1224.
11. Fulwood, R.; Parker, D., *Tetrahedron-Asymmetry* **1992,** 3, 25.
12. Hulst, R.; de Vries, N. K.; Feringa, B. L., *J. Org. Chem.* **1994,** 59, 7453.

13. Cordova, A.; Zou, W.; Dziedzic, P.; Ibrahem, I.; Reyes, E.; Xu, Y., *Chem. Eur. J.* **2006,** 12, 5383.
14. Lalonde, M. P.; Mathieu, P.; Chen, Y.; Jacobsen, E. N., *Angew. Chem., Int. Ed.* **2006,** 45, 6366.
15. Tsogoeva, S. B.; Wei, S., *Chem. Commun.* **2006**, 1451.
16. Braddock, D. C.; Hermitage, S. A.; Redmond, J. M.; White, A. J. P., *Tetrahedron-Asymmetry* **2006,** 17, 2935.
17. Braddock, D. C.; Redmond, J. M.; Hermitage, S. A.; White, A. J. P., *Adv. Synth. Catal.* **2006,** 348.
18. Guangyou, Z.; Yuquing, L.; Zhaohui, W.; Nohira, H.; Hirose, T., *Tetrahedron-Asymmetry* **2003,** 14, 3297.
19. Pikul, S.; Corey, E. J., *Org. Synth.* **1993,** 71, 22.
20. Larrow, J. F.; Jacobsen, E. N., *Org. Synth.* **1998,** 75, 1.
21. Schanz, H.-J.; Linseis, M. A.; Gilheany, D. G., *Tetrahedron-Asymmetry* **2003,** 14, 2763.
22. Whitney, T. A., *J. Org. Chem.* **1980,** 45, 4214.
23. Armstrong, D. W.; He, L.; Yu, T.; Lee, J. T.; Liu, Y., *Tetrahedron-Asymmetry* **1999,** 10, 37.
24. Kelly, A. M.; Bull, S. D.; James, T. D., *Tetrahedron-Asymmetry* **2008,** 19, (4), 489-494.
25. Irving, A. M.; Vogels, C. M.; Nikolcheva, L. G.; Edwards, J. P.; He, X.-F.; Hamilton, M. G.; Baerlocher, M. O.; Baerlocher, F. J.; Decken, A.; Westcott, S. A., *New J. Chem.* **2003,** 27, 1419.
26. Marson, C. M.; Schwarz, I., *Tetrahedron-Asymmetry* **2000,** 41, 8999.

2.4 A Novel Chiral Derivatising Agent for Determination of the Enantiomeric Excess of Chiral Amino Alcohols

2.4.1 Chiral Derivatising Agents for Amino Alcohols

There are few examples of chiral derivatisation protocols for the determination of the enantiopurity of chiral amino alcohols reported in the literature.[1] In 1997, Lindner *et al* reported the synthesis of a new chiral derivatising agent which acts as a stable, selective reagent for the indirect resolution of chiral primary and secondary amino alcohols.[2] Their reagent, (1*S*,2*S*)-*N*-((2-isothiocyanato)-cyclohexyl)-pivaloyl amide **139** ((1*S*,2*S*)-PIDTC), prepared from enantiopure cyclohexane-1,2-diamine *via* a two-step synthesis, then reacts with a pair of enantiomers of an amino alcohol to generate corresponding pairs of diastereomeric thioureas which can then be separated by non-chiral high performance liquid chromatography (HPLC) techniques (Scheme 1).

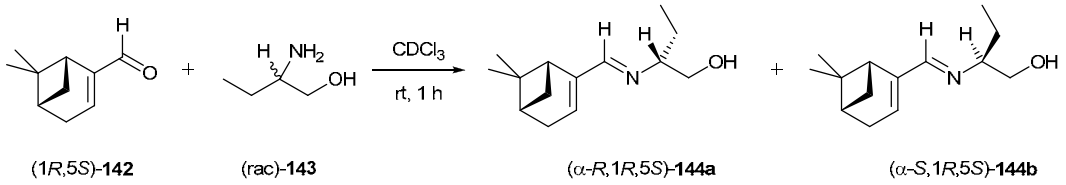


Scheme 1: Chiral derivatisation of parent amino alcohol (*rac*)-**140**.

Although this pre-column derivatisation process showed dramatic improvement on its literature precedents, and relatively good separation between the diastereomers was observed, this method still relies on HPLC analysis which is more costly, less reliable, and less readily available than NMR spectroscopic techniques.

In 2006, Galanski *et al* published work employing (-)-myrtenal **142**, a bicyclic monoterpene, as a chiral derivatising agent for β-amino alcohols.[3] This technique

allowed for determination of the enantiomeric excess of primary amines and amino alcohols using NMR techniques (Scheme 2).



(1*R*,5*S*)-**142** (rac)-**143** (α-*R*,1*R*,5*S*)-**144a** (α-*S*,1*R*,5*S*)-**144b**

Scheme 2: Derivatisation of an amino alcohol using (-)-myrtenal affords a pair of diastereomeric imines.

Whilst this technique was primarily useful for determination of the enantiopurity of chiral primary amines, the authors also reported the successful derivatisation of two amino alcohols; (*rac*)-2-aminobutanol (*rac*)-**143** and (*rac*)-2-amino-4-methyl-1-pentanol (*rac*)-**145**. ^{1}H NMR spectroscopy failed to successfully determine the enantiopurity of these amino alcohols because the resolution of the diastereomers was not sufficient to allow for accurate integration of the diastereomeric resonances. However, in the ^{13}C NMR spectrum, resolution of the diastereomers was observed with baseline separation of the resonances of between $\Delta\delta$ = 0.2 - 0.3 ppm for 2-aminobutanol and $\Delta\delta$ = 0.3 ppm for leucinol. When a racemic mixture of 2-aminobutanol **143** was employed, the relative integration of corresponding diastereomers was determined to be 48.2 : 51.8 ((*R*) : (*S*)) from the ^{13}C NMR spectrum. This fell well within the accepted error limits for determination of enantiopurity using spectroscopic techniques.

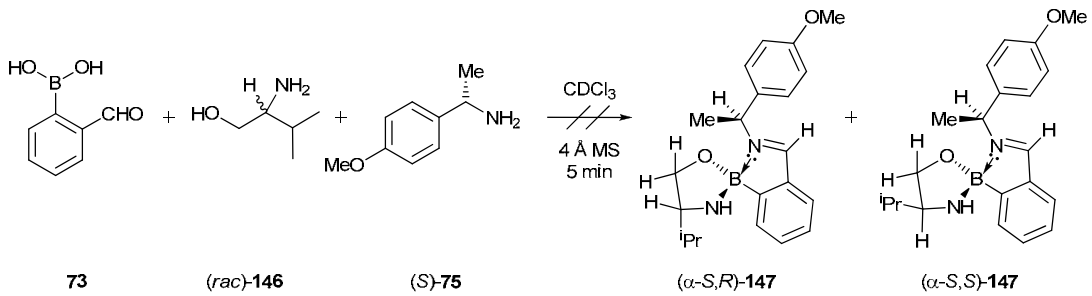
It is clear that the development of a novel chiral derivatisation protocol for determination of the enantiopurity of chiral amino alcohols would be of great use to the synthetic community. Simple extension of literature protocol for primary amines, while successfully applied in the above instances, often results in problematic cyclisation to afford partial oxazolidine side products which impedes successful integration.

2.4.2 Unsuccessful 3-Component Coupling Protocol for Formation of Oxazolidine Boronates

Having completed a successful investigation into the determination of the enantiomeric excess of synthetically useful chiral diamines 1,2-diphenylethane-1,2-diamine **124** and cyclohexane-1,2-diamine **125**, our attention then turned to expanding this protocol to consider chiral amino alcohols.

We postulated that a simple 3-component protocol involving condensation of the amino alcohol with 2-formylphenylboronic acid **73** and tandem imine formation with (*S*)-4-methoxy-α-methylbenzylamine (*S*)-**75** would afford a pair of diastereoisomeric oxazaborolidines which might exhibit resolved pairs of resonances as previously described for chiral diols (Scheme 3).

Therefore, 1.0 equivalent of 2-formylphenylboronic acid **73** was stirred with 1.0 equivalent of (*S*)-4-methoxy-α-methylbenzylamine (*S*)-**75** and 1.0 equivalent of (*rac*)-valinol (*rac*)-**146** in $CDCl_3$ in the presence of 4 Å molecular sieves for 5 minutes (Scheme 3) and its ^{1}H NMR acquired.



73 (*rac*)-**146** (*S*)-**75** (α-*S*,*R*)-**147** (α-*S*,*S*)-**147**

Scheme 3 Postulated formation of diastereoisomeric oxazaborolidine complexes.

Instead of forming the expected oxazaborolidines, the ^{1}H NMR spectrum showed complete selectivity for imine formation on the amino alcohol nitrogen with free unreacted (*S*)-4-methoxy-α-methylbenzylamine remaining in solution (Figure 1).

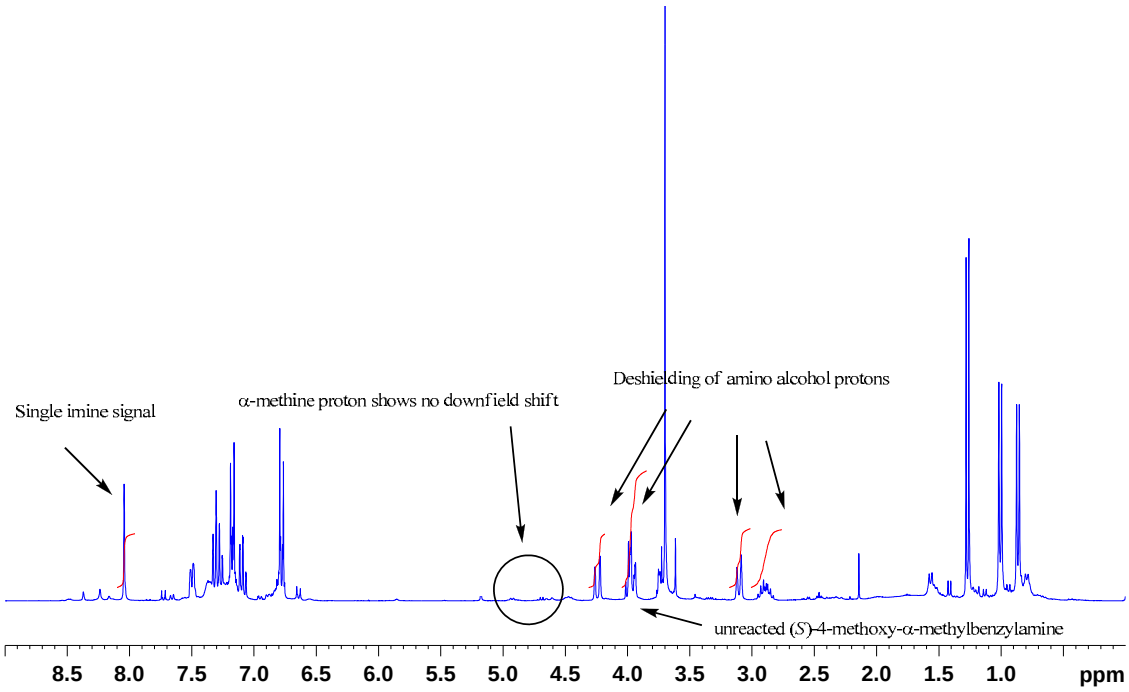


Figure 1 Selective imine formation for the stabilised aminoalcohol iminoboronic acid (300 MHz, $CDCl_3$).

We postulated that this selectivity was due to added stabilisation from an O→B interaction driving the equilibrium towards iminoboronic acid formation with the amino alcohol (Figure 2).

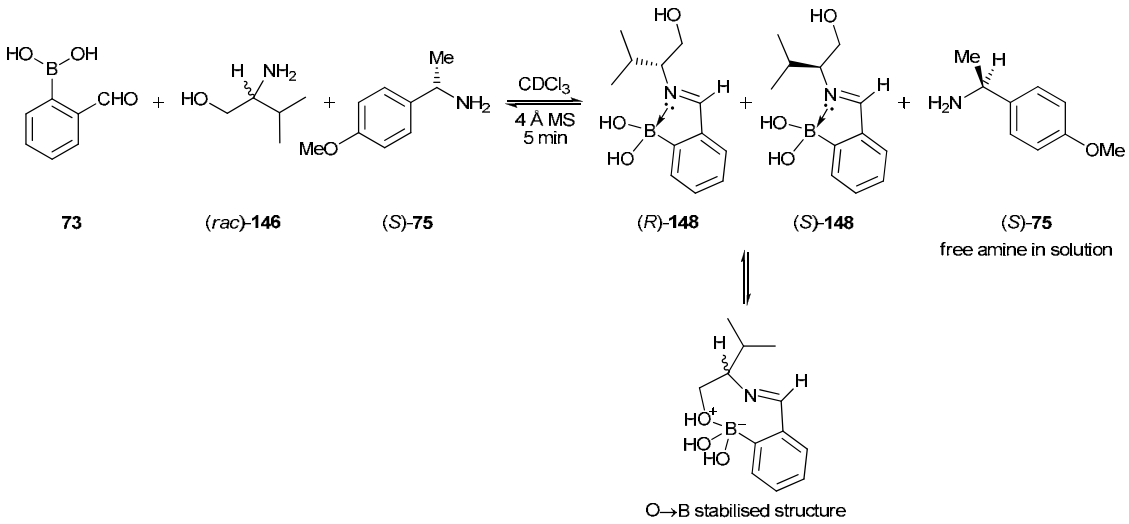
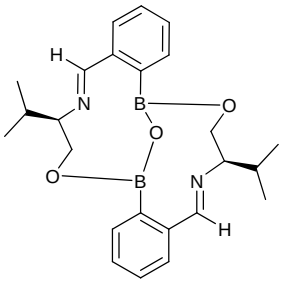


Figure 2 Cyclic iminoboronate ester formation proposed to drive selectivity in imine formation.

However, subsequent X-ray crystallographic analysis (Appendix II) revealed *in situ* formation of a highly stabilised oxygen-bridged di-boron species through dehydration of two imino alcohol boronic acid molecules (Figure 3).

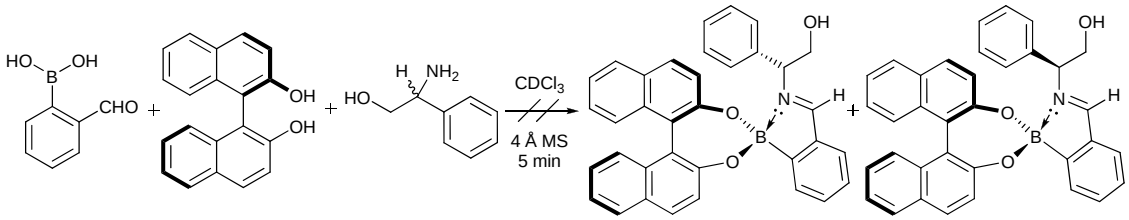


(*R*,*R*)-**149**

Figure 3 Stable oxygen-bridged di-boron species.

Having observed complete selectivity for imine formation from the amino alcohol in the presence of the competing (*S*)-4-methoxy-α-methylbenzylamine (*S*)-**75**, we decided to consider an alternative protocol similar to that used for determination of the enantiomeric excess of chiral diols. It was hoped that imine formation with a racemic amino alcohol followed by condensation of an enantiopure diol with 2-formylphenylboronic acid **73** would afford a pair of diastereomeric iminoboronate ester derivatives which would be distinguishable by ^{1}H NMR analysis.

Therefore, 1.0 equivalent of 2-formylphenylboronic acid **73** was stirred with 1.0 equivalent of (*rac*)-2-phenylglycinol (*rac*)-**150** and 1.0 equivalent of (*R*)-BINOL (*R*)-**74** in $CDCl_3$ in the presence of 4 Å molecular sieves (Scheme 4). An aliquot was removed after 5 minutes and its ^{1}H NMR spectrum acquired.



73 (*R*)-**74** (*rac*)-**150** (α-*R*,*R*)-**151** (α-*S*,*R*)-**151**

Scheme 4 Envisaged 3-component coupling protocol for determination of the *ee* of amino alcohols.

However, the resultant ^{1}H NMR spectrum showed a complicated mixture of products including resonances ascribed to the expected iminoboronate esters, along with peaks from a small amount of cyclised oxazolidine structures, presumably formed *via* a similar pathway to the imidazolidines observed previously, as well as possible oxygen-bridged di-boron species (Figure 4).

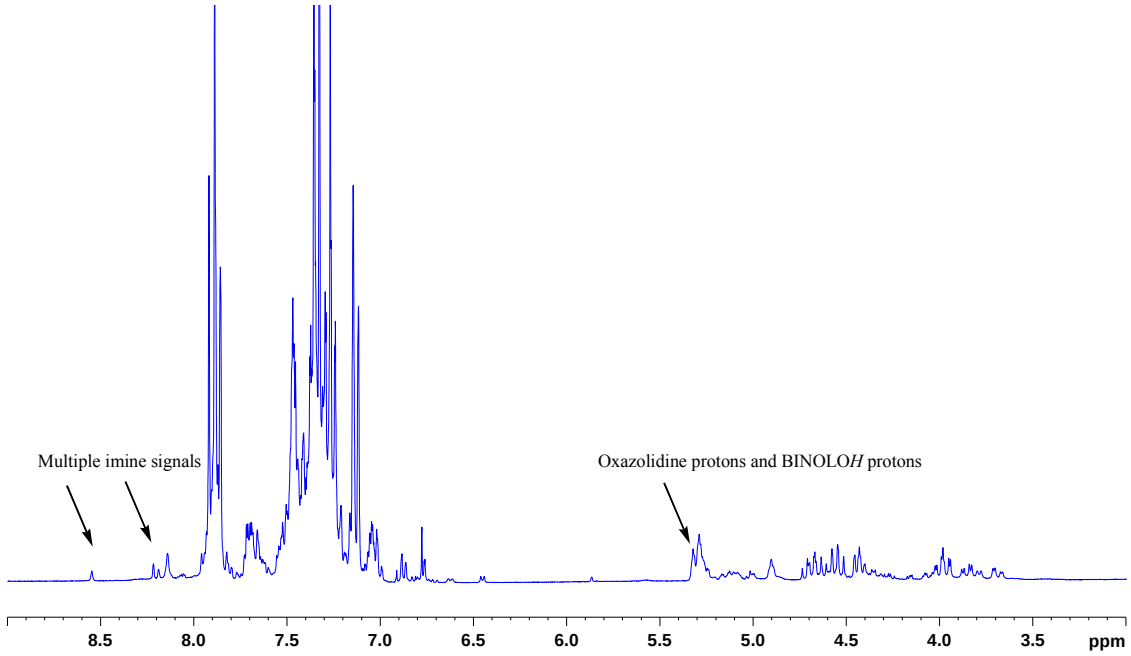


Figure 4 300 MHz ^{1}H NMR spectrum of racemic phenylglycinol (*rac*)-**150** and (*R*)-BINOL (*R*)-**74** showing multiple products.

As in our previous investigation toward determining the *ee* of chiral diamines, it appeared that a mixture of ring-open and closed forms were present with the equilibrium lying predominantly towards cyclised oxazolidine products (Figure 5).

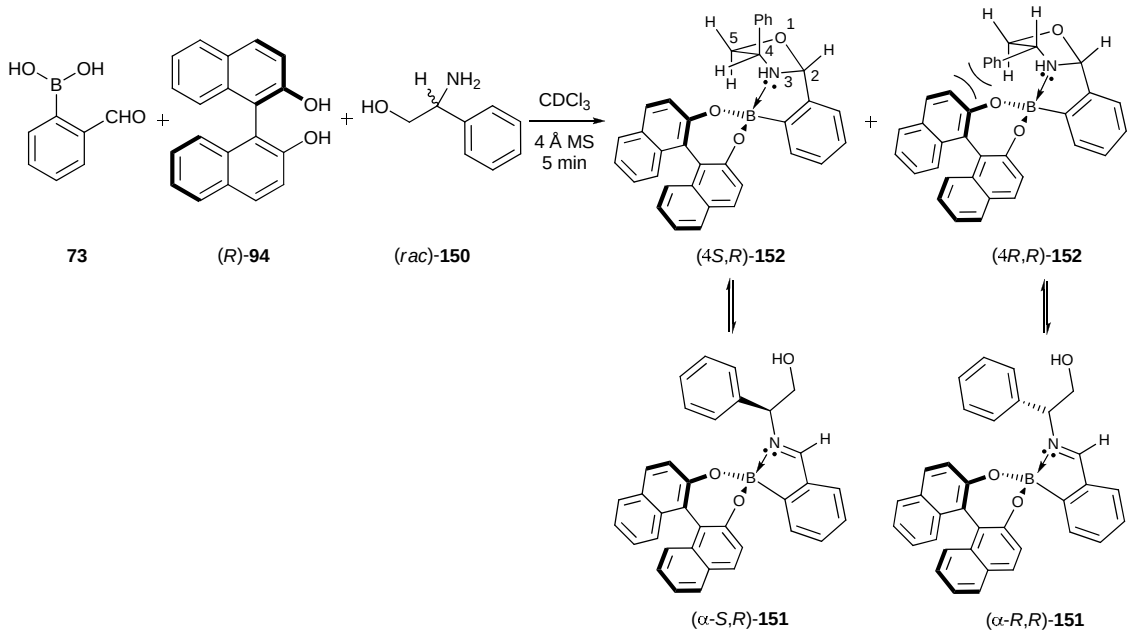


Figure 5 Incomplete ring-closure for (*R*)- and (*S*)-2-phenylglycinol **150** due to steric crowding with the BINOL rings.

Furthermore, the ratio of cyclised : ring-opened products was shown to depend on the individual diastereomer being formed, which is presumably dependant on the different degrees of steric crowding between the proximal binaphthyl rings and the α-substituents that sit axially or equatorially within the oxazolidine ring as determined by the configuration of the amino alcohol enantiomer being derivatised.

Thus, since enantiopure BINOL did not promote complete cyclisation or block it - thereby forming the desired pair of iminoboronate esters - an alternative approach was required. Worthy of note is that in this instance, unlike cyclohexane-1,2-diamine **125**, neither enantiomer of the amino alcohol when derivatised independently afforded a single diastereomer of completely cyclised oxazolidine product. We concluded that this might be due to either the lower nucleophilicity of the oxygen atom driving the cyclisation or the increased steric bulkiness of the phenyl substituent on the oxazolidine ring.

Consequently, we proceeded to derivatise a short series of chiral amino alcohols with racemic BINOL (*rac*)-**74** and 2-formylphenylboronic acid **73** to investigate whether incomplete cyclisation was independent of the amino alcohol α-substituent (Figure 6). In all cases a mixture of ring-open and closed forms were observed for both oxazolidine diastereoisomers. Therefore, it was concluded that this approach was unsuitable for determination of the enantiopurity of a chiral amino alcohol.

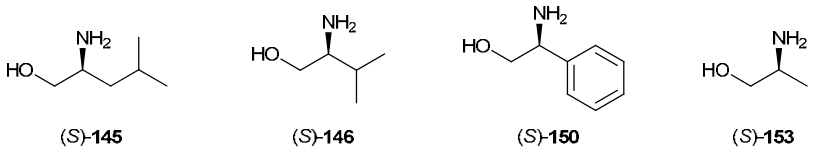
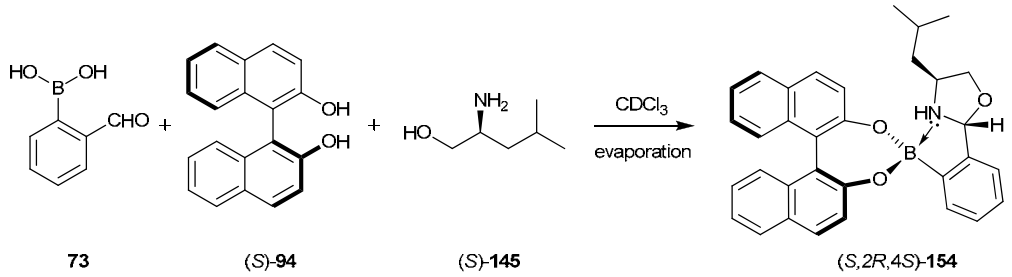


Figure 6 Short series of amino alcohols screened with 2-formylphenylboronic acid **73** and (*rac*)-BINOL (*rac*)-**74**.

Fortuitously, during the derivatisation of (*S*)-leucinol (*S*)-**145** (Scheme 5), selective crystallisation of oxazolidine boronate ester (*S*,2*R*,4*S*)-**154** from the crude mixture afforded crystals suitable for X-ray crystallographic analysis.



73 (*S*)-**94** (*S*)-**145** (*S*,2*R*,4*S*)-**154**

Scheme 5 Crystallisation of (*S*,2*R*,4*S*)-**154** confirmed oxazolidine formation.

The resultant structure confirmed the presence of an oxazolidine ring, with an intramolecular N→B interaction that had presumably assisted *O*-nucleophilic attack onto an imine intermediate, thus facilitating cyclisation (Figure 7).

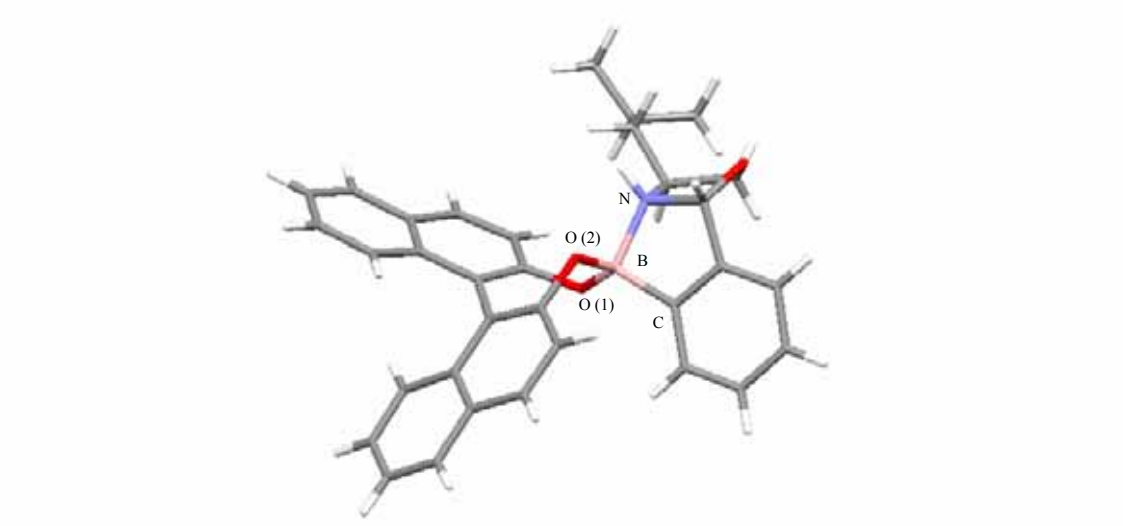


Figure 7 X-ray structure of oxazolidine (*S*,2*R*,4*S*)-**154**.

The X-ray structure confirmed that the boron atom adopts the expected sp^3 geometry, consistent with ^{11}B NMR spectroscopic data which showed a broad singlet at δ 11.6. This indicates some N→B dative interaction in solution. The tetrahedral bond character of the boron centre was calculated from the crystallography data allowing for comparison of the strength of the N→B interaction with the solution phase ^{11}B NMR data. The tetrahedral bond character of an N→Boron centre can be calculated from structural data using two different formulae, both of which use values of bond angles around the boron atom from the diffraction data (Table 1).

Table 1 Bond angles and bond lengths for (*S*,2*R*,4*S*)-**154**.

Bond	Bond Length / Å	Bonds A-B-C	Angle / °
B – N	1.665	O(1) – B – O(2)	112.99
B – O (1)	1.448	O(1) – B – C	115.30
B – O (2)	1.471	O(2) – B – C	113.87
B – C	1.586	O(1) – B – N	112.90
		O(2) – B – N	101.44
		C – B – N	98.55

The most recent approach is that reported by Höpfl who expanded on earlier work by Ōki and co-workers which considered the three bond angles between the boron atom and its covalently-bonded neighbours to considering all six bond angles including those arising from the N→B coordination.[4, 5]

$$THC_{OKI}[\%] = \frac{\sum_{n=1-3}(120 - \theta_n)}{31.5^o} \times 100$$

Equation 1 THC equation as reported by Ōki *et al*.

$$THC_{DA}[\%] = \left[1 - \frac{\sum_{n=1-6}|109.5 - \theta_n|^o}{90^o}\right] \times 100$$

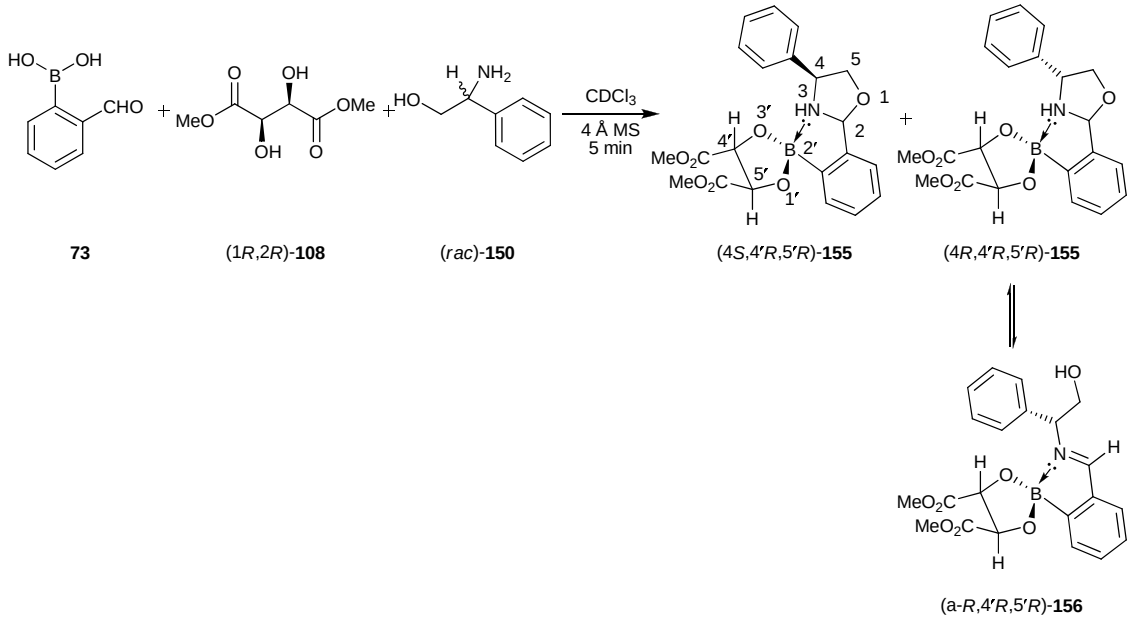
Equation 2 Donor – Acceptor equation for determination of Tetrahedral Bond Character.

Using the methods reported by Ōki and Höpfl, the tetrahedral bond character of the boron atom in (*S*,2*R*,4*S*)-**154** was determined to be 57% and 98% respectively. Both values indicate a strong interaction between the Lewis basic nitrogen atom and the Lewis acidic boron atom. In 2001, Wiskur *et al.* proposed that when a boron atom was in an sp^2 trigonal planar environment, the ^{11}B NMR shift would be approximately 30 ppm and when in a tetrahedral sp^3 environment, the resonance would be closer to 0 ppm.[6] If we compare our two tetrahedral bond character results, the ^{11}B NMR shift and the report by Wiskur, the 57% sp^3 character calculated for THC_{OKI} would agree closer with the ^{11}B NMR data in this case. Therefore, it would appear that the equation

reported by Ōki *et al.* provides a more accurate representation of the strength of our N→B interaction.

Since BINOL had proven unsuccessful, our attention turned to tuning the diol used derivatisation, as previously attempted in our diamine work, to try and confer complete cyclisation whilst retaining diastereoselectivity at the newly generated chiral centre. Dimethyl-L-tartrate **108** was selected as our chiral diol unit again since it is much less sterically demanding than BINOL and its individual enantiomers are both commercially available.

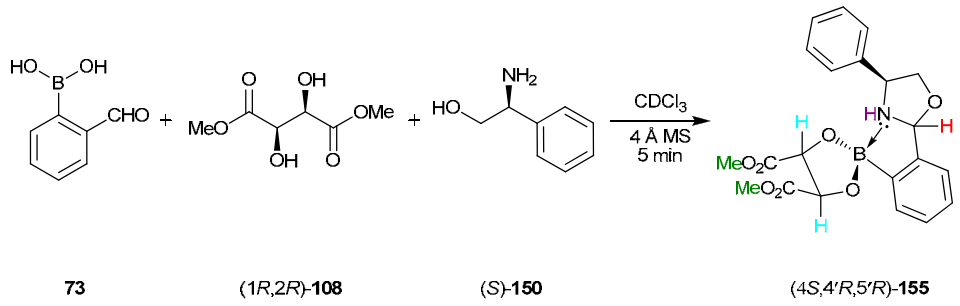
Therefore, 1.0 equivalent of dimethyl-L-tartrate (1*R*,2*R*)-**108** was stirred with 1.0 equivalent of 2-formylphenylboronic acid **73** and 1.0 equivalent of (*rac*)-2-phenylglycinol (*rac*)-**151** in $CDCl_3$ in the presence of 4 Å molecular sieves (Scheme 6) with an aliquot being removed after 5 minutes and its ^{1}H NMR spectrum acquired.



Scheme 6 Incomplete cyclisation of a single diastereomer with dimethyl-L-tartrate **108**.

Once again, a mixture of multiple diastereoisomeric products was observed, with signals corresponding to two oxazolidine boronates ((4*S*,4′*R*,5′*R*)-**155** and (4*R*,4′*R*,5′*R*)-**155**) along with a set of resonances corresponding to a single diastereomer of un-cyclised imine (α-*R*,4′*R*,5′*R*)-**156**. Although some resolution was observed between the two oxazolidines, significant broadening of the resonances of the tartrate moiety

impeded their integration. Therefore, it appeared that while one diastereomer showed complete cyclisation to the ring-closed oxazolidine (Scheme 7), the other was in equilibrium with its open-chain, uncyclised form with the equilibrium lying toward the oxazolidine product.



73 (1*R*,2*R*)-**108** (*S*)-**150** (4*S*,4′*R*,5′*R*)-**155**

Scheme 7 Quantitative oxazolidine formation using (*S*)-2-phenylglycinol (*S*)-**176**.

Variable temperature studies were performed on diastereomerically pure (4*S*,4′*R*,5′*R*)-**155** since its ^{1}H NMR spectrum at 298 K showed significant broadening of the resonances corresponding to the dimethyl singlets and the two C*H*(OB) protons (Figure 8). We postulated that the broadening of the diol protons was due to rapid rotation about the C-B bond at 298 K. ^{11}B NMR spectroscopic analysis showed a broad signal at δ 14.3 ppm which is in accordance with the partial sp^{3} character (unbind-rotate-bind N→B interaction) expected for a rapidly rotating C-B bond.

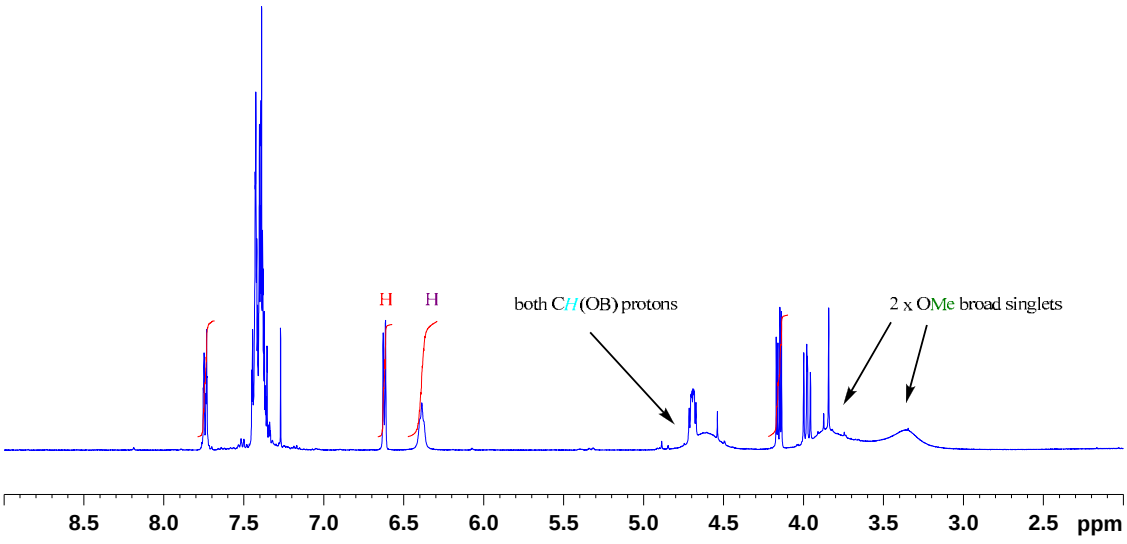


Figure 8 Room temperature ^{1}H NMR spectrum of (4*S*,4′*R*,5′*R*)-**155** showing signal broadening of the protons on the boronate ester ring and both CO_2Me resonances (400 MHz, $CDCl_3$).

The temperature was raised stepwise to 368 K (sample temperature after calibration, all high temperature spectra were run in toluene-d_8) and some sharpening of the signals was observed (Figure 9).

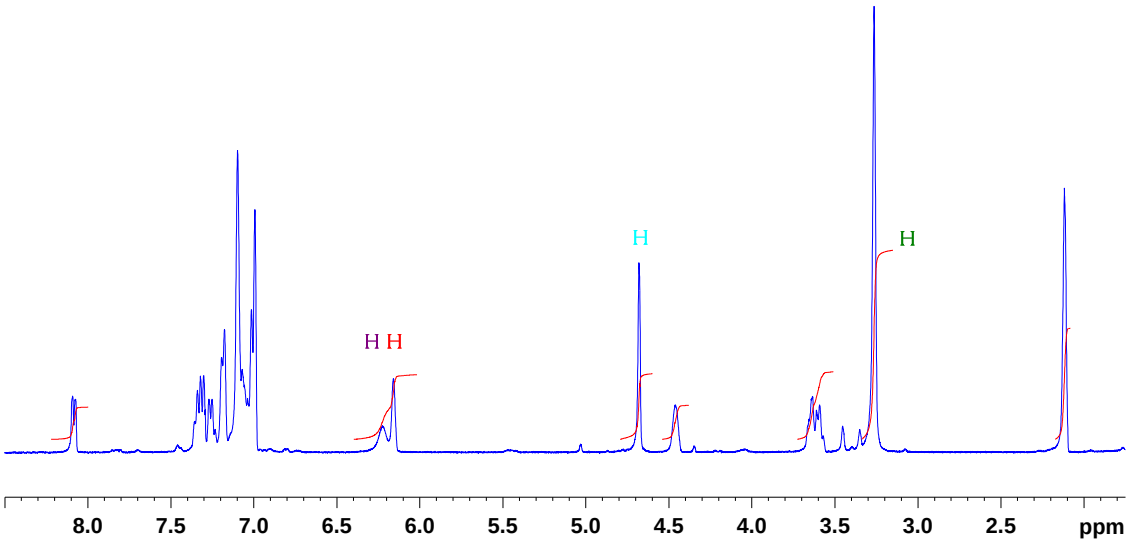


Figure 9 ^{1}H NMR spectrum of (4*S*,4′*R*,5′*R*)-**155** at 368 K (400 MHz, toluene-d_8).

The two methoxy CH_3 resonances coalesced to a single 6H singlet (δ 3.24 ppm), as did the two C*H*(OB) protons (δ 4.68 ppm). The two oxazolidine CH_AH_B ring protons were found as a 2H multiplet (δ 3.68 - 3.52 ppm) and significant deshielding was observed of an aromatic proton (δ 8.08 ppm).

Signal sharpening extended only to the broad signals of the diol protons with all resonances showing a loss of fine coupling. Despite this, sufficient sharpening of the spectrum confirmed the formation of a single diastereomer, crucial if accurate determination of enantiopurity is required.

The temperature was also lowered stepwise to 250 K (sample temperature after calibration, all low temperature spectra were run in $CDCl_3$). Again, sharpening of the peaks was observed, this time with retention of some fine coupling of certain signals (Figure 10).

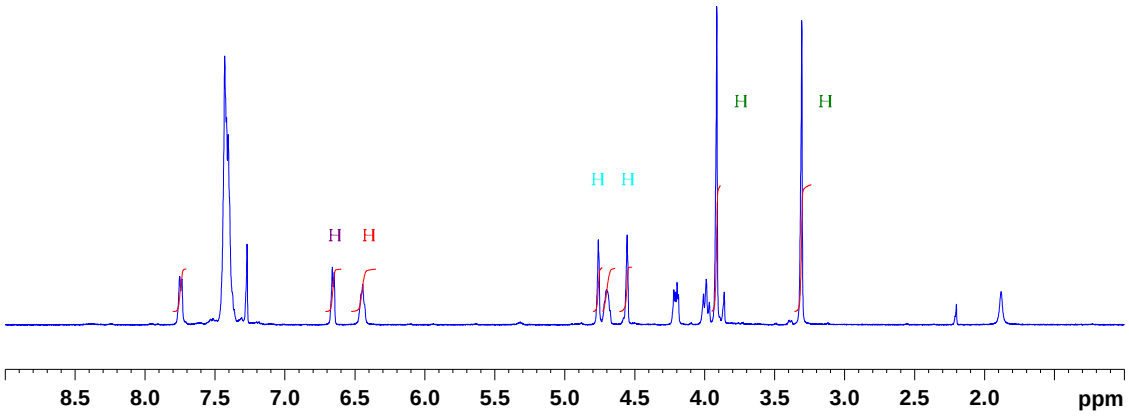
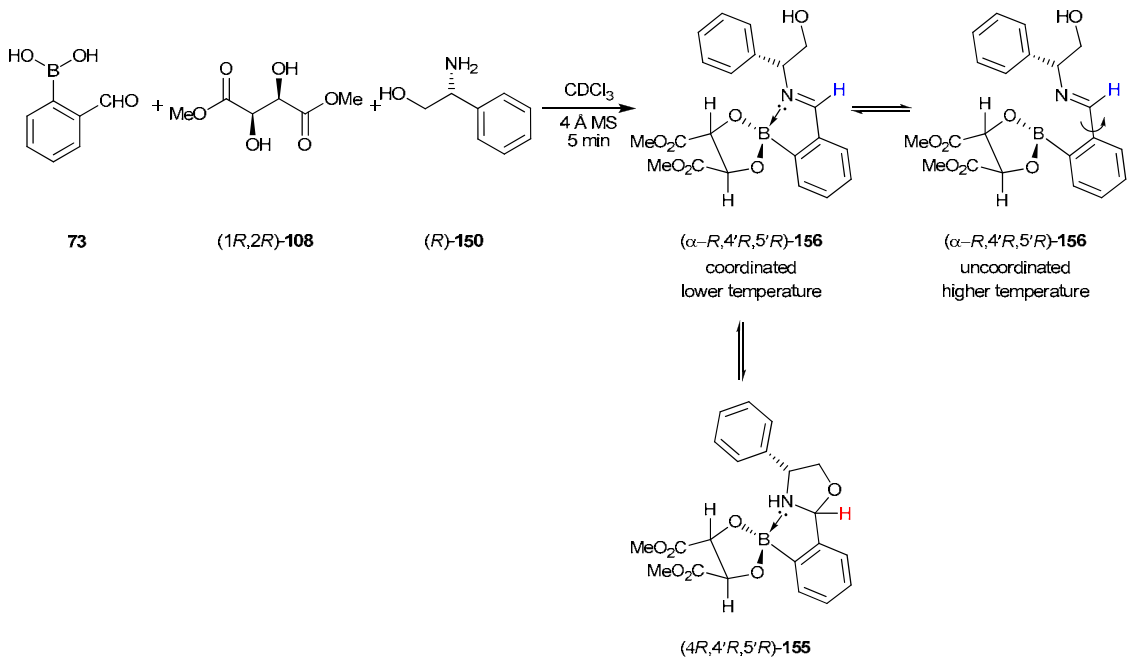


Figure 10 250 K ^{1}H NMR spectrum showing well resolved pairs of CO_2Me and C*H*OB signals (400 MHz, $CDCl_3$).

At lower temperatures, we see discrimination of the individual CO_2CH_3 singlets (δ 3.82 and 3.20 ppm) with significant splitting (Δδ = 0.62 ppm) between the two. The two C*H*(OB) protons also appear as sharp singlets (δ 4.68 and 4.45 ppm), Δδ = 0.23 ppm.

^{11}B NMR showed a small upfield shift to δ 11.5 ppm (from 13.5 ppm), slightly more shielded than at 298 K, inferring a more sp^3 environment at the boron centre. This proved particularly interesting since varying the sample temperature allowed rotation about the C-B bond to be controlled such that both freely rotating and locked structures could be observed by ^{1}H NMR spectroscopy.

We thought that if (4*S*,4′*R*,5′*R*)-**155** showed less facile dissociation of the N→B bond at lower temperatures, it should also be the case for the problematic (4*R*,4′*R*,5′*R*)-**155** diastereoisomer. The imine carbon might then be more electrophilic at lower temperature favouring cyclisation to afford its oxazolidine ring. Therefore, diastereoisomer (4*R*,4′*R*,5′*R*)-**155** was prepared from 1.0 equivalent of (*S*)-2-phenylglycinol (*S*)-**150**, 2-formylphenylboronic acid **73** and dimethyl-L-tartrate (1*R*,2*R*)-**108** which were stirred in $CDCl_3$ in the presence of 4 Å molecular sieves for 5 minutes (Scheme 8) before a ^{1}H NMR spectrum of the crude product was recorded.



Scheme 8 Equilibrium between oxazolidine and iminoboronate ester forms of (4*R*,4′*R*,5′*R*)-**155**.

As in the racemate, resonances corresponding to both oxazolidine and imine products were observed in the ^{1}H NMR spectrum (Figure 11). By comparing the relative integrals of the oxazolidine (δ 6.50 ppm) and imine protons (δ 8.43 ppm), we found that the equilibrium lay slightly towards the cyclised oxazolidine, the two found in a 1 : 0.90 ratio.

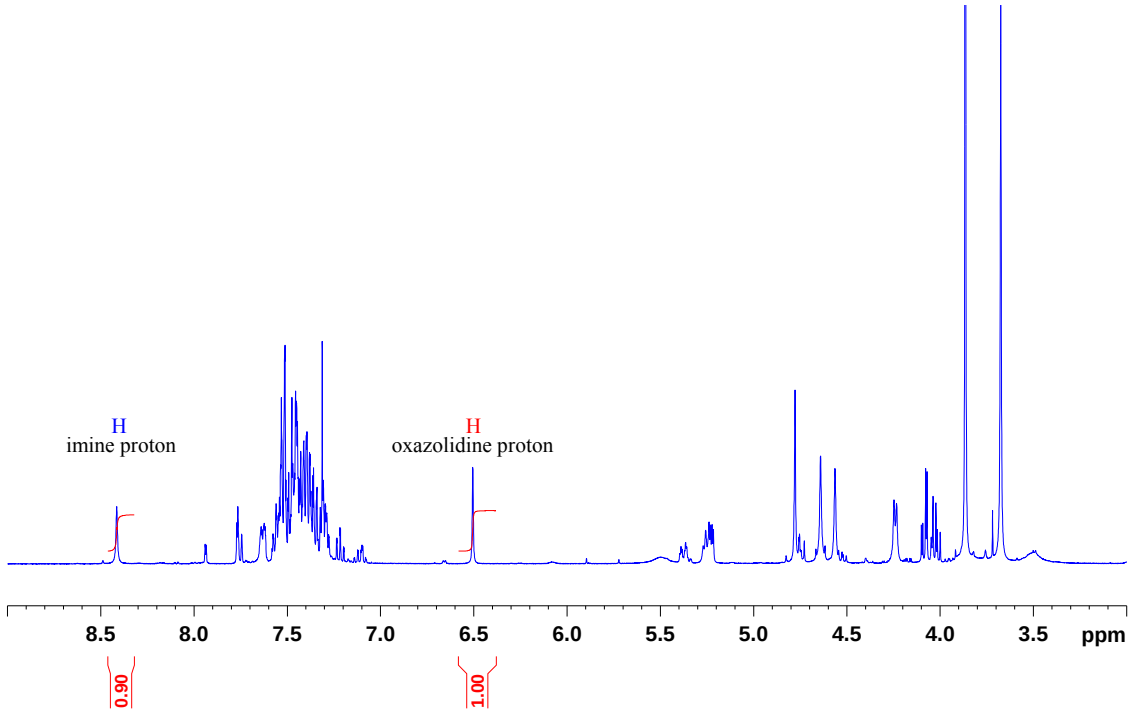


Figure 11 298 K ^{1}H NMR spectrum of (*4R*,4′*R*,5′*R*)-**155** showing both imine and oxazolidine products (400 MHz, $CDCl_3$).

The temperature was then lowered stepwise to 250 K (sample temperature after calibration) to look for a change in the ratio of the two competing structures (Figure 12). Interestingly, as the temperature was lowered a change in the ratio of the two products was observed, with the equilibrium shifting towards the ring-closed oxazolidine. However, the equilibrium did not shift completely to the oxazolidine product, with a 1 : 0.61 ratio the best ratio observed at 250 K (Figure 12).

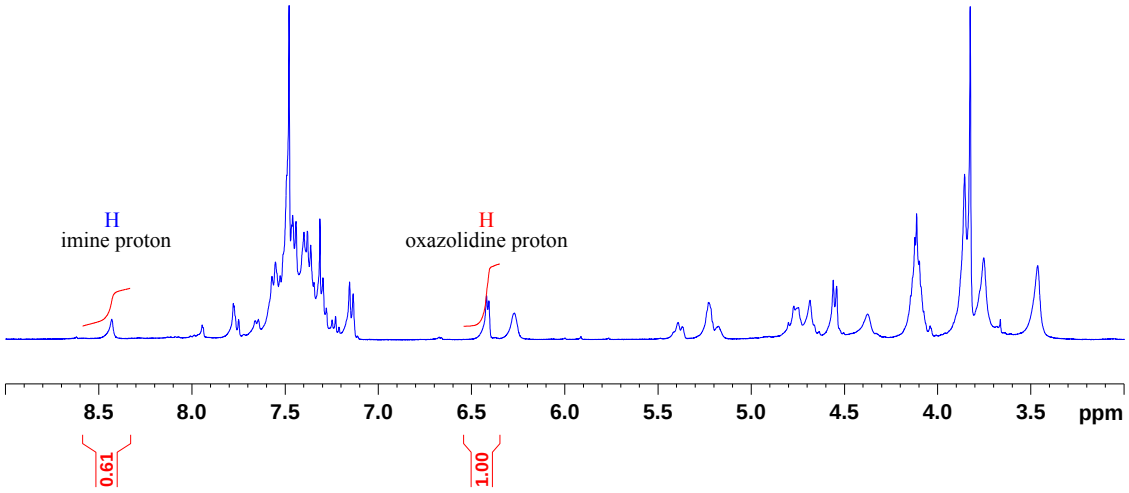


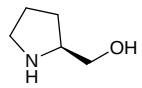
Figure 12 250 K ^{1}H NMR of (4*R*,4′*R*,5′*R*)-**155** (400 MHz, $CDCl_3$).

Following all variable temperature analysis, the NMR samples were re-analysed at room temperature and showed the same broad signals for (4*S*,4′*R*,5′*R*)-**155** and the same ratio of oxazolidine : imine for (4*R*,4′*R*,5′*R*)-**155**.

Despite (4*S*,4′*R*,5′*R*)-**155** showing successful cyclisation and complete stereocontrol at its new stereogenic centre, the incomplete ring-closure seen for (4*R*,4′*R*,5′*R*)-**155** clearly demonstrated that dimethyl-tartrate **108** was not a suitable diol for determining the *ee* of amino alcohols using this protocol.

Following the previous successful use of hydrobenzoin **112** for determining the *ee* of chiral diamines, we screened a range of the chiral diols from our previous investigation to look for a diol that promotes stereoselective cyclisation in both diastereomeric oxazolidine products. We decided to use secondary amino alcohol 2-pyrrolidinemethanol **157** since it would result in formation of an iminium ion which would be highly susceptible to nucleophilic attack (Figure 13). This should ensure

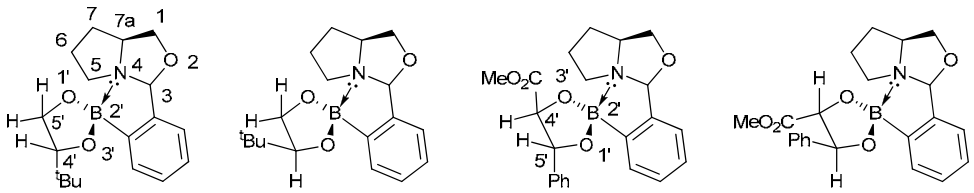
complete oxazolidine formation allowing us to assess the facial selectivity afforded by the diol.



(*S*)-**157**

Figure 13 Secondary amino alcohol used to screen diols for stereoselective oxazolidine formation.

Therefore, 1.0 equivalent of (*S*)-(+)-2-pyrrolidinemethanol (*S*)-**157** was stirred with 1.0 equivalent of a racemic diol and 1.0 equivalent of 2-formylphenylboronic acid **73** in $CDCl_3$ for 5 minutes in the presence of 4 Å molecular sieves before an aliquot was removed and their ^{1}H NMR spectra acquired. Two diols ((*rac*)-3,3-dimethyl-1,2-butane diol (*rac*)-**105** and (*rac*)-methyl-2,3-dihydroxy-3-phenylpropionate (*rac*)-**106**) showed quantitative cyclisation to afford pairs of oxazolidine diastereomers (Figure 14) with sufficient stereocontrol for a 1 : 1 mixture of diastereoisomers to be observed *via* integration of oxazolidine ring protons in their ^{1}H NMR spectra.



(4'*R*,7a*S*)-**158a** (4'*S*,7a*S*)-**158b** (4'*S*,5'*R*,7a*S*)-**159a** (4'*R*,5'*S*,7a*S*)-**159b**

Figure 14 Successful formation of two pairs of oxazolidine diastereoisomers in 1 : 1 ratios.

Disappointingly, when these diols were screened with chiral amino alcohols, neither showed complete stereoselectivity at the new oxazolidine centre for both diastereoisomers.

2.4.3 Alternative *O*-Protection Strategy for Determination of Enantiomeric Excess of Amino Alcohols

Having been unable to find a suitable protocol for formation of a pair of diastereoisomeric oxazolidine boronate esters from the parent chiral amino alcohol, we decided to pursue a protection - derivatisation strategy similar to that employed with demanding chiral diamines described previously.

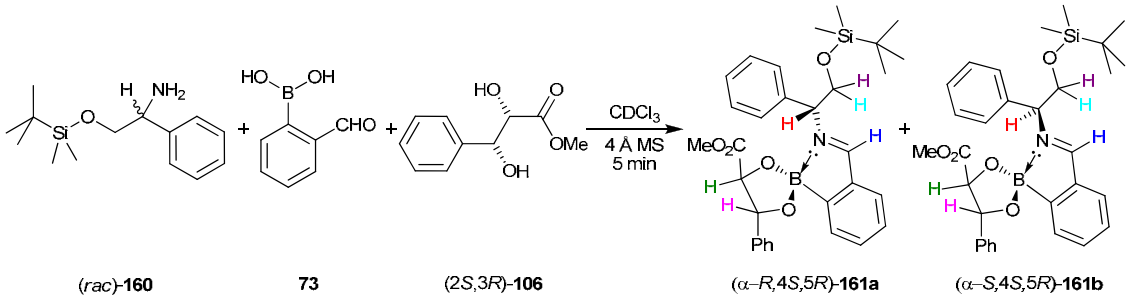
Therefore, we proposed a facile silyl protection strategy for the amino alcohol oxygen moiety which would remove the nucleophilicity of the oxygen and block any cyclisation onto the imine (Scheme 9).

(*rac*)-**150** (*rac*)-**160**

Scheme 9 *O*-protection strategy to impede oxazolidine formation.

Protection of the oxygen functionality of racemic phenylglycinol proceeded cleanly to afford a quantitative yield of *O*-silyl protected alcohol (*rac*)-**160**.

Following the protection of (*rac*)-2-phenylglycinol (*rac*)-**150** as its TBDMS ether, work within the group by Miss Magdalena Powell proceeded to employ the 3-component protocol described previously for the determination of the *ee* of chiral diols to form a pair of diastereomeric iminoboronate esters who are spectroscopically distinct using ^{1}H NMR analysis.[7] She has shown that methyl-2,3-dihydroxy-3-phenylpropionate **106** afforded the greatest resolution of diastereomers (Scheme 10).



Scheme 10 Formation of diastereoisomeric iminoboronate esters from parent *O*-protected (*rac*)-**160**.

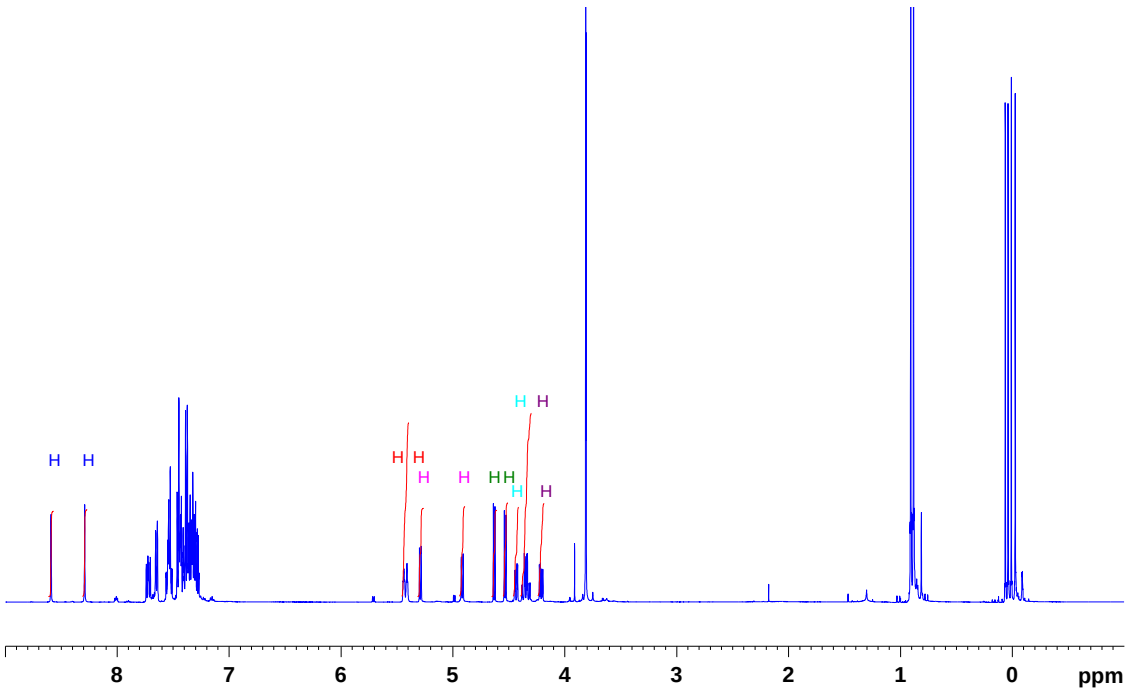


Figure 15 Resolution of 6 sets of signals of (α-*R*,4*S*,5*R*)-**161a** and (α-*S*,4*S*,5*R*)-**161b** (500 MHz, $CDCl_3$).

The ^{1}H NMR spectrum showed successful formation of a pair of diastereomerically independent iminoboronate esters with no signals corresponding to any oxazolidine product. Therefore, it appears that imine formation proceeds quantitatively, followed swiftly by N→B assisted diol condensation as expected. Importantly, no kinetic resolution was observed, confirmed by the relative integrals for the two diastereoisomers being in a 1 : 1 equimolar ratio. A pair of baseline-resolved imine singlets were observed (δ 8.27 and 8.57, Δδ = -0.30 ppm) as well as two distinct resonances for the α-*N* proton (Δδ = 0.05 ppm) and the two protons on the boronate ring (C*H*(Ph)OB and *CH*(CO_2Me)OB *Δδ* = 0.37 ppm and Δδ = 0.10 ppm respectively), all of which may be used to determine the *ee* of the parent amino alcohol (Figure 15).

Further work by Miss Magdalena Powell has used this as a basis for the determination of the enantiomeric excess of a wide range of *O*-silyl amino alcohols (Figure 16).[7]

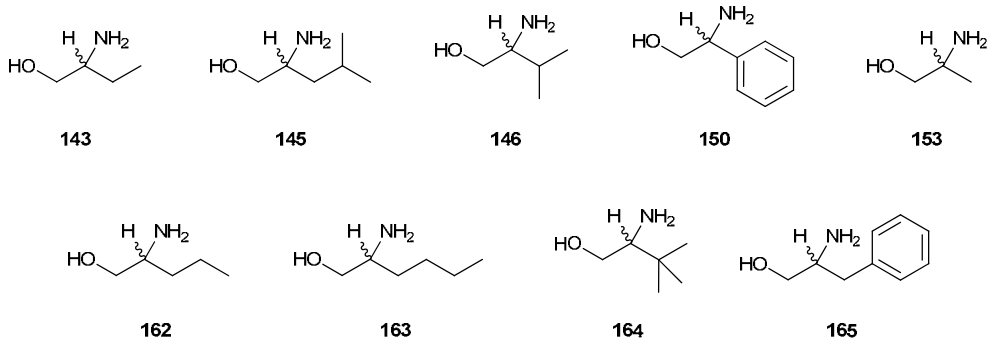


Figure 16 Series of chiral amino alcohols used to test the derivatisation protocol.

^{1}H NMR spectroscopy revealed that in every case a pair of diastereomeric iminoboronate esters were formed in a 1 : 1 ratio. Baseline resolution was achieved for up to six separate resonances and a chemical shift difference was obtained for at least one set of protons independent of the *O*-silyl amino alcohol under investigation. In all cases, splitting of the imine signal was observed in a region of the ^{1}H NMR spectrum that was free of any other resonances.

We have therefore developed a series of expeditious protocols for the determination of the enantiomeric excess of a wide range of chiral compounds bearing primary amine, diol, diamine or amino alcohol functionalities. These procedures involve the condensation of 2-formylphenylboronic acid, a chiral diol and either a primary amine or diamine. This affords a pair of diastereoisomeric iminoboronate esters or imidazolidine boronate esters whose protons show sufficient baseline resolution in their ^{1}H NMR spectrum for accurate determination of their enantiomeric excess to be performed.

2.5 Synthesis and Application of Novel Chiral Oxygen-bridged Di-boron Complexes

2.5.1 Selective Imine-formation for Amino Alcohols over Primary Amines

During our previous investigation towards the development of a protocol for the determination of the enantiomeric excess of chiral amino alcohols, we observed complete selectivity towards imine formation from the amino alcohol amine moiety, while the chiral amine remained unreacted in solution (Figure 2). At the time, it was proposed that this selectivity arose from intramolecular zwitterion formation arising from coordination of the amino alcohol hydroxyl group with the boron centre.

Crystals suitable for x-ray analysis were obtained after evaporation from $CHCl_3$. X-ray data revealed the formation of a di-boron species linked by a bridging oxygen atom (Figure 17).

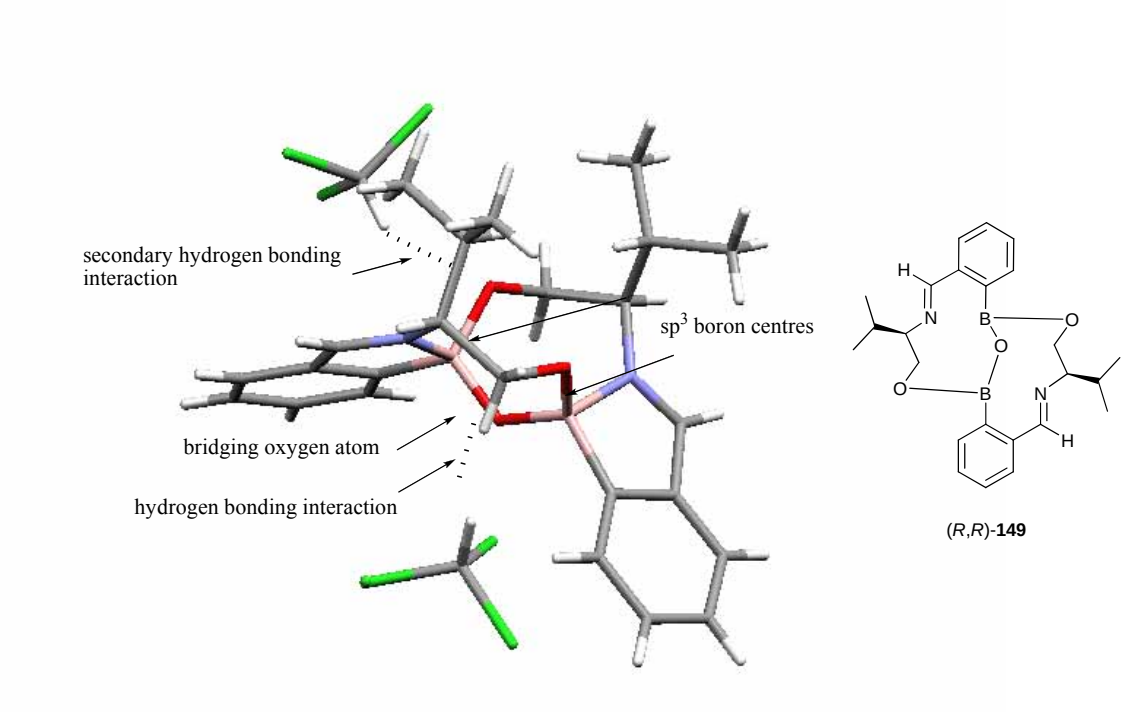


Figure 17 Oxygen-bridged di-boron 'bowl' structure observed by X-ray crystallography.

The structure obtained by X-ray diffraction showed several interesting points. Firstly, the 'bowl' structure is formed by apparent condensation of two imino boronic acid molecules with loss of three equivalents of water to leave an oxygen bridge.

Secondly, both boron atoms adopt an sp^3 geometry in the crystalline state. ^{11}B NMR spectroscopic data showed a broad singlet at δ 10.70, comparable to the ^{11}B NMR data for the sp^3 iminoboronate esters reported previously and indicates some N→B dative interaction in solution. Applying the two tetrahedral bond character formulae for determination of the degree of sp^3 character at the two boron centres shows a strong N→B interaction in both instances.

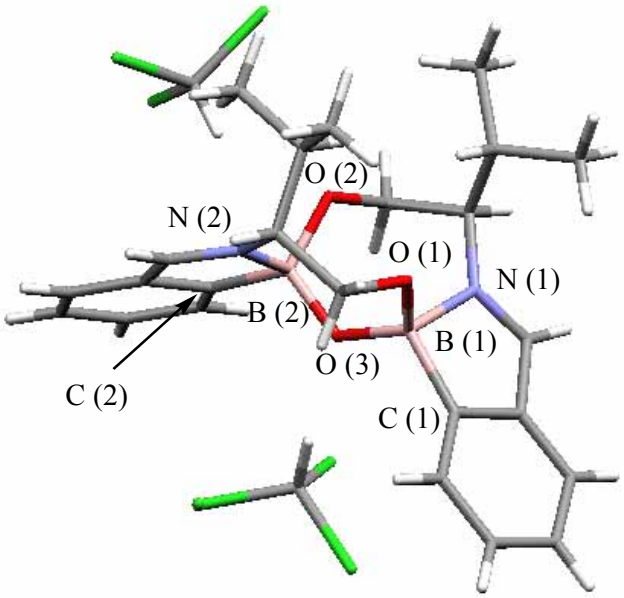


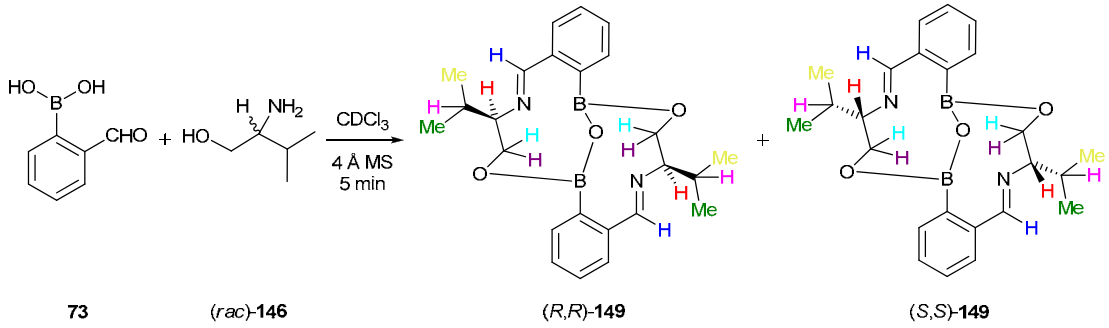
Figure 18 Atom labelling for determination of tetrahedral bond character of 'bowl' species.

Table 2 Bond angles and bond lengths

Bond	Bond Length / Å	Bonds A-B-C	Angle / °
B (1) – N (1)	1.684	O (1) – B (1) – O (3)	116.00
B (1) – O (1)	1.454	O (1) – B (1) – C (1)	115.72
B (1) – O (3)	1.425	O (3) – B (1) – C (1)	113.44
B (1) – C (1)	1.629	O (1) – B (1) – N (1)	106.58
		O (3) – B (1) – N (1)	106.95
		C (1) – B (1) – N (1)	95.28

Bond	Bond Length / Å	Bonds A-B-C	Angle / °
B (2) – N (2)	1.658	O (2) – B (2) – O (3)	115.94
B (2) – O (2)	1.463	O (2) – B (2) – C (2)	114.60
B (2) – O (3)	1.427	O (3) – B (2) – C (2)	113.28
B (2) – C (2)	1.627	O (2) – B (2) – N (2)	104.57
		O (3) – B (2) – N (2)	109.42
		C (2) – B (2) – N (2)	96.69

Using the formulae proposed by Ōki, the two boron centres have tetrahedral bond characters of 47% and 51%, while application of the donor – acceptor formulae proposed by Höpfl suggests a stronger tetrahedral character of 97% in both cases. Comparison with ^{11}B NMR spectroscopic data (δ 10.70 ppm) again suggests that the equation reported by Ōki provides a more accurate assessment of the tetrahedral bond character of the boron centres in these structures. We can now consider the ^{1}H NMR data again in light of the X-ray diffraction information.



Scheme 11 Formation of a di-boron oxygen bridged bowl structure.

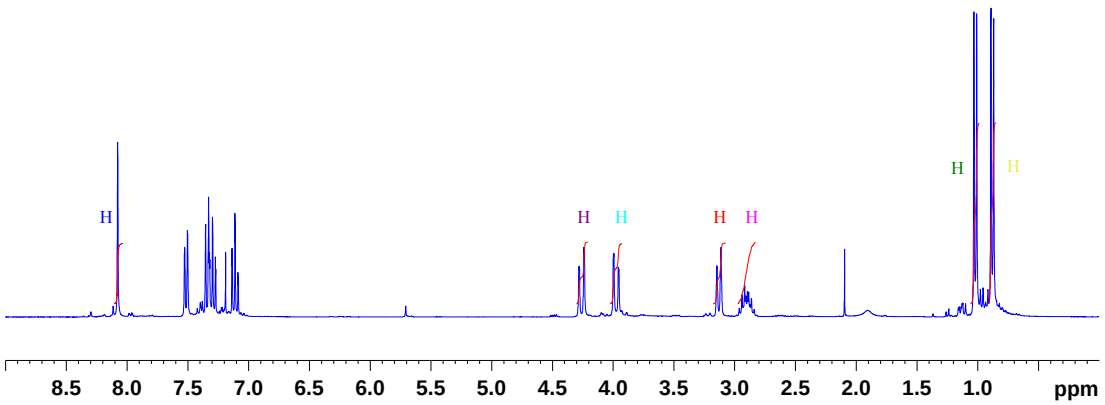


Figure 19 300 MHz ^{1}H NMR data showing clean formation of (*R*,*R*)-**149** and (*S*,*S*)-**149**.

A single set of signals is observed in the ^{1}H NMR spectrum of (*R*,*R*)-**149** and (*S*,*S*)-**149** which we can now rationalise as being due to the axis of symmetry in the 'bowl' structure rendering the two imine signals, for example, identical. Furthermore, to substantiate the proposal that the 'bowl' structures remain un-dissociated in solution, the apparent total selectivity of this imine formation, over the competing formation with (*S*)-(-)-4-methoxy-α-methylbenzylamine indicates that formation of these molecules are non-reversible under these conditions, thus pulling any equilibrium between iminoboronic acids towards this structure.

The extended structure of the 'bowl' molecule shows hydrogen bonding between two hydroxyl groups on the molecule and chloroform-hydrogen atoms in the solvent (Figure 20).

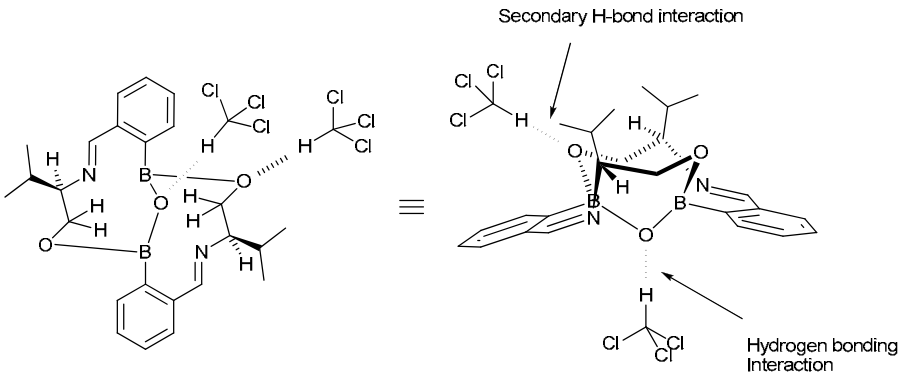


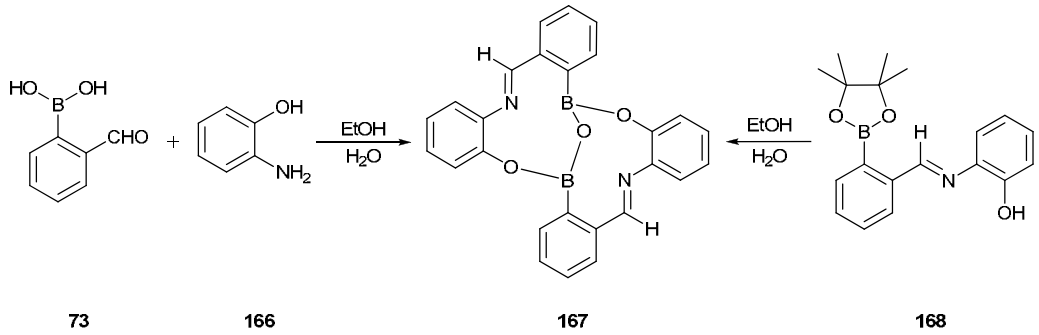
Figure 20 Two molecules of $CHCl_3$ hydrogen bonded to the 'bowl' structure (*R*,*R*)-**149**.

We then proceeded to synthesise a range of these di-boron oxygen bridged structures with a variety of chiral amino alcohols to investigate the general applicability of this procedure.

2.5.2 Synthesis of a Range of Oxygen-Bridged Complexes

A recent publication by Norman *et al.* reported the synthesis of several achiral iminoboronic acid structures as novel Schiff bases.[8] They reported the generation of an oxygen-bridged structure of the type described above using the parent amino alcohol 2-

aminophenol **166** and either the pinacol protected, or unprotected, 2-formylphenylboronic acid (Scheme 12).



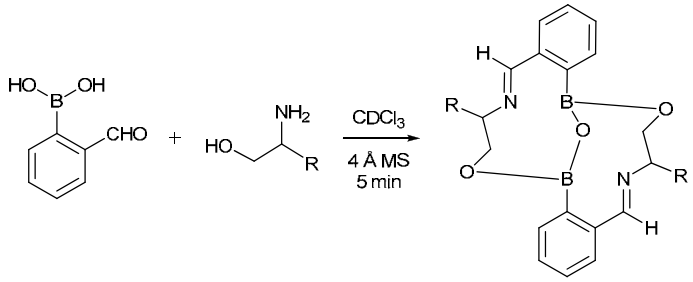
73 166 167 168

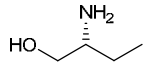
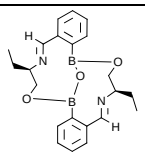
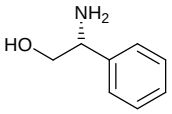
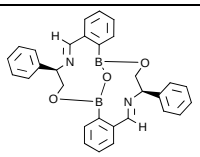
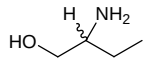
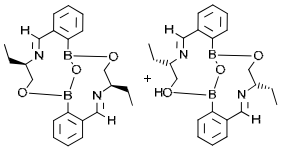
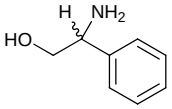
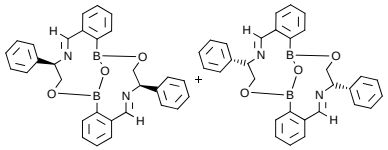
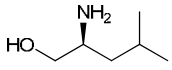
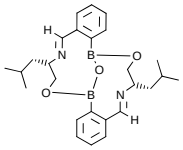
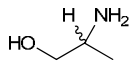
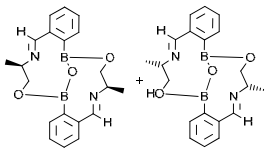
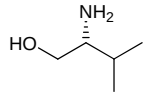
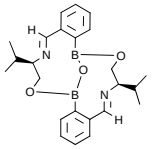
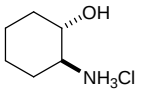
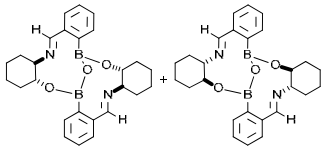
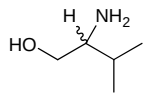
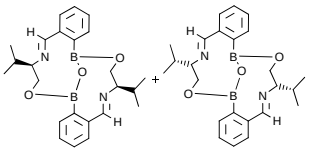
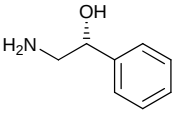
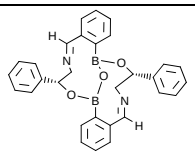
Scheme 12 Formation of an oxygen-bridged di-boron species first reported by Norman *et al.*

Using the tetrahedral bond character equation reported by Ōki, the above species was found to have a 65% tetrahedral character, comparable to our chiral 'bowl' (*R*,*R*)-**149**. Formation was reported in an EtOH / H_2O mix which is both coordinating to the boron and can potentially hydrolyse the imine bond, indicating that formation of the 'bowl' structure is energetically favourable, with complexation occurring despite requiring initial deprotection of the pinacol group, and highly stable since imine hydrolysis is common in aqueous conditions. This seems to fit with our experimental data which shows selective imine condensation due to the formation of the bowl.

We then proceeded to synthesise a range of oxygen-bridged di-boron species using a variety of chiral amino alcohols (Table 3). 1.0 equivalent of the amino alcohol was stirred with 1.0 equivalent of 2-formylphenylboronic acid **73** in $CDCl_3$ for 5 minutes in the presence of 4 Å molecular sieves before an aliquot was removed and its ^{1}H NMR spectrum acquired. Where the HCl salt form of the amino alcohol was used, 1.0 equivalent of $CsCO_3$ was added to form the free amine *in situ*.

Table 3 Synthesis of a series of chiral bowls.



Amino Alcohol	Bowl	Amino Alcohol	Bowl
 (*R*)-**143**	 (*R*,*R*)-**171**	 (*R*)-**150**	 (*R*,*R*)-**173**
 (*rac*)-**143**	 (*R*,*R*)-**171** (*S*,*S*)-**171**	 (*rac*)-**150**	 (*R*,*R*)-**173** (*S*,*S*)-**173**
 (*S*)-**145**	 (*S*,*S*)-**172**	 (*rac*)-**153**	 (*R*,*R*)-**174** (*S*,*S*)-**174**
 (*R*)-**146**	 (*R*,*R*)-**149**	 *trans*-**169**	 (1*R*,2*R*,1'*R*,2'*R*)-**175** (1*S*,2*S*,1'*S*,2'*S*)-**175**
 (*rac*)-**146**	 (*R*,*R*)-**149** (*S*,*S*)-**149**	 (*R*)-**170**	 (*R*,*R*)-**176**

Mass spectrometry was used to confirm the formation of the bridged species since ^{1}H NMR data alone was not conclusive. In several cases, ^{1}H NMR analysis showed a single set of resonances when a racemic amino alcohol was employed. This strongly indicated that complete homocoupling was occurring, affording a 50 : 50 mixture of (*R*,*R*)- and (*S*,*S*)-bowls which were then spectroscopically identical. However, sole formation of the heterochiral (*R*,*S*)-bowl would also give the same spectrum. X-ray data

for (*R*,*R*)-**149**, a crystallised product of the reaction of (*rac*)-**146**, showed homocoupling which indicates that this is the most likely explanation for observing a single species by NMR.

However, this is not observed consistently, with two overlapping sets of signals observed in the complicated ^{1}H NMR spectrum when some racemic amino alcohols are used. This is particularly evident with parent amino alcohol 2-amino-1-butanol (*R*)-**143** and (*rac*)-**143**. Here, we clearly see a second set of resonances in its ^{1}H NMR spectrum, while mass spectrometry again confirms formation of the bowl structure (Figure 21).

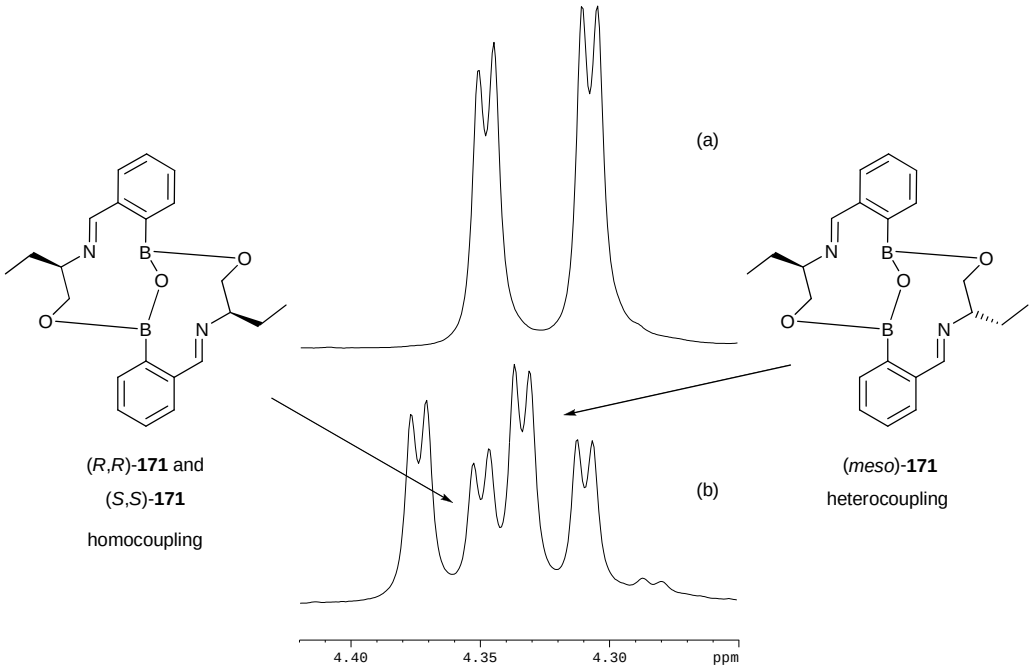


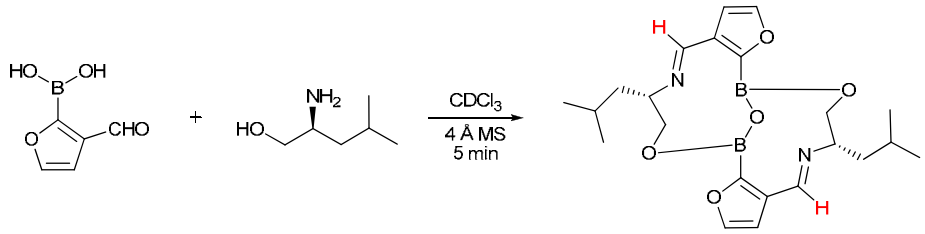
Figure 21: Two sets of resonances observed in the ^{1}H NMR spectrum where (*rac*)-2-amino-1-butanol is used (b) (300 MHz, $CDCl_3$).

As expected, a single set of peaks is observed when enantiopure (*R*)-2-amino-1-butanol (*R*)-**143** is used (Figure 21(a) above). When the same racemic amino alcohol is used, Figure 21(b), two pairs of signals are found in the ^{1}H NMR spectrum. Those overlapping with the original peaks (a) are therefore due to the homochiral pairs (*R*,*R*)-**171** and (*S*,*S*)-**171**, which being enantiomers of one another are indistinct by ^{1}H NMR analysis. The second set of peaks correspond to the newly formed heterochiral pair (*meso*)-**171** which is a diastereomer of the homochiral pairs and show some resolution in the ^{1}H NMR spectrum.

Following the formation of bowls using a variety of enantiopure and racemic amino alcohols, it would appear that the steric demands of the chiral substituent on the β-carbon controls the selectivity of homo : heterocoupling. Amino alcohols with less steric bulk such as 2-amino-1-propanol **153** and 2-amino-1-butanol **143** affords a mixture of both homo and heterocoupling whereas the larger 2-amino-3-methyl-1-butanol **146** or 2-phenylglycinol **150** show predominantly the homocoupling products by ^{1}H NMR spectroscopy, although partial heterochiral formation is still observed.

2.5.3 Variation of Boronic Acid Scaffold

In order to consider these structures further, we decided to replace 2-formylphenylboronic acid **73** with 3-formylfuran-2-boronic acid **177**. This boronic acid was chosen since it presented a more challenging bowl formation due to the larger B-C-C-C-O bond angle than 2-formylphenylboronic acid. Therefore, 1.0 equivalent of 3-formylfuran-2-boronic acid **177** was stirred with 1.0 equivalent of (*S*)-leucinol **145** in $CDCl_3$ for 5 minutes in the presence of 4 Å molecular sieves (Scheme 13) before an aliquot was removed and its ^{1}H NMR acquired.



177 (*S*)-**145** (*S*,*S*)-**178**

Scheme 13 Formation of bowl structure using 3-formylfuran-2-boronic acid.

The bowl structure was again confirmed using mass spectrometry which showed an $[M + H]^{+}$ molecular ion peak at m/z 425. ^{1}H NMR analysis showed a shielded imine signal at δ 8.13 ppm, a characteristic found in several 2-formylphenylboronic acid-based bowl structures (Figure 22).

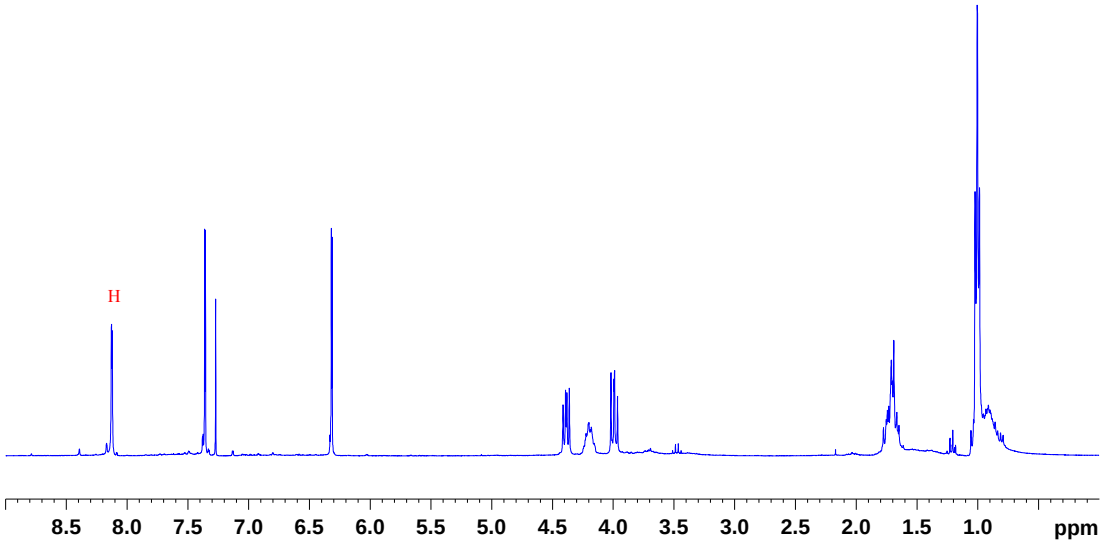
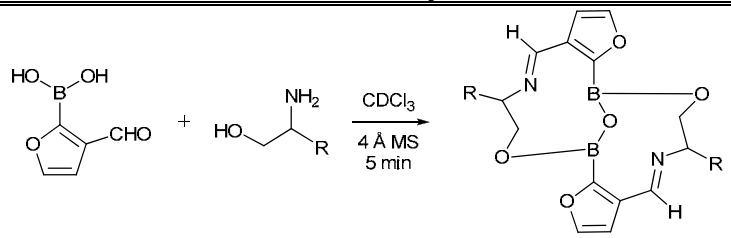


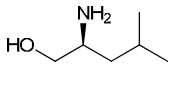
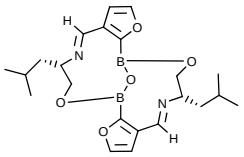
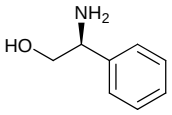
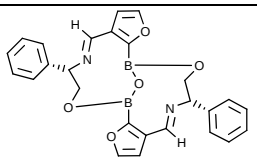
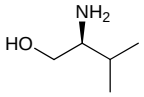
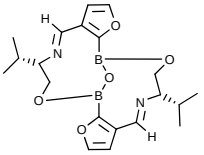
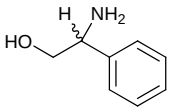
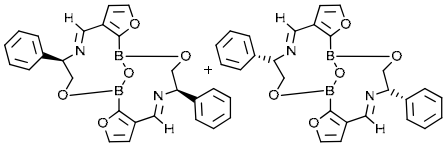
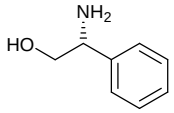
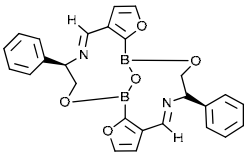
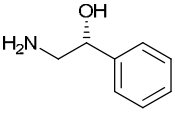
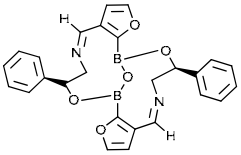
Figure 22: Quantitative formation of (*S*,*S*)-**178** using 3-formylfuran-2-boronic acid **177** (300 MHz, $CDCl_3$).

^{11}B NMR spectroscopic data showed a broad resonance at δ 5.1 ppm. This is consistent with a tetrahedral boron centre and indicates a strong N→B coordinate bond, stronger (δ ~ 4 - 7 ppm) than the 2-formylphenylboronic acid bowls (δ ~ 10 - 13 ppm). A series of chiral bowls were then synthesised from a range of parent amino alcohols with successful formation confirmed using mass spectrometry (Table 4**Error! Reference source not found.**).

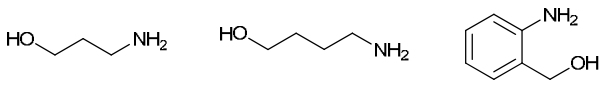
Unlike with bowls formed from 2-formylphenylboronic acid, a mixture of homo and heterocoupling was seen when the sterically demanding (*rac*)-2-phenylglycinol (*rac*)-**150** was used. This is potentially due to the more rigid nature of the 3-formylfuran-2-boronic acid-based structures although it is not completely clear why this is the case. These structures are currently being analysed using computational methods.

Table 4 Several chiral bowl structures formed from 3-formylfuran-2-boronic acid.



Amino Alcohol	Bowl	Amino Alcohol	Bowl
 (*S*)-**145**	 (*S*,*S*)-**178**	 (*S*)-**150**	 (*S*,*S*)-**180**
 (*S*)-**146**	 (*S*,*S*)-**179**	 (*rac*)-**150**	 (*R*,*R*)-**180** (*S*,*S*)-**180**
 (*R*)-**150**	 (*R*,*R*)-**180**	 (*R*)-**170**	 (*R*,*R*)-**181**

A further variation of the structure was considered by changing the ring size to use more remote amino alcohols (Figure 23). However, this did not afford any bowl structures.



182 **183** **184**

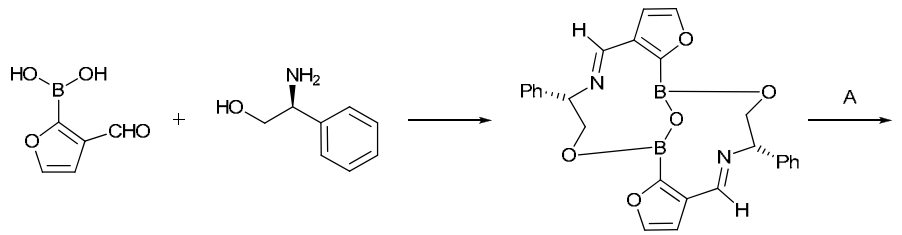
Figure 23 Variation of chain length does not result in the formation of bowls.

2.5.4 Application of the Di-Boron Bridged Species as a Receptor

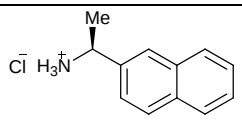
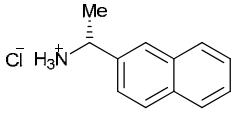
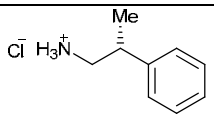
Following our successful syntheses of a wide variety of chiral bowl structures, we proceeded to consider their application as chiral receptors, potentially exploiting the twin electron deficient boron centres in host-guest binding of nucleophiles or anions.

Towards this end, we carried out a preliminary screen using chiral bowl (*S*,*S*)-**180** and a series of primary amine hydrochloride salts. Using Mass Spectrometry analysis, it would appear that there is some interaction between the amines and the chiral bowl, although this is difficult to quantify and no apparent change is observed in the ^{1}H NMR spectra of the crude mixtures (Table 5).

Table 5 Mass Spectrometry analysis of interaction with 3-formylfuran-2-boronic acid bowl (*S*,*S*)-**180**.



177 (*S*)-**150** (*S*,*S*)-**180**

Chiral Amine (A)	Equiv.	Bowl (%) ◡	Ball (%) ◯	Bound to Bowl (%) ◡A	Bound to Ball (%) ◯A
 (*S*)-**77**	1.0	100	15	25	53
 (*R*)-**77**	1.0	100	17	27	56
 (*R*)-**185**	1.0	100	21	24	49

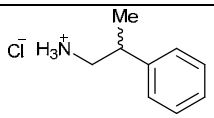
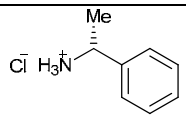
 (*rac*)-**185**	1.0	100	22	25	57
 (*R*)-**76**	1.0	100	16	30	43

Table 4 shows intensities in their Mass Spectrum relative to the chiral bowl.

These results are at a very preliminary stage and further work is ongoing within the group.

2.2.5 References

1. Ager, D. J.; Prakash, I.; Schaad, D. R., *Chem. Rev.* **1996,** 96, 835.
2. Kleidernigg, O. P.; Lindner, W., *Chromatography* **1997,** 44, 465.
3. Dufrasne, F.; Gelbecke, M.; Galanske, M., *Spectrochim. Acta, Part A* **2006,** 65, 869.
4. Hopfl, H., *J. Organomet. Chem.* **1999,** 581, (1-2), 129-149.
5. Toyota, S.; Oki, M., *Bull. Chem. Soc. Jpn.* **1992,** 65, (7), 1832-1840.
6. Wiskur, S. L.; Lavigne, J. J.; Ait-Haddou, H.; Lynch, V.; Hung Chiu, Y.; Canary, J. W.; Anslyn, E. V., *Org. Lett.* **2001,** 3, 1311-1314.
7. Powell, M., *Investigations into a Novel Chiral Derivatisation Protocol for Amino Alcohols*. 2007.
8. Norman, D. W.; Edwards, J. P.; Vogels, C. M.; Decken, A.; Westcott, S. A., *Can. J. Chem.* **2002,** 80, 31-40.

3.1 General Procedures

The solvents and reagents that were used throughout this project were reagent grade unless otherwise stated and were purchased from Acros Organics, Alfa Aesar, Fisher Scientific UK, Frontier Scientific Europe Ltd., Sigma-Aldrich Company Ltd., and were used without further purification.

Infra-red spectra were recorded on a Perkin Elmer Spectrum RX spectrometer between 4400 cm^{-1} and 450 cm^{-1}. Samples were either evaporated from $CHCl_3$ on a NaCl disc (neat) or mixed with KBr in a mortar and pressed into a KBr disc (KBr). All vibrations (n) are given in cm^{-1}.

Nuclear magnetic resonance spectra were run in $CDCl_3$, CD_3OD or $(CD_3)_2CO$. A Bruker AVANCE 300 was used to acquire most NMR spectra, ^{1}H-NMR spectra were recorded at 300.22 MHz, ^{11}B-NMR spectra at 96.32 MHz and {1H}-^{13}C-NMR spectra at 75.50 MHz. ^{19}F-NMR spectra were recorded on a Bruker AVANCE 400 at 376.5 MHz. For greater resolution of signals, some spectra were recorded on a Bruker AVANCE 500 at 500.13 MHz. Chemical shifts (δ) are expressed in parts per million and are reported relative to the residual solvent peak or to tetramethylsilane as an internal standard in ^{1}H and {1H}-^{13}C NMR spectra, boron trifluoride diethyl etherate as an external standard in ^{11}B NMR spectra and $CFCl_3$ as an external standard for ^{19}F NMR spectra. The multiplicities and general assignments of the spectroscopic data are denoted as: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quin), sextet (sxt), doublet of doublets (dd), doublet of triplets (dt), triplet of doublets (td), unresolved multiplet (m), broad (br) and aryl (Ar). Coupling constants (*J*) are expressed in Hertz.

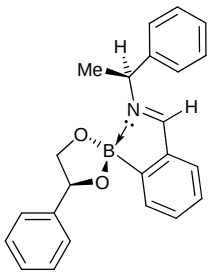
The Mass Spectra used in this report were recorded either by the EPSRC National Mass Spectrometry Service Centre, Swansea, or using a micrOTOFQ electrospray time-of-flight (ESI-TOF) mass spectrometer (Bruker Daltonik GmbH) at the University of Bath. The National Mass Spectrometry Service Centre records mass spectra using electron impact (EI), chemical ionisation (CI) or electrospray (ESI) techniques. A Micromass Quattro II triple quadrupole was used for low resolution measurements using ammonia as the CI reagent gas. A MAT900 high resolution spectrometer was

used for high resolution measurements. The micrOTOFQ spectrometer was coupled to an Agilent Technologies 1200 LC system. 10 μL of sample was directly injected into the mass spectrometer. The nebulising gas used was nitrogen, which was applied at a pressure of 1 bar. Nitrogen was also used as a drying gas, supplied at a flow rate of 8 L/min and a temperature of 110 °C.

Optical rotations were recorded on an Optical Activity Limited AA-10 automatic polarimeter with a path length of 1 dm. Concentrations (c) are quoted in g/100 mL.

All capillary melting points were recorded using a Büchi 535 melting point apparatus. The readings were taken from a mercury-in-glass thermometer and were reported uncorrected as the meniscus point. Where the sample changed colour or evolved gas during or after the melt, thermal decomposition (dec) is noted.

All reactions were carried out at room temperature unless otherwise stated.

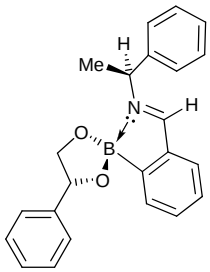


(α-*S*,*R*)-102a

(*S*,*E*)-*N*-((*R*)-2-((*R*)-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

(*R*)-(+)-1-Phenylethane-1,2-diol (*R*)-**102** (55 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (139 mg, 98%); $[\alpha]_D^{20}$ -49.35 (*c* 1.925, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.00 (1H, s, C*H*N), 7.56 (1H, d, *J* 7.0, Ar*H*), 7.57-7.12 (13H, m, Ar*H*), 5.25 (1H, app t, *J* 7.3, C*H*(OB)Ph), 5.09

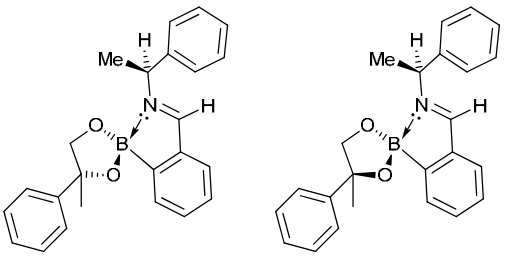
(1H, q, *J* 6.8, C*H*(CH_3)N), 4.32 (1H, app t, *J* 7.3, C$H_A$$H_B$(OB)), 3.78 (1H, app t, *J* 7.3, CH_AH_B(OB)), 1.67 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 165.2 (*C*=N), 142.2, 139.1, 136.7, 132.1, 129.8, 127.8, 127.6, 127.3, 127.2, 127.1, 126.9, 126.8, 126.4, 126.2, 126.0, 125.3, 124.5, 117.5, 71.4, 57.5, 28.6 and 20.1; δ_B (100 MHz; $CDCl_3$) 15.9; *m*/*z* LRMS (CI^+) 356 [$(M+H)^+$, 100%], 210.1 (64), 122.1 (27), 52.2 (10); HRMS (ESI^+) found 356.1816 ($[M+H]^+$ $C_{23}H_{22}BNO_2$ requires 356.1816).



(α-*S*,*S*)-102b

(*S*,*E*)-*N*-((*S*)-2-((*S*)-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

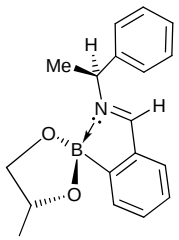
(*S*)-(-)-1-Phenylethane-1,2-diol (*S*)-**102** (55 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (137 mg, 96%); $[\alpha]_D^{20}$ -44.18 (*c* 1.725, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.06 (1H, s, C*H*N), 7.56 (1H, d, *J* 7.1, Ar*H*), 7.37-7.10 (13H, m, Ar*H*), 5.11-5.02 (2H, m, C*H*(OB)Ph and C*H*(CH_3)N), 4.35 (1H, app t, *J* 7.7, C$H_A$$H_B$(OB)), 3.75 (1H, app t, *J* 7.7, CH_AH_B(OB)), 1.61 (3H, d, *J* 6.9, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 165.1 (*C*=N), 142.3, 139.4, 136.7, 132.0, 129.8, 127.8, 127.5, 127.3, 127.2, 126.9(4), 126.9(1), 126.8, 126.3, 126.2, 126.0, 125.3, 124.7, 124.6, 71.5, 57.7, 28.6 and 20.3; δ_B (100 MHz, $CDCl_3$) 16.4; *m*/*z* LRMS (CI^+) 356 [$(M+H)^+$, 20%], 210.1 (100), 122.1 (40), 106.1 (22), 52.2 (11); HRMS (ESI^+) found 356.1818 ($[M+H]^+$ $C_{23}H_{22}BNO_2$ requires 356.1816).



(α-*S*,*R*)-103a and (α-*S*,*S*)-103b

A 50 : 50 mixture of (*S*,*E*)-*N*-((*R*)-2-((*R*)-4-methyl-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine and (*S*,*E*)-*N*-((*S*)-2-((*S*)-4-methyl-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

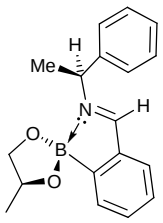
2-Phenylpropane-1,2-diol (*rac*)-**103** (61 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (146 mg, 99%); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (1H, s, C*H*N), 8.06 (1H, s, C*H*N), 7.53-7.13 (28H, m, Ar*H*), 5.00-4.90 (2H, m, 2 x C*H*(CH_3)N), 4.18-4.09 (3H, m, 2 x CH_AH_B(OB) and CH_AH_B(OB)), 4.03 (1H, d, *J* 8.3, CH_AH_B(OB)), 1.66 (3H, s, C(CH_3)OB), 1.63 (3H, s, C(CH_3)OB), 1.59 (6H, m, 2 x C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 166.3 (*C*=N), 166.2 (*C*=N), 149.0, 148.9, 141.1, 140.8, 138.7, 138.6, 133.4(9), 133.4(7), 131.8(4), 131.8(2), 131.7(9), 131.7(0), 129.4, 129.3, 129.2(8), 129.2(6), 129.0(3), 129.0(0), 128.8, 128.7, 128.6(7), 128.6(5), 128.5(8), 128.5(6), 128.4, 128.3, 127.8, 127.6, 127.0(5), 127.0(0), 126.8(4), 126.8(1), 126.2, 126.1, 125.3, 125.2, 81.8(2), 81.8(0), 59.1, 58.9, 31.4(4), 31.4(2), 31.3, 31.2, 22.0 and 21.7; δ_B (100 MHz, $CDCl_3$) 16.9; *m*/*z* LRMS (CI^+) 370 [$(M+H)^+$, 100%], 210.2 (30), 122.1 (6), 106.1 (8); HRMS (ESI^+) found 370.1972 ($[M+H]^+$ $C_{24}H_{24}BNO_2$ requires 370.1973).



(α-*S*,*R*)-104a

(*S*,*E*)-*N*-((*R*)-2-((*R*)-4-methyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

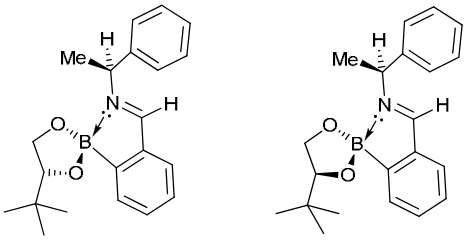
(*R*)-(+)-1,2-Propanediol (30 mg, 0.4 mmol) (*R*)-**104**, 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (116 mg, 99%); $[\alpha]_D^{20}$ -29.14 (*c* 1.750, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $(CD_3)_2CO$) 8.08 (1H, s, C*H*N), 7.50 (1H, d, *J* 7.4, Ar*H*), 7.33-7.12 (8H, m, Ar*H*), 4.92 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.37 (1H, app q, *J* 12.2 and 6.1, CH_AH$_B$(OB)), 4.07 (1H, app t, *J* 12.2, CH$_A$$H_B$(OB)), 3.54 (1H, m, C*H*(CH_3)(OB)), 1.62 (3H, d, *J* 6.8, C(CH_3)(H)N), 1.22 (3H, d, *J* 6.0, C(CH_3)(OB)); δ_C (75 MHz; $CDCl_3$) 163.7 (*C*=N), 140.2, 137.3, 131.2, 130.3, 127.7, 127.5(3), 127.5(0), 127.2(3), 127.2(0), 126.7, 126.2, 125.4, 71.1, 70.9, 59.3, 20.7 and 20.4; δ_B (100 MHz, $CDCl_3$) 18.8; *m*/*z* LRMS (CI^+) 294 [$(M+H)^+$, 100%], 210.2 (58); HRMS (ESI^+) found 294.1656 ($[M+H]^+$ $C_{18}H_{20}BNO_2$ requires 294.1660).



(α-*S*,*S*)-104b

(*S*,*E*)-*N*-((*S*)-2-((*S*)-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

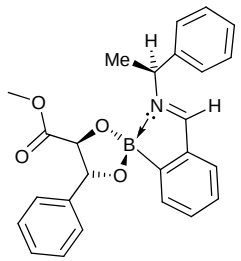
(*S*)-(-)-1,2-Propanediol (*S*)-**104** (30 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**94** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (115 mg, 98%); $[\alpha]_D^{20}$ -30.30 (*c* 0.825, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $(CD_3)_2CO$) 8.12 (1H, s, C*H*N), 7.49 (1H, d, *J* 7.1, Ar*H*), 7.36-7.16 (8H, m, Ar*H*), 4.91 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.28 (1H, app q, 12.8 and 6.4, CH_AH$_B$(OB)), 4.08 (1H, app t, *J* 12.8, CH$_A$$H_B$(OB)), 3.53 (1H, m, C*H*(CH_3)(OB)), 1.62 (3H, d, *J* 6.8, C(CH_3)(H)N), 1.24 (3H, d, *J* 6.0, C(CH_3)(OB)); δ_C (75 MHz; $CDCl_3$) 163.7 (*C*=N), 140.3, 137.3, 131.3, 130.3, 127.9, 127.7, 127.6, 127.2, 126.7, 126.1, 125.7, 125.4, 71.1, 70.9, 59.4, 20.9 and 20.4; δ_B (100 MHz, $CDCl_3$) 19.0; *m*/*z* LRMS (CI^+) 294 [$(M+H)^+$, 41%], 249.2 (11), 210.1 (78), 122.1 (100), 106.1 (20); HRMS (ESI^+) found 294.1660 ($[M+H]^+$ $C_{18}H_{20}BNO_2$ requires 294.1660).



(α-*S*,*R*)-105a and (α-*S*,*S*)-105b

A 50 : 50 mixture of (*S*,*E*)-*N*-((*R*)-2-((*R*)-4-tert-butyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine and (*S*,*E*)-*N*-((*S*)-2-((*S*)-4-tert-butyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenylethanamine

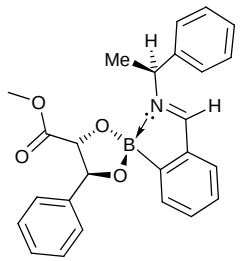
3,3-Dimethylbutane-1,2-diol (*rac*)-**105** (61 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (127 mg, 95%); ν_{max} (film)/cm^{-1} 1636 (C=N); δ_H (300 MHz; $CDCl_3$) 8.52 (1H, s, C*H*N), 8.45 (1H, s, C*H*N), 7.74 (2H, app d, 7.1, Ar*H*), 7.69-7.34 (16H, m, Ar*H*), 5.08-4.96 (2H, m, 2 x C*H*(CH_3)N), 4.21-4.01 (6H, m, 2 x CH_AH_B(OB) and 2 x C*H*(CH_3)(OB)), 1.80 (6H, m, 2 x C(CH_3)(H)N), 1.05 (9H, s, C(CH_3)$_3$), 1.01 (9H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 163.9(4) (*C*=N), 163.9(1) (*C*=N), 142.9, 142.7, 139.8, 139.7, 136.2(4), 136.2(1), 133.5, 133.4, 132.8, 132.7, 132.0, 131.9, 131.4, 131.2, 129.4, 129.3(5), 129.0(4), 129.0(0), 127.9, 127.8, 127.5, 127.3, 127.2, 127.1(1), 85.8, 84.7, 67.0, 66.9, 63.2, 34.2, 34.1, 31.3, 25.7, 25.6(6), 25.6(0), 25.5(4), 25.5(1), 25.1, 23.1 and 22.9; δ_B (100 MHz, $CDCl_3$) 22.8; *m*/*z* LRMS (CI^+) 336 [$(M+H)^+$, 100%], 210.2 (35), 121.9 (66), 105.9 (27), 52.2 (49); HRMS (ESI^+) found 336.2128 ($[M+H]^+$ $C_{21}H_{26}BNO_2$ requires 336.2129).



(α-*S*,4*S*,5*R*)-106a

(4*S*,5*R*)-methyl 5-phenyl-2-(2-((*E*)-((*S*)-1-phenylethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4-carboxylate

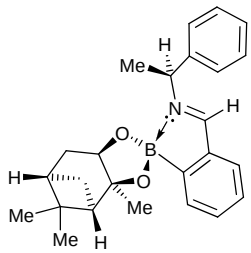
Methyl-(2*S*,3*R*)(-)-2,3-dihydroxy-3-phenylpropionate (2*S*,3*R*)-**106** (78 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (164 mg, 99%); $[\alpha]_D^{20}$ -28.04 (*c* 2.675, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1731 (C=O), 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 7.95 (1H, s, C*H*N), 7.49 (1H, d, *J* 7.0, Ar*H*), 7.47-7.15 (13H, m, Ar*H*), 5.49 (1H, q, *J* 6.8, C*H*(CH_3)N), 5.33 (1H, d, *J* 7.6, C*H*(Ph)(OB)), 4.60 (1H, d, *J* 7.6, C*H*CO_2 CH_3), 3.73 (3H, s, CO_2CH_3), 1.74 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 174.3 (*C*=O), 168.4 (*C*=N), 143.0, 139.9, 137.8, 134.1, 134.0, 130.8, 129.4, 129.3, 129.2, 128.9, 128.8(5), 128.6, 128.4, 128.3, 128.0, 126.6, 126.3, 126.0, 82.8, 81.3, 57.1, 52.4, and 21.0; δ_B (100 MHz, $CDCl_3$) 14.1; *m*/*z* LRMS (CI^+) 414 [$(M+H)^+$, 100%], 239.1 (18), 210.1 (51), 106.0 (17), 52.1 (60); HRMS (ESI^+) found 414.1872 ($[M+H]^+$ $C_{25}H_{24}BNO_4$ requires 414.1871).



(α-*S*,4*R*,5*S*)-106b

(4*R*,5*S*)-methyl-5-phenyl-2-(2-((*E*)-((*S*)-1-phenylethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4-carboxylate

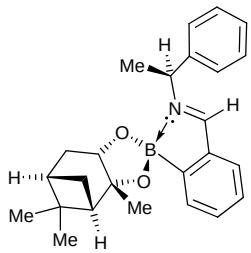
Methyl-(2*R*,3*S*)(+)-2,3-dihydroxy-3-phenylpropionate (2*R*,3*S*)-**106** (78 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (161 mg, 97%); $[\alpha]_D^{20}$ -21.43 (*c* 2.450, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1731 (C=O), 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.35 (1H, s, C*H*N), 7.68 (1H, d, *J* 7.0, Ar*H*), 7.40-7.11 (13H, m, Ar*H*), 5.38 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.81 (1H, d, *J* 7.7, C*H*(Ph)(OB)), 4.47 (1H, d, *J* 7.7, C*H*CO_2CH_3), 3.73 (3H, s, CO_2CH_3), 1.74 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 174.2 (*C*=O), 167.9 (*C*=N), 143.0, 140.8, 137.8, 134.1, 130.9, 129.2, 129.1, 128.7(3), 128.7(0), 128.6(9), 128.5, 128.4(8), 127.9, 127.6, 127.5(6), 126.7, 126.6(6), 126.5(9), 82.7, 80.8, 57.5, 52.3 and 22.0; δ_B (100 MHz, $CDCl_3$) 14.4; *m*/*z* LRMS (CI^+) 414 [$(M+H)^+$, 100%], 210.2 (48); HRMS (ESI^+) found 414.1871 ([M+H] $^+$ $C_{25}H_{24}BNO_4$ requires 414.1871).



(α-*S*,3a*S*,7a*S*,10*S*,11*R*)-107a

(*S*,*E*)-*N*-((10*S*,11*R*)-2-((3a*S*,7a*S*)-3a,5,5-trimethyl-bicyclo[3.1.1]hepto[d][1,3,2] dioxaborol-2-yl)benzylidene)-1-phenylethanamine

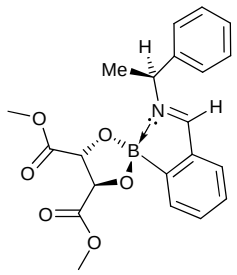
(1*S*,2*S*,3*R*,5*S*)-(+)-Pinan-2,3-diol (1*S*,2*S*,3*R*,5*S*)-**107** (68 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (148 mg, 96%); $[\alpha]_D^{20}$ +6.06 (*c* 1.625, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1637 (C=N); δ_H (300 MHz; $CDCl_3$) 8.81 (1H, s, C*H*N), 7.91 (1H, d, *J* 7.4, Ar*H*), 7.66 (1H, dd, *J* 7.0 and 1.2, Ar*H*), 7.37-7.09 (7H, m, Ar*H*), 4.57 (1H, q, *J* 6.7, C*H*(CH_3)N), 4.30 (1H, dd, *J* 8.3 and 1.3, C*H*(OB)), 2.33-2.22 (1H, m, C$H_A$$H_B$C(OB)), 2.19-2.10 (1H, m, C$H_A$$H_B$C(OB)), 2.05 (1H, app t, *J* 5.0, C*H*C(CH_3)(OB)), 1.88-1.82 (2H, m, C$H_A$$H_B$CH), 1.53 (3H, d, *J* 6.7, C(CH_3)(H)N), 1.38 (3H, s, C(CH_3)OB), 1.20 (4H, br s, C(CH_3)$_{eq}$(CH_3)$_{ax}$ and C*H*C(CH_3)$_2$), 0.77 (3H s, C(CH_3)$_{eq}$(CH_3)$_{ax}$); δ_C (75 MHz; $CDCl_3$) 161.9 (*C*=N), 145.2, 142.0, 135.5, 130.9, 130.0, 128.9, 128.8(1), 128.7, 127.4, 127.3, 127.2(3), 127.2(0), 86.4, 78.5, 68.7, 52.0, 40.0, 38.6, 36.0, 29.1, 27.6, 26.9, 24.6 and 24.5 δ_B (100 MHz, $CDCl_3$) 31.8; *m*/*z* LRMS (CI^+) 388 [$(M+H)^+$, 100%], 210.1 (54), 196.2 (16), 122.1 (39); HRMS (ESI^+) found 388.2445 ($[M+H]^+$ $C_{25}H_{30}BNO_2$ requires 388.2442).



(α-*S*,3a*R*,7a*R*,10*R*,11*S*)-107b

(*S*,*E*)-*N*-((10*R*,11*S*)-2-((3a*R*,7a*R*)-3a,5,5-trimethyl-bicyclo[3.1.1]hepto[d][1,3,2] dioxaborol-2-yl)benzylidene)-1-phenylethanamine

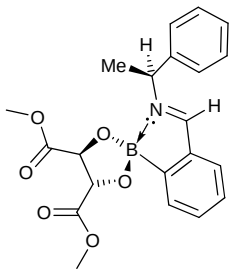
(1*R*,2*R*,3*S*,5*R*)-(-)-Pinan-2,3-diol (1*R*,2*R*,3*S*,5*R*)-**107** (68 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (142 mg, 91%); $[\alpha]_D^{20}$ -4.15 (*c* 1.625, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1637 (C=N); δ_H (300 MHz; $CDCl_3$) 8.84 (1H, s, C*H*N), 7.92 (1H, d, *J* 8.6, Ar*H*), 7.66 (1H, dd, *J* 7.0 and 1.2, Ar*H*), 7.37-7.09 (7H, m, Ar*H*), 4.56 (1H, q, 6.7, C*H*(CH_3)N), 4.31 (1H, dd, *J* 8.5 and 1.5, C*H*(OB)), 2.33-2.23 (1H, m, CH_AH_BC(OB)), 2.19-2.11 (1H, m, CH_AH_BC(OB)), 2.05 (1H, app t, *J* 5.0, C*H*C(CH_3)(OB)), 1.88-1.81 (2H, m, CH_AH_BCH), 1.53 (3H, d, *J* 6.7, C(CH_3)(H)N), 1.36 (3H, s, C(CH_3)OB), 1.21 (4H, br s, $C(CH_3)_{eq}(CH_3)_{ax}$ and C*H*C(CH_3)$_2$), 0.78 (3H s, $C(CH_3)_{eq}(CH_3)_{ax}$); δ_C (75 MHz; $CDCl_3$) 161.9 (*C*=N), 145.4, 142.0, 136.0, 135.5, 133.4, 130.9, 130.0, 129.3, 128.7, 127.4, 127.2, 127.1, 86.5, 78.6, 68.7, 52.0, 40.0, 38.6, 36.0, 29.1, 27.6, 26.9, 24.6 and 24.5; δ_B (100 MHz, $CDCl_3$) 31.9; *m*/*z* LRMS (CI^+) 388 [$(M+H)^+$, 100%], 284.3 (4), 210.2 (8); HRMS (ESI^+) found 388.2443 ($[M+H]^+$ $C_{25}H_{30}BNO_2$ requires 388.2442).



(α-*S*,4*R*,5*R*)-108a

(4*R*,5*R*)-dimethyl-2-(2-((*E*)-((*S*)-1-phenylethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4,5-dicarboxylate

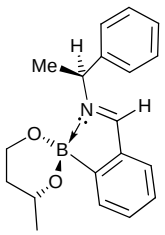
Dimethyl-L-tartrate (1*R*,2*R*)-**108** (71 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (146 mg, 92%); $[\alpha]_D^{20}$ +39.05 (*c* 1.575, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1740 (C=O), 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.25 (1H, s, C*H*N), 7.47 (1H, d, *J* 7.0, Ar*H*), 7.44-7.09 (8H, m, Ar*H*), 5.32 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.58 (2H, s, CH_A(OB)CH_B(OB)), 3.75 (6H, s, 2 x CH_3CO), 1.68 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 173.6 (*C*=O), 173.5 (*C*=O), 168.7 (*C*=N), 140.6, 137.6, 134.2, 131.0, 129.1, 128.9, 128.4, 128.3, 127.4, 126.6, 126.5, 115.0, 77.4, 77.2, 56.8, 52.9, 52.6 and 21.8; δ_B (100 MHz, $CDCl_3$) 14.3; *m*/*z* LRMS (CI^+) 396 [$(M+H)^+$, 100%], 221.1 (10), 210.1 (21), 122.1 (15); HRMS (ESI^+) found 396.1613 ($[M+H]^+$ $C_{21}H_{22}BNO_6$ requires 396.1613).



(α-*S*,4*S*,5*S*)-108b

(4*S*,5*S*)-dimethyl-2-(2-((*E*)-((*S*)-1-phenylethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4,5-dicarboxylate

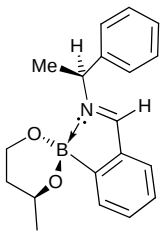
Dimethyl-D-tartrate (1*S*,2*S*)-**128** (71 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (151 mg, 96%); $[\alpha]_D^{20}$ -48.33 (*c* 2.525, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1740 (C=O), 1631 (C=N); δ_H (300 MHz; $CDCl_3$) 7.94 (1H, s, C*H*N), 7.53 (1H, d, *J* 6.8, Ar*H*), 7.40-7.09 (8H, m, Ar*H*), 5.44 (1H, q, *J* 7.0, C*H*(CH_3)N), 4.87 (2H, s, CH_A(OB)CH_B(OB)), 3.73 (6H, s, 2 x CH_3CO), 1.68 (3H, d, *J* 7.0, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 173.6 (*C*=O), 172.2 (*C*=O), 169.3 (*C*=N), 139.8, 137.5, 134.2, 131.0, 129.4, 129.3, 128.8, 128.3, 127.1, 126.6, 126.5, 118.9, 72.6, 72.5, 56.5, 53.3, 52.9 and 20.8; δ_B (100 MHz, $CDCl_3$) 14.7; *m*/*z* LRMS (CI^+) 396 [$(M+H)^+$, 13%], 210.1 (46), 122.1 (100) 106.1 (21); HRMS (ESI^+) found 396.1613 ($[M+H]^+$ $C_{21}H_{22}BNO_6$ requires 396.1613).



(α-*S*,*R*)-109a

(*S*,*E*)-*N*-((*R*)-2-((*R*)-4-methyl-1,3,2-dioxaborinan-2-yl)benzylidene)-1-phenylethanamine

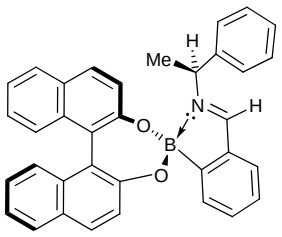
(*R*)-(-)-1,3-Butanediol (*R*)-**109** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (114 mg, 93%); $[\alpha]_D^{20}$ +18.23 (*c* 1.975, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1644 (C=N); δ_H (300 MHz; $(CD_3)_2CO$) 8.70 (1H, s, C*H*N), 7.76-7.71 (1H, m, Ar*H*), 7.67-7.62 (1H, m, Ar*H*), 7.47-7.25 (7H, m, Ar*H*), 4.71 (1H, q, *J* 6.7, C*H*(CH_3)N), 4.27-3.96 (3H, m, CH_AH_B(OB) and C*H*(CH_3)(OB)), 1.96-1.81 (2H, m, CH_AH_BC(OB)), 1.68 (3H, d, *J* 6.7, C(CH_3)(H)N), 1.34 (3H, d, *J* 6.3, C(CH_3)(OB)); δ_C (75 MHz; $CDCl_3$) 162.0 (*C*=N), 145.3, 140.4, 133.3, 130.4, 130.3, 129.7, 129.5, 128.8, 128.7(5), 127.2, 127.1(6), 127.1(3), 68.5, 68.1, 62.0, 34.7, 24.6 and 23.5; δ_B (100 MHz, $CDCl_3$) 27.9; *m*/*z* LRMS (CI^+) 308 [$(M+H)^+$, 100%], 210.1 (10); HRMS (ESI^+) found 308.1815 ($[M+H]^+$ $C_{19}H_{22}BNO_2$ requires 308.1816).



(α-*S*,*S*)-109b

(*S*,*E*)-*N*-((*S*)-2-((*S*)-4-methyl-1,3,2-dioxaborinan-2-yl)benzylidene)-1-phenylethanamine

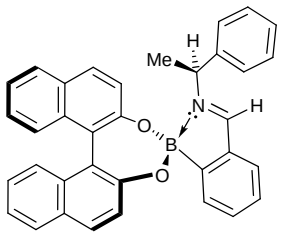
(*S*)-(+)-1,3-Butanediol (*S*)-**109** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (116 mg, 94%); $[\alpha]_D^{20}$ +16.66 (*c* 1.800, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1641 (C=N); δ_H (300 MHz; $(CD_3)_2CO$) 8.72 (1H, s, C*H*N), 7.77-7.71 (1H, m, Ar*H*), 7.67-7.64 (1H, m, Ar*H*), 7.48-7.26 (7H, m, Ar*H*), 4.70 (1H, q, *J* 6.7, C*H*(CH_3)N), 4.26-4.20 (1H, m, C*H*(CH_3)(OB)), 4.15-4.09 (1H, m, CH_AH_B(OB)), 4.07-3.98 (1H, m, CH_AH_B(OB)), 1.95-1.80 (2H, m, CH_AH_BC(OB)), 1.69 (3H, d, *J* 6.7, C(C*H*$_3$)(H)N), 1.33 (3H, d, *J* 6.3, C(C*H*$_3$)(OB)); δ_C (75 MHz; $CDCl_3$) 160.5 (*C*=N), 143.9, 139.0, 131.9, 128.7, 128.0, 127.9(8), 127.3, 127.2, 127.1(7), 127.1(1), 125.7(4), 125.7(0), 67.0, 66.6, 60.3, 33.2, 23.1 and 22.0; δ_B (100 MHz, $CDCl_3$) 27.7; *m*/*z* LRMS (CI^+) 308 [$(M+H)^+$, 100%], 210.1 (60), 122.1 (67), 116.1 (94), 105.9 (35), 52.2 (44); HRMS (ESI^+) found 308.1818 ($[M+H]^+$ $C_{19}H_{22}BNO_2$ requires 308.1816).



(α-*S*,*R*)-110a

(*S*,*E*)-*N*-((*R*)-2-((*R*)-naphtho[2,1,6,7-def][1,3,2]dioxaborepin-4-yl)benzylidene)-1-phenylethanamine

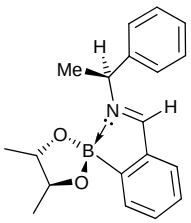
(*R*)-BINOL (*R*)-**74** (115 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a white solid (197 mg, 98%); m.p. 165-172 °C (dec); $[\alpha]_D^{20}$ -561.55 (*c* 1.375, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1626 (C=N); δ_H (300 MHz; $CDCl_3$) 7.93 (1H, s, C*H*N), 7.81-7.57 (4H, m, Ar*H*), 7.36-6.96 (16H, m, Ar*H*), 6.72 (1H, d, *J* 7.0, Ar*H*), 4.80 (1H, q, *J* 7.0, C*H*(CH_3)N), 1.60 (3H, d, *J* 7.0, C(C*H*$_3$)(H)N); δ_C (75 MHz; $CDCl_3$) 169.5 (*C*=N), 155.0, 154.6, 140.5, 137.3, 134.2, 133.9, 133.6, 131.7, 130.7, 130.6, 130.1, 129.3, 129.1, 129.0, 128.8, 128.7(6), 128.7(1), 128.3, 128.1, 127.8, 127.6, 127.5, 126.8, 125.6, 125.5, 124.4, 123.8, 123.7, 123.6, 123.4, 123.2, 122.2, 57.0 and 21.1; δ_B (100 MHz, $CDCl_3$) 12.5; *m*/*z* LRMS (CI^+) 504 [$(M+H)^+$, 100%], 237.2 (9), 210.2 (10); HRMS (EI^+) found 503.2055 ($[M]^{+\bullet}$ $C_{35}H_{26}BNO_2$ requires 503.2051).



(α-*S*,*S*)-110b

(*S*,*E*)-*N*-((*S*)-2-((*S*)-naphtho[2,1,6,7-def][1,3,2]dioxaborepin-4-yl)benzylidene)-1-phenylethanamine

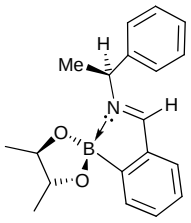
(*S*)-BINOL (*S*)-**74** (115 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (193 mg, 96%); m.p. 167-173 °C (dec); $[\alpha]_D^{20}$ +353.00 (*c* 1.700, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1625 (C=N); δ_H (300 MHz; $CDCl_3$) 8.08 (1H, s, C*H*N), 7.80-7.57 (4H, m, Ar*H*), 7.33-6.95 (16H, m, Ar*H*), 6.72 (1H, d, *J* 6.9, Ar*H*), 4.94 (1H, q, *J* 6.9, C*H*(CH_3)N), 1.40 (3H, d, *J* 6.9, C(C*H*$_3$)(H)N); δ_C (75 MHz; $CDCl_3$) 169.3 (*C*=N), 154.9, 154.5, 139.7, 137.1, 134.2, 134.1, 133.8, 133.7, 130.8, 130.6, 130.2, 129.6, 129.4, 129.2, 129.0, 128.6, 128.4, 128.2, 128.0, 127.7, 127.6, 127.0, 126.9, 125.8, 125.7(6), 123.9, 123.7, 123.5, 123.4, 123.3, 122.3, 118.4, 59.0 and 21.5; δ_B (100 MHz, $CDCl_3$) 12.7; *m*/*z* LRMS (CI^+) 504 [$(M+H)^+$, 25%], 237.1 (16), 210.2 (100), 122.0 (44), 105.9 (25); HRMS (EI^+) found 503.2053 ($[M]^{+\bullet}$ $C_{35}H_{26}BNO_2$ requires 503.2051).



(α-*S*,4*S*,5*S*)-111a

(*E*,1*S*)-*N*-2-((4*S*,5*S*)-4,5-dimethyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

(2*S*,3*S*)-Butane-2,3-diol (2*S*,3*S*)-**111** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (113 mg, 92%); $[\alpha]_D^{20}$ -5.00 (*c* 1.375, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.18 (1H, s, C*H*N), 7.48 (1H, d, *J* 7.2, Ar*H*), 7.35-7.12 (8H, m, Ar*H*), 4.93 (1H, q, *J* 7.0, C*H*(CH_3)N), 3.82-3.77 (2H, m, 2 x C*H*(CH_3)O), 1.60 (3H, d, *J* 7.0, C(C*H*$_3$)(H)N), 1.19 (6H, d, *J* 6.0, 2 x C(C*H*$_3$)O); δ_C (75 MHz; $CDCl_3$) 165.3 (*C*=N), 141.8, 138.9, 132.7, 132.4, 132.1, 131.9, 129.1, 128.9, 128.7, 128.2, 127.8, 126.8, 79.7, 77.0, 61.0, 60.8, 22.1 and 20.5; δ_B (100 MHz, $CDCl_3$) 19.3; *m*/*z* LRMS (CI^+) 308 [$(M+H)^+$, 100%], 210.1 (17), 122.1 (14); HRMS (ESI^+) found 308.1816 ($[M+H]^+$ $C_{19}H_{22}BNO_2$ requires 308.1816).

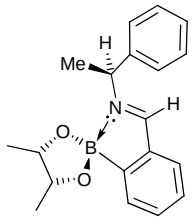


(α-*S*,4*R*,5*R*)-111b

(*E*,1*S*)-*N*-2-((4*R*,5*R*)-4,5-dimethyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

(2*R*,3*R*)-Butane-2,3-diol (2*R*,3*R*)-**111** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The

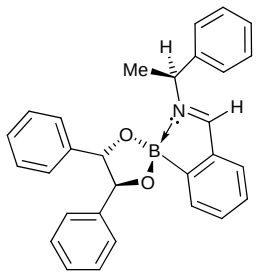
sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (118 mg, 96%); $[\alpha]_D^{20}$ -4.33 (*c* 0.925, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.16 (1H, s, C*H*N), 7.51 (1H, d, *J* 7.0, Ar*H*), 7.38-7.12 (8H, m, Ar*H*), 4.93 (1H, q, *J* 7.0, C*H*(CH_3)N), 3.85-3.69 (2H, m, 2 x C*H*(CH_3)O), 1.62 (3H, d, *J* 7.0, C(C*H*$_3$)(H)N), 1.19 (6H, d, *J* 4.7, 2 x C(C*H*$_3$)O); δ_C (75 MHz; $CDCl_3$) 165.2 (*C*=N), 142.1, 138.9, 132.7, 132.3, 132.0, 129.1, 128.8, 128.5, 128.0, 127.8, 127.6, 126.8, 79.6, 77.1, 61.3, 61.2, 22.5 and 20.5; δ_B (100 MHz, $CDCl_3$) 19.5; *m*/*z* LRMS (CI^+) 308 [$(M+H)^+$, 100%], 210.2 (16), 122.1 (15); HRMS (ESI^+) found 308.1818 ($[M+H]^+$ $C_{19}H_{22}BNO_2$ requires 308.1816).



(α-*S*,4*R*,5*S*)-111c

(*E*,1*S*)-*N*-2-((4*R*,5*S*)-4,5-dimethyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

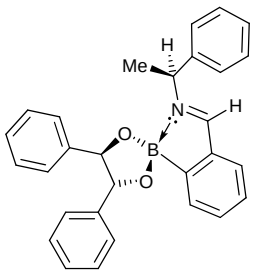
(2*R*,3*S*)-Butane-2,3-diol (2*R*,3*S*)-**111** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (119 mg, 97%); $[\alpha]_D^{20}$ -2.00 (*c* 1.875, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (1H, s, C*H*N), 7.49 (1H, d, *J* 7.2, Ar*H*), 7.37-7.13 (8H, m, Ar*H*), 4.94 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.36-4.24 (2H, m, 2 x C*H*(CH_3)O), 1.62 (3H, d, *J* 6.8, C(C*H*$_3$)(H)N), 1.16 (3H, d, *J* 6.4, C(C*H*$_3$)O), 1.13 (3H, d, *J* 6.4, C(C*H*$_3$)O); δ_C (75 MHz; $CDCl_3$) 164.9 (*C*=N), 142.0, 139.1, 132.9, 132.5, 132.0, 129.1, 128.8, 128.4, 128.1, 127.6, 126.9, 74.8, 74.7, 61.5, 61.2, 22.4, 17.7 and 17.3; δ_B (100 MHz, $CDCl_3$) 19.8; *m*/*z* LRMS (CI^+) 308 [$(M+H)^+$, 100%], 210.2 (52), 122.1 (18), 106.1 (13), 52.1 (17); HRMS (ESI^+) found 308.1819 ($[M+H]^+$ $C_{19}H_{22}BNO_2$ requires 308.1816).



(α-*S*,4*S*,5*S*)-112a

(*E*,1*S*)-*N*-(2-((4*S*,5*S*)-4,5-diphenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

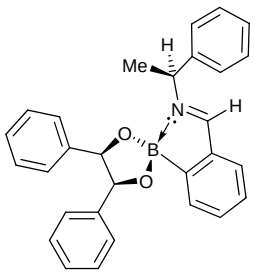
(1*S*,2*S*)-1,2-Diphenylethane-1,2-diol (*S*,*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (160 mg, 93%); m.p. 151-154 °C; $[\alpha]_D^{20}$ -30.00 (*c* 0.650, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1631 (C=N); δ_H (400 MHz; $CDCl_3$) 8.27 (1H, s, C*H*N), 7.91 (1H, d, *J* 6.6, Ar*H*), 7.51 (1H, m, Ar*H*), 7.45-6.95 (17H, m, Ar*H*), 5.68 (1H, q, *J* 6.8, C*H*(CH_3)N), 5.00 (2H, s, 2 x C*H*(Ph)O), 1.82 (3H, d, *J* 6.8, C(C*H*$_3$)(H)N); δ_C (75 MHz; $CDCl_3$) 167.9 (*C*=N), 141.9, 140.7, 140.3, 140.0, 134.0, 131.1, 130.7, 130.4, 130.3(6), 130.3(2), 130.2, 130.0, 129.5, 129.4(9), 129.2, 128.5, 128.4(7), 128.4(0), 127.7(3), 127.7(1), 127.0, 126.9, 126.8, 126.4, 87.6, 85.7, 58.2 and 21.9; δ_B (100 MHz, $CDCl_3$) 14.4; *m*/*z* LRMS (CI^+) 432 [$(M+H)^+$, 64%], 343.2 (39), 210.1 (100), 122.0 (63), 106.0 (35); HRMS (ESI^+) found 432.2127 ($[M+H]^+$ $C_{29}H_{26}BNO_2$ requires 432.2129).



(α-*S*,4*R*,5*R*)-112b

(*E*,1*S*)-*N*-(2-((4*R*,5*R*)-4,5-diphenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

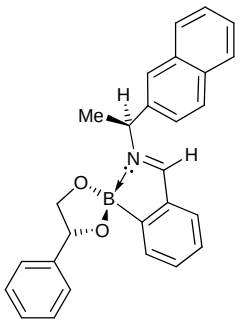
(1*R*,2*R*)-1,2-Diphenylethane-1,2-diol (*R*,*R*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (171 mg, 99%); m.p. 150-152 °C; $[\alpha]_D^{20}$ +31.66 (*c* 2.225, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1631 (C=N); δ_H (300 MHz; $CDCl_3$) 8.18 (1H, s, C*H*N), 7.80 (1H, d, *J* 7.2, Ar*H*), 7.46-6.93 (18H, m, Ar*H*), 5.46 (1H, q, *J* 7.0, C*H*(CH_3)N), 4.89 (2H, s, 2 x C*H*(Ph)O), 1.81 (3H, d, *J* 7.0, C(C*H*$_3$)(H)N); δ_C (75 MHz; $CDCl_3$) 166.6 (*C*=N), 140.1, 140.0, 138.8, 138.7, 136.4, 132.5, 129.4, 129.1, 128.6, 128.2, 128.1, 127.8, 127.4(3) 127.4(0), 127.3(8), 127.3(3), 127.1, 126.9, 126.5, 126.3, 125.7, 125.4, 125.3, 124.9, 86.1, 84.6, 56.6 and 20.2; δ_B (100 MHz, $CDCl_3$) 14.6; *m*/*z* LRMS (CI^+) 432 [$(M+H)^+$, 100%], 210.2 (77), 122.0 (12), 120.1 (14), 106.1 (17); HRMS (ESI^+) found 432.2133 ($[M+H]^+$ $C_{29}H_{26}BNO_2$ requires 432.2129).



(α-*S*,4*R*,5*S*)-112c

(*E*,1*S*)-*N*-(2-((4*R*,5*S*)-4,5-diphenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-phenyl ethanamine

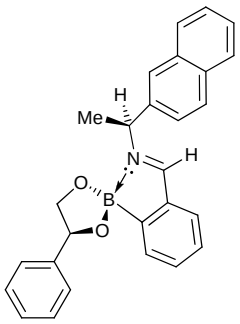
(1*R*,2*S*)-1,2-Diphenylethane-1,2-diol (*R*,*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-phenylethylamine (*S*)-**76** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a dark yellow solid (159 mg, 91%); m.p. 150-152 °C; $[\alpha]_D^{20}$ -26.28 (*c* 1.115, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (1H, s, C*H*N), 7.82 (1H, d, *J* 7.2, Ar*H*), 7.57-6.95 (18H, m, Ar*H*), 5.44 (1H, d, *J* 7.5, CH_ACH$_B$(Ph)O), 5.42 (1H, d, *J* 7.5, CH$_A$CH_B(Ph)O), 5.32 (1H, q, *J* 7.0, C*H*(CH$_3$)N), 1.82 (3H, d, *J* 7.0, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 166.3 (*C*=N), 141.6, 141.5, 140.8, 138.8, 133.6, 132.0, 129.4, 129.3, 129.1, 128.8, 128.1, 128.6, 128.2, 127.9, 127.8, 127.7(9), 127.7(6), 127.6(5), 127.6(3), 127.4, 127.3, 127.2(9), 127.1(6), 126.9, 82.7, 82.5, 59.9 and 22.0; δ_B (100 MHz, $CDCl_3$) 17.4; *m*/*z* LRMS (CI$^+$) 432 [(M+H)$^+$, 100%], 210.2 (27); HRMS (ESI$^+$) found 432.2129 ([M+H]$^+$ $C_{29}H_{26}BNO_2$ requires 432.2129).



(α-*S*,*R*)-113a

(*E*,1*S*)-*N*-(2-((*R*)-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

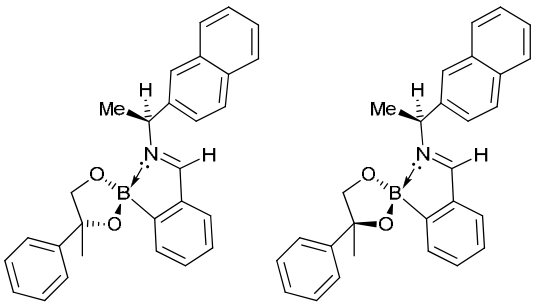
(*R*)-(+)-1-Phenylethane-1,2-diol (*R*)-**102** (55 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a pale yellow solid (149 mg, 92%) m.p. 138-140 °C; $[\alpha]_D^{20}$ +22.00 (*c* 1.000, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1632 (C=N); δ_H (300 MHz; $CDCl_3$) 8.07 (1H, s, C*H*N), 7.76-7.73 (4H, m, Ar*H*), 7.60 (1H, d, *J* 7.0, Ar*H*), 7.43-7.15 (11H, m, Ar*H*), 5.30-5.17 (2H, m, C*H*(CH_3)N and C*H*(Ph)O), 4.41 (1H, t, *J* 8.1, CH_AH_BO), 3.82 (1H, t, *J* 8.1, CH_AH_BO), 1.83 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 167.1 (*C*=N), 143.9, 138.2(4), 138.2(2), 133.7, 133.6, 133.5(9), 133.5(0), 131.3, 129.7, 129.6, 129.3(3), 129.3(1), 128.7, 128.6(7), 128.5(5), 128.2, 127.6, 127.0, 126.9, 126.3, 126.2, 126.1, 78.1, 73.0, 59.0 and 21.6; δ_B (100 MHz, $CDCl_3$) 16.3; *m*/*z* LRMS (CI^+) 406 [$(M+H)^+$, 22%], 262.2 (25), 260.1 (76), 172.2 (46), 155.1 (61), 107.9 (100); HRMS (EI^+) found 404.1926 (^{10}B) ($[M]^{+\bullet}$ $C_{27}H_{24}BNO_2$ requires 404.1931).



(α-*S*,*S*)-113b

(*E*,1*S*)-*N*-(2-((*S*)-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

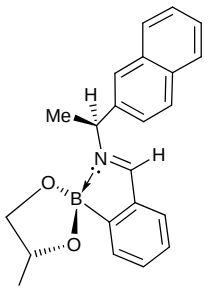
(*S*)-(+)-1-Phenylethane-1,2-diol (*S*)-**102** (55 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (151 mg, 92%); $[\alpha]_D^{20}$ +15.33 (*c* 1.375, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.02 (1H, s, C*H*N), 7.80-7.75 (4H, m, Ar*H*), 7.59 (1H, d, *J* 6.8, Ar*H*), 7.46-7.33 (6H, m, Ar*H*), 7.26-7.13 (5H, m, Ar*H*), 5.33-5.26 (2H, m, C*H*(CH_3)N and C*H*(Ph)O), 4.39 (1H, t, *J* 8.3, CH_AH_BO), 3.82 (1H, t, *J* 8.3, CH_AH_BO), 1.81 (3H, d, *J* 7.0, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 167.2 (*C*=N), 143.7, 138.2, 138.0, 133.7, 133.6(8), 133.5, 131.2, 129.4, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 127.9, 127.5, 127.4(9), 127.4(7), 126.8, 126.5, 126.3, 126.0, 78.2, 73.0, 58.7 and 21.4; δ_B (100 MHz, $CDCl_3$) 16.0; *m*/*z* LRMS (CI^+) 406 [$(M+H)^+$, 10%], 260.2 (19), 172.1 (48), 155.1 (53), 107.9 (100), 106.1 (64); HRMS (EI^+) found 403.1851 (^{10}B) ($[M-H]^+ \bullet$ $C_{27}H_{24}BNO_2$ requires 403.1853).



(α-*S*,*R*)-114a and (α-*S*,*S*)-114b

A 50:50 mixture of (*E*,1*S*)-*N*-(2-((*R*)-4-methyl-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine and (*E*,1*S*)-*N*-(2-((*S*)-4-methyl-4-phenyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

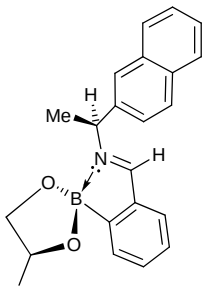
2-Phenylpropane-1,2-diol (*rac*)-**103** (61 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (163 mg, 97%); ν_{max} (film)/cm^{-1} 1633 (C=N); δ_H (300 MHz; $CDCl_3$) 8.32 (1H, s, C*H*N), 8.22 (1H, s, C*H*N), 7.96-7.88 (7H, m, Ar*H*), 7.81 (1H, br s, Ar*H*), 7.73-7.69 (2H, m, Ar*H*), 7.64-7.29 (22H, m, Ar*H*), 5.29 (2H, m, 2 x C*H*(CH_3)N), 4.41-4.29 (3H, m, 2 x CH_AH$_B$O and CH$_A$$H_B$O), 4.21 (1H, d, *J* 8.5, CH$_A$$H_B$O), 1.90-1.83 (12H, m, 2 x C(CH_3)(H)N and 2 x C(CH_3)(Ph)O); δ_C (75 MHz; $CDCl_3$) 173.3(3), 173.3(1), 169.3 (*C*=N), 169.0 (*C*=N), 137.8, 137.7(7), 137.7(4), 137.2(2), 137.2(0), 137.1(1), 137.1(0), 134.0, 133.9, 133.3, 133.2(8), 133.2(4), 133.2(1), 133.1(7), 133.1(4), 133.0(9), 133.0(6), 130.8, 130.7, 129.1, 128.9, 128.8(8), 128.8(5), 128.8(2), 128.2(4), 128.2(0), 128.1, 128.0, 127.8, 127.7, 126.6(3), 126.6(0), 126.5, 126.4(9), 126.4(6), 126.4(1), 126.3(3), 126.3(1), 126.2(7), 126.2(3), 125.6(4), 125.6(2), 77.6(2), 77.6(0), 56.5, 56.2, 52.4(3), 52.4(0), 52.3(6), 52.3(1), 21.3 and 20.4; δ_B (100 MHz, $CDCl_3$) 16.7; *m*/*z* LRMS (CI$^+$) 420 [(M+H)$^+$, 100%], 335.2 (23), 286.1 (11), 191.1 (10); HRMS (ESI$^+$) found 420.2131 ([M+H]$^+$ $C_{28}H_{26}BNO_2$ requires 420.2129).



(α-*S*,*R*)-115a

(*E*,1*S*)-*N*-(2-((*R*)-4-methyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

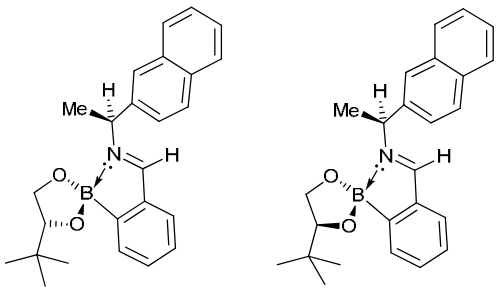
(*R*)-(+)-1,2-Propanediol (*R*)-**104** (30 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (125 mg, 91%); m.p. 130-133 °C; $[\alpha]_D^{20}$ +3.00 (*c* 2.050, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.25 (1H, s, C*H*N), 7.95-7.87 (4H, m, Ar*H*), 7.69 (1H, d, *J* 7.5, Ar*H*), 7.54-7.43 (5H, m, Ar*H*), 7.30 (1H, t, *J* 7.2, Ar*H*), 5.28 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.53 (1H, br s, C*H*(CH_3)O), 4.29 (1H, br t, *J* 7.4, CH_AH$_B$O), 3.74 (1H, t, *J* 7.4, CH$_A$$H_B$O), 1.90 (3H, d, *J* 6.8, C(CH_3)(H)N), 1.40 (3H, d, *J* 5.8, C(CH_3)(H)O); δ_C (75 MHz; $CDCl_3$) 165.9 (*C*=N), 138.9, 138.6, 133.7, 133.3, 133.0, 131.7, 129.1, 128.7, 128.5, 128.1, 128.0(5), 128.0(0), 126.8, 126.7, 126.3, 126.2, 72.6, 72.5, 60.3, 22.3 and 21.9; δ_B (100 MHz, $CDCl_3$) 18.5; *m*/*z* LRMS (CI$^+$) 344 [(M+H)$^+$, 100%], 190.1 (70), 155.1 (10); HRMS (ESI$^+$) found 344.1817 ([M+H]$^+$ $C_{22}H_{22}BNO_2$ requires 344.1816).



(α-*S*,*S*)-115b

(*E*,1*S*)-*N*-(2-((*S*)-4-methyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

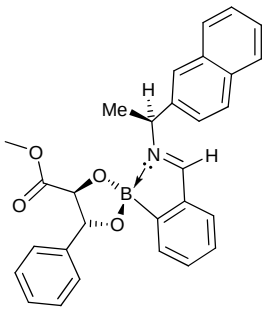
(*S*)-(-)-1,2-Propanediol (*S*)-**104** (30 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a pale yellow solid (135 mg, 99%); m.p. 134-135 °C; $[\alpha]_D^{20}$ +4.18 (*c* 0.675, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.29 (1H, s, C*H*N), 7.96-7.87 (4H, m, Ar*H*), 7.68 (1H, d, *J* 7.0, Ar*H*), 7.59-7.40 (5H, m, Ar*H*), 7.33-7.29 (1H, m, Ar*H*), 5.29 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.60-4.50 (1H, m, C*H*(CH_3)O), 4.30 (1H, t, *J* 7.7, C$H_A$$H_B$O), 3.73 (1H, t, *J* 7.7, C$H_A$$H_B$O), 1.91 (3H, d, *J* 6.8, C(CH_3)(H)N), 1.39 (3H, d, *J* 6.0, C(CH_3)(H)O); δ_C (75 MHz; $CDCl_3$) 165.8 (*C*=N), 139.0, 138.7, 133.7, 133.3, 133.0, 131.7, 129.1, 128.7, 128.6, 128.5, 128.1, 127.0, 126.8, 126.7, 126.1, 125.8, 72.6, 72.4, 60.5, 22.1 and 21.9; δ_B (100 MHz, $CDCl_3$) 18.7; *m*/*z* LRMS (CI^+) 344 [$(M+H)^+$, 100%], 190.1 (77), 155.1 (12); HRMS (ESI^+) found 344.1813 ($[M+H]^+$ $C_{22}H_{22}BNO_2$ requires 344.1816).



(α-*S*,*R*)-116a and (α-*S*,*S*)-116b

A 50:50 mixture of (*E*,1*S*)-*N*-(2-((*R*)-4-*tert*-butyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine and (*E*,1*S*)-*N*-(2-((*S*)-4-*tert*-butyl-1,3,2-dioxaborolan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

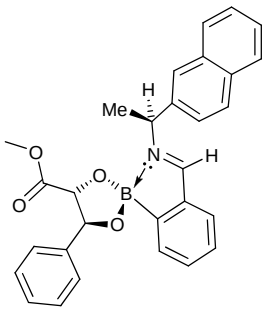
3,3-Dimethylbutane-1,2-diol (*rac*)-**105** (61 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (131 mg, 85%); ν_{max} (film)/cm^{-1} 1634 (C=N); δ_H (300 MHz; $CDCl_3$) 8.48 (1H, s, C*H*N), 8.40 (1H, s, C*H*N), 7.95-7.83 (8H, m, Ar*H*), 7.70 (2H, d, *J* 7.2, Ar*H*), 7.63-7.45 (10H, m, Ar*H*), 7.40-7.30 (2H, m, Ar*H*), 5.18-5.10 (2H, m, 2 x C*H*(CH_3)N), 4.17-4.00 (6H, m, 2 x C*H*(^{t}Bu)O, 2 x C$H_A$$H_B$O and 2 x C$H_A$$H_B$O), 1.86-1.82 (6H, m, 2 x C(CH_3)(H)N), 1.01 (9H, s, C(CH_3)$_3$), 0.95 (9H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 163.9 (*C*=N), 163.8 (*C*=N), 140.0, 139.8, 139.5, 139.4(4), 139.4(1), 133.6, 133.4, 132.9, 132.7, 132.6, 132.5, 132.4(9), 132.4(0), 131.7, 131.3, 131.1, 131.0, 129.7, 129.0, 128.9, 128.5, 128.1, 128.0, 127.8, 127.7, 126.8, 126.3, 126.2, 126.1(5), 126.1(2), 126.0(2), 126.0(0), 125.7, 125.6(8), 125.6(0), 125.5, 125.4(8), 125.4(3), 84.4, 84.3, 63.0, 62.8, 33.8, 33.7, 25.2 (3C, C(*C*H_3)$_3$), 25.1 (3C, C(*C*H_3)$_3$), 22.6 and 22.4; δ_B (100 MHz, $CDCl_3$) 22.7; *m*/*z* LRMS (ESI^+) 386 [$(M+H)^+$, 100%], 301.2 (7), 232.2 (25), 155.1 (4); HRMS (ESI^+) found 386.2286 ($[M+H]^+$ $C_{25}H_{28}BNO_2$ requires 386.2286).



(α-*S*,4*S*,5*R*)-117a

(4*S*,5*R*)-methyl-2-(2-((*E*)-((*S*)-1-(naphthalen-3-yl)ethylimino)methyl)phenyl)-5-phenyl-1,3,2-dioxaborolane-4-carboxylate

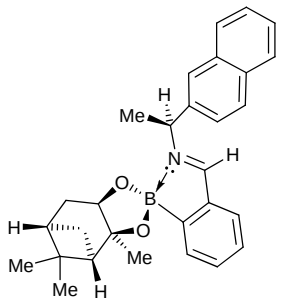
Methyl-(2*S*,3*R*)(-)-2,3-dihydroxy-3-phenylpropionate (2*S*,3*R*)-**106** (78 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a white solid (182 mg, 98%); m.p. 146-148 °C; $[\alpha]_D^{20}$ -12.42 (*c* 1.880, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1736 (C=O), 1632 (C=N); δ_H (300 MHz; $CDCl_3$) 8.35 (1H, s, C*H*N), 7.95-7.84 (4H, m, Ar*H*), 7.82 (1H, d, *J* 7.4, Ar*H*), 7.61-7.28 (11H, m, Ar*H*), 5.64 (1H, q, *J* 6.8, C*H*(CH_3)N), 5.09 (1H, d, *J* 7.7, C*H*(Ph)O), 4.67 (1H, d, *J* 7.7, C*H*(CO_2 CH_3)O), 3.89 (3H, s, CO_2CH_3), 2.03 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 173.9 (*C*=O), 168.0 (*C*=N), 142.6, 137.8, 137.6, 137.5, 134.8, 134.2, 133.9, 133.2, 133.1, 133.0, 130.6, 128.9, 128.4, 128.1, 127.8, 127.6, 126.5, 126.4(7), 126.4(1), 126.1, 125.8, 125.6, 82.4, 80.6, 57.2, 52.0 and 21.3; δ_B (100 MHz, $CDCl_3$) 14.6; *m*/*z* LRMS (ESI^+) 464 [$(M+H)^+$, 100%], 310.1 (15), 278.2 (10), 230.1 (10), 202.2 (6), 155.1 (9); HRMS (ESI^+) found 464.2028 ($[M+H]^+$ $C_{29}H_{26}BNO_4$ requires 464.2028).



(α-*S*,4*R*,5*S*)-117b

(4*R*,5*S*)-methyl-2-(2-((*E*)-((*S*)-1-(naphthalen-3-yl)ethylimino)methyl)phenyl)-5-phenyl-1,3,2-dioxaborolane-4-carboxylate

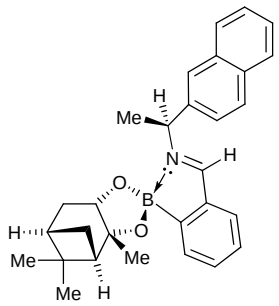
Methyl-(2*R*,3*S*)-(-)-2,3-dihydroxy-3-phenylpropionate (2*R*,3*S*)-**106** (78 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (183 mg, 99%); $[\alpha]_D^{20}$ +10.57 (*c* 1.005, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1735 (C=O), 1632 (C=N); δ_H (300 MHz; $CDCl_3$) 8.10 (1H, s, C*H*N), 8.05 (1H, br s, Ar*H*), 7.99-7.85 (3H, m, Ar*H*), 7.80 (1H, d, *J* 7.6, Ar*H*), 7.70-7.30 (11H, m, Ar*H*), 5.77 (1H, q, *J* 6.8, C*H*(CH_3)N), 5.50 (1H, d, *J* 7.5, C*H*(Ph)O), 4.76 (1H, d, *J* 7.5, C*H*(CO_2CH_3)), 3.86 (3H, s, CO_2CH_3), 2.01 (3H, d, 6.8, C(C*H*$_3$)(H)N); δ_C (75 MHz; $CDCl_3$) 174.0 (*C*=O), 168.3 (*C*=N), 142.7, 137.5, 137.1, 133.8, 133.3, 133.1, 133.2, 131.7, 131.1, 130.5, 130.0, 129.2, 128.5, 128.3, 128.1, 127.8, 127.7, 126.7, 126.6(5), 126.6(0), 126.3, 126.0, 82.5, 81.0, 56.8, 52.1 and 20.6; δ_B (100 MHz, $CDCl_3$) 14.4; *m*/*z* LRMS (ESI^+) 464 [$(M+H)^+$, 100%], 310.1 (17), 202.3 (14), 155.1 (6); HRMS (ESI^+) found 464.2030 ($[M+H]^+$ $C_{29}H_{26}BNO_4$ requires 464.2028).



(α-*S*,3a*S*,7a*S*,10*S*,11*R*)-118a

(*S*,*E*)-*N*-((10*S*,11*R*)-2-((3a*S*,7a*S*)-3a,5,5-trimethyl-bicyclo[3.1.1]hepto[d][1,3,2] dioxaborol-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

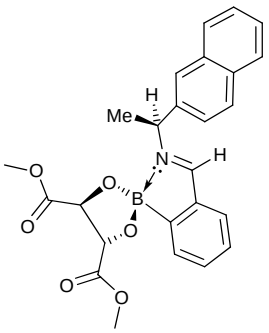
(1*S*,2*S*,3*R*,5*S*)-(+)-Pinan-2,3-diol (1*S*,2*S*,3*R*,5*S*)-**107** (68 mg, 0.4 mmol), (61 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a light yellow solid (171 mg, 98%); m.p. 125-129 °C; $[\alpha]_D^{20}$ +2.00 (*c* 1.975, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1639 (C=N); δ_H (300 MHz; $CDCl_3$) 8.11 (1H, s, C*H*N), 7.95 (1H, br s, Ar*H*), 7.91-7.86 (5H, m, Ar*H*), 7.65 (1H, dd, *J* 8.5 and 1.7, Ar*H*), 7.53-7.44 (4H, m, Ar*H*), 4.92 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.43 (1H, dd, *J* 7.0 and 1.9, C*H*(OB)), 2.46-2.38 (1H, m, CH_AH$_B$C(OB)), 2.32-2.24 (1H, m, CH$_A$$H_B$C(OB)), 2.15 (1H, app t, *J* 5.0, C*H*C(CH_3)(O)), 2.07-1.97 (2H, m, C$H_A$$H_B$CH), 1.80 (3H, d, *J* 6.8, C(CH_3)(H)N), 1.52 (3H, s, C(CH_3)O), 1.35 (4H, br s, C(CH_3)$_{eq}$(CH_3)$_{ax}$ and C*H*C(CH_3)$_2$), 0.75 (3H, s, C(CH_3)$_{eq}$(CH_3)$_{ax}$); δ_C (75 MHz; $CDCl_3$) 161.9 (*C*=N), 142.3, 141.6, 135.1, 133.6, 132.7, 130.6, 129.7, 128.0(4), 128.0(1), 127.6, 127.3, 127.1, 126.0, 125.7, 125.6, 125.2, 86.1, 78.1, 68.3, 51.6, 39.6, 38.2, 35.6, 28.7, 27.2, 26.5, 24.1 and 24.0; δ_B (100 MHz, $CDCl_3$) 30.4; *m*/*z* LRMS (ESI$^+$) 438 [(M+H)$^+$, 100%], 353.2 (6), 229.1 (9); HRMS (ESI$^+$) found 438.2600 ([M+H]$^+$ $C_{29}H_{32}BNO_2$ requires 438.2599).



(α-*S*,3a*R*,7a*R*,10*R*,11*S*)-118b

(*S*,*E*)-N-((10*R*,11*S*)-2-((3a*R*,7a*R*)-3a,5,5-trimethyl-bicyclo[3.1.1]hepto[d][1,3,2] dioxaborol-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

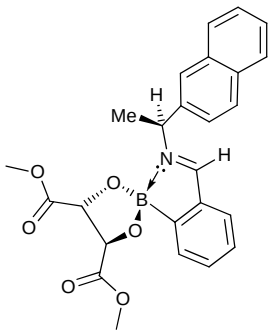
(1*R*,2*R*,3*S*,5*R*)-(-)-Pinan-2,3-diol (1*R*,2*R*,3*S*,5*R*)-**107** (68 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a pale cream solid (164 mg, 94%); m.p. 125-127 °C; $[\alpha]_D^{20}$ -5.66 (*c* 1.555, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1639 (C=N); δ_H (300 MHz; $CDCl_3$) 8.08 (1H, s, C*H*N), 7.95 (1H, br s, Ar*H*), 7.90-7.86 (5H, m, Ar*H*), 7.64 (1H, m, Ar*H*), 7.58-7.46 (4H, m, Ar*H*), 4.93 (1H, q, *J* 6.6, C*H*(CH_3)N), 4.42 (1H, dd, *J* 8.7 and 1.9, C*H*(OB)), 2.45-2.38 (1H, m, C$H_A$$H_B$CO), 2.33-2.25 (1H, m, CH$_A$$H_B$CO), 2.15 (1H, app t, *J* 5.0, C*H*C(CH_3)(O)), 2.08-1.94 (2H, m, C$H_A$$H_B$CH), 1.80 (3H, d, *J* 6.6, C(CH_3)(H)N), 1.51 (3H, s, C(CH_3)O), 1.37 (4H, br s, C(CH_3)$_{eq}$(CH_3)$_{ax}$ and C*H*C(CH_3)$_2$), 0.72 (3H, s, C(CH_3)$_{eq}$(CH_3)$_{ax}$); δ_C (75 MHz; $CDCl_3$) 161.9 (*C*=N), 142.3, 141.6, 135.1, 133.6, 133.1, 132.7, 130.8, 130.6, 129.8, 128.1, 127.7, 127.2, 126.0, 125.8, 125.6, 123.9, 86.1, 78.1, 68.3, 51.6, 39.7, 38.2, 35.7, 28.8, 27.2, 26.5, 24.2 and 24.1; δ_B (100 MHz, $CDCl_3$) 30.3; *m*/*z* LRMS (ESI$^+$) 438 [(M+H)$^+$, 100%], 355.3 (52), 324.2 (11), 212.1 (15), 155.1 (29); HRMS (ESI$^+$) found 438.2599 ([M+H]$^+$ $C_{29}H_{32}BNO_2$ requires 438.2599).



(α-*S*,4*R*,5*R*)-119a

(4*R*,5*R*)-dimethyl-2-(2-((*E*)-((*S*)-1-(naphthalen-3-yl)ethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4,5-dicarboxylate

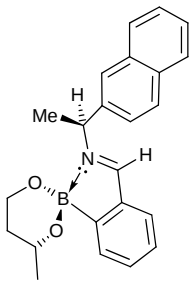
Dimethyl-L-tartrate (1*R*,2*R*)-**108** (71 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (164 mg, 92%); $[\alpha]_D^{20}$ +10.82 (*c* 1.335, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1744 (C=O), 1631 (C=N); δ_H (300 MHz; $CDCl_3$) 8.30 (1H, s, C*H*N), 7.96-7.80 (4H, m, Ar*H*), 7.68 (1H, d, *J* 7.2, Ar*H*), 7.62-7.48 (4H, m, Ar*H*), 7.38 (1H, d, *J* 7.3, Ar*H*), 7.31 (1H, dt, *J* 7.5 and 0.9, Ar*H*), 5.58 (1H, q, *J* 6.8, C*H*(CH_3)N), 4.80 (2H, s, $CH_A(O)CH_B(O)$), 3.88 (6H, s, 2 x CO_2CH_3), 1.95 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 173.6(5) (*C*=O), 173.6(1) (*C*=O), 169.3 (*C*=N), 138.1, 137.6, 134.4, 134.2, 134.1, 133.5, 133.3, 131.2, 129.2, 128.5, 128.1, 126.9, 126.8, 126.6, 126.0, 125.9, 78.0, 77.9, 56.8, 56.6, 52.7 and 21.6; δ_B (100 MHz, $CDCl_3$) 13.6; *m*/*z* LRMS (ESI^+) 446 [$(M+H)^+$, 100%], 292.1 (19), 230.1 (6), 155.1 (5); HRMS (ESI^+) found 446.1765 ([$M+H^+$ $C_{25}H_{24}BNO_6$ requires 446.1769).



(α-*S*,4*S*,5*S*)-119b

(4*S*,5*S*)-dimethyl-2-(2-((*E*)-((*S*)-1-(naphthalen-3-yl)ethylimino)methyl)phenyl)-1,3,2-dioxaborolane-4,5-dicarboxylate

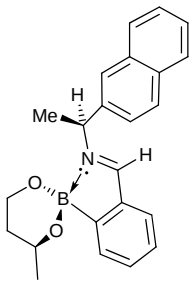
Dimethyl-D-tartrate (1*S*,2*S*)-**108** (71 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (170 mg, 96%); $[\alpha]_D^{20}$ +12.00 (*c* 1.000, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1744 (C=O), 1631 (C=N); δ_H (300 MHz; $CDCl_3$) 8.03 (1H, s, C*H*N), 7.99 (1H, br s, Ar*H*), 7.95-7.80 (3H, m, Ar*H*), 7.63-7.47 (5H, m, Ar*H*), 7.30-7.22 (2H, m, Ar*H*), 5.71 (1H, q, *J* 7.0, C*H*(CH_3)N), 5.01 (2H, s, $CH_A(O)CH_B(O)$), 3.88 (6H, s, 2 x CO_2CH_3), 1.95 (3H, d, *J* 7.0, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 173.3(7) (*C*=O), 173.3(2) (*C*=O), 169.2 (*C*=N), 137.2, 137.0, 134.0, 133.2(4), 133.2(3), 130.7, 129.1, 128.2, 127.7, 126.6(5), 126.6(1), 126.4, 126.3, 126.2, 126.0, 125.9, 77.7, 72.1, 56.2, 53.1, 52.4 and 20.4; δ_B (100 MHz, $CDCl_3$) 14.4; *m*/*z* LRMS (ESI^+) 446 [$(M+H)^+$, 100%], 363.2 (28), 292.1 (27), 155.1 (26); HRMS (ESI^+) found 446.1766 ($[M+H]^+$ $C_{25}H_{24}BNO_6$ requires 446.1769).



(α-*S*,*R*)-120a

(*E*,1*S*)-*N*-(2-((*R*)-4-methyl-1,3,2-dioxaborinan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

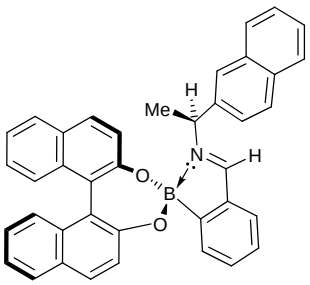
(*R*)-(-)-1,3-Butanediol (*R*)-**109** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (141 mg, 99%); m.p. 120-123 °C; $[\alpha]_D^{20}$ -3.33 (*c* 1.750, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1632 (C=N); δ_H (300 MHz; $CDCl_3$) 8.79 (1H, s, C*H*N), 7.97 (1H, br s, Ar*H*), 7.94-7.89 (3H, m, Ar*H*), 7.83-7.80 (1H, m, Ar*H*), 7.75-7.72 (1H, Ar*H*), 7.65 (1H, dd, *J* 8.5 and 1.7, Ar*H*), 7.57-7.45 (4H, m, Ar*H*), 4.91 (1H, q, *J* 7.0, C*H*(CH_3)N), 4.30-3.99 (1H, m, C*H*(CH_3)O), 3.98-3.88 (1H, m, CH_AH_BO), 3.87-3.77 (1H, m, CH_AH_BO), 1.94-1.86 (2H, m, $CH_AH_BC(CH_3)O$), 1.81 (3H, d, *J* 7.0, C(CH_3)(H)N), 1.35 (3H, d, *J* 6.6, C(CH_3)O); δ_C (75 MHz; $CDCl_3$) 162.4 (*C*=N), 142.9, 140.4, 134.5, 133.4, 133.0, 130.4, 129.6, 129.0, 128.5, 128.4, 128.3, 128.1, 126.4, 126.0, 125.4, 125.0, 68.5, 61.9, 36.2, 34.8, 24.7 and 23.6; δ_B (100 MHz, $CDCl_3$) 28.0; *m*/*z* LRMS (ESI^+) 358 [$(M+H)^+$, 100%], 273.2 (9), 254.1 (13), 204.1 (23), 155.1 (7); HRMS (ESI^+) found 358.1976 ($[M+H]^+$ $C_{23}H_{24}BNO_2$ requires 358.1973).



(α-*S*,*S*)-120b

(*E*,1*S*)-*N*-(2-((*S*)-4-methyl-1,3,2-dioxaborinan-2-yl)benzylidene)-1-(naphthalen-3-yl)ethanamine

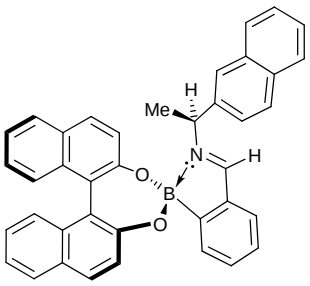
(*S*)-(+)-1,3-Butanediol (*S*)-**109** (36 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a cream solid (140 mg, 98%); m.p. 121-123 °C; $[\alpha]_D^{20}$ -4.92 (*c* 1.645, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1632 (C=N); δ_H (300 MHz; $CDCl_3$) 8.78 (1H, s, C*H*N), 7.98 (1H, br s, Ar*H*), 7.96-7.90 (3H, m, Ar*H*), 7.82-7.79 (1H, m, Ar*H*), 7.75-7.72 (1H, m, Ar*H*), 7.66 (1H, dd, *J* 8.9 and 1.9, Ar*H*), 7.57-7.48 (4H, m, Ar*H*), 4.93 (1H, q, *J* 6.6, C*H*(CH_3)N), 4.22-4.06 (3H, m, C*H*(CH_3)O, CH_AH_BO and CH_AH_BO), 1.94-1.90 (2H, m, $CH_AH_BC(CH_3)O$), 1.80 (3H, d, *J* 6.6, C(C*H*$_3$)(H)N), 1.36 (3H, d, *J* 6.2, C(C*H*$_3$)O); δ_C (75 MHz; $CDCl_3$) 162.4 (*C*=N), 142.9, 140.3, 133.9, 133.3, 133.0, 130.4, 129.5, 128.8, 128.4, 128.0, 126.4, 126.0, 125.9, 125.8, 125.3, 124.7, 68.6, 68.1, 62.0, 34.7, 24.7 and 23.5; δ_B (100 MHz, $CDCl_3$) 28.0; *m*/*z* LRMS (ESI^+) 358 [$(M+H)^+$, 100%], 282.2 (25), 254.1 (45), 204.2 (30), 155.1 (8); HRMS (ESI^+) found 358.1979 ($[M+H]^+$ $C_{23}H_{24}BNO_2$ requires 358.1973).



(α-*S*,*R*)-121a

(*S*,*E*)-*N*-((*R*)-naphtho[2,1,6,7-*def*][1,3,2]dioxaborepin-4-yl)benzylidene)-1-(naphthalen-2-yl)ethanamine

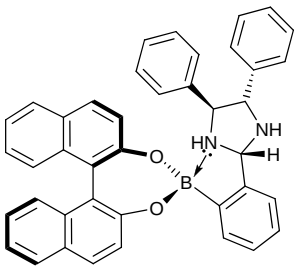
(*R*)-BINOL (*R*)-**74** (114 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a bright yellow solid (208 mg, 94%); mp 159-164 °C (dec); $[\alpha]_D^{20}$ -415.02 (*c* 2.750, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1639 (C=N); δ_H (300 MHz; $CDCl_3$) 8.20 (1H, s, C*H*N), 8.03-7.87 (7H, m, Ar*H*), 7.74 (1H, d, *J* 8.9, Ar*H*), 7.66-7.38 (9H, m, Ar*H*), 7.33-7.28 (5H, m, Ar*H*), 6.98 (1H, d, *J* 7.1, Ar*H*), 5.34 (1H, q, *J* 6.8, C*H*(CH_3)N), 1.78 (3H, d, *J* 6.8, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 169.1 (*C*=N), 154.6, 154.2, 136.8, 136.7, 133.9, 133.5, 133.4(8), 133.4(0), 133.2, 131.2, 130.5(3), 130.5(1), 130.3, 129.8, 129.3, 129.2(7), 129.2(5), 129.1, 128.8, 128.3, 128.2, 128.1, 127.9, 127.8(8), 127.8(3), 126.9, 126.8, 126.6, 126.4, 126.1, 125.7, 125.4, 123.5, 123.3, 123.1, 121.9, 58.7 and 21.1; δ_B (100 MHz, $CDCl_3$) 12.4; *m*/*z* LRMS (ESI^+) 554 [$(M+H)^+$, 3%], 415.2 (16), 358.2 (18), 299.1 (100), 199.0 (32); HRMS (ESI^+) found 554.2287 ([M-H]$^+$ $C_{39}H_{28}BNO_2$ requires 554.2288).



(α-*S*,*S*)-121b

(*S*,*E*)-*N*-((*S*)-naphtho[2,1,6,7-*def*][1,3,2]dioxaborepin-4-yl)benzylidene)-1-(naphthalen-2-yl)ethanamine

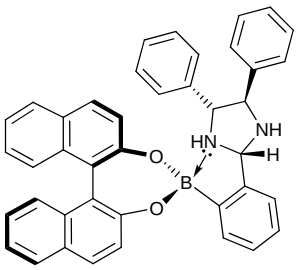
(*S*)-BINOL (*S*)-**74** (114 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(-)-1-(naphthalen-3-yl)ethanamine (*S*)-**77** (68 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a bright yellow solid (204 mg, 92%); mp 161-166 °C (dec); $[\alpha]_D^{20}$ +353.80 (*c* 1.405, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1638 (C=N); δ_H (300 MHz; $CDCl_3$) 8.38 (1H, s, C*H*N), 8.00-7.90 (4H, m, Ar*H*), 7.82-7.74 (2H, m, Ar*H*), 7.66-7.21 (16H, m, Ar*H*), 6.97 (1H, d, *J* 6.8, Ar*H*), 5.23 (1H, q, *J* 7.0, C*H*(CH_3)N), 1.97 (3H, d, *J* 7.0, C(CH_3)(H)N); δ_C (75 MHz; $CDCl_3$) 169.4 (*C*=N), 154.8, 154.3, 152.8, 137.5, 137.0, 133.9, 133.7, 133.4, 133.0, 131.3, 130.4, 130.3, 129.9, 129.5, 129.0, 128.8, 128.5, 128.2, 128.1, 127.8, 127.7, 127.4, 127.2, 126.6, 126.5, 125.8, 125.4, 125.3, 124.4, 124.0, 123.6, 123.4, 123.1, 123.0, 122.0, 117.9, 56.9 and 20.7; δ_B (100 MHz, $CDCl_3$) 12.2; *m*/*z* LRMS (ESI^+) 554 [$(M+H)^+$, 6%], 415.1 (12), 299.1 (100), 199.0 (27); HRMS (ESI^+) found 554.2282 ([M+H]$^+$ $C_{39}H_{28}BNO_2$ requires 554.2288).



(*R*,2*S*,4*S*,5*S*)-126a

(2*S*,4*S*,5*S*)-2-(2-((*R*)-naphtho[2,1,9,14-*def*][1,3,2]dioxaborepin-4-yl)phenyl)-4,5-diphenylimidazolidine

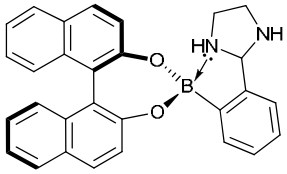
(1*S*,2*S*)-1,2-Diphenyl-1,2-ethanediamine (1*S*,2*S*)-**124** (85 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*R*)-BINOL (*R*)-**74** (114 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a bright yellow solid (233 mg, 98%), mp 220-222 °C (dec); $[\alpha]_D^{20}$ -302.19 (*c* 1.150, CH_2Cl_2); δ_H (400 MHz; $CDCl_3$) 8.01-7.93 (2H, m, Ar*H*), 7.78 (1H, d, *J* 7.8, Ar*H*), 7.55-7.22 (18H, m, Ar*H*), 7.17-7.13 (1H, m, Ar*H*), 6.89 (2H, t, *J* 6.0, Ar*H*), 6.75 (1H, d, *J* 6.0, Ar*H*), 6.69 (1H, d, *J* 8.6, Ar*H*), 6.14 (1H, dd, *J* 12.3 and 5.8, C*H*$(NH)_2$), 4.95 (1H, app t, *J* 5.8, N*H*(→B)), 4.89 (1H, dd, *J* 10.6 and 5.8, C*H*(Ph)N→B), 4.75 (1H, dd, *J* 12.3 and 10.6, C*H*(Ph)NH), 2.80 (1H, app t, *J* 12.3, N*H*); δ_C (75 MHz; $CDCl_3$); 154.6, 153.5, 153.1, 139.9, 136.3(3), 136.3(2), 133.9, 133.7, 133.5, 131.7, 130.9, 130.6, 130.5, 129.9, 129.8, 129.4, 129.2, 128.8(4), 128.8(1), 128.5(1), 128.5(0), 128.0, 127.8, 127.6, 127.4, 127.3, 125.7, 124.7, 124.4, 124.0, 123.8, 123.7(6), 123.7(5), 123.3, 123.0, 121.6, 118.2, 111.6, 85.5, 73.4, 67.3; δ_B (100 MHz, $CDCl_3$) 13.3; *m*/*z* LRMS (ESI^+) 595 [$(M+H)^+$, 39%], 395 (44), 363 (52), 309 (70), 292 (100); HRMS (ESI^+) found 595.2551 ([$M+H]^+$ $C_{41}H_{31}BN_2O_2$ requires 595.2551).



(*R*,2*S*,4*R*,5*R*)-126b

(2*S*,4*R*,5*R*)-2-(2-((*R*)-naphtho[2,1,9,14-*def*][1,3,2]dioxaborepin-4-yl)phenyl)-4,5-diphenylimidazolidine

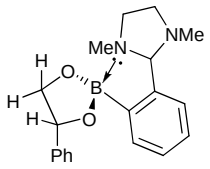
(1*R*,2*R*)-1,2-Diphenyl-1,2-ethanediamine (1*R*,2*R*)-**126** (85 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*R*)-BINOL (*R*)-**74** (114 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a bright yellow solid (222 mg, 95%), mp 220-222 °C (dec); $[\alpha]_D^{20}$ +314.61 (*c* 1.725, CH_2Cl_2); δ_H (400 MHz; $CDCl_3$) 8.00-7.93 (2H, m, Ar*H*), 7.87 (1H, d, *J* 9.0, Ar*H*), 7.82 (1H, d, *J* 8.1, Ar*H*), 7.69 (1H, d, *J* 9.1, Ar*H*), 7.50-7.03 (20H, m, Ar*H*), 6.61 (1H, d, *J* 7.1, Ar*H*), 6.17 (1H, dd, *J* 12.6 and 5.8, C*H*$(NH)_2$), 5.42 (1H, app t, *J* 5.8, N*H*(→B)), 5.17 (1H, dd, *J* 9.3 and 5.8, C*H*(Ph)N→B), 4.75 (1H, dd, *J* 12.6 and 9.3, C*H*(Ph)NH), 2.82 (1H, app t, *J* 12.6, N*H*); δ_C (75 MHz; $CDCl_3$) 154.3, 153.8, 153.0, 140.6, 137.1, 136.4, 133.9, 133.8, 133.7, 131.6, 131.4, 130.8, 129.8, 129.6, 129.4, 129.3, 129.0(4), 129.0(0), 128.9, 128.7, 128.5, 128.1, 127.8, 127.6, 127.5, 127.4, 127.3, 125.6, 124.7, 124.4, 124.0, 123.8, 123.6, 123.5, 123.3, 121.4, 118.2, 111.7, 84.7, 72.7 and 66.9; δ_B (100 MHz, $CDCl_3$) 13.8; *m*/*z* LRMS (ESI^+) 595 [$(M+H)^+$, 8%] 489.4 (50), 268.3 (84), 239.2 (100); HRMS (EI^+) found 594.2469 ($[M]^{+\bullet}$ $C_{41}H_{31}BN_2O_2$ requires 594.2473).



(*R*)-130

2-(2-((*R*)-naphtho[2,1,9,14-*def*][1,3,2]dioxaborepin-4-yl)phenyl)imidazolidine

(*R*)-BINOL (*R*)-**74** (114 mg, 0.4 mmol), 2-formylphenylboronic acid **91** (60 mg, 0.4 mmol) and ethylenediamine **129** (27 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (166 mg, 94%); $[\alpha]_D^{20}$ -30.66 (*c* 1.150, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1469 (s), 1381 (s), 1095 (s); δ_H (300 MHz; $CDCl_3$) 7.98 (1H, d, *J* 8.3, Ar*H*), 7.85-7.63 (4H, m, Ar*H*), 7.41-7.03 (7H, m, Ar*H*), 6.95-6.90 (1H, m, Ar*H*), 6.83 (1H, d, *J* 8.7, Ar*H*), 6.65 (1H, d, *J* 9.0, Ar*H*), 6.41 (1H, d, *J* 7.4, Ar*H*), 6.27 (1H, br s, N*H*(→B)), 5.74 (1H, br s, C*H*$(NH)_2$), 2.76-2.65 (1H, m, CH_{ax}(N→B)), 2.43 (1H, br s N*H*), 2.22-2.09 (1H, m, CH_{ax}(NH)) and 1.62-1.45 (2H, m, CH_{eq}(N→B) and CH_{eq}(NH)); δ_C (75 MHz; $CDCl_3$) 154.1, 153.0, 137.7, 136.2, 133.8, 131.3(4), 131.3(2), 130.9, 129.8, 129.6, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 127.7, 127.5, 125.8, 125.3, 124.3, 124.1, 123.5, 123.0, 121.1, 89.5, 47.4 and 44.7; δ_B (100 MHz, $CDCl_3$) 11.9; *m*/*z* LRMS (ESI^+) 443 [$(M+H)^+$, 2%], 463.3 (10), 241.3 (30), 189.0 (100), 157.0 (73), 61.3 (58); HRMS (ESI^-) found 441.1780 ([M-H] $C_{29}H_{23}BN_2O_2$ requires 441.1785).

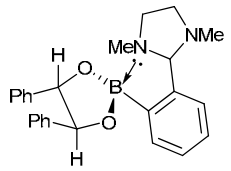


(*R*)-132

1,3-dimethyl-2-(2-((*R*)-4-phenyl-1,3,2-dioxaborolan-2-yl)phenyl)imidazolidine

(*R*)-1-Phenyl-1,2-ethanediol (*R*)-**102** (51 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and *N*,*N*'-dimethylethylamine **131** (43 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The

sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (116 mg, 90%); $[\alpha]_D^{20}$ +49.31 (*c* 1.600, CH_2Cl_2); ν_{max} (film)/cm^{-1} 2859 (s), 2789 (s), 1456 (s), 1223 (s); δ_H (300 MHz; $CDCl_3$) 7.67 (1H, d, *J* 6.8, Ar*H*), 7.53-7.52 (2H, m, Ar*H*), 7.43-7.39 (2H, m, Ar*H*), 7.36-7.31 (3H, m, Ar*H*), 7.24 (1H, d, *J* 7.8, Ar*H*), 5.28 (1H, dd, *J* 8.6 and 6.6, C*H*(Ph)O), 4.45 (1H, dd, *J* 8.6 and 6.6, CH_AH$_B$O), 4.40 (1H, s, C*H*$(NCH_3)_2$), 3.87 (1H, app t, *J* 8.6, CH$_A$*H*$_B$O), 3.72-3.66 (1H, m, CH_{ax}(N→B)), 3.62-3.55 (1H, m, C$H_{ax}$$(NCH_3)$), 2.95-2.87 (2H, m, C$H_{eq}$(N→B) and C$H_{eq}$$(NCH_3)$), 2.66 (3H, s, (N→B)C$H_3$), 2.65 (3H, s, NC$H_3$); δ_C (75 MHz; $CDCl_3$) 143.8, 140.7, 131.9, 129.3, 129.1, 129.0, 128.7, 128.5, 128.2, 127.5, 126.2, 124.2, 95.3, 78.0, 72.7, 54.1, 53.9, 42.5 and 42.3; δ_B (100 MHz, $CDCl_3$) 16.1; *m*/*z* LRMS (ESI^+) 323 [$(M+H)^+$, 66%], 266.1 (11), 219.1 (34), 191.1 (100), 175.1 (9); HRMS (ESI^+) found 323.1924 ([M+H]$^+$ $C_{19}H_{23}BN_2O_2$ requires 323.1925).

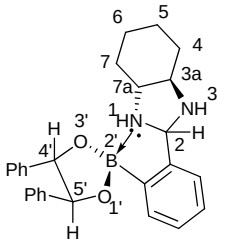


(4S,5S)-133

1,3-dimethyl-2-(2-((4*S*,5*S*)-4,5-diphenyl-1,3,2-dioxaborolan-2-yl)phenyl) imidazolidine

(1*S*,2*S*)-Hydrobenzoin (1*S*,2*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and *N*,*N*'-dimethylethylamine **131** (43 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (156 mg, 98%); $[\alpha]_D^{20}$ +111.73 (*c* 2.175, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1495 (s), 1214 (s), 1059 (s); δ_H (300 MHz; $CDCl_3$) 7.94 (1H, d, *J* 7.6, Ar*H*), 7.54-7.28 (7H, m, Ar*H*), 7.18-7.05 (6H, m, Ar*H*), 4.98 (2H, s, CH_A(O)CH_B(O)), 4.38 (1H, s, C*H*$(NCH_3)_2$), 3.87-3.60 (2H, m, CH_{ax}(N→B) and C$H_{ax}$$(NCH_3)$), 3.07-2.97 (2H, C$H_{eq}$(N→B) and C$H_{eq}$$(NCH_3)$), 2.82 (3H, s, C$H_3$(N→B)), and 2.70 (3H, s, NCH_3); δ_C (75 MHz; $CDCl_3$) 141.9, 141.1, 132.6, 130.3, 130.1, 129.5, 129.4, 128.6, 128.4, 127.8, 127.6, 127.4, 127.3, 127.1, 126.9, 126.5, 124.7, 124.1, 95.5, 86.0, 82.3, 54.4, 53.6, 43.2, and 42.4; δ_B (100 MHz, $CDCl_3$) 15.3; *m*/*z* LRMS (ESI^+) 399 [$(M+H)^+$, 45%],

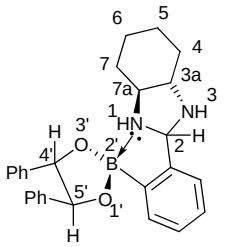
191.1 (100), 175.1 (19); HRMS (ESI$^+$) found 399.2243 ([M+H]$^+$ $C_{25}H_{27}BN_2O_2$ requires 399.2244).



(2*S*,3a*R*,4′*S*,5′*S*,7a*R*)-134a

(3a*R*,7a*R*)-octahydro-2-(2-((4′*S*,5′*S*)-4′,5′-diphenyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-*H*-benzo[*d*]imidazole

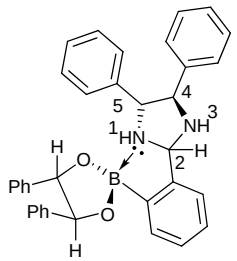
(1*S*,2*S*)-Hydrobenzoin (1*S*,2*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **91** (60 mg, 0.4 mmol) and (1*R*,2*R*)-cyclohexane-1,2-diamine (1*R*,2*R*)-**125** (46 mg, 0.4 mmol) in were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a light yellow solid (164 mg, 98%); m.p. 147-149 °C (dec); $[\alpha]_D^{20}$ +75.00 (*c* 1.625, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3054 (s), 1455 (s), 1257 (s); δ_H (500 MHz; $CDCl_3$) 7.63 (1H, d, Ar*H*), 7.51-6.98 (12H, m, Ar*H*), 6.63 (1H, d, Ar*H*), 6.49 (1H, br s, C*H*(NH)$_2$), 5.08 (1H, d, *J* 7.6, CH_A(O)CH_B(O)), 4.89 (1H, s, N*H*(→B)), 4.54 (1H, d, *J* 7.6, CH_A(O)CH_B(O)), 2.46 (1H, q, *J* 11.0, C*H*(N→B)), 2.22 (1H, br s, N*H*), 1.99 (1H, d, *J* 11.7, C*H*), 1.74 (1H, d, *J* 11.7, C*H*), 1.61 (1H, d, *J* 13.2, C*H*), 1.38-1.04 (4H, m, C_2H_4), 0.89 (1H, q, *J* 13.2, C*H*), -0.14 (1H, q, *J* 11.0, C*H*NH); δ_C (75 MHz; $CDCl_3$) 142.1, 141.6, 130.2, 130.1, 130.0, 129.5, 129.4(9), 129.4(3), 129.1, 129.0, 128.9, 128.7, 128.1, 127.2, 127.1, 126.4, 125.7, 123.2, 87.8, 86.7, 83.4, 65.9, 63.8, 29.7, 27.3, 24.9 and 24.2; δ_B (100 MHz, $CDCl_3$) 12.6; *m*/*z* LRMS (ESI$^+$) 425 [(M+H)$^+$, 22%], 345.2 (19), 303.3 (100); HRMS (ESI$^+$) found 425.2395 ([M+H]$^+$ $C_{27}H_{29}BN_2O_2$ requires 425.2395).



(2*S*,3a*S*,4′*S*,5′*S*,7a*S*)-134b

(3a*S*,7a*S*)-octahydro-2-(2-((4′*S*,5′*S*)-4′,5′-diphenyl-1,3,2-dioxaborolan-2-yl)phenyl)-1-*H*-benzo[*d*]imidazole

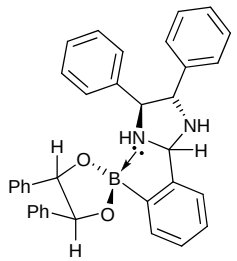
(1*S*,2*S*)-Hydrobenzoin (1*S*,2*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (1*S*,2*S*)-cyclohexane-1,2-diamine (1*S*,2*S*)-**125** (46 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a gold solid (166 mg, 99%); m.p. 148-150 °C (dec); $[\alpha]_D^{20}$ -88.53 (*c* 1.825, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3054 (s), 1455 (s), 1257 (s); δ_H (500 MHz; $CDCl_3$) 7.61-7.45 (6H, m, Ar*H*), 7.30-7.23 (6H, m, Ar*H*), 7.02 (1H, t, *J* 7.3, Ar*H*), 6.58 (1H, d, *J* 7.3, Ar*H*), 6.21 (1H, br s, C*H*(NH)$_2$), 5.18 (1H, s, N*H*(→B)), 4.78 (1H, d, *J* 8.8, CH_A(O)CH_B(O)), 4.66 (1H, d, *J* 8.8, CH_A(O)CH_B(O)), 2.39 (1H, q, *J* 10.4, C*H*(N→B)), 2.23 (1H, br s, N*H*), 1.97 (1H, d, *J* 10.4, C*H*), 1.89 (1H, d, *J* 12.9, C*H*), 1.63 (1H, d, *J* 12.9, C*H*), 1.44 (1H, m, C*H*), 1.32-0.90 (4H, m, C_2H_4) and 0.10 (1H, q, *J* 10.4, C*H*(NH)); δ_C (75 MHz; $CDCl_3$) 141.9(4), 141.9(0), 132.8, 132.6, 132.1, 132.0, 131.7, 131.1, 130.8, 130.6, 130.5, 130.1, 129.1, 128.9, 128.6, 127.7, 126.4, 122.7, 87.6, 86.2, 83.4, 66.6, 63.8, 29.5, 27.7, 25.2 and 24.5; δ_B (100 MHz, $CDCl_3$) 13.1; *m*/*z* LRMS (ESI$^+$) 425 [(M+H)$^+$, 3%], 407.3 (13), 303.3 (100); HRMS (ESI$^+$) found 425.2399 ([M+H]$^+$ $C_{27}H_{29}BN_2O_2$ requires 425.2395).



(4′*S*,4*R*,5*R*,5'*S*)-135a

(4*R*,5*R*)-4,5-diphenyl-2-(2-((4′*S*,5′*S*)-4′,5′-diphenyl-1,3,2-dioxaborolan-2-yl)phenyl)imidazolidine

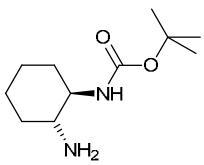
(1*S*,2*S*)-Hydrobenzoin (1*S*,2*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (1*R*,2*R*)-1,2-diphenylethane-1,2-diamine (1*R*,2*R*)-**124** (85 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a pale grey solid (206 mg, 99%); m.p. 184-186 °C; $[\alpha]_D^{20}$ -149.66 (*c* 2.225, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3054 (s), 1449 (s), 1272 (s); δ_H (500 MHz; $CDCl_3$) 7.73 (1H, d, *J* 7.3, Ar*H*), 7.48 (1H, t, *J* 7.3, Ar*H*), 7.40-7.18 (13H, m, Ar*H*), 7.12-7.04 (9H, m, Ar*H*), 6.39 (1H, t, *J* 6.3, N*H*(→B)), 5.70 (1H, dd, *J* 10.7 and 6.3, C*H*(NH)$_2$), 4.92 (1H, dd, *J* 10.7 and 6.3, C*H*(Ph)(N→B)), 4.77 (2H, br s, CH_A(O)CH_B(O)), 3.95 (1H, br t, *J* 10.7, C*H*(Ph)(NH)), 2.34 (1H, br t, *J* 10.7, N*H*); δ_C (75 MHz; $CDCl_3$) 141.2, 140.9, 140.8(7), 140.8(5), 140.8(1), 140.6, 140.3, 140.0, 139.9, 139.8, 139.6, 139.2, 138.7, 138.4, 137.7, 136.8, 136.6, 130.4, 129.7, 129.3, 129.2, 128.9(4), 128.9(3), 128.8(8), 128.8(2), 127.8, 127.7, 127.4, 127.2, 123.4, 85.7, 83.4, 73.3, 66.8 and 31.4; δ_B (100 MHz, $CDCl_3$) 14.0; *m*/*z* HRMS (ESI$^+$) found 523.2553 ([M+H]$^+$ $C_{35}H_{31}BN_2O_2$ requires 523.2553).



(4′*S*,4*S*,5*S*,5'*S*)-135b

(4*R*,5*R*)-4,5-diphenyl-2-(2-((4′*S*,5′*S*)-4′,5′-diphenyl-1,3,2-dioxaborolan-2-yl)phenyl)imidazolidine

(1*S*,2*S*)-Hydrobenzoin (1*S*,2*S*)-**112** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (1*S*,2*S*)-1,2-diphenylethane-1,2-diamine (1*S*,2*S*)-**124** (85 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a white solid (203 mg, 98%); m.p. 184-186 °C; $[\alpha]_D^{20}$ -144.33 (*c* 1.975, CH_2Cl_2); ν_{max} (film)/cm^{-1} 3054 (s), 1449 (s), 1272 (s); δ_H (500 MHz; $CDCl_3$) 7.67 (1H, d, *J* 7.6, Ar*H*), 7.47 (1H, dt, *J* 6.9 and 1.6, Ar*H*), 7.43-7.26 (8H, m, Ar*H*), 7.15-6.80 (14H, m, Ar*H*), 5.91 (1H, br s, N*H*(→B)), 5.22 (1H, br s, C*H*(NH)$_2$), 4.75 (1H, br s, C*H*(Ph)(N→B)), 4.68-4.52 (3H, m, CH_B(Ph(NH)) and CH_A(O)CH_B(O)) and 2.55 (1H, br s, N*H*); δ_C (75 MHz; $CDCl_3$) 141.6, 141.4, 141.3, 141.1, 141.0, 139.8, 139.7, 139.6, 139.2, 139.0, 138.7, 138.6(3), 138.6(1), 138.4, 138.0, 137.3, 135.8, 131.7, 130.1, 130.0, 129.5, 129.2, 129.1, 128.9, 128.5, 128.2, 127.7, 127.4, 126.9, 123.6, 86.5, 83.1, 74.5, 67.9 and 31.4; δ_B (100 MHz, $CDCl_3$) 17.3; *m*/*z* HRMS (ESI$^+$) found 523.2563 ([M+H]$^+$ $C_{35}H_{31}BN_2O_2$ requires 523.2553).

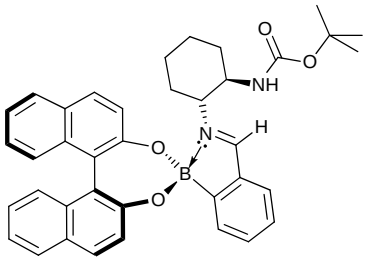


(1*R*,2*R*)-137

***tert*-butyl-(1*R*,2*R*)-2-aminocyclohexylcarbamate**

(1*R*,2*R*)-Cyclohexane-1,2-diamine (1*R*,2*R*)-**125** (0.90 g, 7.9 mmol) and 2-(*tert*-butoxycarbonyloxyimino)-2-phenylacetonitrile **136** (1.95 g, 7.9 mmol) were heated to

reflux in absolute ethanol (50 mL) for 24 hours. The solution was then allowed to cool to room temperature and the solvent removed *in vacuo*. The crude product was re-dissolved in CH_2Cl_2 (30 mL), extracted with water (3 x 20 mL) and brine (2 x 20 mL) before being dried ($MgSO_4$) and the CH_2Cl_2 evaporated to afford the title compound as a brown solid (156 mg, 98%); m.p. 98-101 °C; $[\alpha]_D^{20}$ -12.00 (*c* 1.150, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1707 (C=O); δ_H (300 MHz; $CDCl_3$) 8.03 (1H, s, N*H*(Boc)), 5.08 (2H, br s, NH_2), 3.80 (1H, m, C*H*(NHBoc), 3.15 (1H, m, C*H*NH_2), 1.80-1.72 (2H, m, CH_2CNH), 1.57-1.41 (2H, m, CH_2CNH_2), 1.38 (9H, s, C(CH_3)$_3$), 1.32-1.06 (4H, m, C_2H_4); δ_C (75 MHz; $CDCl_3$) 156.1 (*C*=O), 79.3, 61.0, 55.0, 35.4, 32.3, 29.1 (3C, C(*C*H_3)$_3$) and 23.6 (2C, *C*$_2$H$_4$); *m*/*z* LRMS (ESI$^+$) 216 [(M+H), 100%], 159.1 (5); HRMS (ESI$^+$) found 216.1777 ([M+H]$^+$ $C_{11}H_{22}N_2O_2$ requires 216.1780).

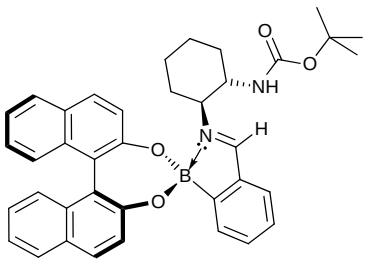


(*S*,1*R*,2*R*)-138a

***tert*-butyl-(*E*,1*R*,2*R*)-2-((2-((*S*)-naphtho[15,10,1,2-*def*][1,3,2]dioxaborepin-4-yl) phenyl)methyleneamino)cyclohexylcarbamate**

tert-butyl-(1*R*,2*R*)-2-aminocyclohexylcarbamate (1*R*,2*R*)-**138** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-BINOL (*S*)-**74** (114 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (236 mg, 99%), m.p. 170-175 °C (dec); $[\alpha]_D^{20}$ -429.29 (*c* 1.050, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1708 (C=O), 1620 (C=N); δ_H (400 MHz; $CDCl_3$) 8.56 (1H, s, C*H*N), 7.82-7.75 (4H, m, Ar*H*), 7.48-7.45 (1H, m, Ar*H*), 7.34-7.05 (10H, m, Ar*H*), 6.78-6.74 (1H, m, Ar*H*), 4.66 (1H, d, *J* 10.0, N*H*CO_2^tBu), 3.89-3.76 (1H, m, C*H*NHBoc), 3.20 (1H, dt, *J* 11.3 and 3.8, C*H*N=C), 2.36-2.30 (1H, m, CH_{eq}CNHBoc), 1.99-1.93 (1H, m, CH_{eq}CN=C), 1.58-0.99 (14H, m, C_4H_5 and CO_2^tBu), 0.83-0.67 (1H, m, CH_2); δ_C (75 MHz; $CDCl_3$) 169.6 (*C*=O), 154.9

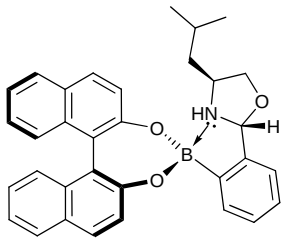
(*C*=N), 137.6, 134.0, 133.6, 131.5, 130.7, 130.5, 130.4, 130.3, 130.2, 130.0, 129.5, 128.9, 128.8, 128.3, 128.1, 127.7, 127.4, 126.9, 125.5, 124.8, 123.9, 123.7, 123.6, 123.2, 123.1, 122.6, 118.3, 80.8, 63.9, 52.2, 35.3, 34.0, 25.3 and 25.1 (3C, C(*C*H$_3$)$_3$); δ_B (100 MHz, $CDCl_3$) 12.0; *m*/*z* LRMS (CI^+) 597 [$(M+H)^+$, 23%], 268.2 (100), 239.1 (97), 211.2 (76); HRMS (EI^+) found 595.2351 ($[M]^{+\bullet}$ $C_{38}H_{37}BN_2O_4$ (^{10}B) requires 595.2353).



(*S*,1*S*,2*S*)-139b

***tert*-butyl (*E*,1*S*,2*S*)-2-((2-((*S*)-naphtho[15,10,1,2-*def*][1,3,2]dioxaborepin-4-yl) phenyl)methyleneamino)cyclohexylcarbamate**

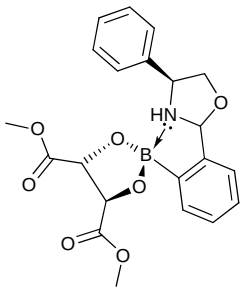
tert-butyl-(1*S*,2*S*)-2-aminocyclohexylcarbamate (1*S*,2*S*)-**138** (86 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-BINOL (*S*)-**74** (114 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (222 mg, 95%), m.p. 170-173 °C (dec); $[\alpha]_D^{20}$ +414.00 (*c* 1.975, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1707 (C=O), 1617 (C=N); δ_H (400 MHz; $CDCl_3$) 8.47 (1H, s, C*H*N), 7.85-7.73 (4H, m, Ar*H*), 7.45 (1H, app d, *J* 7.5, Ar*H*), 7.36-7.06 (10H, m, Ar*H*), 6.82 (1H, app d, *J* 6.8, Ar*H*), 5.43 (1H, d, *J* 8.1, N*H*COO^{t}Bu), 3.60-3.48 (1H, m, C*H*NHBoc), 3.09 (1H, dt, *J* 11.9 and 3.4, C*H*N=C), 2.34-2.29 (1H, m, CH_{eq}CNHBoc), 1.95-1.91 (1H, m, CH_{eq}CN=C), 1.76-0.71 (15H, m, C_4H_6 and $CO_2{}^tBu$) δ_C (75 MHz; $CDCl_3$) 169.4 (*C*=O), 156.7 (*C*=N), 137.6, 134.2, 133.6(4), 133.6(1), 131.4, 130.8, 130.5, 130.3, 129.8, 129.4, 129.2, 128.8, 128.5, 128.2, 127.5, 127.2, 125.8, 125.7, 125.0, 124.9, 124.2, 123.9, 123.7, 123.6, 122.6, 122.3, 79.6, 61.0, 55.5, 34.1, 33.3, 28.6, 25.1 and 25.0 (3C, C(*C*H$_3$)$_3$); δ_B (100 MHz, $CDCl_3$) 12.1; *m*/*z* LRMS (ESI^+) 597 [$(M+H)^+$, 10%], 561.4 (26), 347.2 (100), 329.2 (85), 273.1 (24); HRMS (ESI^+) found 619.2741 ($[M+Na]^+$ $C_{38}H_{37}BN_2O_4$ requires 619.2740).



(*S*,2*R*,4*S*)-**154**

(4*S*)-4-isobutyl-2-(2-((*S*)-naphtho[2,1,9,14-*def*][1,3,2]dioxaborepin-4-yl)phenyl)oxazolidine

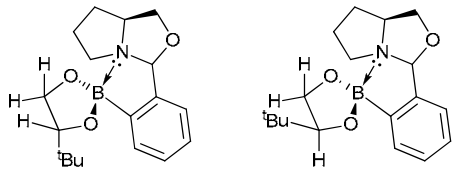
(*S*)-BINOL (*S*)-**74** (114 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-leucinol (*S*)-**145** (47 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the title compound selectively crystallised from the crude solution as pale cream needles (32 mg, 16%); mp 161-163 °C (dec); $[\alpha]_D^{20}$ +218.57 (*c* 2.355, CH_2Cl_2); ν_{max} (film)/cm^{-1} 2959 (s), 1467 (s), 1173 (s); δ_H (300 MHz; $CDCl_3$) 7.86-7.78 (4H, m, Ar*H*), 7.30-7.03 (11H, m, Ar*H*), 6.89 (1H, d, *J* 8.1, Ar*H*), 6.49 (1H, m, N*H*), 5.28 (1H, br s, C*H*(NH)(O)), 4.31 (1H, app d, *J* 11.3, CH_AH_BO), 3.88-3.81 (1H, m, CH_AH_BO), 3.39-3.31 (1H, m, C*H*(NH)), 2.11-2.00 (1H, m, $CH(CH_3)_2$), 1.63-1.47 (2H, m, $CH_AH_BC(CH_3)_2$), 0.88-0.81 (6H, m, $C(CH_3)_2$); δ_C (75 MHz; $CDCl_3$) 153.9, 153.2, 136.6, 134.1, 133.9, 133.5, 131.0, 129.7, 129.4, 128.9, 128.7, 128.6, 128.3, 127.4, 126.7, 126.2, 126.0, 125.9, 125.8(7), 125.8(0), 124.1, 123.8, 123.5, 123.1, 121.5, 112.2, 96.0, 66.6, 62.5, 40.6, 24.7, 23.0 and 22.9; δ_B (100 MHz, $CDCl_3$) 11.6; *m*/*z* LRMS (ESI^+) 500 [$(M+H)^+$, 9%], 268.2 (53), 239.2 (45), 214.2 (48), 158.1 (100); HRMS (ESI^+) found 499.2425 (^{10}B) ($[M+H]^+$ $C_{33}H_{30}BNO_3$ requires 499.2428).



(4*S*,4′*R*,5′*R*)-155

(4′*R*,5′*R*)-dimethyl-2-(2-((4*S*)-4-phenyloxazolidin-2-yl)phenyl)-1,3,2-dioxaborolane-4′,5′-dicarboxylate

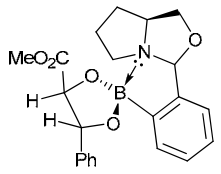
Dimethyl-L-tartrate (1*R*,2*R*)-**108** (71 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-phenylglycinol (*S*)-**150** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a white solid (156 mg, 95%); m.p. 125-127 °C; $[\alpha]_D^{20}$ -41.66 (*c* 1.470, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1735 (C=O); δ_H (300 MHz; $CDCl_3$); 7.80-7.77 (1H, m, Ar*H*), 7.49-7.38 (8H, m, Ar*H*), 6.66 (1H, d, *J* 6.1, C*H*(NH)(O)), 6.43 (1H, br t, *J* 6.1, N*H*), 4.76-4.71 (1H, m, C*H*(Ph)), 4.70-4.55 (2H, br s, CH_A(O)CH_B(O)), 4.20 (1H, dd, *J* 9.1 and 4.0, $CH_{eq}H_{ax}O$), 4.02 (1H, dd, *J* 9.1 and 7.8, $CH_{ax}H_{eq}O$), 3.97-3.75 (3H, br s, CO_2CH_3) and 3.54-3.26 (3H, br s, CO_2CH_3); δ_C (75 MHz; $CDCl_3$) 142.4, 139.1, 137.8, 137.4, 137.0, 135.5, 132.3, 132.1, 131.7, 130.3, 129.8, 129.4, 128.5, 123.4, 95.1, 77.9, 72.5, 61.0, 60.7, 53.4 and 53.2; δ_B (100 MHz, $CDCl_3$) 13.5; *m*/*z* LRMS (CI$^+$) 412 [(M+H)$^+$, 73%], 196.1 (47), 164.1 (44), 120.1 (61), 106.0 (100); HRMS (ESI$^+$) found 412.1563 ([M+H]$^+$ $C_{21}H_{22}BNO_7$ requires 412.1561).

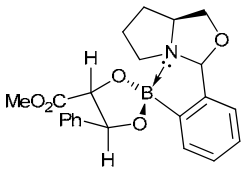


(4′*R*,7a*S*)-**158a and** (4′*S*,7a*S*)-**158b**

A 50 : 50 mixture of (7a*S*)-3-(2-((4′*R*)-4′-*tert*-butyl-1,3,2-dioxaborolan-2-yl)phenyl)-hexahydropyrrolo[1,2-*c*]oxazole and (7a*S*)-3-(2-((4′*S*)-4′-*tert*-butyl-1,3,2-dioxaborolan-2-yl)phenyl)-hexahydropyrrolo[1,2-*c*]oxazole

3,3-Dimethyl-1,2-butane diol (*rac*)-**105** (47 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(+)-2-pyrrolidinemethanol (*S*)-**157** (40 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (120 mg, 95%); ν_{max} (film)/cm^{-1} 2955 (s), 2873 (s), 1109 (s); δ_H (300 MHz; $CDCl_3$) 7.43-7.37 (2H, m, Ar*H*), 7.26-7.13 (6H, m, Ar*H*), 5.74 (1H, s, C*H*(N)(O)), 5.70 (1H, s, C*H*(N)(O)), 4.13-4.06 (2H, m, C*H*CH_2O), 3.95-3.60 (12H, m, 2 x CH_AH_BO, 2 x CH_AH_BN, 2 x CH_AH_BOB and 2 x C*H*(^{t}Bu)(O)), 3.04-2.91 (2H, m, CH_AH_BN), 2.19-1.65 (8H, m, CH_2CH_2CH), 0.90 (9H, s, C(CH_3)$_3$) and 0.86 (9H, s, C(CH_3)$_3$); δ_C (75 MHz; $CDCl_3$) 140.7, 140.6, 130.9, 129.6, 129.5, 128.2, 128.1(9), 128.1(6), 128.1(0), 127.5, 123.2, 123.0, 102.7, 102.6, 84.5, 84.0, 71.8, 71.7, 67.0, 66.7, 64.5, 64.4, 55.1, 54.9, 34.3, 34.2, 32.6, 32.4, 26.7, 26.4, 25.9 (3C, C(*C*H$_3$)$_3$) and 25.8 (3C, C(*C*H$_3$)$_3$); δ_B (100 MHz, $CDCl_3$) 15.4; *m*/*z* LRMS (ESI$^+$) 316 [(M+H)$^+$, 100%], 299.2 (32), 280.2 (16), 239.2 (10); HRMS (ESI$^+$) found 316.2075 ([M+H]$^+$ $C_{18}H_{26}BNO_3$ requires 316.2076).

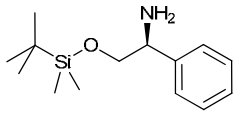




(4′*S*,5′*R*,7a*S*)-**159a and** (4′*R*,5′*S*,7a*S*)-**159b**

A 50 : 50 mixture of methyl-2-(2-((7a*S*)-hexahydropyrrolo[1,2-c]oxazol-3-yl)phenyl)-(4′*S*,5′*R*)-5′-phenyl-1,3,2-dioxaborolane-4′-carboxylate and methyl-2-(2-((7a*S*)-hexahydropyrrolo[1,2-c]oxazol-3-yl)phenyl)-(4′*S*,5′*R*)-5′-phenyl-1,3,2-dioxaborolane-4′-carboxylate.

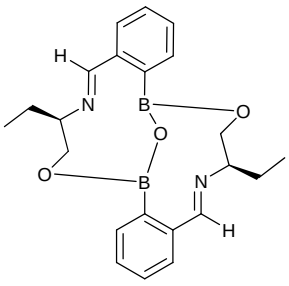
(*rac*)-Methyl-2,3-dihydroxy-3-phenylpropionate (*rac*)-**106** (78 mg, 0.4 mmol), 2-formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-(+)-2-pyrrolidinemethanol (*S*)-**157** (40 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil as a 50 : 50 mixture (154 mg, 98%); ν_{max} (film)/cm^{-1} 1745 (C=O); δ_H (300 MHz; $CDCl_3$) 7.56 (1H, d, *J* 7.4, Ar*H*), 7.50-7.44 (3H, m, Ar*H*), 7.37-7.16 (14H, m, Ar*H*), 5.86 (1H, s, C*H*(N)(O)), 5.80 (1H, s, C*H*(N)(O)), 5.11 (1H, d, *J* 7.4, C*H*(Ph)), 5.04 (1H, d, *J* 7.9, C*H*(Ph)), 4.48 (1H, d, *J* 7.4, C*H*(CO_2CH_3)), 4.43 (1H, d, *J* 7.9, C*H*(CO_2CH_3)), 4.41-4.34 (1H, m, C*H*CH_2O), 4.23-4.15 (1H, m, C*H*CH_2O), 3.71-3.57 (12H, m, 2 x CO_2CH_3, 2 x CH_AH_BO, 2 x CH_AH_BO and 2 x CH_AH_BN), 3.19-3.12 (1H, m, CH_AH_BN), 3.05-2.97 (1H, m, CH_AH_BN), 2.42-2.26 (1H, m, CH_AH_BCH), 2.20-2.09 (1H, m, CH_AH_BCH) and 2.05-1.66 (6H, m, 2 x CH_AH_BCH and 2 x CH_2CH_2CH); δ_C (75 MHz; $CDCl_3$) 174.3, 173.0, 143.0, 142.5, 140.5, 140.0, 137.4, 134.2, 130.6, 130.5, 130.3, 129.9, 129.8, 129.0, 128.9(8), 128.9(5), 128.9(2), 128.8, 128.6, 128.5, 128.2, 126.5, 126.3, 123.1, 122.8, 120.3, 118.0, 117.6, 104.0, 103.3, 83.2, 81.7, 81.1, 72.2, 65.2, 65.2, 55.7, 55.1, 52.4, 52.1, 32.6, 32.3, 26.4 and 26.3; δ_B (100 MHz, $CDCl_3$) 14.5; *m*/*z* LRMS (ESI$^+$) 394 [(M+H)$^+$, 100%], 306.2 (11), 280.2 (7); HRMS (ESI$^+$) found 394.1822 ([M+H]$^+$ $C_{22}H_{24}BNO_5$ requires 394.1820).



(*S*)-**160**

(*S*)-2-(*tert*-butyldimethylsilyloxy)-1-phenylethanamine

tert-Butyldimethylsilyl chloride (301 mg, 2.0 mmol), (*S*)-2-phenylglycinol (*S*)-**150** (274 mg, 2.0 mmol) and Et_3N (0.56 mL, 4.0 mmol) were stirred in CH_2Cl_2 (20 mL) at room temperature for 18 hours. The crude solution was washed with brine (2 x 10 mL) and saturated sodium bicarbonate solution (2 x 10 mL) before drying ($MgSO_4$), filtration and evaporation afforded the title compound as a colourless oil (467 mg, 93%); $[\alpha]_D^{20}$ +5.44 (*c* 1.100, CH_2Cl_2); υ_{max} (film)/cm^{-1} 1089 (O-Si), 700 (O-Si); δ_H (300 MHz, $CDCl_3$) 7.36-7.14 (5H, m, Ar*H*), 4.02 (1H, dd, *J* 8.4 and 4.0, C*H*Ph), 3.68 (1H, dd, *J* 9.8 and 4.0, CH_AH$_B$(O)), 3.48 (1H, dd, *J* 9.8 and 8.4, CH$_A$$H_B$(O)), 1.73 (2H, br s, NH_2), 0.88 (9H, s, C(CH_3)$_3$) and 0.00 (6H, s, Si(CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 142.9, 128.7, 128.5, 127.7, 127.6, 127.3, 68.4, 51.1, 18.6 (3C, C(*C*H$_3$)$_3$) -2.8 and -5.1 (2C, Si(*C*H$_3$)$_2$); *m*/z HRMS (ESI$^+$) found 253.1790 ([M+H]$^+$ $C_{14}H_{25}NOSi$ requires 253.1797).

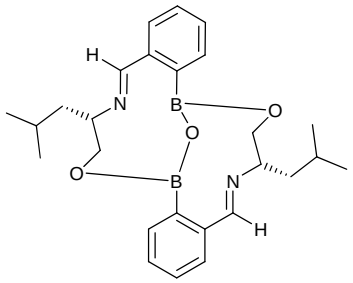


(*R*,*R*)-**171**

(*R*,*E*)-2-((1-hydroxybutan-2-yl-imino)methyl)phenyldiboronate

2-Formylphenylboronic acid **91** (60 mg, 0.4 mmol) and (*R*)-2-amino-1-butanol (*R*)-**143** (38 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (76 mg, 98%); $[\alpha]_D^{20}$ +14.67 (*c* 1.875, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1628 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (2H, s, C*H*N), 7.50 (2H, t, *J* 7.4, Ar*H*), 7.36-7.26 (4H, m, Ar*H*), 7.12-7.07 (2H, m,

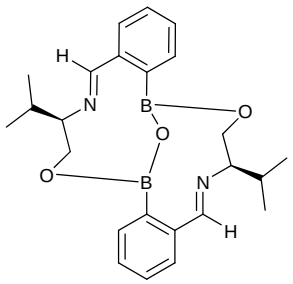
Ar*H*), 4.33 (2H, dd, *J* 12.0 and 1.7, CH_AH_B(O)), 3.78 (2H, dd, *J* 12.0 and 1.7, CH_AH_B(O)), 3.51 (2H, m, C*H*(Et)(N)), 2.20-2.09 (4H, m, CH_AH_BCH_3) and 0.93 (6H, t, *J* 7.6, CH_3); δ_C (75 MHz; $CDCl_3$) 167.3 (*C*=N), 136.9, 133.5, 133.3, 129.3, 127.2, 126.2, 70.7, 62.4, 24.8 and 11.5; δ_B (100 MHz; $CDCl_3$) 11.2; *m*/*z* LRMS (CI^+) 389 [$(M+H)^+$, 6%], 188.2 (50), 106.0 (46), 72.0 (100); HRMS (EI^+) found 388.2126 ($[M]^{+\bullet}$ $C_{22}H_{26}B_2N_2O_3$ requires 388.2128).



(*S*,*S*)-**172**

(*S*,*E*)-2-((1-hydroxy-4-methylpentan-2-ylimino)methyl)phenyldiboronate

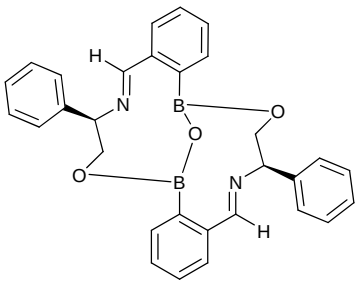
2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-leucinol (*S*)-**145** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow solid (83 mg, 93%); m.p. 116-120 °C (dec); $[\alpha]_D^{20}$ -26.10 (*c* 1.025, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1628 (C=N); δ_H (300 MHz; $CDCl_3$) 8.16 (2H, s, C*H*N), 7.51 (2H, d, *J* 7.4, Ar*H*), 7.36-7.27 (4H, m, Ar*H*), 7.11 (2H, dt, *J* 7.4 and 1.1, Ar*H*), 4.35 (2H, dd, *J* 11.9 and 1.7, CH_AH_B(O)), 3.81-3.73 (4H, m, CH_AH_B(O) and C*H*(N)), 2.16-2.06 (2H, m, CH_AH_BC(N)), 2.02-1.92 (2H, m, CH_AH_BC(N)), 1.72-1.63 (2H, m, C*H*$(CH_3)_2$) and 0.90 (12H, app t, *J* 6.8, C$(CH_3)_2$); δ_C (75 MHz; $CDCl_3$) 166.9 (*C*=N), 136.9, 133.5, 133.1, 129.4, 127.2, 126.1, 66.7, 62.5, 40.4, 24.8, 23.0 and 22.9; δ_B (100 MHz; $CDCl_3$) 11.5; *m*/*z* LRMS (ESI^+) 445 [$(M+H)^+$, 14%], 412.4 (100), 292.2 (66), 227.2 (15); HRMS (ESI^+) found 445.2833 ($[M+H]^+$ $C_{26}H_{34}B_2N_2O_3$ requires 445.2832).



(*R*,*R*)-**149**

(*R*,*E*)-2-((1-hydroxy-3-methylbutan-2-ylimino)methyl)phenyldiboronate

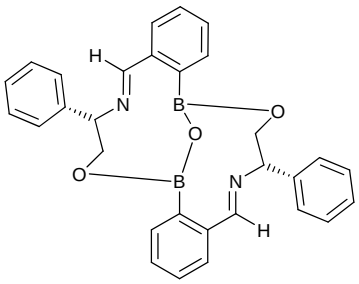
2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*R*)-2-amino-3-methyl-1-butanol (*R*)-**146** (45 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (81 mg, 98%); $[\alpha]_D^{20}$ +22.77 (*c* 1.520, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1628 (C=N); δ_H (300 MHz; $CDCl_3$) 8.08 (2H, s, C*H*N), 7.51 (2H, d, *J* 7.4, Ar*H*), 7.35-7.27 (4H, m, Ar*H*), 7.11 (2H, dt, *J* 7.4 and 1.1, Ar*H*), 4.26 (2H, dd, *J* 12.2 and 1.3, $CH_AH_B(O)$), 3.98 (2H, dd, *J* 12.2 and 1.3, $CH_AH_B(O)$), 3.13 (2H, m, C*H*(^{i}Pr)(N)), 2.96-2.83 (2H, m, C*H*(CH_3)$_2$), 1.02 (6H, d, *J* 6.8, C(C*H*$_3$)(CH_3)) and 0.88 (6H, d, *J* 6.8, C(CH_3)(C*H*$_3$)); δ_C (75 MHz; $CDCl_3$) 167.3 (*C*=N), 136.8, 133.6, 129.4, 127.2, 127.0, 126.2, 76.0, 60.9, 27.0, 21.1 and 19.4; δ_B (100 MHz; $CDCl_3$) 10.7; *m*/*z* LRMS (ESI^+) 417 [$(M+H)^+$, 13%], 283.2 (100), 200.1 (2); HRMS (ESI^+) found 417.2521 ($[M+H]^+$ $C_{24}H_{30}B_2N_2O_3$ requires 417.2518).



(*R*,*R*)-**173**

(*R*,*E*)-2-((2-hydroxy-1-phenylethylimino)methyl)phenyldiboronate

2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*R*)-2-phenylglycinol (*R*)-**150** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (88 mg, 91%); $[\alpha]_D^{20}$ +21.10 (*c* 2.005, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1627 (C=N); δ_H (300 MHz; $CDCl_3$) 7.66-7.63 (4H, m, C*H*N and Ar*H*), 7.43-7.30 (12H, m, Ar*H*), 7.20 (2H, br t, *J* 7.4, Ar*H*), 7.09 (2H, dt, *J* 7.4 and 0.8, Ar*H*), 5.25 (2H, m, CH_AH_B(O)), 4.65 (2H, dd, *J* 11.9 and 10.4, C*H*(Ph)(N)) and 3.95 (2H, m, CH_AH_B(O)); δ_C (75 MHz; $CDCl_3$) 166.1 (*C*=N), 137.0, 135.7, 133.9, 133.5, 132.3, 130.0, 129.9, 129.7, 129.5, 127.2, 126.8, 126.7, 71.4 and 69.1; δ_B (100 MHz; $CDCl_3$) 11.3; *m*/*z* LRMS (ESI^+) 485 [$(M+H)^+$, 9%], 368.2 (10), 312.1 (100), 278.2 (16); HRMS (ESI^+) found 485.2208 ($[M+H]^+$ $C_{30}H_{26}B_2N_2O_3$ requires 485.2208).

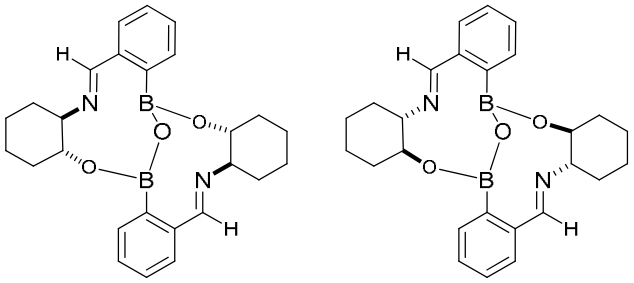


(*S*,*S*)-**173**

(*S*,*E*)-2-((2-hydroxy-1-phenylethylimino)methyl)phenyldiboronate

2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) and (*S*)-2-phenylglycinol (*S*)-**150** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å

molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (92 mg, 95%); $[\alpha]_D^{20}$ -21.10 (*c* 1.450, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1627 (C=N); δ_H (300 MHz; $CDCl_3$) 7.65-7.63 (4H, m, C*H*N and Ar*H*), 7.43-7.30 (12H, m, Ar*H*), 7.20 (2H, br t, *J* 7.4, Ar*H*), 7.09 (2H, dt, *J* 7.4 and 0.8, Ar*H*), 5.25 (2H, m, CH_AH$_B$(O)), 4.65 (2H, dd, *J* 11.7 and 10.6, C*H*(Ph)(N)), 3.95 (2H, m, CH$_A$$H_B$(O)); δ_C (75 MHz; $CDCl_3$) 166.0 (*C*=N), 137.0, 135.6, 133.9, 133.5, 132.3, 130.0, 129.9, 129.7, 129.4, 128.0, 127.3, 126.8, 71.3, and 65.8; δ_B (100 MHz; $CDCl_3$) 10.8; *m*/*z* LRMS (ESI$^+$) 485 [(M+H)$^+$, 27%], 312.1 (100); HRMS (ESI$^+$) found 485.2206 ([M+H]$^+$ $C_{30}H_{26}B_2N_2O_3$ requires 485.2208).

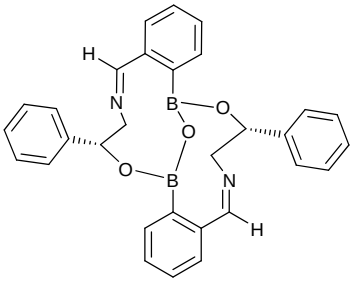


(1*R*,2*R*,1′*R*,2′*R*)-**175 and** (1*S*,2*S*,1′*S*,2′*S*)-**175**

A 50 : 50 mixture of 2-((*E*)-((1*R*,2*R*)-2-hydroxycyclohexylimino)methyl)phenyldiboronate and 2-((*E*)-((1*S*,2*S*)-2-hydroxycyclohexylimino)methyl)phenyldiboronate

2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) was stirred with *trans*-2-aminocyclohexanol hydrochloride **169** (61 mg, 0.4 mmol) and cesium carbonate (130 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. Cesium carbonate and molecular sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a yellow oil (85 mg, 96%); m.p. 142-144 °C (dec); ν_{max} (film)/cm^{-1} 1625 (C=N); δ_H (300 MHz; $CDCl_3$) 8.20 (2H, s, C*H*N), 8.19 (2H, s, C*H*N), 7.47 (4H, d, *J* 6.8, Ar*H*), 7.35 (4H, d, *J* 7.4, Ar*H*), 7.28 (4H, app dt, *J* 7.5 and 1.1, Ar*H*), 7.10 (4H, app dt, *J* 7.5 and 1.1, Ar*H*), 3.96-3.88 (4H, m, C*H*(N)), 3.79-3.70 (4H, m, C*H*(O)), 2.26 (4H, br d, *J* 12.0, CH_AH$_B$C(N)), 1.88-1.81 (8H, m, CH$_A$$H_B$C(N) and C$H_AH_B$C(O)), 1.71-1.66 (4H, m, CH$_A$$H_B$C(O)) and 1.50-1.12 (16H, m, C(N)C$_2$$H_4$); δ_C (75 MHz; $CDCl_3$) 164.0 (*C*=N), 137.2, 133.2, 129.9, 129.1, 126.9, 126.3, 65.6, 36.3, 29.8, 27.3, 24.9 and 24.8; δ_B (100

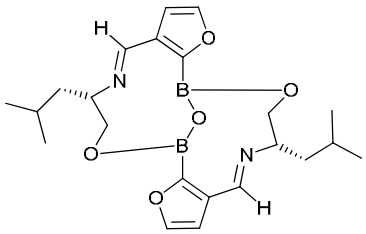
MHz; $CDCl_3$) 10.8; *m*/*z* LRMS (ESI^+) 441 [$(M+H)^+$, 100%], 290.2 (15); HRMS (ESI^+) found 441.2519 ($[M+H]^+$ $C_{26}H_{30}B_2N_2O_3$ requires 441.2519).



(*R*,*R*)-**176**

(*R*,*Z*)-2-((2-hydroxy-2-phenylethylimino)methyl)phenyldiboronate

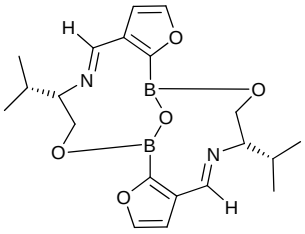
2-Formylphenylboronic acid **73** (60 mg, 0.4 mmol) was stirred with (*R*)-(-)-2-amino-1-phenylethanol (*R*)-**170** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a bright yellow solid (140 mg, 95%); m.p. 145-147 °C (dec); $[\alpha]_D^{20}$ +19.43 (*c* 1.355, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1635 (C=N); δ_H (300 MHz; $CDCl_3$) 8.25 (2H, s, C*H*N), 7.64 (2H, d, *J* 7.0, Ar*H*), 7.48-7.14 (16H, m, Ar*H*), 5.46 (2H, br d, *J* 9.8, CH_AH_B(N)), 4.50-4.42 (2H, m, C*H*(Ph)(O)) and 4.03 (2H, br d, *J* 9.8, CH_AH_B(N)); δ_C (75 MHz; $CDCl_3$) 167.0 (*C*=N), 143.5, 137.0, 134.6, 134.2, 133.5, 129.8, 129.5, 128.8, 127.6, 126.9, 126.8, 126.2, 72.3 and 62.9; δ_B (100 MHz; $CDCl_3$) 10.5; *m*/*z* LRMS (ESI^+) 485 [$(M+H)^+$, 100%], 312.1 (99); HRMS (ESI^+) found 485.2209 ($[M+H]^+$ $C_{30}H_{26}B_2N_2O_3$ requires 485.2208).



(*S*,*S*)-**178**

(*S*,*E*)-3-((1-hydroxy-4-methylpentan-2-ylimino)methyl)furan-2-yldiboronate

3-Formylfuran-2-boronic acid **177** (56 mg, 0.4 mmol) was stirred with (*S*)-leucinol (*S*)-**145** (51 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a red oil (82 mg, 97%); $[\alpha]_D^{20}$ -34.04 (*c* 1.650, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1649 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (1H, s, C*H*N), 8.12 (1H, s, C*H*N), 7.36 (2H, d, *J* 1.9, C*H*C(C=N)), 6.32 (2H, d, *J* 1.9, C*H*C(O)), 4.39 (1H, dd, *J* 8.9 and 6.0, CH_AH_B(O)), 4.24-4.15 (2H, m, C*H*(N)), 3.99 (2H, dd, *J* 8.9 and 7.4, CH_AH_B(O)), 1.77-1.65 (6H, m, $CH_AH_BCH(CH_3)_2$) and 1.00 (12H, br t, *J* 5.5, $C(CH_3)_2$); δ_C (75 MHz; $CDCl_3$) 157.2 (*C*=N), 144.7, 132.7, 122.8, 110.0, 71.9, 52.2, 32.6, 20.5, 8.9 and 8.1; δ_B (100 MHz; $CDCl_3$) 4.6; *m*/*z* LRMS (ESI^+) 425 [$(M+H)^+$, 32%], 412.4 (27), 389.3 (35), 375.2 (100); HRMS (ESI^+) found 425.2422 ($[M+H]^+$ $C_{22}H_{30}B_2N_2O_5$ requires 425.2419).

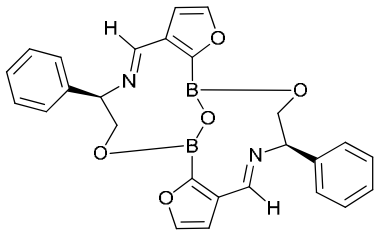


(*S*,*S*)-**179**

(*S*,*E*)-3-((1-hydroxy-3-methylbutan-2-ylimino)methyl)furan-2-yldiboronate

3-Formylfuran-2-boronic acid **177** (56 mg, 0.4 mmol) and (*S*)-2-amino-3-methyl-1-butanol (*S*)-**146** (45 μL, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a dark brown solid (74

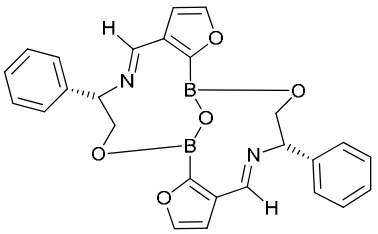
mg, 93%); m.p. 131-134 °C (dec); $[\alpha]_D^{20}$ -36.75 (*c* 1.950, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1649 (C=N); δ_H (300 MHz; $CDCl_3$) 8.13 (1H, s, C*H*N), 8.12 (1H, s, C*H*N), 7.35 (2H, d, *J* 1.9, C*H*C(C=N)), 6.33 (2H, d, *J* 1.9, C*H*C(O)), 4.39 (2H, dd, *J* 9.4 and 6.2, CH_AH_B(O)), 4.15 (2H, dd, *J* 9.4 and 4.0, CH_AH_B(O)), 3.90-3.84 (2H, m, C*H*(N)), 2.28-2.17 (2H, m, C*H*$(CH_3)_2$), 1.06 (6H, d, *J* 6.0, C(CH_3)$_2$), 1.04 (6H, d, *J* 6.0, C(CH_3)$_2$); δ_C (75 MHz; $CDCl_3$) 157.2 (*C*=N), 144.5, 132.6, 123.3, 110.2, 69.3, 63.5, 32.6, 20.0 and 17.4; δ_B (100 MHz; $CDCl_3$) 4.7; *m*/*z* LRMS (ESI^+) 397 [$(M+H)^+$, 9%], 345.2 (100), 283.2 (36); HRMS (ESI^+) found 397.2102 ($[M+H]^+$ $C_{20}H_{26}B_2N_2O_5$ requires 397.2104).



(*R*,*R*)-**180**

(*R*,*E*)-3-((2-hydroxy-1-phenylethylimino)methyl)furan-2-yldiboronate

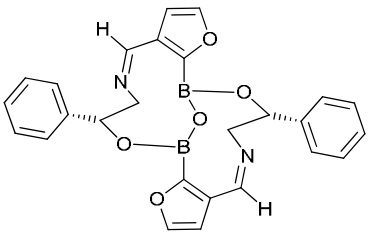
3-Formylfuran-2-boronic acid **177** (56 mg, 0.4 mmol) was stirred with (*R*)-2-phenylglycinol (*R*)-**150** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a red solid (88 mg, 95%); m.p. 115-118 °C (dec); $[\alpha]_D^{20}$ +39.58 (*c* 1.125, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1657 (C=N); δ_H (300 MHz; $CDCl_3$) 7.83 (1H, s, C*H*N), 7.82 (1H, s, C*H*N), 7.53-7.44 (10H, m, Ar*H*), 7.42 (2H, d, *J* 1.9, C*H*C(C=N)), 6.24 (2H, d, *J* 1.9, C*H*C(O)), 5.35-5.28 (2H, m, C*H*(Ph)(N)), 4.57-4.45 (4H, m, CH_AH_B(O)); δ_C (75 MHz; $CDCl_3$) 158.3 (*C*=N), 144.9, 136.6, 131.4, 129.8, 129.6, 129.5(9), 129.5(5), 129.5(0), 124.6, 110.3, 71.3 and 70.4; δ_B (100 MHz; $CDCl_3$) 5.4; *m*/*z* LRMS (ESI^+) 465 [$(M+H)^+$, 100%], 415.2 (33), 335.2 (36), 292.1 (32), 215.1 (10); HRMS (ESI^+) found 465.1794 ($[M+H]^+$ $C_{26}H_{22}B_2N_2O_5$ requires 465.1793).



(*S*,*S*)-**180**

(*S*,*E*)-3-((2-hydroxy-1-phenylethylimino)methyl)furan-2-yldiboronate

3-Formylfuran-2-boronic acid **177** (56 mg, 0.4 mmol) was stirred with (*S*)-2-phenylglycinol (*S*)-**150** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a dark red solid (90 mg, 97%); m.p. 115-118 °C (dec); $[\alpha]_D^{20}$ -39.58 (*c* 2.010, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1657 (C=N); δ_H (300 MHz; $CDCl_3$) 7.83 (1H, s, C*H*N), 7.82 (1H, s, C*H*N), 7.53-7.44 (10H, m, Ar*H*), 7.42 (2H, d, *J* 1.9, C*H*C(C=N)), 6.24 (2H, d, *J* 1.9, C*H*C(O)), 5.35-5.28 (2H, m, C*H*(Ph)(N)), 4.57-4.45 (4H, m, CH_AH_B(O)); δ_C (75 MHz; $CDCl_3$) 158.3 (*C*=N), 144.9, 136.6, 131.4, 129.8, 129.6, 129.5(9), 129.5(5), 129.5(0), 124.6, 110.3, 71.3 and 70.4; δ_B (100 MHz; $CDCl_3$) 5.4; *m*/*z* LRMS (ESI^+) 465 [$(M+H)^+$, 75%], 415.2 (56), 292.1 (100); HRMS (ESI^+) found 465.1793 ($[M+H]^+$ $C_{26}H_{22}B_2N_2O_5$ requires 465.1793).



(*R*,*R*)-**181**

(*R*,*E*)-3-((2-hydroxy-2-phenylethylimino)methyl)furan-2-yldiboronate

3-Formylfuran-2-boronic acid **177** (56 mg, 0.4 mmol) was stirred with (*R*)-2-amino-1-phenylethanol (*R*)-**170** (55 mg, 0.4 mmol) were stirred in $CDCl_3$ (5 mL) for 5 minutes in the presence of 4 Å molecular sieves. The sieves were removed using gravity filtration and the solvent removed *in vacuo* to afford the title compound as a dark

brown solid (85 mg, 92%); m.p. 124-126 °C (dec); $[\alpha]_D^{20}$ +18.51 (*c* 1.155, CH_2Cl_2); ν_{max} (film)/cm^{-1} 1662 (C=N); δ_H (300 MHz; $CDCl_3$) 8.26 (2H, br s, C*H*N), 7.56 (4H, br d, Ar*H*), 7.45 (2H, d, *J* 1.9, C*H*C(C=N)), 7.39-7.26 (6H, m, Ar*H*), 6.34 (2H, d, *J* 1.9, C*H*C(O)), 5.56-5.51 (2H, m, CH_AH_B(N)) and 4.11-4.08 (4H, m, CH_AH_B(N), C*H*(Ph)(O)); δ_C (75 MHz; $CDCl_3$) 157.7 (*C*=N), 145.1, 142.1, 129.7, 129.0, 128.8, 128.6, 128.1, 126.7, 124.5, 110.4, 76.2 and 63.7; δ_B (100 MHz; $CDCl_3$) 5.0; *m*/*z* LRMS (ESI^+) 465 [$(M+H)^+$, 65%], 415.2 (100), 323.2 (83); HRMS (ESI^+) found 465.1793 ($[M+H]^+$ $C_{26}H_{22}B_2N_2O_5$ requires 465.1793).

4 Appendix

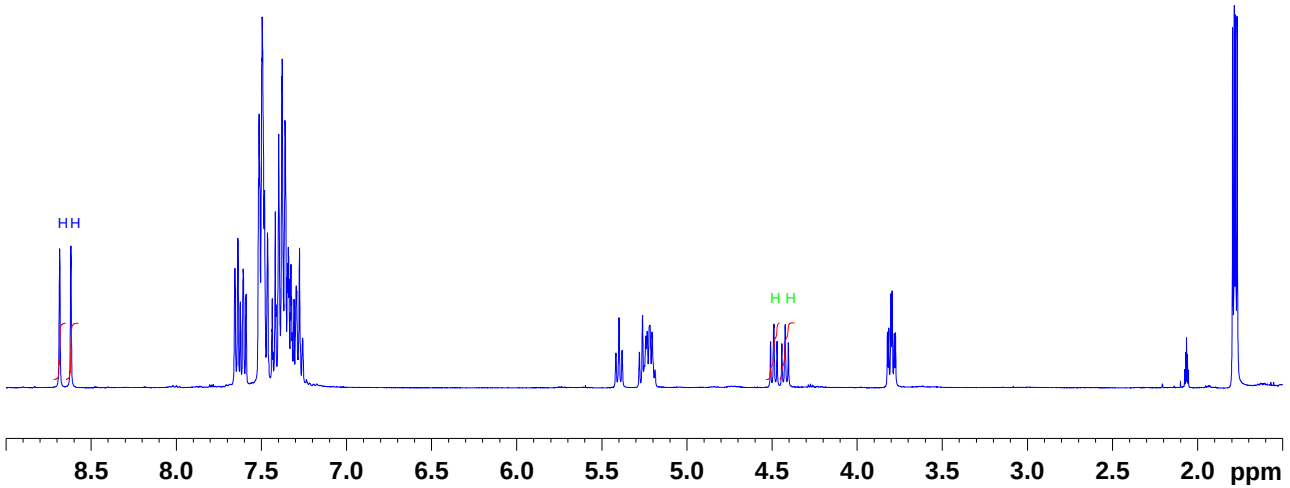
4.1 ^{1}H NMR Spectra from the Derivatisation of Racemic Samples of Chiral Diols

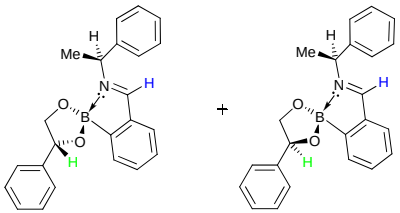
4.1.1 (*S*)-(-)- α-methylbenzylamine

5.1.2 (*S*)-(-)-1-(naphthalen-2-yl)ethanamine

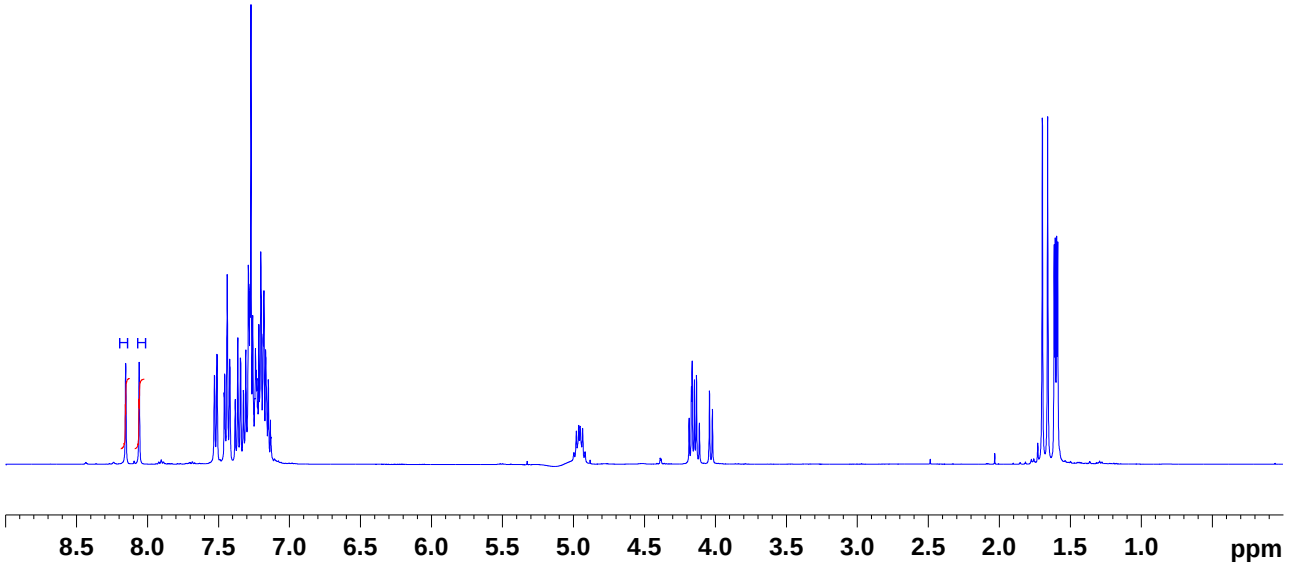
5.2 ^{1}H NMR Spectra from the Derivatisation of Racemic Samples of Chiral Diamines

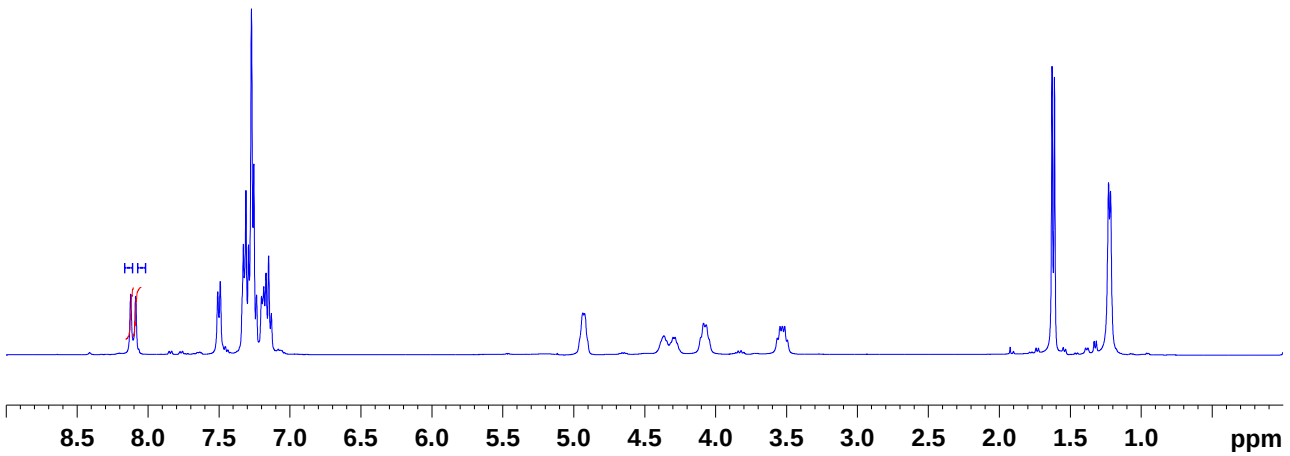
5.3 ^{1}H NMR Spectrum for the Derivatisation of Racemic *O*-Protected Amino Alcohol 2-phenylglycinol



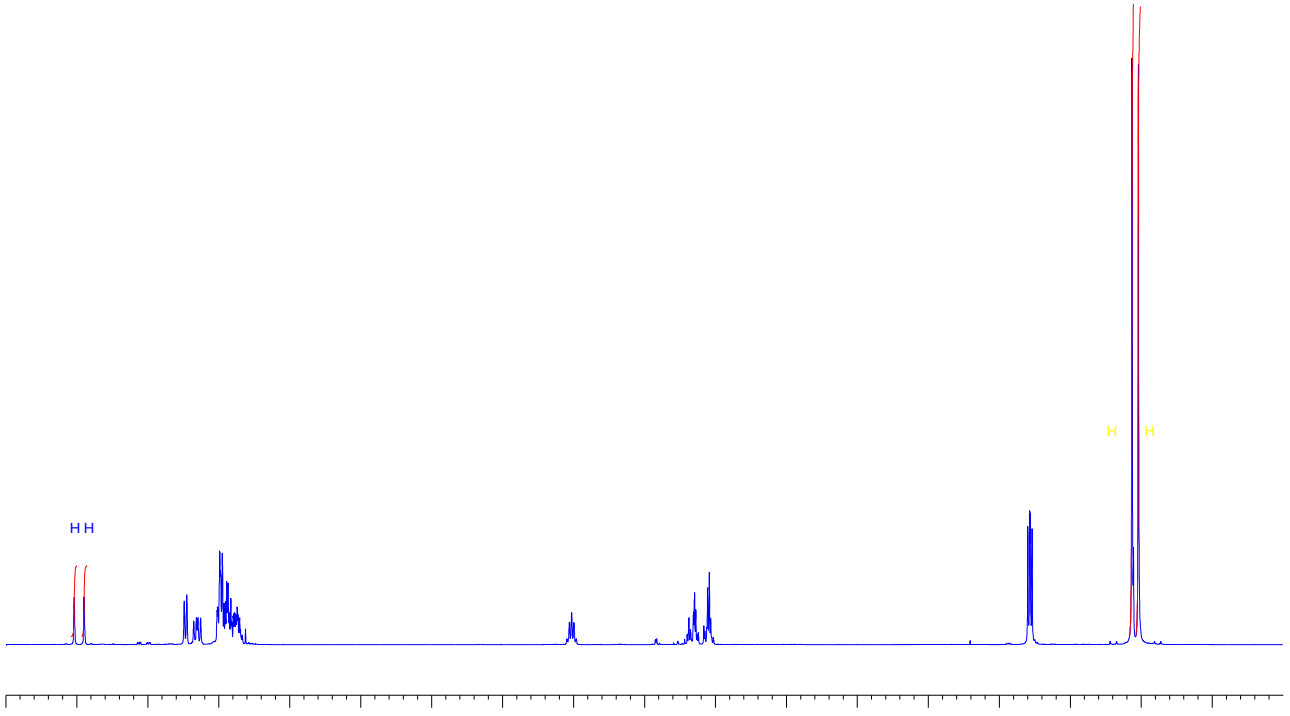


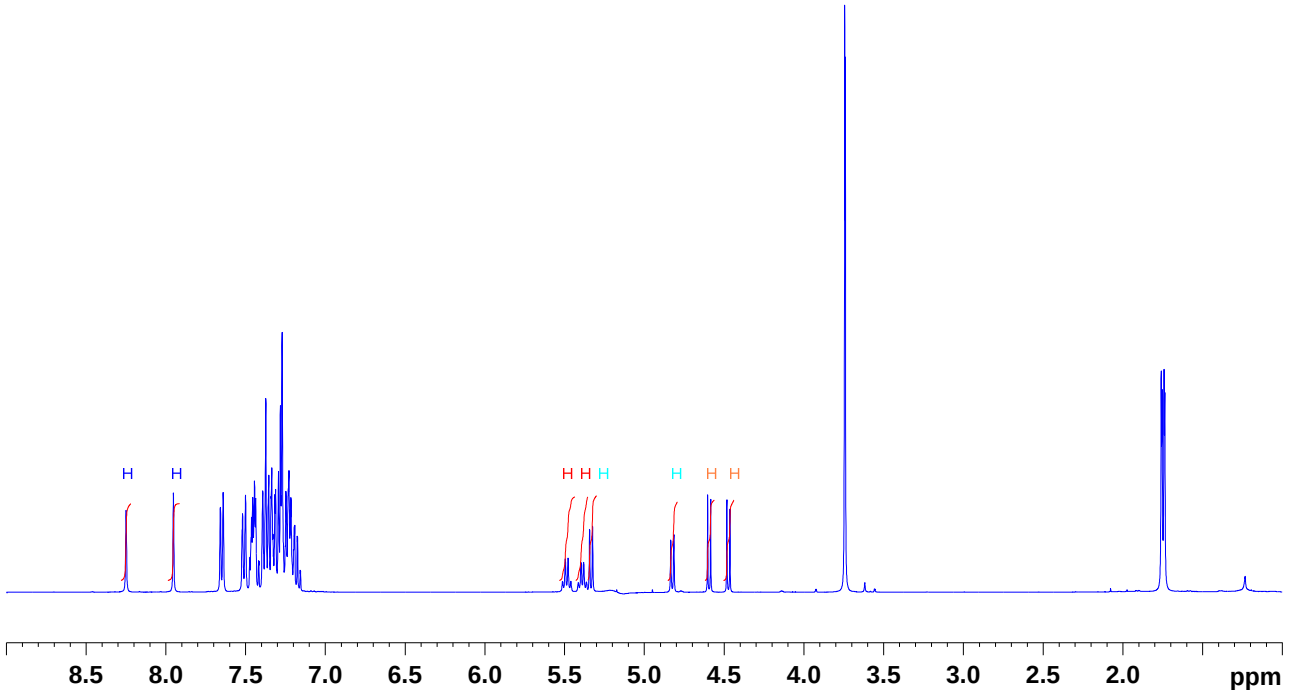
(α-*S*,*R*)-**102a** + (α-*S*,*S*)-**102b**


H H
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
Me
H
N
H
O
B
O
+
(α-S,R)-103a
(α-S,S)-103b

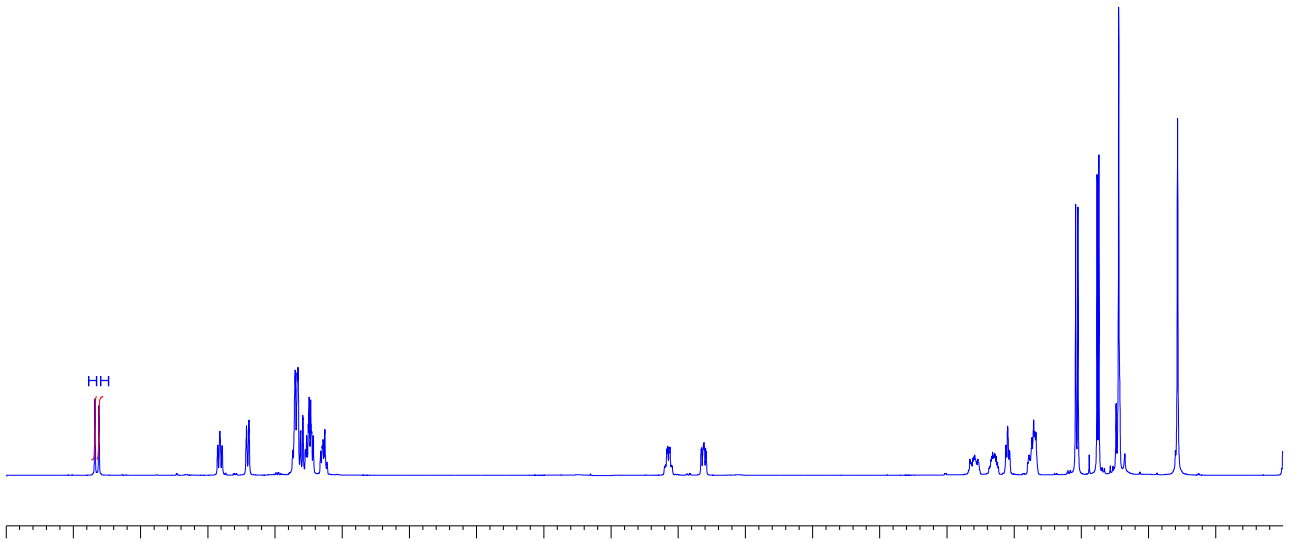


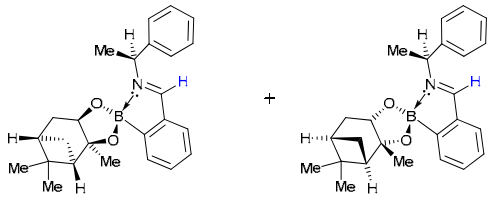
(α-*S*,*R*)-**104a** (α-*S*,*S*)-**104b**


H H
H H
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
Me
H
N
H
O
B
O
H3C
CH3
CH3
+
(α-S,R)-105a
(α-S,S)-105b

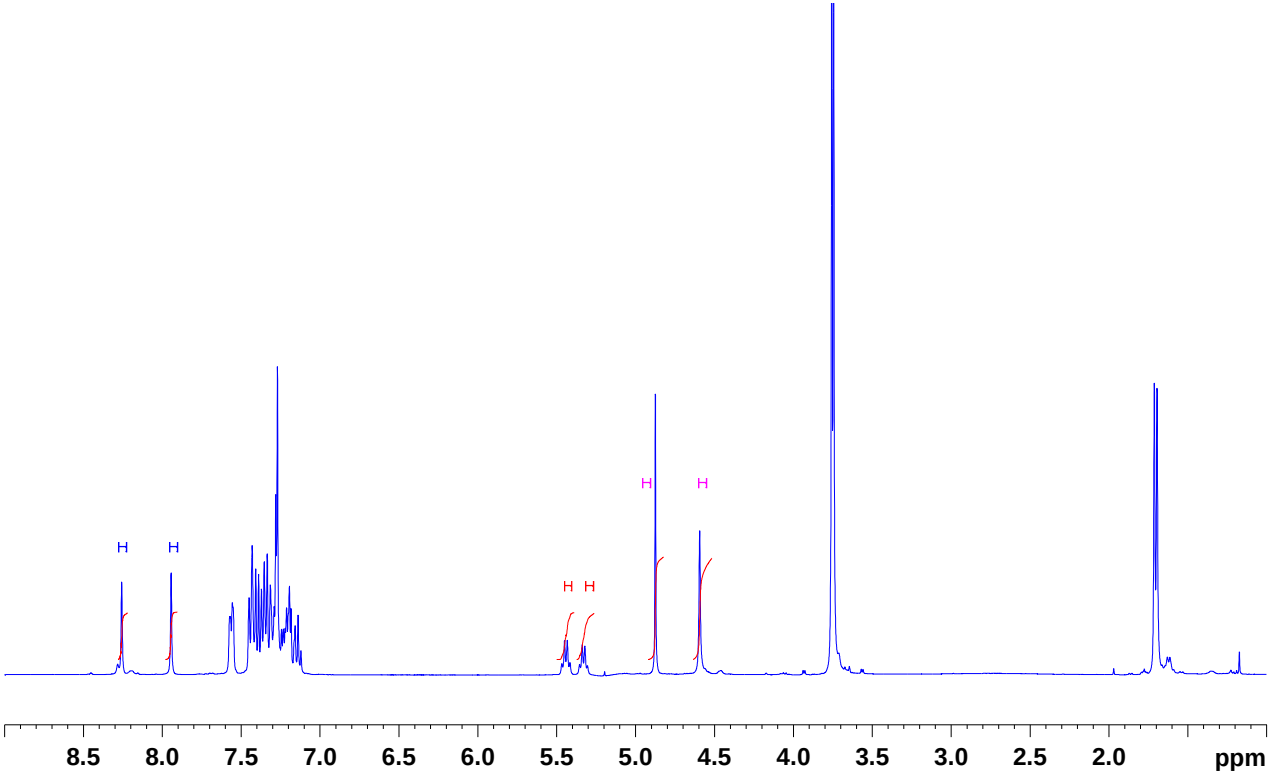


(α-*S*,4*S*,5*R*)-**106a** (α-*S*,4*R*,5*S*)-**106b**

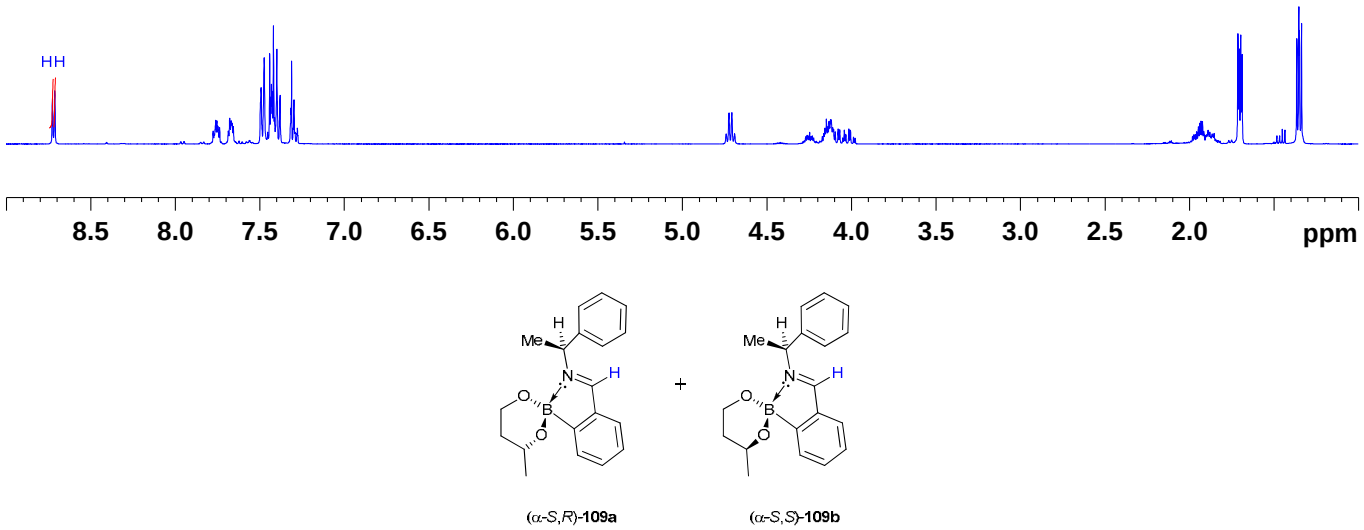




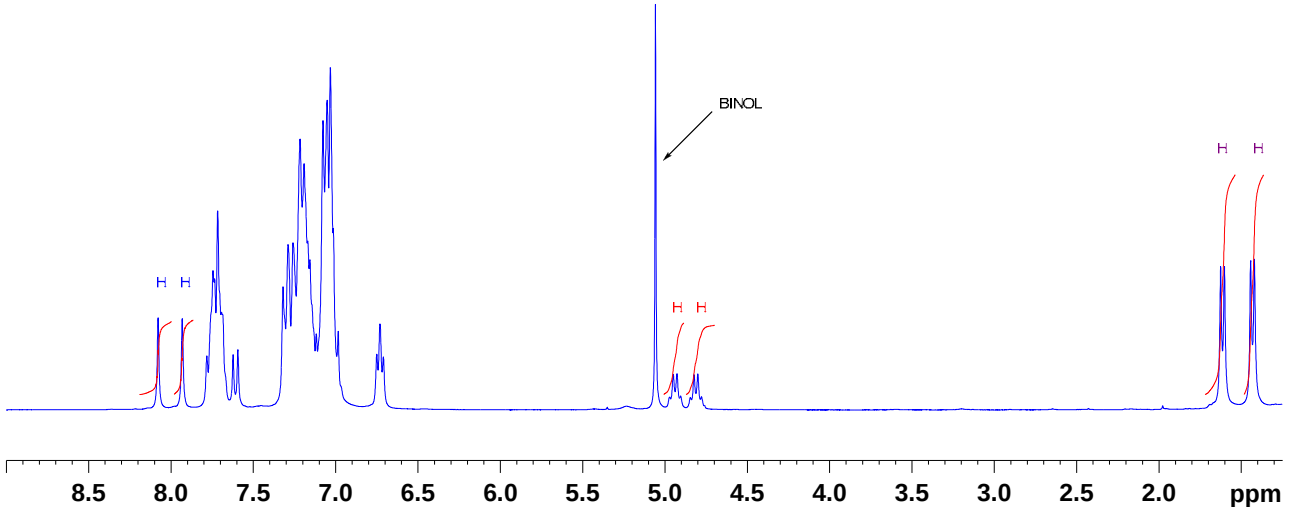
(α-*S*,3a*S*,7a*S*,10*S*,11*R*)-**107a** + (α-*S*,3a*R*,7a*R*,10*R*,11*S*)-**107b**



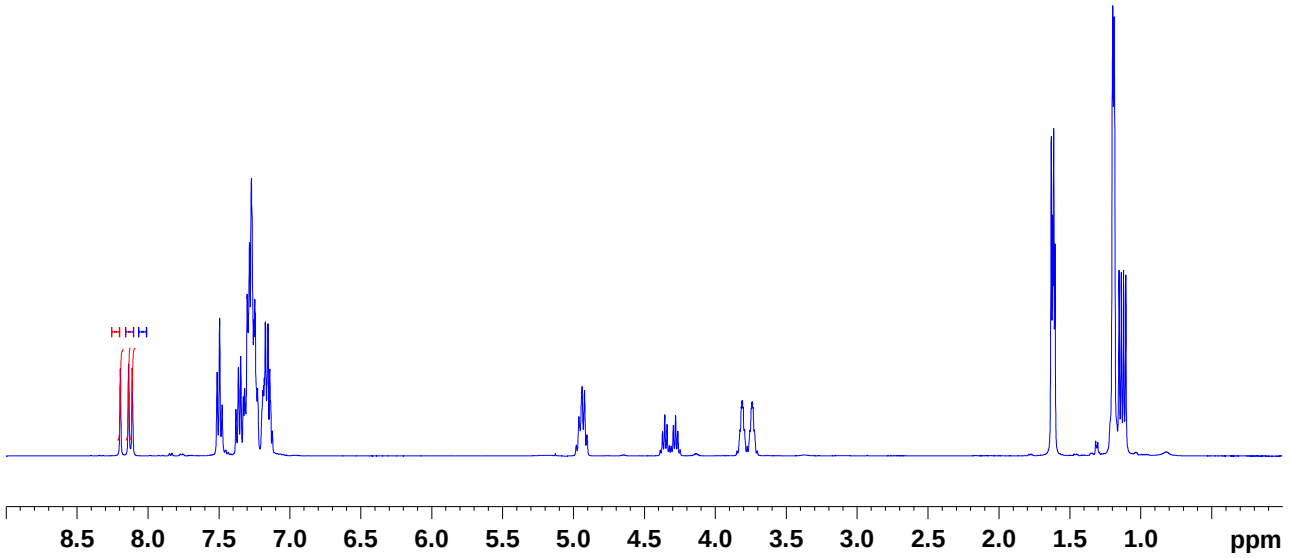
(α-*S*,4*R*,5*R*)-**108a** (α-*S*,4*S*,5*S*)-**108b**

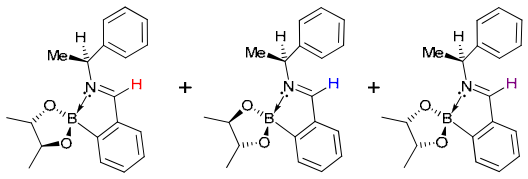


(α-*S*,*R*)-**109a** (α-*S*,*S*)-**109b**

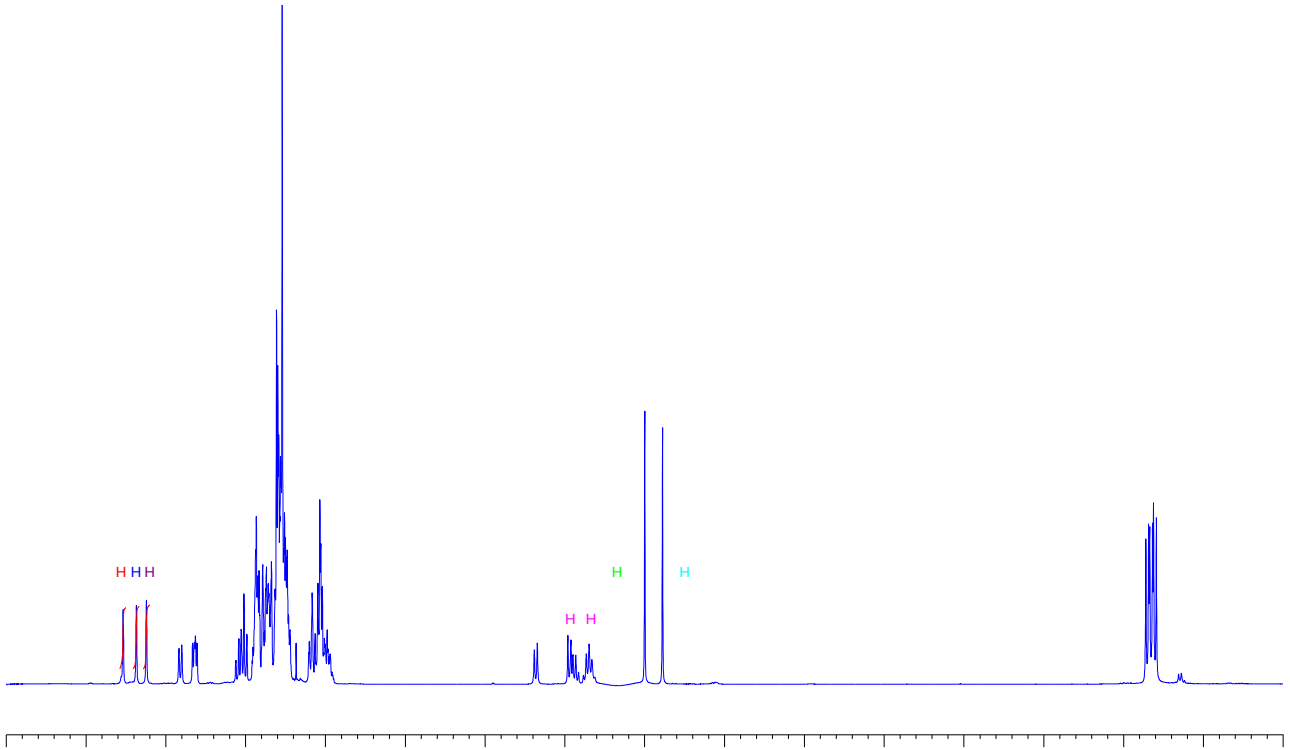


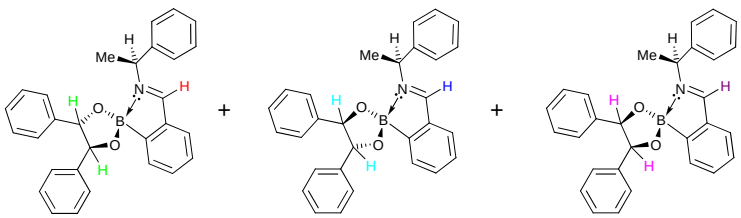
(α-*R*,*S*)-**110a** (α-*S*,*S*)-**110b**



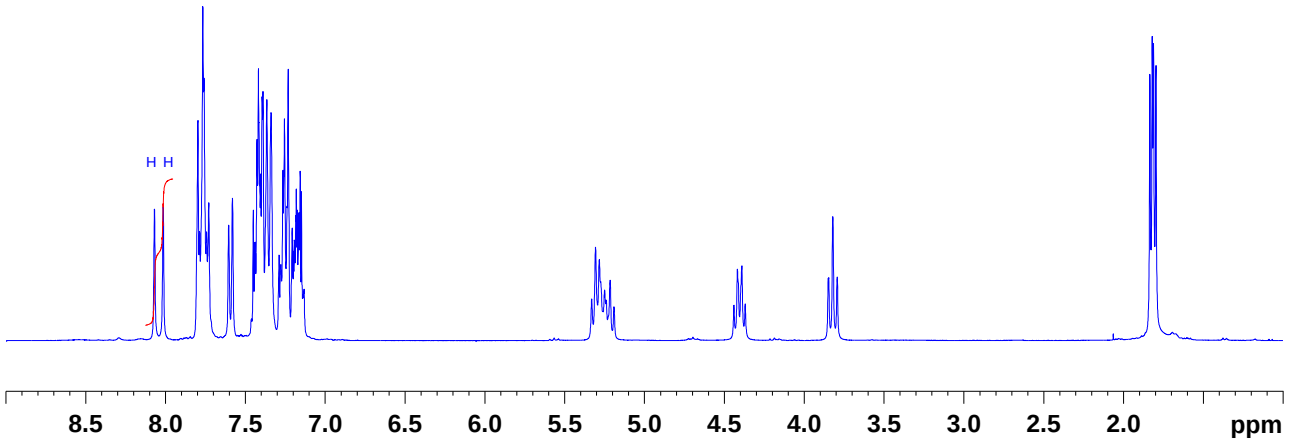


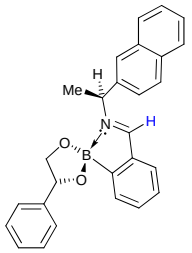
(α-*S*,4*S*,5*S*)-**111a** (α-*S*,4*R*,5*R*)-**111b** (α-*S*,4*S*,5*R*)-**111c**



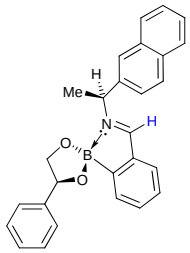


(α-*S*,4*S*,5*S*)-**112a** (α-*S*,4*R*,5*R*)-**112b** (α-*S*,4*R*,5*S*)-**112c**

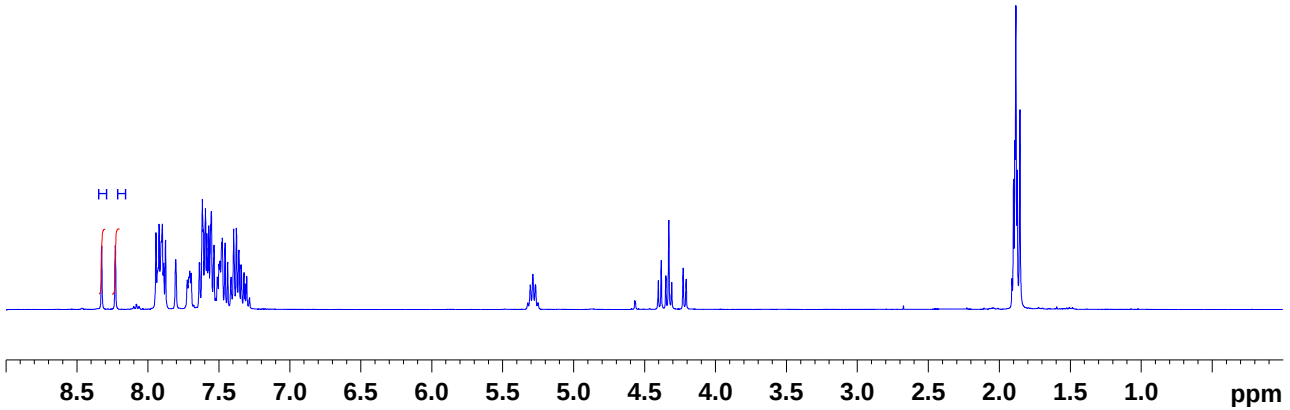


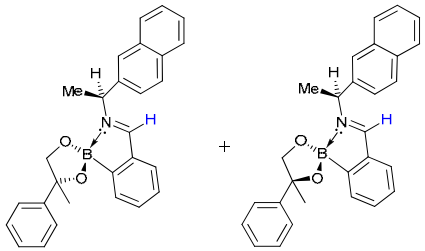


(α-*S*,*R*)-**113a**



(α-*S*,*S*)-**113b**

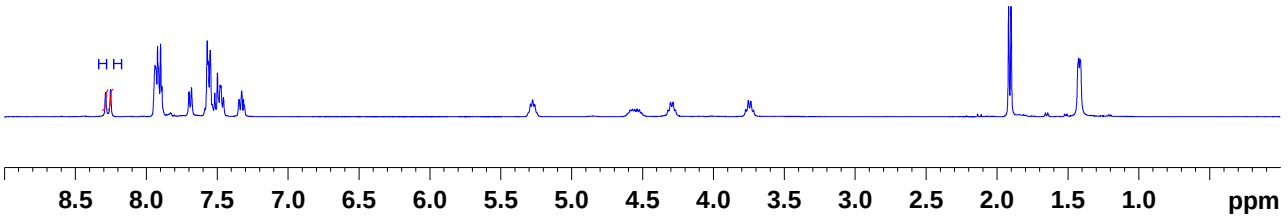


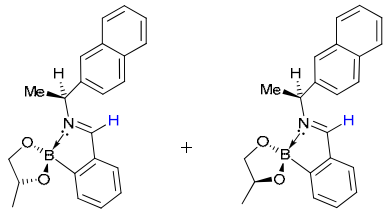


(α-*S*,*R*)-**114a**

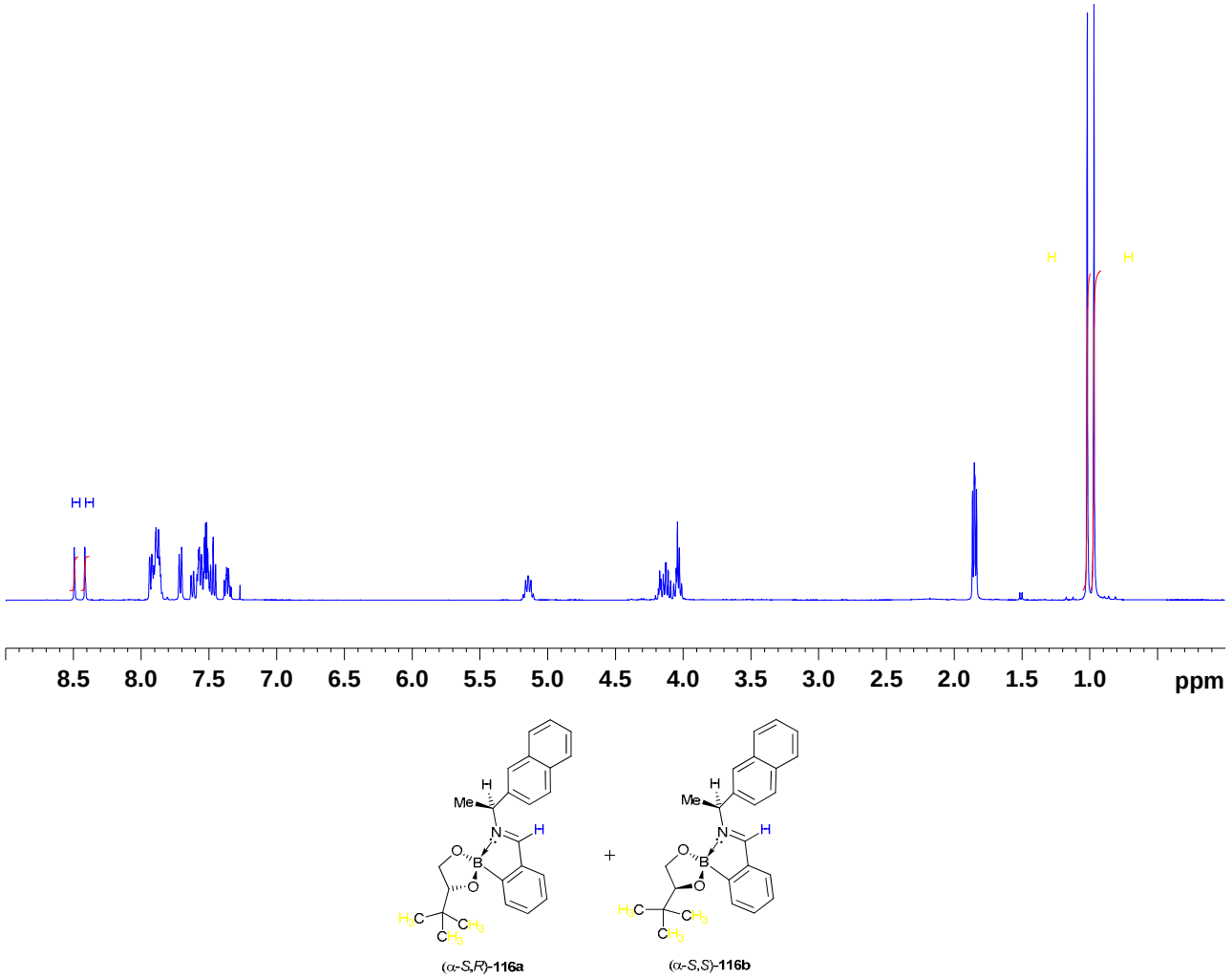
+

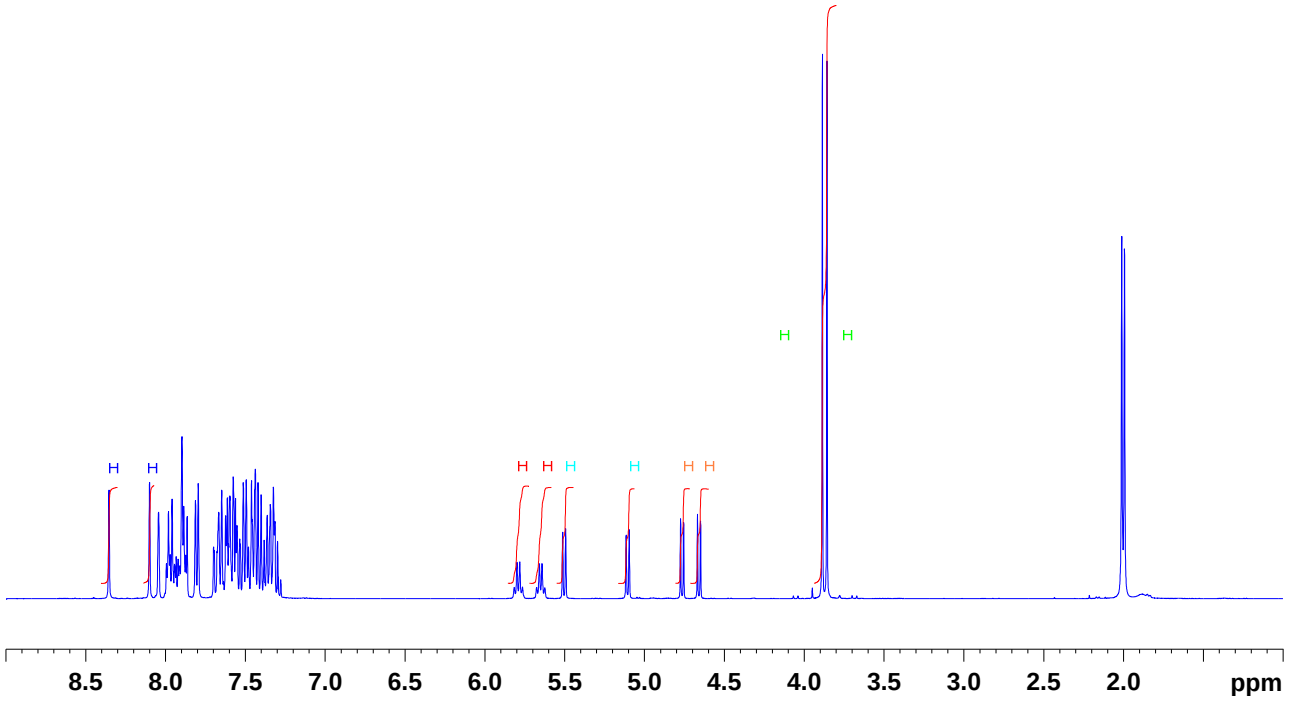
(α-*S*,*S*)-**114b**



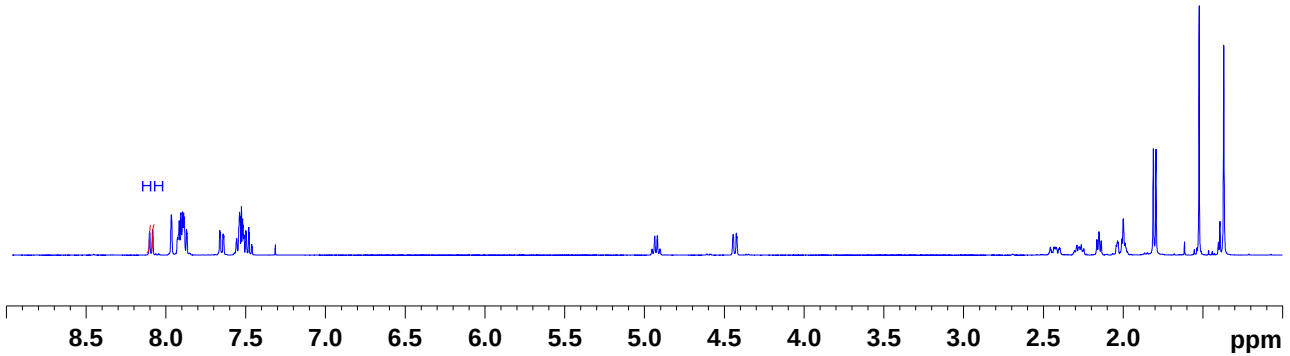


(α-*S*,*R*)-**115a** + (α-*S*,*S*)-**115b**

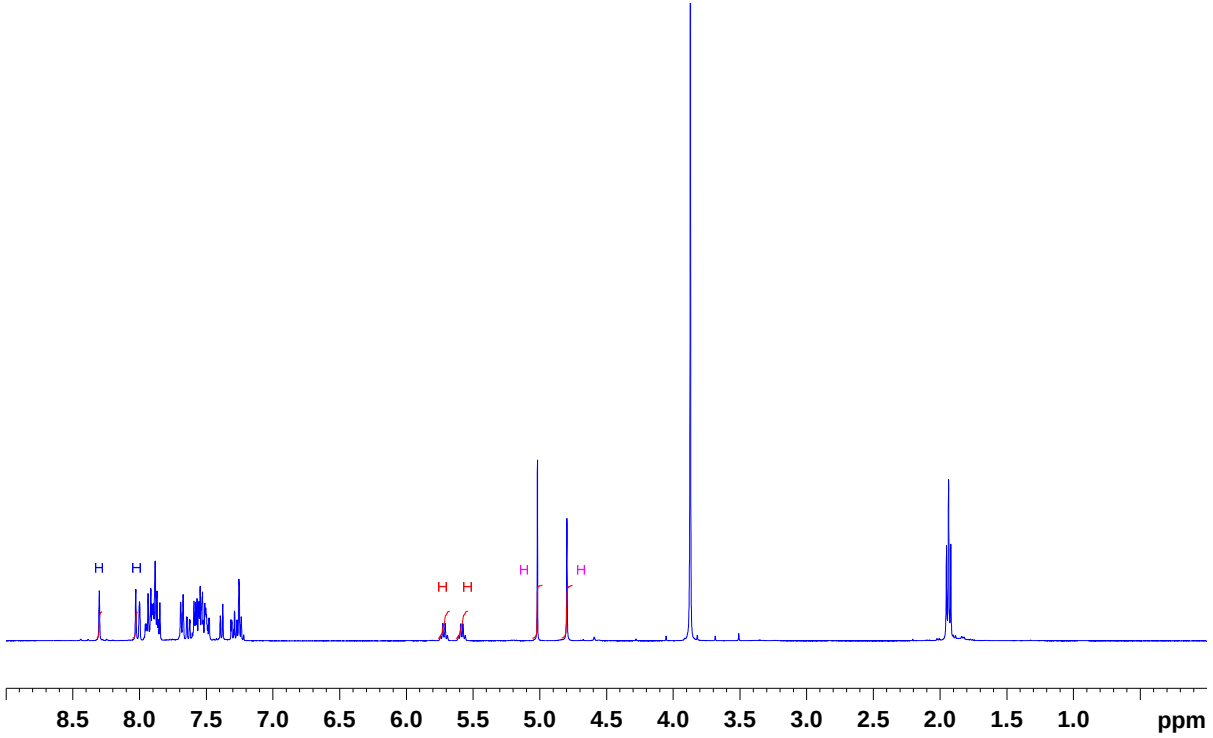

H H
H H
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
Me
H
N
H
O
B
O
H3C
CH3
CH3
+
(α-S,R)-116a
(α-S,S)-116b



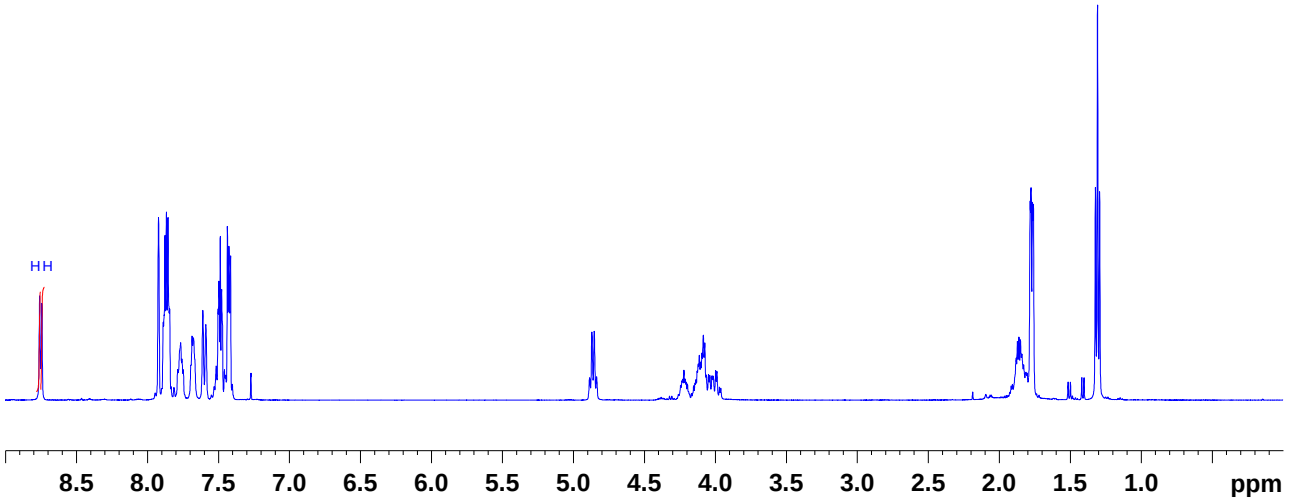
(α-*S*,4*S*,5*R*)-**117a** (α-*S*,4*R*,5*S*)-**117b**



(α-*S*,3a*S*,7a*S*,10*S*,11*R*)-**118a** + (α-*S*,3a*R*,7a*R*,10*R*,11*S*)-**118b**



(α-*S*,4*R*,5*R*)-**119a** (α-*S*,4*S*,5*S*)-**119b**


HH
8.5
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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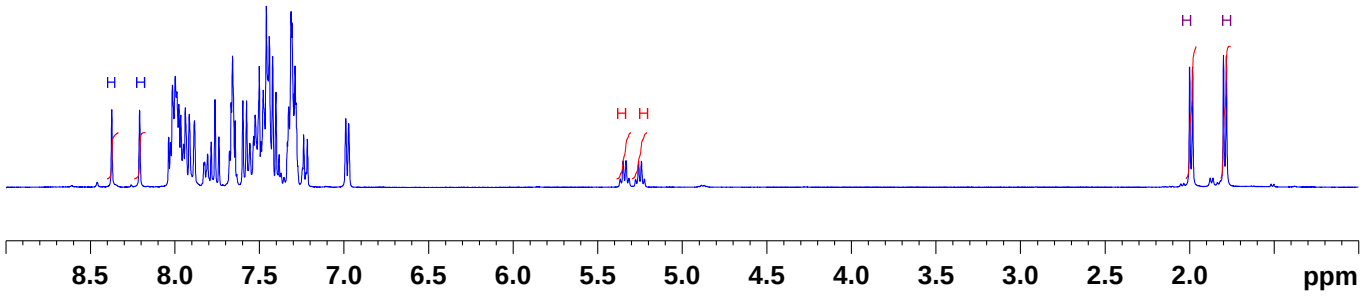
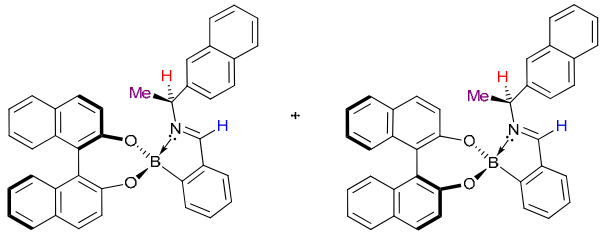
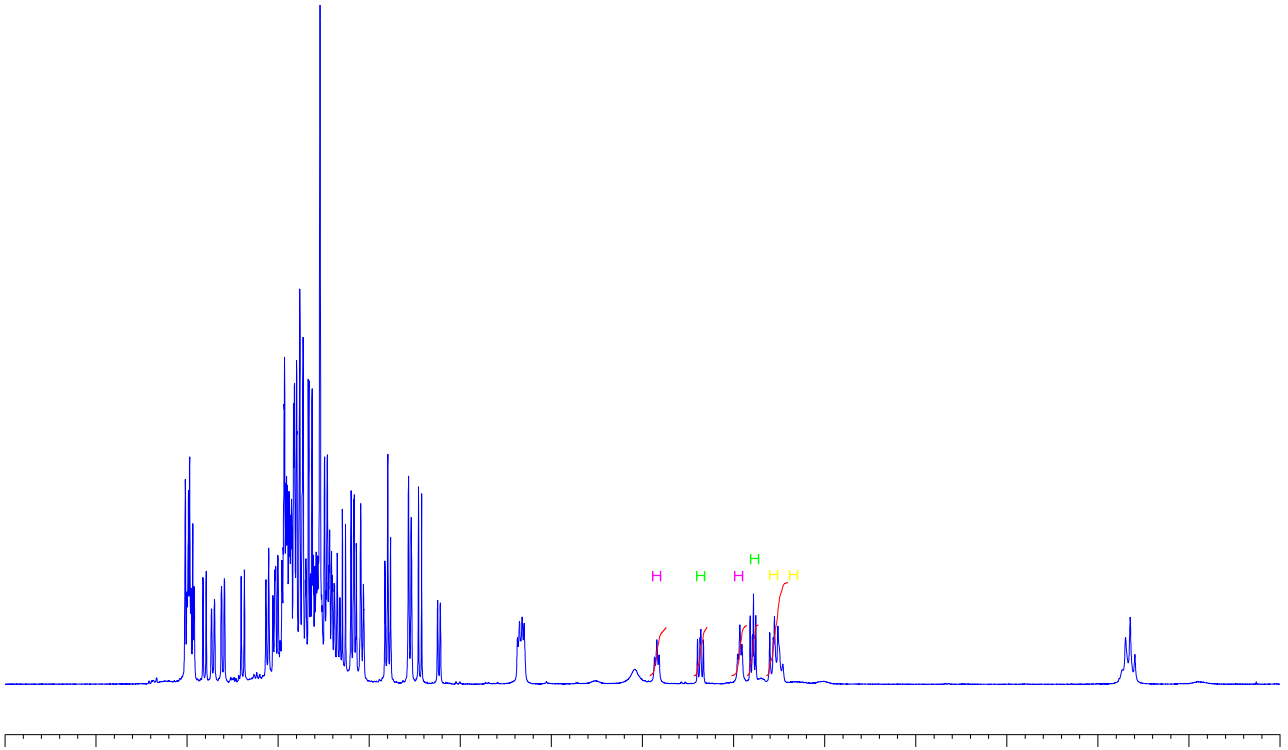
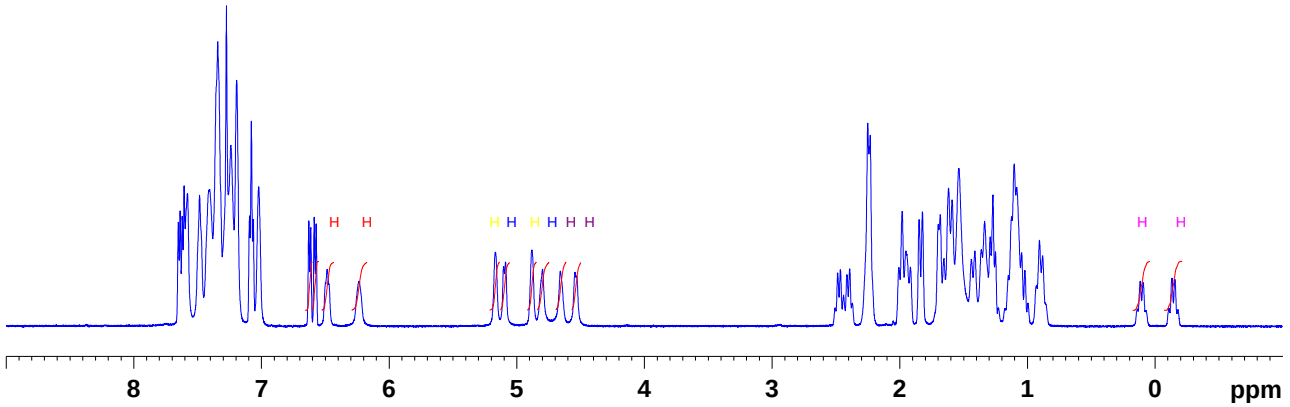
2.5
2.0
1.5
1.0
ppm
Me
H
N
H
O
B
O
+
(α-*S*,*R*)-**120a**
(α-*S*,*S*)-**120b**

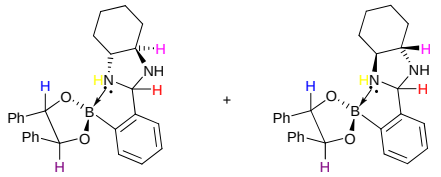




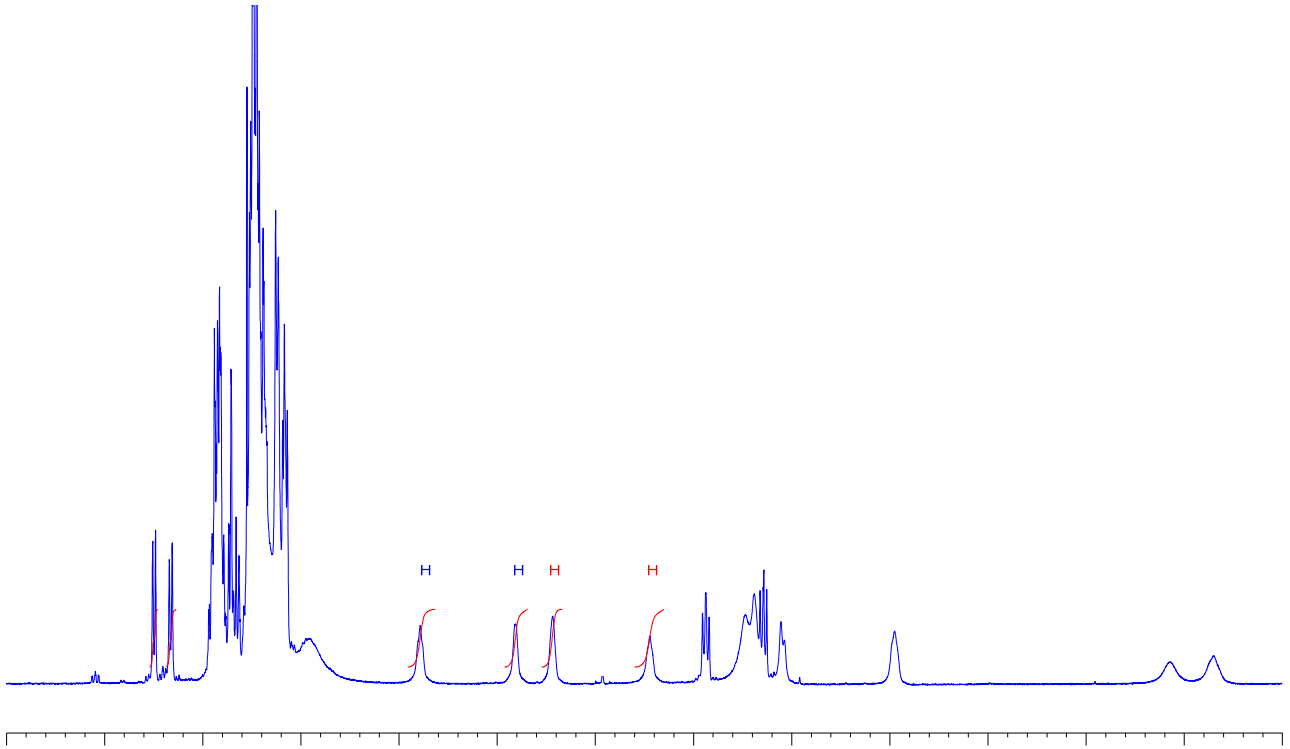
(α-*S*,*R*)-**121a** (α-*S*,*S*)-**121b**

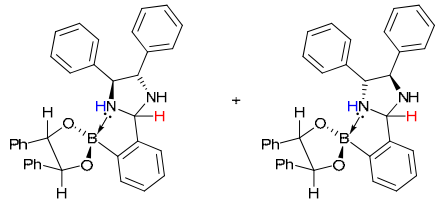

H
H H H H H
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 ppm
(R,2S,4S,5S)-126a
+
(R,2S,4R,5R)-126b



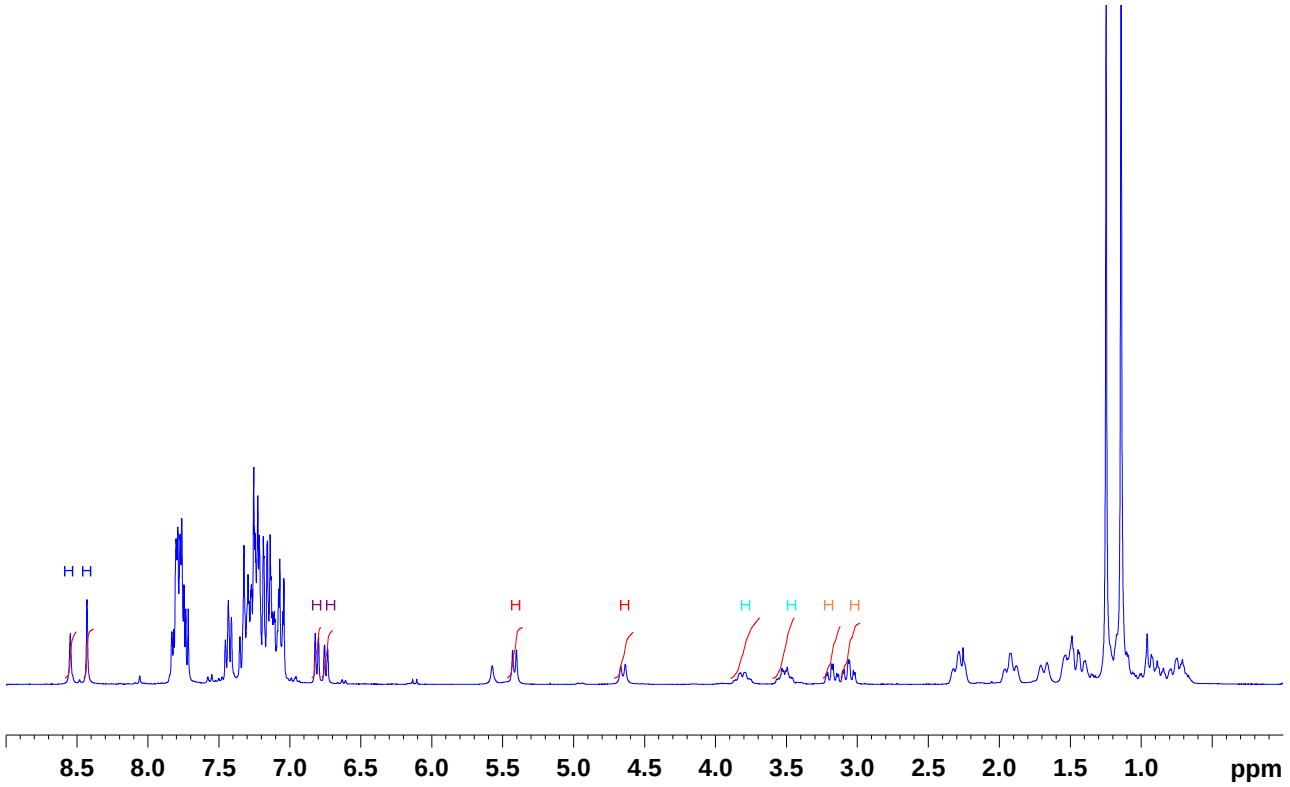


(3a*R*,4′*S*,5′*S*,7a*R*)-**134a** (3a*S*,4′*S*,5′*S*,7a*S*)-**134b**

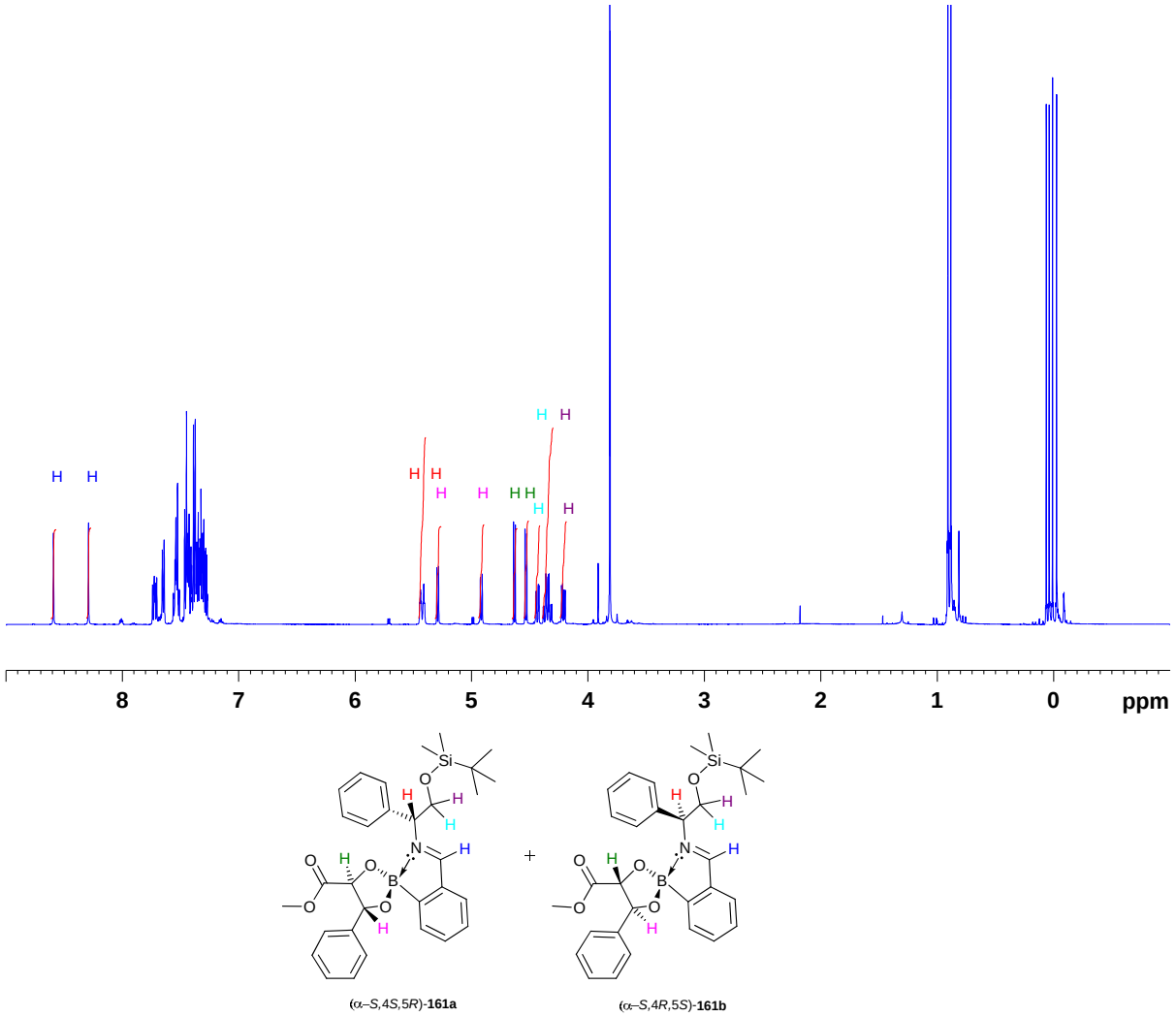




(4′*S*,4*S*,5*S*,5′*S*)-**135a** (4′*S*,4*R*,5*R*,5′*S*)-**135b**



(*S*,1*R*,2*R*)-**138a** (*S*,1*S*,2*S*)-**138b**



(α–*S*,4*S*,5*R*)-**161a** + (α–*S*,4*R*,5*S*)-**161b**

5.1 X-Ray Crystallography Data

Table 1. Crystal data and structure refinement for (*S*,2*R*,4*S*)-**154**.

Identification code	(*S*,2*R*,4*S*)-**154**
Empirical formula	C33 H30 B N O3
Formula weight	499.39
Temperature	150(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P 2_1
Unit cell dimensions	a = 8.1770(2) A alpha = 90 deg. b = 14.8410(5) A beta = 94.8390(10) deg. c = 10.5950(3) A gamma = 90 deg.
Volume	1281.17(6) A^3
Z, Calculated density	2, 1.295 Mg/m^3
Absorption coefficient	0.081 mm^-1
F(000)	528
Crystal size	0.35 x 0.35 x 0.25 mm
Theta range for data collection	6.27 to 27.51 deg.
Limiting indices	-10<=h<=10, -19<=k<=18, -13<=l<=13
Reflections collected / unique	15517 / 5671 [R(int) = 0.0875]
Completeness to theta =	27.51 97.7 %
Max. and min. transmission	0.9799 and 0.9720
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5671 / 1 / 347
Goodness-of-fit on F^2	1.031
Final R indices [I>2sigma(I)]	R1 = 0.0514, wR2 = 0.1221
R indices (all data)	R1 = 0.0681, wR2 = 0.1329

Absolute structure parameter	-0.3(11)
Largest diff. peak and hole	0.230 and -0.232 e.A^-3

Table 2.
Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for (*S*,2*R*,4*S*)-**154**.

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
B	4797(3)	1032(2)	7371(2)	28(1)
N	2785(2)	886(1)	7426(2)	28(1)
O(1)	5551(2)	1500(1)	8471(1)	29(1)
O(2)	4851(2)	1552(1)	6193(1)	28(1)
O(3)	1058(2)	-364(1)	7335(2)	37(1)
C(1)	5442(2)	2421(2)	8530(2)	27(1)
C(2)	4685(3)	2787(2)	9566(2)	32(1)
C(3)	4490(3)	3690(2)	9678(2)	33(1)
C(4)	5018(3)	4282(2)	8746(2)	29(1)
C(5)	4691(3)	5220(2)	8785(2)	35(1)
C(6)	5125(3)	5780(2)	7846(2)	36(1)
C(7)	5911(3)	5429(2)	6818(2)	34(1)
C(8)	6245(3)	4526(2)	6756(2)	30(1)
C(9)	5823(2)	3920(2)	7718(2)	26(1)
C(10)	6115(2)	2975(2)	7654(2)	25(1)
C(11)	7089(2)	2550(2)	6681(2)	26(1)
C(12)	8740(3)	2815(2)	6498(2)	28(1)
C(13)	9574(3)	3515(2)	7204(2)	32(1)
C(14)	11161(3)	3744(2)	7003(2)	36(1)
C(15)	12004(3)	3290(2)	6081(2)	39(1)
C(16)	11248(3)	2600(2)	5415(2)	35(1)
C(17)	9611(2)	2349(2)	5592(2)	29(1)
C(18)	8838(3)	1609(2)	4914(2)	33(1)
C(19)	7291(3)	1350(2)	5124(2)	30(1)
C(20)	6413(2)	1824(1)	6006(2)	26(1)
C(21)	5313(2)	8(2)	7247(2)	29(1)
C(22)	6860(3)	-400(2)	7341(2)	32(1)
C(23)	7006(3)	-1312(2)	7064(2)	37(1)
C(24)	5620(3)	-1819(2)	6687(2)	40(1)
C(25)	4074(3)	-1432(2)	6587(2)	37(1)
C(26)	3951(3)	-519(2)	6864(2)	30(1)
C(27)	2371(3)	8(2)	6732(2)	31(1)
C(28)	1474(3)	-207(2)	8653(2)	35(1)
C(29)	2162(3)	761(2)	8731(2)	29(1)
C(30)	921(3)	1491(2)	8991(2)	33(1)
C(31)	683(3)	1646(2)	10397(2)	37(1)
C(32)	101(4)	813(3)	11070(3)	58(1)
C(33)	-452(4)	2440(3)	10535(3)	61(1)

Table 3. Bond lengths [A] for (*S*,2*R*,4*S*)-**154**.

B-O(1)	1.448(3)
B-O(2)	1.471(3)
B-C(21)	1.586(3)
B-N	1.665(3)
N-C(27)	1.521(3)
N-C(29)	1.525(3)
N-H	0.90(3)
O(1)-C(1)	1.372(3)
O(2)-C(20)	1.370(2)
O(3)-C(27)	1.408(3)
O(3)-C(28)	1.428(3)
C(1)-C(10)	1.388(3)
C(1)-C(2)	1.413(3)
C(2)-C(3)	1.355(3)
C(3)-C(4)	1.416(3)
C(4)-C(5)	1.418(4)
C(4)-C(9)	1.425(3)
C(5)-C(6)	1.366(4)
C(6)-C(7)	1.411(3)
C(7)-C(8)	1.372(3)
C(8)-C(9)	1.424(3)
C(9)-C(10)	1.425(3)
C(10)-C(11)	1.495(3)
C(11)-C(20)	1.383(3)
C(11)-C(12)	1.435(3)
C(12)-C(13)	1.421(3)
C(12)-C(17)	1.422(3)
C(13)-C(14)	1.375(3)
C(14)-C(15)	1.413(4)
C(15)-C(16)	1.362(4)
C(16)-C(17)	1.418(3)
C(17)-C(18)	1.430(3)
C(18)-C(19)	1.358(3)
C(19)-C(20)	1.412(3)
C(21)-C(26)	1.393(3)
C(21)-C(22)	1.399(3)
C(22)-C(23)	1.391(4)
C(23)-C(24)	1.391(4)
C(24)-C(25)	1.384(4)
C(25)-C(26)	1.391(3)
C(26)-C(27)	1.507(3)
C(28)-C(29)	1.543(3)
C(29)-C(30)	1.525(3)
C(30)-C(31)	1.536(3)
C(31)-C(33)	1.515(4)
C(31)-C(32)	1.523(4)

Table 4. Bond lengths [A] and angles [deg] for (*S*,2*R*,4*S*)-**154**.

O(1)-B-O(2)	112.99(18)
O(1)-B-C(21)	115.30(18)
O(2)-B-C(21)	113.87(18)
O(1)-B-N	112.90(17)
O(2)-B-N	101.44(16)
C(21)-B-N	98.55(16)
C(27)-N-C(29)	104.85(16)
C(27)-N-B	105.97(16)
C(29)-N-B	117.00(16)
C(27)-N-H	109.8(19)
C(29)-N-H	104.7(17)
B-N-H	114.1(18)
C(1)-O(1)-B	119.24(16)
C(20)-O(2)-B	111.88(15)
C(27)-O(3)-C(28)	104.63(17)
O(1)-C(1)-C(10)	121.94(18)
O(1)-C(1)-C(2)	116.89(19)
C(10)-C(1)-C(2)	121.1(2)
C(3)-C(2)-C(1)	120.6(2)
C(2)-C(3)-C(4)	120.6(2)
C(3)-C(4)-C(5)	121.3(2)
C(3)-C(4)-C(9)	119.1(2)
C(5)-C(4)-C(9)	119.5(2)
C(6)-C(5)-C(4)	121.0(2)
C(5)-C(6)-C(7)	120.0(2)
C(8)-C(7)-C(6)	120.3(2)
C(7)-C(8)-C(9)	121.5(2)
C(8)-C(9)-C(4)	117.7(2)
C(8)-C(9)-C(10)	122.37(19)
C(4)-C(9)-C(10)	119.87(19)
C(1)-C(10)-C(9)	118.24(18)
C(1)-C(10)-C(11)	118.41(19)
C(9)-C(10)-C(11)	123.34(18)
C(20)-C(11)-C(12)	118.93(19)
C(20)-C(11)-C(10)	118.24(18)
C(12)-C(11)-C(10)	122.62(18)
C(13)-C(12)-C(17)	117.73(18)
C(13)-C(12)-C(11)	123.04(19)
C(17)-C(12)-C(11)	119.21(19)
C(14)-C(13)-C(12)	121.1(2)
C(13)-C(14)-C(15)	120.7(2)
C(16)-C(15)-C(14)	119.4(2)
C(15)-C(16)-C(17)	121.4(2)
C(16)-C(17)-C(12)	119.6(2)
C(16)-C(17)-C(18)	121.2(2)
C(12)-C(17)-C(18)	119.17(18)
C(19)-C(18)-C(17)	120.84(19)
C(18)-C(19)-C(20)	120.0(2)
O(2)-C(20)-C(11)	119.42(18)
O(2)-C(20)-C(19)	118.81(19)
C(11)-C(20)-C(19)	121.77(19)
C(26)-C(21)-C(22)	118.2(2)
C(26)-C(21)-B	110.54(18)
C(22)-C(21)-B	130.9(2)
C(23)-C(22)-C(21)	120.0(2)
C(24)-C(23)-C(22)	120.3(2)

C(25)-C(24)-C(23)	120.9(2)
C(24)-C(25)-C(26)	118.0(2)
C(25)-C(26)-C(21)	122.6(2)
C(25)-C(26)-C(27)	124.2(2)
C(21)-C(26)-C(27)	113.2(2)
O(3)-C(27)-C(26)	115.8(2)
O(3)-C(27)-N	105.30(17)
C(26)-C(27)-N	104.23(17)
O(3)-C(28)-C(29)	105.06(18)
N-C(29)-C(30)	110.82(17)
N-C(29)-C(28)	102.29(17)
C(30)-C(29)-C(28)	115.19(18)
C(29)-C(30)-C(31)	114.96(18)
C(33)-C(31)-C(32)	111.6(2)
C(33)-C(31)-C(30)	109.8(2)
C(32)-C(31)-C(30)	113.7(2)

Table 5.
Anisotropic displacement parameters (A^2 x 10^3) for (*S*,2*R*,4*S*)-**154**.
The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
B	28(1)	26(1)	29(1)	2(1)	4(1)	-2(1)
N	28(1)	26(1)	30(1)	3(1)	3(1)	0(1)
O(1)	34(1)	24(1)	29(1)	2(1)	2(1)	-4(1)
O(2)	29(1)	27(1)	28(1)	2(1)	3(1)	-3(1)
O(3)	32(1)	34(1)	46(1)	-2(1)	7(1)	-7(1)
C(1)	29(1)	23(1)	29(1)	1(1)	0(1)	-4(1)
C(2)	33(1)	35(1)	28(1)	1(1)	5(1)	-6(1)
C(3)	32(1)	36(1)	31(1)	-8(1)	6(1)	-3(1)
C(4)	27(1)	31(1)	30(1)	-6(1)	1(1)	-2(1)
C(5)	34(1)	32(1)	37(1)	-8(1)	0(1)	2(1)
C(6)	42(1)	24(1)	42(1)	-3(1)	-4(1)	3(1)
C(7)	39(1)	27(1)	36(1)	3(1)	0(1)	-1(1)
C(8)	30(1)	30(1)	30(1)	-1(1)	1(1)	0(1)
C(9)	27(1)	25(1)	27(1)	-2(1)	0(1)	-2(1)
C(10)	26(1)	26(1)	25(1)	-1(1)	1(1)	-2(1)
C(11)	28(1)	24(1)	25(1)	1(1)	3(1)	-1(1)
C(12)	31(1)	27(1)	27(1)	5(1)	2(1)	1(1)
C(13)	32(1)	30(1)	33(1)	2(1)	0(1)	-2(1)
C(14)	31(1)	36(1)	41(1)	1(1)	-3(1)	-7(1)
C(15)	27(1)	47(2)	41(1)	7(1)	5(1)	-4(1)
C(16)	31(1)	40(1)	36(1)	6(1)	9(1)	2(1)
C(17)	28(1)	30(1)	28(1)	4(1)	4(1)	2(1)
C(18)	35(1)	35(1)	29(1)	0(1)	7(1)	3(1)
C(19)	35(1)	28(1)	28(1)	-3(1)	4(1)	-1(1)
C(20)	29(1)	24(1)	26(1)	3(1)	4(1)	1(1)
C(21)	31(1)	27(1)	28(1)	1(1)	5(1)	-2(1)
C(22)	30(1)	34(1)	32(1)	2(1)	5(1)	3(1)
C(23)	40(1)	35(1)	37(1)	2(1)	12(1)	7(1)
C(24)	53(1)	28(1)	40(1)	-2(1)	16(1)	3(1)
C(25)	44(1)	30(1)	37(1)	-5(1)	10(1)	-9(1)
C(26)	32(1)	29(1)	30(1)	-1(1)	6(1)	-3(1)
C(27)	32(1)	28(1)	34(1)	-1(1)	3(1)	-6(1)
C(28)	34(1)	31(1)	42(1)	5(1)	8(1)	-1(1)
C(29)	27(1)	30(1)	30(1)	3(1)	5(1)	0(1)
C(30)	32(1)	30(1)	36(1)	3(1)	4(1)	4(1)
C(31)	36(1)	40(1)	36(1)	0(1)	5(1)	4(1)
C(32)	74(2)	57(2)	46(2)	2(1)	23(1)	-12(2)
C(33)	66(2)	70(2)	47(2)	-11(2)	10(1)	26(2)

Table 6.
Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for (*S*,2*R*,4*S*)-**154**.

	x	y	z	U(eq)
H(2)	4310	2396	10191	38
H(3)	3996	3927	10386	39
H(5)	4164	5462	9475	41
H(6)	4896	6407	7886	44
H(7)	6210	5820	6166	41
H(8)	6769	4299	6055	36
H(13)	9027	3830	7826	38
H(14)	11696	4213	7488	43
H(15)	13087	3464	5928	46
H(16)	11831	2280	4819	42
H(18)	9414	1294	4309	39
H(19)	6799	851	4678	36
H(22)	7811	-55	7593	38
H(23)	8057	-1588	7133	44
H(24)	5735	-2440	6496	48
H(25)	3126	-1779	6336	44
H(27)	2031	128	5818	37
H(28A)	2309	-645	8998	42
H(28B)	491	-260	9134	42
H(29)	3109	788	9393	35
H(30A)	-152	1328	8547	39
H(30B)	1276	2065	8624	39
H(31)	1777	1814	10824	44
H(32A)	863	314	10965	87
H(32B)	-997	645	10704	87
H(32C)	63	944	11974	87
H(33A)	-42	2964	10094	91
H(33B)	-493	2583	11435	91
H(33C)	-1557	2288	10165	91
H	2170(30)	1330(20)	7070(30)	35(7)

Table 1. Crystal data and structure refinement for (*R*,*R*)-**149**.

Identification code	(*R*,*R*)-**149**
Empirical formula	C26 H32 B2 Cl6 N2 O3
Formula weight	654.86
Temperature	150(2) K
Wavelength	0.71073 A
Crystal system	monoclinic
Space group	P 2_1
Unit cell dimensions	a = 12.8270(2) A alpha = 90 deg. b = 9.1150(2) A beta = 90.4400(10) deg. c = 13.5150(3) A gamma = 90 deg.
Volume	1580.10(6) A^3
Z, Calculated density	2, 1.376 Mg/m^3
Absorption coefficient	0.574 mm^-1
F(000)	676
Crystal size	0.50 x 0.40 x 0.25 mm
Theta range for data collection	4.16 to 27.48 deg.
Limiting indices	-16<=h<=16, -11<=k<=11, -17<=l<=17
Reflections collected / unique	17416 / 6826 [R(int) = 0.0302]
Completeness to theta =	27.48 99.4 %
Max. and min. transmission	0.8697 and 0.7622
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6826 / 1 / 372
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0437, wR2 = 0.1027
R indices (all data)	R1 = 0.0475, wR2 = 0.1059

Absolute structure parameter	0.45(5)
Largest diff. peak and hole	0.613 and -0.649 e.A^-3

Table 2.
Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (A^2 x 10^3) for (*R*,*R*)-**149**.

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
B(1)	773(2)	4849(3)	1701(2)	26(1)
B(2)	2107(2)	5704(3)	2905(2)	27(1)
N(1)	1083(2)	5931(2)	737(1)	29(1)
N(2)	2439(2)	4122(2)	3424(1)	29(1)
O(1)	1309(1)	3463(2)	1549(1)	29(1)
O(2)	2883(1)	5933(2)	2133(1)	30(1)
O(3)	1048(1)	5632(2)	2578(1)	26(1)
C(1)	-476(2)	4841(3)	1470(2)	28(1)
C(2)	-1313(2)	4109(3)	1899(2)	31(1)
C(3)	-2326(2)	4339(3)	1540(2)	37(1)
C(4)	-2516(2)	5292(4)	755(2)	40(1)
C(5)	-1700(2)	6026(3)	308(2)	37(1)
C(6)	-703(2)	5766(3)	670(2)	32(1)
C(7)	261(2)	6405(3)	294(2)	33(1)
C(8)	2139(2)	6470(3)	495(2)	32(1)
C(9)	2749(2)	5252(3)	-32(2)	39(1)
C(10)	2243(3)	4864(4)	-1024(2)	50(1)
C(11)	3881(3)	5705(5)	-187(2)	57(1)
C(12)	2644(2)	7055(3)	1442(2)	33(1)
C(13)	2270(2)	6715(3)	3886(2)	31(1)
C(14)	2186(2)	8218(3)	4061(2)	39(1)
C(15)	2383(2)	8782(4)	5004(2)	50(1)
C(16)	2680(2)	7856(4)	5771(2)	55(1)
C(17)	2778(2)	6346(4)	5625(2)	49(1)
C(18)	2581(2)	5817(3)	4677(2)	35(1)
C(19)	2639(2)	4291(3)	4349(2)	34(1)
C(20)	2408(2)	2677(3)	2951(2)	32(1)
C(21)	3367(2)	2436(3)	2288(2)	37(1)
C(22)	3389(2)	849(3)	1916(2)	44(1)
C(23)	4386(2)	2769(4)	2844(3)	54(1)
C(24)	1372(2)	2526(3)	2386(2)	31(1)
C(30)	-560(2)	7703(3)	3613(2)	38(1)
Cl(1)	-1860(1)	7260(1)	3292(1)	44(1)
Cl(2)	-252(3)	9444(4)	3101(2)	68(1)
Cl(3)	-371(3)	7745(9)	4883(3)	65(1)
Cl(2A)	-357(6)	9521(8)	3520(20)	124(5)
Cl(3A)	-396(7)	7080(20)	4882(6)	70(3)
C(40)	4977(2)	7163(3)	3308(2)	34(1)
Cl(4)	5537(1)	5944(1)	4139(1)	86(1)
Cl(5)	5599(1)	7114(2)	2190(1)	104(1)
Cl(6)	5045(1)	8908(1)	3833(1)	103(1)

Table 3. Bond lengths [A] for (*R*,*R*)-**149**.

B(1)-O(3)	1.425(3)
B(1)-O(1)	1.454(3)
B(1)-C(1)	1.629(4)
B(1)-N(1)	1.684(3)
B(2)-O(3)	1.427(3)
B(2)-O(2)	1.463(3)
B(2)-C(13)	1.627(3)
B(2)-N(2)	1.658(3)
N(1)-C(7)	1.282(3)
N(1)-C(8)	1.480(3)
N(2)-C(19)	1.283(3)
N(2)-C(20)	1.465(3)
O(1)-C(24)	1.419(3)
O(2)-C(12)	1.417(3)
C(1)-C(2)	1.394(3)
C(1)-C(6)	1.401(3)
C(2)-C(3)	1.400(4)
C(3)-C(4)	1.391(4)
C(4)-C(5)	1.385(4)
C(5)-C(6)	1.385(4)
C(6)-C(7)	1.462(4)
C(8)-C(12)	1.527(3)
C(8)-C(9)	1.536(4)
C(9)-C(11)	1.525(4)
C(9)-C(10)	1.527(4)
C(13)-C(14)	1.395(4)
C(13)-C(18)	1.401(4)
C(14)-C(15)	1.395(4)
C(15)-C(16)	1.389(5)
C(16)-C(17)	1.396(5)
C(17)-C(18)	1.391(4)
C(18)-C(19)	1.462(4)
C(20)-C(24)	1.534(3)
C(20)-C(21)	1.543(3)
C(21)-C(22)	1.531(4)
C(21)-C(23)	1.533(4)
C(30)-Cl(2A)	1.681(8)
C(30)-Cl(3)	1.732(5)
C(30)-Cl(1)	1.766(3)
C(30)-Cl(2)	1.777(4)
C(30)-Cl(3A)	1.815(10)
C(40)-Cl(5)	1.716(3)
C(40)-Cl(4)	1.732(3)
C(40)-Cl(6)	1.743(3)

Table 4. Bond angles [deg] for (*R*,*R*)-**149**.

O(3)-B(1)-O(1)	116.0(2)
O(3)-B(1)-C(1)	113.44(19)
O(1)-B(1)-C(1)	115.72(19)
O(3)-B(1)-N(1)	106.95(18)
O(1)-B(1)-N(1)	106.58(18)
C(1)-B(1)-N(1)	95.28(18)
O(3)-B(2)-O(2)	115.94(19)
O(3)-B(2)-C(13)	113.28(19)
O(2)-B(2)-C(13)	114.6(2)
O(3)-B(2)-N(2)	109.42(19)
O(2)-B(2)-N(2)	104.57(18)
C(13)-B(2)-N(2)	96.69(18)
C(7)-N(1)-C(8)	122.3(2)
C(7)-N(1)-B(1)	111.13(19)
C(8)-N(1)-B(1)	125.97(19)
C(19)-N(2)-C(20)	122.6(2)
C(19)-N(2)-B(2)	110.9(2)
C(20)-N(2)-B(2)	126.25(18)
C(24)-O(1)-B(1)	115.76(17)
C(12)-O(2)-B(2)	115.30(18)
B(1)-O(3)-B(2)	120.63(18)
C(2)-C(1)-C(6)	116.9(2)
C(2)-C(1)-B(1)	133.0(2)
C(6)-C(1)-B(1)	110.1(2)
C(1)-C(2)-C(3)	120.0(2)
C(4)-C(3)-C(2)	121.0(3)
C(5)-C(4)-C(3)	120.3(3)
C(4)-C(5)-C(6)	117.5(2)
C(5)-C(6)-C(1)	124.2(2)
C(5)-C(6)-C(7)	126.2(2)
C(1)-C(6)-C(7)	109.6(2)
N(1)-C(7)-C(6)	113.5(2)
N(1)-C(8)-C(12)	108.26(19)
N(1)-C(8)-C(9)	109.5(2)
C(12)-C(8)-C(9)	115.3(2)
C(11)-C(9)-C(10)	109.9(2)
C(11)-C(9)-C(8)	110.9(2)
C(10)-C(9)-C(8)	111.1(3)
O(2)-C(12)-C(8)	112.9(2)
C(14)-C(13)-C(18)	117.8(2)
C(14)-C(13)-B(2)	133.2(3)
C(18)-C(13)-B(2)	109.0(2)
C(15)-C(14)-C(13)	120.2(3)
C(16)-C(15)-C(14)	120.3(3)
C(15)-C(16)-C(17)	121.2(3)
C(18)-C(17)-C(16)	117.2(3)
C(17)-C(18)-C(13)	123.3(3)
C(17)-C(18)-C(19)	126.9(3)
C(13)-C(18)-C(19)	109.8(2)
N(2)-C(19)-C(18)	113.5(2)
N(2)-C(20)-C(24)	108.6(2)
N(2)-C(20)-C(21)	111.3(2)
C(24)-C(20)-C(21)	112.9(2)
C(22)-C(21)-C(23)	109.3(2)
C(22)-C(21)-C(20)	110.0(2)
C(23)-C(21)-C(20)	111.5(2)
O(1)-C(24)-C(20)	112.79(19)
Cl(2A)-C(30)-Cl(3)	91.6(8)

Cl(2A)-C(30)-Cl(1)	110.7(4)
Cl(3)-C(30)-Cl(1)	111.9(2)
Cl(2A)-C(30)-Cl(2)	19.5(10)
Cl(3)-C(30)-Cl(2)	109.7(3)
Cl(1)-C(30)-Cl(2)	108.73(17)
Cl(2A)-C(30)-Cl(3A)	110.9(6)
Cl(3)-C(30)-Cl(3A)	19.4(4)
Cl(1)-C(30)-Cl(3A)	105.3(3)
Cl(2)-C(30)-Cl(3A)	128.4(5)
Cl(5)-C(40)-Cl(4)	111.15(16)
Cl(5)-C(40)-Cl(6)	111.08(17)
Cl(4)-C(40)-Cl(6)	107.63(14)

Table 5.
Anisotropic displacement parameters (A^2 x 10^3) for (*R*,*R*)-**149**.
The anisotropic displacement factor exponent takes the form:

-2 pi^2 [h^2 a*^2 U11 + ... + 2 h k a* b* U12]

	U11	U22	U33	U23	U13	U12
B(1)	33(1)	26(1)	20(1)	-1(1)	5(1)	-5(1)
B(2)	28(1)	30(1)	22(1)	-4(1)	5(1)	-2(1)
N(1)	39(1)	26(1)	22(1)	-2(1)	5(1)	-6(1)
N(2)	28(1)	34(1)	26(1)	2(1)	4(1)	-3(1)
O(1)	37(1)	27(1)	23(1)	-2(1)	5(1)	-2(1)
O(2)	30(1)	31(1)	28(1)	-3(1)	8(1)	-4(1)
O(3)	31(1)	29(1)	20(1)	-5(1)	3(1)	-2(1)
C(1)	34(1)	30(1)	22(1)	-5(1)	0(1)	-2(1)
C(2)	34(1)	34(1)	23(1)	-3(1)	1(1)	-5(1)
C(3)	34(1)	50(2)	26(1)	-7(1)	0(1)	-7(1)
C(4)	35(1)	53(2)	32(1)	-7(1)	-4(1)	1(1)
C(5)	44(1)	40(1)	27(1)	1(1)	-3(1)	4(1)
C(6)	40(1)	29(1)	26(1)	-2(1)	0(1)	-1(1)
C(7)	44(1)	32(1)	23(1)	1(1)	2(1)	-1(1)
C(8)	39(1)	31(1)	27(1)	2(1)	8(1)	-9(1)
C(9)	45(2)	43(2)	28(1)	-3(1)	13(1)	-6(1)
C(10)	64(2)	55(2)	31(1)	-9(1)	7(1)	-5(2)
C(11)	50(2)	71(2)	50(2)	-16(2)	22(1)	-13(2)
C(12)	36(1)	28(1)	33(1)	-3(1)	7(1)	-10(1)
C(13)	23(1)	43(1)	29(1)	-11(1)	4(1)	-3(1)
C(14)	29(1)	43(2)	46(2)	-20(1)	3(1)	-4(1)
C(15)	38(1)	61(2)	51(2)	-32(2)	3(1)	-1(1)
C(16)	39(1)	85(3)	40(2)	-37(2)	5(1)	-8(2)
C(17)	41(2)	79(2)	26(1)	-15(1)	2(1)	-6(2)
C(18)	27(1)	51(2)	28(1)	-9(1)	5(1)	-7(1)
C(19)	29(1)	46(2)	28(1)	0(1)	2(1)	-4(1)
C(20)	36(1)	29(1)	31(1)	4(1)	2(1)	-1(1)
C(21)	39(1)	33(1)	39(1)	2(1)	8(1)	6(1)
C(22)	45(2)	43(2)	44(2)	-14(1)	-5(1)	9(1)
C(23)	37(1)	45(2)	81(2)	-20(2)	9(1)	-5(1)
C(24)	38(1)	26(1)	29(1)	1(1)	4(1)	-5(1)
C(30)	33(1)	41(2)	38(1)	0(1)	2(1)	4(1)
Cl(1)	39(1)	49(1)	44(1)	-7(1)	-1(1)	-3(1)
Cl(2)	47(1)	59(1)	98(2)	30(1)	-22(1)	-15(1)
Cl(3)	37(1)	125(3)	34(1)	-8(2)	3(1)	5(2)
Cl(2A)	49(2)	32(2)	293(15)	2(5)	14(6)	0(2)
Cl(3A)	41(2)	135(7)	33(2)	-3(4)	-3(1)	-6(4)
C(40)	26(1)	39(1)	38(1)	1(1)	-3(1)	-2(1)
Cl(4)	84(1)	65(1)	108(1)	44(1)	-52(1)	-25(1)
Cl(5)	51(1)	217(2)	44(1)	-18(1)	14(1)	-37(1)
Cl(6)	77(1)	60(1)	171(1)	-52(1)	-54(1)	30(1)

Table 6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (A^2 x 10^3) for (*R*,*R*)-**149**.

	x	y	z	U(eq)
H(2)	-1195	3453	2435	37
H(3)	-2892	3837	1836	44
H(4)	-3210	5441	524	48
H(5)	-1819	6682	-227	44
H(7)	278	7103	-227	40
H(8)	2060	7309	23	39
H(9)	2742	4358	396	46
H(10A)	1519	4563	-918	75
H(10B)	2628	4057	-1331	75
H(10C)	2257	5723	-1460	75
H(11A)	4255	4911	-520	85
H(11B)	4210	5904	455	85
H(11C)	3903	6592	-597	85
H(12A)	3292	7582	1271	39
H(12B)	2165	7768	1754	39
H(14)	1994	8860	3537	47
H(15)	2314	9805	5121	60
H(16)	2820	8257	6408	66
H(17)	2970	5707	6151	58
H(19)	2808	3501	4779	41
H(20)	2423	1916	3484	38
H(21)	3313	3106	1704	45
H(22A)	3998	707	1493	65
H(22B)	2752	646	1536	65
H(22C)	3432	180	2483	65
H(23A)	4373	3783	3084	82
H(23B)	4976	2639	2396	82
H(23C)	4459	2098	3407	82
H(24A)	1288	1497	2166	37
H(24B)	792	2757	2838	37
H(30)	-85	6950	3323	45
H(40)	4228	6894	3206	41