SYNTHESIS
OF
BORON-CENTRED TRIPODAL LIGANDS

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"Tudo vale a pena se a alma não é pequena"

(All is worthwhile if the soul is not small)

Fernando Pessoa

To my family and Laurent

DECLARATION

I hereby declare that this thesis has been entirely composed by myself and that the work described herein is my own except where clearly mentioned either in acknowledgement, reference or text. It has not been submitted, in whole or in part, for any other degree, diploma or other qualification.

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ABSTRACT

Since their introduction, the hydrotris(pyrazolyl)borate and the hydrotris(methimazolyl)borate ligands have drawn the attention of many research groups. These boron-centred ligand systems have been studied, modified and applied in different areas of chemistry from medicinal to surface chemistry and catalysis.

The synthesis of new tripodal ligands of the type $[LB(mt)_3]$ (L = neutral Lewis base; mt = methimazolyl) with boron substituted by various nitrogen donors (L) is the aim of the work reported in this thesis. In this work a new synthetic method to obtain these ligands is presented. This new method consists of the substitution of dimethylamine in $[(HNMe_2)B(mt)_3]$ by a neutral N-donor under reflux in toluene. The evidence that the dimethylamine in $[(HNMe_2)B(mt)_3]$ can be substituted with N-donors contradicts the previously proposed mechanism for the "one-pot" reactions with tris(dimethylamino)borane reported previously. From this synthetic work, a new mechanism for the formation of ligands of the type $[(L)B(mt)_3]$ is proposed.

The N-donors used in this work were mainly tertiary amines and imines but also a primary amine, benzylamine was successfully used. The functionalization of the boron central atom of these ligands with primary amines broadens the possibility of synthesis of new ligands.

In order to explore an alternative to methimazole, two new boron-centred tripodal ligands with sulphur donors, $[(HNMe_2)B(1,4,5\text{-trimethylimidazolyl-2-thione})_3]$ and $[(HNMe_2)B(1\text{-methyl-benzimidazolyl-2-thione})_3]$, were synthesized. These ligands present a more protective environment around the boron bridgehead created by the substituents in the 4^{th} and 5^{th} position of methimazole.

The chiral tripodal ligand, [(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] was successfully obtained, and after its coordination to molybdenum tricarbonyl two diastereoisomeric complexes in a 1:7 ratio were obtained. Although, it was sought to obtain a single diastereisomer form of the complex, this is a very promising result indicating that this system can still be improved in order to obtain chiral boron-centred tripodal ligand complexes.

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ABBREVIATIONS

An	Anisyl
Ar	Aryl
ATH	Asymmetric Transfer Hydrogenation
$B(NMe_2)_3$	Tris(dimethylamino)borane
BINAP	2,2′-dihydroxy-1,1′-binaphthyl
BINOL	2,2′-bis(diphenylphosphino)-1,1′-binaphthyl
Bn	Benzyl
BOX	Bisoxazoline
br	broad
BuLi	Butyllithium
Bz	Benzyl
Cp	Cyclopentadiene
Cy	Cyclohexyl
cym	cymene
d	Doublet
DABCO	1,4-diazabicyclo[2.2.2]octane
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	Dichloromethane
DFT	Density Functional Theory
DMAP	Dimethylaminopyridine
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
e.e.	Enantiomeric excess
ES-MS	Electrospray Mass Spectrometry
Et	Ethyl
EtOH	Ethanol
Et_2O	Diethyl ether
FAB-MS	Fast atomic absortion mass spectrometry
fac	facial
Hmt	Methimazole, 2-mercapto-1-methylimidazole
$HNMe_2$	Dimethylamine
Hpz	Pyrazole
Hz	Hertz
i-Pr	Isopropyl
IR	Infrared
J	spin-spin coupling constant
K	Kelvin
Kj mol-1	Kilojoule per mol
LDA	Lithium diisopropyl amide
m	Multiplet

m	Meta
M.p.	melting point
Me	ethyl
MeCN	Acetonitrile
MeCOCl	Acetyl chloride
MeCOOH	Acetic acid
MeI	Methyl Iodide
MeLi	Methyl lithium
MeOH	Methanol
Mes	Mesityl
MS	Mass specrometry
mt	methimazolyl
NaOMe	Sodium Methoxide
NH_4PF_6	Ammonium hexafluorophosphate
NMe_2	Dimethylamine
NMR	Nuclear Magnetic Ressonance
o	Ortho
p	Para
Ph	Phenyl
PhCOCl	Benzoyl chloride
PPh_3	Triphenylphosphine
ppm	parts per million
pz	pyrazolyl
q	Quartet
s	Singlet
S_N1	Nucleophilic Substitution 1
S_N2	Nucleophilic Substitution 2
t	Triplet
T-Bu	Ter-Butyl
Tbz	Hydrotris(2-mercapto-benzoyhiazoline)borate
THF	Tetrahydrofuran
Tm	Hydrotris(methimazolyl)borate
TMEDA	Tetramethylethylenediamine
Tol	Tolyl
Tp	Hydrotris(pyrazolyl)borate
Tpm	Hydrotris(2-thiopyridone)borate
TRISOX	Trisoxazoline
Tt	Hydrotris(trioxotriazolyl)borate
Tz	Hydrotris(2-mercaptothiazoline)borate

CHAPTER I

BORON-CENTRED LIGANDS WITH THIONE DONORS

1.1. INTRODUCTION

The synthesis of new boron-functionalized tripodal ligand analogues of hydrotris(methimazolyl)borate (Tm) is the main concern of this thesis. The efforts towards the synthesis of these tripodal ligands will be described and discussed in the next chapters. This chapter will provide an introduction to the Tm tripodal ligand system which is necessary to contextualize this thesis work.

1.2. FROM HARD TO SOFT SCORPIONATE LIGANDS

Five decades ago, Trofimenko introduced the tris(pyrazolyl)borate (Tp) ligand, and described it as "a creature (that) grabs its prey with two identical claws and then may proceed to sting it with the sharp point of the curving tail"(Fig.1.1).[1] Following this metaphor the poly(pyrazolyl)borates were coined as scorpionate ligands.

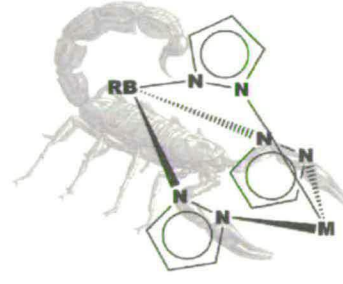
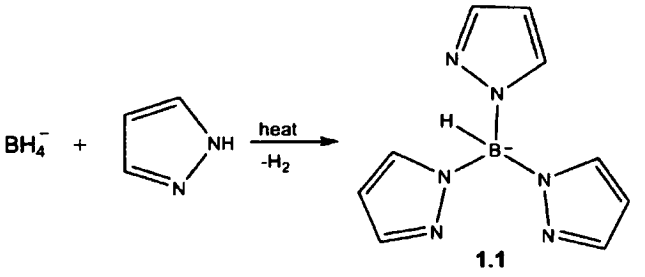


Fig.1.1. *Tris(pyrazolyl)borate ligand coordinated to a metal centre (M) mimicking a scorpion attack.*

The anionic hydrotris(pyrazolyl)borate was synthesized by heating pyrazole and alkali-metal borohydrides under solvent-free conditions (Scheme 1.1).[1] This

methodology has now also been employed to synthesise a wide range of Tp ligand analogues.[2]



1.1

Scheme 1.1. *Synthesis of the anionic hydrotris(pyrazolyl)borate ligand.*[1]

The tris(pyrazolyl)borate ligand is often compared to the cyclopentadienyl (Cp) ligand, as both systems are anionic, $6e^-$ donor face-capping ligands. However, there are also differences between these ligands systems such as, the relatively hard σ-donor character of Tp and the softer character of Cp which has some π-acceptor ability. Other differences between these ligand systems are the topology and the number of possible substitutable positions. There are five possible substitutable positions in the Cp ligand and ten substitutable positions in the Tp ligand (one on the boron and three on each of the pyrazole rings). Then, the tris(pyrazolyl)borate ligands can be tuned sterically and electronically and this versatility is reflected in the number of applications of Tp ligand derivatives in various fields of study such as catalysis, bioinorganic models and metal extractions.[2]

It is also possible to modify the scorpionate ligands by replacing the pyrazole with another heterocycle, or by replacing the central boron atom by another element. The replacement of the pyrazole rings can affect the size of the chelate rings formed on metal complexation, though the negative charge of the ligand is maintained.

Furthermore, the anionic character of the ligand can be changed if the boron is replaced with a different atom.[2]

The possibility of changing the pyrazole rings in the Tp ligand by other heterocycles with different donor atoms is attractive since it can lead to scorpionate ligands with different donor properties. As Tp ligand complexes were used to mimic sulphur-donor protein complexes with biological activity, it became interesting to explore the introduction of sulphur donor heterocycles into tris(pyrazolyl)borate derivatives.[3] However, the choice of another molecule to use in the synthesis of new derivatives to replace the pyrazole was restrained to the presence of an N-H acidic proton to enhance the condensation with the borohydride under solvent free conditions.

The first scorpionate ligand with heterocycles bearing sulphur donors was reported by Reglinski and Spicer in 1996.[4] They used 1-methylimidazole-2-thione (methimazole) to replace the pyrazole in the Tp ligand structure and obtained the hydrotris(methimazolyl)borate (Tm) ligand (Fig.1.2).[4]

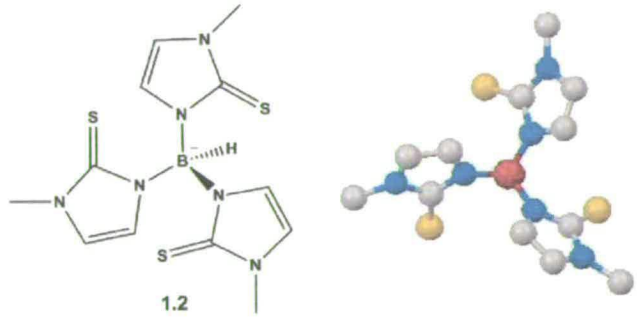


Fig.1.2. *Hydrotris(methimazolyl)borate (Tm) ligand and its crystal structure (hydrogens and the counter ion omitted for clarity).*[5, 4]

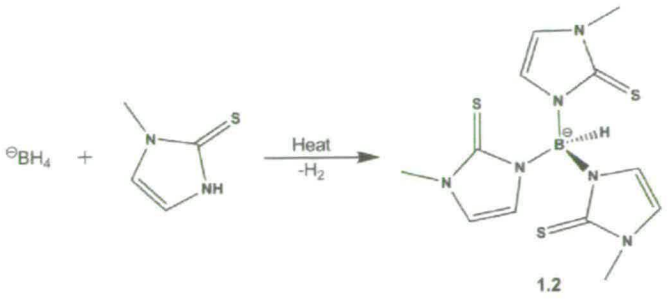
Methimazole can exist in two tautomeric forms, thiol and thione (Fig.1.3). Despite being commercialized as 1-methyl-2-imidazolethiol, NMR spectroscopy studies proved that the thione tautomer is the more favourable structure for this compound.[6] In this form it presents the acidic N-H proton which allows the condensation with borohydride during the synthesis of hydrotris(methymazolyl)borate ligand.[4]

Fig.1.3. *Thiol and thione tautomers of methimazole.*

1.3. TRIS(METHIMAZOLYL)BORATE (TM) LIGAND

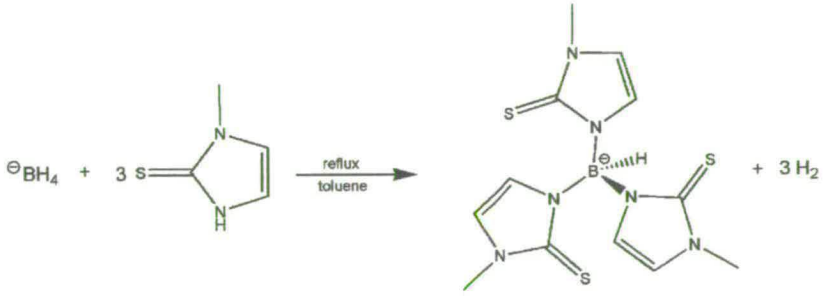
1.3.1. Synthesis

The Tm ligand can be synthesised employing a similar method as used to obtain the Tp ligand, a melt reaction with an alkali-metal borohydride and methimazole. This synthesis does not require solvent and can be followed by measuring the quantities of hydrogen gas produced after the solids start to melt.[4]



Scheme 1.2. *Synthesis of Tm ligand via melt reaction.*

This synthesis is limited by the thermal stability of the product formed since decomposition can occur if the reaction is heated beyond 180°C.[7, 8] The thermal limitation of this reaction can be related to methimazole's properties, as its melting point is around 145°C. The Tm ligand can also be obtained when a solution of methimazole and sodium borohydride in toluene is heated under reflux. This synthetic route can prevent thermal decomposition of the reactants, however it can take up to 36 hours to reach completion (Scheme 1.3).[9, 7]



Scheme 1.3. *Alternative Tm ligand synthesis: heating a solution of methimazole and borohydride in toluene until reflux.*

Some analogues of the Tm ligand with thioimidazole derivatives can be synthesised by heating a mixture of a substituted thioimidazole and sodium borohydride in toluene under reflux.[9]

1.3.2. Tm ligand derivatives

Derivatives of the Tm ligand can be obtained by replacing and/or functionalizing the N-methyl group and the 4- and 5- positions of the methimazole ring, or the boron central atom. The ten possible sites which can allow modifications on the Tm ligand are represented in Fig.1.4.

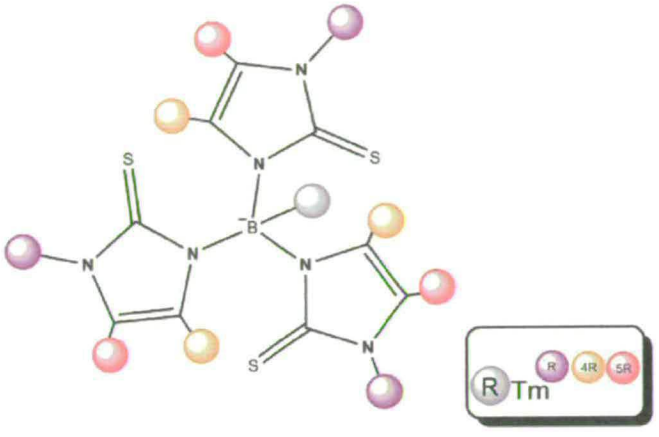


Fig.1.4. *Substitutable positions on the Tm ligand structure and respective abbreviation system.*

There are many examples of Tm ligand derivatives using methimazole analogues with different alkyl and aryl groups instead of the N-methyl group. Some of these methimazole derivatives used for the synthesis of Tm ligand analogues are displayed in Fig.1.5. The common abbreviation for these analogues is Tm^R, where R is the substituent of the thioimidazole nitrogen atom.

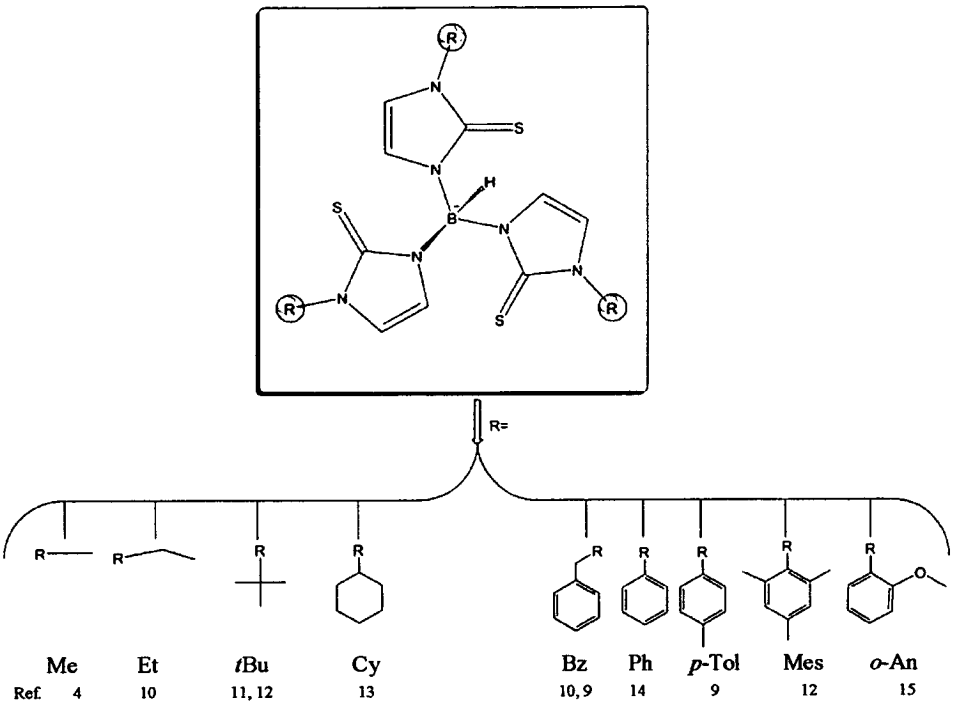
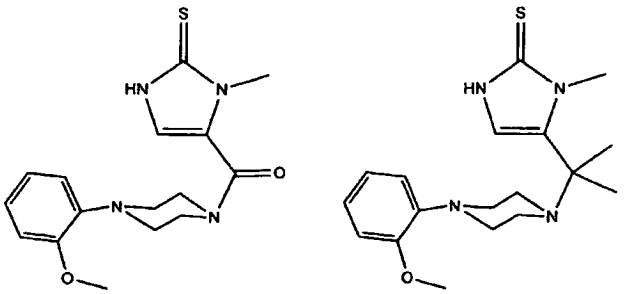


Fig.1.5. *Tm ligand derivatives with 1-R-imidazole-2-thiones.*

Usually, the 1-R-imidazole-2-thiones are easy to synthesize or are commercially available which makes them an interesting replacement for methimazole in the Tm ligand. The ligands synthesized with the imidazole-2-thiones may present different steric properties depending on the size of the R group which affects the encapsulation of the metal upon complexation. The creation of a cavity which can accommodate the metal centre is an attractive feature explored when this ligand system is applied to modelling metalloenzyme sites.

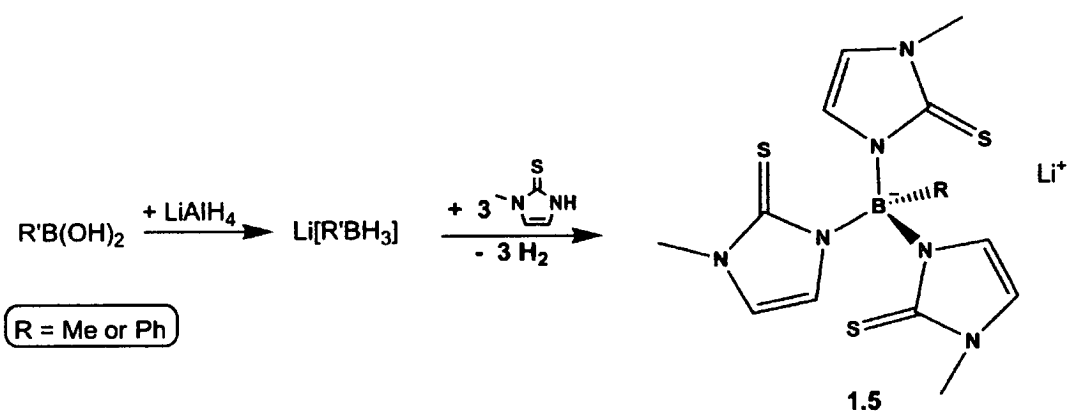
The 1-R-imidazole-2-thiones can also accommodate different groups on the 4- and 5- positions such as **1.3** and **1.4** shown in Fig. 1.6..



1.3 1.4

Fig.1.6. *Methimazole functionalized in the 5-position by piperazine derivatives: 1-methyl-5-[4-(2'-methoxyphenyl)-1-piperazinyl)carbonyl]-imidazole-2-thione* ***1.3*** *and 1-methyl-5-[4-(2'-methoxyphenyl)-1-piperazinyl)methyl]-imidazole-2-thione* ***1.4****.*[16]

As shown on Fig. 1.4, it is also possible to replace the hydride on the boron by alkyl or aryl groups without affecting the overall negative charge of the ligand. The first synthesis of a ligand with a different group on the boron instead of the hydride was reported by Santos and co-workers. They used methyl and phenyl groups to functionalize the boron atom by synthesising the ligands for precursors $RB(OH)_2$ (Scheme 1.4).[17]

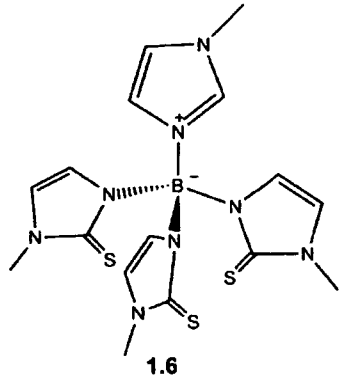


Scheme 1.4. *Synthesis of LiRTm^{Me}* ***1.5*** *reported by Santos and co-workers.*[17]

Other groups have been used to replace the hydride on the boron central atom of the Tm ligand, giving rise to ligands such as *n*BuTm^{Me} and *p*-$FC_6H_4Tm^{Me}$.[3] Other

approaches, such as the oxidative reaction of metallaboratranes was also used to insert groups, such as Cl or Br or an alkoxide group on the boron central atom. [18, 3]

The functionalization of the boron atom on the Tm framework with neutral N-donors to form new neutral ligands was reported by Bailey's research group.[19] The introduction of these zwitterionic ligands also brought to light a new synthetic method to generate Tm ligand analogues from tris(dimethylamino)borane. With this new synthesis, neutral tris(methimazolyl)borate derivatives can be obtained through a one-pot reaction with N-donor, $B(NMe_2)_3$ and methimazole in a 1:1:3 ratio in a toluene solution heated under reflux to obtain the product in high yield (more than 80 %).[19] This method will be discussed in more detail in Chapter II of this thesis.



1.6

Fig.1.7. *Neutral boron-centred tripodal ligand [(N-methylimidazole)B(methimazolyl)] **1.6** introduced by Bailey.*[19]

It is also possible to obtain ligands with a similar backbone structure as Tm by using other five-membered ring heterocycles with thione functions such as thiazolidine-2-thione[7] (**1.7**), 1,2,4-triazole-5-thione[20] (**1.8**) or 1,3,4-thiadiazole-2-thione[21] (**1.9**) and 1-methyl-5-thiotetrazole[22] (**1.10**) (Fig. 1.8). However, some of these heterocycles (**1.8** and **1.9**) can provide boron-centred tripodal ligands with the

ability to coordinate through two different donor atoms (sulphur or nitrogen). More detail of these ligands and examples of complexes needed.

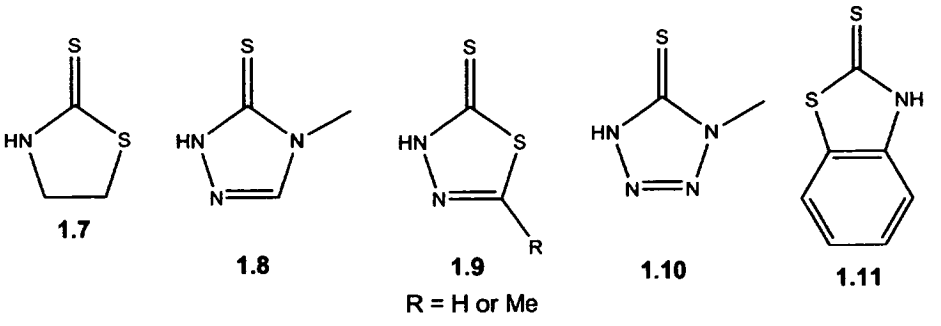
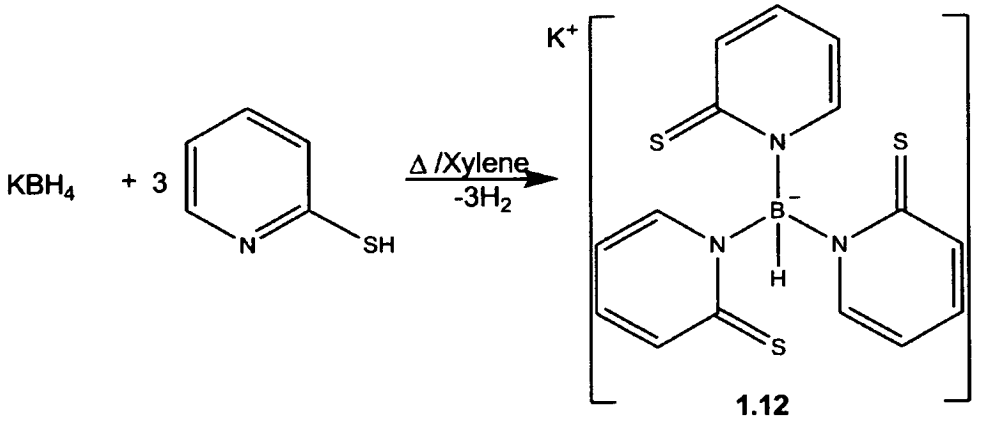


Fig.1.8. *Range of other heterocycles which can be used in the synthesis of Tm ligand derivatives.*[3]

Recently, it was reported the synthesis of a new boron-centred tripodal ligand with thione donors using 2-mercaptopyridine. This new ligand was prepared by heating under reflux a xylene suspension of potassium borohydride and 2-mercaptopyridine (Scheme 1.5).[23]



Scheme 1.5. *Synthesis of hydrotris(2-thiopyridone)borate (Tmp) ligand reported by Owen.*[23]

The 2-mercaptopyridine presents two tautomeric forms, the thione and thiolate. The thione form provides more electron density on the sulphur which can enhance the donor properties of the ligand (Fig 1.9).

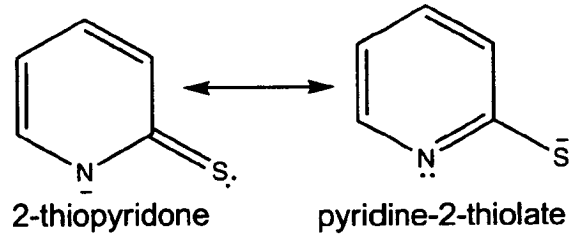


Fig.1.9. Resonance structures present on 2-mercaptopyridone.[23]

The anionic Tmp ligand can also present two resonance forms, as the negative charge can be on one of the sulphur donors or on the boron central atom. Fig.1.10.[23] However, Owen observed by ^{13}C NMR and X-ray single crystal diffraction that K[Tmp] structure presents thione donors which shows that the thiopyridone form is predominant.[23]

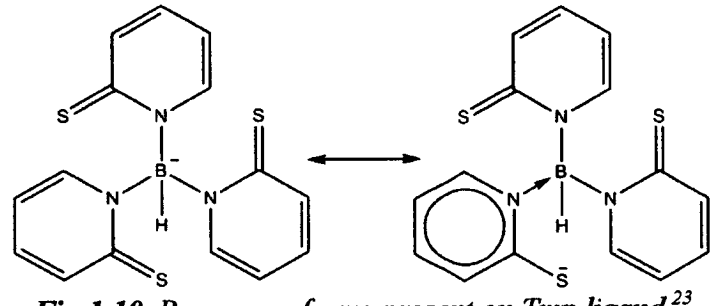


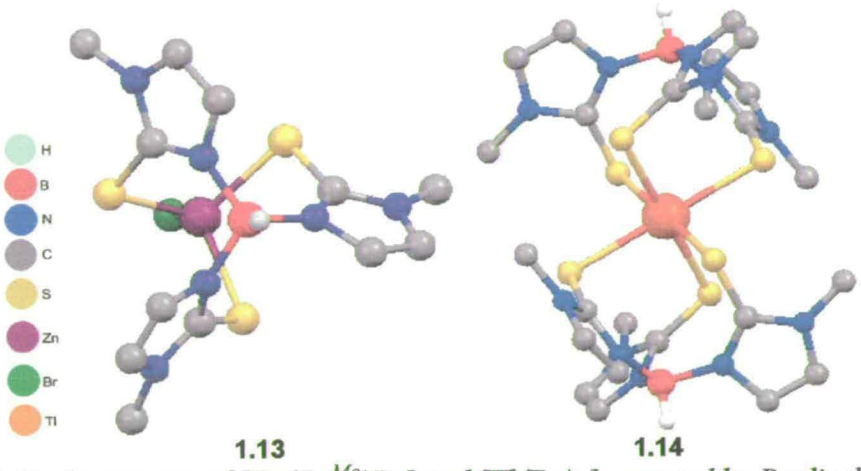
Fig.1.10. Resonance forms present on Tmp ligand.[23]

As the negative charge of Tmp ligand can be on the sulphur, the B-H bond can activated which makes these ligands potential precursors of metallaboratranes. [23, 24]

1.4. COORDINATION CHEMISTRY

1.4.1. Symmetry of metal complexes

The [(Tm)ZnBr] was the first complex of the Tm ligand reported by Reglinski.[4] In this complex it was possible to observe that this tridentate ligand forms a C_3-symmetric complex with a "propeller-like" conformation.[4] Fig.1.11 shows a metal an example of a tetrahedral **1.13** and an octahedral **1.14** metal complex of Tm ligand.



1.13 **1.14**

Fig.1.11. *Structures of [Zn(Tm^{Me})Br] and [Tl(Tm)$_2$] reported by Reglinski and Spicer.*[4, 25]

The Tm ligand differs from the Tp ligand system by the insertion of hexocyclic sulphur donor atoms on the methimazole ring. This results in the formation of eight-membered rings upon complexation instead of the six-membered rings formed in complexes with tris(pyrazolyl)borate (Tp) ligands. The Tm ligand complexes present C_3-symmetry due to twisting of the chelate rings to minimize angle-strain and maximize the π overlaping. This contrasts with the C_{3v}-symmetry presented by the tridentate Tp ligand metal complexes (Fig.1.12).

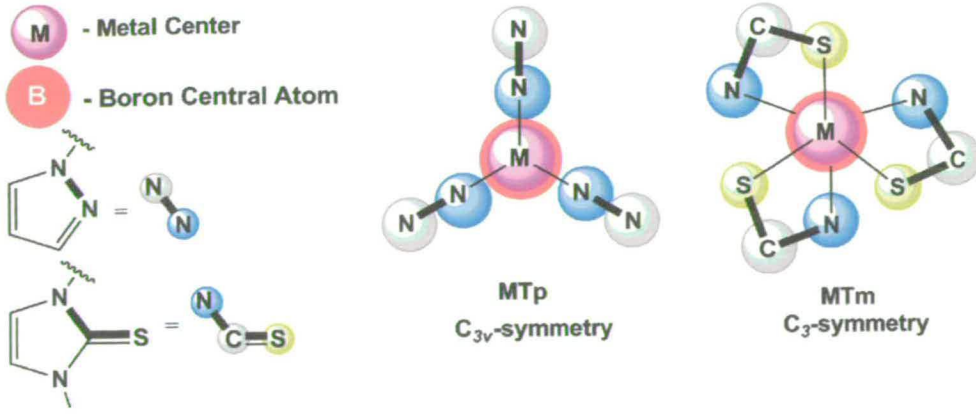


Fig.1.12. *Symmetry differences between Tp and Tm metal complexes.*

The helical rotation around the H-B···M axis of the tridimensional-cage structure present on the Tm ligand complexes generates two enantiomeric conformations (Fig.1.13).

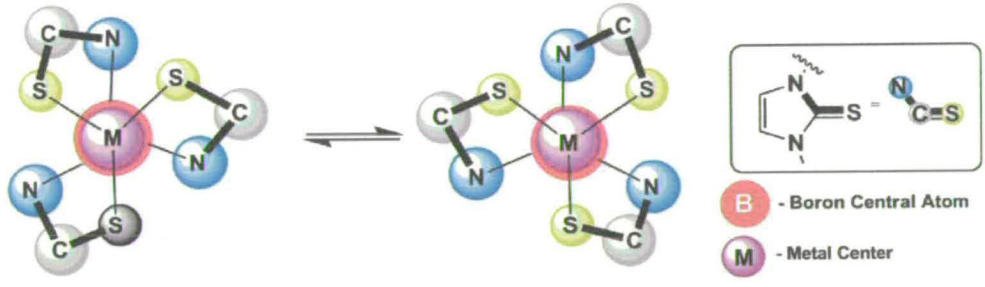


Fig.1.13. *Rotational enantiomers of MTm complexes.*

The crystal structures of these complexes show the presence of the two enantiomers. In solution it is possible to observe the racemisation process of Tm^R complexes presenting diastereotopic CH_2 protons adjacent to N in the 1-position of methimazole through ^1H NMR analysis. The racemisation of the complexes can occur by two different mechanisms: a non-dissociative mechanism and a dissociative mechanism (Fig.1.14).

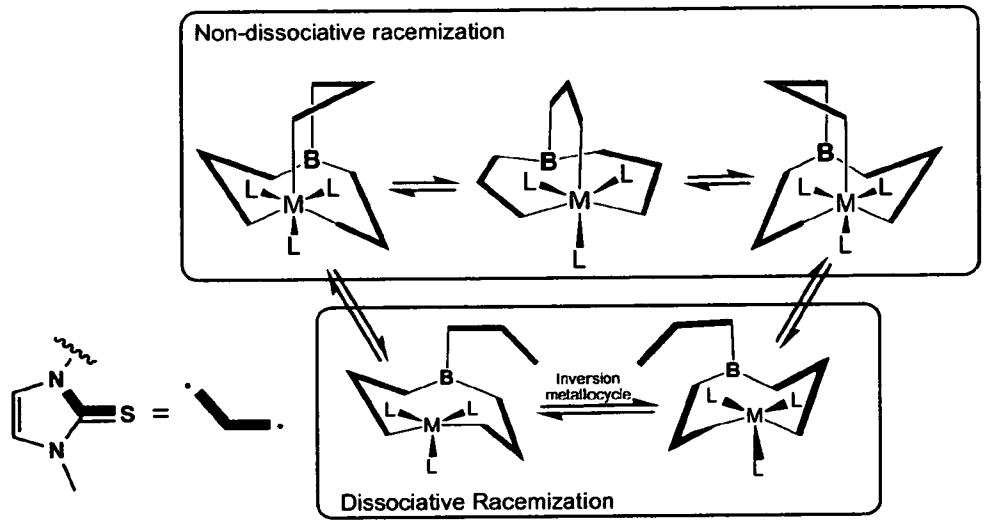
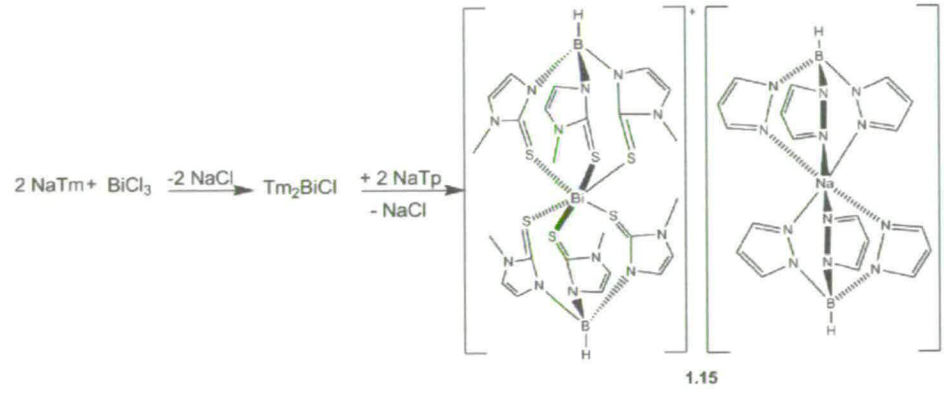


Fig.1.14. *Two possible racemization processes of metal complexes with Tm^R ligands.*[26]

The chirality of these Tm ligand systems will be discussed in more detail in the introduction to Chapter IV.

1.4.2. Donor properties

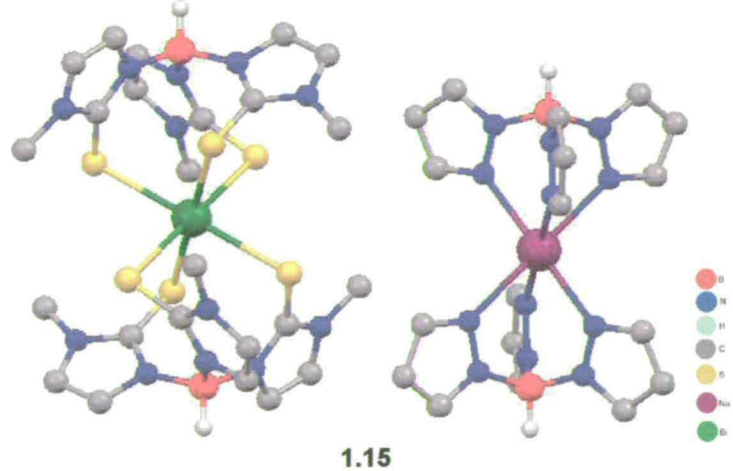
The presence of three sulphur donor atoms in the hydrotris(methimazolyl)borate ligand makes it a "softer" derivative of the ubiquitous hydrotris(pyrazolyl)borate (Tp) with its set of three hard nitrogen donors. A good example of the different hard-soft properties of these ligands was demonstrated by Reglinski and collaborators through a sequential reaction of $BiCl_3$ with NaTm and NaTp (Scheme 1.6).[27] The complex $[Bi(Tm)_2]^+[Na(Tp)_2]^-$ was obtained showing the soft sulphur donors of Tm coordinated to the bismuth and the hard nitrogen donors of Tp coordinated to the sodium (Fig.1.13) showing the coordination preferences of both ligands.[27]



1.15

Scheme 1.6. *Sequential reaction with hard and soft donor ligands reported by Reglinski.*[27]

The result of the reaction presented in Scheme 1.6 was also confirmed by *ab initio* calculations of the complexation energies for NaTp and NaTm, which showed a lower energy for the formation of the sodium tris(pyrazolyl)borate complex.[8] This confirms the softer donor character of the Tm ligand.



1.15

Fig.1.15. *Structure of $[Bi(Tm)_2]^+[Na(Tp)_2]^-$ reported by Reglinski.*[27]

Since its introduction, the Tm ligand has been related with other $6e^-$ face-capping ligands, such as, the well known Tp and Cp (cyclopentadienyl) ligands. The donor properties of these ligands can be determined by observing the IR carbonyl stretching bands of similar metal carbonyl complexes of these ligands. This was achieved by comparison of the carbonyl stretching frequencies in tungsten carbonyl complexes $[LW(CO)_3I]$ with the Tm, Tp and Cp ligands (Table 1.1).[28]

Table 1.1. *C-O stretching frequencies for $[LW(CO)_3I]$ complexes with Cp, Tp and Tm ligands.*[28]

Complex	υ(CO) / cm^{-1}			Ref.
$[CpW(CO)_3I]$	2030	1944	1936	29
$[TpW(CO)_3I]$	2021	1942	1904	30
$[TmW(CO)_3I]$	2004	1916	1902	28

Observing Table 1.1., it is possible to order the ligands in a series of decreasing donor strength as: Tm → Tp → Cp. In this series, Tm ligand is the stronger donor due to its sulphur lone pairs π-donation to the metal centre. However, the π-donation from the Tp ligand to the metal centre is very small which is related to its strong σ-donation from the pyrazole nitrogen atoms. The Cp is the worst donor of this series as it acts as a π-acceptor and competes with the carbonyl groups for electron density and therefore the C-O stretching energy for $[CpW(CO)_3I]$ is high.[28]

The strong π-donation of the Tm ligand to the metal centre was also observed in other carbonyl complexes with metals such as, molybdenum,[31] tungsten,[31] rhenium [32] and manganese.[33]

Another important aspect to describe the Tm ligands is its ligand-field properties. The magnetic behaviour of three sandwich-type complexes of Fe(II) with Tm, Tp and Cp (ferrocene) showed how different these complexes can be in terms of ligand field splitting. For instance, $[Fe^{II}(Cp)_2]$ (ferrocene) is a low-spin diamagnetic complex while $[Fe^{II}(Tp)_2]$ shows spin crossover properties[34] and $[Fe^{II}(Tm)_2]$ has a high spin paramagnetic d^6 iron (II).[35] This indicates that the order of these ligands in the spectrochemical series is Cp > Tp > Tm.[35, 36]

The spectroscopic analysis of the distorted octahedral $[Ni(Tm)_2]$ complex showed that hydro(trismethimazolyl)borate generates a weak ligand field with an estimated *Dq* of 816 cm^{-1}. This estimation allowed the placement of Tm ligand between the Cl^- (Dq = 680 cm^{-1}) and the H_2O (Dq = 850 cm^{-1}) ligands in the spectrochemical series.[35, 3]

1.4.2.1. Donor properties of neutral RTm ligands

The synthesis of analogues of Tm ligand with replacement N-donor substituents on the boron is the focus of this thesis. The insertion of these groups on the boron neutralizes the charge of the anionic Tm and can change its donor properties upon coordination to a metal centre. The effect of the insertion of different donors in boron-centred ligands can be illustrated with the comparison of the CO stretching frequencies of different manganese(I)triscarbonyl complexes with anionic and neutral pyrazolyl tripodal ligands (Table 1.2).

Table 1.2. CO stretching frequencies of manganese tricarbonyl complexes with anionic and neutral pyrazolyl tripodal ligands

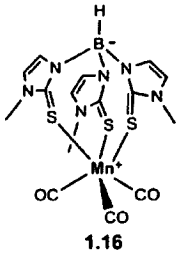
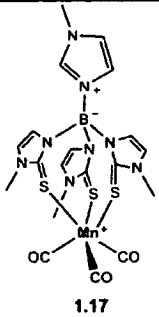
Complex	υ_{co}/cm^{-1}	Medium	Ref.
[{HB(3,5-Me_2pz)$_3$]Mn(CO)$_3$]	2023,1912	KBr	37
[{HB(pz)$_3$}Mn(CO)$_3$]	2036, 1932	MeCN	38
[{1-methylimidazole)B(pz)$_3$}Mn(CO)$_3$]$^+$	2041, 1941	MeCN	39
[{HC(3,5-Me_2pz)$_3$}Mn(CO)$_3$]$^+$	2044, 1949	CH_2Cl_2	40
[(HC(pz)$_3$}Mn(CO)$_3$]$^+$	2051, 1956	CH_2Cl_2	40

It is possible to observe on Table 1.2. that the anionic pyrazolyl ligands generate neutral complexes whereas neutral ligands, such as [1-methylimidazole)B(pz)$_3$] forms cationic complexes. The CO stretching frequencies of an anionic complex are expected to be lower than in the neutral complex, as in the latter the positive charge of the metal will affect directly the attached carbonyl ligands. This is also verified by the IR data on Table 1.2, as the donor strength of the ligand decreases if its negative charge is neutralized by the insertion of another group on the boron tripodal central atom. Replacing the boron atom by a carbon atom on the tripodal ligand not only affects the electronic charge of the ligand but also its electron donation to the metal. By comparison of CO stretching energies of the complexes [(HB(pz)$_3$}Mn(CO)$_3$] and [(HC(pz)$_3$}Mn(CO)$_3$]$^+$ it is possible to note a decrease of electronic donation to the metal from the neutral complex as indicated by the higher CO stretching frequency. Moreover, the insertion of an N-donor, as 1-methylimidazole, on the boron bridgehead in the Tp ligand structure also decreases the donor strength of this anionic ligand. This can be observed by comparison

between the two CO stretching frequencies on [{$HB(pz)_3$}$Mn(CO)_3$] and [{1-methylimidazole)$B(pz)_3$}$Mn(CO)_3$]$^+$. With the data on Table 1.2, it is possible to place the ligand [{1-methylimidazole)$B(pz)_3$} between the anionic Tp and the neutral [$(HC(pz)_3$}$Mn(CO)_3$]$^+$ according to its donor properties. This can be due to the stabilization of the positive charge on the 1-methylimidazole ring which is located away from the metal. In the tris(pyrazolyl)methane ligands this charge localization is not possible which makes them the weakers donors than the other ligand on Table 1.2.

A similar situation is observed for the methimazolyl ligands, as the CO stretching frequencies of manganese(I)tricarbonyl complexes with the neutral ligand [(N-methylimidazole)$B(methimazolyl)_3$] was compared to the anionic Tm ligand by IR spectroscopy. This IR data is displayed in Table 1.3.

Table 1.3. *C-O stretching frequencies for manganese(I)triscarbonyl complexes with Tm and [(N-methylimidazole)Tm ligands.*

Complex	 **1.16** [$TmMn(CO)_3$]	 **1.17** [(N-methylimidazole)$Tm(CO)_3$]$^+$
υ(C-O) / cm^{-1}	2003, 1905	2007, 1914
Medium	Toluene	Acetonitrile
Ref.	41	39

Observing Table 1.3, it is possible to see that the anionic Tm is only a slightly stronger donor than the neutral ligand, indicating that the interaction between the positive charge on N-methylimidazole and the metal centre is very small. This is possibly caused by the delocalisation of the azole charge within the ring as shown on Fig.1.16. [39]

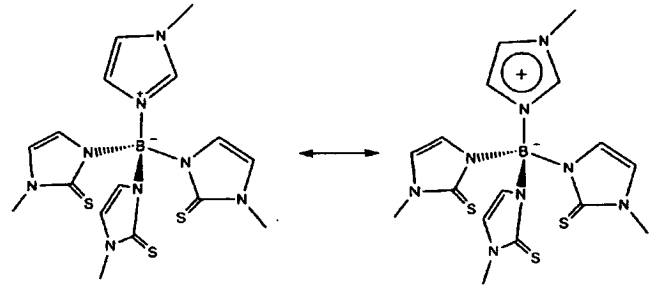


Fig.1.16. *Localization of the charge on N-methylimidazole in the neutral boron-centred tripodal ligand.*[39]

1.4.3. Coordination modes

The tris(methimazolyl)borates have shown great flexibility of coordination and have been found to adopt six different coordination modes (Fig.1.17). This versatility of coordination gives this ligand system a range of alternative steric and electronic properties which can be explored for different applications.

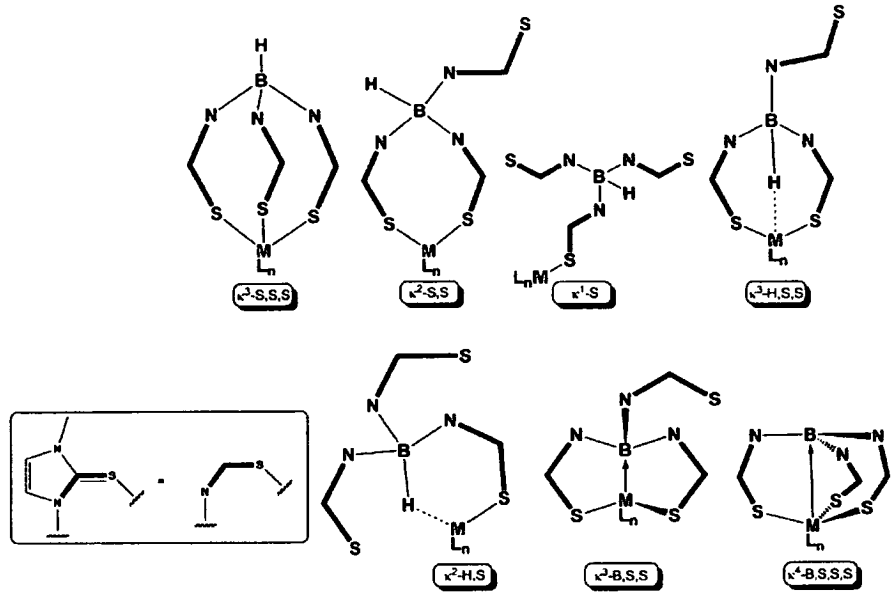


Fig.1.17. *Possible coordination modes of boron-centred tripodal ligands with thione donors ligand.*

There is a wide range of complexes reported where these boron-centred ligands present these different types of coordination and it is interesting to consider the possible metal geometries that can be found in some of these metal complexes.

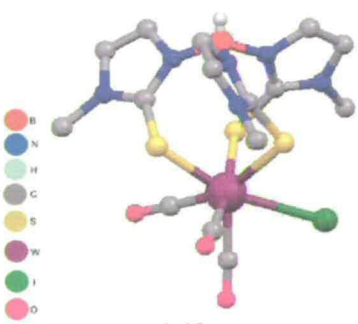
1.4.3.1. κ^3-*S,S,S* coordination mode

The most common complexes of the RTm ligand present the three sulphur atoms coordinated to the metal centre in a κ^3-S,*S,S* coordination. The coordination through three sulphur donors is the most expected pre-organization of these ligands.[3]

The tris(methimazolyl)borates can form bis-ligand complexes, when two Tm units coordinate in a κ^3-*S,S,S* fashion to a metal centre in an octahedral S_6

coordination sphere. In the literature, it is possible to find $[M(Tm)_2]^{n+}$ complexes with In(III),[42] Tl(III),[25] Sn(IV),[43] As(III),[44] Bi(III),[42] Fe(II),[35] and Ni(II).[35] A bismuth complex of this type was displayed on the Fig.1.15. It is also common to find octahedral complexes were one tris(methimazolyl)borate occupies three positions of the coordination sphere. $[Mn(Tm)(CO)_3]$, [Ru(Tm)(*p*-cymene)]Cl and [Ru(Tm)(Cp)] are some examples of complexes that were previously reported and studied.[10, 45, 33] It was observed that complexes of these tridentate ligands with tungsten can form a seven coordinate complex, $[W(Tm)(CO)_3I]$ (Fig.1.18).[28]

Tetrahedral complexes of zinc bearing the tridentate Tm^R ligands have also been reported as they have been shown to have some applications as metalloenzyme mimics.[46]

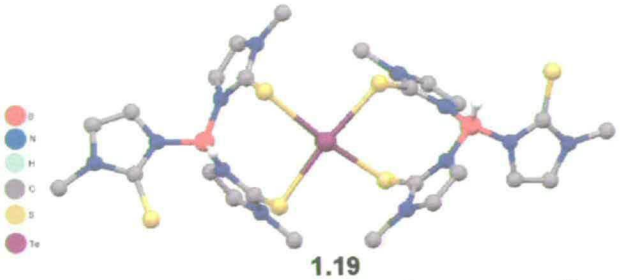


1.18

Fig.1.18. *Structure of the seven coordinate complex $[W(Tm)(CO)_3I]$.*[28]

1.4.3.2. κ^2-*S,S* coordination mode

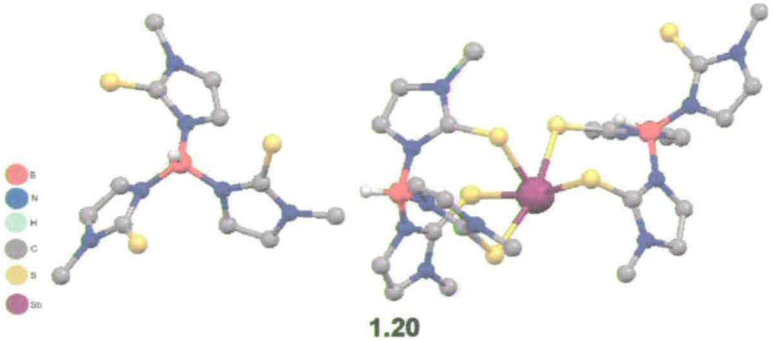
The tris(methimazolyl)borate also can coordinate by two sulphur donors as a $4e^-$ donor ligand, an example of this coordination mode is the tellurium complex $[Te(\kappa^2\text{-}S,S\text{-}Tm)_2]$. This complex has a distorted square-planar geometry as shown in Fig.1.19. This geometry has previously been observed in other Te(II) complexes with thione donors.[47]



1.19

Fig.1.19. *Structure of [Te(κ^2-S,S-Tm)$_2$].*[47]

The square-pyramidal antimony complex, [Sb(κ^3-*S,S,S*-Tm)(κ^2-*S,S*-Tm)]Tm, has two Tm ligands coordinated in κ^2 and κ^3 modes and a third Tm unit is present a the counter anion (Fig.1.20).[48]



1.20

Fig.1.20. *Structure [Sb(κ^3-S,S,S-Tm)(κ^2-S,S-Tm)]Tm.* [48]

1.4.3.3. κ^1- *S* coordination mode

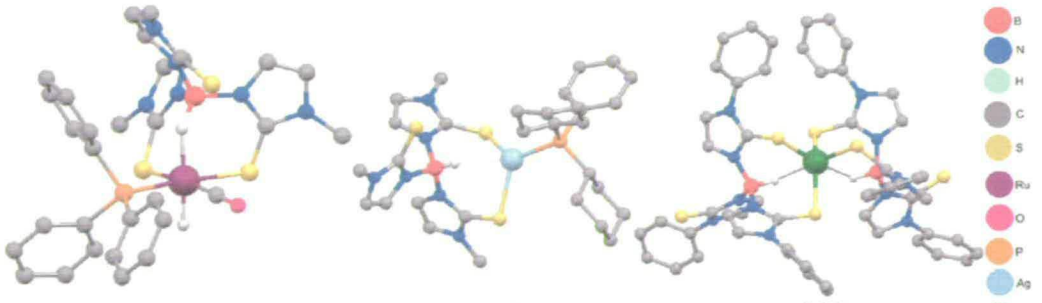
The tris(methimazolyl)borates can also bind to a metal centre by only one sulphur donor in a κ^1-*S* fashion. This coordination mode is not very common amongst these ligands and the tetra coordinated tin complex [$Ph_3Sn(\kappa^1$-*S*-Tm)] and [Ag(PhTm)(PPh_3)] are the few examples that can be found in the literature.[49, 50]

1.4.3.4. κ^3-*H,S,S* and κ^2-*H,S* coordination modes

The B-H in hydrotris(methimazolyl)borates can be close to the metal centres creating a M···H-B interaction. It is difficult to evaluate the nature of this "bond" and it is many times referred as an agostic bond. Although, agostic is a term that is generally used to describe M···H-C interactions, it may not be most appropriate to describe the M···H-B interaction. Recently, Spicer and Reglinski[3] introduced a classification system where these interactions are classified into three types. These classes are defined by Δr which is the difference between the observed M···H distance (d(M···H)) and the sum of the metal and hydrogen covalent radii (r_{cov}) (Equation 1.1).[3]

$$\Delta r = d(M\cdots H) - (r_{cov}(M) + r_{cov}(H)) \qquad \textbf{Equation 1.1}$$

The first type of M···H interaction is when the metal and the hydride are close (Δr < 0.25 Å). When, Δr is between 0.25 Å and 0.75 Å the interaction M···H is of the second type and finally all other complexes that present longer interactions (0.75 < Δr) belong to the third type.[3] This classification system quantifies the M···H-B interaction and allows the understanding of the nature of this "bond" as resultant from 3-centre 2 electron bond or dependant of electrostatic or steric factors.[3] Fig.1.21 shows three complexes with Tm^R ligands coordinated in a κ^3-*H,S,S* mode.



1.21 [Ru(Tm)(PPh$_3$)(CO)H] 1.22 [Ag(Tm)(PCy$_3$)] 1.23 [Fe(Tm^{Ph})$_2$]

Fig.1.21. *Complexes with tris(methimazolyl)borates presenting* κ^3*-H,S,S coordination.*[51-53]

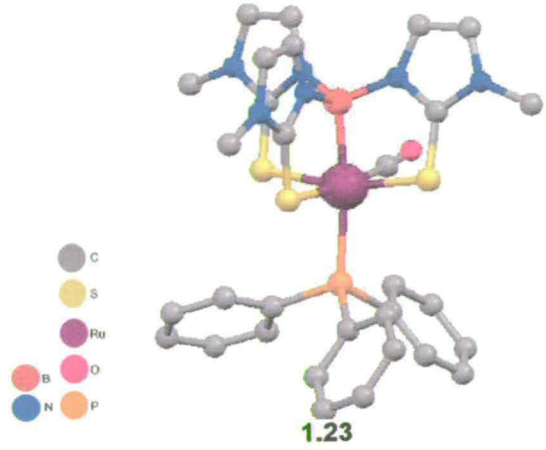
From the complexes showed in Fig.1.21, the octahedral complex [Ru(Tm)(PPh$_3$)(CO)H] presents a M···H-B interaction of the first category with short distance between the ruthenium and the hydride.[51] The other two complexes in Fig.1.21 display M···H-B interaction of the second type.[52, 3, 53] The Tm^R ligands can also coordinate in a κ^2-*H,S* mode however complexes with this type of coordination are rare.

1.4.3.5. κ^3-*B,S,S* and κ^4-*B,S,S,S* coordination modes

The formation of complexes with tris(methimazolyl)borane coordinated in a κ^3-*B,S,S* or a κ^4-*B,S,S,S* mode can occur when the boron loses the hydride during the complex synthesis. This has been shown to occur during the reaction of [Ir(PPh$_3$)$_2$(CO)Cl] with KTm^{tBu} generating {[(κ^3-*B,S,S*-B(mt)$_3$]Ir(PPh$_3$)(CO)H}.[54] The synthesis of this complex involves the metathesis of Cl by the tris(methimazolyl)borate and the cleavage of the B-H bond to allow the formation the M→B interaction. The type of structure formed has been named as

metallaboratranes.[54]

A metallaboratrane is formed by the coordination of the three sulphur atoms of the tris(methimazolyl)borates and a dative bond between the boron and the metal centre and presents a structure with three five membered chelate rings. These types of complexes with Rh(I),[55, 54] Ir(I),[54] Ru(II),[56] Os(0) [57] and other platinum group elements have been reported and studied. An example of a ruthenaboratrane structure is displayed in Fig.1.22.



1.23

Fig.1.22. *Structure of [Ru(κ⁴-B(mt)₃)(PPh₃)(CO)].*[58]

The nature of the M→B interaction was investigated using computational methods and it was observed that in a metallaboratrane the metal has a d^6 configuration instead of the expected d^8 configuration according to the metal oxidation number. Parkin's studies of M→B bonding in the metallaboratrane {[(κ⁴-B(mt)₃]Ir(PPh₃)Cl} showed that there is a 3-centre 4-electron interaction between Cl-Ir-B orbitals resulting in decrease of 2 electrons in the metal d^8 electron orbital configuration.[54]

1.5. CONCLUSION

Since it was introduced the tris(methimazolyl)borates have been used to model sulphur-rich metalloenzyme sites.[59, 46] Technetium complexes with this ligand system have been studied and applied as radiopharmaceutical drugs.[17, 32, 60] The application of the Tm ligand in surface coatings has also been reported.[61] Other applications of this ligand in mass spectrometry of organometallic analytes[62] and in catalysis have as well been investigated.[63]

Due to the particularly large variety of coordination modes, tris(methimazolyl)borate ligands have the ability to "tune" the metal centre in terms of geometry and/or electronic and steric properties. Thus, its uses are very diverse making this system attractive and applicable in different areas of chemistry.

REFERENCES

1. S. Trofimenko, *J. Am. Chem. Soc.*, 1966, **88**, 1842.
2. S. Trofimenko, *Scorpionates: The Coordinational Chemistry of Polypyrazolylborate Ligands*, Imperial College Press, London, 1999.
3. M. D. Spicer and J. Reglinski, *Eur. J. Inorg. Chem.*, 2009, 1553.
4. M. Garner, J. Reglinski, I. Cassidy, M. D. Spicer and A. R. Kennedy, *Chem. Commun.*, 1996, **16**, 1975.
5. A. Biernat, M. Schwalbe, D. Wallace, J. Reglinski and M. D. Spicer, *Dalton Trans.*, 2007, 2242.
6. M. Garner, D. R. Armstrong, J. Reglinski, W. E. Smith, R. Wilson and J. H. McKillop, *Bioorg. Med. Chem. Lett.*, 1994, **4**, 1357.
7. J. F. Ojo, P. A. Slavin, J. Reglinski, M. Garner, M. D. Spicer, A. R. Kennedy and S. J. Teat, *Inorg. Chim. Acta*, 2001, **313**, 15.
8. J. Reglinski, M. Garner, I. D. Cassidy, P. A. Slavin, M. D. Spicer and D. R. Armstrong, *J. Chem. Soc., Dalton Trans.*, 1999, 2119.
9. S. Bakbak, V. K. Bhatia, C. D. Incarvito, A. L. Rheingold and D. Rabinovich, *Polyhedron*, 2001, **20**, 3343.
10. P. J. Bailey, A. Dawson, C. McCormack, S. A. Moggach, D. H. Oswald, S. Parsons, D. W. H. Rankin and A. Turner, *Inorg. Chem.*, 2005, **44**, 8884.
11. D. J. Mihalcik, J. L. White, J. M. Tanski, L. N. Zakharov, G. P. A. Yap, C. D. Incarvito, A. L. Rheingold and D. Rabinovich, *Dalton Trans.*, 2004, 1626.
12. M. Tesmer, M. Shu and H. Vahrenkamp, *Inorg. Chem.*, 2001, **40**, 4022.
13. M. M. Ibrahim, M. Shu and H. Vahrenkamp, *Eur. J. Inorg. Chem.*, 2005, **2005**, 1388.

14. C. Kimblin, B. M. Bridgewater, D. G. Churchill and G. Parkin, *Chem. Commun.*, 1999, 2301.

15. J. Seebacher, M. Shu and H. Vahrenkamp, *Chem. Commun.*, 2001, 1026.

16. R. Garcia, Y. H. Xing, A. Paulo, A. Domingos and I. Santos, *J. Chem. Soc., Dalton Trans.*, 2002, 4236.

17. R. Garcia, A. Paulo, A. Domingos and I. Santos, *Dalton Trans.*, 2003, 2757.

18. J. S. Figueroa, J. G. Melnick and G. Parkin, *Inorg. Chem.*, 2006, **45**, 7056.

19. P. J. Bailey, D. Lorono-Gonzales, C. McCormack, F. Millican, S. Parsons, R. Pfeifer, P. Pinho, F. Rudolphi and A. S. Perucha, *Chem. Eur. J.*, 2006, **12**, 5293.

20. P. J. Bailey, M. Lanfranchi, L. Marchio and S. Parsons, *Inorg. Chem.*, 2001, **40**, 5030.

21. R. M. Silva, C. Gwengo, S. V. Lindeman, M. D. Smith and J. R. Gardinier, *Inorg. Chem.*, 2006, **45**, 10998.

22. Y.-L. Wang, R. Cao and W.-H. Bi, *Polyhedron*, 2005, **24**, 585.

23. G. Dyson, A. Hamilton, B. Mitchell and G. R. Owen, *Dalton Trans.*, 2009, 6120.

24. G. R. Owen, P. H. Gould, J. P. H. Charmant, A. Hamilton and S. Saithong, *Dalton Trans.*, 2010, **39**, 392.

25. P. A. Slavin, J. Reglinski, M. D. Spicer and A. R. Kennedy, *J. Chem. Soc., Dalton Trans.*, 2000, 239.

26. P. J. Bailey, D. Lorono-Gonzales, C. McCormack, F. Millican, S. Parsons, R. Pfeifer, P. P. Pinho, F. Rudolphi and A. S. Perucha, *Chem. Eur. J.*, 2006, **12**, 5293.

27. J. Reglinski, M. D. Spicer, M. Garner and A. R. Kennedy, *J. Am. Chem. Soc.*, 1999, **121**, 2317.

28. M. Garner, M.-A. Lehmann, J. Reglinski and M. D. Spicer, *Organometallics*, 2001, **20**, 5233.

29. R. H. Hill, A. Becalska and N. Chiem, *Organometallics*, 1991, **10**, 2104.

30. H. P. Kim, S. Kim, R. A. Jacobson and R. J. Angelici, *Organometallics*, 1986, **5**, 2481.

31. M. R. Foreman, A. F. Hill, A. J. White and D. J. Williams, *Organometallics*, 2003, **22**, 3831.

32. R. Garcia, A. Paulo, Â. Domingos and I. Santos, *J. Organomet. Chem.*, 2001, **632**, 41.

33. L. A. Graham, A. R. Fout, K. R. Kuehne, J. L. White, B. Mookherji, F. M. Marks, G. P. A. Yap, L. N. Zakharov, A. L. Rheingold and D. Rabinovich, *Dalton Trans.*, 2005, 171.

34. J. P. Jesson, S. Trofimenko and D. R. Eaton, *J. Am Chem. Soc.*, 1967, **89**, 3158.

35. M. Garner, K. Lewinski, A. Pattek-Janczyk, J. Reglinski, B. Sieklucka, M. D. Spicer and M. Szaleniec, *Dalton Trans.*, 2003, 1181.

36. M. Schwalbe, P. C. Andrikopoulos, D. R. Armstrong, J. Reglinski and M. D. Spicer, *Eur. J. Inorg. Chem.*, 2007, 1351.

37. J. E. Joachim, C. Apostolidis, B. Kanellakopulos, R. Maier, N. Marques, D. Meyer, J. Müller, A. Pires de Matos, B. Nuber, J. Rebizant and M. L. Ziegler, *J. Organometal. Chem.*, 1993, **448**, 119.

38. J. H. MacNeil, A. W. Roszak, M. C. Baird, K. F. Preston and A. L. Rheingold, *Organometallics*, 1993, **12**, 4402.

39. P. J. Bailey, L. Budd, F.A. Cavaco, S. Parsons, A. Sanchez-Perucha and F. White, *Chem. Eur. J.*, 2010, **16**, 2819.

40. D. L. Reger, T. C. Grattan, K. J. Brown, C. A. Little, J. J. S. Lamba, A. L. Rheingold and R. D. Sommer, *J. Organometal. Chem*, 2000, **607**, 120.

41. P. J. Bailey, D. J. Lorono-Gonzales, C. McCormack, S. Parsons and M. Price, *Inorg. Chim. Acta*, 2003, **354**, 61.

42. C. A. Dodds, J. Reglinski and M. D. Spicer, *Chem. Eur. J.*, 2006, **12**, 931.

43. C. Kimblin, B. M. Bridgewater, D. G. Churchill, T. Hascall and G. Parkin, *Inorg. Chem.*, 2000, **39**, 4240.

44. C. A. Dodds, M. Jagoda, J. Reglinski and M. D. Spicer, *Polyhedron*, 2004, **23**, 445.

45. P. J. Bailey, D. J. Lorono-Gonzales, C. McCormack, S. Parsons and M. Price, *Inorg. Chim. Acta*, 2003, **354**, 61.

46. G. Parkin, *New J. Chem.*, 2007, **31**, 1996–2014.

47. C. A. Dodds, A. R. Kennedy, J. Reglinski and M. D. Spicer, *Inorg. Chem.*, 2003, **43**, 394.

48. C. A. Dodds, J. Reglinski and M. D. Spicer, *Chem. Eur. J.*, 2006, **12**, 931.

49. A. F. Hill and M. K. Smith, *Chem. Commun.*, 2005, 1920.

50. D. Wallace, E. J. Quinn, D. R. Armstrong, J. Reglinski, M. D. Spicer and W. E. Smith, *Inorg. Chem.*, **49**, 1420.

51. M. R. Foreman, A. F. Hill, G. R. Owen, A. J. P. White and D. J. Williams, *Organometallics*, 2003, **22**, 4446.

52. C. Kimblin, D. G. Churchill, B. M. Bridgewater, J. N. Girard, D. A. Quarless and G. Parkin, *Polyhedron*, 2001, **20**, 1891.

53. C. Santini, C. Pettinari, G. Gioia Lobbia, R. Spagna, M. Pellei and F. Vallorani, *Inorg. Chim. Acta*, 1999, **285**, 81.

54. V. Landry, J. G. Melnick, D. Buccella, K. Pang, J. C. Ulichny and G. Parkin, *Inorg. Chem.*, 2006, **45**, 2588.

55. I. R. Crossley, M. R. Foreman, A. F. Hill, A. J. P. White and D. J. Williams, *Chem. Commun.*, 2005, 221.

56. M. R. S. J. Foreman, A. F. Hill, G. R. Owen, A. J. P. White and D. J. Williams, *Organometallics*, 2003, **22**, 4446.

57. M. R. Foreman, A. F. Hill, A. J. P. White and D. J. Williams, *Organometallics*, 2004, **23**, 913.

58. A. F. Hill, G. R. Owen, A. J. P. White and D. J. Williams, *Angew. Chem. Int. Ed.*, 1999, **38**, 2759.

59. J. G. Melnick and G. Parkin, *Science*, 2007, **317**, 225.

60. R. Garcia, A. Paulo, A. Domingos, I. Santos, K. Ortner and R. Alberto, *J. Am. Chem. Soc.*, 2000, **122**, 11240.

61. J. Reglinski, M. D. Spicer, J. F. Ojo, G. D. McAnally, A. Skorska, S. J. Smith and W. E. Smith, *Langmuir*, 2003, **19**, 6336.

62. M. F. Wyatt, B. K. Stein and A. G. Brenton, *Anal. Chem.*, 2005, **78**, 199.

63. M. Jiménez-Tenorio, M. C. Puerta and P. Valerga, *Organometallics*, 2009, **28**, 2787.

CHAPTER II

STUDIES INTO THE SYNTHESIS OF BORON-CENTRED TRIPODAL LIGANDS FROM TRIS(DIMETHYLAMINO)BORANE

2.1. INTRODUCTION

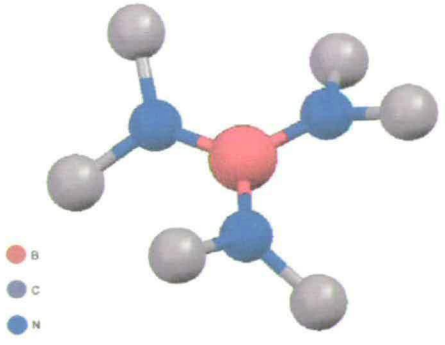
The synthesis of new tripodal ligands of the type $[LB(mt)_3]$ (L = neutral Lewis base; mt = methimazolyl) with boron substituted by various nitrogen donors (L) is the aim of this work. These ligands can be synthesized via a "one-pot" reaction with tris(dimethylamino)borane, as mentioned in the previous chapter, or through substitution of the dimethylamine in $[(HNMe_2)B(mt)_3]$. In this chapter, the results towards the study and development of the latter synthetic method will be presented and discussed. To support the understanding of this work, an introduction to the reactivity of tris(dimethylamino)borane and the synthesis of these ligands via a "one-pot" reaction will be presented. The application of a similar synthetic route to obtain $[(L)B(pz)_3]$ (pz = pyrazole) will also be included in this chapter.

2.2. TRIS(DIMETHYLAMINO)BORANE

The source of boron of the majority of the ligands synthesized and studied in this work was tris(dimethylamino)borane. In order to understand the $[LB(mt)_3]$ ligand system synthesis it is important to consider some structural features and reactivity of $B(NMe_2)_3$.

X-ray diffraction and gas phase electron diffraction studies have shown that tris(dimethylamino)borane has D_3 symmetry in which $B\text{-}N_3$ is planar (Fig.2.1). Although, it was observed that two of the three dimethylamino groups of this compound can twist through a variable angle between 28 to 35° ($N(CH_3)_2$ twist

angle).[1,2] This twist is due to the steric strain relief of the amine groupes. The B-N bond lengths were found to be between 1.43-1.44(8) Å, which is shorter than in tetrahedral borane compounds, such as H_3BNH_3 where the B-N distance is 1.56 Å.[1, 3] The short distance between the vacant *p*-orbital of the boron and the delocalized lone pairs of the nitrogen atoms creates a π-interaction.



2.1

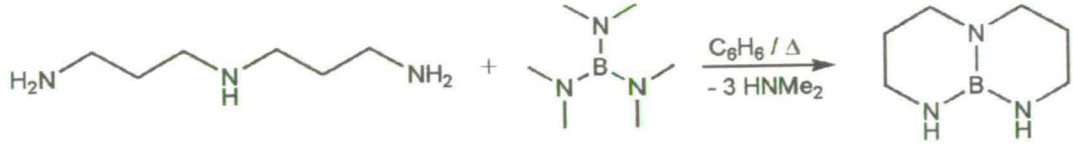
Fig. 2.1. *Structure of tris(dimethylamino)borane* ***2.1***. [2]

NMR studies by Beckett and co-workers demonstrated that this B-N π-interaction decreases the Lewis acidity of tris(dimethylamino)borane relative to tris(methoxy)borane and trifluoroborane, and this can be understood in terms of the relative electronegativities of nitrogen, oxygen and fluor.[4]

Tris(dimethylamino)borane can easily react with primary and secondary amines by transamination reactions to form tris(amino)boranes.[5] These reactions are facilitated by the fact that liberated dimethylamine gas is readily lost from the reaction, thus driving the equilibrium to the transamination product (Eq. 2.1).[6]

$$B(NMe_2)_3 + 3\,RNH_2 \rightleftharpoons B(NHR)_3 + 3\,HNMe_2\,(g) \qquad \textit{Eq. 2.1.}$$

Other heterocyclic aminoboranes, such as that formed with 3,3,2-diaminodipropylamine, can be obtained via the reaction with triamines, as represented in Scheme 2.1.



Scheme 2.1. *Synthesis of 1,5,7-triaza-6-borabicyclo[4.4.0]decane from tris(dimethylamino)borane.* [6]

Interesting work on the reactivity of $B(NMe_2)_3$ with pyridines and anilines was developed by Braun and Nöth. They reported the synthesis of three tris(amino)boranes synthesized via transamination of tris(dimethylamino)borane with aniline, 2-aminopyridine and 8-quinolinamine. For all these reactions the respective amine was reacted with tris(dimethylamino)borane under reflux in toluene.[7, 8] The structures of tris(anilino)borane **2.2**, tris(2-pyridylamino)borane **2.3**, and tris(8-quinolinoamino)borane **2.4** are represented on Fig.2.2.[8]

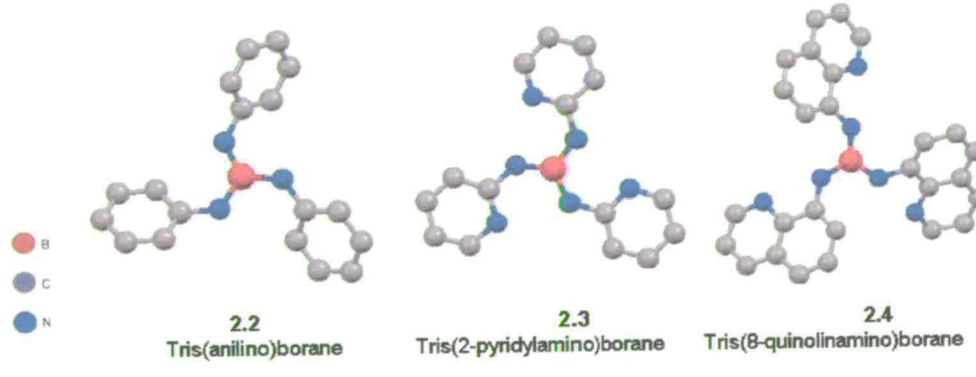
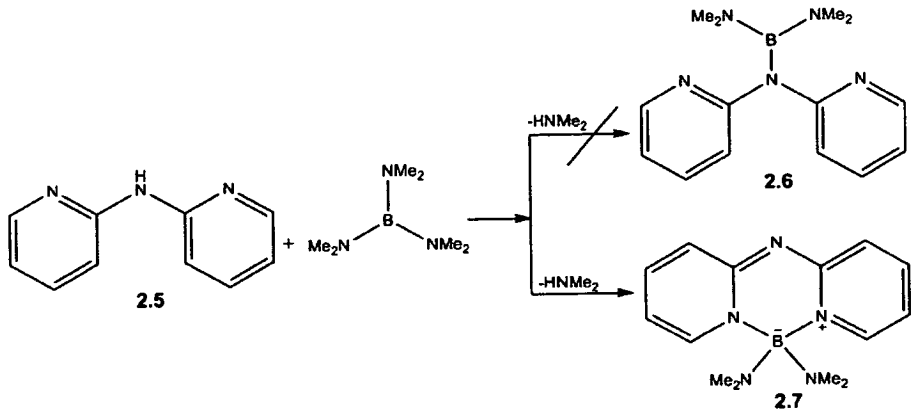


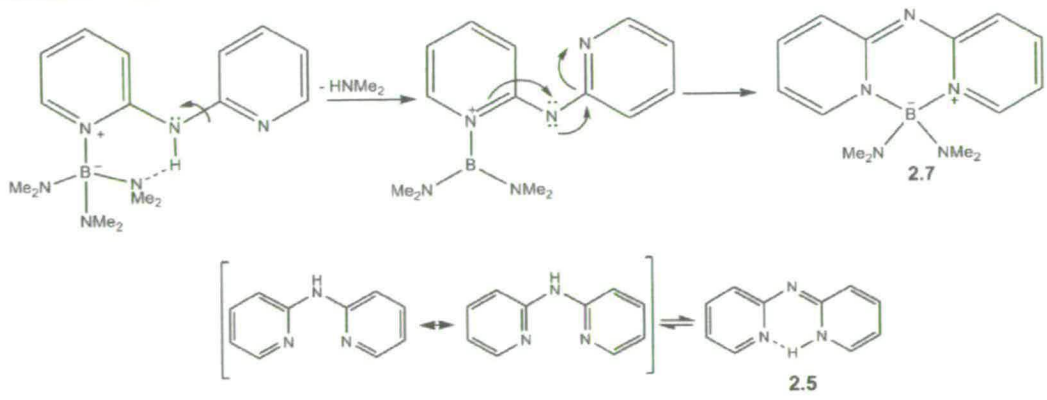
Fig.2.2. *Trisaminoboranes synthesized from tris(dimethylamino)borane(hydrogens are not shown).*[8]

Braun and Nöth also investigated the reactivity of $B(NMe_2)_3$ with di(pyrid-2-yl)amine **2.5** expecting to obtain bis(dimethylamino)di(pyridyl-2-yl)borane **2.6** (Scheme 2.3). This reaction was unsuccessful and the product formed was the heterocyclic 2-aminopyridine(dimethylamino)borane **2.7** (Scheme 2.3).[7]



Scheme 2.3. *Product obtained and expected of the reaction of tris(dimethylamino)borane with di(pyrid-2-yl)amine.* [7]

According to Braun and Nöth, the mechanism of this reaction was different from the previous reactions with pryridines and anilines. In this case, the boron coordinates first with one of the pyridine nitrogen atoms instead of reacting with the nitrogen bearing the acidic N-H proton, which is less accessible sterically. Dimethylamine gas is formed and eliminated due to the formation of an N-H···N hydrogen bridge bond. The rotation of the C-N bond of the non-coordinated pyridyl moiety allows the cyclization and consequently formation of the six-membered ring anion. The electron delocalization of di(pyrid-2-yl)amine 2.5 also affects strongly this mechanism, which is shown on Scheme 2.4.[7]



Scheme 2.4. *Mechanism of the synthesis of the 2-aminopyridine(dimethylamino)borane and the electron delocalization of di(pyrid-2-yl)amine reported by Braun and Nöth.*[7]

When this 2-aminopyridine(dimethylamino)borane reacts with aluminium trichloride one of the dimethylamine groups is easily removed. This may be due to the disparity of the B-N bond lengths of the dimethylamino groups which are different (1.63(8) Å and 1.45(9) Å), which may indicate a weaker B-N bond. This is observed in the structure of 2-aminopyridine(dimethylamino)borane **2.7**, also reported by Braun and Nöth (Fig.2.3.).[7]

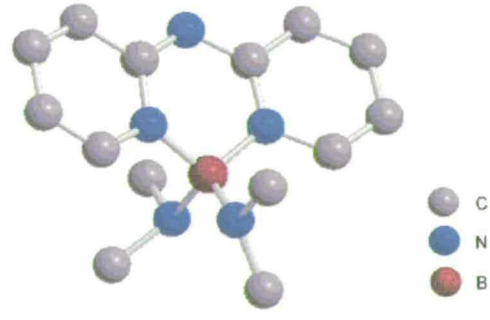
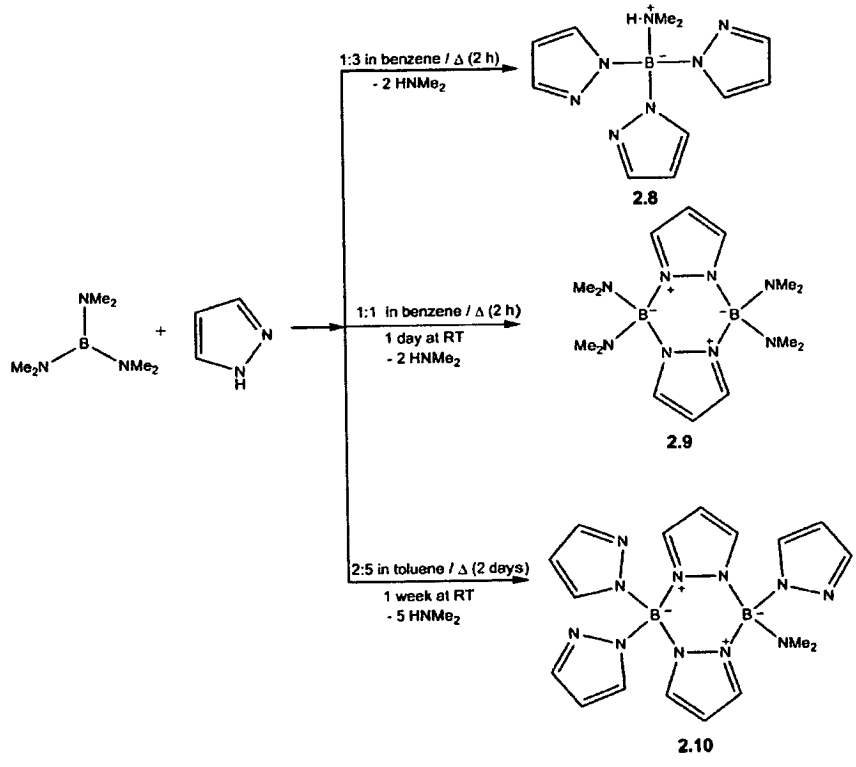


Fig.2.3. *Structure of 2-aminopyridine(dimethylamino)borane* ***2.7*** *reported by Braun and Nöth (hydrogens not shown for clarity).*[7]

Niedenzu also investigated the reactivity of tris(dimethylamino)borane with pyrazole in the synthesis of pyrazaboles. In this work, $B(NMe_2)_3$ was reacted with different equivalents of pyrazole under benzene or toluene reflux where some dimethylamine gas evolution was observed. In the case of pyrazabole formation, the mixture was left reacting at room temperature until dimerization occured. The conditions of these reactions and the products obtained, dimethylamine-tris(pyrazolyl)borate **2.8** and two different pyrazaboles (**2.9** and **2.10**), are displayed in Scheme 2.5.



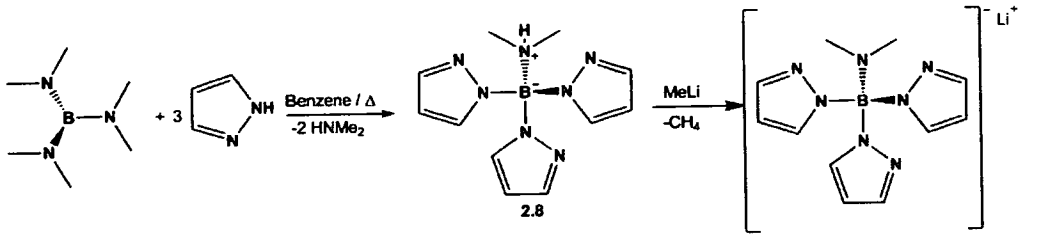
Scheme 2.5. *Niedenzu reactions with $B(NMe_2)_3$ and pyrazole.*[9]

According to Niedenzu, the driving force for these reactions is the formation of a very reactive tetrahedral intermediate, $[(HNMe_2)(NMe_2)B(pz)_2]$, that reacts readily with pyrazole in solution releasing dimethylamine gas. Niedenzu's work showed that it was possible to synthesize a tris(pyrazolyl)borate analogue from tris(dimethylamino)borane. [9, 10]

2.3. SYNTHESIS OF LIGANDS OF THE TYPE $[LB(MT)_3]$

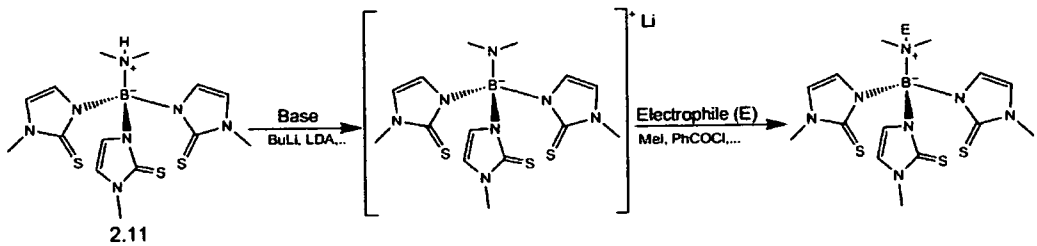
2.3.1. Ligand synthesis via a "one-pot" reaction: genesis and mechanism

Tris(pyrazolyl)borate ligand derivatives with functionalized boron can be synthesized from boronic acids and boron trihalides.[11] As mentioned previously, tris(dimethylamino)borane was used in the synthesis of $[(HNMe_2)B(pz)_3]$ **2.8** as reported by Niedenzu (Scheme 2.5).[9] It was observed in the low temperature ^1H NMR spectrum that the dimethylamine N-H proton can interchange site between the NMe_2 group and pyrazole nitrogen atoms, and the ligand can be represented as $[(HNMe_2)B(pz)_3]$ or $H[(NMe_2)B(pz)_3]$. This is reinforced by its easy deprotonation, so when this ligand reacts with MeLi the lithium salt, $Li[(NMe_2)B(pz)_3]$, is formed (Scheme 2.6).[12]



Scheme 2.6. *Synthesis of [(HNMe$_2$)B(pz)$_3$] 2.8 from B(NMe$_2$)$_3$ and respective lithium salt reported by Niedenzu.*[9, 12]

This route was exploited by Bailey to obtain derivatives of the hydrotris(methimazolyl)borate (Tm) ligand in which the boron bound hydride is replaced by alternative groups, [(L)B(mt)$_3$], as the synthesis of these ligands could not be achieved directly from [(H)B(mt)$_3$] due to the strong covalent character of the B-H bond.[13, 14] After establishing that [(HNMe$_2$)B(mt)$_3$] could also be obtained by heating a solution of tris(dimethylamino)borane and methimazole in toluene under reflux, Bailey and co-workers first attempted to prepare these derivatives of Tm was via N-H deprotonation of [(HNMe$_2$)B(mt)$_3$] with a strong base followed by the addition of an electrophile in order to convert HNMe$_2$ into a good leaving group which could be substituted by the desired groups (L) (Scheme 2.7). Despite the use of different bases (BuLi, MeLi, NaH, NaOMe, LDA) and electrophiles (MeI, Me$_3$OBF$_4$, MeCOCl, PhCOCl), this method failed as only methimazole and/or its derivative resulting from electrophilic addition could be isolated. The attempts to isolate the anion [(NMe$_2$)B(mt)$_3$]$^-$ were also unsuccessful possibly due to product decomposition during the deprotonation step.[14]



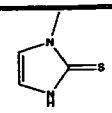
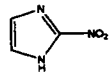
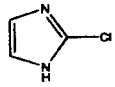
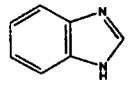
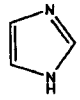
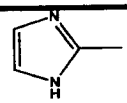
2.11

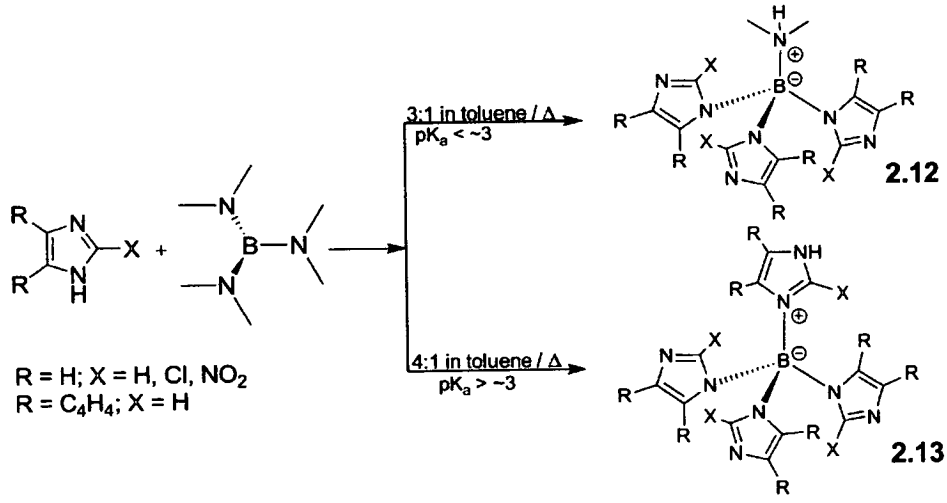
Scheme 2.7. *Synthetic approach attempted by Bailey and co-workers to obtain Tm ligand derivatives via deprotonation of the dimethylamine group in* $[(HNMe_2)B(mt)_3]$.[14]

The ligand decomposition and consequent formation of the methimazolyl anion in the presence of a strong base suggests a weaker coordination of the methimazole rings to the boron than pyrazole under these conditions. This disparity is likely to be related to the stability of the anionic heterocycles anions and can be expressed by the acidic pK_a which is a measure of its Brønsted acidity and therefore stability of conjugate base (heterocycle anion). Thus, methimazole (pK_a = 12)[15] is expected to provide a more stable anion than pyrazole (pK_a= 14 in $EtOH/H_2O$).[16] Following these observations, Bailey and co-workers sought the reactivity of tris(dimethylamino)borane with a range of imidazoles. The different imidazoles used to react with the borane under toluene reflux are displayed in Table 2.1.[14]

These reactions lead to the isolation of two different types of product: $[(HNMe_2)B(azolyl)_3]$ **2.12** and $H[B(azolyl)_4]$ **2.13** (Scheme 2.8). The basic pK_a of the heterocycles appeared to be the main feature which determines the outcome of these reactions. It was observed that azoles with basic pK_a higher than ~3 give the $H[B(azolyl)_4]$ **2.13** system and azoles with basic pK_a lower than ~3 form $[(HNMe_2)B(azolyl)_3]$ **2.12** (Scheme 2.8).

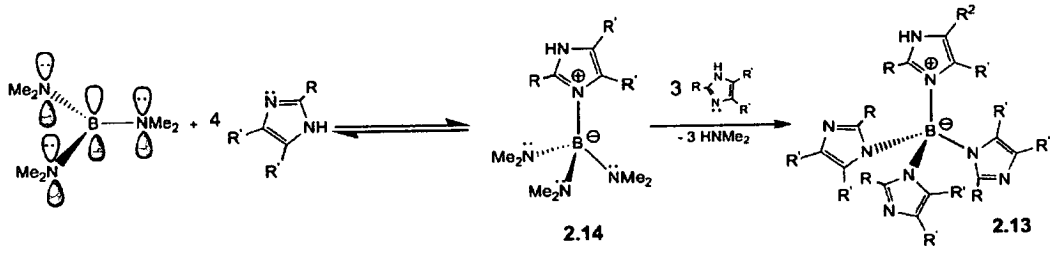
Table 2.1. *Range of azoles reacted with $B(NMe_2)_3$ by Bailey and co-workers.*[14]

	Azole	Basic pK_a	Acidic pK_a
	1-methylimidazole-2-thione (methimazole)	-1.0 [17]	12.0 [15]
	2-nitro-imidazole	-0.8 [18] (DMF/H_2O)	7.5 [19] ($MeOH/H_2O$)
	pyrazole	2.5 [20] (H_2O)	14.0 [16] ($EtOH/H_2O$)
	2-cloro-imidazole	3.5 [21] (H_2O)	10.5 [22]
	benzimidazole	5.7 [23] (H_2O)	12.8 [23] (H_2O)
	imidazole	7.0 [18] (DMF/H_2O)	14.9 [18] (DMF/H_2O)
	2-methylimidazole	7.8 [18] (DMF/H_2O)	14.1 [24]



Scheme 2.8. *Influence of azole basic pK_a and its reactivity with tris(dimethylamino)borane.*[25]

Bailey and co-workers initially explained these observations as resulting from a two step mechanism via a reactive intermediate. The first step in the formation of H[B(azolyl)$_4$] **2.13** was proposed to be the formation a tetrahedral reactive intermediate [(azole)B(NMe$_2$)$_3$] **2.14** (Scheme 2.9) by coordination of the azole to tris(dimethylamino)borane. It was suggested that, despite the weak Lewis acidity of B(NMe$_2$)$_3$, the strong basicity of the azole (basic pK_a higher than ~3) enables its coordination. The formation of this tetrahedral intermediate [(azole)B(NMe$_2$)$_3$] **2.14** (Scheme 2.9) removes the N-B π-bonding within B(NMe$_2$)$_3$ and substantially increases the basicity of the NMe$_2$ groups bound to the boron and these then react with the remaining azole heterocycle in solution through a transamination reaction to form the tetra(azolyl) system **2.13** (Scheme 2.9). This is analogous to the initial formation of [(HNMe$_2$)(NMe$_2$)B(pz)$_2$] proposed by Niezendu during the formation of pyrazole borates,[9] although without the proton transfer from the azole to NMe$_2$.

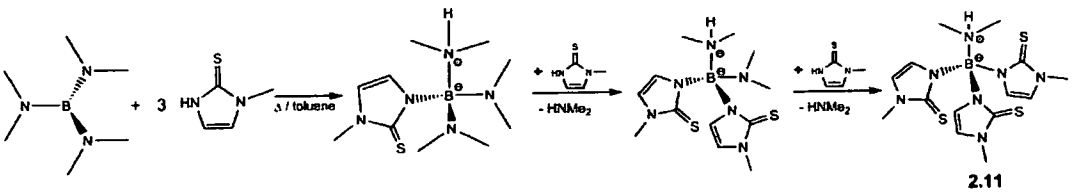


R=H, R'=H (imidazole), C_4H_4 (benzimidazole)
R= Cl (2-chloroimidazole), Me (2-methylimidazole), R'=H

Scheme 2.9. *Bailey and co-workers proposed mechanism for the reaction of strongly basic azoles with tris(dimethylamino)borane to afford a tetrasubstituted borane.*[14]

If the azole was not basic enough (basic pK_a lower than ~3, e.g. methimazole or pyrazole) it cannot coordinate to the borane to form the [(azole)B(NMe$_2$)$_3$] **2.14** (Scheme 2.10) intermediate. In this case, transamination directly from B(NMe$_2$)$_3$ proceeds to provide initially [(azolyl)B(NHMe$_2$)(NMe$_2$)$_2$] and subsequently

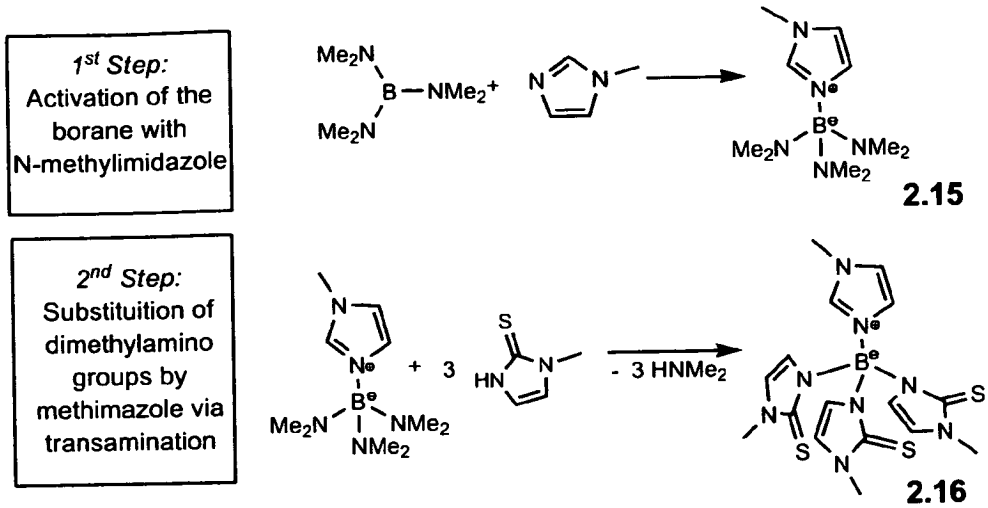
[(HNMe$_2$)B(azolyl)$_3$] **2.12** via subsequent transamination steps (Scheme 2.10); this being the mechamism proposed by Niedenzu for the reaction with pyrazole.



Scheme 2.10. *Transamination reaction between methimazole and tris(dimethylamino)borane.*

In all of these reactions the reactivity of tris(dimethylamino)borane with the basic azole heterocycles is affected by its weak Lewis acidity, as the boron *p*-orbital in the planar B(NMe$_2$)$_3$ is stabilized by B-N π-bonding by donation of the nitrogen lone pairs to the boron. In this view of the mechanism, the strongly basic heterocycles may be regarded as activating the B(NMe$_2$)$_3$, as they form the reactive tetrahedral borane species to promote the reaction with the azoles.

As a result of this interpretation, Bailey and his collaborators reported a new method to synthesize ligands of the type [LB(mt)$_3$] via a "one-pot" reaction. Through this method [(N-methylimidazole)B(methimazolyl)$_3$] could be obtained in high yield (yield > 80 %) from a mixture of tris(dimethylamino)borane, N-methylimidazole and methimazole in a 1:1:3 ratio in a toluene solution under reflux (Scheme 2.11).[14]

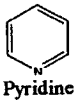
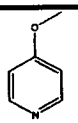
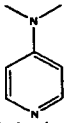
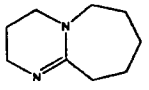


Scheme 2.11. *The proposed two step mechanism of [(N-methylimidazole)B(mt)$_3$] synthesis in a "one-pot" reaction reported by Bailey.*[14]

The idea behind this approach was that one equivalent of the strongly basic N-methylimidazole would coordinate to $B(NMe_2)_3$ to form a more reactive intermediate, [(N-methylimidazole)$B(NMe_2)_3$] **2.15** (Scheme 2.11). Since N-methylimidazole lacks an acidic proton, the transamination reaction only occurs when this intermediate reacts with the acidic N-H proton of methimazole to form [(N-methylimidazole)B(mt)$_3$] **2.16**. As dimethylamine was released from the reaction, the concentration of [(N-methylimidazole)$B(NMe_2)_3$] **2.15** in the mixture was very low and it was never possible to observe its presence by NMR analysis.

The scope of this reaction with some different basic activators other than N-methylimidazole was also studied by Bailey and Perucha, and further investigated through the work presented in this thesis. Perucha's results on the scope of basic activators of borane using this synthetic method are presented on Table 2.2.[25]

Table 2.2. *Work developed by Perucha on the scope of neutral N donor heterocycles (L) as borane activators in the synthesis of [LB(mt)$_3$].*[25]

	Heterocycles				
	 Pyridine	 4-methoxypyridine	 4-dimethylaminopyridine	 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)	 Triethylamine
Basic pK$_a$	5.14 [26] (H_2O)	6.2 [27] (H_2O)	9.2 [28] (H_2O)	12.0 [29] (DMSO)	9.07 [30] (DMSO)
Reaction time	16 h	8 h	6 h	1 h	— *

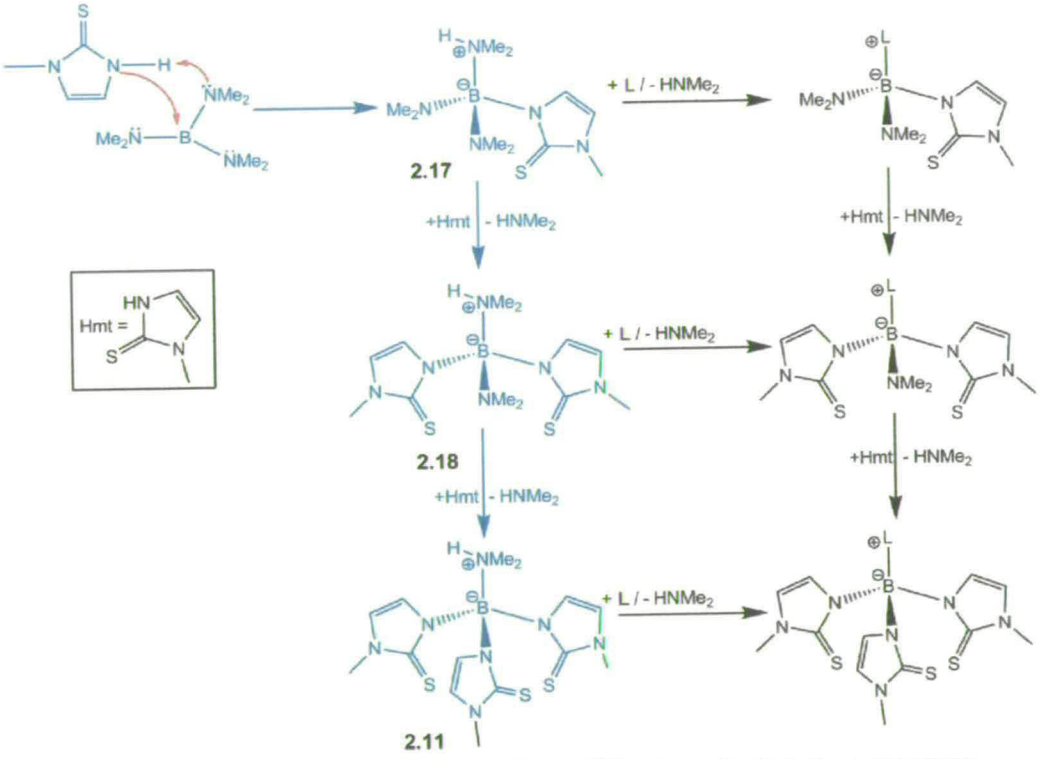
*No reaction due to steric effects

In all these reactions the three components were combined in toluene solution and heated to reflux. The time until dimethylamine ceases to be evolved marks the time to reaction completion, at which point the product has generally precipitated from the reaction mixture. At first glance, these results indicate a correlation between the heterocycle basicity and reaction time, but this is not conclusive since no further kinetic studies with a wider range of borane activators were done. The reaction with triethylamine was not successful as only [(HNMe$_2$)B(mt)$_3$] could be isolated in the end, despite its high basic pK$_a$. This indicates that steric effects also affect the synthesis of these ligands through this route. It should be noted that in the absence of an "activating base" the reaction between B(NMe$_2$)$_3$ and methimazole proceeds to form [(HNMe$_2$)B(mt)$_3$] in 2 h.

2.3.2. Ligand synthesis via [(HNMe$_2$)B(mt)$_3$]

The aim of this work is the synthesis of chiral boron-centred tripodal ligands type [(L*)B(mt)$_3$] following the previous work of Perucha. However a more extensive study of the influence of the basic pK_a of the bases used to activate tris(dimethylamino)borane and the outcome of these "one-pot" reactions showed that the mechanism explained above cannot be correct. As mentioned before, there is a correlation between the basicity of the borane activator and the reaction time, as stronger bases react readily with the borane decreasing the overall ligand synthesis reaction time. Consequently, the formation of the tetrahedral borane species with a strongly basic activator base appears to be the rate-determining step of this reaction. Comparing, the basic pK_a of dimethylamine (pK_a = 10.7)[26] with some other borane activators, as 4-dimethylaminopyridine (pK_a = 9.2),[28] showed that it could also activate the borane while it is present in solution during reaction. Besides, it was seen that when pyridine (pK_a = 5.14)[31] acts as borane activator it takes around sixteen hours until no dimethylamine evolution ceases. In reactions with all other activating bases the products LB(mt)$_3$ are obtained in a pure state, however the product of this reaction with pyridine is contaminated with [(HNMe$_2$)B(mt)$_3$], which can be obtained after just a few hours of reaction. This was intriguing and the hypothesis that [(HNMe$_2$)B(mt)$_3$] could react with strong neutral N-donors (L) to afford the desired ligand type [(L)B(mt)$_3$] by direct substitution of its HNMe$_2$ group was raised. Since [(HNMe$_2$)B(mt)$_3$] is formed in just 2 hours in the absence of an "activating base", the question arises as to why the slower reactions with activating base do not form products contaminated with this species.

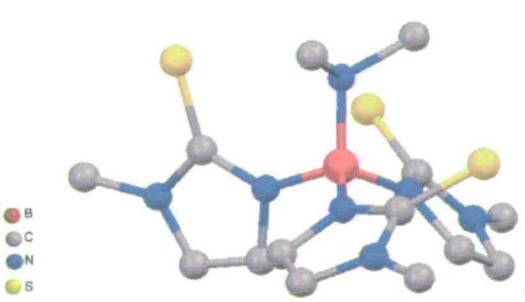
In order to investigate this hypothesis, a series of ligands were synthesized by both methods: the "one-pot" reaction and from the reaction of $[(HNMe_2)B(mt)_3]$ with a strong base. An analysis of both synthetic methods and the discussion of the obtained results with both syntheses will be presented in the Section 2.4 of this chapter.



Scheme 2.12. *Proposed mechanism for the synthesis of these ligands.*

This investigation proved that it is possible to substitute the dimethylamine in $[(HNMe_2)B(mt)_3]$ **2.11** with neutral nitrogen donors to obtain the desired neutral boron substituted ligand, $[(L)B(mt)_3]$. Therefore, the previously reported mechanism has been shown to be erroneous and the proposed mechanism for this synthesis is represented in Scheme 2.12.

According to the results obtained, the first step of the synthesis of $[(L)B(mt)_3]$ from $[(HNMe_2)B(mt)_3]$ is the formation of a neutral tetrahedral species **2.17,** $[(HNMe_2)(NMe_2)_2B(methimazolyl)]$ (Scheme 2.12) from a reaction between methimazole's acidic proton with one of the borane dimethylamino groups with coordination of the resulting methimazolyl group to boron. The borane thus loses its B-N π-bonding and changes its hybridization from sp^2 to sp^3. In the absence of an added base (*L*), this more reactive tetrahedral borane species reacts with two more equivalents of methimazole to afford the ligand $[(HNMe_2)B(mt)_3]$ by transamination reactions. In the presence of an added base, the dimethylamine group of one of the three tetrahedral borane intermediates (**2.17**, **2.18** or **2.11** on Scheme 2.12) can be replaced. Although this base substituted borane intermediate could not be isolated, the outcome of this reaction was the desired substituted neutral ligand. Whether the substitution of $HNMe_2$ can occur in the intermediates **2.17** or **2.18** could not be determined, however it was established that it can be achieved in $[(HNMe_2)B(mt)_3]$ **2.11** to provide the ultimate product $[LB(mt)_3]$.



2.11

Fig.2.4. *Structure of dimethylamino-tris(methimazolyl)borate 2.11 reported by Bailey (hydrogens atoms are hidden for clarity).*[14]

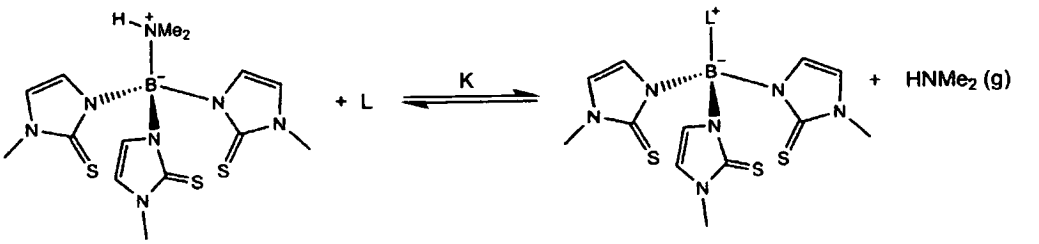
It has therefore been established that it is possible to substitute the $HNMe_2$ in $[(HNMe_2)B(mt)_3]$ by another basic N-donor, providing a new route to obtain ligands of the type $[(L)B(mt)_3]$. The substitution of $HNMe_2$ of $[(HNMe_2)B(pz)_3]$ has also been investigated and this is discussed in Section 2.7.

2.4. ANALYSIS OF BOTH SYNTHETIC METHODS

Both synthetic methods, the "one-pot" reaction (method 1) and the reaction of $[(HNMe_2)B(mt)_3]$ with added N-donor (method 2), are effective for the synthesis of $[LB(mt)_3]$. The procedures are quite similar, as the products are obtained by heating the starting materials under reflux in a high boiling point solvent, usually toluene. Generally, the final product precipitates while the mixture is still heated under reflux or after cooling and can be recovered in high yield (more than 80%) and purity after filtration.

Another common feature of these syntheses is their irreversibility due to the evolution of dimethylamine gas. This characteristic is important because it favours the formation of the boron functionalized Tm ligand analogue. During the reaction $[(HNMe_2)B(mt)_3]$ and the final product are in equilibrium (Scheme 2.13). This equilibrium is shifted if dimethylamine gas is released from the reaction vessel, allowing the formation of the desired final product. It was observed that these reactions are faster when nitrogen is bubbled into the reaction vessel to sweep the $HNMe_2$ away. This procedure assures the irreversibility of this reaction as it allows a better degasification of the mixture. The release of dimethylamine facilitates the

monitoring of this reaction by testing the pH of the gases exhausted while the mixture is heated.



L = neutral N-donor

Scheme 2.13. *Species in equilibrium during the reaction of [(HNMe$_2$)B(mt)$_3$] with a neutral N-donor (L).*

The position of the equilibrium represented on Scheme 2.13 will be determined by the nature of the added donor L, and may be correlated with its basic pK_a as the reaction is favoured by the stronger donors (higher pK_a). The basic pK_a of $HNMe_2$ is 10.8[26] and thus its substitution with weaker bases (e.g. pyridine, pKa 5.14 [31]), would be unfavourable and provide a small value of K (Scheme 2.13). However, the loss of $HNMe_2$ as a gas drives the reaction to completion. Since these reactions can be quantitative, the measure of accurate stoichiometric amount of starting materials favours the high purity of the final product, which can be obtained just by solvent removal or after washing the precipitated product with an inert solvent.

2.4.1. Ligands synthesized by both methods

In order to study and understand the synthetic methods a series of ligands was synthesized via both routes (Fig.2.5). This study started with the synthesis of previously reported ligands obtained by the "one-pot" reaction (method 1), [(N-

methylimidazole)B(methimazolyl)$_3$] **2.16** and [(4-dimethylaminopyridine)B(methimazolyl)$_3$] **2.20**, but using [(dimethylamine)B(methimazolyl)$_3$] as starting material (method 2) instead of tris(dimethylamino)borane.

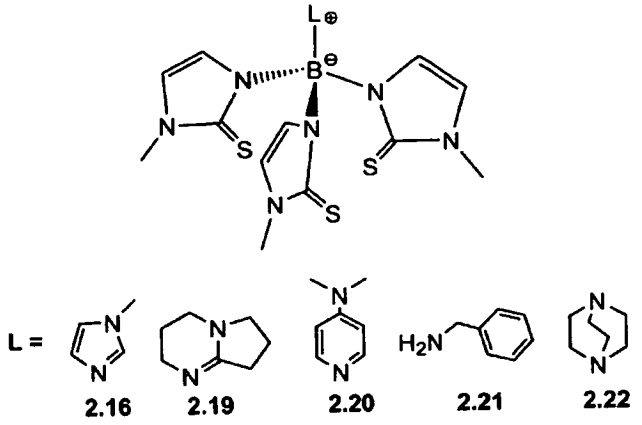


Fig. 2.5. *Series of ligands synthesized.*

Following Bailey's methods, [(dimethylamine)B(methimazolyl)$_3$] was obtained by heating under reflux a 1:3 mixture of tris(dimethylamino)borane and methimazole in toluene. After a few hours, the product precipitated from the mixture and isolated by filtration, washed with diethylether, dried under vacuum and used as starting material for this work.

The procedure used for both methods was very similar: heating under reflux a suspension of reactants in toluene. Although, during these reactions [(dimethylamine)B(methimazolyl)$_3$] never completely dissolves in the toluene, this solvent has been chosen for the base exchange reactions (method 2). Tetrahydrofuran and dichloromethane were also tried for method 2. Although [(dimethylamine)B(methimazolyl)$_3$] is soluble in these solvents, the reactions were

very slow due to their lower boiling points and sometimes the final product was contaminated with starting materials. The results obtained with both synthetic methods are displayed on Table 2.3.

For this study, the basicity was the main feature for selecting N-donors other than N-methylimidazole or 4-dimethylaminopyridine, but the possibility to use a chiral analogue of these bases was also important.

The choice of 1,5-diazabicyclo[4,3,0]non-5-ene (DBN) for this work was based on previous work done by Perucha with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and with a perspective to functionalize the boron with a chiral DBN analogue.

Table 2.3. *Results obtained for the synthesis of ligands of type [LB(mt)$_3$] via method 1 ("one-pot" reaction) or by method 2 (from a reaction of a base with [(HNMe$_2$)B(mt)$_3$]).*

N-donor (L)	pK_a	Ligand (product number)	Method 1		Method 2	
			Reaction time* (h)	Yield %	Reaction time* (h)	Yield %
N-methylimidazole	7.8[18] (DMF/H_2O)	2.16	2	71	3	75
1,5-diazabicyclo[4,3,0]non-5-one (DBN)	12.0[32]	2.19	4	78	5	72
4-dimethylaminopyridine (DMAP)	9.20[28]	2.20	4	87	4	76
Benzylamine	8.74[33] (MeCN/H_2O)	2.21	9	54	12	40
1,4-diazabicyclo[2.2.2]octane (DABCO)	9.06[30]	2.22	48	83	36	78

* As measured by the time of cessation of $HNMe_2$ formation.

The successful ligand synthesis with benzylamine (ligand **2.21**) showed that primary amines can also be used to functionalize the borane; all previous work had been done with tertiary amines or imines.

The DABCO (1,4-diazabicyclo[2.2.2]octane) was selected for this work as an alternative to triethylamine, since its nitrogen lone pairs of electrons are more accessible. It was also interesting to investigate the reactivity of a diamine in these ligand syntheses. An interesting result was obtained from a "one-pot" reaction with tris(dimethylamino)borane, methimazole and 1,4-diazabicyclo[2.2.2]octane, in 1:3:1 proportion respectively. This reaction was stopped before all dimethylamine gas was released and a solid was isolated after solvent removal under vacuum. The analysis through electro-spray mass spectrometry (Fig. 2.6.) and ^{1}H NMR (Fig.2.7) showed that this powder was a mixture of three different species.

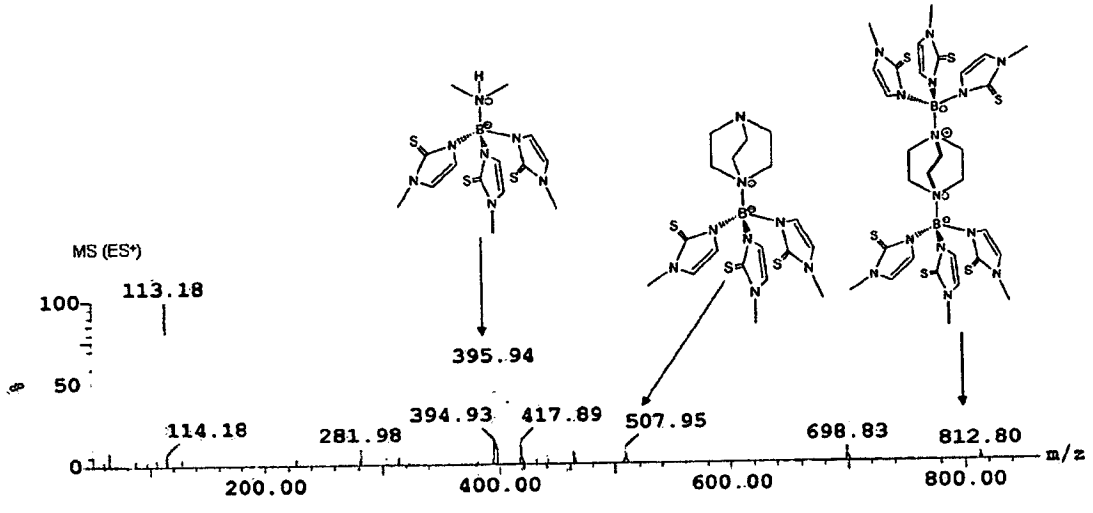


Fig.2.6. *Positive electro-spray mass spectrum of the mixture obtained from the "one-pot" ligand synthesis with DABCO.*

The ^{1}H NMR of this mixture of products shows five different signals between 3.65 and 2.9 ppm which correspond to the DABCO protons and to the methyl groups

of the methimazole moieties of the ligands (Fig. 2.7). There are two different signals for the DABCO protons; one at 2.91 ppm which corresponds to the mono substituted product and another signal of small intensity at 3.56 ppm for the bis substituted ligand. The ^{1}H NMR of this mixture also shows three different signals at 3.49, 3.58 and 3.61 ppm which were assigned to the three different methimazole methyl groups of the species present in the mixture, [(1,4-diazabicyclo[2.2.2]octane){B(methimazolyl)$_3$}$_2$], (1,4-diazabicyclo[2.2.2]octane){B(methimazolyl)$_3$ and [(dimethylamine)B(methimazolyl)$_3$] (Fig. 2.7).

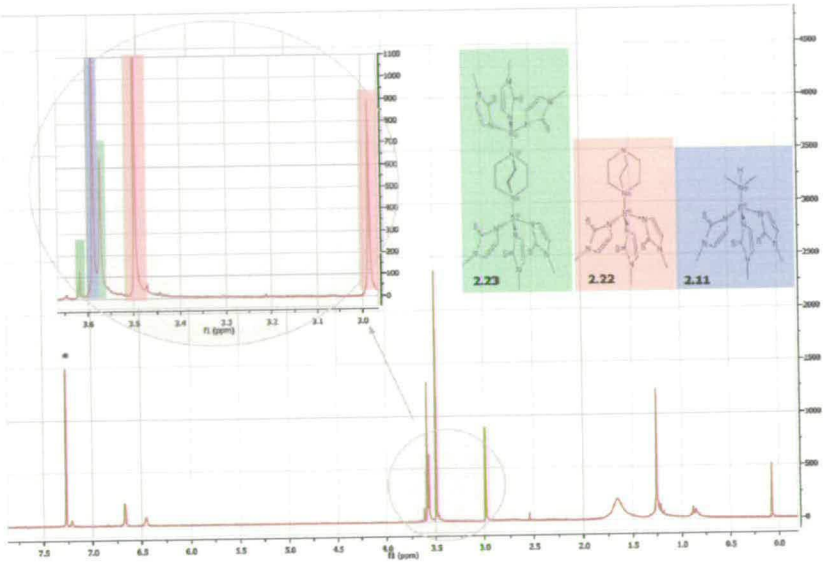
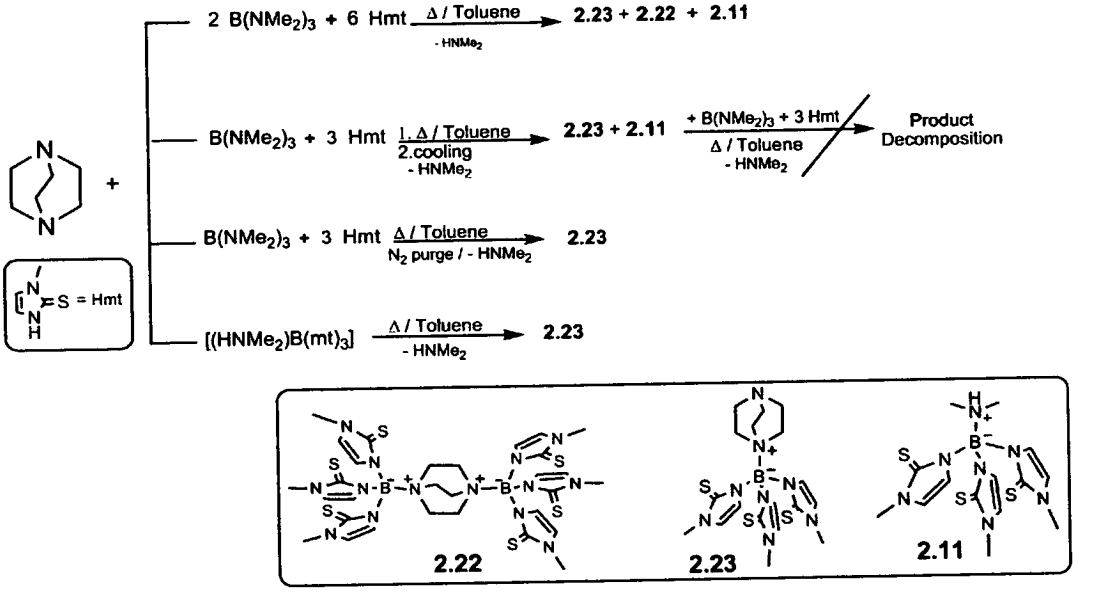


Fig.2.7. *^{1}H NMR of the mixture obtained from the "one-pot" ligand synthesis with DABCO in $CDCl_3$ (detail over region between 3.65-3.45 ppm where are the different proton signals of the three products).*

The presence of [(dimethylamine)B(methimazolyl)$_3$] in this mixture indicates that this ligand was an intermediate formed during a "one-pot" reaction. Also, it is interesting to note that the mixture contains the bis-substituted DABCO species, [(1,4-diazabicyclo[2.2.2]octane){B(methimazolyl)$_3$}$_2$] (Fig. 2.7). The formation of

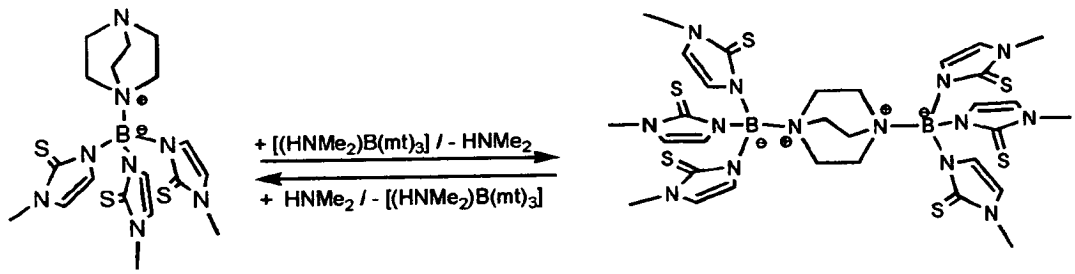
this product indicates that the basicity of the 2nd DABCO nitrogen atom in $[(DABCO)B(mt)_3]$ is sufficiently high to substitute $HNMe_2$ in $[(HNMe_2)B(mt)_3]$. Many attempts were made to separate this mixture or to synthesise [(1,4-diazabicyclo[2.2.2]octane)$_2$] exclusively but all of them failed due to product decomposition or inefficient separation. The synthetic approaches attempted for this synthesis are displayed on Scheme 2.14.



Scheme 2.14. *Attemped synthetic apporoaches to obtain [(1,4-diazabicyclo[2.2.2]octane){B(methimazolyl)$_3$}$_2$].*

The [(1,4-diazabicyclo[2.2.2]octane){B(methimazolyl)$_3$}$_2$] seems to be an unstable product thus, it was not possible to isolate. Analysis of the decomposition product obtained by ^{1}H NMR show that small quantities of $[(HNMe_2)B(mt)_3]$ (one singlet at 3.58 ppm) and $[(DABCO)B(mt)_3]$ (two singlet signals at 3.50 and 2.90 ppm) were also present within the mixture. This indicates that there is an equilibrium

between [(DABCO)B(mt)$_3$] and [(DABCO){B(mt)$_3$}$_2$] that depends on the presence of [(HNMe$_2$)B(mt)$_3$] and dimethylamine dissolved in solution. The instability of [(DABCO){B(mt)$_3$}$_2$] favours the equilibrium towards the formation of [(DABCO)B(mt)$_3$], which is the final product of this reaction (Scheme 2.15).



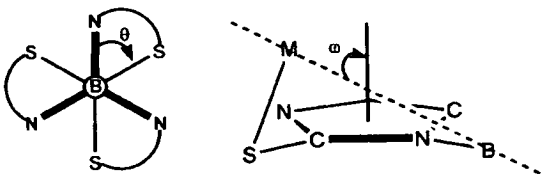
Scheme 2.15. *Equilibrium that can occur during the reaction of [(HNMe$_2$)B(mt)$_3$] and DABCO.*

2.5. METAL COMPLEXES

As mentioned in Chapter I, the Tm ligand and its derivatives synthesized in this work give metal complexes with C_3 symmetry. In this chapter the synthesized ruthenium and molybdenum complexes will be introduced and discussed.

2.5.1. Structural parameters

The structures of the C_3 - symmetric complexes of Tm^{Me} ligand have been described by Hill in terms of two parameters θ° and ω° (Fig. 2.8).[34]



θ ω

λ (θ < 0°)

δ (θ > 0°)

Fig 2.8. *Parameters introduced by Hill and co-workers to characterize the C_3-symmetric metal complexes of Tm ligand or its derivatives.*[34]

These parameters are used to describe the rotational deformation that the metal complexes of the Tm ligand and its derivatives (including ligands of the type [(L)B(mt)$_3$]) metal complexes exhibit. When coordinated to a metal this type of ligand forms a bicyclo[3,3,3] cage that twists due to its inherent angle strain. The formation of two rotational enantiomers, $\lambda\lambda\lambda$ and $\delta\delta\delta$, is a consequence of the helical twist of this cage. Hill introduced the θ parameter to describe the absolute configuration of the rotational enantiomers. This parameter is the measure of the tortional angle N-B-M-S (Fig.2.8.).[34] Therefore, for a complex with λ enantiomeric configuration the parameter θ is < 0° and if θ is > 0° the enantiomeric configuration of the complex is δ (Fig. 2.8). The measure of the three θ angles (θ^m) in a complex allows the determination of the absolute rotational enantiomeric configuration of the complex, since λ and δ configurations cannot coexist in the same complex, though the two enantiomers can coexist in the same unit cell of the whole crystal structure lattice.[34]

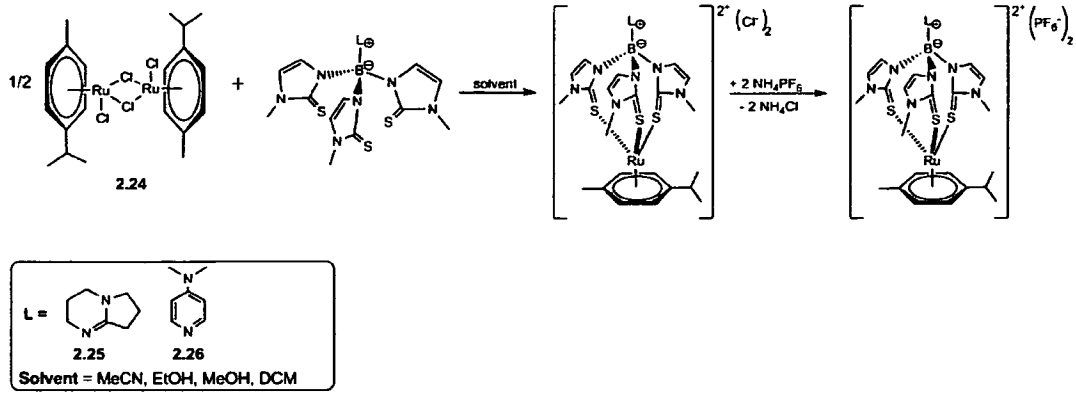
The angle between the normal to the plane of the methimazole ring, which makes with the B→M vector is the second parameter, ω, defined by Hill (Fig.2.8.).[34] This angle measures the displacement of the metal (M) from the methimazole planes

and is related to the flexibility of hybridization of the sulphur atoms. This parameter is usually presented as ω^m, which is the mean of all the three ω angles.[34]

2.5.1. Complexation to Ruthenium (II)

In this work, some of the ligands were coordinated to the $[Ru(p\text{-cymene})]^{2+}$ fragment. Ruthenium was used for this work due to its properties and its potential applications in catalysis. Ruthenium (II) forms low spin diamagnetic complexes, and it easily coordinates to molecules containing heteroatoms (e.g. nitrogen, oxygen, phosphorus...).[35] The complexes of η^6- arene Ru(II) are usually stable to hydrolysis and the metal not easily oxidized to Ru(III) due to the strong π interaction between the metal and the arene.[36] Moreover, ruthenium complexes have shown good catalytic activity in hydrogenations and transfer hydrogenations[37] and on olefin metathesis.[38] The potential catalytic applications of ligands of the type $[(L^*)B(mt)_3]$, (with chiral groups attached to the boron) coordinated to rutheninum (II) can also be interesting in a further investigation as future work.

The synthesis of the Ru(II) complexes described in this work followed a similar method which was previously reported by Bailey and Perucha for the synthesis of $[Ru(p\text{-cymene})(N\text{-methylimidazole})B(methimazolyl)_3][Cl]_2$ (Scheme 2.16).[14]



Scheme 2.16. *Synthetic route used to obtain the ruthenium complexes 2.25 and 2.26.*

A ruthenium (II) complex of [(1,5-diaza-bicylo-(4.3.0)non-5-ene)B(methimazolyl)$_3$] 2.25 was formed by reaction of the ligand with dichloro(*p*-cymene)ruthenium dimer in ethanol followed by a salt metathesis with NH_4PF_6 to exchange the chloride counter-ions (Scheme 2.16). Generally, this last procedure facilitate the purification of the complex, since the hexafluorophosphate anions usually make the complex precipitate, thus render it easy to isolate via filtration.

Compared to that of the free ligand, the ^{1}H NMR spectrum of the complex shows a shift upfield of the proton signals of 1,5-diaza-bicylo-(4.3.0)non-5-ene which indicates that the complex was formed. The other signals of the ^{1}H and ^{13}C NMR for **2.25** confirm the solid state structure found by X-Ray anaysis.

The complex was crystallized by slow diffusion of ether into a concentrated acetonitrile solution. The structure of the obtained crystals contains both $\lambda\lambda\lambda$ and $\delta\delta\delta$ enantiomers within the unit cell. One of the rotational enantiomers of this crystal structure can be seen on Fig.2.9.

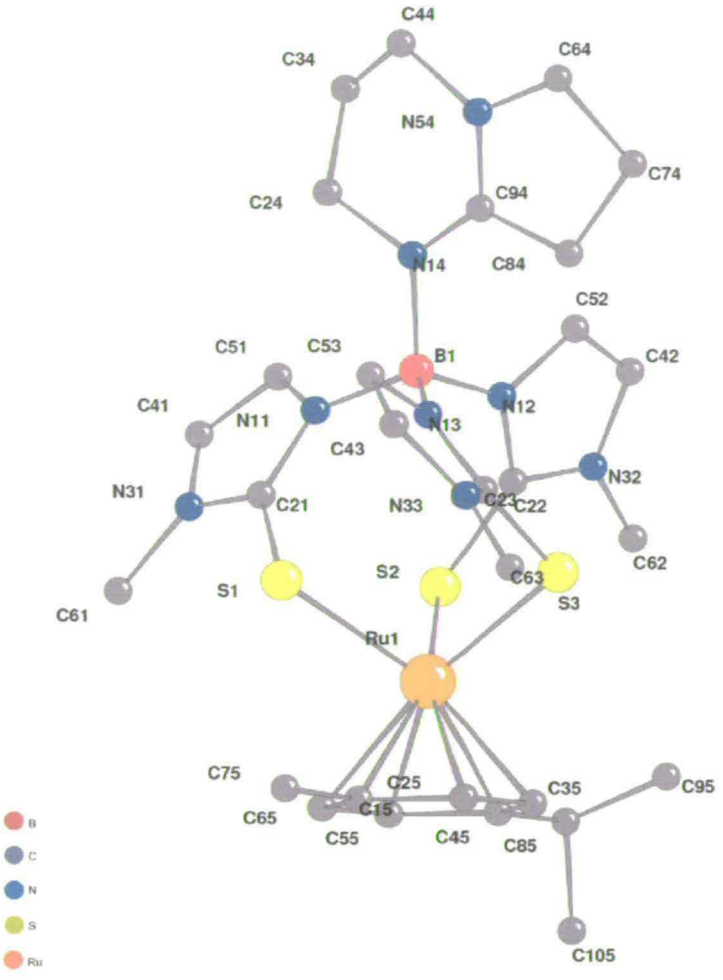


Fig.2.9. *Crystal stucture of Λ enantiomer of [{(1,5-diaza-bicylo-(4.3.0)non-5-ene)B(methimazolyl)$_3$}Ru(p-cymene)][PF_6]$_2$* ***2.25*** *(hexafluorophosphate counter-ions and hydrogens not shown for clarity). The selected bond lengths and angles for this complex are presented on Table 2.4.*

Table 2.4. *Selected angles (°) and bond lengths (Å) of [{(1,5-diaza-bicylo-(4.3.0)non-5-ene)B(methimazolyl)$_3$}Ru(p-cymene)][PF$_6$]$_2$ 2.25*

B-N$_{mt}$(13)	1.538(5)	Ru-S(2)	2.403(9)
B-N$_{mt}$(11)	1.553(4)	Ru-S(3)	2.425(8)
B-N$_{mt}$(12)	1.561(4)	Ru-S(1)	2.454(9)
B-N$_{DBN}$(14)	1.569(5)	N(13)-B-N(11)	109.6(3)
S(1)-C(21)	1.721(3)	N(13)-B-N(12)	116.7(3)
S(2)- C(22)	1.729(3)	N(11)-B-N(12)	105.0(3)
S(3)-C(23)	1.719(3)	N(13)-B-N(14)	104.5(3)
Ru-C$_{p\text{-cym}}$ (55)	2.183(4)	N(11)-B-N(14)	111.5(3)
Ru-C$_{p\text{-cym}}$ (35)	2.185(3)	N(12)-B-N (14)	109.6(3)
Ru-C$_{p\text{-cym}}$ (65)	2.196(4)	S(2)-Ru-S(1)	90.90(3)
Ru-C$_{p\text{-cym}}$ (25)	2.196(4)	S(3)-Ru-S(1)	95.69(3)
Ru-C$_{p\text{-cym}}$ (45)	2.213(4)	S(2)-Ru-S(3)	87.08(3)
Ru-C$_{p\text{-cym}}$ (15)	2.226(4)		

The ruthenium (II) complex of [(DMAP)B(methimazolyl)$_3$] was obtained by an analogous method (Scheme 2.16.) as the previously presented complex. Compared to the free ligand, the ^{1}H NMR of **2.25** shows a shift downfield of the two doublet signals of the DMAP pyridine moiety and the olefinic protons of the methimazole rings. The analysis of **2.25** by FAB-MS, showed the molecular peak of the complex with loss of the counterions (M^+ = 708.7). This complex was crystallized by slow diffusion of diethyl ether in acetonitrile. These crystals were analysed by X-ray crystallography, however its structure could not be refined as the crystal lattice was not regular due to solvent loss and decomposition of the complex. The structure presented on this chapter shows only the relative position of the atoms.

The crystals analysed showed to have the λλλ and δδδ enatiomers present in the crystal unit cell as seen in Fig.2.10.

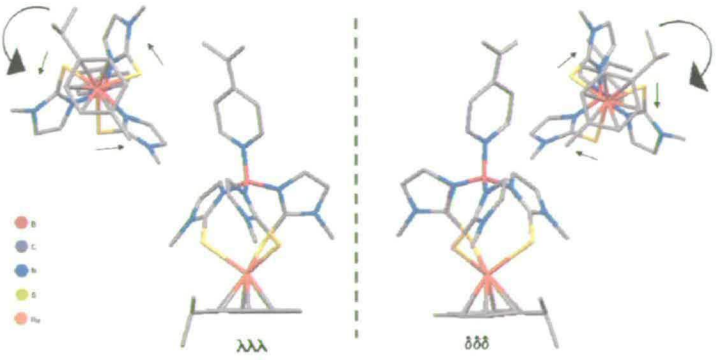


Fig.2.10. *Crystal structure of [{(DMAP)B(methimazolyl)$_3$}Ru(p-cymene)][PF$_6$]$_2$ **2.26** showing the axial enantiomers λλλ and δδδ (hydrogen atoms and counter-ions were hidden for clarity).*

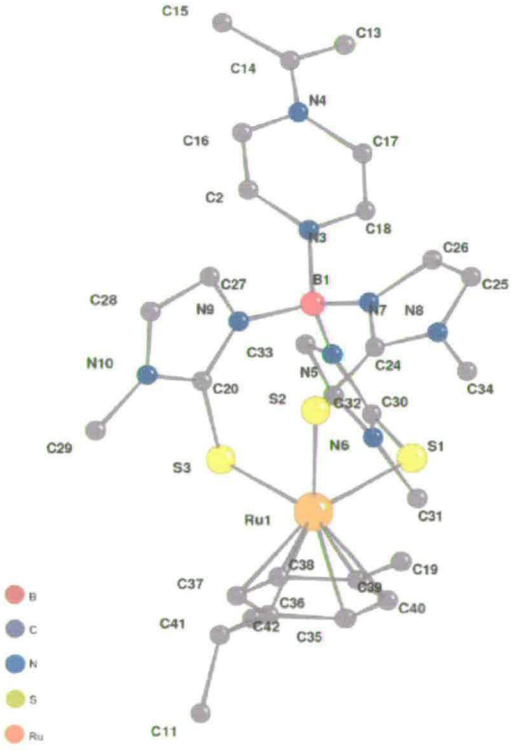


Fig.2.11. *Crystal stucture of δδδ enantiomer of [{(DMAP)B(methimazolyl)$_3$}Ru(p-cymene)][PF$_6$]$_2$ **2.26** showing the atomic numbering scheme (hexafluorophosphate counter-ions and hydrogens not shown for clarity). The selected bond lengths and angles for this complex are presented on Table 2.4.*

Table 2.5. *Selected angles (°) and bond lengths (Å) of Λ enantiomer of [{(DMAP)B(methimazolyl)$_3$}Ru(p-cymene)][PF$_6$]$_2$* **2.26** *(this structure could not be refined due loss of solvent))*

B-N$_{mt}$ (18)	1.592	Ru-S(2)	2.414
B-N$_{mt}$ (7)	1.541	Ru-S(3)	2.432
B-N$_{mt}$(25)	1.538	Ru-S(1)	2.412
B-N$_{DMAP}$ (9)	1.584	N(18)-B-N(7)	111.92
S(1)-C(21)	1.713	N(7)-B-N(25)	105.91
S(2)- C(22)	1.728	N(25)-B-N(18)	115.78
S(3)-C(23)	1.718	N(13)-B-N(9)	103.50
Ru-C$_{p\text{-cym}}$ (55)	2.177	N(11)-B-N(9)	109.28
Ru- C$_{p\text{-cym}}$ (35)	2.189	N(12)-B-N(9)	110.46
Ru- C$_{p\text{-cym}}$ (65)	2.206	S(2)-Ru-S(1)	92.59
Ru- C$_{p\text{-cym}}$ (15)	2.220	S(3)-Ru-S(1)	87.11
Ru- C$_{p\text{-cym}}$ (25)	2.203	S(2)-Ru-S(3)	92.54
Ru- C$_{p\text{-cym}}$ (45)	2.213		

The structure of complex **2.26** was not fully solved as the R-factor was above 30%, thus the measurements on this crystal do not present any standard deviations. The structures presented on Fig.2.10 and Fig.2.11 were based on the atomic position assigned for the crystals obtained.

The structure of complexes **2.25** and **2.26** show that the ligand is coordinated in a facial κ^3-S,S,S mode to the metal centre. The average S-Ru distances and S-Ru-S angles are 2.42 Å and 91.23° for **2.25** and 2.41 Å and 90.74° for **2.26**. The distances and angles present on **2.25** are very similar to the ones found in [{(N-methylminidazole)B(methimazolyl)$_3$}Ru(p-cymene)][PF$_6$]$_2$ (Ru-S 2.42 Å and S-Ru-S 90.77°) reported by Bailey and Perucha.[14, 25] In both of the complexes the ruthenium is π bonded to the *p*-cymene ligand with an average Ru-C bond distance of 2.19 Å for **2.25** and 2.20 Å for **2.26**. The separation between the metal centre and

the arene ligand centroid is 1.68 Å **2.25** and 1.70 Å **2.26**. The average B-N_{mt} bond length is 1.55 Å **2.25** and 1.56 Å **2.26** of the nitrogen atoms of the methimazole rings coordinated to the boron. The mean N_{mt}-B-N_{mt} angle of complex **2.26** is 111.20°. For complex **2.25** the mean N_{mt}-B-N_{mt} angle is 110.43° which is close to 109.45° found in {(N-methylminidazole)B(methimazolyl)$_3$}Ru(p-cymene)][PF_6]$_2$ (The structural parameter θ^m for **2.25** and **2.26** is respectively, -49.23° and 49.3 and -49.0° for the displayed structures. The ω^m tortional parameter is -56.22° ($\lambda\lambda\lambda$ enantiomer of **2.25**) and -56.34° and 56.33° for $\lambda\lambda\lambda$ and $\delta\delta\delta$ enantiomers of **2.26**, respectively. The value of θ^m and ω^m value for complex **2.25** is in the range for octahedral Tm ligand complexes (θ 42.8–49.8° and ω 50.6–61.7°).[14]

The complexation of [(benzylamine)B(methimazolyl)$_3$] with ruthenium (II) by a similar procedure as presented on Scheme 2.16 was attempted. Before recrystallization, the ^{1}H NMR analysis of this complex indicated the presence of [{(benzylamine)B(methimazolyl)$_3$}Ru(p-cymene)]$^{2+}$, since the four aromatic protons of the benzylamine appeared as a multiplet between 7.60 and 7.54 ppm and the correspondent singlet signals at 3.91 ppm for the CH_2 group and at 5.90 ppm for the NH_2 moiety. Recrystallization of the product was performed by slow diffusion of diethyl ether in acetonitrile and yielded crystals suitable for X-Ray analysis. However, this analysis showed that these crystals presented an unexpected structure containing only three methimazole ligands coordinated to ruthenium *p*-cymene (Fig.2.12). This may be due to complex decomposition by moisture/air or light during crystallization or it is also possible that the previously analysed complex was contaminated with benzylamine from the ligand decomposition.

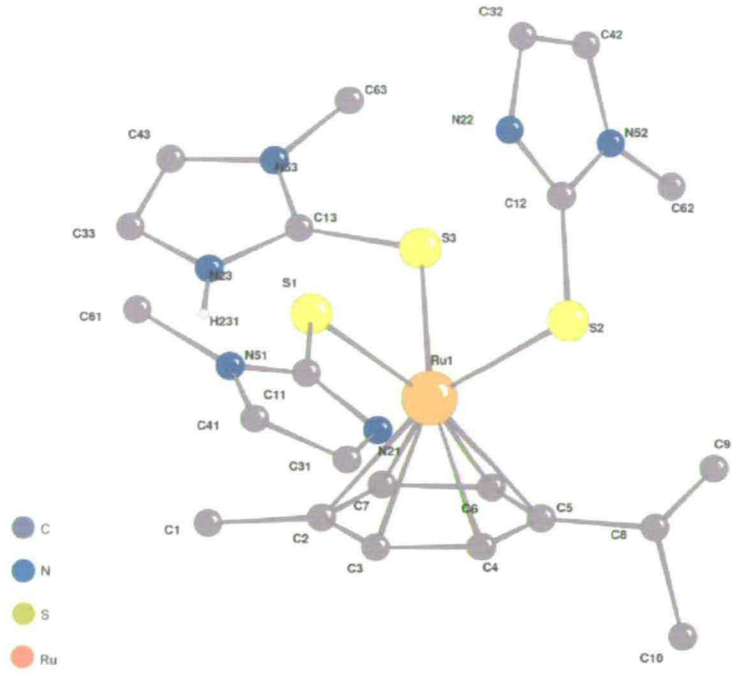


Fig.2.12. *Crystal structure of [(methimazole)$_3$Ru(p-cymene)][PF$_6$]$_2$* **2.27** *(some hydrogen atoms and counter-ions were hidden for clarity). The selected bond lengths and angles for this complex are presented on Table 2.6.*

Table 2.6. *Selected angles (°) and bond lengths (Å) [(methimazole)$_3$Ru(p-cymene)][PF$_6$]$_2$* **2.27.**

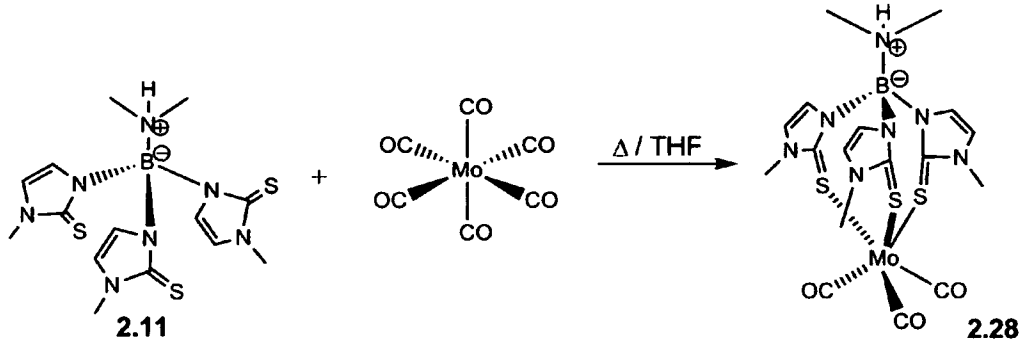
S(1)-C(11)	1.707(6)	Ru- $C_{p\text{-cym}}$ (5)	2.260(6)
S(2)-C(12)	1.716(6)	Ru- $C_{p\text{-cym}}$ (6)	2.226(5)
S(3)-C(13)	1.700(6)	Ru- $C_{p\text{-cym}}$ (7)	2.189(6)
Ru-S(1)	2.401(15)	N(21)-C(11)-S(1)	129.1(4)
Ru-S(2)	2.427(16)	N(22)-C(12)-S(2)	127.4(4)
Ru-S(3)	2.408(14)	N(23)-C(13)-S(3)	130.1(4)
Ru-$C_{p\text{-cym}}$ (2)	2.241(6)	S(1)-Ru-S(3)	83.60(5)
Ru- $C_{p\text{-cym}}$ (3)	2.204(5)	S(1)-Ru-S(2)	88.40(5)
Ru- $C_{p\text{-cym}}$ (4)	2.201(6)	S(2)-Ru-S(3)	87.51(5)

The structure of complex **2.27** shows three independent methimazole rings and a *p*-cymene ring coordinated to ruthenium. The arene ligand is π bonded to the

metal centre with an average Ru-C bond distance 2.20 Å which is very close to the Ru-C average bond found in [TmRu(*p*-cymene)]$^+$ (2.21 Å) reported by Bailey.[39] The separation between the arene centroid and the metal centre is 1.71 Å. The average S-Ru bond distances in complex **2.27** is 2.43 Å which are similar to the Ru-S average bonds found for the cationic [TmRu(*p*-cymene)]$^+$ (average S-Ru bonds 2.41 Å). Unexpectedly, these values are similar to the ones found in the previously presented structures **2.25** and **2.26** and for the ones found in [TmRu(*p*-cymene)]$^+$, despite the absence of the boron centre. This may indicate that the coordination of the methimazole to boron does not significantly influence the donor properties of the sulphur atoms in the tripodal ligands. An interesting feature of this complex is the S···H-N hydrogen bond present between two of the three methimazole rings coordinated to the ruthenium. For this interaction, the S···H distance is 2.73 Å and the S···H-N angle is 123.73°, which fall on the range of typical sulphur containing hydrogen bonds.[40] These hydrogen bonds, which are commonly present amongst proteins, are relatively weaker and generally are related to the stabilization of the sulphur atom by an acidic proton.[40] In the case of the complex **2.27** this hydrogen-sulphur interaction affects the position of the Ru coordinated methimazole rings. This is reflected on the average S-Ru-S angles for complex **2.27** (average S-Ru-S angle 86.5°) relatively to the ones found in [TmRu(*p*-cymene)]$^+$ (average S-Ru-S angle 91.7°). [39]

2.5.2. Complexation to Molydenum(0)

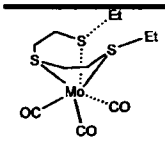
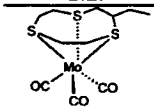
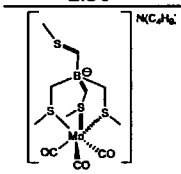
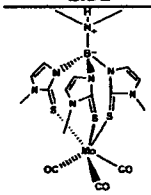
The ligand [(HNMe$_2$)B(methimazolyl)$_3$] was reacted with molybdenum hexacarbonyl under reflux of tetrahydrofuran, to obtain {[(HNMe$_2$)B(methimazolyl)$_3$]Mo(CO)$_3$} (Scheme2.17).



Scheme 2.17. *Synthesis of [{(dimethylamine)B(methimazolyl)$_3$}Mo(CO)$_3$].*

The synthesis of **2.28** was followed by IR spectroscopy until the molybdenum hexacarbonyl characteristic C=O frequency band (2004 cm^{-1}) could no longer be observed. The appearance of two new C=O frequency bands at 1982 and 1921 cm^{-1} indicated the reaction was complete and the complex **2.28** was formed. The product **2.28** was recovered as a white solid after washing the crude product with diethyl ether and removing the remaining solvent under high vacuum. The ^{1}H and ^{13}C NMR and electrospray mass spectroscopy analysis confirmed the presence of **2.28**. The ^{11}B NMR of this compound presented a single peak at 5.98 ppm which is in the range for tetrahedral boron compounds.[41] This diamagnetic stable complex allowed the study of the ligand properties by comparing the Infra-Red C=O stretching frequencies with those observed for complexes with other tridentate sulphur donor ligands (Table 2.7).

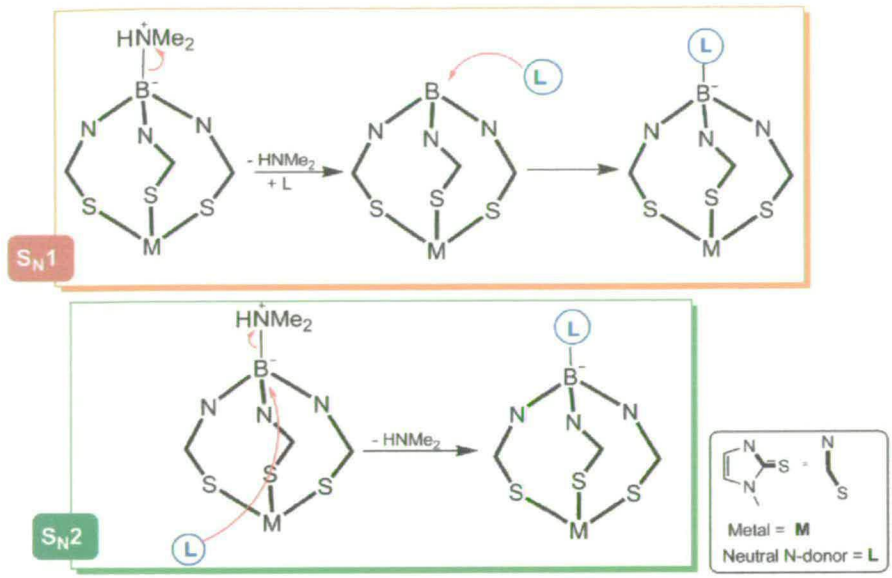
Table 2.7. *Infra-red C=O stretching frequencies of [{(HNMe$_2$)B(mt)$_3$}Mo(CO)$_3$] and other three tridentate sulphur donor molybdenum (0) triscarbonyl complexes.*

Complex		$\upsilon_{C=O}$ (cm^{-1})	Medium	Ref
 2.29	[(3,6,9-trithioundecane)(triscarbonyl)molybdenum (0)]	1930, 1820	CH_2Cl_2	42
 2.30	[(2-ethyl-1,4,7-trithiocyclononane)(tricarbonyl)molybdenum (0)]	1936, 1827	CH_2Cl_2	42
 2.31	[tetrabutylammonium][tetrakis(methylthio)methyl)-borate)(tricarbonyl)molybdenum(0)]	1899, 1784	THF	43, 44
 2.28	[{(dimethylamine)tris(methimazoly)borate(tricarbonyl)molybdenum (0)]	1987, 1957	Hexane	This work

The C=O frequencies observed are higher in 2.28 that in the previously reported complexes. This indicates that the C=O bonds in this complex are stronger that in the other three complexes, which means that [(HNMe$_2$)B(mt)$_3$] is the weakest donor of this group. The lower carbonyl stretching frequencies observed for the other three complexes indicate weaker C=O bonds. This is due a stronger Mo-CO π^* backbonding that is influenced by the higher electronic donation of the sulphur atoms coordinated to the metal. This difference may be attributed to the sp^2 hybridization of the methimazolyl sulphur atom resulting in a π donation to the metal in comparison to the sp^3 hybridization of the sulphur donors in the other three complexes which are σ donors.

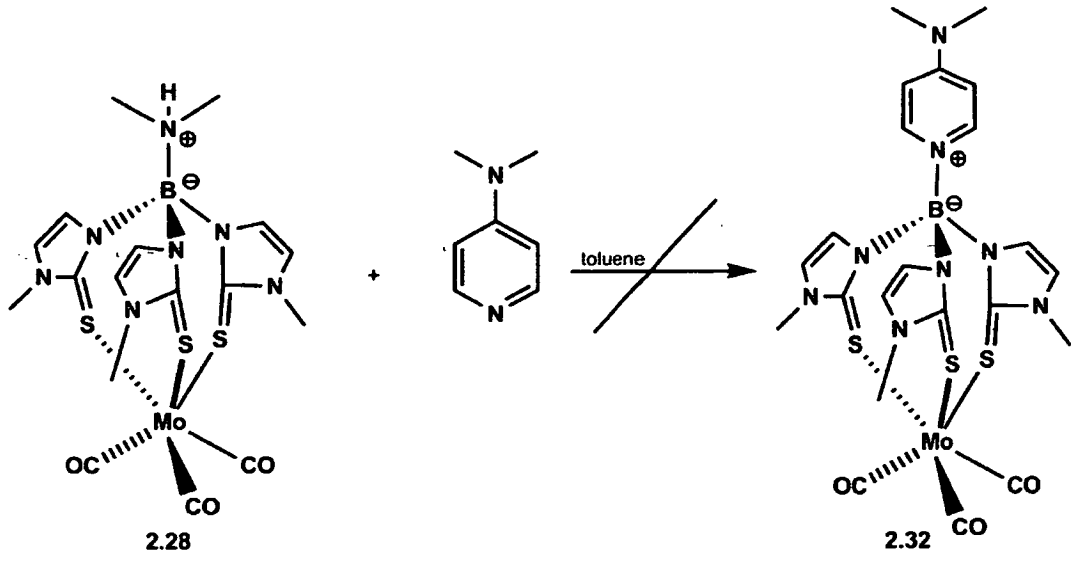
2.6. FURTHER INVESTIGATION OF THE LIGAND SYNTHESIS MECHANISM

Since the dimethylamine could be substituted in $[(HNMe_2)B(mt)_3]$, its substitution in metal complexes of this ligand was investigated. The aim of this study was to attempt to identify if the $HNMe_2$ substitution in $[(HNMe_2)B(mt)_3]$ follows a S_N1 or S_N2 type of process. If this substitution follows a dissociative mechanism type S_N1, the reaction occurs in two steps. The first step is the formation of a 3-coordinate borane species after the dimethylamine is release. Then this reactive borane species reacts with the added N-donor to produce the substituted complex (Scheme 2.18). If this substitution follows a S_N2 process the release of the dimethylamine and the coordination with an N-donor will be simultaneous. This process cannot occur within a complex since the hindrance created by the coordinated metal to the ligand would not allow the N-donor backside attack and the evolution of $HNMe_2$ will not be observed. Although a bimolecular substitution is possible to occur within the free ligand $[(HNMe_2)B(mt)_3]$ (Scheme 2.18).



Scheme 2.18. *Possible mechanisms for the substitution of $HNMe_2$ in metal complexes of $[(HNMe_2)B(mt)_3]$.*

For this study, [{(dimethylamine)B(methimazolyl)$_3$}Mo(CO)$_3$] was dissolved in toluene and 4-dimethylaminopyridine was added. The mixture was heated under reflux for one hour and after cooling it was stirred at room temperature until no evolution of dimethylamine gas was observed. The isolated off-white solid obtained was analysed by infra-red and ^{11}B NMR spectroscopy to seek, respectively, the presence of carbonyl characteristic vibration bands and boron isotope nuclei. Despite the fact that dimethylamine gas was released during the reaction, this product has been shown to be a complex mixture of decomposition products without any boron or carbonyl groups.



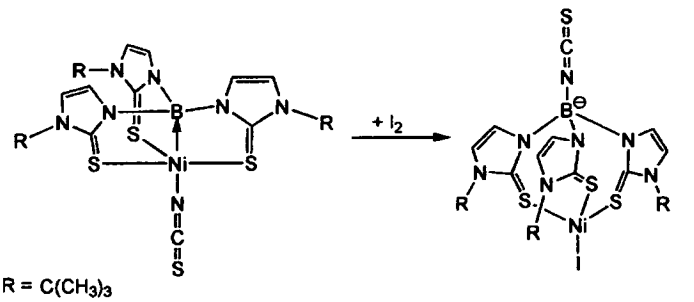
Scheme 2.19. *Attempted substituition of dimethylamine for 4-dimethylaminopyridine within a molybdenum complex.*

The results from this study are therefore inconclusive since this reaction was performed only once, and lead to the decomposition of the product. Further investigation of this type of reactions with different metal complexes and different N-donors may indicate the which mechanism type can occur when the ligand $[LB(mt)_3]$ is synthesized from $[(HNMe_2)B(mt)_3]$.

2.6.1. Functionalization of boron by N-donors within complexes: reactivity of metallaboratranes

Nickel complexes with tris(2-mercapto-1-tert-butylimidazolyl)borate with the boron functionalized on the 4th position by a N-donor have been obtained from the reaction of the respective metallaboratrane. This observation was made by Parkin and co-workers who reacted a nickel metallaboratrane complex, $[\kappa^4\text{-}B(mt^{t\text{-}Bu})_3]NiCl$

with potassium thiocyanate or sodium azide in the presence of iodine (Scheme 2.20).[45]



Scheme 2.20. *Synthesis of[(SCN)B(mt$^{t\text{-}Bu}$)$_3$]NiI by reaction of {[κ^4-B(mt$^{t\text{-}Bu}$)$_3$]Ni(NCS)} with iodine.*[45]

More investigation of this route may lead to an alternative route to synthesize boron functionalized complexes. However, the mechanism of this synthesis is still uncertain and more investigation is required to provide a better understanding of the reactivity of metallaboratranes.[45]

2.7. SYNTHESIS OF [RB(PZ)$_3$] TYPE OF LIGANDS

The chemistry of hydrotris(pyrazolyl)borate or scorpionate ligand and its analogues has been under investigation since their introduction by Trofimenko.[46] Many analogues of Tp ligand have been reported and used for a broad range of applications, from catalysis to radiopharmaceutical drugs.

Due to its importance, the synthesis of Tp ligand analogues in which the B-H is replaced by a neutral N-donor was also investigated in this work. The dimethylamine substituition on [(HNMe$_2$)B(pz)$_3$] was also investigated to afford the respective boron substituted Tp ligands analogues of the type [LB(pz)$_3$].

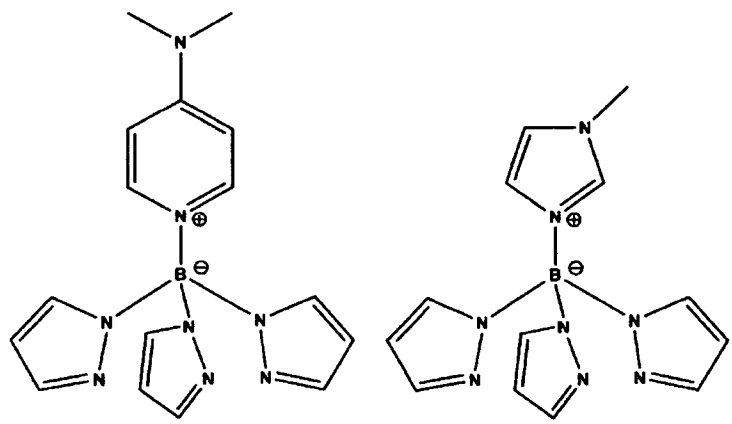
2.7.1 Synthesis of $[(HNMe_2)B(pz)_3]$

As discussed on Section 2.2, Niedenzu studied the reactivity of tris(dimethylamino)borane and pyrazole under various conditions (e.g. reflux time, further stirring time at room temperature) and solvents (benzene or toluene) and the different products that could be obtained (Scheme 2.5). The reaction of pyrazole reaction with $B(NMe_2)_3$ is exothermic with immediate evolution of dimethylamine, and a range of boranes from $[(HNMe_2)B(pz)_3]$ to pyrazaboles can be obtained depending on the reactional conditions.[9] For this work it was necessary to improve and modify these conditions in order to obtain exclusively $[(HNMe_2)B(pz)_3]$. Many attempts were made until the desired product was obtained in relatively high yield and good purity. The product was obtained by a slow addition of $B(NMe_2)_3$ to a solution of pyrazole in cyclohexane followed by heating under reflux for one hour. This procedure slows the reaction of tris(dimethylamino)borane with pyrazole and avoids the formation of dimers and/or pyrazaboles, favouring the formation of $[(HNMe_2)B(pz)_3]$.

2.7.2. Synthesis of $[LB(pz)_3]$ ligands from $[(HNMe_2)B(pz)_3]$

Since the substitution of dimethylamine in $[(HNMe_2)B(pz)_3]$ **2.8** by neutral N-donors could be achieved it was investigated whether this method could be applied to tris(pyrazolyl)borate analogues.

The ligands **2.33** and **2.34** were synthesized by heating a solution of $[(HNMe_2)B(pz)_3]$ under reflux with a neutral N-donor (Fig. 2.13). The loss of $HNMe_2$ during these reactions was observed with damp pH paper. The ^1H NMR analysis of the crude product of these reactions showed the absence of the characteristic singlet for the $HNMe_2$ group at 2.26 ppm of **2.8,** indicating the successful synthesis of both ligands.



2.33 **2.34**

Fig.2.13. *Ligands synthesized by substituition of $HNMe_2$ in $[(dimethylamine)B(pyrazolyl)_3]$.*

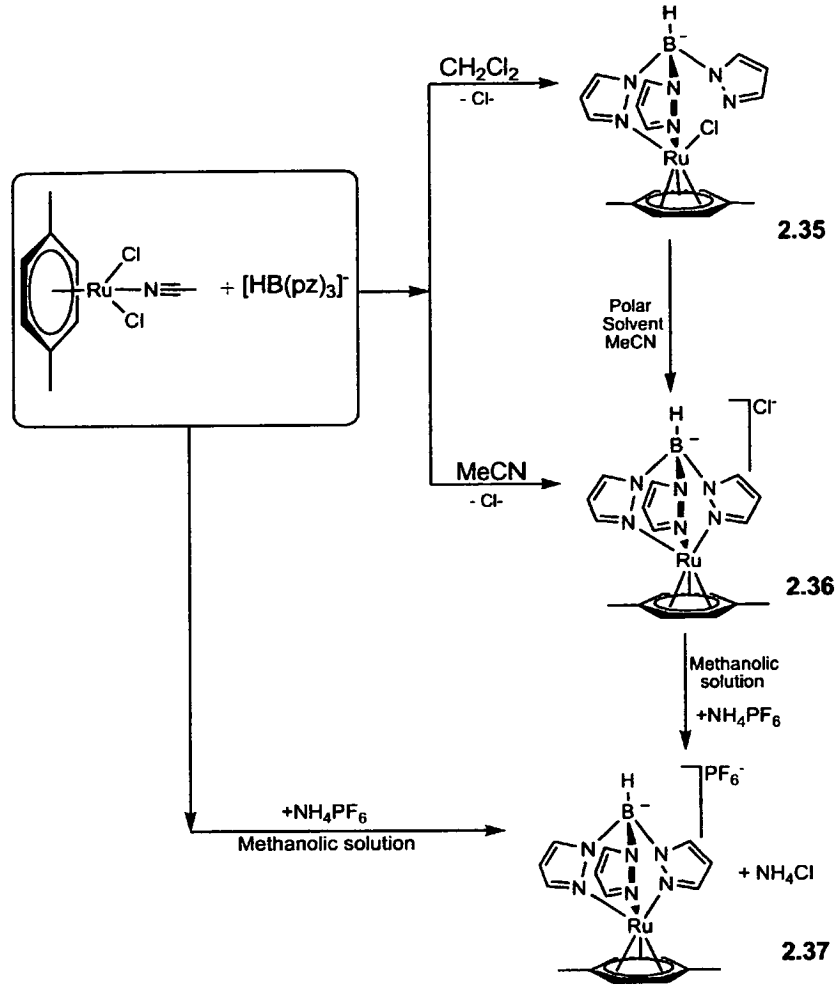
The ligand [(N-methylimidazole)B(pyrazolyl)$_3$] had been previously synthesized by Perucha via a "one-pot" reaction[25] of tris(dimethylamino)borane, pyrazole and N-methylimidazole, and it was reproduced via a base exchange reaction to compare the efficiency of both methods in the synthesis of this compound. The ^1H NMR characterization of this compound was very similar to the analysis of the same ligand obtained by Perucha.[25]

This base exchange method was also used to obtain [(DMAP)B(pyrazolyl)$_3$] which is an analogue of one of the ligands previously obtained from [(HNMe$_2$)B(mt)$_3$]. The analysis of this product by ^{1}H and ^{13}C NMR are consistent with the proposed ligand structure.

2.7.3. Complexation to Ruthenium (II)

Ruthenium complexes of poly(pyrazolyl)borates ligands have been shown to have many interesting applications in catalysis, such as C-H activation, proton transfer reactions and C-C bond formation amongst others.[47-50]

For this work, a ruthenium (II) complex of [(DMAP)B(pyrazolyl)$_3$] was synthesized by a method similar reported by Tocher (Sheme 2.21).[48]



Scheme 2.21. *Synthetic approaches reported by Tocher for the synthesis of [Ru(η^6-p-MeC$_6$H$_4$){κ^3-HB(pz)$_3$}][PF$_6$].*[48]

The ligand was added to a methanolic solution of dichloro(*p*-cymene)ruthenium dimer and left stirring for an hour This was followed by a salt metathesis reaction with addition of NH_4PF_6. The obtained yellow powder was crystallized from diethyl ether diffusion into a concentrated acetonitrile solution. The crystal structure of this complex is displayed on Fig.2.14.

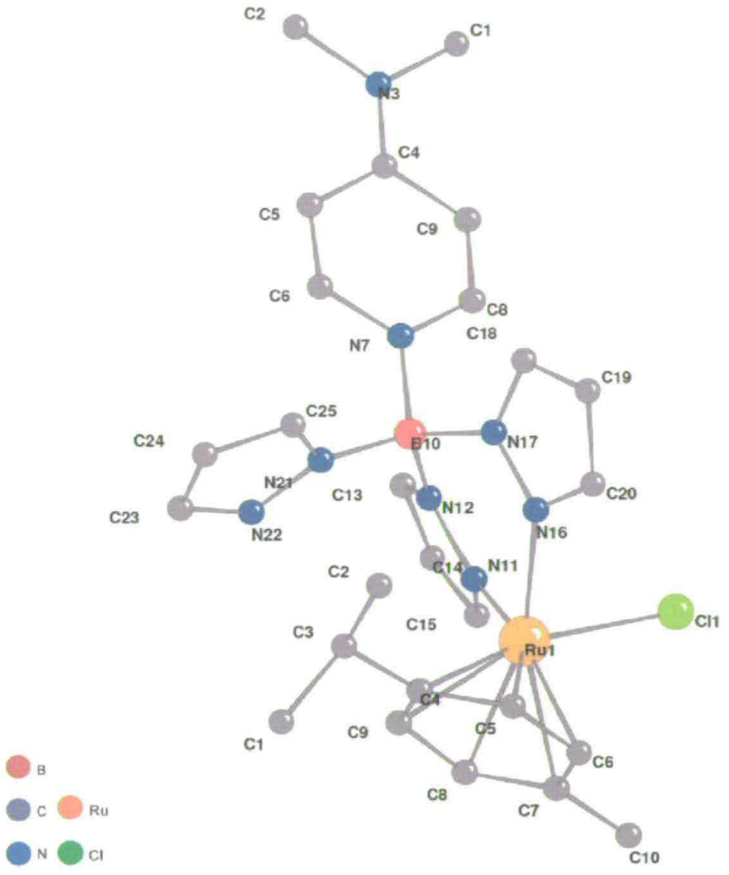


Fig.2.14. *Crystal structure of [{(DMAP)B(pz)$_3$}Ru(p-cymene)Cl] PF_6* ***2.38.*** *(hydrogen atoms and hexafluorophosphate counter-ion were omitted for clarity).*

One chloride ligand is still coordinated to ruthenium and the ligand is κ^2-N,N coordinated. This was unexpected since the synthetic method used was the analogous to the one reported by Tocher and collaborators (Scheme 2.21) which provides the κ^3- *N,N,N* coordinated ligand.[48] The analysis of this product by ^{1}H and ^{13}C NMR showed the presence of two types of pyrazole signals in a 1:2 ratio, which was concordant with the structure found in the solid state.

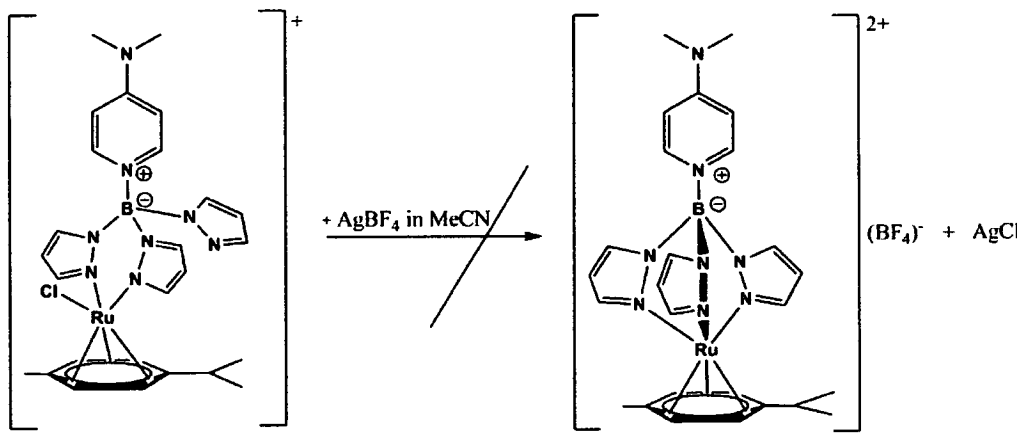
Table 2.8. *Selected angles (°) and bond lengths (Å)* for *[{(DMAP)B(pz)$_3$}Ru(p-cymene)Cl] PF_6 2.38.*

B-N $_{DMAP}$(7)	1.569(4)	Ru- $C_{p\text{-cym}}$ (9)	2.159(3)
B-N $_{pz}$ (21)	1.521(4)	Ru-Cl	2.390(7)
B-N $_{pz}$(12)	1.531(4)	Ru-N(11)	2.076(2)
B-N $_{pz}$ (17)	1.540(4)	Ru-N(16)	2.086(2)
N(21)-N(22)	1.367(4)	N(11)-Ru-N(16)	86.76(8)
N(12)-N(11)	1.361(3)	N(16)-Ru-Cl	84.92(6)
N(16)-N(17)	1.370(3)	N(11)-Ru-Cl	84.82(6)
Ru-$C_{p\text{-cym}}$ (4)	2.224(3)	N(21)-B-N(17)	109.7(2)
Ru- $C_{p\text{-cym}}$ (5)	2.192(3)	N(7)-B-N(12)	105.9(2)
Ru- $C_{p\text{-cym}}$ (6)	2.184(3)	N(7)-B-N(21)	110.4(2)
Ru- $C_{p\text{-cym}}$ (7)	2.217(3)	N(17)-B-N(12)	111.4(2)
Ru- $C_{p\text{-cym}}$ (8)	2.187(2)		

In this complex the [(DMAP)B(mt)$_3$] ligand binds the metal in a κ^2-N,N coordination mode with an average Ru-N distance of 2.08 Å. The ruthenium is π bonded to the *p*-cymene ligand with an average Ru-C distance of 2.19 Å and it is 1.67 Å separated from the arene centroid. The Ru-Cl distance is 2.39 Å. The angle of the chelating ligand and the metal (N-Ru-N) is 84.87°. These distances and angles are very similar to the ones found in [Ru(η^6-*p*-MeC$_6$H$_4$){κ^2-HB(pz)$_3$}Cl] (average Ru-C_{arene} 2.20 Å, Ru-Cl distance 2.39 Å, N-Ru-N angle 84.8°) which was previously reported by Tocher [48] The average B-N distance of the three pyrazole N atoms to the boron center is 1.53 Å and the B-N distance between DMAP's nitrogen coordinated to the boron is 1.57 Å which is slightly longer than the other B-N bonds.

In order to investigate the possible conversion of the κ^2-*N,N* coordination of the ligand to κ^3-*N,N,N* the complex was dissolved in acetonitrile and $AgBF_4$ was added and the formation of AgCl was observed in solution (Scheme 2.22).

The solution was filtered and the remaining yellow solution was evaporated to dryness under vacuum. The ^{1}H NMR spectrum of the resulting product showed three different signals for the pyrazole rings indicating that the ligand was not coordinated in a κ^3-N,N,N mode and/or there was a mixture of products resulting from complex decomposition. Attempted purification of this product by crystallization was unsuccessfully.



2.38 **2.39**

Scheme 2.22. *Attempted synthesis of [{(DMAP)B(pz)$_3$}Ru(p-cymene)](PF$_6$)(BF$_4$) (hexafluorophosphate counter-ions are omitted for clarity).*

The retention of the chloride ligand to the ruthenium centre in the structure of **2.38** was responsible for the κ^2 coordination of the tripodal ligand thus influencing the position of the uncoordinated pyrazole ligand. The attempt to recoordinate this pyrazole ring to the ruthenium failed since it required decoordination of the chloride and one of the pyrazole ring to form the κ^3 coordinated complex.

2.8. CONCLUSION

The work presented in this chapter shows that it is possible to synthesize ligands of the type $[(L)B(mt)_3]$ by substitution of dimethylamine in $[(HNMe_2)B(mt)_3]$ when it is reacted with a neutral N-donors under reflux in toluene. The N-donors used in this work were mainly tertiary amines and imines but also a primary amine, benzylamine was successfully used. The possibility to use primary amines to functionalize the boron broadens the range of N-donors that can be applied in the synthesis of new ligands. Hence, there are more possible ways to functionalize the boron of the Tm ligand derivatives with chiral groups. The synthesis of the ligand with a chiral primary amine, α-methylbenzylamine, is presented on Chapter IV.

This synthetic route can also be applied to ligands with pyrazole instead of methimazole, although only two reactions were performed and more of the reactivity of these ligands requires further investigation.

The evidence that the dimethylamine in $[(HNMe_2)B(mt)_3]$ can be substituted with N-donors contradicts the previously proposed mechanism for the "one-pot" reactions with (dimethylamino)borane reported by Bailey and Perucha.[14, 25] In the light of this work, another mechanism for the formation of ligands of the type $[(L)B(mt)_3]$ is proposed. However, it was not possible to determine whether the process is a dissociative or a bimolecular substitution. This investigation will require further work in the reactivity of dimethylamino(trismethimazolyl)borate metal complexes with N-donors.

REFERENCES

1. A. H. Clark and G. A. Anderson, *J. Chem. Soc., Dalton Trans.*, 1969, 1082.
2. G. Schmid, R. Boese and D. Blaser, *Z. Naturforsch., B: Chem. Sci.*, 1982, **37**, 1230.
3. E. W. Hughes, *J. Am. Chem. Soc.*, 1956, **78**, 502.
4. M. A. Beckett, G. C. Strickland, J. R. Holland and K. Sukumar Varma, *Polymer*, 1996, **37**, 4629.
5. H. Steinberg and R. J. Brotherton, *Organoboron Chemistry*, Interscience, New York, 1966.
6. K. Niedenzu, P. Fritz and J. W. Dawson, *Inorg. Chem.*, 1964, **3**, 1077.
7. U. Braun and H. Nöth, *Eur. J. Inorg. Chem.*, 2007, 2296.
8. U. Braun, T. Habereder, H. Nöth, H. Piotrowski and M. Warchhold, *Eur. J. Inorg. Chem.*, 2002, 1132.
9. K. Niedenzu and W. W. Seelig, *Z. Anorg. Allg. Chem.*, 1981, **483**, 51.
10. K. Niedenzu and K. R. Woodrum, *Inorg. Chem.*, 1989, **28**, 4022.
11. R. Garcia, A. Paulo, A. Domingos and I. Santos, *Dalton Trans.*, 2003, 2757.
12. K. Niedenzu and S. Trofimenko, *Inorg. Chem.*, 1985, **24**, 4222.
13. A. Biernat, M. Schwalbe, D. Wallace, J. Reglinski and M. D. Spicer, *Dalton Trans.*, 2007, 2242.
14. P. J. Bailey, D. Lorono-Gonzales, C. McCormack, F. Millican, S. Parsons, R. Pfeifer, P. Pinho, F. Rudolphi and A. S. Perucha, *Chem. Eur. J.*, 2006, **12**, 5293.
15. Z. Fijalek and P. Zuman, *Anal. Lett.*, 1990, **23**, 1213.
16. K. Kostka and M. M. Strawiak, *Pol. J. Chem.*, 1984, **58**, 647.

17. H. N. Po, Z. Shariff, J. A. Masse, F. Freeman and M. C. Keindl-yu, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1991, **63**, 1.

18. T. Akutagawa and G. Saito, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 1753.

19. G. G. Gallo, C. R. Pasqualucci, P. Radaelli and G. C. Lancini, *J. Org. Chem.*, 1964, **29**, 862.

20. J. Catalán and J. Elguero, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1869.

21. K. H. Kim and Y. C. Martin, *J. Med. Chem.*, 1991, **34**, 2056.

22. K. Schofield, M. R. Grimmett and B. R. T. Keene, *Heteroaromatic nitrogen compounds: the azoles*, Cambridge University Press, 1976.

23. J. Catalan, R. M. Claramunt, J. Elguero, J. Laynez, M. Menendez, F. Anvia, J. H. Quian, M. Taagepera and R. W. Taft, *J. Am. Chem. Soc.*, 1988, **110**, 4105.

24. Y. Takeuchi, K. L. Kirk and L. A. Cohen, *J. Org. Chem.*, 1978, **43**, 3570.

25. A. S. Perucha, PhD Thesis, *University of Edinburgh*, 2007.

26. H. K. Hall, *J. Am. Chem. Soc.*, 1957, **79**, 5441.

27. H. H. Jaffé and G. O. Doak, *J. Am. Chem. Soc.*, 1955, **77**, 4441.

28. S. J. Angyl and C. L. Angyal, *J. Chem. Soc.*, 1952, 1461.

29. D. D. Perrin, *J. Chem. Soc.*, 1965, 5590.

30. M. R. Crampton and I. A. Robotham, *J. Chem. Res. (S)*, 1997, 22.

31. J. D. Roberts, *J. Am. Chem. Soc.*, 1956, **78**, 886.

32. D. J. Cram, R. A. Carmack and R. C. Helgeson, *J. Am. Chem. Soc.*, 2002, **110**, 571.

33. S. M. C. Buckenmaier, D. V. McCalley and M. R. Euerby, *J. Chromatogr. A*, 2003, **1004**, 71.

34. M. R. Foreman, A. F. Hill, A. P. White and D. J. Williams, *Organometallics*, 2003, **22**, 3831.

35. E. Wiberg, N. Wiberg and A. Frederick Holleman, *Inorganic Chemistry*, Academic Press, 2001.

36. R. N. M. Kitamura, in *Ruthenium in Organic Synthesis*, ed. S.-I. Murahashi, John Wiley & Sons, Inc., 2005, pp. 3-52.

37. O. Novakova, H. Chen, O. Vrana, A. Rodger, P. J. Sadler and V. Brabec, *Biochemistry*, 2003, **42**, 11544.

38. T. M. T. Robert H. Grubbs, in *Ruthenium in Organic Synthesis*, ed. S.-I. Murahashi, John Wiley & Sons, Inc., 2005, pp. 153-177.

39. P. J. Bailey, D. J. Lorono-Gonzales, C. McCormack, S. Parsons and M. Price, *Inorg. Chim. Acta*, 2003, **354**, 61.

40. P. Zhou, F. Tian, F. Lv and Z. Shang, *Proteins*, 2009, **76**, 151.

41. J. Mason, *Multinuclear NMR*, Plenum Press, New York, 1987.

42. O. P. Siclovan and R. J. Angelici, *Inorg. Chem.*, 1998, **37**, 432.

43. P. Ge, B. S. Haggerty, A. L. Rheingold and C. G. Riordan, *J. Am. Chem. Soc.*, 1994, **116**, 8406.

44. A. L. Sargent, E. P. Titus, C. G. Riordan, A. L. Rheingold and P. Ge, *Inorg. Chem.*, 1996, **35**, 7095.

45. K. Pang, J. M. Tanski and G. Parkin, *Chem. Commun.*, 2008, 1008.

46. S. Trofimenko, *Chem. Rev.*, 1993, **93**, 943.

47. R. J. Abernethy, A. F. Hill, N. Tshabang, A. C. Willis and R. D. Young, *Organometallics*, 2009, **28**, 488.

48. S. Bhambri and D. A. Tocher, *J. Chem. Soc., Dalton Trans.*, 1997, 3367.

49. C. Bruneau and P. H. Dixneuf, *Acc. Chem. Res.*, 1999, **32**, 311.

50. M. Jiménez-Tenorio, M. C. Puerta and P. Valerga, *Organometallics*, 2009, **28**, 2787.

CHAPTER III

BORON-CENTRED TRIPODAL LIGANDS WITH HETEROCYCLES OTHER THAN METHIMAZOLE

3.1. INTRODUCTION

Previously, the work towards the synthesis of analogues of tris(methimazolyl)borate ligands with boron functionalized with a neutral N-donor has been presented. Subsequently, the synthesis of these ligands with different sulphur and selenium donor heterocycle analogues of methimazole has been investigated. This work will be presented in this chapter. The heterocycles used for this work were 1-methyl-benzimidazole-2-thione, 1,4,5-trimethyl-imidazole-2-thione and 1-mesityl-imidazole-2-selone (Fig.3.1).

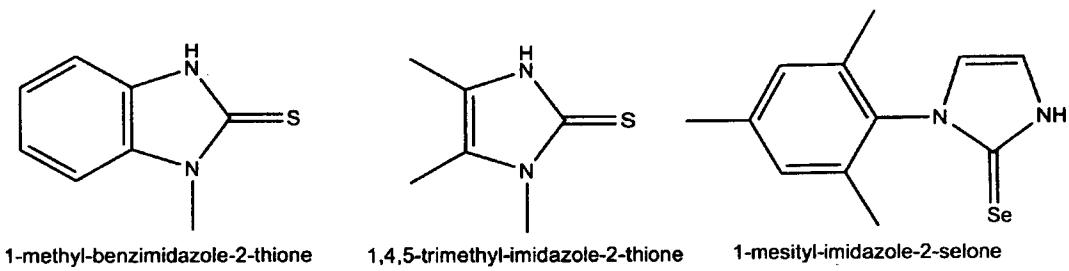


Fig.3.1. *Heterocycles used for the ligand synthesis.*

As some of these compounds were not readily available for purchase, their synthesis will also be discussed in this chapter. Dimethylamine and N-methylimidazole were used to functionalize the boron forth position in these new ligands.

3.2. BORON-CENTRED TRIPODAL LIGANDS WITH SOFT DONOR ATOMS

The ubiquitous tris(pyrazolyl)borate ligand system can be derivatized in order to control the steric environment of the binding site. This derivatization can be done

by replacing the pyrazole rings by substituted pyrazole rings and/or by other heterocycles.[1, 2] The substitution of the pyrazole by methimazole rings in this type of system gave rise to another generation of scorpionates or boron-centred tripodal ligands with soft donors.

The tris(methimazolyl)borate ligand system framework can be described as $[E(L_2D)_3]$ (E = central tripod atom, L = linking atom and D = donor atom) with many possibilities for variation by changing E, L and D (Fig.3.2.).[3] In this work only the ligand systems with boron as central tripodal atom, as $[B(L_2D)_3]$ with soft donor atoms will be considered.

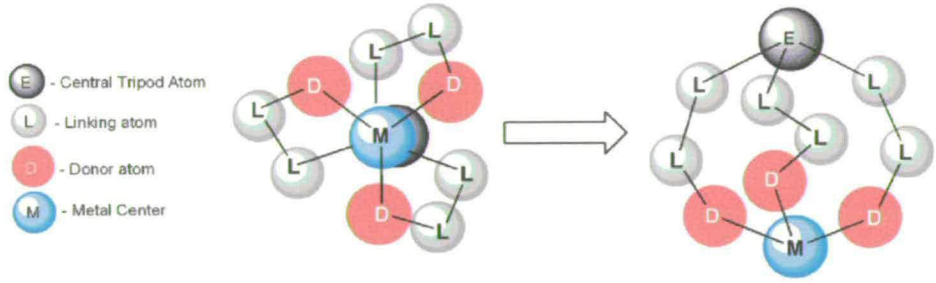


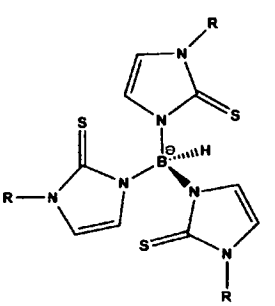
Fig.3.2. *Coordination of a $[E(L_2D)_3]$ ligand system to a metal centre (M) (two different views showing the bicyclo[3,3,3]cage).*

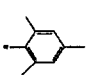
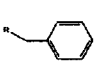
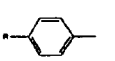
In these ligands the coordination of the three donor atoms to a metal forms C_3-symmetric complexes with a bicyclo[3,3,3]cage that presents chirality through the twisted conformation of the cage.[4, 5] Modification of the heterocycles that provide the donor atoms can be used to tune this system electronically and sterically.

3.2.1. Boron-centred tripodal ligands with sulphur donors

As mentioned in Chapter 1, the Tm ligand has been used to model metalloenzyme sites,[6] since it can create a protective encapsulation for a metal centre. This metal protection can be achieved by substituting the methimazole N-methyl group on the Tm ligand structure. To explore the biomimetic applications of this ligand system, many new ligands have been prepared with methimazole derivatives containing different functional groups (R) in the methimazole ring 3-position. The common abbreviation used for these analogues is Tm^R. Some of these analogues are listed on Table 3.1

Table 3.1. *Some Tm ligand derivatives with methimazole analogues substituted in the third position.*



Substituent		Abreviation	Ref.
Methyl	R——	**Tm or Tm^{Me}**	1
Phenyl		**Tm^{Ph}**	7
Mesityl		**Tm^{Mes}**	7
t-Butyl		**$Tm^{t\text{-}Bu}$**	8
Benzyl		**Tm^{Bz}**	9
***p*-Tolyl**		**$Tm^{p\text{-}Tol}$**	9
***o*-Anisyl**		**$Tm^{o\text{-}An}$**	10
Xylene		**Tm^{Xyl}**	11

The metal protection in complexes with Tm ligand analogues depends on the orientation and the nature of the functional group in the methimazole 3-position. Vahrenkamp and co-workers have studied some zinc complexes with Tm^{Mes}, $Tm^{p\text{-}Tolyl}$ and Tm^{Xyl} and compared the orientation of the three different N-substituents of the thioimidazole relative to the B-Zn axis. A schematic view of this comparison is displayed in Fig.3.3.

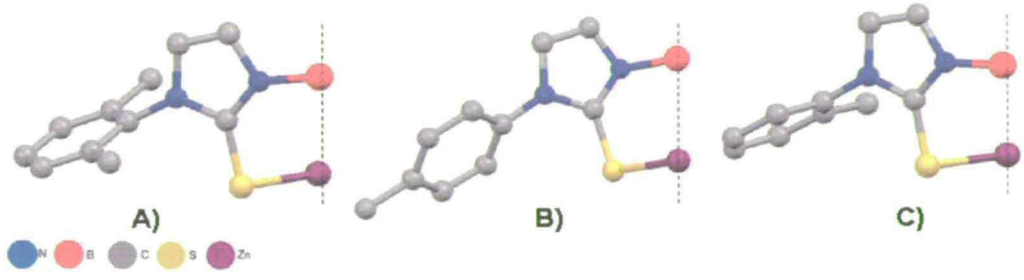
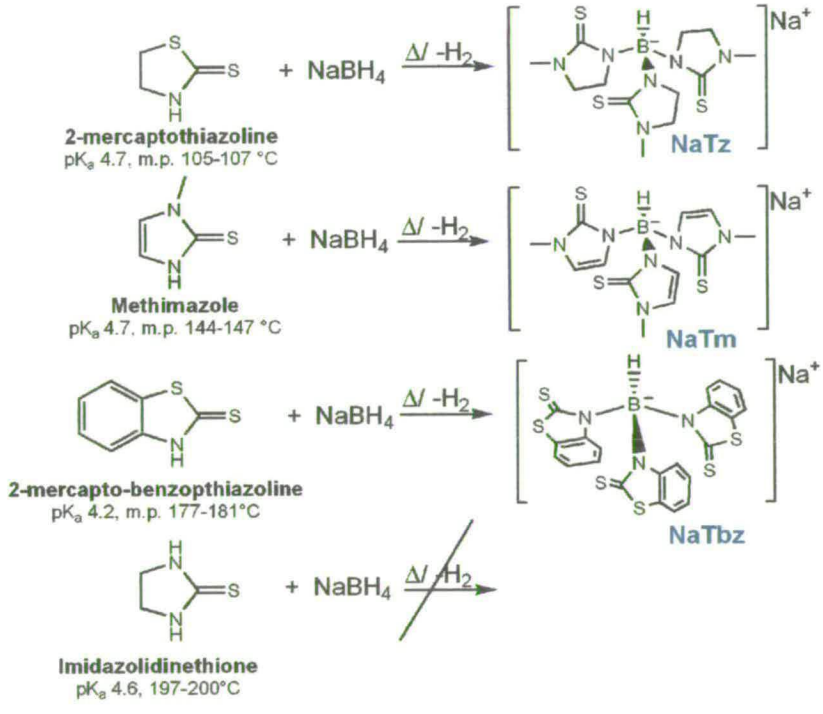


Fig.3.3. *Partial view of tripodal ligand arms bonded to zinc in three different complexes with: A) Tm^{Xyl}; B)$Tm^{p\text{-}Tolyl}$ and C) $Tm^{o\text{-}Tolyl}$.*[11]

According to Fig.3.3 it is possible to create more encapsulation of the metal if *para*-substituted aromatic thioimidazoles are used in the Tm backbone.[11] The chirality of the metal complexes containing these Tm ligand analogues can also be influenced by variation of the nitrogen substituents of the methimazole. Since these ligands form a cage with helical rotation, the size and shape of these groups can create a hindrance that restrain the motion of this cage. Bailey and collaborators investigated a range of complexes and studied the possible racemisation processes and their energetic barriers.[12, 13] This work will be discussed in more detail as an

introduction to Chapter IV, as this chapter is more focused on the modifications of the methimazole rings to obtain new ligands.

It is also possible to synthesize analogues of the Tm ligand using heterocycles other than methimazole, but always keeping the sulphur donors atoms. Ojo and Regliski reported the synthesis of new soft tripodal ligands from the reaction of borohydride with different thiones.[14] From the three imine-thiones used in their work (2-mercaptothiazoline, 2-mercaptobenzothiazoline and imidazolidinethione) only two reacted successfully with the borohydride to form new ligands (Scheme 3.1.)[14]



Scheme 3.1. *Imine-thiones used by Ojo and Reglinski to synthesize the Tm ligands and two new boron centred-tripodal ligands with soft donors (NaTz and NaTbz).* [14]

The melting point and the pK_a of the different heterocycles were determinant factors in the choice of the thiones used in Ojo and Reglinski's work. The unsuccessful synthesis with imidazolidinethione through a melt reaction showed that

in this case the pK_a of the heterocycle may not be a determinant factor in this synthetic route (Scheme 3.1). In these melt reactions the main cause of decomposition can be the overheating of the mixture. To avoid thermal decomposition during the synthesis, the melting point of the heterocycle has to be considered as an important factor when the thione is selected.

Although, the pK_a of different azoles is an important factor in the synthesis of neutral boron-centred tripodal ligands from $B(NMe_2)_3$. According to previous results, Bailey and Perucha established that the reaction of methimazole and other azoles with pK_a below 3.0 (approximately) with tris(dimethylamino)borane generated the neutral tetrasubstituted species [(azole)B(azolyl)$_3$]. These azoles presented an acidic proton which allows the reaction with $B(NMe_2)_3$ and therefore the synthesis of new ligands with different heterocycles in place of methimazole.[13]

In the next section of this chapter, the work with analogues of methimazole substituted in the 4th and 5th position in order to develop the synthesis of new ligands will be presented.

3.3. BORON-CENTRED TRIPODAL LIGANDS WITH SUBSTITUTED METHIMAZOLE ANALOGUES

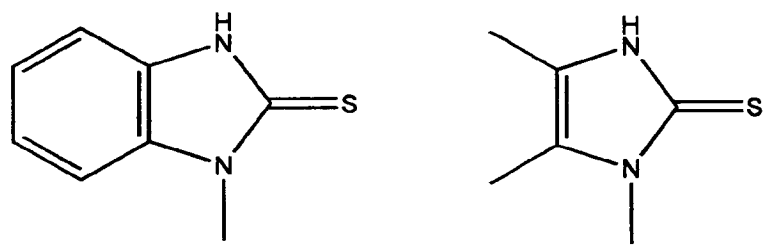
It was mentioned previously that the most common derivatizations made on the Tm ligand system were related to the substitution of the *N*-methyl group of the methimazole with different alkyl or aryl groups. However, it is also possible to use methimazole analogues substituted in the 4- and 5-positions. In this thesis, two analogues of methimazole were synthesized and used to obtain new boron-centred

tripodal ligands. This work will be presented in this section and the synthesis of these new ligands will be presented in presented and discussed on Section 3.4.

The work with these heterocycles will be continued in Chapter IV where chiral neutral N-donors used to functionalize the boron's 4th position will be introduced.

3.3.1. Carbon-substituted analogues of methimazole

For this work two methimazole analogues substituted at the 4- and 5-positions (Fig. 3.4) were used for the ligand synthesis. As in methimazole, these heterocycles present an acidic N-H proton which allows the transamination reaction with $B(NMe_2)_3$.



1-methyl-benzimidazole-2-thione 1,4,5-trimethyl-imidazole-2-thione

Fig.3.4. *Methimazole analogues used to synthesize the ligands presented in this work.*

From the reaction of these thioimidazoles with tris(dimethylamino)borane it is expected to obtain two ligands that, upon complexation, present a protected environment for the remaining axial site at boron as found for the anionic ligand

NaTbz, containing the 2-mercaptobenzothiazoline donors, reported by Ojo and Reglinski (Scheme 3.1 and Fig.3.5).

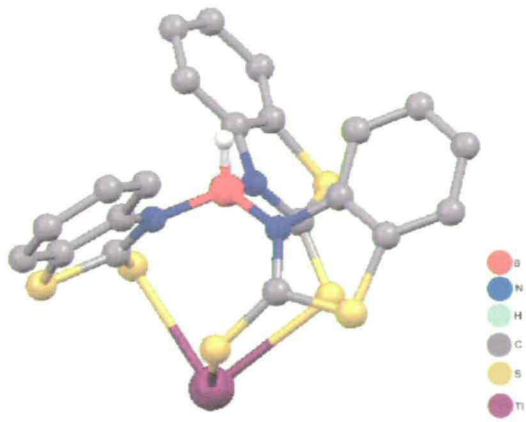


Fig.3.5. *Structure of the anionic Tbz ligand coordinated to thalium reported by Ojo and Reglinski.*[14]

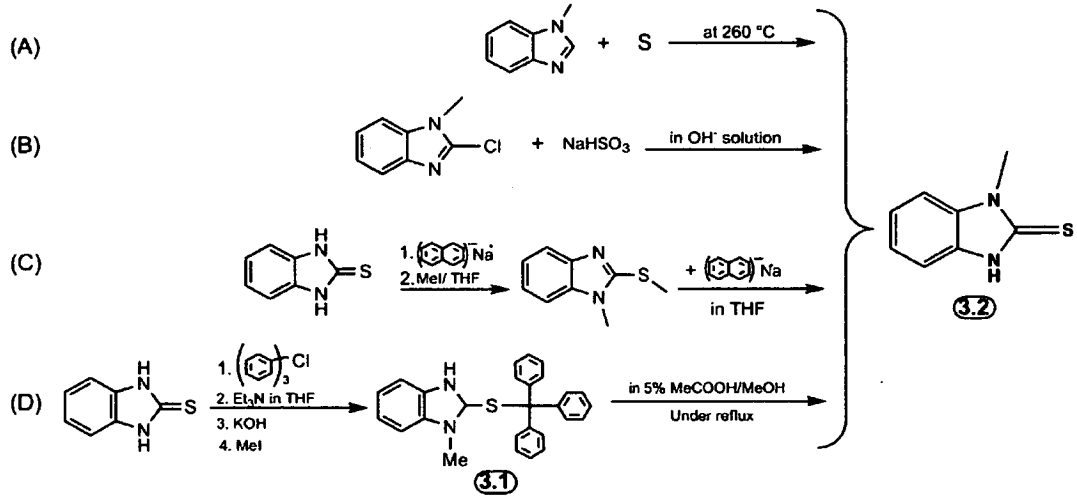
In the structure of the complex displayed in Fig. 3.5, the orientation of the aromatic rings of the benzothiazoline in the Tbz ligand creates a C_3-symmetric cavity around the hydride attached to the boron.

The 1-methyl-benzimidazole-2-thione and the 1,4,5-trimethyl-imidazole-2-thione (Fig.3.4) can also be used to synthesize ligands with chiral N-donors in the boron 4th position. In this case the chiral group coordinated to the boron will be located in the C_3-symmetric cavity thus increasing the transfer of the chirality to the rest of the ligand. In the Chapter IV, the work done towards the synthesis of a new

chiral boron-centred tripodal ligand using 1,4,5-trimethylimidazole-2-thione which will be presented and discussed.

3.3.2. Synthesis of 1-methyl-benzimidazole-2-thione

Several synthetic methods have been reported for the synthesis of 1-methyl-benzimidazole-2-thione. This compound can be synthesized by heating a mixture of 1-methylbenzimidazole and sulphur at 260°C,[15] or by reacting 1-methyl-2-chlorobenzimidazole with sodium bisulphite in sodium hydroxide solution.[16] There are also alternative synthetic routes starting from benzimidazole; the synthetic strategies to obtain 1-methyl-benzimidazole-2-thione are displayed in Scheme 3.7.[17,18]



Scheme 3.2. *Synthetic routes to obtain 1-methyl-benzimidazole-2-thione* ***3.19***;

References: (A),[15] *(B),*[16] *(C),*[17] *(D).*[18]

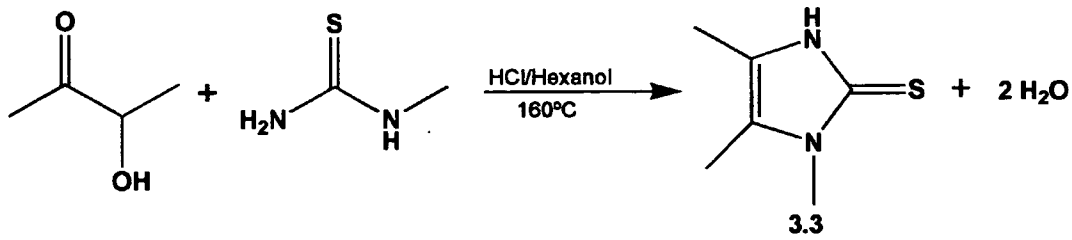
The synthesis of 1-methyl-benzimidazole using 2-thiobenzimidazole as starting material, reported by Doerge and Cooray was undertaken (D of Scheme 3.7).[18] Via this method the methylation of 2-thiobenzimidazole is achieved after protecting the thione sulphur with a trityl group to avoid S- methylation.

This method was successful, as the required benzimidazole was synthesized in gram-scale and high purity. However, it was found that if the trityl protective group was not efficiently removed after methylation, the mixture of the desired benzimidazole and its protected derivative obtained as final product was difficult to separate. Although the separation of these compounds by recrystallization was possible, the reaction yield was substantially affected. These issues are related to an incomplete removal of the trityl group in the last step of this synthesis. After increasing the reaction time from 2h to 36 h to promote the completion of this last step and recrystallizing the product from acetonitrile instead of ethanol, it was possible to produce pure 1-methylbenzimidazole-2-thione in a 71% yield and proceed to the ligand synthesis. The ^{1}H NMR analysis of the 1-methylbenzimidazole-2-thione obtained was consistent with the reported analysis.

3.3.3. Synthesis of 1,4,5-trimethylimidazole-2-thione

The other methimazole analogue synthesized was 1,4,5-trimethylimidazole-2-thione. The synthesis of this compound was reported by Kister,[19, 20] and it involves the condensation of 3-hydroxy-2-butanone and N-methylthiourea in hexanol at 160°C for twelve hours. The water produced during this reaction can be removed by an azeotropic distillation and this product can be purified by preparative

chromatography and/or recrystallization.[20] This method was optimised in order to maximize the yield of this reaction (21%). The best result was obtained when this reaction was carried out in a solution of 4% hydrochloric acid in hexanol and heated to reflux for 16 hours (Scheme 3.3).

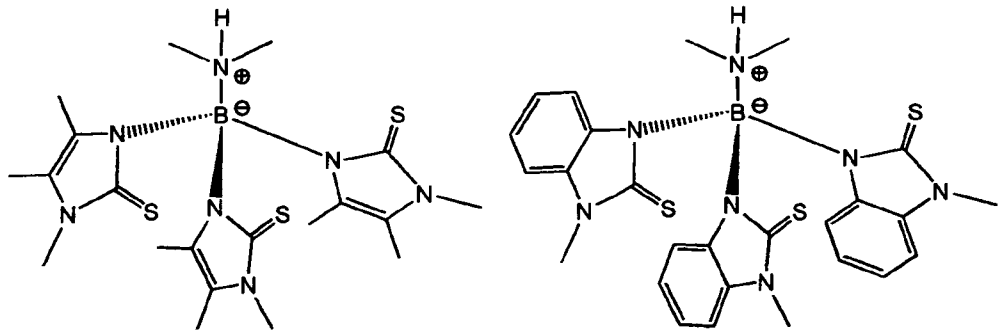


Scheme 3.3. *Synthetic route to obtain 1,4,5-trimethylimidazole-2-thione 3.3.*[19]

The azeotropic removal of water was not necessary. The final crude product was recrystallized from petroleum ether and hexanes and obtained in 30% yield. The ^{1}H NMR analysis of this product was consistent with the literature data.

3.4. LIGAND AND COMPLEX SYNTHESIS

The methimazole analogues,were reacted with tris(dimethylamino)borane in toluene under reflux to afford the respective ligands (**3.4** and **3.5**) shown in Fig.3.6 in respectively 66 and 54% yield.



3.4 3.5

Fig.3.6. *Ligands synthesized with 1-methylbenzimidazol-2-thione 3.4 and 1,4,5-trimethylimidazole-2-thione 3.5.*

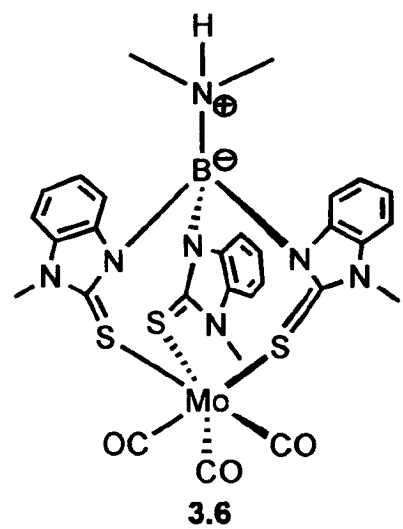
Both tripodal ligands were successfully synthesized and characterized by ^{1}H and ^{13}C NMR and positive ion FAB mass spectrometry.

The ^{1}H NMR spectrum of [($HNMe_2$)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] (**3.4**) showed three singlets at 2.84, 2.08 and 2.04 ppm assigned to the methyl groups of the 1,4,5-trimethylimidazolyl-2-thione groups. The dimethylamino group gives a singlet at 3.48 ppm for the six methyl protons and a broad signal appears at 10.47 ppm for the N-H proton. The ^{13}C NMR spectrum shows six signals for this ligand since the two CH_3-C moieties of 1,4,5-trimethylimidazolyl-2-thione and the two methyl groups of $HNMe_2$ appear at the same chemical shift. The presence of the ligand was confirmed by FAB^+ mass spectrometry ([M+1] = 480) and elemental analysis. Further work with 1,4,5-trimethyl-imidazole-2-thione will be presented in Chapter IV.

The ^{1}H NMR spectrum of [($HNMe_2$)B(1-methyl-benzimidazolyl-2-thione)$_3$] (**3.5**) contained a clear aromatic multiplet in the region 7.19 to 7.13 ppm for the aromatic moiety of the thione heterocycle. The two equivalent methyl groups of the $HNMe_2$ appeared at 3.75 ppm while the methyl groups of the benzimidazolyl moiety

of the ligand give another singlet at 3.80 ppm. The N-H proton produces a broad signal at 10.22 ppm. The ^{13}C NMR exhibits nine signals; eight signals correspond to the three equivalent benzimidazole rings and one signal is assigned to the equivalent methyl groups of $HNMe_2$. The FAB^+ mass spectrometry ([M+1] = 546) and elemental analysis confirmed the presence of the ligand.

In order to study the donor properties of the ligand [$(HNMe_2)$B(1-methyl-benzimidazolyl-2-thione)$_3$] (**3.5**) it was coordinated to molybdenum tricarbonyl to form the complex [{κ^3-$(HNMe_2)$B(1-methyl-benzimidazolyl-2-thione)$_3$}$Mo(CO)_3$] (**3.6**). The complex was synthesized from a mixture of the ligand and $Mo(CO)_6$ in tetrahydrofuran under reflux.



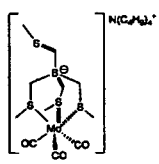
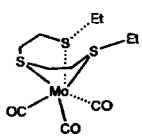
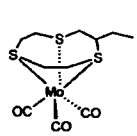
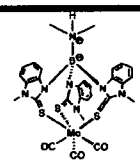
3.6

Fig.3.7. *Complex of [(HNMe$_2$)B(1-methyl -benzimidazolyl-2-thione)$_3$] with molydenum tricarbonyl 3.6.*

The ^1H NMR spectrum of **3.6** shows four sets of signals, as for the free ligand. In comparison to the proton signals of the ligand, this complex shows the

two methyl groups of $HNMe_2$ shifted to slightly higher frequency (from 3.75 ppm to 3.80 ppm). The same happens to the methyl groups of the thiobenzimidazole which shift from 3.80 ppm to 3.88 ppm after complexation. This deshielding is caused by electron density changes on the ligand upon coordination to the molybdenum. The aromatic signals of the thiobenzimidazole appear as a multiplet in the region 7.20 to 7.10 ppm. Despite the deshielding of the methyl groups, the N-H proton of the dimethylamino group appears more shielded (from 10.22 ppm to 9.45 ppm). This may be related to ring-current effects due to the position of the aromatic moieties of the benzimidazole surrounding the $HNMe_2$ group. The CO ligands of this complex provide a characteristic signal at 205.6 ppm in the ^{13}C NMR spectrum. The FAB^+ mass spectrometry ([M+1] = 726) the elemental analysis confirmed the presence of this complex. The Infra-red analysis of **3.6** in hexane solution showed two absortions due to C-O stretching vibrations at 1979 and 1950 cm^{-1}. A comparison of these C-O vibration energies with those observed in other $Mo(CO)_3$ complexes with trisulphur donor ligands is provided on Table 3.2.

Table 3.2. *Infra-red C-O stretching frequencies of complex 3.6 and other tridentate sulphur donor molybdenum (0) tricarbonyl complexes.*

Complex				
				3.6
$\upsilon_{C\equiv O}(cm^{-1})$	**1899, 1784**	**1930, 1820**	**1936, 1827**	**1979,1950**
Medium	**THF**	**CH_2Cl_2**	**CH_2Cl_2**	**Hexane**
Ref.	**21,22**	**23**	**23**	**This work**

In order to do a better comparison of the donor strength of the tripodal sulphur donor molybdenum tricarbonyl complexes on Table 3.2., it only considered the energy of the *A* symmetry (higher energy) C-O vibration mode, where there is a simultaneous C-O stretching of the three carbonyl ligands. In these complexes, the energy of the C-O vibration is directly related to the electron density on the metal, and thus the donor properties of the various sulphur donor ligands. Higher electron density will result in greater electron density in the C-O π^* orbitals and thus lower the C-O stretching energy.

Observing Table 3.2, the complex **3.6** gives the highest energy compared to the other complexes, which indicates that the ligand **3.6** is a weaker donor than the other ligands considered. However, this comparison does not take into account the sulphur hybridization in the different ligands. The sulphur in the thioimidazolyl ligands is sp^2 hybridized and thus can potentially act as a π-acceptor system, while the other ligands have sp^3 hybridized sulphur atoms which have the potential to act as π-donors.

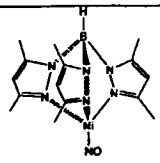
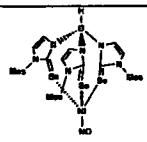
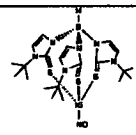
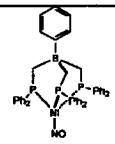
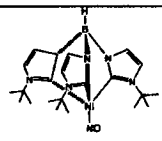
It was established by Reglinski and Spicer that the donor properties of anionic Tm ligand system are affected when the methimazolyl moieties are replaced, or when a group is inserted on the bridgehead boron atom.[24] Complex **3.6** is a good example of this effect where the benzimidazole replaces Tm methimazole rings. This increases the electron density on the ligand and makes it a better donor when compared to a similar system as complex [{$(HNMe_2)B(mt)_3$}$Mo(CO)_3$] ($\nu_{C\text{-}O}$ = 1987 cm^{-1}) presented on Chapter II.

In this case the electronic and steric properties of these boron-centred tripodal ligands can change if the thioimidazoles are replaced by other heterocycles with sulphur donors, since these two properties are related.[24]

3.5. BORON-CENTRED TRIPODAL LIGANDS WITH OTHER DONOR ATOMS

The electronic effects of the ligand on the metal centre are easy to observe when the donor atoms of the heterocycles are changed. Strongly donating ligand systems were reported using heterocycles bearing phosphorus, carbon and selenium atoms which were used as alternatives to the sulphur donor atoms of methimazole. The strong electron donating character of some tripodal ligands with $[P_3]$, $[S_3]$, $[Se_3]$ and $[C_3]$ donor sets can be compared by the N-O stretching frequency in the IR spectra of Ni(0) [LNiNO] complexes, which are displayed in Table 3.3. A decrease in the N-O stretching frequency indicates increased NO π-backbonding from the nickel due to a stronger electron donation from the tripodal ligand to the metal.

Table 3.3. *N-O stretching frequencies for [LNiNO] complexes with boron-centred tripodal ligands with different donor atoms.*

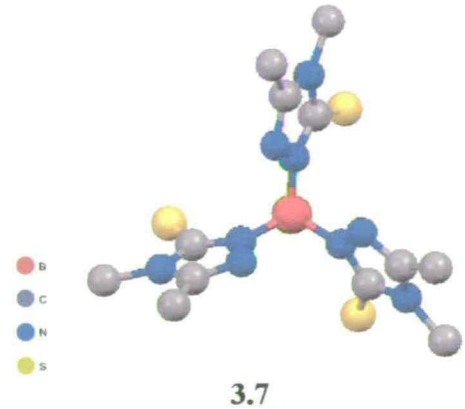
COMPLEX		$\gamma_{(NO)}$/ CM^{-1}	REF.
	{[Tp*]NiNO}	1786	25
	{[TmSe^{Mes}]NiNO}	1763, 1752*	25
	{[Tm^{tBu}]NiNO}	1741	26
	{[PhB(CH$_2$PPh$_2$)$_3$]NiNO}	1737	27
	{[HBIm^{tBu}]NiNO}	1703	28

* Two frequencies observed

Observing N-O stretching energies of the complexes on Table.3.3, it is possible measure the donor ability of these ligands in terms of different donor atoms as $[C_3]>[P_3]>[S_3]>[Se_3]$.[28]

The versatility of this boron centred tripodal ligand system allows the introduction of heterocycles that can hold two types of donor atoms. Bailey previously reported the synthesis of an ambidentate N_3/S_3 tripodal ligand, the

hydridotris(thiooxotriazolyl)borate (Fig.3.8), from the melt reaction of sodium borohydride with 5-thioxo-4,5-dihydro-3,4-dimethyl-1,2,4-triazole.



3.7

Fig.3.8. *Structure of hydridotris(trioxotriazolyl)borate or Tt ligand reported by Bailey.*[3]

This system was explored to give rise to the Janus scorpionates which are systems with simultaneous and controlled soft κ^3-*S,S,S* and hard κ^3-*N,N,N* coordination to a metal. This type of complex has been used in materials chemistry due to their interesting electrochemical properties.[29]

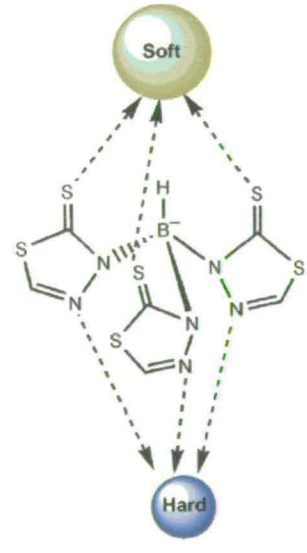
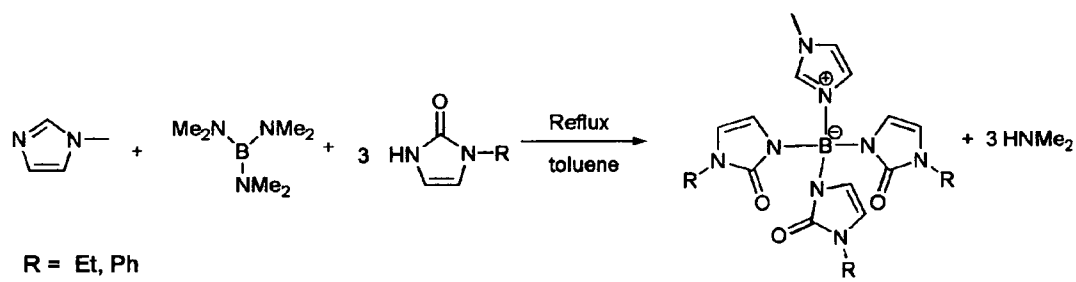


Fig.3.9. *Representation of the binding behaviour of Janus scorpionate ligand.*[29]

The Janus scorpionates profit from the hard nitrogen and the soft sulphur donor atoms to coordinate to a wide range of metals according to Pearson's Hard-Soft Acid-Base concept. [30]

Generally, the derivatives of the Tm ligand are synthesized from melt reactions between sodium borohydride and a heterocycle similar to methimazole, as presented on Scheme 3.1. However, it is also possible to obtain these derivatives from the reaction of a heterocycle bearing a N-H acidic proton and tris(dimethylamino)borane. During their investigation of the synthesis of new ligands Bailey and Perucha observed that imazole derivatives with different donors successfully reacted with $B(NMe_2)_3$ in a "one-pot" reaction. [13, 31] Perucha used imidazolinones to obtain a Tm derivative with oxygen donors (Scheme 3.4). [31]



Scheme 3.4. *Reaction of 1-R-imidazolin-2-one (R = Ph, Et) with tris(dimethylamino)borane and N-methylimidazole to afford new ligand with oxygen donors.* [31]

The 1-R-imidazolin-2-one (R = Ph, Et) is an analogue of methimazole with oxygen donors. According to Perucha, this compound did not react with sodium borohydride in a melt reaction but its reaction with $B(NMe_2)_3$ is successful. [31] Unfortunately, the coordination of these ligands to a metal was not successful due to

instability of the ligand [(N-methylimidazole)B(1-ethyl-imidazolyl-2-one)] or due to the low solubility in the solvent system used.[31]

In order to continue the investigation of the synthesis of these types of ligands with different donors from tris(dimethylamino)borane, some work has been done using imidazoles bearing selenium atoms. In the next section of this thesis the synthetic work done with selenium analogues of methimazole towards the synthesis of a boron-centred tripodal ligand with selenium donor atoms will be presented

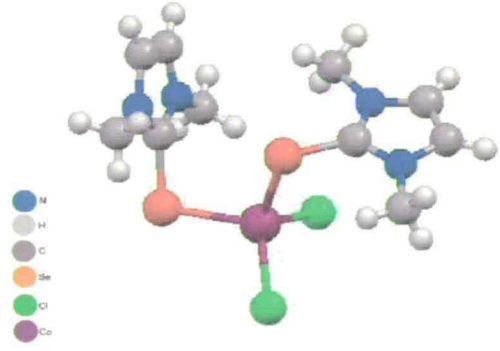
3.6. SYNTHESIS OF BORON FUNCTIONALIZED LIGANDS WITH SELENIUM DONORS

The derivatizations of the Tp and Tm ligand systems by changing the donor atoms have drawn the attention of many research groups. Since boron-centred tripod ligands can accommodate a diversity of donor atoms (carbon, nitrogen, phosphorus, oxygen and sulphur) it is very attractive to investigate new possible donors. Selenium is another chalcogen element with properties similar to sulphur and can be a good donor for this ligand system.

Despite existing in many oxidation states (2^-, 2^+, 0, 4^+, 6^+), Se(II) is commonly used in organic chemistry due to its biological activity and catalytic applications of organoselenium compounds, as diselenides and selenides.[32-34] Since selenium atoms are larger than sulphur, these compounds present a longer Se-C bond (1.98 Å) than the C-S bond (1.81 Å) in organosulphur compounds. In comparison with sulphur, selenium is less electronegative and thus a stronger donor.[32]

To synthesize an analogue of the Tm ligand with Se donors in place of S it is necessary to obtain a selenium analogue of methimazole. The main characteristic that makes the methimazole a good heterocycle for this ligand system is that it exists mainly in its thione form. However, in general selones are more stable than selenols, as the latter easily dimerize under oxidative conditions.[35] The use of a heterocycle with a selone functional group is therefore essential for a successful synthesis of new boron centred tripodal ligands.

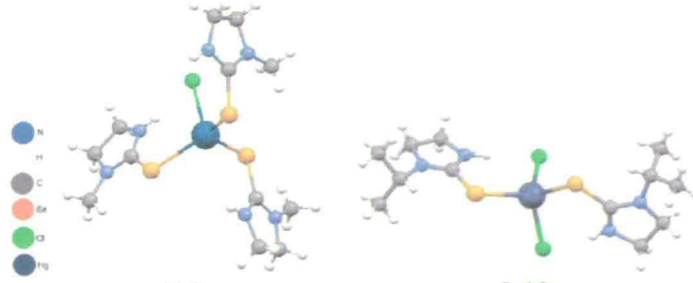
Metal complexes with selone ligands have been synthesized previously by Williams and Wazeer (Fig.3.9 and Fig.3.10).[36-41] Williams and co-workers reported the first complex with two 1,3-dimethylimidazole-2-selone ligands coordinated to cobalt(II) (Fig.3.9).[41]



3.8

Fig.3.9. *Structure of dichlorobis[1,3-dimethylimidazole-2(3H)selone-Se]cobalt(II) reported by Williams and co-workers.*[41]

Other complexes of Au(II), Ag(II) and Hg(II) with imidazolidine-2-selone and imidazole-2-selone as ligands can also be found in the published work by Ahmad and Wazeer.[36-38, 40]



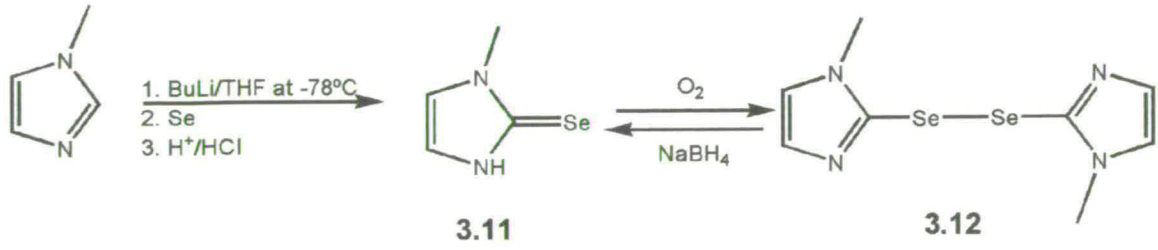
3.9 **3.10**

Fig.3.10. *Structures of {chloro-tris[N-methyl-2(3H)-imidazolidine-2-selone]mercury(II)}chloride* ***3.9*** [38] *and dichloro-bis(N-isopropyl-imidazolidine-2-selone)mercury(II)* ***3.10***.[39]

3.6.1. Selenium analogue of methimazole: synthesis and ligands

The first synthesis of the selenium analogue of methimazole, 1-methyl-imidazole-2-selone, was presented and characterized by Guziec in 1994 in order to study its activity to inhibit the thyroid hormone synthesis. As for methimazole, this seleno-imidazole also can exist in two tautomeric forms, selenol and selone, one more stable than the other.[42] According to Guziek, the synthesized selenium version of methimazole was very similar to the sulphur analogue, thus the product obtained was likely to be a selone. To continue this investigation on anti-thyroid inhibitors, Mugesh and co-workers improved Guziek's synthesis and proved that the previously reported selone was in fact a di-selenide species produced by oxidation. The formation of this dimer was an indication that the product synthesized was in the selenol rather than in the selone tautomeric form as this oxidative dimerization is very common amongst selenols.[35] Mugesh also reported that this dimerization can be

reversible by reacting the di-selenide with sodium borohydride to afford the respective selone (Scheme 3.5).[43, 44]

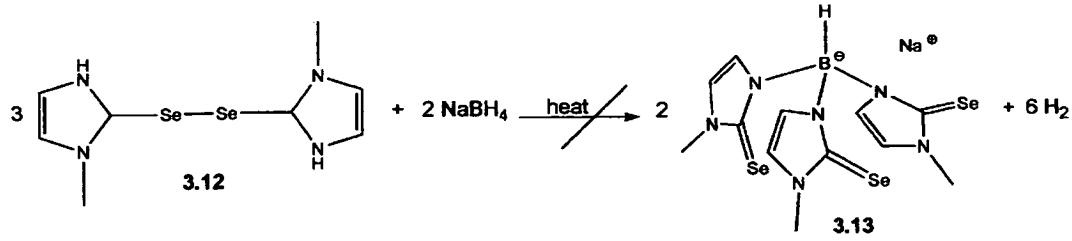


3.11 **3.12**

Scheme 3.5. *Synthesis of 1-methyl-imidazole-2-selene* ***3.11*** *and its dimer* ***3.12***.[42-44]

From Mugesh's and Guziek's presented work it was not clear which tautomeric form of the selenium analogue of methimazole was more stable. Nevertheless, some work on the synthesis of this selenium analogue of methimazole was developed for this thesis and syntheses of some ligands were attempted.

For this work, the selenium analogue of methimazole was synthesized from 1-methylimidazole following the methodology represented in Scheme 3.5. However, only the di-selenide form of 1-methyl-imidazole-2-selone could be isolated due to aerial oxidation. The fact that borohydride could be used to reduce this dimer back to the selone, and could also be used to synthesise the anionic Tm ligand led to the investigation of a different approach in order to synthesise the target boron-centred tripodal ligand with selenium donors. It was investigated whether the target ligand could be obtained from the melting reaction of the diselenide with an excess of $NaBH_4$ (Scheme 3.6).



Scheme 3.6. *Attempted synthesis of hydrotris(1-methylimidazolyl-2-selone)borane 3.11 from the dimeric form of 1-methylimidazole-2-selone 3.12.*

This approach was unsuccessful since analysis of the solid product obtained did not reveal any traces of the desired ligand.

While this work was being developed, a study on the stability of this selenium analogue of methimazole was reported by Parkin and collaborators, which helped to clarify the incongruous conclusions of Mugesh and Guziek on the stability of the selone and selenol tautomers.[45]

3.6.2. Selenol/selone tautomerism

The structural study by Parkin and co-workers was focused on two systems of molecules, 1-R-2-hydroselenoimidazole/1-R-imidazole-2-selone, (R as methyl or mesityl groups; Fig.3.11).

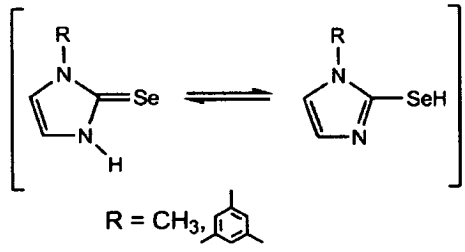


Fig.3.11. *Selone/selenol tautomersism of (1-R-2-hydroselenoimidazole/1-R-imidazole-2-selone) studied by Parkin and co-workers.*[45]

Parkin chose to synthesize a selenoimidazole substituted in the 1-position by a mesityl group due to its easy preparation, and to apply it to the synthesis of a selenium donor ligand analogue of Tm^{Mes}. The insertion of a bulky mesityl group provides greater stability against rapid oxidation of this selenium compound. Parkin's study was based on characterization by NMR and X-ray analysis of both mono and dimeric forms of the two systems 1-methyl-2-hydroselenoimidazole/1-methyl-imidazole-2-selone and 1-mesityl-2-hydroselenoimidazole/1-mesityl-imidazole-2-selone.

The X-ray diffraction analysis of the selenium analogue of methimazole (R = Me) indicated the presence of a hydrogen atom attached to nitrogen, showing that the selone tautomer was crystallized. As for methimazole, the structure of these crystals is constituted by pairs of hydrogen bonded dimers (Fig.3.12).[46,47]

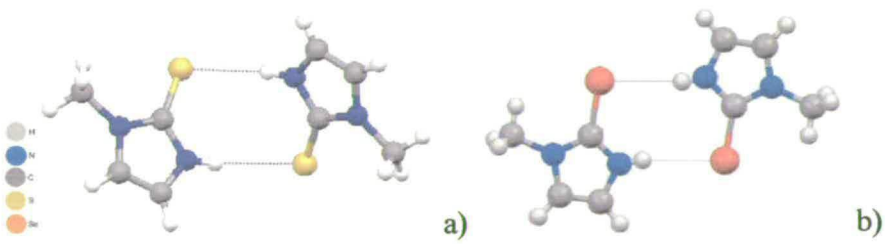


Fig.3.12. *Methimazole (a) and its selenium analogue (b).* [47, 48]

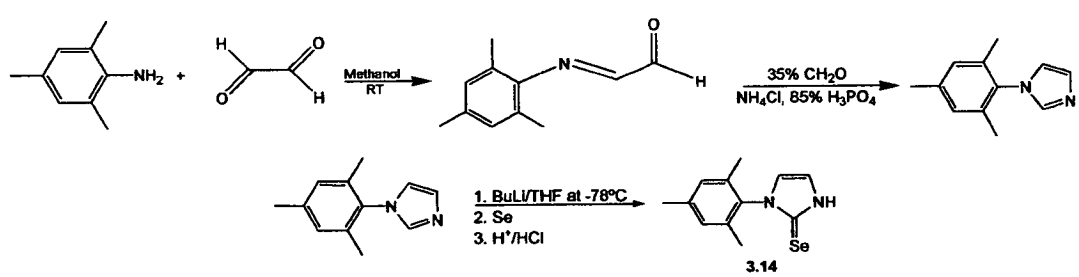
The interaction of the selenium atoms with the hydrogen were also found in the structure of the 1-mesityl-imidazole-2-selone.

A short time after Parkin's research group published this structural study, Mugesh reported the crystal structure of 1-methyl-imidazole-2-selone and also concluded that the selone was the stable tautomer.[49]

3.6.3. Attempted ligand synthesis with 1-mesitylimidazole-2-selone

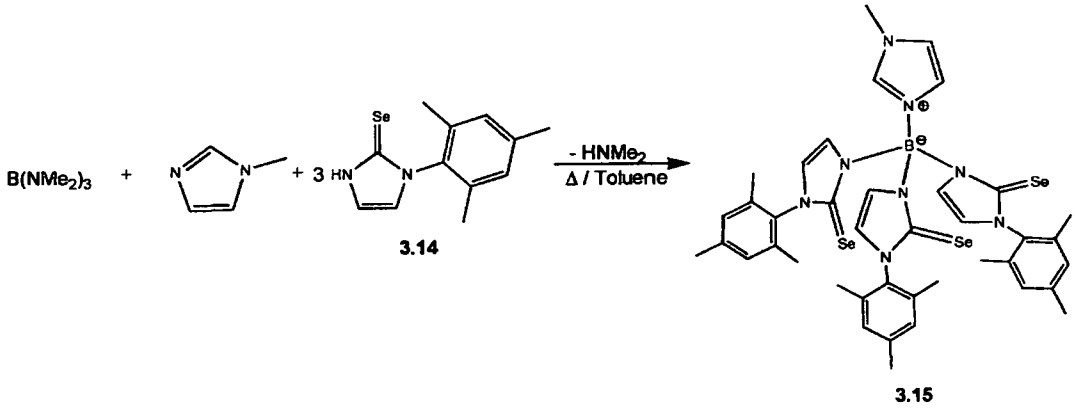
Since the 1-mesityl-imidazole-2-selone was more stable towards oxidation than its methyl analogue, it was attempted to synthesize a boron-centred tripodal ligand functionalized in the 4th position by N-methylimidazole. This ligand was targeted since previous work was developed with [(N-methylimidazole)B(mt)$_3$] and a good comparison of the donor properties of the novel ligand could be readily observed.

As 1-mesitylimidazole is not a commercial product, it was synthesized as reported by Zhao and collaborators.[50] The synthetic route followed is represented in Scheme 3.7.



Scheme 3.7. *Synthesis of 1-mesitylimidazole-2-selone 3.14*.[50, 45]

The target ligand was obtained from a one pot-reaction between tris(dimethylamino)borane, 1-mesitylimidazole-2-selone and *N*-methylimidazole in a 1:3:1 ratio (Scheme 3.8).



Scheme 3.8. Synthesis of [(N-methylimidazole)B(1-mesitylimidazolyl-2-selone)$_3$].

The ligand formed, [(N-methylimidazole)B(1-mesitylimidazolyl-2-selone)$_3$] (**3.15**), was analysed by ^{1}H NMR and by positive ion (FAB$^+$) mass spectrometry. The mass spectrum of this ligand is shown in Fig.3.13.

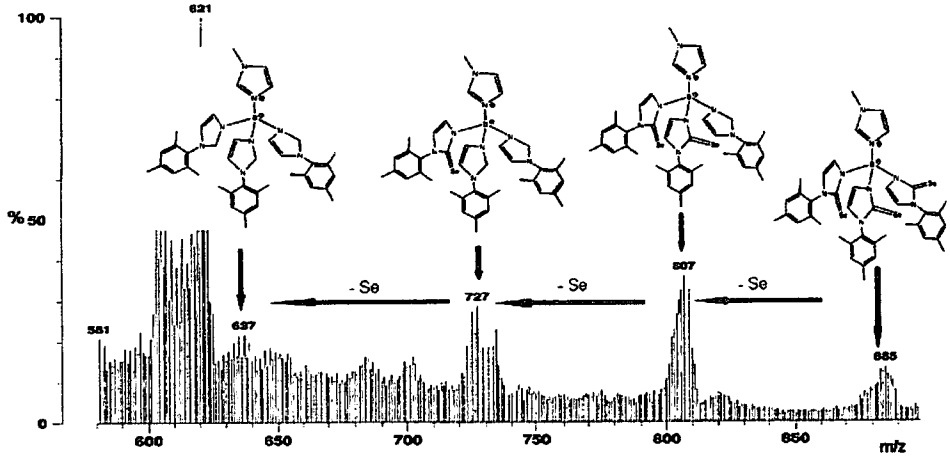
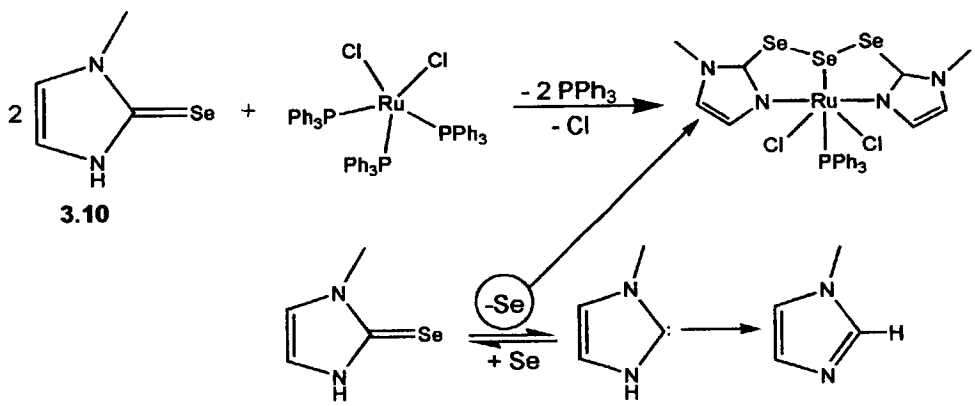


Fig.3.13. *Fab$^+$ of [(N-methylimidazole)B(1-mesitilimidazole-2-selone)$_3$] with evidence of loss of selenium atoms.*

The FAB^+ spectrum showed the decomposition of the ligand via loss of the selenium atoms with formation of a species that could be the respective carbene species. A similar decomposition via loss of selenium on 1-methylimidazole-2-selone was also speculated by Hill and co-workers to explain the insertion of a third Se atom in the structure of a new diorganotriselenane ruthenium complex (Scheme.3.9).[51]



Scheme 3.9. *Synthesis of [Ru{(κ^3- Se,N,N'-Se(mt^{Se})$_2$}$Cl_2(PPh_3)$]reported by Hill, showing a possible decomposition of the1-methylimidazole-2-selone via carbene formation.*[51]

For this work, the synthesis of these boron-centred tripodal ligands with selenium derivatives of methimazole started before the Parkin's research group reported the Tm^{Se} ligand and its stability studies.[45, 52] Then, the importance of this project for this thesis was then limited due to lack of novelty. Therefore, it was decided to not continue further investigation on these ligands, despite its interesting potential.

3.7. CONCLUSION

Since the introduction of the Tm ligand, its derivatization has been studied extensively. This system is versatile and can easily be tuned electronically and sterically. In this chapter, two different thioimidazole analogues of methimazole substituted at the 4- and 5-positions (1-methyl-benzimidazole-2-thione and 1,4,5-trimethyl-imidazole-2-thione) have been prepared in order to synthesize two new boron-centred tripodal ligands with sulphur donors: $[(HNMe_2)B(1,4,5\text{-trimethylimidazolyl-2-thione})_3]$ **(3.4)** and $[(HNMe_2)B(1\text{-methyl-benzimidazolyl-2-thione})_3]$ **(3.4)**. It is expected that these ligands present a protective environment around the boron bridgehead created by the methimazole substituents. Further investigation of the ligand $[(L^*)B(1,4,5\text{-trimethylimidazolyl-2-thione})_3]$ (L^* - chiral N-donor) will be presented in the next chapter.

The ligand $[(HNMe_2)B(1\text{-methyl-benzimidazolyl-2-thione})_3]$ was coordinated to molybdenum tricarbonyl to afford the respective metal complex. The C-O stretching vibrations of this complex allowed the study of the donor properties of the ligand by comparison with other molybdenum tricarbonyl complexes. It was then observed that this ligand is a better donor than the ligand $[(HNMe_2)B(mt)_3]$ presented in Chapter II, due to the electronic enrichment around the ligand promoted by the benzimidazole rings.

In this chapter the work towards the synthesis of a boron-centred tripodal ligand system bearing selenium donor atoms was also presented. Work was done on the synthesis of selenium analogues of methimazole, but was abandoned due to its wide interest from other research groups despite its potential use for carbene chemistry.

REFERENCES

1. M. Garner, J. Reglinski, I. Cassidy, M. D. Spicer and A. R. Kennedy, *Chem. Commun.*, 1996, **16**, 1975.
2. S. Trofimenko, *Chem. Rev.*, 1993, **93**, 943.
3. P. J. Bailey, M. Lanfranchi, L. Marchio and S. Parsons, *Inorg. Chem.*, 2001, **40**, 5030.
4. P. J. Bailey, A. Dawson, C. McCormack, S. A. Moggach, D. H. Oswald, S. Parsons, D. W. H. Rankin and A. Turner, *Inorg. Chem.*, 2005, **44**, 8884.
5. M. R. Foreman, A. F. Hill, A. P. White and D. J. Williams, *Organometallics*, 2003, **22**, 3831.
6. M. I. Mohamed, S. Mouhai and V. Heinrich, *Eur. J. Inorg. Chem.*, 2005, **2005**, 1388.
7. C. Kimblin, B. M. Bridgewater, D. G. Churchill and G. Parkin, *Chem. Commun.*, 1999, 2301.
8. M. Tesmer, M. Shu and H. Vahrenkamp, *Inorg. Chem.*, 2001, **40**, 4022.
9. S. Bakbak, V. K. Bhatia, C. D. Incarvito, A. L. Rheingold and D. Rabinovich, *Polyhedron*, 2001, **20**, 3343.
10. J. Seebacher, M. Shu and H. Vahrenkamp, *Chem. Commun.*, 2001, 1026.
11. M. M. Ibrahim, M. Shu and H. Vahrenkamp, *Eur. J. Inorg. Chem.*, 2005, **2005**, 1388.
12. P. J. Bailey, C. McCormack, S. Parsons, F. Rudolphi, A. S. Perucha and P. Wood, *Dalton Trans.*, 2007, 476.

13. P. J. Bailey, D. Lorono-Gonzales, C. McCormack, F. Millican, S. Parsons, R. Pfeifer, P. Pinho, F. Rudolphi and A. S. Perucha, *Chem. Eur. J.*, 2006, **12**, 5293.

14. J. F. Ojo, P. A. Slavin, J. Reglinski, M. Garner, M. D. Spicer, A. R. Kennedy and S. J. Teat, *Inorg. Chim. Acta*, 2001, **313**, 15.

15. A. V. El'tsov and K. M. Krivozheiko, *Zh. Obshch. Khim.*, 1966, **2**, 189.

16. D. Harrison and J. T. Ralph, *J. Chem. Soc.*, 1965, 3132.

17. T. R. Lee and K. Kim, *J. Heterocycl. Chem.*, 1989, **26**, 747.

18. D. R. Doerge and N. M. Cooray, *Synth. Commun.*, 1991, **21**, 1789.

19. J. Kister, G. Assef, G. Mille and J. Metzger, *Can. J. Chem.*, 1979, **57**, 822.

20. J. Kister, G. Assef, G. Mille and J. Metzger, *Can. J. Chem.*, 1979, **57**, 813.

21. P. Ge, B. S. Haggerty, A. L. Rheingold and C. G. Riordan, *J. Am. Chem. Soc.*, 1994, **116**, 8406.

22. A. L. Sargent, E. P. Titus, C. G. Riordan, A. L. Rheingold and P. Ge, *Inorg. Chem.*, 1996, **35**, 7095.

23. O. P. Siclovan and R. J. Angelici, *Inorg. Chem.*, 1998, **37**, 432.

24. M. Schwalbe, P. C. Andrikopoulos, D. R. Armstrong, J. Reglinski and M. D. Spicer, *Eur. J. Inorg. Chem.*, 2007, 1351.

25. V. K. Landry, K. Pang, S. M. Quan and G. Parkin, *Dalton Trans.*, 2007, 820.

26. L. S. Maffett, K. L. Gunter, K. A. Kreisel, G. P. A. Yap and D. Rabinovich, *Polyhedron*, 2007, **26**, 4758.

27. C. E. MacBeth, J. C. Thomas, T. A. Betley and J. C. Peters, *Inorg. Chem.*, 2004, **43**, 4645.

28. J. M. Smith, *Comments Inorg. Chem.*, 2008, **29**, 189.

29. J. R. Gardinier, R. M. Silva, C. Gwengo and S. V. Lindeman, *Chem. Commun.*, 2007, 1524.

30. R. G. Pearson, *J. Am. Chem. Soc.*, 1963, **85**, 3533.

31. A. S. Perucha, PhD Thesis, *University of Edinburgh*, 2007.

32. N. N. Greenwood and A. Earnshaw, *Chemistry of the Elements*, 2nd edn., Oxford, 1997.

33. P. C. Taylor and J. F. S. L. Apps, *Annu. Rep. Prog. Chem., Sect. B: Org. Chem.*, 2008, **104**, 49.

34. W. Thomas, *Angew. Chem. Int. Ed.*, 2000, **39**, 3740.

35. C. Santi, S. Santoro, L. Testaferri and M. Tiecco, *Synlett*, 2008, 1471.

36. S. Ahmad, A. A. Isab, A. R. Al-Arfaj and A. P. Arnold, *Polyhedron*, 2002, **21**, 2099.

37. S. Ahmad, A. A. Isab and A. P. Arnold, *J. Coord. Chem.*, 2003, **56**, 539.

38. A.-H. D. Al-Amri, M. Fettouhi, M. I. M. Wazeer and A. A. Isab, *Inorg. Chem. Commun.*, 2005, **8**, 1109.

39. A. A. Isab, M. I. M. Wazeer, M. Fettouhi, S. Ahmad and W. Ashraf, *Polyhedron*, 2006, **25**, 2629.

40. M. I. M. Wazeer and A. A. Isab, *Spectrochim. Acta, Part A*, 2005, **62**, 880.

41. D. J. Williams, T. A. Jones, E. D. Rice, K. J. Davis, J. A. Ritchie, W. T. Pennington and G. L. Schimek, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1997, **53**, 837.

42. L. J. Guziec and F. S. Guziec, Jr., *J. Org. Chem.*, 1994, **59**, 4691.

43. G. Roy and G. Mugesh, *J. Am. Chem. Soc.*, 2005, **127**, 15207.

44. G. Roy, M. Nethaji and G. Mugesh, *J. Am. Chem. Soc.*, 2004, **126**, 2712.

45. V. K. Landry, M. Minoura, K. Pang, D. Buccella, B. V. Kelly and G. Parkin, *J. Am. Chem. Soc.*, 2006, **128**, 12490.

46. H. T. Flakus, A. Miros and P. G. Jones, *Spectrochim. Acta, Part A*, 2002, **58**, 225.

47. C. Laurence, M.J. El Ghomari, J.-Y. Le Questel, M. Berthelot and R. Mokhlisse, *J. Chem. Soc., Perkin Trans. 2*, 1998, 1545.

48. V. Gabriella, B. Stefania, S. Fabio, M. Luca and A. Luciano, *J. Heterocycl. Chem.*, 1995, **32**, 227.

49. G. Roy, D. Das and G. Mugesh, *Inorg. Chim. Acta*, 2007, **360**, 303.

50. J. Liu, J. Chen, J. Zhao and Y. Zhao, *Synthesis*, 2003, **17**, 2661.

51. R. D. Dewhurst, A. R. Hansen, A. F. Hill and M. K. Smith, *Organometallics*, 2006, **25**, 5843.

52. M. Minoura, V. K. Landry, J. G. Melnick, K. Pang, L. Marchio and G. Parkin, *Chem. Commun.*, 2006, 3990.

CHAPTER IV

CHIRAL SUBSTITUTED BORON-CENTRED TRIPODAL LIGANDS

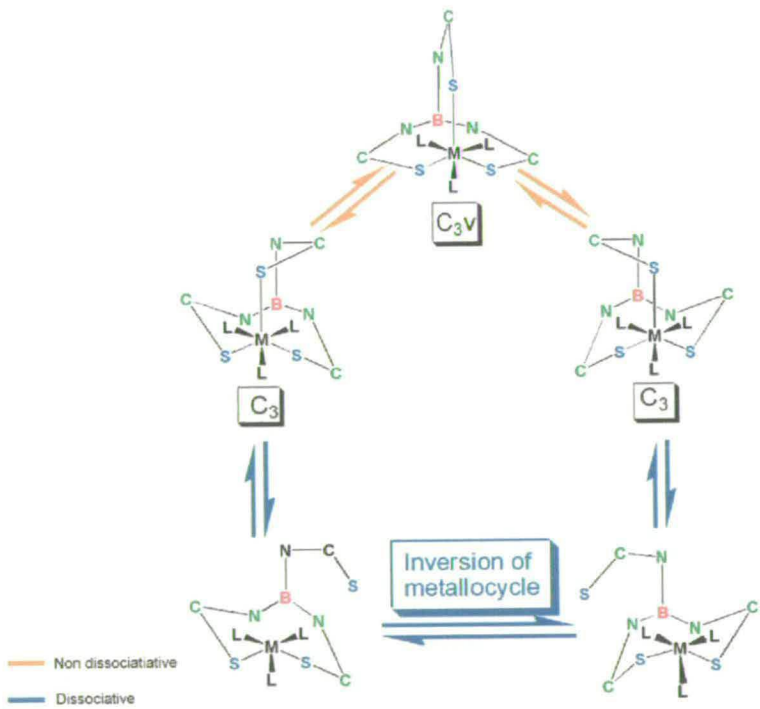
4.1. INTRODUCTION

The approach towards the synthesis of new boron-centred tripodal ligands with a chiral group on the boron bridgehead will be presented in this chapter. The work introduced in the previous chapters contributed to an understanding of the synthetic method adopted and the derivatization of this tripodal ligand system. The synthesis of a boron-centred tripodal ligand functionalized in the 4th position by a chiral, neutral N-donor such as (*S*)-(-)-α-methylbenzylamine will be presented and discussed. The different attempts undertaken to coordinate N-donors to the boron bridgehead will also be presented in this chapter. In order to introduce the work presented, an overview of the chirality of these ligands and their chiral complexes is provided, as well as the previous methodologies employed to obtain chiral Tm ligand derivatives. Finally, potential catalytic activity in asymmetric transfer hydrogenation using these chiral ligands will be discussed in the end of this chapter as future work.

4.2. CHIRALITY OF TM^R LIGAND METAL COMPLEXES

Metal complexes of the hydrotris(methimazolyl)borate (TM) ligand with κ^3-*S,S,S* coordination mode are C_3-symmetric and present a three-dimensional bicyclo[3,3,3]cage. This structure presents a type of atropisomerism by helical rotation about the B-M axis due to the angle strain within this cage. The interconversion between the two rotational enantiomers, *λλλ* and *δδδ*, can result from an associative or a dissociative process (Scheme 4.1).[1,2]

The dissociative racemization process involves a low energy inversion of an eight-membered metallocycle formed after the de-coordination of one of the tripodal ligand arms from the metal centre (Scheme 4.1). After the inversion of the metallocycle, the tripodal arm re-coordinates to the metal centre to form the enantiomeric structure. This mechanism depends essentially on the dissociative energy between the metal and the donor atom which is related to the lability of the metal centre and can be influenced by the trans effect of other ligands bound to the metal.[2]



Scheme 4.1. *Processes of interconvertion of the rotational enatiomers on Tm ligand metal complexes.*[1, 2]

In the non-dissociative mechanism the enantiomers are interconverted by a conformational twist of the cage via a highly strained C_{3v}-symmetric transition state. The energy of the process is determined by the angle strain of the metal-ligand cage in this transition-state structure.[2]

4.2.1. Racemization of Tm ligand metal complexes

Bailey and co-workers reported some studies on the energy of racemization of a range of metal complexes containing Tm ligand analogues with diastereotopic protons, Tm^{Et} **4.1** and Tm^{Bz} **4.2** (Fig. 4.1), in four-coordinate complexes: $[Tm^{Et}ZnCl]$, $[Tm^{Bz}ZnCl]$, $[Tm^{Et}CdCl]$, $[Tm^{Et}HgCl]$, $[Tm^{Et}CuPPh_3]$, $[Tm^{Et}AgPPh_3]$; and in six-coordinate complexes: $[Tm^{Et}Ru(p\text{-cymene}]Cl$, $[Tm^{Et}Ru(p\text{-cymene}]PF_6$ and $[Tm^{Et}Mn(CO)_3]$.

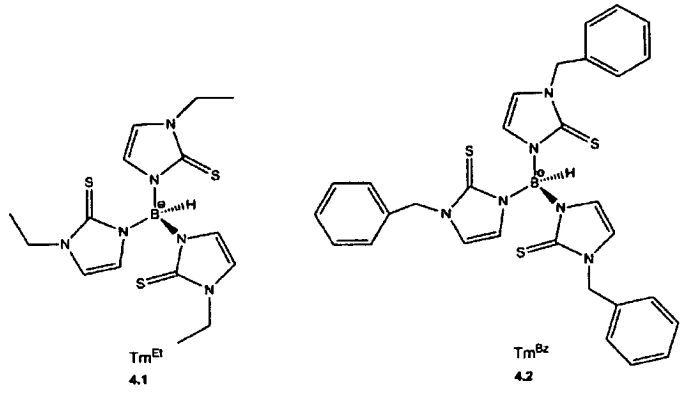


Fig.4.1. *Ligands used in the study of the barriers of C_3 symmetric of complexes reported by Bailey and co-workers.*[1]

In these studies, the activation energy of the racemization process was calculated from the coalescence temperature measured by variable temperature NMR experiments for the complexes in donor solvents, such as dimethylsulphoxide and acetonitrile, and in a non-donor solvents (tetrachloroethane and chloroform).[1] Fig.4.2 displays the variable temperature ^1H NMR spectra of $[ZnTm^{Et}Cl]$ in deuterated

acetonitrile. The coalescence temperature is identified by the fast-exchange limit in which the methylene groups are no longer observed as diastereotopic.

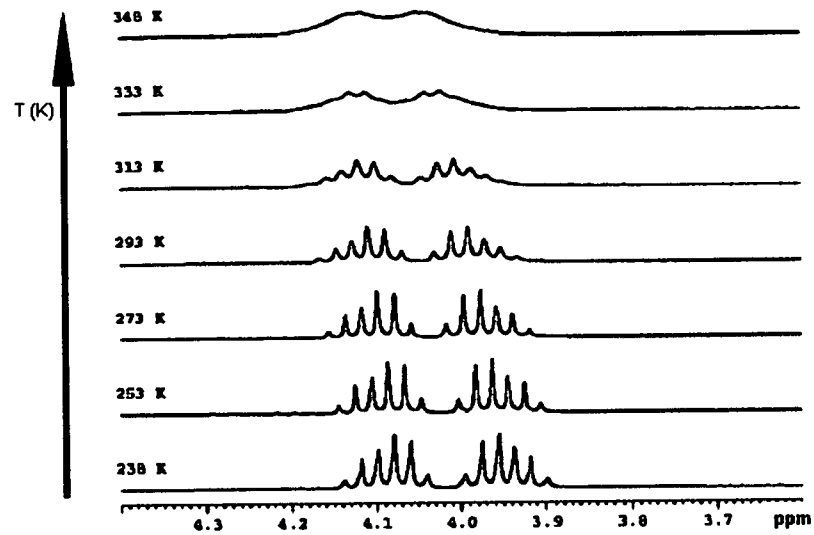


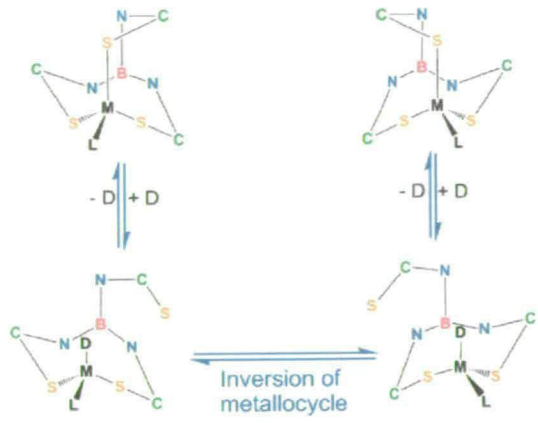
Fig.4.2. *VT NMR spectrum of the diastereotopic methylene proton signals of [ZnTm^{Et}Cl] in acetonitrile reported by Bailey and co-workers.*[1]

The activation energy of the racemisation process $\Delta G^{\ddagger}$ was determinated by Equation 4.1, using the coalescence temperature (*Tc*) and the frequency of separation of the NMR signals in the slow exange limit (Δv).[1]

$$\Delta G^{\ddagger} = RTc\,[22.96 + \ln(Tc / \Delta v)] \qquad \textbf{Equation 4.1}$$

The reported study revealed that the barrier of racemization for the four-coordinate complexes falls between 55 and 77 kJ.mol^{-1} and was reduced by donor solvents. These low energies can be related to the substituition lability at d^{10} metal ions. In the light of these observations, Bailey concluded that these complexes followed a dissociative mechanism for the racemization process. Scheme 4.2 shows

the dissociative mechanism of racemization assisted by a donor solvent of a four coordinate complex.



Scheme 4.2. *Dissociative mechanism of racemization assisted by a donor solvent in a four coordinate complex.*[1]

This energetic barrier could not be determined experimentally for the six-coordinate complexes, as the energy of the process was found to be higher than the limit of the method used (VT NMR line shape analysis). Consequently, the mechanism of racemization in these complexes remains uncertain. However, the high energy of the process in these complexes (>100 $kJ.mol^{-1}$), and the lack of any solvent effects, indicate that a non-dissociative mechanism is followed as would be anticipated for these low-spin d^6 metal ions.[1]

To complement this study, the energy between the C_3-symmetric (ground-state) and the C_{3v}-symmetric (transition state) conformations for the non-dissociative mechanism in both $[HB(C_3H_3N_2S)_3ZnCl]$ and $[HB(C_3H_3N_2S)_3Mn(CO)_3]$ were also calculated *ab initio* by Bailey's research collaborators. The energy profile of this racemization mechanism, for the formation of two enantiomers is represented schematically in Fig.4.3. These DFT calculations estimated that this energy

difference was 121 kJmol^{-1} for the four-coordinate Zn(II) complex and 163 kJmol^{-1} for the six-coordinate Mn(I) tricarbonyl complex.[1]

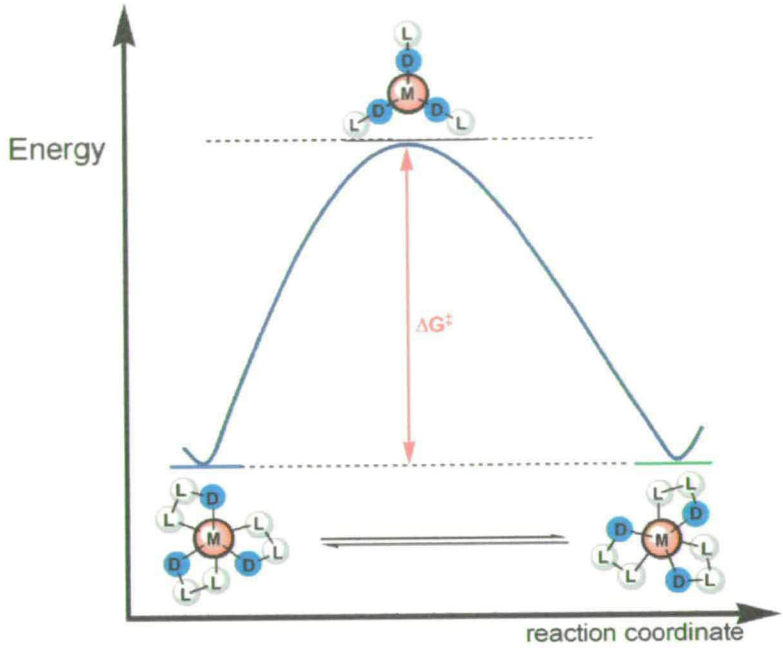


Fig.4.3. *Schematic energy profile of a non-dissociative mechanism of racemization for the formation of the enantiomers in C_3-symmetric complexes containing a bicyclo[3,3,3]cage.*

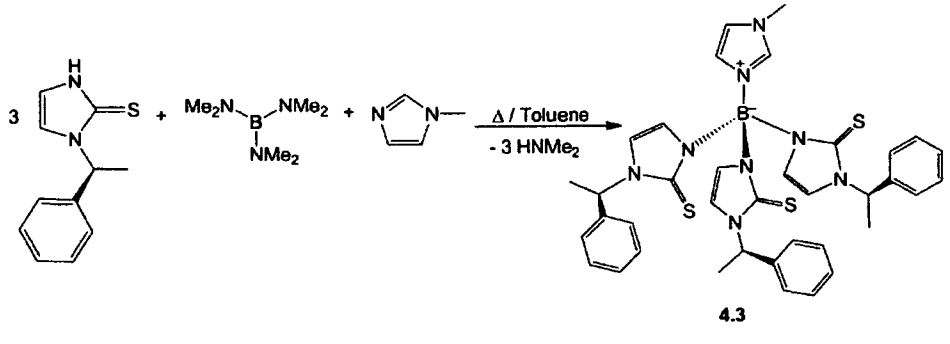
The racemization energy for the octahedral complexes studied by Bailey's group has been shown to be higher than 100 kJ.mol^{-1}. This indicates that the separation of the racemate is possible, however hitherto not accomplished. The understanding of the racemization mechanism in these different complexes is an important tool for the synthesis and isolation of single enantiomeric complexes, which is an objective of this thesis.

4.3. INTRODUCING CHIRALITY INTO THE TM LIGAND FRAMEWORK

The introduction of chirality into the Tm ligand framework may enable the synthesis of a chiral ligand which, upon coordination, can generate a single diasteroisomeric complex. Chirality may be introduced into the structure of boron-centred tripodal ligands at two different positions; it can be achieved by using chiral derivatives of methimazoles or by introducing a chiral group on the boron central tripodal atom. For this work only the latter approach was attempted. The synthetic methodologies employed previously by Bailey and Perucha to obtain a chiral ligand containing chiral groups on the methimazole N-atoms will first be discussed.

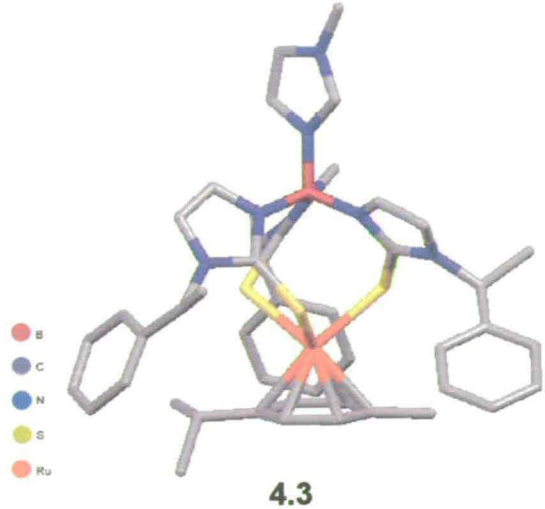
4.3.1. Ligands with chiral methimazoles

Bailey and Perucha reported the synthesis of a ligand containing enantiomerically pure α-methylbenzyl groups in place of N-methyl groups of the methimazole parent.[3, 4] The synthetic route used to produce this ligand is shown in Scheme 4.3.



Scheme 4.3. *Synthesis of [(N-methylimidazole)B(1-(S)α-methylbenzylimidazole-2-thione)$_3$] via a one-pot reaction.*[3]

This ligand was reacted with $[Ru(p\text{-cymene})Cl_2]_2$ and NH_4PF_6 to afford the respective Ru(II) arene complex with hexafluorophosphate counterions, [{(*N*-methylimidazole)B(1-(S)α-methylbenzylimidazole-2-thione)$_3$}Ru(*p*-cymene)][PF_6]$_2$ (**4.3**). The structure of this complex is shown in Fig.4.4.



4.3

Fig.4.4. *Structure of the λλλ diastereoisomer of[{(N-methylimidazole)B(1-(S)α-methylbenzylimidazole-2-thione)$_3$}Ru(p-cymene)][PF_6]$_2$ (**4.3**) reported by Bailey.*[3, 4]

The ^{1}H NMR analysis of complex **4.3** showed only one pair of doublets for the diastereotopic protons of the *p*-cymene ^{i}Pr methyl groups which indicates the presence of only one diastereotopic species. The crystal structure of this complex showed the presence of a single molecule per unit cell instead of an enantiomeric pair found in other achiral systems such as [{(N-methylimidazole)B(mt)$_3$}Ru(*p*-cymene)][PF_6]$_2$, confirming the presence of a single diastereoisomer. This complex presents a (*λλλ-S)* configuration in a pseudo C_3 symmetric environment. The (*δδδ-S)* diastereisomer of this complex is not observed in the crystal. The conformations, *λλλ* and *δδδ*, have different energies and thus one is formed in preference during the synthesis of the complex. In this case the S-configuration of the α-methylbenzyl

groups favours the λλλ form of the metal-ligand cage structure. The energetic profile for the formation of these two diastereisomers therefore resembles Fig.4.5.

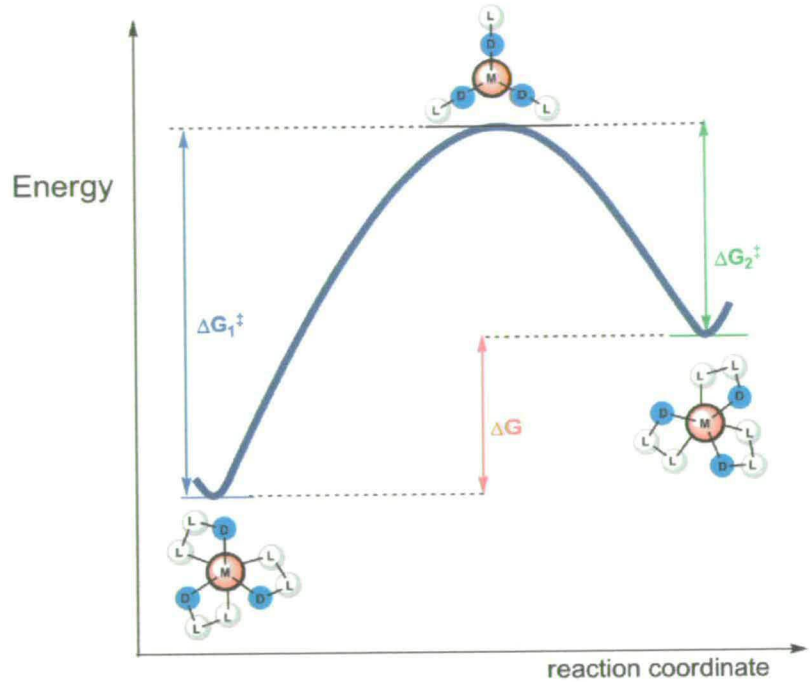


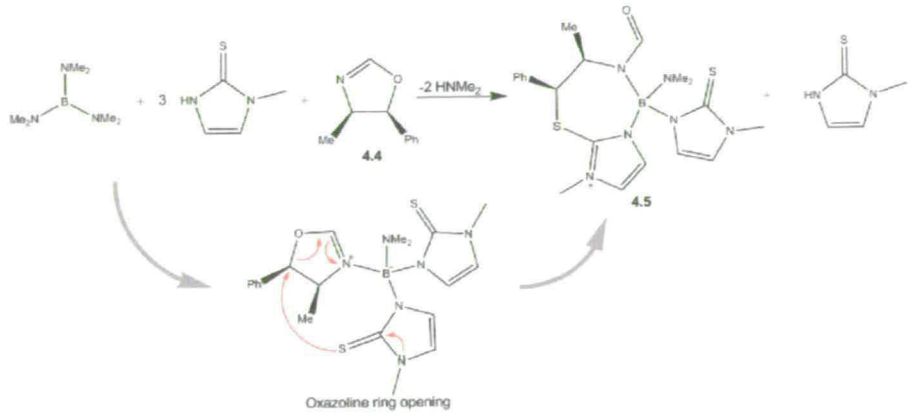
Fig.4.5. *Schematic representation of the energetic profile for the formation of two energetically different diastereisomers through a non-dissociative mechanism of racemization.*

This demonstrates that it is possible to synthesise two diasterisomers with substantially different energies by incorporating chirality into the methimazole donors.[3]

It was also observed in this complex that the Ru-S bonds lengths are longer than in Ru(II) complexes of other Tm analogues, indicating the steric protection at the metal binding site induced by the chiral benzylamine groups on the methimazole.[3] This can limit the applicability of these complexes if metal reactivity is required, as in catalytic processes.

4.3.2 Introducing chirality on the boron atom

The insertion of chiral N-donors on the boron bridgehead of the tris(methimazolyl)borate framework is an alternative to the use of chiral methimazole analogues to synthesize single diastereomer complexes containing only the λλλ or δδδ metal-ligand cage. This approach was also used by Bailey and Perucha in order to obtain chiral ligands. Following their work on the synthesis of new ligands with tris(dimethylamino)borane, they sought to use chiral oxazolines to functionalize boron's bridgehead on analogues of Tm ligand. Their first attempt at the synthesis of a new chiral ligand was the reaction of (4R,5R)-4-methyl-5-phenyl-2-oxazoline with tris(dimethylamino)borane and methimazole on a 1:1:3 ratio under reflux in toluene (Scheme 4.4.).[4] It was expected to obtain an analogue of [(N-methylimidazole)B(mt)$_3$] with the oxazoline replacing the N-methylimidazole.[3] However, the analysis of the obtained product indicated the presence of a tetra-coordinated borane with two methimazole rings, a dimethylamino and a formamide group (**4.5**). A cyclic structure formed via an intramolecular ring-opening reaction between the oxazoline and one methimazole sulphur atom could be the reason to explain the presence of a formamide group on the boron (Scheme 4.4).[3]



Scheme 4.4. *Reaction of (4R,5R)-4-methyl-5-phenyl-2-oxazoline with $B(NMe_2)_3$ and methimazole and the oxazoline ring-opening reaction products.*[3]

To avoid the intramolecular oxazoline ring opening by the methimazole sulphur during the synthesis of new chiral ligands, Bailey co-workers tried to use other chiral oxazolines without a phenyl group at the 5th position which can make the attached carbon more susceptible to a nucleophilic attack. The range of oxazolines used by Bailey and Perucha in their work is shown in Fig.4.6.[3]

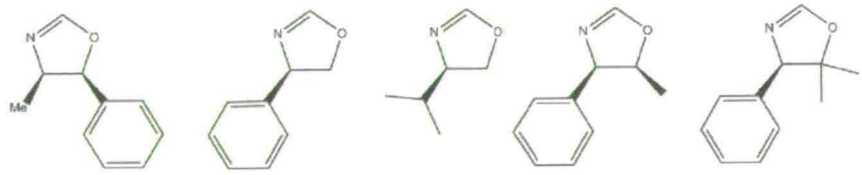
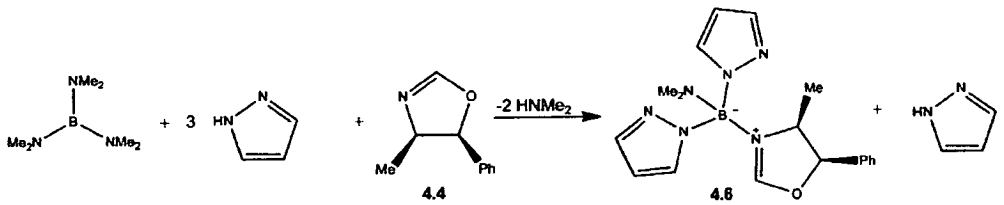


Fig.4.6. *Chiral oxazolines used by Bailey and Perucha in the attempted synthesis of new ligands.*[3]

Despite using other chiral oxazolines to obtain a ligand, the outcome of the reactions was similar to the ring opening product. To investigate the effect of methimazole sulphur on the oxazoline ring opening, they performed a similar ligand synthesis replacing the methimazole by pyrazole rings. The product isolated

presented a tetrahedral borane with two pyrazole rings and an oxazoline attached always retaining the NMe_2 group (Scheme 4.5).[3]

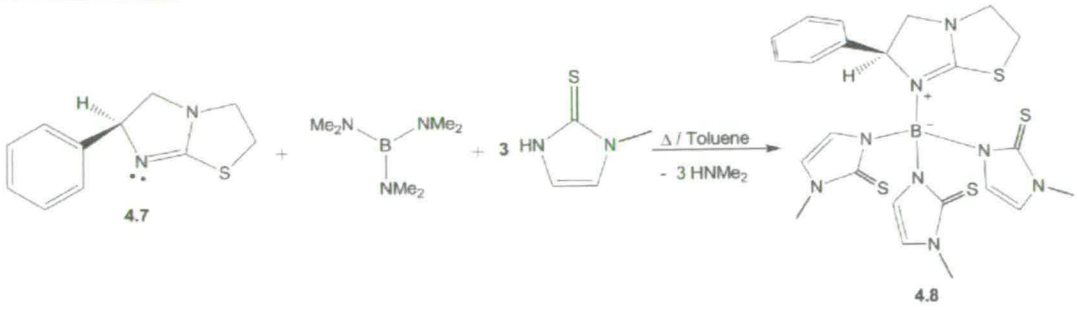


Scheme 4.5. *Reaction of (4R,5R)-4-methyl-5-phenyl-2-oxazoline with $B(NMe_2)_3$ and pyrazole reported by Bailey.*[3]

The retention of the dimethylamino group on the final product of both reactions can be related to the steric hindrance created by the other heterocycles which prevents the transamination reaction with another heterocycle.[3]

If the target chiral ligand was synthesized via substituition of $HNMe_2$ on $[(HNMe_2)B(mt)_3]$ by the chiral oxazoline, by the method described in Chapter II, some of these problems could be avoided. This synthesis was not hitherto accomplished but can be considered as future work on this project.

After the unsuccessful result with the oxazolines, Bailey and Perucha tried to functionalize the boron 4th position in the Tm structure with (-)-tetramisole {(*S*)-(−)-6-phenyl-2,3,5,6-tetrahydroimidazo[2,1-b]thiazole}. This chiral molecule was chosen for the ligand synthesis because of its basic pK_a (8.17 in water)[5] which is in the range of the boron activating bases for the "one-pot"reactions. Then, the ligand [{(-)-tetramisole}B(methimazolyl)$_3$] was synthesized from the reaction of one equivalent of tris(dimethylamino)borane, three equivalents of methimazole and one equivalent of (-)-tetramisole (Scheme 4.6).[4]



Scheme 4.6. *Synthesis of {[(-)-tetramisole]B(methimazolyl)$_3$}.*[4]

The ligand **4.8** was coordinated to [Ru(*p*-cymene)]$^{2+}$ and the obtained chiral complex was characterized by NMR. The ^{1}H NMR of this complex showed the presence of both (*S*, Δ) and (*S*, Λ) diastereoisomers in a 2:1 ratio (Fig.4.7). [4]

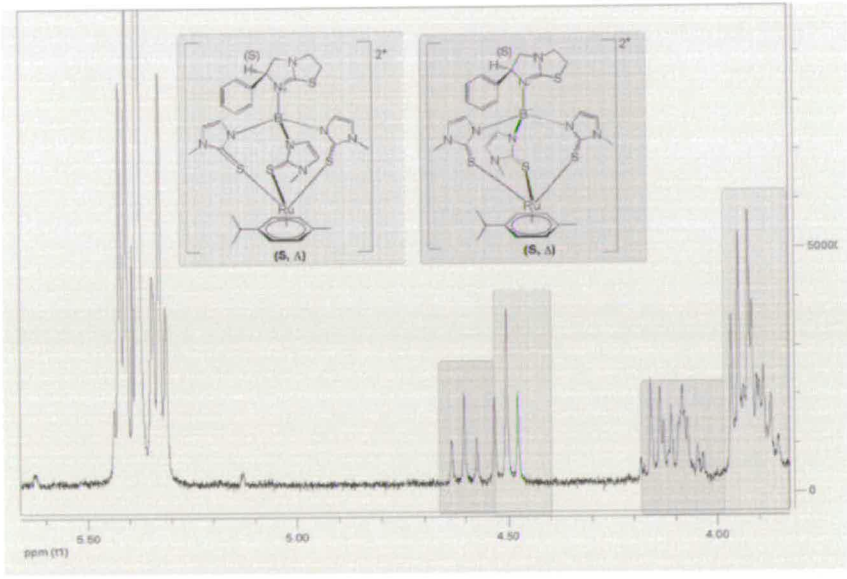
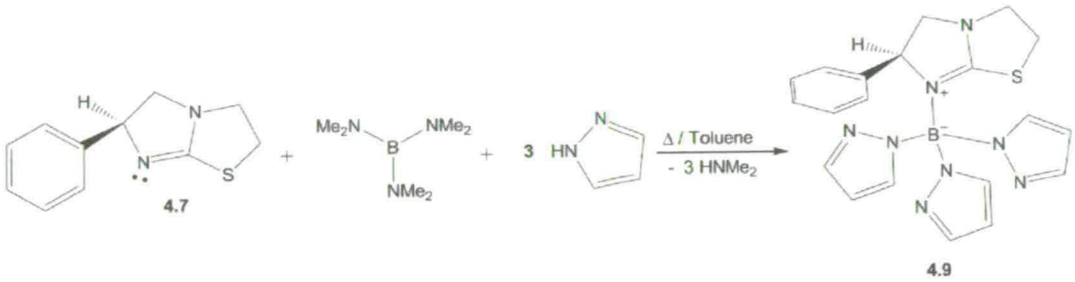


Fig.4.7. *Diasteroisomers (S, Λ) and (S,Δ) of the complex {(-)-(tetramisole)B(methimazolyl)$_3$] Ru(p-cymene)]}$^{2+}$.*[4]

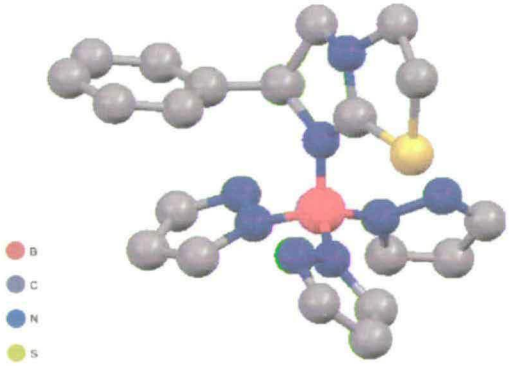
The separation of the diasteoisomers of this complex was not possible despite attempts made by recrystallization and by chromatography.[4] The fact that both diatereoisomers of the complex are formed, albeit in unequal amounts, indicates that the interaction of the chirality of the tetramisole with the bicyclo[3,3,3] cage in this

complex is relatively weak and the energy difference between the two is small. This can be rationalized by the fact that the tetramisole phenyl ring can adopt a position where its interaction with the methimazolyl rings is minimal.

The {[(-)-tetramisole]B(pyrazolyl)$_3$} was also synthesized by Perucha (Scheme 4.7) and its structure was determined by X-ray crystallography (Fig.4.8).[4]



Scheme 4.7. *Synthesis of {[(-)-tetramisole]B(pyrazolyl)$_3$}.*[4]



4.9

Fig.4.8. *Crystal structure of {[(-)-tetramisole]B(pyrazolyl)$_3$}.*[4]

The crystal structure of the ligand **4.9** shows clearly that the tetramisole's phenyl ring is orientated perpendicularly to the C_3-axis of the ligand. It is also assumed that the orientation of this phenyl ring is the same in ligand **4.8** and is maintained in the metal complex which explains the similar energies of the two diastereisomers.

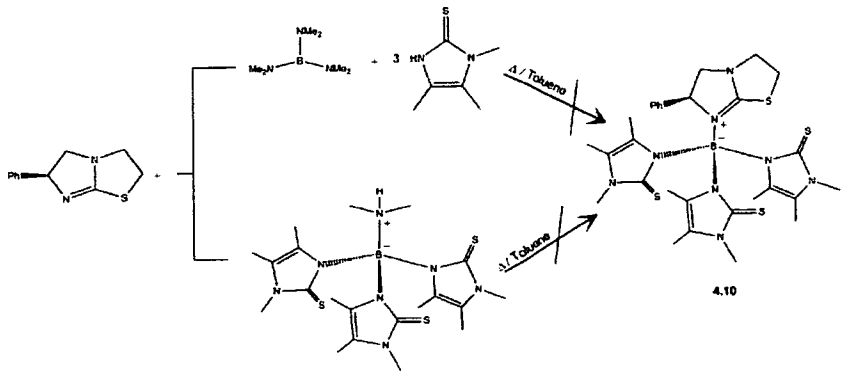
4.4. SYNTHESIS OF BORON-CENTRED TRIPODAL LIGANDS FUNCTIONALIZED WITH CHIRAL MOLECULES

4.4.1. Synthesis of boron centred tripodal ligands functionalized with (-)-tetramisole

In order to continue the work started by Perucha, some attempts at the synthesis of new chiral ligands were made. As observed in the previously synthesized ligands {[(-)-tetramisole]B(methimazolyl)$_3$} and {[(-)-tetramisole]B(pyrazolyl)$_3$}, there is a weak interaction between the phenyl group of tetramisole and the other heterocycles of the ligand. To increase this interaction and to synthesize a new chiral ligand, it was investigated whether the presence of methyl groups on the 4th and 5th position of methimazole would increase the interaction between the tetramisole and the rest of the ligand.

As the chiral heterocycle was only available as (-)-tetramisole hydrochloride it was obtained as the free-base as reported previously by Perucha and used for the ligand synthesis.[4]

The synthesis of a chiral ligand was carried out using 1,4,5-trimethylimidazole-2-thione instead of methimazole or pyrazole. The synthetic approaches to this ligand are displayed in Scheme 4.8.



Scheme 4.8. *Synthetic approaches to a new chiral boron-centred tripodal ligand using tetramisole to functionalize the boron 4th position.*

The two synthetic methodologies adopted were: the "one-pot" reaction using tetramisole, tris(dimethylamino)borane and 1,4,5-trimethylimidazole-2-thione in a 1:1:3 ratio, and the substitution of the dimethylamine in [($HNMe_2$)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] by tetramisole. Both syntheses were set under toluene reflux for 10h or until the evolution of dimethylamine gas ceased. Despite the evolution of $HNMe_2$ and the formation of a white precipitate in the reaction vessel, the product isolated from these reactions was only 1,4,5-trimethylimidazole-2-thione. The ^1H NMR and MS analysis of the recovered solid confirmed the presence of the modified methimazole and some impurities, however no traces of the (-)-tetramisole were found.

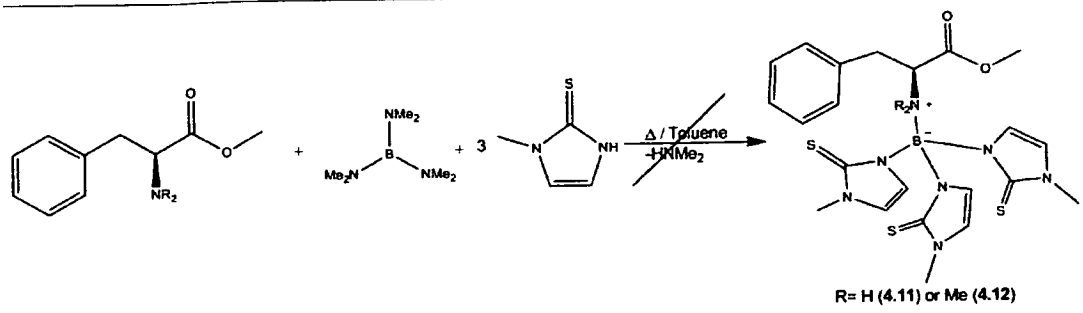
A possible explanation for this is the low reactivity of the $HNMe_2$ moiety due to the protective environment created by the methyl groups on the methimazole. This protected enclosure around the boron 4th position may prevent the coordination of the tetramisole in both syntheses.

4.4.2. Synthesis of boron-centred tripodal ligands functionalized with (-)-phenylalanine derivatives

In pursuance of new chiral molecules to functionalize the borane on the tripodal ligand some work was done with amino acid derivatives.

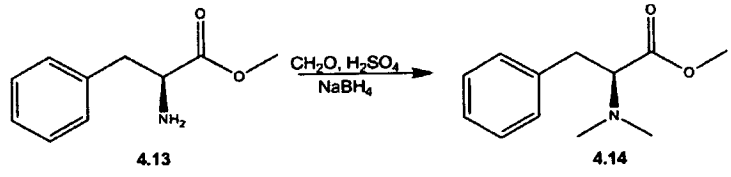
Most α-amino acids are chiral and readily available. The presence of the α-amino group which can coordinate to the boron was an attractive feature to this work. However, the presence of the -COOH group in these compounds could interfere in the ligand synthesis with tris(dimethylamino)borane as the oxygen of the -OH moiety could coordinate to the boron instead of the amine nitrogen. To avoid this problem, it was decided to use α-amino esters and α-phenylalanine methyl ester was chosen for this work. The pK_a of this amino ester is 7.11 (in water)[6] which indicates that it should be able to coordinate to the borane through a "one-pot" reaction.

A ligand synthesis was carried out using α-phenylalanine methyl ester, tris(dimethylamino)borane and methimazole in a 1:1:3 ratio, as shown on Scheme 4.9. The reaction was left under reflux until $HNMe_2$ evolution ceased (18h under reflux) and a white solid was recovered and analysed. The ^1H NMR and MS of the product did not show the presence of the targeted ligand, but proved to be a mixture of products. None of these products could be isolated and identified. At this stage of the investigation, the ligand synthesis with the boron functionalized with primary amines was still in the beginning and since better results were obtained with tertiary amines (which are more basic) it was decided to carry on with the ligand synthesis using a dimethylamine analogue of the α-phenylalanine methyl ester (Scheme 4.9).



Scheme 4.9. *Attempts of tripodal-ligand syntheses with α-phenylalanine methyl ester and with its dimethylamine derivative.*

The dimethylamine derivative of the α-phenylalanine methyl ester was synthesized via a reductive alkylation as reported by Wang and co-workers as shown in Scheme 4.10.[7]



Scheme 4.10. *Synthesis of N,N-dimethyl α-phenylalanine methyl ester.*[7]

The ligand synthesis was attempted using the *N,N*-dimethyl analogue of α-phenylalanine methyl ester (**4.14**) in a "one-pot" reaction as shown in Scheme 4.9. The evolution of dimethylamine was observed during this synthesis; the reaction was heated under reflux for 20 h and a white solid was recovered. The ^{1}H NMR spectrum of this material (Fig.4.9) showed that the product obtained was a mixture and not the target chiral ligand. The presence of a broad signal due to an NH group in the spectrum may be an indication of the presence of $[(HNMe_2)B(mt)_3]$ or unreacted methimazole. The identification of the components of this mixture is difficult due to different methyl protons signals in the spectrum (Fig. 4.9). The MS of this compound does not show the expected molecular ion mass for the desired ligand (M^+: *m/z* =

557). The isolation and characterization of the components of this mixture was not undertaken as other synthetic approaches to insert chirality into the boron were attempted.

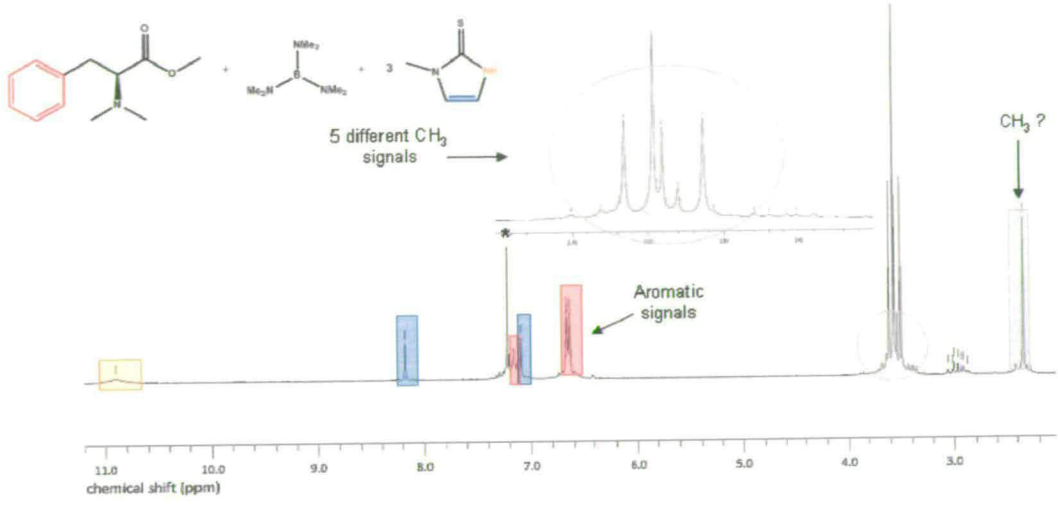
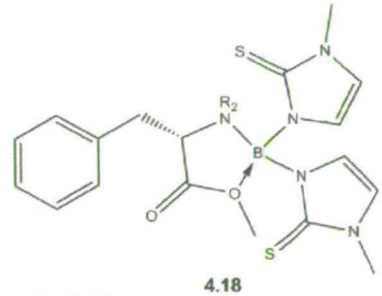


Fig.4.9. *^{1}H NMR of the crude product obtained from the reaction of N,N-dimethyl analogue of α-phenylalanine methyl ester, tris(dimethylamino)borane and methimazole on a 1:1:3 ratio.*

A possible cause for these unsuccessful results can be related to the cyclization of the methyl ester forming a boroxazoline by coordination of one amino ester oxygen atom to the boron (Fig.4.10).



4.18

R= H ; Me

Fig.4.10. *Possible structure of the boroxazoline formed during the ligand synthesis.*

4.4.3. Synthesis of boron-centred tripodal ligands functionalized with α-methylbenzylamine

Benzylamine was one of the N-donors used to substitute the dimethylamine in $[(HNMe_2)B(mt)_3]$ as presented on Chapter II. This base was the first primary amine found to coordinate to the boron atom of tripodal ligand. The easy and readily available chiral analogues of this amine made it an attractive compound to be used in this work. (S)–α-methylbenzylamine was the chiral benzylamine analogue chosen for this work.

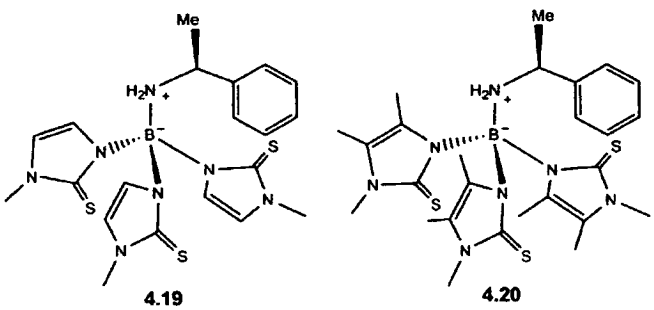
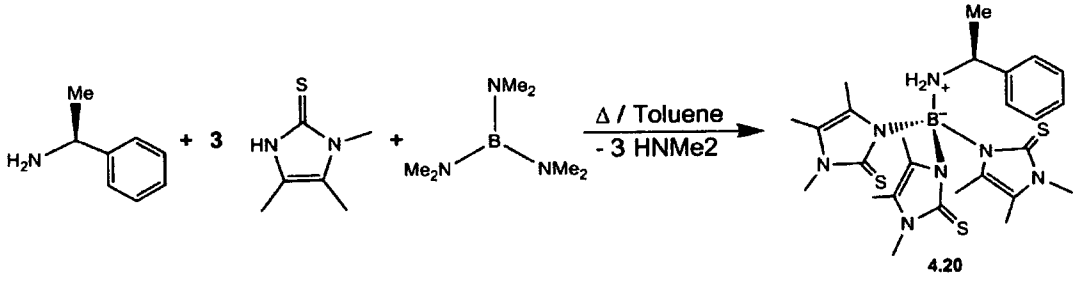


Fig.4.11. *Chiral ligands synthesised for this work.*

The synthesis of two ligands was carried out using the chiral (S)–α-methylbenzylamine to coordinate the boron 4th position. The ligand [{(S)-(-)-α-methylbenzylamine}$B(mt)_3$] **4.19** (Fig.4.11) was obtained via a "one-pot" reaction using methimazole, the chiral amine and tris(dimethylamino)borane in a 1:1:3 ratio in a toluene solution under reflux until the $HNMe_2$ evolution ceased (after 48 h). After removing the toluene under vacuum and washing the remaining precipitate with diethyl ether, a white solid was recovered in 44% yield and analysed. The ^1H NMR in deuterated chloroform of this product showed clearly the presence of the three methimazole rings which appear as a group of three signals: two doublets at

7.04 (three protons) and 6.68 ppm (three protons) for the six CH moieties, and a singlet at 3.42 ppm which corresponds to three methyl groups present in the ligand. In the same spectrum, the (S)–α-methylbenzylamine protons generated four different signals: a broad signal at 10.24 ppm assigned to the NH_2 group, a multiplet from 7.38 to 7.21 ppm corresponding to the phenyl ring, the proton attached to the chiral carbon generated a characteristic quartet at 4.06 ppm, and a doublet at 1.30 ppm which was assigned to the methyl group of the chiral amine. The ^{13}C NMR showed four signals for the three methimazolyl rings which confirm the equivalence of each ring on the ligand. The FAB^+ MS ([M+1] = 472) and the CHN analysis also confirmed the presence of this ligand.

The ligand **4.20** containing the 4,5-dimethylmethimazolyl donors was synthesized from a "one-pot" reaction similar to the one used to obtain **4.19**. However, for this ligand synthesis the methimazole was replaced by its dimethylated derivative, 1,4,5-trimethylimidazole-2-thione, as displayed in Scheme 4.11. This reaction was monitored by observing the evolution of dimethylamine gas using damp pH paper.



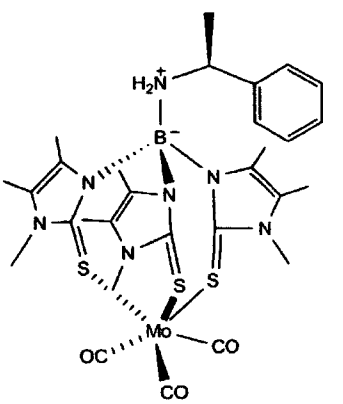
Scheme 4.11. *Synthesis of [((S)-(-)- α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] **4.20**.*

The ligand **4.20** was recovered as a white solid in 31% yield by a similar procedure as employed for the synthesis of **4.19**. The analysis of the product by ^{1}H NMR showed the presence of the three dimethylated methimazole rings as three different singlets at 3.50, 3.47 and 2.02 ppm corresponding to nine protons each. The presence of (S)-α-methylbenzylamine was also confirmed by the presence of similar signals as observed for the ligand **4.19**. A comparison of both ligands signals shows a downfield shift of the chiral benzylamine signals for **4.20**. From the spectrum it is possible to observe five different signals for the chiral benzylamine: a broad signal at 11.54 ppm which corresponds to the NH_2 protons, a multiplet between 7.32 and 7.27 ppm which is assigned to the aromatic protons, the proton and the methyl group attached to the chiral carbon which generate respectively a quartet at 4.11 ppm and a doublet at 1.38 ppm. The ^{13}C NMR showed five signals for the carbons in the dimethyl methimazolyl moiety indicating an equivalency between all the three heterocycles in the ligand **4.20**. The successful formation of this ligand indicates that the methyl groups of 1,4,5-trimethylimidazole-2-thione do not fully block the coordination of donors to the boron. The presence of this ligand was also confirmed by FAB^{+} MS ([M+1] = 556) and the CHN analysis also confirmed the presence of this ligand.

4.5. CHIRAL LIGAND TO METAL COORDINATION

In order to study its donor properties, the ligand **4.20** was coordinated to molybdenum tricarbonyl. The [{(S)-(-)-α-methylbenzylamine)B(1,4,5-

trimethylimidazolyl-2-thione)$_3$}Mo(CO)$_3$] **4.21** was synthesized by reacting the ligand **4.20** with [Mo(MeCN)$_3$(CO)$_3$] prepared from Mo(CO)$_6$ *in situ* in acetonitrile at room temperature for 24 h. This reaction was followed by infra red spectroscopy until completion. The analysis by positive FAB mass spectrometry revealed the molecular ion peak M^+ = 737.3 which confirms the presence of the complex **4.21** (Fig. 4.13).

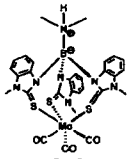
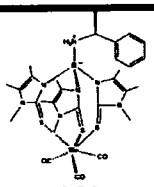


4.21

Fig.4.13. *[{(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$}Mo(CO)$_3$] **4.21**.*

The complex **4.21** was analyzed by infra-red spectroscopy and the observed C-O stretching frequencies were compared with the other two molybdenum complexes synthesized in this work. The C-O vibrations of the three complexes are displayed in Table 4.1.

Table 4.1 *Infra-red C-O stretching frequencies of the molybdenum complexes synthesized for this work.*

Complex	 **3.6**	 **2.28**	 **4.21**
$\upsilon_{C\equiv O}$ (cm^{-1})	1979,1950	1987, 1957	1952, 1957
Medium	Hexane	Hexane	Hexane

From Table 4.1, it is clear that the complex **4.21** presents the lower C-O stretching energy which indicates a higher electron donation from the ligand to the metal. This indicates that the ligand **4.20** is a better donor than the other two ligands synthesized for this thesis. The donor properties of the ligand **4.20** are affected by the presence of the α-methylbenzylamine on the boron bridgehead and the methyl groups on the methimazole 4th and 5th positions. In comparison to the other complexes, **4.21** presents a primary amine coordinated to the boron instead of a secondary amine as on the other two complexes which may affect the charge on the boron atom.

The complex **4.21** was also analysed by ^{1}H and ^{13}C NMR spectroscopy, however some impurities were identified during this analysis maybe caused by decomposition (Fig.4.14 and Fig.4.15). The proton NMR spectrum showed the presence of two sets of signals in 1:7 ratio approximately (Fig.4.14).

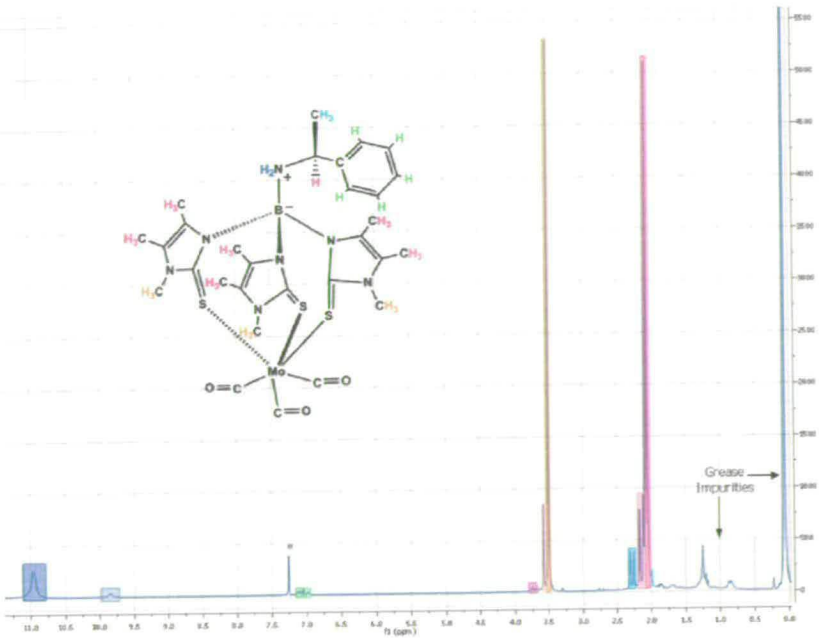


Fig.4.14. *^{1}H NMR of [{(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$}Mo(CO)$_3$] (**4.21**) showing the two sets of signals in a 1:7 ratio.*

This observation was confirmed by the carbon NMR spectrum which clearly showed the two sets of signals (Fig. 4.15).

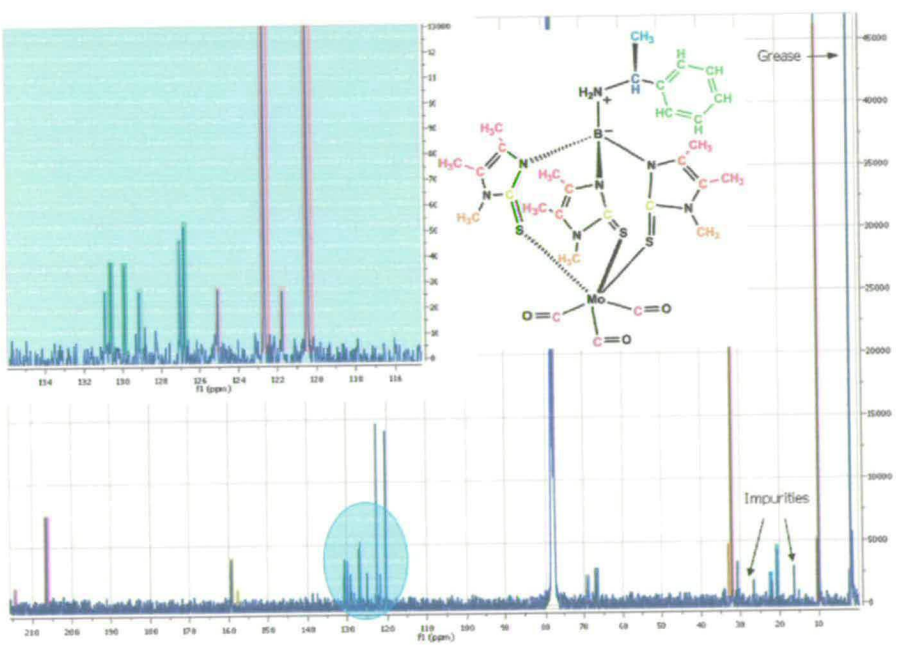


Fig. 4.15. *^{13}C NMR of [{(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$}Mo(CO)$_3$]**4.21** showing the two sets of signals.*

The presence of these two sets of signals indicates the presence of two diastereoisomers due to the complex bicyclo[3,3,3] cage twist. The 1:7 ratio of the two diastereoisomers synthesized shows that a small interaction between the chiral methylbenzylamine and the methyl groups in methimazole 4th and 5th position which allows the twisting of the cage structure. This is a promising result to achieve the single diastereisomer synthesis of this system. The synthesis of a ligand analogue of [{(*S*)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] using 1-methylbenzimidazole-2-thione instead of methimazole can be considered as a future work for this project since the presence of the aromatic rings on the methimazole can interact more with the chiral group on the boron and therefore increase the energy difference between complex diastereoisomers.

4.6. CONCLUSION

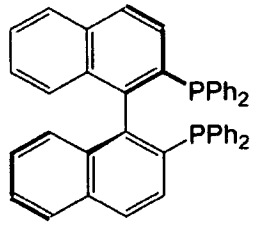
In this chapter, the work towards the synthesis of new boron-centred chiral tripodal ligands in order to obtain a single diastereoisomer of the respective metal complex was presented. For this purpose, it was attempted to improve the chiral ligand {[(-)-tetramisole]B(methimazolyl)$_3$} by replacing the methimazole by its dimethylated analogue, 1,4,5-trimethylimidazole-2-thione. Despite the two synthetic methodologies tried for the ligand synthesis, it was not possible to obtain the target ligand, possibly due to steric constraints between the methyl groups on the methimazole and the phenyl ring of the (-)-tetramisole. Thereafter, it was tried to functionalize the boron 4th position with the chiral phenylalanine ester and its dimethylamine derivative. This approach was not as successful and the aminoester may have undergone cyclization to form the respective boroxazoline. Finally, the synthesis of a chiral ligand was achieved by using (*S*)-(-)-α-methylbenzylamine to coordinate to the boron bridgehead of the tripodal ligand. The chiral ligand, [(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] was successfully synthesized and its coordination to molybdenum tricarbonyl showed to afford two diastereoisomeric complexes in a 1:7 ratio. The formation of two diastereoisomers was surprising since it was expected a greater interaction between the chiral methylbenzylamine coordinated to the boron central atom and the methyl groups on the 4th and 5th position of the methimazole. However, this is a very promising result and indicates that this system can still be improved in order to obtain a single diasteroisomeric complex with ruthenium or rhodium which can be tested as catalyst for asymmetric transfer hydrogenation.

4.7. CATALYTIC APPLICATIONS OF THIS CHIRAL SYSTEM

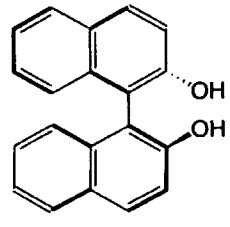
The synthesis of a single diastereisomer of a complex with a chiral boron-centred tripodal ligand was the aim of this work. Although, the synthesis of a single diasterisomer of a complex was not hitherto accomplished, it is important to relate this chiral system with its applicability.

The idea behind this project is to explore the atropisomerism and the C_3-symmetry present in the tris(methymazolyl)borate complexes and to apply it as an effective catalyst for asymmetric transfer hydrogenation.

Several chiral systems displaying atropisomerism have applications in asymmetric catalysis. This type of chirality is present in binaphthyl derivatives, such as BINAP and BINOL ligands (Fig.4.16 and Fig.4.17), commonly used in catalysis, where two enantiomers are formed by restricted rotation around the C-C bond between the two naphthyl rings.[8, 9] The success of these ligand systems in enantioselective catalysis is usually related to two fold symmetry and their type of chirality, which inducts symmetric transformations .[10]



(*R*)-BINAP
2,2'-bis(diphenylphosphino)-1,1'-binaphthyl



(*S*)-BINOL
1,1'-binaphthyl-2-ol

Fig.4.16. *Structures of BINAP and BINOL.*[8, 9]

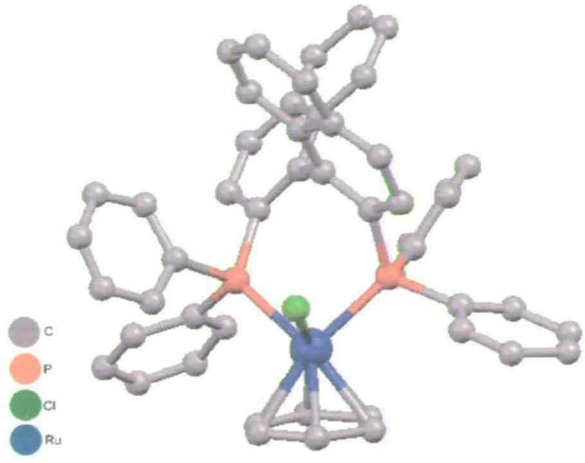


Fig.4.17. *Structure of (η^6-Benzene)-chloro-(2',2'-bis(diphenylphosphino)-1,1'-binaphthyl-P,P')-ruthenium(II) reported by Noyori.*[11]

The two-fold symmetry is a common feature amongst the most successful catalysts used in asymmetric transfer hydrogenations. There are many advantages of the use of C_2-symmetry in catalysis, such as the possibility to reduce the formation of possible isomeric metal complexes and to minimize the number of different catalyst/substrate arrangements. This leads to a reduction of reaction pathways and intermediates which facilitates analysis of the ligand/substrate interaction, which may be crucial in the enantioselective process, and the kinetic studies of the catalytic reaction.[12] The successful chiral recognition in C_2-symmetric bidentate ligand systems is due to the formation of two identical situations upon rotation of 180°. This is an advantage relative to C_1-symmetric systems which can only form two different diastereoisomers. Besides this disparity, other ligands with different topologies and symmetry have also been employed for asymmetric catalysis.

The increase of symmetry of a catalyst employed on asymmetric transformations can reduce the number of intermediate states in catalyzed reactions, as chirality is only compatible with proper rotational axis. This fact contributed for

the exploitation of complexes bearing C_3-symmetric ligands in asymmetric catalysis instead of the usual twofold symmetric ligands, as BINAP, used in chiral transformations.[13] The homotopic sites present in a complex with a twofold bidentate ligand, or in a complex with a threefold symmetric tridentate ligand, depends on the geometry of the complexes. The favourable geometry of the complexes with C_2- and C_3-symmetric ligands is represented in Fig. 4.18.

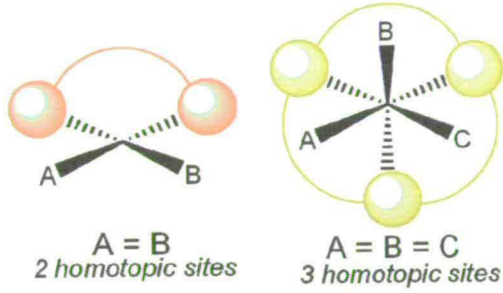
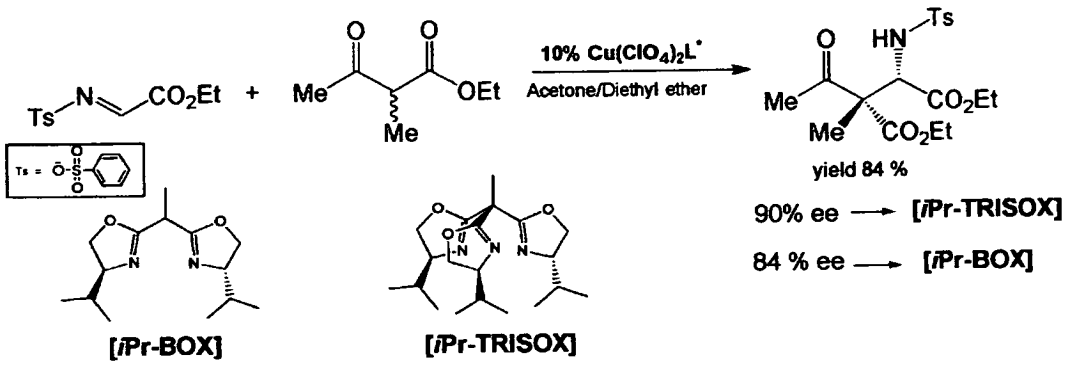


Fig. 4.18. *Homotopic sites present on a tetrahedral complex with a bidentate ligand and of an octahedral complex with a tridentate ligand.*

An increase of the number of homotopic sites of the catalyst reduces the number of intermediate rotamers formed during the reaction and can maximize the probability of success of the chiral recognition during the catalytic process.[13] Although, it is important to establish that this is not a "universal rule" and experimentally the mechanism of a certain reaction can change when the symmetry of the ligand in the catalyst is different.[13]

An example of the effect of increasing the ligand symmetry in a certain catalyzed reaction was verified by Gade and co-workers while comparing the activity of copper (II) complexes with a threefold and a twofold oxazoline ligand system. Gade's studies were focused on an enantioselective Mannich reaction catalyzed by [(*i*Pr-TRIZOX)Cu]$(ClO_4)_2$ and by [(*i*Pr-BOX)Cu]$(ClO_4)_2$ (Scheme 4.12).[14]



Scheme 4.12. *Enantioselective Mannich reaction of ethyl 2-methylacetoacetate with N-tosyl-α-imino methyl ester catalyzed of by [(iPr-TRISOX)Cu](ClO$_4$)$_2$ and by [(iPr-BOX)Cu](ClO$_4$)$_2$].*[14]

For this system, Gade and collaborators observed that with 10% of catalyst the yield obtained was the same, however the enantioselectivity of the catalyst increased when the tripodal oxazoline ligand was employed (Scheme 4.12).[14]

In spite of the success of the TRISOX ligand and other C_3-symmetric tripodal ligands in catalysis,[13] their potency to promote asymmetric transfer hydrogenation has not yet been assessed.

The combination of atropisomerism and three-fold symmetry in the Tm ligand backbone makes it a good candidate as asymmetric transfer hydrogenation catalyst. It is expected that complexes of ruthenium with chiral pseudo-C_3-symmetric ligands can catalyse enantioselective ketone hydrogenations following an inner-sphere mechanism with the formation of a metal hydride as reported in reactions catalysed by $Ru(PPh)_3Cl_2$.[15]

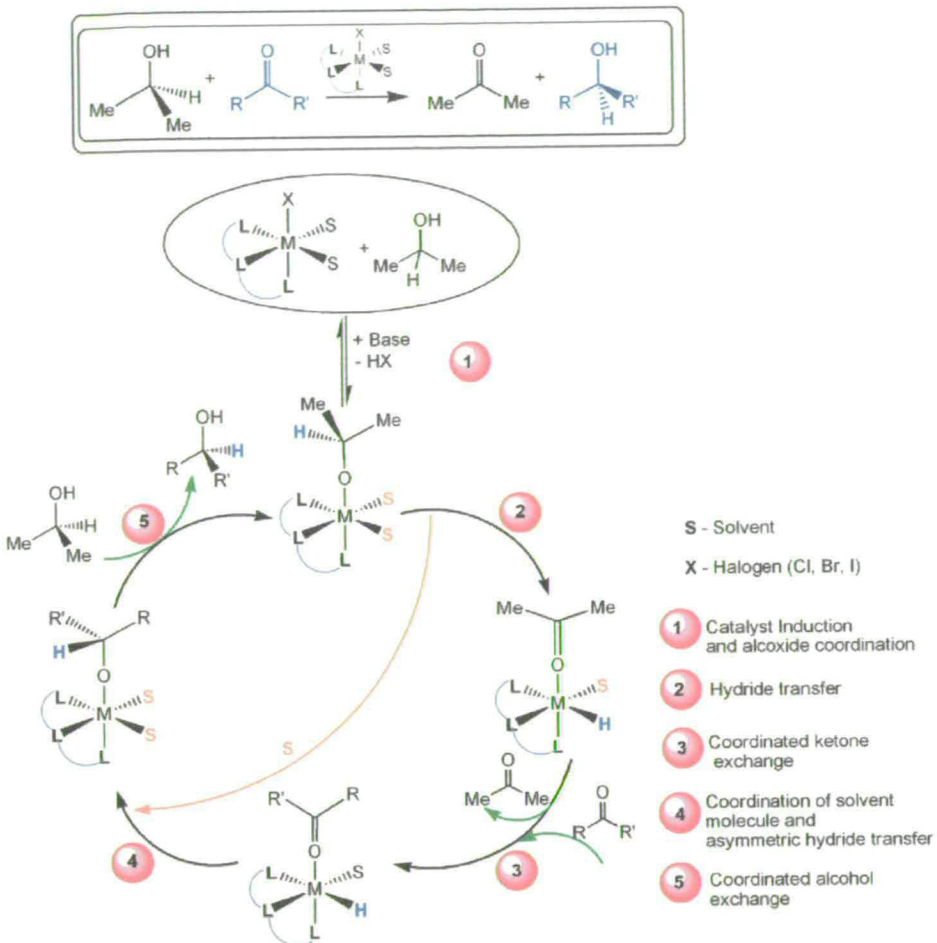


Fig.4.19. *Catalytic cycle for asymmetric transfer hydrogenation catalysed by an octahedral complex with a tridentate ligand via metal-hydride formation.*[15]

REFERENCES

1. P. J. Bailey, A. Dawson, C. McCormack, S. A. Moggach, D. H. Oswald, S. Parsons, D. W. H. Rankin and A. Turner, *Inorg. Chem.*, 2005, **44**, 8884.
2. M. R. Foreman, A. F. Hill, A. P. White and D. J. Williams, *Organometallics*, 2003, **22**, 3831.
3. P. J. Bailey, C. McCormack, S. Parsons, F. Rudolphi, A. S. Perucha and P. Wood, *Dalton Trans.*, 2007, 476.
4. A. S. Perucha, PhD Thesis, University of Edinburgh, 2007.
5. M. Vermeir and N. Boens, *Eur. Biophys. J.*, 1992, **21**, 47.
6. R. D. Skwierczynski and K. A. Connors, *Pharmaceut. Res.*, 1993, **10**, 1174.
7. C.-s. Da, M. Ni, Z.-j. Han, F. Yang and R. Wang, *J. Mol. Catal. A: Chem.*, 2006, **245**, 1.
8. R. Hulst, N. K. de Vries and B. L. Feringa, *Tetrahedron: Asymmetry*, 1994, **5**, 699.
9. A. Miyashita, A. Yasuda, H. Takaya, K. Toriumi, T. Ito, T. Souchi and R. Noyori, *J. Am. Chem. Soc.*, 1980, **102**, 7932.
10. M. Berthod, G. Mignani, G. Woodward and M. Lemaire, *Chem. Rev.*, 2005, **105**, 1801.
11. K. Mashima, K. Kusano, T. Ohta, R. Noyori and H. Takaya, *Chem. Comm.*, 1989, 1208.
12. A. Pfaltz and W. J. Drury, *Proc. Nat. Acad. Sci. U.S.A.*, 2004, **101**, 5723.
13. C. Moberg, *Angew. Chem. Int. Ed.*, 1998, **37**, 248.

14. C. Foltz, B. Stecker, G. Marconi, S. Bellemin-Laponnaz, H. Wadepohl and L. H. Gade, *Chem. Commun.*, 2005, 5115.

15. S. Gladiali and E. Alberico, *Chem. Soc. Rev.*, 2006, **35**, 226.

CHAPTER V

EXPERIMENTAL PART

GENERAL PROCEDURES

All the experiments were performed using Schlenk techniques, under a nitrogen atmosphere, with glassware dried at 160°C. Solvents were distilled and dried by standard methods[1] or used directly from a Glass Contour solvent purification system. All chemicals were obtained from Sigma-Aldrich and used as received. Tris(dimethylamino)borane, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) and N-methylimidazole were used as received and stored under nitrogen atmosphere. [Ru(*p*-cymene)Cl_2]$_2$ was prepared according to the methods reported by Jensen.[2] Mass spectrometry was recorded on two different spectrometers: Micromass Platform II (ES-MS) and Maspec II System. IR spectra were recorded from 4000 to 400 cm^{-1} with a JASCO FT-IR 410 instrument. NMR spectra were recorded on three different spectrometers operating at room temperature: Bruker ARX 250, Bruker DPX 360 and Bruker DMX 500. ^1H chemical shifts are reported in ppm relative to TMS (δ = 0). Peak multiplicity is abbreviated: singlet, s; doublet, d; dd, doublet of doublets; broad, br; triplet, t; multiplet, m; septet, sept; quartet, q.

All ligand syntheses were followed by testing the evolution of dimethylamine gas from the reaction mixture with a simple pH paper test. Reaction times may differ if nitrogen is bubbled through the reaction vessel.

5.1.EXPERIMENTAL PART CHAPTER II

[(dimethylamine)B(pyrazolyl)$_3$] 2.8 [3]

Tris(dimethylamino)borane (0.515 cm^3, 2.90 mmol) was added dropwise to a suspension of pyrazole (600 mg, 8.80 mmol) in 5 cm^3 of dry cyclohexane. This reaction is exothermic and dimethylamine gas evolution is immediate. The mixture was heated under reflux for 2 h. The white solid formed was filtered, washed twice with 5 cm^3 of cold diethyl ether and dried under vacuum. (560 mg, 75%).

^{1}H NMR (250.1 MHz, $CDCl_3$): δ_H 9.78 (1H, br), 6.66 (3H, m), 6.45 (3H, s), 3.58 (15H, s).

[(dimethylamine)B(methimazolyl)$_3$] 2.11 [4]

Tris(dimethylamino)borane (2.44 cm^3, 13.4 mmol) was added to a suspension of methimazole (4.61g, 40.2 mmol) in 15 cm^3 toluene. This mixture was heated under reflux for 4 h. A white precipitate was formed after 1 h. The solvent was removed under vacuum and the white powder was washed twice with 5 cm^3 of diethyl ether, filtered and dried under vacuum (4.18 g, 79%).

^{1}H-NMR (250.1 MHz, $CDCl_3$): δ_H 7.70 (3H, d, ^3J = 1.7 Hz), 7.51 (1H, s), 7.03 (3H, t, ^3J = 2.2 Hz and ^3J = 1.7 Hz), 6.21 (3H, d, ^3J = 1.7 Hz), 2.26 (6H, s).

[(N-methylimidazole)B(methimazolyl)$_3$] 2.16 [4]

Method 1

N-methylimidazole (0.093 cm^3, 1.17mmol) and tris(dimethylamino)borane (0.205 cm^3, 1.17 mmol) were added to a suspension of methimazole (400 mg, 3.50 mmol) in 10 cm^3 of toluene. This mixture was heated under reflux for 4 h. After cooling a white precipitate was observed. The precipitate was filtered by cannula and washed three times with 5 cm^3 of diethyl ether (358 mg, 71%).

Method 2

N-methylimidazole (0.0403 cm3, 0.506 mmol) was added to a suspension of [(dimethylamine)B(methimazolyl)$_3$] (200 mg, 0.506 mmol) in 15 cm^3 of toluene . The mixture was heated under reflux for 3 h. After 1h, the clear solution became cloudy with a white precipitate. The white precipitate was filtered by cannula and washed three times with 5 cm^3 of diethyl ether. (134 mg, 75%)

^{1}H NMR (250.1 MHz, $CDCl_3$): δ_H 7.45 (1H, s), 7.07 (1H, s), 6.69-6.64 (6H, s), 3.70 (3H, s), 3.61 (9H, s).

[(DBN)B(methimazolyl)$_3$] 2.19

Method 1

In 20 cm^3 of toluene, 1,5-diazabicyclo[4.3.0]non-5-ene (0.200 cm3, 1.68 mmol), tris(dimethylamino)borane (0.281 cm3, 1.68 mmol) and methimazole (500 mg, 4.38 mmol) were added together and heated to under reflux. After 1 h a white precipitate had formed from the solution. The solution was heated for a further 3 h. The white solid was filtered via cannula and washed three times with 5 cm^3 of diethyl ether. The ligand was isolated in 78% yield (621 mg).

Method 2

1,5-diazabicyclo[4.3.0]non-5-ene (0.064 cm^3, 0.506 mmol) was added to a suspension of 200 mg (0.506 mmol) [(dimethylamine)B(methimazolyl)$_3$] in 15 cm^3 of toluene. The mixture was heated under reflux for 5 h. After 1 h, the clear solution became cloudy with a white precipitate. The reaction was carried out for a further 4 h. The white precipitate was filtered by cannula and washed three times with 5 cm^3 of diethyl ether (172 mg, 72%).

$C_{19}H_{27}BN_8S_3$ (474.16): calcd.: C, 48.10; H, 5.74; N, 23.61; found: C, 47.60; H, 5.46; N, 23.36 %. MS (FAB$^+$): *m/z* = 474 (M$^+$); ^{1}H NMR (500.1 MHz, $CDCl_3$): δ_H 6.71 (3H, d, ^3J = 2.5 Hz), 6.67 (3H, d, ^3J = 2.2 Hz), 6.6-6.5 (4H, m), 3.6 (9H, s), 3.56-3.49 (4H, m), 3.39-3.33 (2H, m), 2.05-1.9 (2H, br); ^{13}C-NMR (90.5 MHz, DMSO-d_6): δ_C 161.0 (C=S $_{MTI}$), 129.3 ($C_{q\ DBN}$), 120.1 (CH $_{MTI}$), 114.1 (CH $_{MTI}$), 46.9 (CH_2

$_{DBN}$), 43.9 (CH_2 $_{DBN}$), 42.9 (CH_2 $_{DNB}$), 34.9 (CH_2 $_{DBN}$), 30.7 (CH_2 $_{DBN}$), 24.1 (CH_3 $_{MTI}$), 18.3 (CH_2 $_{DBN}$).

[(DMAP)B(methimazolyl)$_3$] 2.20 [5]

Method 1

To a solution of 4-(dimethylamino)pyridine (148 mg, 1.3 mmol) in 20 cm^3 of toluene was added tris(dimethylamino)borane (0.232 cm^3, 1.3 mmol) and methimazole (455 mg, 3.96 mmol). The reaction was heated under reflux. After 2 h a white precipitate was observed in the solution and the mixture was heated for a further 4 h. A white solid was recovered by filtration and washed three times with 5 cm^3 of diethyl ether to yield 534 mg of product (87%).

Method 2

To a solution of 4-(dimethylamino)pyridine (61.7 mg, 0.506 mmol) in 15 cm^3 of toluene was added [dimethylamine)B(methimazolyl)] (200 mg, 0.506 mmol). The mixture was heated under reflux. After 2 h the solution became cloudy with a white precipitate. The reaction was heated for a further 2 h. A white precipitate was formed after cooling and it was isolated by filtration. It was washed three times with 5 cm^3 of diethyl ether to yield 181 mg (76%) of a white powder.

^{1}H NMR (250.1 MHz, $CDCl_3$): δ_H 8.23 (2H, dd, ^3J = 1.6 Hz and ^3J = 6.5 Hz), 6.65 (3H, d, ^3J = 2.4 Hz), 6.61 (3H, d, ^3J = 2.3 Hz), 6.43 (2H, dd, ^3J = 1.6 Hz and ^3J = 6.5 Hz), 3.54 (9H, s), 2.94 (6H, s) .

[(benzylamine)B(methimazolyl)$_3$] 2.21

Method 1

To a suspension of methimazole (300 mg, 2.63 mmol) in 15 cm^3 of toluene were added (0.153 cm^3, 0.877 mmol) tris(dimethylamino)borane and benzylamine (0.0956 cm^3, 0.877 mmol). The mixture was heated under reflux for 9 h. A white precipitate was formed after 3 h. The powder was isolated by cannula filtration and washed three times with 5 cm^3 of diethyl ether (220 mg, 54%).

Method 2

To a suspension of [(dimethylamine)B(methimazolyl)$_3$] (362 mg, 0.917 mmol) in 20 cm^3 of toluene was added benzylamine (0.100 cm^3, 0.917 mmol). The mixture was heated under reflux. A white solid was observed after 1 h of reaction and the reaction was continued for a further 11 h. The powder was filtered and washed three times with 5 cm^3 diethyl ether (167 mg, 40%).

$C_{19}H_{24}BN_7S_3$ (457.4): calcd.: C, 49.89; H, 5.29; N, 21.43; found: C, 49.74; H, 5.56; N, 21.32 %. MS (FAB$^+$): *m/z* = 457.4 (M + 1); ^{1}H NMR (360.1 MHz, $CDCl_3$): δ_H 7.50-7.37 (5H, m), 6.71 (3H, d, ^3J = 2.6 Hz), 6.67 (3H, d, ^3J = 0.8 Hz), 6.35 (2H, s), 3.89 (3H, s), 3.61 (9H, s); ^{13}C NMR (90.5 MHz, $CDCl_3$): δ_C 162.5 (C=S $_{MTI}$), 129.4 (2CH $_{BZA}$), 129.1 (2CH $_{BZA}$), 128.7 (CH $_{BZA}$), 127.5 (CH $_{BZA}$), 121.16 (CH_2 $_{MTI}$), 119.4 (CH_2 $_{MTI}$), 48.62 (CH_2 $_{BZA}$), 35.18 (CH_3 $_{MTI}$).

[(DABCO)B(methimazolyl)$_3$] 2.22

Method 1

To a suspention of 1,4-diazabicyclo[2.2.2]octane (81 mg, 0.725 mmol) in 25 cm^3 of toluene were added tris(dimethylamino)borane (0.255 cm^3, 1.46 mmol) and methimazole (500 mg, 4.35 mmol). The reaction was heated under reflux for 48 h. A white precipitate was observed after cooling the mixture. It was dried and washed with three times with 5 cm^3 of diethyl ether to afford 276 mg (83%) of product.

Method 2

To a suspension of 1,4-diazabicyclo[2.2.2]octane (56.6 mg, 0.506 mmol) in 15 cm^3 toluene was added [(dimethylamine)B(methimazolyl)$_3$] (400 mg, 1.01 mmol). The mixture was heated under reflux for 36 h. A white precipitate was observed after cooling the mixture. The solvent was removed under vacuum and the powder was washed with three portions of 5 cm^3 of diethyl ether to afford 182 mg (78%) of product.

$C_{18}H_{27}BN_8S_3$ (462.47): calcd.: C, 46.75; H, 5.88; N, 24.23; found: C, 46.19; H, 5.08; N, 23.94 %; MS (FAB$^+$): m/z = 463.4 (M + 1); ^{1}H NMR (360.1 MHz, DMSO-d$_6$): δ_H 6.82 (3H, br, CH), 6.65 (3H, d, ^3J = 2.1 Hz), 3.33 (12H, s), 3.04 (9H, s); ^{13}C NMR (90.5 MHz, DMSO-d$_6$): δ_C 161.7 ($C_{q\,MTI}$), 119.3 (CH_{MTI}), 113.9 (CH_{MTI}) 45.5 ($CH_{2\,DABCO}$), 33.7 ($CH_{3\,MTI}$); δ_B (115.5 MHz, DMSO-d$_6$): 3.62.

[Ru(*p*-cymene)Cl_2]$_2$ 2.24 [2]

To a suspension of ruthenium (III) chloride hydrate (3.0 g, 0.014 mol) in 200 cm^3 ethanol was added α-terpinene (15 cm^3, 0.092 mol). The mixture was heated under reflux for 6 h. The solvent was evaporated to half volume and the remaining solution was kept at -10°C for 18 h to allow the product to precipitate. The solid was filtered and washed with cold ethanol. The solvent was removed and 3.3 g (75%) of a red solid was obtained.

^{1}H NMR (250.1 MHz, $CDCl_3$): δ_H 5.47 (4H, d, ^3J = 6.0 Hz), 5.33 (4H, d, ^3J = 6.0 Hz), 2.92 (2H, sept, ^3J = 7.2 Hz), 2.15 (6H, s), 1.28 (6H, d, ^3J = 6.7 Hz).

[{(1,5-diazabicyclo[4.3.0]non-5-ene)B(methimazolyl)$_3$}Ru(*p*-cymene)][PF_6]$_2$ 2.25

[Ru(*p*-cymene)Cl_2]$_2$ (64.6 mg, 0.105 mmol) was dissolved in 15 cm^3 of dried ethanol and stirred at room temperature for 45 minutes. The ligand [(1,5-diazabicyclo[4.3.0]non-5-ene)B(methimazolyl)$_3$] (100 mg, 0.210 mmol) was added in small portions and the mixture stirred for 12 h at room temperature. Then, NH_4PF_6 (171 mg, 1.05 mmol) was added and the precipitation of an orange solid was observed. After filtration by cannula, the solid was washed three times with 7 cm^3 of ethanol and twice with 10 cm^3 of diethyl ether. After drying under vacuum, the complex was obtained with a yield of 76% (171 mg). Crystals suitable for X-ray crystallography were obtained by slow diffusion of diethyl ether in a concentrated solution of the complex in acetonitrile.

$C_{29}H_{41}BF_{12}N_8P_2RuS_3$ (1000.1): calcd.: C, 34.89; H, 4.13; N, 11.21; found: C, 34.16; H, 4.02; N, 11.15%; MS (FAB^+): *m/z* = 501.9 [(M + 1)/2]; ^1H NMR (250.1 MHz, CD_3CN): δ_H 7.15 (3H, d, ^3J = 3.0 Hz), 6.77 (3H , d, ^3J = 3.1 Hz,), 5.53-5.39 (4H, m), 3.91 (1H, sept, ^3J = 6.7 Hz), 3.77-3.71 (4H, m), 3.67 (9H, s), 3.64-3.39 (4H, m), 2.47-2.38 ppm (2H, m), 2.18 pm (3H, s), 1.30 ppm (2H, m), 1.17 ppm (6H, t, ^3J = 7 Hz); ^{13}C NMR (125.7 MHz, $(CH_3)_2CO$): δ_C 172.2 ($C_{q\ DBN}$), 148.9 ($C_{q\ MTI}$), 124.4 ($CH_{\ MTI}$), 124.1($CH_{\ MTI}$), 107.8 ($C_{q\ p\text{-cym}}$), 103.5 ($C_{q\ p\text{-cym}}$), 87.3 ($2CH_{\ p\text{-cym}}$), 86.3 ($CH_{\ p\text{-cym}}$), 85.3 ($2CH_{\ p\text{-cym}}$), 55.3 ($CH_{2\ DBN}$), 46.7 ($CH_{2\ DBN}$), 45.4 ($CH_{2\ DBN}$), 37.1 ($CH_{2\ DBN}$), 36.9 ($CH_{2\ DBN}$), 32.0 ($CH_{3\ MTI}$), 23.5 ($CH_{3\ p\text{-cym}}$), 21.3 ($2CH_{3\ p\text{-cym}}$), 19.5 ($CH_{2\ DBN}$); ^{11}B NMR (115.5 MHz, DMSO-d_6): δ_B 4.15.

Table 5.1 *Crystallographic data and structure refinement details for* ***2.25***

Crystal description	red block
Empirical Formula	$C_{31}\ H_{44}\ B\ F_{12}\ N_9\ P_2\ Ru\ S_3$
M_w	1040.75
T/ K	150(2)
Crystal system	Monoclinic
Space group	$P2_1/c$
***a* /Å**	16.7640(5)
***b* /Å**	13.0602(4)
***c* /Å**	20.5423(6)
α / °	90
β / °	94.485(2)
γ / °	90
V / Å^3	4483.8(2)
Z	4
D / g cm^{-3}	1.542
μ / mm^{-1}	0.646
Reflexions measured	8811
R_{int}	0.0674
Data with $\|F\|>4\sigma(\|F\|)$	7122
Absortion correction type	multiscan
Min/max transmission	0.334 / 0.827
R	0.0452

[{(DMAP)B(methimazolyl)$_3$}Ru(*p*-cymene)][PF$_6$]$_2$ 2.26

[Ru(*p*-cymene)Cl$_2$]$_2$ (153 mg, 0.025 mmol) was dissolved in 14 cm^3 of methanol and left stirring for 90 min. [(DMAP)B(methimazolyl)$_3$] (236 mg, 0.50 mmol) was added and a colour change from orange to red was observed. The reaction was stirred for 16 h at room temperature and was heated for a further 4 h at 55-60 °C. NH_4PF_6 (163 mg, 1.00 mmol) was added to the complex and a red precipitate was formed immediately. The solid was dried and dissolved in 10 cm^3 of acetone. The red solution was filtered to remove the excess of hexafluorophosphate salt. The filtrate was taken to dryness and the remaining product was recrystallised from dichloromethane to obtain 497 mg (90%) of a red solid. Crystals suitable for X-ray crystallography were obtained from slow evaporation of a concentrated solution of the complex in dichloromethane.

$C_{29}H_{39}BF_{12}N_8P_2RuS_3$ (998.68): calcd.: C, 34.91; H, 3.94; N, 11.23; found: C, 34.52; H, 3.89; N,11.11 %; MS (FAB$^+$): *m/z* = 708.7 (M$^+$ with loss of counter-ions); ^{1}H NMR (250.1 MHz, DMSO-d$_6$): δ_H 8.28 (2H, d, ^3J = 7.8 Hz), 7.56 (3H, d, ^3J = 2.4 Hz), 6.98 (2H, d, ^3J = 7.8 Hz), 6.94 (3H, d, ^3J = 2.4 Hz), 5.64-5.76 (4H, m), 3.71 (9H, s), 3.25 (6H, s), 2.91 (1H, sept, ^3J = 6.8 Hz), 2.23 (3H, s), 1.21 (3H, s), 1.18 (3H, s); ^{13}C NMR (90.1 MHz, DMSO-d$_6$): δ_C 162.6 ($C_{q\ MTI}$), 158.3 ($C_{q\ DMAP}$), 145.7 (CH_{DMAP}), 108.9 (CH_{MTI}), 108.4 ($C_{q\ p\text{-}cym}$), 103.1 ($C_{q\ p\text{-}cym}$), 86.8 (CH_{DMAP}), 86.4 ($CH_{p\text{-}cym}$), 85.9 (CH_{MTI}), 84.8 ($CH_{p\text{-}cym}$), 41.2 ($CH_{p\text{-}cym}$), 36.8 ($CH_{3\ DMAP}$), 32.0 ($CH_{3\ MTI}$), 23.5 ($CH_{3\ p\text{-}cym}$), 19.6 ($CH_{3\ p\text{-}cym}$).

The refinement of the structure of **2.26** was not possible due to the loss of solvent which affected the quality of the obtained crystals. The R-factor found for the

refinement of this structure was above 30%. Apart from the atomic coordinates, no further crystallographic data was obtained,

[(methimazolyl)$_3$Ru(*p*-cymene)][PF$_6$]$_2$ 2.27

A solution of [Ru(*p*-cymene)]Cl$_2$]$_2$ (330 mg, 0.5 mmol) in 23 cm^3 methanol was stirred for 90 min at room temperature. The ligand [(benzylamine)B(methimazolyl)$_3$] (395 mg, 1.00 mmol) was added and a colour change from orange to dark red occurred. Then the mixture was stirred at room temperature for 16 h and heated for a further 4 h at 55-60 °C. Then NH_4PF_6 (326 mg, 2.00 mmol) was added and an orange precipitate was formed. The solid was dried under vacuum and dissolved in 10 cm^3 acetone. The red solution was filtered to remove the excess of hexafluorophosphate salt. The filtrate was dried and the remaining product was precipitated from a mixture of dichloromethane and hexane (4:1) to obtain 640 mg (70%) of a red/orange solid. Crystals suitable for X-ray crystallography were obtained by slow diffusion of diethyl ether in a concentrated solution of the complex in acetonitrile.

(867.7): calcd.: C, 30.45; H, 3.72; N, 9.69; found: C, 30.08; H, 3.68; N,9.54 %; MS(FAB$^+$): *m/z* = 577.8 (M$^+$ with loss of counter-ions); ^{1}H NMR (250.1 MHz, CD_3CN): δ_H 10.70 (3H, br), 7.03 (6H, dd, ^3J = 2.2 Hz and ^3J=12.0 Hz), 7.01 (3H, d, ^3J = 2.2 Hz), 5.60 (2H, d, ^3J = 6.3 Hz), 5.44 (2H, d, J = 6.3 Hz), 3.66 (9H, s), 2.81 (1H, sept, J = 6.9 Hz), 2.11 (3H, s), 1.26 (3H, s), 1.23 (3H, s); ^{13}C NMR (62.8 MHz, $CDCl_3$): δc 154.0 ($C_{q\ MTI}$), 123.4 ($C_{q\ p\text{-cym}}$), 118.0 ($C_{q\ p\text{-cym}}$), 108.4 (CH_{MTI}), 105.7 (CH_{MTI}), 88.6 ($CH_{p\text{-cym.}}$), 86.0 ($CH_{p\text{-cym}}$), 35.5 ($CH_{p\text{-cym}}$), 31.2 ($CH_{3\ MTI}$), 22.3 ($CH_{3\ p\text{-cym}}$), 17.9 ($CH_{3\ p\text{-cym}}$).

Table 5.2. *Crystallographic data and structure refinement details for* **2.26**.

Crystal description	Red rod
Empirical Formula	$C_{22}H_{32}F_{12}N_6P_2RuS_3$
M_w	867.73
T/ K	150
Crystal system	Monoclinic
Space group	P 1 2_1 / n 1
a /Å	15.1385(10)
b /Å	15.2072(10)
c /Å	15.4226(11)
α / °	90
β / °	115.370(1)
γ / °	90
V / Å^3	3212.3(4)
Z	4
D / g cm^{-3}	1.794
μ / mm^{-1}	0.880
Reflexions measured	6574
R_{int}	0.080
Data with $\|F\|>4\sigma(\|F\|)$	5071
Absortion correction type	Semi-empirical from equivalents
Min/max transmission	0.63 / 0.94
R	0.0651

[(dimethylamine)B(methimazolyl)$_3$Mo(CO)$_3$] 2.28

[(dimethylamine)B(methimazolyl)$_3$] (0.2 mg, 0.5 mmol) was dissolved in 15 cm^3 of tetrahydrofuran and then Mo(CO)$_6$ (133 mg, 0.5 mmol) was added. The mixture was heated under reflux. After 2 h the solution became yellow. The mixture was heated for a further 3 h. The solvent was removed under vacuum and the solid was washed three times with 5 cm^3 of diethyl ether and dried under vacuum to afford 112 mg (38%) of an off-white powder.

$C_{17}H_{25}BMoN_7O_3S_3$ (578.4): calcd.: C, 35.30; H, 4.36; N, 16.95; found: C, 34.90; H, 4.67; N, 17.12.%; MS(ES): *m/z* = 579 (M + 1); ^{1}H NMR (360.1 MHz, $CDCl_3$): δ_H

9.75 (NH, br), 6.69 (3H, d, ^3J = 2.2 Hz), 6.68 (3H, d, ^3J = 2.2 Hz), 3.61 (9H, s), 3.68 (6H,s); ^{13}C NMR (90.5 MHz, $CDCl_3$): δ_C 207.4 (C = O), 163.2 (C=S), 119.4 (CH_{MTI}), 114.0 (CH_{MTI}), 35.4 ($CH_{3\ MTI}$), 25.2 (CH_3); ^{11}B (115.5 MHz, $CDCl_3$): δ_B 5.98; IR (hexane): 1987, 1957 cm^{-1} (C ≡ O).

Attempted synthesis of [{(DMAP)B(methimazolyl)$_3$}Mo(CO)$_3$] 2.32

[{(dimethylamine)B(methimazolyl)$_3$}Mo(CO)$_3$] (20 mg, 0.034 mmol) was dissolved in toluene and DMAP (4 mg, 0.34 mmol) was added. The mixture was heated under reflux for 1 h and evolution of dimethylamine gas was monitored by pH paper test. The mixture was cooled and left stirring at room temperature for 3 h. The solvent was removed under vacuum and the product was washed with 2 cm^3 of diethyl ether. The product analysis by ^{11}B magnetic resonance spectroscopy showed no boron signal and IR spectroscopy showed no bands for C ≡ O vibrations.

[(DMAP)B(pyrazolyl)$_3$] 2.33

To a suspension of [(dimethylamine)B(pyrazolyl)$_3$] (300 mg, 1.16 mmol) in 15 cm^3 of toluene was added 4-(dimethylamino)pyridine (143 mg, 1.16 mmol). The reaction was heated under reflux for 12 h. A white powder was recovered by filtration. It was washed twice with 5 cm^3 of diethyl ether and dried under vacuum. The ligand was obtained with 90% (350 mg) yield.

$C_{16}H_{19}BN_8$ (334.19): calcd.: C, 57.50; H, 5.73; N, 33.53; found: C, 57.01; H, 5.39; N, 33.38 %; MS (FAB$^+$): *m/z* = 335.3 (M + 1); ^{1}H NMR (360.1 MHz, $CDCl_3$): δ_H 8.31

(2H, d, ^3J = 7.4 Hz), 7.74 (3H, d, ^3J = 0.8 Hz), 7.12 (3H, d, ^3J = 2.2 Hz), 6.56 (2H, d, ^3J = 7.5 Hz), 6.25 (3H, t, ^3J = 1.7 Hz and ^3J = 0.9 Hz), 3.16 (6H, s); ^{13}C NMR (90.5 MHz, CD_3CN): δ_C 156.1 ($C_{q\ DMAP}$), 145.4 ($3CH_{pz}$), 135.3 ($3CH_{pz}$), 129.1 ($3CH_{DMAP}$), 106.6 ($3CH_{pz}$), 105.7 ($2CH_{DMAP}$), 39.9 ($2CH_{3\ DMAP}$).

[(N-methylimidazole)B(pyrazolyl)$_3$] 2.34 [5]

To a suspension of [(dimethylamine)B(pyrazolyl)$_3$] (300 mg, 1.16 mmol) in 15 cm^3 of toluene was added N-methylimidazole (0.0922 cm^3, 1.16 mmol). The mixture was heated under reflux for 4 h. A white solid was recovered by filtration, washed three times with 5 cm^3 of diethyl ether and dried under vacuum. The ligand was obtained in 88% yield (304 mg).

^{1}H NMR (360.1 MHz, $CDCl_3$): δ_H 8.58 (1H, s), 7.72 (3H, d, ^3J = 1.7 Hz), 7.57 (1H, t, ^3J = 2.2 Hz and ^3J = 3.1 Hz), 6.96 (3H, d, ^3J = 2.2 Hz), 6.92 (1H, t, ^3J = 1.7 Hz and ^3J = 1.3 Hz), 6.24 (3H, t, ^3J = 1.7 Hz and ^3J = 2.2 Hz), 3.77 (1H, s).

[{κ^2-N,N (DMAP)B(pz)$_3$}Ru(*p*-cymene)Cl]PF$_6$ 2.38

[Ru(*p*-cymene)Cl_2]$_2$ (110 mg, 0.0179 mmol) was dissolved in 10 cm^3 of methanol and stirred for 1 h. Then, [(DMAP)B(pz)$_3$] (120 mg, 0.36 mmol) was added in small portions and a colour change of the mixture from orange to yellow was observed. The reaction was stirred for a further 24 h at room temperature. NH_4PF_6 (60 mg, 0.37 mmol) was added to the solution and a yellow precipitate was formed. The precipitate was dried and washed with ether to afford 120 mg (37%) of a yellow

solid. The product was crystallized by slow diffusion of diethyl ether into an acetonitrile solution to obtain crystals suitable for X-ray crystallography.

$C_{26}H_{33}BC_lF_6N_8PRu$ (749.9): calcd.: C, 41.64; H, 4.44; N, 14.94; found: C, 41.53; H, 4.35; N,14.56 %; MS (FAB^+) *m/z* = 605.2 (M^+ complex without counter-ion); ^1H NMR (360.1 MHz, DMSO-d_6): δ_H 8.18 (2H, d, ^3J = 2.2 Hz), 7.82 (1H, d, ^3J = 1.3 Hz), 7.46 (2H, d, ^3J = 2.6 Hz), 7.08 (1H, d, ^3J = 2.1 Hz), 7.03 (2H, d, ^3J = 7.8 Hz), 6.90 (2H, d, ^3J = 7.4 Hz), 6.68 (2H, t, ^3J = 2.2 Hz), 6.53 (1H, t, ^{3}J = 1.7 Hz), 5.77 (2H, d, ^3J = 6.1 Hz), 4.92 (2H d, ^3J = 6.1 Hz), 3.22 (6H, s), 2.66 (1H, sept, ^3J = 6.5 Hz), 1.56 (3H, s), 1.76 (6H, d, ^3J = 6.5 Hz); ^{13}C NMR (90.5 MHz, DMSO-d_6): δ_C 160.9 ($C_{q\ DMAP}$), 156.8 ($2CH_{\ DMAP}$), 148.6 ($C_{q\ p\text{-cym}}$), 142.3 ($2CH_{\ pz}$), 138.2 (CH pz), 133.6 (CH pz), 128.8 (2CH pz), 108.3 (2CH DMAP), 107.8 (2CH pz), 107.7 (CH pz), 102.6 ($2CH_{\ p\text{-cym}}$), 102.0 ($2CH_{\ p\text{-cym}}$), 87.28 ($C_{q\ p\text{-cym}}$), 80.48 ($CH_{\ p\text{-cym}}$), 29.8 ($CH_{3\ DMAP}$), 22.2 ($CH_{3\ p\text{-cym}}$), 17.5 ($CH_{3\ p\text{-cym}}$).

Table 5.3. Crystallographic data and structure refinement details for 2.38

Crystal description	Orange block
Empirical Formula	$C_{26}\ H_{33}B\ F_6\ N_8\ P\ Ru$
M_w	749.90
T/ K	150(2)
Crystal system	Monoclinic
Space group	$P2_1/c$
***a* /Å**	15.3059(5)
***b* /Å**	10.1443(3)
***c* /Å**	20.8293(7)
α / °	90.00
β / °	106.854(2)
γ / °	90.00
V / Å^3	3095.20 (17)
Z	4
D / g cm^{-3}	1.609
μ / mm^{-1}	0.713
Reflexions measured	6359
R_{int}	0.0578
Data with $\|F\|>4\sigma(\|F\|)$	5123
Absortion correction type	multiscan
Min/max transmission	0.7707 / 0.9168
R	0.0347

Attempted synthesis of [{(DMAP)B(pz)$_3$}Ru(*p*-cymene)](PF$_6$)(BF$_4$) 2.39

[{(DMAP)B(pz)$_2$}Ru(p-cymene)Cl]PF$_6$ (60 mg, 0.08 mmol) was dissolved in 5 cm^3 of acetonitrile and silver tetrafluoroborate (23 mg, 0.12 mmol) was added. A precipitate of AgCl was formed after 10 min and the mixture was stirred for 30 min. The precipitate was filtered off and the filtrate was concentrated to half volume and left to crystallise by slow diffusion of ether. Product analysis by NMR spectroscopy shows three more sets of signals for the pyrazole rings of the complex. This could be a mixture of products or decomposition of the complex.

5.2. EXPERIMENTAL PART CHAPTER III

S-trityl-benzimidazole-2-thione 3.1 [6]

Benzimidazole-2-thione (6.0 g, 40 mmol) was dissolved in 120 cm^3 tetrahydrofuran and triethylamine (5.2 g, 52 mmol) and triphenylmethyl chloride (11.16 g, 40 mmol) were added to the solution. The mixture was stirred at room temperature for 30 h. The NEt$_3$.HCl precipitated and was filtered. The filtrate was concentrated and the solid obtained, S-trityl-benzimidazole-2-thione, was recrystallised from toluene and was used to prepare 1-methylbenzimidazole-2-thione (14.6 g, 93%).

1-methylbenzimidazole-2-thione 3.2 [6]

S-trityl-benzimidazole-2-thione (14.6 g, 37 mmol) was dissolved in 160 cm^3 of freshly distilled acetone and ground potassium hydroxide (12.6 g, 226 mmol). This mixture was stirred for 40 min, and then methyl iodide (9.3 g, 66 mmol) was added. After stirring for a further 3 h, 200 cm^3 of toluene were added and the mixture was extracted with 80 cm^3 of water and 80 cm^3 of brine. The organic phase was dried over anhydrous sodium sulphate and dried under vacuum. The solid obtained was dissolved in 120 cm^3 of a solution 5% (v/v) acetic acid in methanol and it was heated under reflux for 32 h. The solvent was removed under vacuum and the crude product was dissolved in dichloromethane and extracted three times with 40 cm^3 of 10% (w/w) aqueous sodium bicarbonate solution. The organic phase was dried over anhydrous sodium sulphate, dried under vacuum and the solid obtained was recrystallized from acetonitrile. The crystals were washed with hexane to afford 4.3 g (71%) of a white solid.

^1H (250.1 MHz, $CDCl_3$): δ_H 9.57 (1H, br), 7.21 (4H, m), 3.78 (3H, s).

1,4,5-trimethylimidazole-2-thione 3.3 [7]

To a mixture of 3-hydroxybutanone (8.8 g, 0.1 mol) and N-methylthiourea (9.0 g, 0.1 mol) in 50 cm^3 of hexanol was added 2 cm^3 of concentrated hydrochloric acid (37%). The reaction mixture was heated under reflux for 12 h. Then, it was cooled and placed in an ice bath. The mixture formed was filtered immediately and the precipitate was washed with two portions of hexane (15 cm^3) and three portions of

diethyl ether (25 cm^3). The product was then recrystallized from petroleum ether to afford 4.2 g (30%) of pure compound. ^1H NMR (250.1 MHz, $CDCl_3$): δ_H 10.95 (1H, br), 3.50 (3H, s), 2.08 (3H, s), 2.05 (3H, s)

[(HNMe$_2$)B(1,4,5-trimethylimidazole-2-thione)$_3$] 3.4

To a suspension of 1,4,5-trimethylimidazole-2-thione (500 mg, 3.52 mmol) in 10 cm^3 of toluene was added tris(dimethylamino)borane (0.205 cm^3, 1.17 mmol). The mixture was heated to reflux for 12 h. The solvent was evaporated and the crude product was washed three times with 5 cm^3 of diethyl ether. The pure product was obtained as a white powder in 66 % (434 mg) yield.

$C_{20}H_{34}BN_7S_3$ (479.5): calcd.: C, 50.09; H, 7.15; N, 20.45; found: C, 49.96; H, 7.13; N, 20.38 %; MS (FAB^+): *m/z* = 480.4 (M + 1); ^1H NMR (500.1 MHz, $CDCl_3$): δ_H 10.47 (1H, br), 3.48 (6H, s), 2.84 (9H, s), 2.08 (9H, s), 2.04 (9H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 157.9 (Cq), 121.5 (CH), 119.5 (CH), 39.3 (CH_3), 31.1 ($2CH_3$), 8.9 ($2CH_3$).

[(HNMe$_2$)B(1-methylbenzimidazole-2-thione)$_3$] 3.5

1-methylbenzimidazole-2-thione (500 mg, 3.04 mmol) was dissolved in 15 cm^3 of xylene and tris(dimethylamino)borane (0.117 cm^3, 1.02 mmol) was added. The mixture was heated under reflux for 24 h, during which time the solution became cloudy. The mixture was cooled to room temperature and the solvent was removed

under vacuum. The white solid was washed twice with 5 cm^3 of diethyl ether and dried under vacuum to afford 300 mg (54%) of product.

$C_{26}H_{28}BN_7S_3$ (545.6): calcd.: C, 57.24; H, 5.17; N, 17.97; found: C, 57.05 ;H, 5.15; N, 17.91 %; MS(FAB^+): *m/z* = 546 (M + 1); ^1H NMR (360.1 MHz, $CDCl_3$): δ_H 10.22 (1H, br), 7.19-7.13 (12H, m), 3.80 (6H, s), 3.75 (6H, s); ^{13}C NMR (90.5 MHz, $CDCl_3$): δ_C 169.9 (CS), 135.9 (C_q), 127.9 (C_q), 124.9 (CH), 123.7 (CH), 110.8 (CH), 109.8 (CH), 31.4 (CH_3), 18.6 ($2CH_3$).

[{(HNMe$_2$)B(1-methylbenzimidazole-2-thione)$_3$}Mo(CO)$_3$] 3.6

To a suspension of [(HNMe$_2$)B(1-methylbenzimidazole-2-thione)$_3$] (200 mg, 0.360 mmol) in 15 cm^3 of tetrahydrofuran was added molybdenum hexacarbonyl (97.0 mg, 0.360 mmol). The mixture was refluxed for 6 h and the reaction was monitored by IR spectroscopy. During the reflux the solution became pale green. The tetrahydrofuran was removed under vacuum and the product was dissolved in chloroform and impurities were filtered off. The filtrate was dried to afford 82 mg (31%) of a yellow solid.

$C_{29}H_{28}BMoN_7O_3S_3$ (725.5): calcd.: C, 48.01; H, 3.89; N, 13.51; found: C, 47.87; H, 3.86; N, 13.47 %; MS (FAB^+): *m/z* = 726 (M + 1); ^1H NMR (360.1 MHz, $CDCl_3$): δ_H 9.45 (1H, br), 7.20-7.10 (12H, m), 3.88 (9H, s), 3.80 (6H, s); ^{13}C NMR (90.5 MHz, $CDCl_3$): δ_C 205.6 (CO), 169.3 (CS), 132.3 (C_q), 132.6 (C_q), 127.6 (CH), 124.7 (CH), 110.1 (CH), 109.4 (CH), 30.7 (CH_3), 15.1 ($2CH_3$); ^{11}B NMR (119.1 MHz, $CDCl_3$): δ_B 18.8. IR (hexane solution): 1982, 1950 cm^{-1} (C ≡ O).

5.3 .EXPERIMENTAL PART CHAPTER IV

[((S)-(-)-α-methylbenzylamine)B(methimazolyl)$_3$] 4.19

To a solution of (S)-(−)-α-methylbenzylamine (0.188 cm^3, 1.45 mmol) in 15 cm^3 of toluene were added methimazole (500 mg, 4.36 mmol) and tris(dimethylamino)borane (0.253 cm^3, 1.45 mmol). The mixture was heated under reflux for 48 h. Then, the toluene was removed under vacuum and the remaining solid was washed three times with 5 cm^3 of diethyl ether. The product was obtained in 44% (305 mg) yield.

$C_{20}H_{26}BN_7S_3$ (471.5): calcd.: C, 50.95; H, 5.56; N, 20.80; found: C, 57.51; H, 5.53; N, 19.98 %; MS (FAB$^+$): *m/z* = 472 (M + 1); ^{1}H NMR (360.1 MHz, DMSO-d$_6$): δ_H 10.24 (2H, br), 7.38-7.21 (5H, m), 7.04 (3H, d, ^3J = 2.1 Hz), 6.86 (3H, d, ^3J = 2.4), 4.06 (1H, q, ^3J = 6.5), 3.42 (9H, s), 1.30 (3H, d, ^3J = 6.5 Hz); ^{13}C NMR (90.5 MHz, DMSO-d$_6$): δ_C 160.8 (C=S), 128.1 (2CH $_{MBZA}$), 126.4 ($C_{q\ MBZA}$), 125.8 (2CH $_{MBZA}$), 124.9 ($C_{q\ MBZA}$), 119.6 (CH $_{MTI}$), 114.2 (CH $_{MTI}$), 50.5 (CH $_{MBZA}$), 33.5 ($CH_{3\ MTI}$), 22.3 ($CH_{3\ MBZA}$).

[((S)-(-)- α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$] 4.20

To a suspension of 1,4,5-trimethyl-imidazole-2-thione (600 mg, 4.22 mmol) in 15 cm^3 of toluene were added tris(dimethylamino)borane (0.246 cm^3, 1.14 mmol) and (S)-(-)-α-methylbenzylamine (0.181 cm^3,1.14 mmol). The mixture was heated under reflux for 60 h. The solvent was removed under vacuum and the remaining solid was

washed twice with 5 cm^3 of diethyl ether. The product was recovered as a white powder solid in 31% yield (240 mg).

$C_{26}H_{38}BN_7S_3$ (555.6): calcd.: C, 56.20; H, 6.89; N, 17.65; found: C, 55.97 ; H, 6.86; N, 17.57 %; MS (FAB^+): *m/z* = 556 (M + 1); ^1H NMR (360.1 MHz, $CDCl_3$): δ_H 11.54 (2H, br), 7.32-7.27 (5H, m), 4.11 (1H, q, ^3J = 6.5 Hz), 3.50 (9H, s), 3.47 (9H, s), 2.02 (9H, s), 1.37 (3H, d, ^3J = 6.5 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 157.9 (C=S), 144.9 ($C_{q\ aromatic\ MBZA}$), 131.1 (CH_{MBZA}), 130.2 (CH_{MBZA}), 125.9 (CH_{MBZA}), 125.1 (CH_{MBZA}), 122.9 (C_q), 119.6 (C_q), 31.2 (CH_3), 11.9 ($CH_{3\ MBZA}$), 8.9 ($2CH_3$).

[{(S)-(-)-α-methylbenzylamine)B(1,4,5-trimethylimidazolyl-2-thione)$_3$}Mo(CO)$_3$] 4.21

A suspension of molybdenum hexacarbonyl (40 mg, 0.151 mmol) in 20 cm^3 of acetonitrile was heated under reflux for 3 h. The solution became yellow and was added via cannula to a schlenk flask containing (S)-(-)-α-methylbenzylamine)B(1,4,5-trimethyl-imidazolyl-2-thione)$_3$ (70 mg, 0.126 mmol). The solution was stirred at room temperature for 24 h. The resulting green solution obtained was evaporated under vacuum and the product was dissolved in a mixture chloroform/hexane (1:1) and filtered. The filtrate was dried under vacuum to obtain a 15 mg (16%) of product.

$C_{29}H_{40}BMoN_7O_3S_3$ (737.6): calcd.: C, 47.22; H, 5.47; N, 13.29; decomposition prevented satisfactory analysis; MS (FAB^+): *m/z* = 737.3 (M^+); ^1H NMR (360.1

MHz, $CDCl_3$): δ_H 6.70-6.67 (5H, m), 3.74 (1H, q, ^3J = 6.5 Hz), 3.61 (9H, s), 3.59 (9H, s), 2.49 (3H, d, ^3J = 6.0 Hz), 2.43 (2H, s), 1.25 (9H, s); ^{13}C NMR (90.1 MHz, $CDCl_3$): δ_C 205.3 (CO), 158.3 (CS), 136.4 ($C_{q\ aromatic\ MBZA}$), 129.5 (CH_{MBZA}), 128.91 (CH_{MBZA}), 125.9 (CH_{MBZA}), 125.7 (CH_{MBZA}), 121.6 (CH_{MBZA}), 120.6 (C_q), 119.4 (C_q), 31.8 (CH_{MBZA}), 31.1 (CH_3), 19.1 ($CH_{3\ MBZA}$), 8.02 ($2CH_3$) ; ^{11}B NMR (119.1 MHz, $CDCl_3$): δ_B 5.28; IR (hexane solution): 1952, 1957 cm^{-1} (C ≡ O).

REFERENCES

1. W. L. F. Armarego and C. L. L. Chai, in *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Burlington, 5th edn., 2003, pp. 578-584.
2. S. B. Jensen, S. J. Rodger and M. D. Spicer, *J. Organomet. Chem.*, 1998, **556**, 151.
3. K. Niedenzu and W. W. Seelig, *Z. Anorg. Allg. Chem.*, 1981, **483**, 51.
4. P. J. Bailey, D. Lorono-Gonzales, C. McCormack, F. Millican, S. Parsons, R. Pfeifer, P. Pinho, F. Rudolphi and A. S. Perucha, *Chem. Eur. J.*, 2006, **12**, 5293.
5. A. S. Perucha, PhD Thesis, *University of Edinburgh*, 2007.
6. D. R. Doerge and N. M. Cooray, *Synth. Commun.*, 1991, **21**, 1789.
7. J. Kister, G. Assef, G. Mille and J. Metzger, *Can. J. Chem.*, 1979, **57**, 813.