

# The development of non-heme N<sub>4</sub>-tetradentate Manganese(II) complexes for alcohol oxidation

**V Vermaak**

 **orcid.org 0000-0002-7408-4046**

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|                |               |
|----------------|---------------|
| Supervisor:    | Dr AJ Swarts  |
| Co-supervisor: | Prof DA Young |

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## ABSTRACT

A series of known and novel non-heme N<sub>4</sub>-tetradentate ligands, ***R,R***- and ***S,S***-**L5 - L12**, of the BPMCN type (BPMCN = N,N'-dimethyl-N,N'-bis(2-pyridylmethyl)-(R,R/S,S)-1,2-diaminocyclohexane) containing different N-donors (pyridine or 1-methylimidazole), substituents on the N-donor (methyl or bromo), degrees of amination (secondary or tertiary) and enantiomers (*R,R* and *S,S*), were prepared via an indirect reductive amination and methylation procedure. The ligands were characterised by Fourier transform infrared (FT-IR) and nuclear magnetic resonance (NMR) spectroscopy. The N<sub>4</sub>-tetradentate ligands were reacted with Mn(OTf)<sub>2</sub> to produce the non-heme Mn(II)-complexes, ***R,R***- and ***S,S***-**C1 - C8**, with general formula [(L)Mn(OTf)<sub>2</sub>]. The prepared Mn(II)-complexes were characterised by magnetic susceptibility, melting point analysis, atmospheric pressure chemical ionisation mass spectrometry (APCI-MS), ultraviolet-visible (UV-visible) spectroscopy, single crystal x-ray diffraction (SC-XRD) and CHNS elemental analysis, which confirmed the molecular structure and bulk purity of the complexes. Screening of the complexes against benzyl alcohol oxidation revealed that the tertiary diamine complexes, ***R,R***- and ***S,S***-**C5 - C8**, were more stable than their secondary diamine counterparts, ***R,R***- and ***S,S***-**C1 - C4**. Complexes containing the BMIMCN ligand system, ***R,R***- and ***S,S***-**C8**, showed the highest activity due to the ligands' higher electron donating abilities. Complexes with a ligand system containing a substituent in the C6 position, ***R,R***- and ***S,S***-**C2, C3, C6 and C7** displayed lower catalytic activity due to increased steric constraints in the coordination sphere of the metal. No difference in activity was found between the *R,R*- and *S,S*-configurations of the Mn(II)-complexes, which confirmed the identical active site accessibility as established by solid-state structural analysis. The best performing complex, ***S,S***-**C8**, was used to optimise various reaction parameters, i.e. catalyst, H<sub>2</sub>O<sub>2</sub> and AcOH concentration. It was found that an increase in all of the parameters resulted in an increase in substrate conversion; however, selectivity towards the aldehyde product decreased. This was due to over-oxidation resulting in the formation of benzoic acid in the product mixture. The optimal conditions from the different parameters were consequently used to oxidise a variety of linear, cyclic, bicyclic and benzylic alcohols. Although primary alcohol substrates could be oxidised with high conversions (97%), they suffered from reduced selectivity and side-reactions. It was decided to extend the study towards secondary alcohol substrates and excellent conversions of up to 100% with isolated yields of up to 86% for the ketone products were achieved. In addition, no unwanted side-reactions or selectivity issues were observed. These results indicated that the novel non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes, ***R,R***- and ***S,S***-**C8**, showed high catalytic activity towards a variety of alcohol substrates and, in some cases, proved to be superior to previous Mn(II)-complex systems utilised in catalytic alcohol oxidation.

Key terms: alcohol oxidation, non-heme, N<sub>4</sub>-tetradentate ligand, Mn(II)

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### Chapter 4

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## LIST OF ABBREVIATIONS

|                                    |                                                                                       |
|------------------------------------|---------------------------------------------------------------------------------------|
| APCI-MS                            | Atmospheric pressure chemical ionisation mass spectrometry                            |
| BM                                 | Bohr magnetons                                                                        |
| BMIMCN                             | Bis(1-methylimidazole-2-methyl)-cyclohexane-1,2-diamine                               |
| Bn-TPEN                            | N-benzyl-N,N',N''-tris(2-pyridylmethyl)-ethane-1,2-diamine                            |
| BPMCN                              | Bis(2-pyridylmethyl)-cyclohexane-1,2-diamine                                          |
| BPMEN                              | Bis(2-pyridylmethyl)-ethane-1,2-diamine                                               |
| BQCN                               | Bis(6-quinolylmethyl)cyclohexane-1,2-diamine                                          |
| BQEN                               | Bis(6-quinolylmethyl)-ethane-1,2-diamine                                              |
| $^{13}\text{C} \{^1\text{H}\}$ NMR | Carbon-13 proton decoupled nuclear magnetic resonance                                 |
| DACH                               | 1,2-diaminocyclohexane                                                                |
| FT-IR                              | Fourier transform infrared                                                            |
| $^1\text{H}$ NMR                   | Proton nuclear magnetic resonance                                                     |
| MCP                                | N,N'-dimethyl-bis(2-pyridylmethylpinene)-cyclohexane-1,2-diamine                      |
| MEPP                               | N,N'-dimethyl-bis(2-pyridylmethylpinene)-ethane-1,2-diamine                           |
| N <sub>4</sub>                     | N,N',N'',N'''                                                                         |
| NDO                                | Naphthalene dioxygenase                                                               |
| PDP                                | 2-({(S)-2-[(S)-1-(pyridin-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-yl}methyl)-pyridine |
| PyTACN                             | Pyridylmethyl-1,4,7-triazacyclononane                                                 |
| RDO                                | Rieske dioxygenase                                                                    |
| SC-XRD                             | Single crystal x-ray diffraction                                                      |
| TMTACN                             | N,N',N''-trimethyl-1,4,7-triazacyclononane                                            |
| TON                                | Turnover number                                                                       |
| TPA                                | Tris(2-pyridylmethyl)amine                                                            |
| UV-visible                         | Ultraviolet-visible                                                                   |

## CONFERENCE CONTRIBUTIONS AND PUBLICATIONS

### Conferences attended

Vermaak, V.; Young, D.A.; Swarts, A.J. Regulating the activity of alcohol oxidation via the steric and electronic properties of non-heme manganese(II) catalysts. Poster presented at: 28<sup>th</sup> annual conference of the Catalysis Society of South Africa. 19 - 22 November 2017. Pilanesberg, South Africa.

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# **Chapter 1**

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**Introduction towards catalytic alcohol  
oxidation with non-heme N<sub>4</sub>-tetradentate  
manganese(II) complexes**

# *Chapter 1: Introduction towards catalytic alcohol oxidation with non-heme N<sub>4</sub>-tetradentate manganese(II) complexes*

## **1.1 Introduction**

The activation of hydrocarbon bonds through catalytic oxidation has become an important research area in the last few decades.<sup>1</sup> In addition to alkane and alkene oxidation, the oxidation of alcohol substrates also provides the fine chemicals industry with useful and economically valuable products.<sup>2-4</sup> Even though various methods to oxidise alcohols have proven to be successful, severe oxidisers and expensive and toxic metals are needed.<sup>5-9</sup> To overcome this problem, a new method, which is much greener towards the environment and uses more benign conditions, has been developed. It includes the use of non-heme N<sub>4</sub>-tetradentate manganese(II) complexes that utilise hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) as the terminal oxidant with acetic acid (AcOH) as a co-catalyst.

Inspiration for this research originated from nature, where enzymes, i.e. cytochrome P450 and Rieske dioxygenase, are found.<sup>10</sup> These enzymes are capable of stereoselectively catalysing the oxidation of various hydrocarbon substrates in living organisms. It was found that the Rieske dioxygenase enzymes, containing a non-heme ligand system, show much greater versatility and activity towards the substrates compared to cytochrome P450.<sup>11</sup> From these observations, it was decided to extend research towards non-heme iron(II) complexes for catalytic hydrocarbon oxidation. However, the catalytic activity of the iron(II) complexes was low, which resulted in research shifting towards non-heme manganese(II) complexes that display higher activity.<sup>12</sup>

The only drawback when non-heme manganese(II) complexes are used is the requirement of a carboxylic acid co-catalyst, i.e. AcOH, in the reaction mixture.<sup>9</sup> It is believed that AcOH aids in the activation of H<sub>2</sub>O<sub>2</sub>, which occurs via the heterolysis of the peroxo (O-O) bond to form high valent Mn<sup>V</sup>-oxo (Mn<sup>V</sup>=O) species. Further investigations have found that AcOH also suppresses disproportionation of H<sub>2</sub>O<sub>2</sub>, which results in more H<sub>2</sub>O<sub>2</sub> being available as oxidant.

Another important factor to consider during the development of non-heme manganese(II) complexes is the ligand system used. Changing the nitrogen donor and substituents in the ligand system has an impact on the electronic and steric properties of the catalyst, and ultimately affects the selectivity and activity thereof.<sup>13-14</sup> Numerous studies employing non-heme N<sub>4</sub>-tetradentate manganese(II) complexes have been conducted on the oxidation of alkanes and alkenes.<sup>12-15</sup> However, less research has been conducted on the catalytic oxidation of alcohols with non-heme manganese(II) complexes, which causes a gap in this research field.<sup>5, 16-17</sup>

# *Chapter 1: Introduction towards catalytic alcohol oxidation with non-heme N<sub>4</sub>-tetradentate manganese(II) complexes*

## **1.2 Aims and objectives**

The aim of the current study was to develop novel non-heme N<sub>4</sub>-tetradentate manganese(II) complexes that differ according to their N-donors, substituents, degree of amination and configuration, and to test their performance towards the catalytic oxidation of various alcohol substrates.

The objectives that were set to achieve this goal are as follows:

- a) Synthesis of various non-heme N<sub>4</sub>-tetradentate ligands, which differ according to their N-donors, substituents, degree of amination and configuration.
- b) Synthesis of Mn(OTf)<sub>2</sub> complexes bearing the non-heme N<sub>4</sub>-tetradentate ligands.
- c) Evaluation of the complexes as catalyst precursors in benzyl alcohol oxidation to determine the best performing complex.
- d) Employing the best performing complex for the optimisation of reaction parameters, i.e. catalyst, oxidant (H<sub>2</sub>O<sub>2</sub>) and co-catalyst (AcOH) concentrations to ensure the best oxidation results.
- e) Having established the optimal reaction conditions, catalytic oxidation of various primary and secondary alcohol substrates will be conducted with the best performing complex.

## **1.3 Outline of dissertation**

In *Chapter 2*, a brief history of hydrocarbon oxidation will be given with an emphasis on how inspiration from nature led to the development of non-heme manganese(II) complexes as oxidation catalysts. A discussion regarding the ligand systems used in these complexes will also be included to illustrate how they affect the oxidation reaction.

In *Chapter 3*, the synthesis and characterisation of the novel non-heme N<sub>4</sub>-tetradentate ligand systems with their corresponding manganese(II) complexes that were used in the current study will be discussed.

In *Chapter 4*, the results obtained from screening of the various non-heme N<sub>4</sub>-tetradentate manganese(II) complexes against benzyl alcohol oxidation will be discussed. Optimisation of the reaction parameters will follow and it will end with the results obtained from the oxidation of various primary and secondary alcohol substrates.

*Chapter 1: Introduction towards catalytic alcohol oxidation with non-heme  
N<sub>4</sub>-tetradentate manganese(II) complexes*

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## **Chapter 2**

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**The history and development of  
non-heme manganese(II) complexes for  
catalytic hydrocarbon oxidation**

## *Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation*

### **2.1 Introduction**

A great amount of effort has been spent on the oxidation of hydrocarbons in the last couple of decades by employing various efficient methods to produce alcohols, epoxides and carbonyl compounds. Many of these products serve as important intermediates and feedstocks in the fine chemicals and perfume industry.<sup>1-3</sup> Although there are processes currently being used to oxidise hydrocarbons with great efficiency, they require severe oxidisers, i.e.  $\text{HNO}_3$ ,  $\text{KMnO}_4$  and  $\text{CrO}_3$ , which are hazardous towards the environment.<sup>4-5</sup> In addition, toxic and expensive metals, i.e. Au, Pt, Cr and W, are needed along with high temperatures to ensure the success of the oxidation reaction.<sup>6-8</sup>

To overcome this problem, the chemical research community has found inspiration from nature to develop catalytic systems that are greener, use more benign reaction conditions, and promote better selectivity during catalytic oxidation reactions. Initially, cytochrome P450, which possesses a heme ligand system, was discovered,<sup>9</sup> which led to the discovery of non-heme Rieske dioxygenase enzymes<sup>10</sup> and resulted in the development of non-heme Fe(II)-complexes.<sup>11</sup> Following the development of Fe(II)-systems, several Mn(II)-complexes bearing a non-heme ligand system have emerged, which display higher catalytic activity compared to their Fe(II) counterparts.<sup>12</sup>

Non-heme Mn(II)-complexes have been used in a variety of hydrocarbon oxidations, i.e. alkane and alkene, and showed high activity and selectivity towards a wide variety of substrates.<sup>12-15</sup> However, a significant gap is the lack of research in the field of alcohol oxidation with these types of complexes. Although some alcohol oxidation studies have been conducted, utilising similar ligand systems as those used in alkane and alkene oxidation,<sup>4, 16-17</sup> there is still a need to extend research towards novel ligand systems or derivatives of those already tested to improve catalytic activity and selectivity.

Here follows a brief history of hydrocarbon oxidation and how the development of biomimetic non-heme catalysts changed this research field to become greener and more selective. Although the current non-heme complexes are able to activate hydrocarbon bonds, the risk of over-oxidation still remains a problem. This is because the oxygenated products are more reactive than the substrates.<sup>18</sup> Therefore, the goal is to develop catalysts that can selectively transform substrates into valuable products under benign conditions.

## *Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation*

### **2.2 A brief history of hydrocarbon oxidation**

This section will focus on the origin of hydrocarbon oxidation and how research has developed to improve the activity and selectivity thereof. It is not meant to be exhaustive, due to the vast amount of literature available on this subject. Therefore, only certain studies will be discussed to highlight key developments in hydrocarbon oxidation over the last 160 years.

One of the first experiments conducted on the oxidation of hydrocarbons was reported by Würtz in 1859. According to Evans and Witzemann, Würtz succeeded in oxidising propylene glycol to lactic acid using potassium permanganate ( $\text{KMnO}_4$ ) as the oxidising agent, with platinum (Pt) black as the catalyst.<sup>19</sup> The oxidation reaction involved the regioselective oxidation of a terminal hydroxyl group to a carboxyl group. This began a new era of hydrocarbon oxidation reactions in which different metals and oxidising agents were used to oxidise hydrocarbons. Among the most important hydrocarbons to be oxidised were alkanes, alkenes and alcohols.

The main challenge, however, during these oxidations was to selectively oxidise the substrates, which was not always possible due to over-oxidation. To prevent over-oxidation, experiments had to be conducted at milder conditions. It was speculated that some of the oxidised products from propylene glycol possibly resulted from the selective oxidation of the methyl group, rather than the alcohol group. However, according to Weyl, it was impossible to oxidise a methyl group directly to a secondary ( $2^\circ$ ) alcohol,<sup>19</sup> and oxidation from a methyl group to an aldehyde or carboxylic acids was even rarer. This resulted in little research being done on alkane oxidation and researchers decided to invest more time in the oxidation of alcohols.

An attempt was made in 1914 to employ alkaline hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) for the oxidation of an alcohol-containing compound.<sup>20</sup> Maltose was successfully oxidised to produce glucosido acids – compounds containing a carboxyl ( $\text{COOH}$ ) group – which are the result of over-oxidation. Ethanol was also oxidised in the presence of neutral and alkaline  $\text{KMnO}_4$  solutions to determine the oxidation products.<sup>21</sup> It was found that acetic acid ( $\text{AcOH}$ ) was the major oxidation product during the reaction, which also formed due to over-oxidation.

Although  $\text{KMnO}_4$  and  $\text{H}_2\text{O}_2$  were starting to become common oxidising agents, it was found that the introduction of a metal catalyst improved the rate of the hydrocarbon oxidation reaction.<sup>22</sup> Metal catalysts, hetero- and homogeneous, not only aided in the oxidation of hydrocarbon bonds, but also improved the selectivity and activity of the oxidation reaction.

## *Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation*

### **2.2.1 Development of metal catalysts for hydrocarbon oxidation**

In 1983, the oxidation activity of different metals was tested during a study on the oxidation temperature of various hydrocarbons.<sup>23</sup> Oxidation was carried out using air as the oxidant, and asbestos impregnated with finely divided metals as the catalyst. The metals studied included palladium (Pd), iridium (Ir), rhodium (Rh), gold (Au), ruthenium (Ru), osmium (Os) and Pt. Lightweight alkane (methane up to heptane) gases and alkenes (ethylene, propene and isobutene) were among the main substrates used in the oxidation reaction. It was determined that water (H<sub>2</sub>O) and carbon dioxide (CO<sub>2</sub>) were the only products formed, concluding that complete oxidation of the substrates occurred. During the comparative study, it was also found that the metals studied can be arranged in order of increasing activity: Au, Rh, Ir, Ru, Pt, Pd and Os.

To determine the role of a metal catalyst in the oxidation of alcohols, ethanol, isopropanol and butanol were employed as substrates, with air as the oxidant, and several different metal oxides as catalysts.<sup>24</sup> The catalysts were oxide mixtures of copper (Cu), silver (Ag), vanadium (V), uranium (U), molybdenum (Mb), tungsten (W) and alloys of zinc (Zn), Cu, Pt, Pd, bismuth (Bi), Au and manganese (Mn). The major products of oxidation were found to be aldehydes and ketones, with yields of up to 76%, but no comparison between the ratio of aldehydes and ketones was made, as they were treated as one.

The introduction of metal catalysts was found to not only increase the efficiency of alcohol oxidation, but could also be used for the oxidation of aromatic compounds containing aliphatic substituents. Ethylbenzene was studied as a substrate with oxygen (O<sub>2</sub>) as oxidant in the presence of manganese acetate as the catalyst.<sup>25</sup> Not only was the yield of the acetophenone product increased 10-fold when the catalyst was introduced relative to the blank experiment, but the reaction rate also improved. Other metal acetates, i.e. cobalt (Co), Ni, Fe and V, were also used in the same study to investigate the oxidation of acetaldehyde to AcOH, but showed similar results to that of manganese acetate.

During another study, ethylbenzene was oxidised with oxygen employing MnO<sub>2</sub> as the catalyst, and the reaction was conducted at temperatures above 100 °C.<sup>26</sup> The catalyst increased the reaction rate and yield of acetophenone (major product) more than 20-fold relative to a blank experiment without the catalyst, which demonstrated the importance of the catalyst. Product analysis showed that the alcohol (1-phenylethanol) is produced as by-product. However, the alcohol readily oxidised to the ketone due to over-oxidation, and it was found that benzoic acid is also present in the product mixture.

## *Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation*

The introduction of metal catalysts also became important for the selective oxidation of alkenes, leading to the formation of epoxides. Due to the high reactivity of the epoxide ring, it can further be used as a feedstock for the production of alcohols, lubricants and stabilisers for polymers.<sup>27</sup> A study on the oxidation of ethylene without a catalyst and at elevated temperatures (600 °C) needed four hours to produce 21% ethylene oxide.<sup>28</sup> A comparative study demonstrated that the introduction of molybdenum (Mo) along with barium oxide (BaO) as co-catalyst significantly improved the reaction rate.<sup>29</sup> In only 25 min. and at a lower temperature (120 °C), a 90% conversion of 1-octene, with 95% epoxide selectivity, was achieved when the metal catalyst was present.

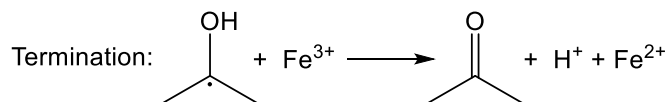
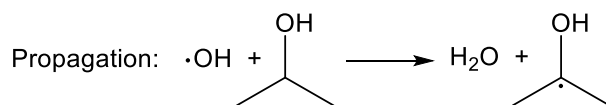
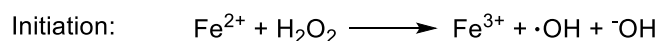
Mn(II)-salts were later employed to also catalyse olefin epoxidation reactions in the presence of bicarbonate as a buffer and H<sub>2</sub>O<sub>2</sub> as oxidant.<sup>30-31</sup> Evaluating the catalyst concentration illustrated that 0.01 mol % of MnSO<sub>4</sub> increased the yield four- to six-fold compared to experiments that did not contain any catalyst. Furthermore, the introduction of MnSO<sub>4</sub> also resulted in higher epoxide yields (94%) compared to other metal sulfates, i.e. Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub> (28%), CuSO<sub>4</sub> (23%) and NiSO<sub>4</sub> (24%). It was found that a variety of cyclic, benzylic and linear (internal and terminal) alkenes could be epoxidised by the MnSO<sub>4</sub> catalyst. However, an excess of H<sub>2</sub>O<sub>2</sub> (5-25 equivalents compared to the substrate) was needed.

From the studies described above, it can be seen that the introduction of a metal catalyst in the reaction mixture has a significant advantage to ensure faster and more selective hydrocarbon oxidations. It was, however, still necessary to make use of high temperatures to produce oxygenated products and over-oxidation was a drawback. As the years progressed, more earth-abundant transition metals, i.e. Fe and Mn, were employed along with a greener oxidant, i.e. H<sub>2</sub>O<sub>2</sub>, which only decomposes into O<sub>2</sub> and H<sub>2</sub>O. Due to H<sub>2</sub>O<sub>2</sub> becoming a more frequently used oxidant, further discussions will mainly focus on the use H<sub>2</sub>O<sub>2</sub> as oxidant.

### **2.2.2 Fenton chemistry**

When Fenton combined H<sub>2</sub>O<sub>2</sub> and Fe<sup>2+</sup>-ions in 1894, he observed that the radical species produced were capable of oxidising hydrocarbons.<sup>32</sup> The combination of these two chemicals became known as Fenton's reagent. Fenton's reagent, as proposed by Haber and Weiss,<sup>33</sup> produced OH radicals (•OH) and it was thought that these radicals serve as the active oxidant during hydrocarbon oxidations, as illustrated in Scheme 2.1.

## Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation



**Scheme 2.1:** Initiation, propagation and termination steps of Fenton chemistry applied to alcohol oxidation.<sup>33-34</sup>

During the propagation step of the oxidation reaction, alkyl radicals are produced as a result of the reaction between the alcohol substrate and  $\cdot\text{OH}$ .<sup>34</sup> The alkyl radicals can then undergo various reactions, i.e. either react with other alkyl radicals to form chains or react with the  $\text{Fe}^{2+}$ -ions to yield carbocations. The carbocations can then be hydrolysed to form alcohols. Later studies on Fenton chemistry determined that the  $\cdot\text{OH}$  does not exist and neither carbon radicals nor aryl adducts are formed. It was found that the  $\text{Fe}^{2+}$ -ions, after interaction with  $\text{H}_2\text{O}_2$ , would rather form  $\text{Fe}^{3+}$ -hydroperoxo ( $\text{Fe}^{3+}\text{-OOH}$ ) intermediates, which can react with and oxidise organic substrates.<sup>35-38</sup>

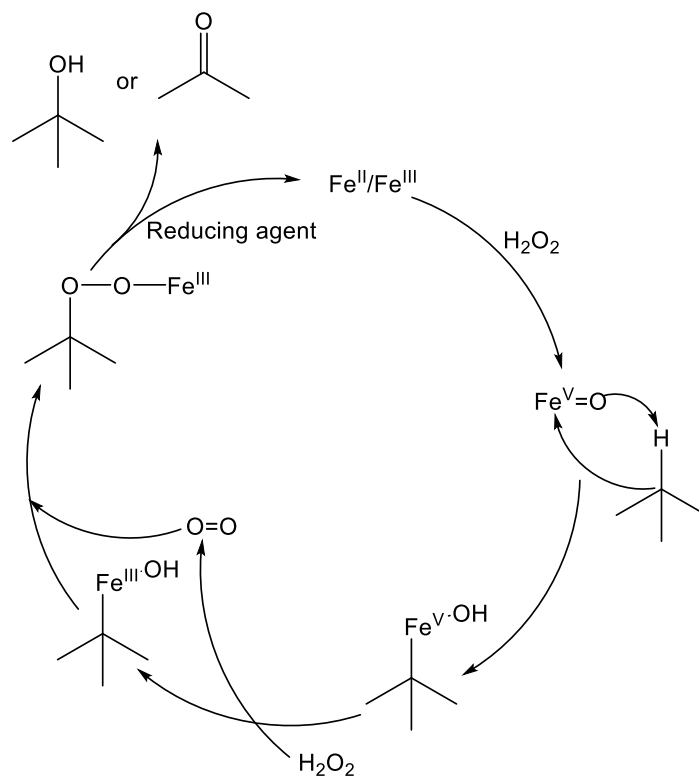
### 2.2.3 Gif chemistry

The hydroxyl radicals produced from the interaction between  $\text{Fe}^{2+}$ -ions and  $\text{H}_2\text{O}_2$  caused controversy and led to the development of a new type of system, known as Gif chemistry. Derek Barton developed the concept of Gif chemistry to provide a much simpler description that omits radicals to explain the abovementioned interaction. Barton hypothesised a world a few billion years ago where the Fe present used  $\text{O}_2$  from photosynthesising plants to oxidise saturated hydrocarbons.<sup>39</sup> Further investigations by Barton into the oxidation of hydrocarbons, using  $\text{H}_2\text{O}_2$  with  $\text{Fe(II)}$ - and  $\text{Cu(II)}$ -ions, illustrated the absence of free carbon radicals as intermediates during the reaction.<sup>40</sup>

According to an earlier study by Kremer, the oxidation of a hydrocarbon occurs when  $\text{Fe}^{2+}$ -ions and  $\text{H}_2\text{O}_2$  react to form a high-valent  $\text{Fe}^{\text{V}}$ -oxo ( $\text{Fe}^{\text{V}}=\text{O}$ ) species from  $\text{Fe}^{\text{III}}\text{-OOH}$ .<sup>41-42</sup> These  $\text{Fe}^{\text{V}}=\text{O}$  species are involved in a phenomenon known as the Sleeping Beauty effect.<sup>40</sup> The terminology comes from the active species that is in a dormant state ('sleeping beauty') until it interacts with the saturated hydrocarbon ('the prince') and oxidises ('kisses') the hydrocarbon bond. Oxidation

## Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation

of the hydrocarbon occurs via the formation of an iron-carbon bond and the rest of the oxidation reaction follows, as illustrated in Scheme 2.2, to produce the active  $\text{Fe}^{\text{V}}=\text{O}$  species again.



**Scheme 2.2: Oxidising saturated hydrocarbons via the Sleeping Beauty effect.<sup>40</sup>**

Barton explained that the  $\text{Fe}^{\text{V}}=\text{O}$  species has a higher affinity for secondary carbons,<sup>43</sup> which is due to a compromise between bond strength considerations and steric effects. Although the steric effects are larger in tertiary carbons compared to primary carbons, the energy required to activate the C-H bond in primary carbons is higher than their tertiary counterparts. For these reasons, tertiary carbons are more readily oxidised than primary carbons are. The products resulting from oxidation are produced when  $\text{O}_2$  is present resulting from  $\text{H}_2\text{O}_2$  decomposition, followed by the addition of a reducing agent. The type of reducing agent used will then determine whether an alcohol or ketone is formed.

The mechanism and active species involved during the hydrocarbon oxidation reaction, as proposed by Barton for Gif chemistry, became more accepted when similar results were obtained in biochemical studies at that time. During investigations on cytochrome P450, it was discovered that an iron species with a high oxidation state ( $\text{Fe}^{\text{IV}}=\text{O}$ ) was an active intermediate in the catalytic cycle of the enzyme.<sup>40</sup>

## *Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation*

### **2.2.4 Cytochrome P450**

The indirect discovery of cytochrome P450 occurred in 1958, when Klingenberg investigated the liver microsomes of rats in which he found pigments.<sup>44</sup> The pigments showed an absorption band at 450 m $\mu$ , determined by difference spectrophotometry, when the microsomes were treated with carbon monoxide (CO). The CO molecule also shows an absorption band at 450 m $\mu$ , confirming that CO was bound to the pigment. Furthermore, it was found that only the reduced pigment had an affinity for CO. Apart from CO, ethylisocyanide and nitric oxide also showed an affinity for the pigment.<sup>45</sup> These observations led to the belief that the pigment was a new microsomal heme protein. The same study revealed that the pigment is labile under aerobic conditions, and a follow-up study confirmed that a reduced form of the pigment rapidly reoxidises when exposed to O<sub>2</sub>.<sup>46</sup> The study also suggested that the pigment had cytochrome b (an Fe-centre bound to protoheme IX) properties and due to the absorption band at 450 m $\mu$  the pigment was labelled cytochrome P450.

Cytochrome P450 was also isolated from the microsomes of the adrenal cortex and found to perform selective alkane and aromatic hydroxylations as well as alkene oxidations.<sup>47</sup> After several mechanistic and structural studies, the classification of cytochrome P450 became clear. Cytochrome P450 was classified as a class of monooxygenase enzymes capable of catalysing the oxidation of various hydrocarbons.<sup>9</sup> The oxidation of the hydrocarbon occurs with the incorporation of only one oxygen atom from O<sub>2</sub> into the substrate.

Structural studies have found that the active site of this enzyme comprises a central Fe<sup>III</sup>-atom surrounded by a N<sub>4</sub>-tetradentate cyclic ligand, as illustrated in Figure 2.1.<sup>11, 48</sup> The ligand is a porphyrin ring, otherwise known as a heme group. An axial Fe-S bond is connected via a cysteine residue, which links the active site to the protein part of the enzyme. The other axial position assists in the binding of O<sub>2</sub> for the initiation of oxidation reactions.

Another enzyme, also responsible for the oxidation of hydrocarbons, is present in soil micro-organisms, called *Pseudomonads*. They thrive in mineral salts that are rich in naphthalene, because they are used as a food source that they are able to metabolise.<sup>49</sup> During metabolic reactions, dihydroxylation reactions are performed on the naphthalene substrate by enzymes known as Rieske oxygenases. Only a small percentage of Rieske oxygenases are monooxygenase enzymes, while the majority function as dioxygenases.<sup>50</sup>

## Chapter 2: The history and development of non-heme manganese(II) complexes for catalytic hydrocarbon oxidation

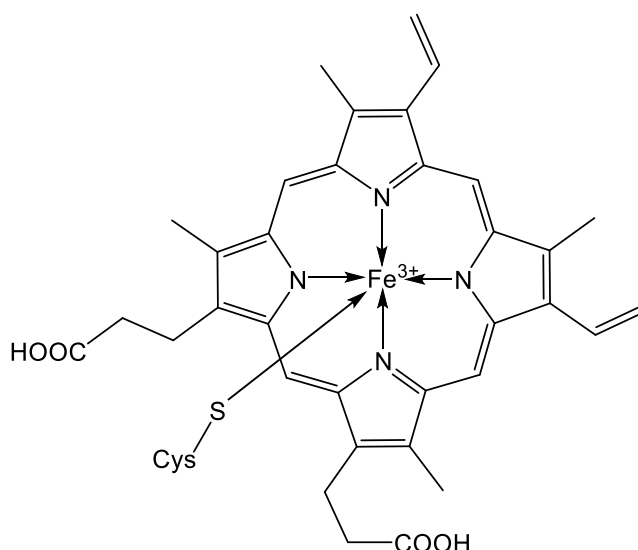


Figure 2.1: Structure of cytochrome P450.<sup>48</sup>

### 2.2.5 Rieske dioxygenases

Rieske dioxygenase (RDO) enzymes are non-heme enzymes, meaning that they possess a central metal atom that is not surrounded by a porphyrin ring. Instead of a porphyrin ring, the coordination sphere of the metal can contain other groups, such as those found in naphthalene 1,2-dioxygenase (NDO). NDO is an  $\alpha_3\beta_3$  hexamer with an alpha subunit containing a  $\beta$ -sheet within the active centre. The active site consists of an iron(II) ion surrounded by two histidines (His<sub>208</sub> and His<sub>213</sub>), a bidentate aspartic acid (Asp<sub>362</sub>) and a H<sub>2</sub>O molecule in the axial position.<sup>10</sup> The other axial position is available for substrate binding and activation. The structure of NDO is illustrated in Figure 2.2.

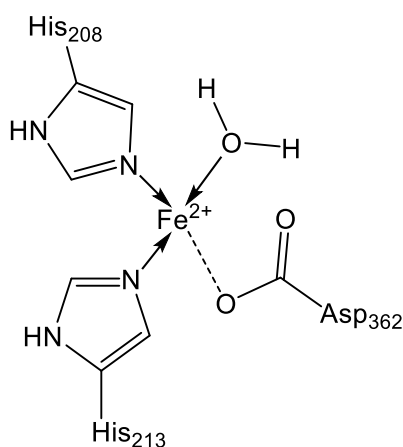
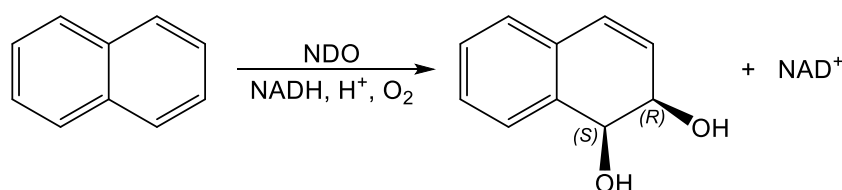


Figure 2.2: Structure of naphthalene 1,2-dioxygenase.<sup>10</sup>

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NDO has the ability to stereoselectively dihydroxylate aromatic substrates using atmospheric oxygen.<sup>50</sup> It has been observed that both the oxygen atoms from O<sub>2</sub> are incorporated into the final product and this is where the dioxygenase terminology comes from. One of the most notable reactions of NDO is the stereoselective dihydroxylation of naphthalene to cis-(1*R*,2*S*)-1,2-dihydro-1,2-naphthalenediol. The product was observed when a mutant strain of *Pseudomonas putida* produced the naphthalene diol from naphthalene.<sup>51</sup> Naphthalene is oxidised by NDO, according to the catalytic reaction in Scheme 2.3, but Rieske dioxygenases are also responsible for the catalytic dihydroxylation of benzylic substrates.<sup>52</sup>



**Scheme 2.3: The catalytic oxidation of naphthalene with NDO.**<sup>51</sup>

The non-heme enzymes are important when it comes to their oxidative catalytic properties. They tend to show high reactivity and selectivity during various oxidation reactions of natural hydrocarbons, which makes them attractive for industrial applications.<sup>10, 50</sup> RDO enzymes also display greater versatility than cytochrome P450, because of their ability to catalyse a variety of oxidative transformations.<sup>53</sup> The abovementioned properties started an era where new metal catalysts with non-heme N<sub>4</sub>-tetradentate ligand systems were synthesised to mimic non-heme enzymes found in nature.<sup>54</sup>

### 2.3 Development of biomimetic non-heme catalysts for hydrocarbon oxidation

Much research has gone into the investigation of bio-inspired catalysis with an emphasis on mimicking metalloenzymes involved in oxidation reactions.<sup>55</sup> These catalytic reactions are conducted by employing H<sub>2</sub>O<sub>2</sub> as an oxidant for the activation of various hydrocarbon bonds, i.e. C-H, C=C and C-OH bonds.<sup>11</sup> Although high activity and yields are important during these reactions, selectivity should also be considered a priority.

The selectivity can be affected by altering the ligand system, which, in turn, affects the stabilisation of the active M<sup>V</sup>=O, M<sup>IV</sup>=O or M<sup>III</sup>-OOH intermediates in the catalytic cycle, with M representing Fe or Mn.<sup>11</sup> Another result of altering the ligand system is a change in the activity of the catalyst. The main advantage to developing these catalysts is that they are non-toxic, environmentally friendly and energy efficient.<sup>11</sup> Below follows a description of the various Fe(II)- and Mn(II)-catalyst systems that have been used to catalyse alkane, alkene and alcohol

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oxidation reactions. More emphasis will be placed on Mn(II)-systems as they are the focus of the current study.

### 2.3.1 Non-heme Fe(II)-based catalysts

Fe is an environmentally friendly and non-toxic metal, which makes it a suitable candidate for catalytic reactions.<sup>56</sup> It is also a cheap source of metal because it is found in copious amounts in the earth's crust. These properties make it evident that Fe-complexes show good potential for being used as catalysts during hydrocarbon oxidation.<sup>57</sup> Several hydrocarbon oxidations, i.e. aliphatic hydroxylation, alkene epoxidation and alcohol oxidation, have been performed over the years using non-heme Fe(II)-complexes as catalysts. Here follows a short summary of the ligand systems and their corresponding complexes used for these catalytic oxidations, and how their electronic and steric properties affected the reaction.

#### 2.3.1.1 Alkane oxidation

In 1997, one of the first stereoselective aliphatic hydroxylation studies with an Fe(II)-complex was reported. The study employed a variety of hydrocarbon substrates, i.e. cyclohexane, 2-hexene and derivatives thereof. Aliphatic hydroxylation was achieved using oxidant-limiting conditions with 1 mole%  $\text{H}_2\text{O}_2$  as the oxidant and a tris(2-pyridylmethyl)amine (TPA) ligated Fe(II)-complex of the type  $[(\text{TPA})\text{Fe}(\text{MeCN})_2](\text{ClO}_4)_2$  (Figure 2.3) to catalyse the oxidation reaction in 15 minutes at room temperature.<sup>53</sup> The reactions yielded turnover numbers (TONs) of up to 3.6 for the alcohol products. It was, however, found that some of the alcohol products over-oxidised to the ketone product.

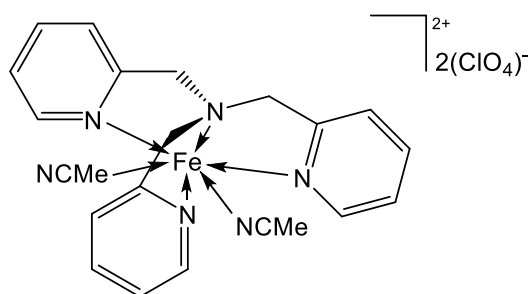


Figure 2.3:  $[(\text{TPA})\text{Fe}(\text{MeCN})_2](\text{ClO}_4)_2$  complex used to catalyse aliphatic hydroxylation.<sup>53</sup>

As the years progressed, several other ligand systems have been utilised to synthesise non-heme Fe(II)-based complexes. These complexes showed excellent activity and stereoselectivity when alkanes were catalytically oxidised. The ligand systems utilised in these

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complexes were chosen because they are able to stabilise the active high valent  $\text{Fe}^{\text{V}}$ -intermediate via the electron donating properties of their N-donor moieties.<sup>11</sup>

An  $\text{Fe}(\text{II})$ -complex bearing pyridylmethyl-1,4,7-triazacyclononane (PyTACN) as a  $\text{N}_4$ -tetradentate ligand,  $[(\text{PyTACN})\text{Fe}(\text{OTf})_2]$ , as shown in Figure 2.4, was found to be an active catalyst in the hydroxylation of alkanes.<sup>58</sup> A 1000 equivalents of cyclohexane compared to the catalyst were oxidised under oxidant-limiting conditions, employing 10 to 100 equivalents of  $\text{H}_2\text{O}_2$  over 30 minutes at 25 °C. Employing these reaction conditions, a maximum TON of 64 towards cyclohexanol could be achieved, which is already better than the  $[(\text{TPA})\text{Fe}(\text{MeCN})_2](\text{ClO}_4)_2$  complex, due to the smaller amount of  $[(\text{PyTACN})\text{Fe}(\text{OTf})_2]$  complex needed. It was also found that a decrease in the alcohol:ketone ratio occurred when the amount of  $\text{H}_2\text{O}_2$  increased, which was concluded to be due to over-oxidation because the alcohol product is more reactive than the alkane substrate.

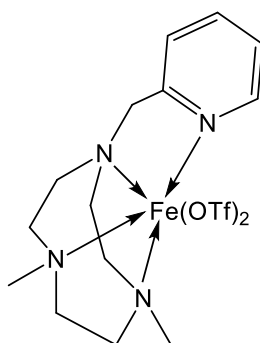


**Figure 2.4:**  $[(\text{PyTACN})\text{Fe}(\text{OTf})_2]$  complex to catalyse the hydroxylation of cyclohexane.<sup>58</sup>

It was later seen that a trend towards bis(aminopyridyl) ligands and derivatives thereof started to emerge. An  $\text{Fe}(\text{II})$ -complex bearing a 2-((S)-2-[(S)-1-(pyridin-2-ylmethyl)pyrrolidin-2-yl]pyrrolidin-1-yl)methyl)pyridine (PDP) ligand system,  $[(\text{PDP})\text{Fe}(\text{MeCN})_2](\text{SbF}_6)_2$  (Figure 2.5), with 1.2 equivalents of  $\text{H}_2\text{O}_2$  was used to catalyse the hydroxylation of 4-methylcyclohexyl pivalate, an aliphatic compound.<sup>59</sup> Unfortunately, only 15% conversion towards 4-hydroxy-4-methylcyclohexyl pivalate was achieved after 30 minutes at room temperature. Upon the addition of 0.5 equivalents of  $\text{AcOH}$ , the percentage conversion increased to 42%. A similar observation in percentage conversion was made when bis(2-pyridylmethyl)-ethane-1,2-diamine (BPMEN) was utilised as the ligand system (41% from 12%), but the selectivity (calculated as yield divided by conversion) was higher (90% compared to 60%). The only drawback was the high amount of complex needed in the reaction (5 mole%), which highlighted the difficulty of activating C-H bonds for oxidation.

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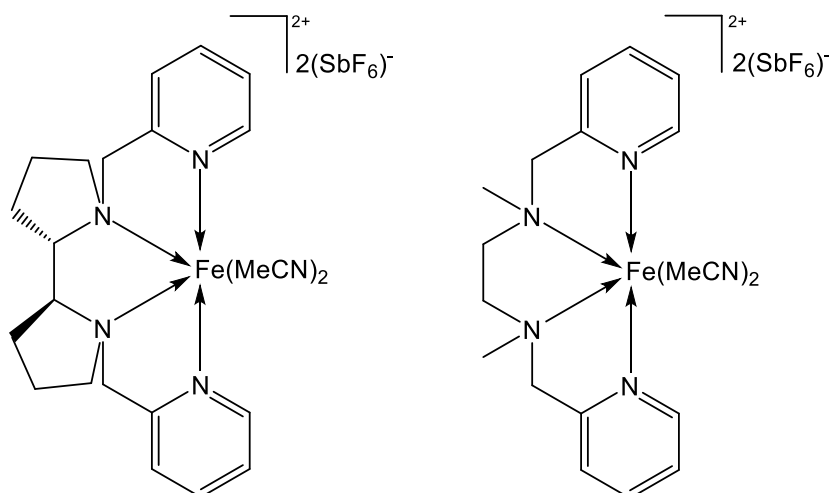


**Figure 2.5:**  $[(\text{PDP})\text{Fe}(\text{MeCN})_2](\text{SbF}_6)_2$  and  $[(\text{BPMEN})\text{Fe}(\text{MeCN})_2](\text{SbF}_6)_2$  complexes used to catalyse the hydroxylation of alkanes.<sup>59</sup>

Gomez and co-workers later employed a variety of ligand systems, i.e. PyTACN, BPMEN and a newly developed derivative containing a pinene substituent, N,N'-dimethyl-bis(2-pyridylmethylpinene)-cyclohexane-1,2-diamine (MCPP, Figure 2.6) and N,N'-dimethyl-bis(2-pyridylmethylpinene)-ethane-1,2-diamine (MEPP), to determine their effectiveness in catalytic hydrocarbon oxidation.<sup>60</sup> Catalytic hydroxylation of cis-1,2-dimethylcyclohexane (cis-DMCH) was conducted using 1 mole% catalyst concentration, 1.2 equivalents  $\text{H}_2\text{O}_2$  and 50 mole% AcOH over 16 minutes at 0 °C. It was found that the complexes containing the MCPP and MEPP ligands provided the highest alcohol product yield, 57% and 49%, respectively, of all the tested ligands, with PyTACN coming in third place. The researchers concluded that a stabilisation effect from the bulky pinene groups may be the reason for their higher activity.

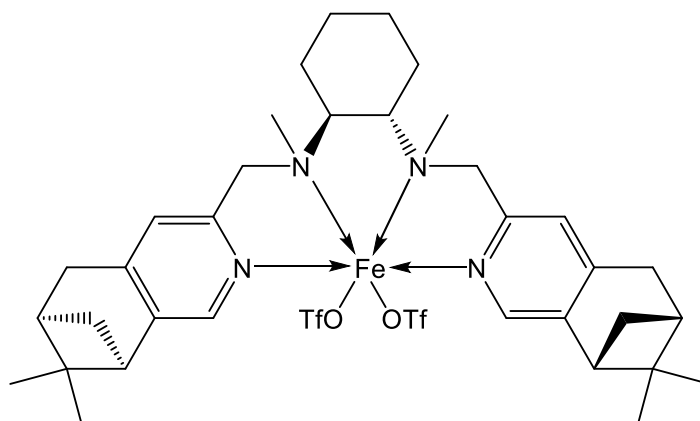


**Figure 2.6:**  $[(\text{MCPP})\text{Fe}(\text{OTf})_2]$  complex used to catalyse the oxidation of cis-DMCH.<sup>60</sup>

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### 2.3.1.2 Alkene oxidation

Various non-heme Fe(II)-complexes containing similar ligands to those described previously have also been utilised in alkene oxidation studies. In one study, the epoxidation and dihydroxylation of cyclic and linear alkenes were studied utilising BPMEN and TPA ligand systems coordinated to Fe(OTf)<sub>2</sub> precursors.<sup>61</sup> A catalyst concentration of 0.5 mole% was used with 1.5 equivalents of H<sub>2</sub>O<sub>2</sub> over 30 minutes at room temperature. No significant difference between the complexes was found regarding percentage conversion. However, the complex bearing a BPMEN ligand system showed greater selectivity towards epoxide formation (11:1) compared to TPA, which showed similar selectivity towards epoxide and diol formation ( $\approx$  1:1). Furthermore, the addition of AcOH did not only increase conversion by 21% for both, but also resulted in better selectivity towards the epoxide product (225:1 and 45:1). This study demonstrated that non-heme Fe(II)-complexes show higher activity towards alkene oxidation compared to alkane oxidation resulting in less catalyst and oxidant needed during the reaction.

Zang and co-workers later studied the catalytic cis-dihydroxylation of alkenes with the use of a bis(6-quinolylmethyl)cyclohexane-1,2-diamine (BQCN) ligated non-heme Fe(OTf)<sub>2</sub> complex, as illustrated in Figure 2.7, which was studied along with derivatives thereof containing different backbones and substituents.<sup>62</sup> The reaction utilised three equivalents of H<sub>2</sub>O<sub>2</sub> as the oxidant and the catalyst concentration was 3 mole%, which contradicts the observation made previously regarding less catalyst load and H<sub>2</sub>O<sub>2</sub> needed for alkene oxidation. In this study, however, the need for higher catalyst and oxidant concentrations is caused by the bulky groups that form part of the ligand system, decreasing access to the active centre.

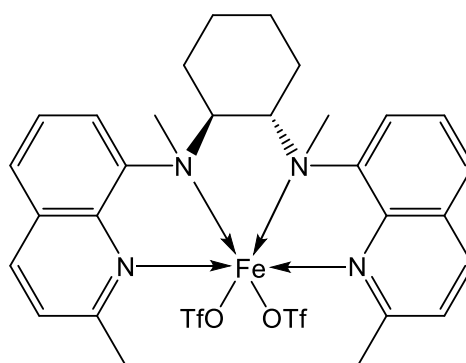


Figure 2.7: [(BQCN)Fe(OTf)<sub>2</sub>] complex utilised for alkene oxidation.<sup>62</sup>

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### 2.3.1.3 Alcohol oxidation

Although numerous studies have been conducted on alkane and alkene oxidation with non-heme Fe-complexes, research dedicated to the oxidation of alcohols is comparatively low. One study employed the use of different bidentate  $\alpha$ -iminopyridine ligated  $\text{Fe}(\text{OTf})_2$  complexes of the type  $\text{ML}_2\text{X}_2$ , as shown in Figure 2.8, in which the ligands occupy four positions in the coordination sphere of the metal, similar to tetradentate ligands.<sup>56</sup> Oxidation of benzylic, linear and cyclic alcohols (all secondary) was conducted with four equivalents of *tert*-butyl hydroperoxide (t-BuOOH) instead of the usual  $\text{H}_2\text{O}_2$  with 3 mole% catalyst concentration. Unfortunately, only 23 to 47% conversion towards the ketone product could be achieved after four hours and 30 minutes at room temperature.

In a different study, phenylene dipicolineamide-ligated  $\text{FeCl}_2$  systems, which differed according to the backbone substituents and counter ions (Figure 2.9), were utilised to oxidise several primary and secondary linear, benzylic and cyclic alcohols using 1.5 equivalents of t-BuOOH as oxidant.<sup>63</sup> However, a co-catalyst, i.e. N-hydroxyphthalimide, was also included. Although excellent conversions of up to 100% could be achieved with a 2 mole% catalyst concentration, reaction times were long (7 hours) and elevated temperatures were required (50 °C). The other drawback was the occurrence of over-oxidation towards the carboxylic acid product when primary alcohols were used as substrates.

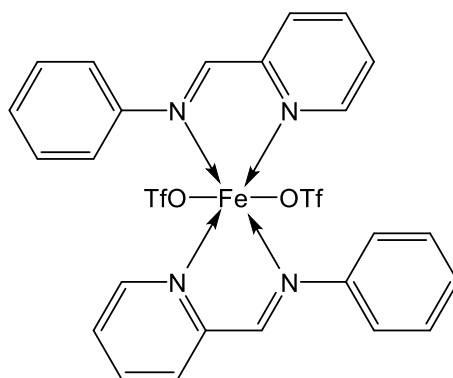


Figure 2.8:  $\alpha$ -iminopyridyl ligated  $\text{Fe}(\text{OTf})_2$  complex used for alcohol oxidation.<sup>56</sup>

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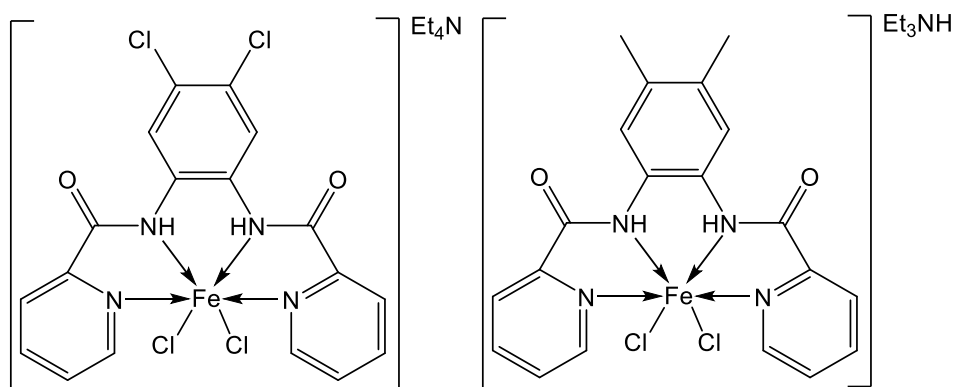


Figure 2.9: Phenylene dipicolineamide ligated  $\text{FeCl}_2$  complexes used in the oxidation of alcohols.<sup>63</sup>

### 2.3.2 Non-heme Mn(II)-based catalysts

From the abovementioned studies, it is clear that numerous studies have been conducted on catalytic hydrocarbon oxidation with the use of non-heme Fe(II)-complexes, which displayed high activity and selectivity. It was, however, found that Mn(II)-salts and their complexes displayed higher activity compared to their Fe counterparts.<sup>12, 31, 64</sup>

A thermodynamic study was conducted to compare the active Fe and Mn intermediates during oxidation reactions.<sup>64</sup> It was found that the activation energy of Mn(II)-species to the active high valent  $\text{Mn}^{\text{IV}}=\text{O}$  species is significantly lower compared to that of Fe(II) to  $\text{Fe}^{\text{III}}\text{-OOH}$  activation, as illustrated in Figure 2.10. The activation of Mn(II) is therefore much easier compared to Fe(II), highlighting the increased activity seen for Mn(II)-complexes during hydrocarbon oxidation.

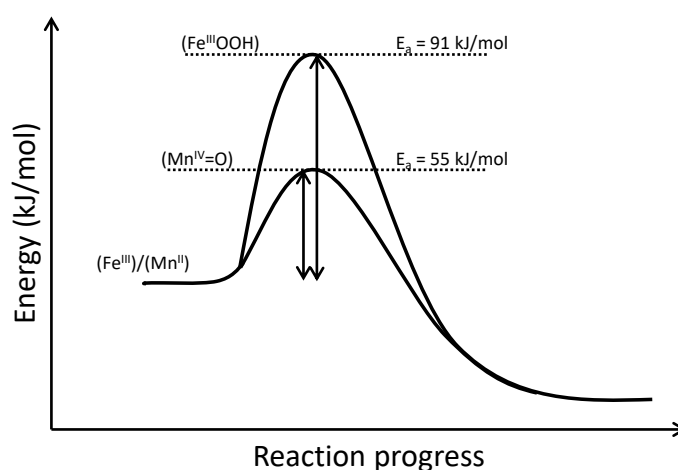


Figure 2.10: Difference in the activation energy of Fe(II)- and Mn(II)-complexes.<sup>64</sup>

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This study was supported by experimental evidence when oxidation reactions employing Mn(II)- and Fe(II)-complexes, under similar conditions, were compared. Catalytic epoxidation of terminal and internal alkenes with non-heme Fe(II)- and Mn(II)-complexes containing a PDP ligand system and H<sub>2</sub>O<sub>2</sub> as oxidant was conducted.<sup>14</sup> Under similar reaction conditions, it was found that higher percentage conversions for several alkene substrates were achieved with the Mn(II)-complex compared to the Fe(II)-complex, suggesting superior activity for Mn. Furthermore, the Mn(II)-complex required a lower catalyst (0.1 mole%) and lower oxidant concentration (1.3 equivalents), while the Fe(II)-complex needed 1 mole% and two equivalents, respectively.

From these results, it became apparent that it is better to utilise non-heme Mn(II)-complexes in catalytic hydrocarbon oxidations rather than non-heme Fe(II)-complexes. This resulted in numerous studies being conducted on alkane, alkene and alcohol oxidation with the use of non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes.

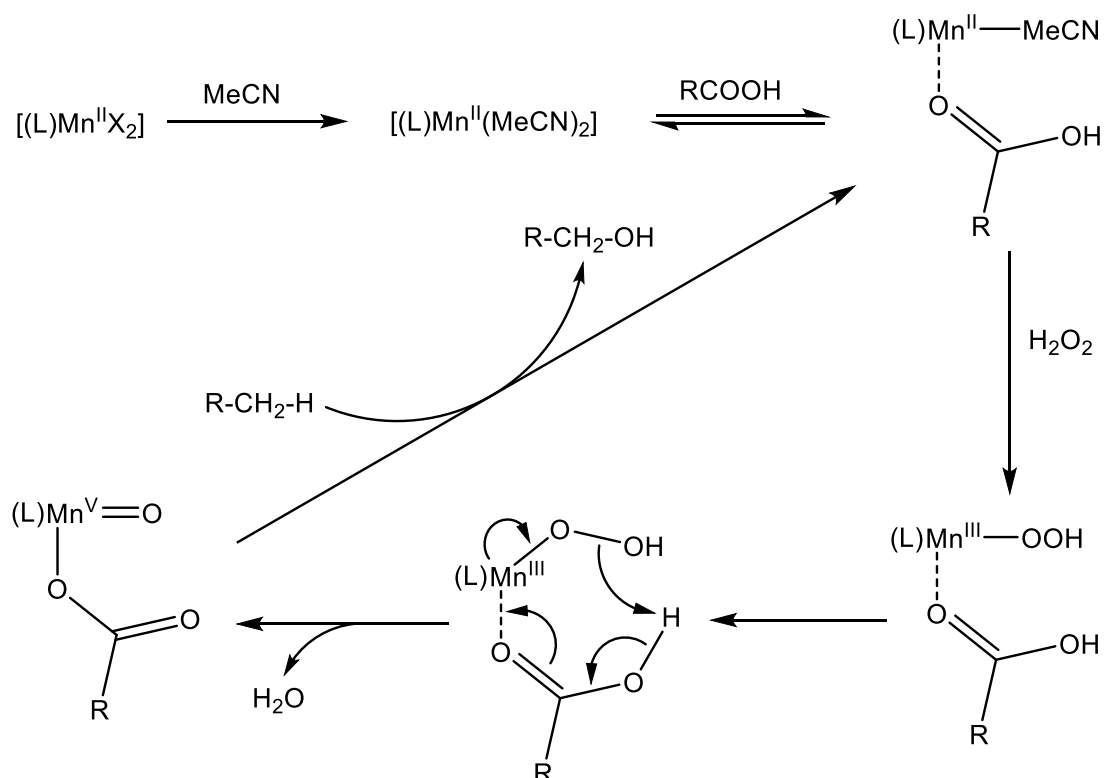
### **2.3.2.1 Requirement of carboxylic acid as co-catalyst**

Although non-heme Mn(II)-complexes show higher activity than their Fe(II) counterparts do, they have one drawback. They require the use of a co-catalyst in the form of a carboxylic acid (RCOOH).<sup>12-13</sup> The reason behind this observation is still vague, but studies have illustrated that it not only facilitates the activation,<sup>14</sup> but also suppresses the disproportionation of H<sub>2</sub>O<sub>2</sub>.<sup>12</sup>

When it facilitates the activation process, it promotes the fast heterolysis of the peroxo (O-O) bond present in the intermediate Mn<sup>III</sup>-OOH species.<sup>12, 14</sup> Heterolysis of the O-O bond leads to the formation of a more active high valent Mn<sup>V</sup>=O species, which becomes the active oxidant responsible for hydrocarbon oxidation, as shown in Scheme 2.4.

The pathway described in Scheme 2.4 is a generalised mechanism for the catalytic oxidation of alkanes and alkenes with non-heme Mn(II)-complexes assisted by a carboxylic acid co-catalyst. Several catalytic oxidation studies conducted on alkane and alkene substrates with these complexes have shown that the abovementioned pathway is followed via the different Mn-species illustrated. However, no evidence is yet available to support this mechanistic pathway during catalytic alcohol oxidation with non-heme Mn(II)-complexes. Here follows a discussion of the catalytic oxidation studies of alkanes, alkenes and the less studied alcohol substrates, employing non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes as the catalyst utilising a terminal oxidant and carboxylic acid co-catalyst.

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**Scheme 2.4: Formation of the active high valent  $Mn^V=O$  species responsible for hydrocarbon oxidation via the carboxylic acid assisted pathway.<sup>11, 14</sup>**

### 2.3.2.2 Alkane oxidation

The catalytic oxidation of alkanes with non-heme Mn(II)-complexes has been studied rather intensely due to the challenge of activating 'inert' C-H bonds. Some of the non-heme aminopyridine ligand systems utilised for alkane oxidation include Mn-triflate complexes ligated by bis(6-quinolylmethyl)-ethane-1,2-diamine (BQEN) and BPMCN, as illustrated in Figure 2.11.<sup>65</sup> In a comparative study employing these two complexes, cyclohexane, 1,2-dimethylcyclohexane (DMCH) and adamantane were oxidised under oxidant-limiting conditions, using peracetic acid (AcOOH) as oxidant (100 equivalents per Mn). Yields of up to 78% were achieved in 20 minutes at 25 °C utilising 0.2 mole% catalyst and it was found that the BQEN complex showed higher activity (3-11% higher yields) than BPMCN.

The oxidation of other hydrocarbon substrates, i.e. alkenes and alcohols, was also investigated and it was found that the complexes showed a higher affinity for alkenes and alcohols compared to alkanes. It was concluded that C-H bonds are more inert compared to C=C and C-OH bonds. This statement was supported during a comparative kinetic study at 25 °C where a N-benzyl-N,N',N''-tris(2-pyridylmethyl)-ethane-1,2-diamine (Bn-TPEN) ligated  $Mn(OTf)_2$

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complex, shown in Figure 2.12, was screened against different hydrocarbons, which had similar structures.<sup>66</sup> It was found that the rate constant ( $k$ ) for hydrocarbon oxidation with a Bn-TPEN ligated non-heme Mn(II) complex increases in the following order: alkane ( $2.7 \times 10^{-2}$ ) < alcohol ( $4.9 \times 10^{-2}$ ) < aromatic ( $9.4 \times 10^{-2}$ ) < alkene ( $3.2 \times 10^{-1}$ ). When ultraviolet-visible (UV-visible) spectroscopy was employed, it was found that the activation of C-H bonds is the result of an active mononuclear  $\text{Mn}^{\text{IV}}=\text{O}$  complex.

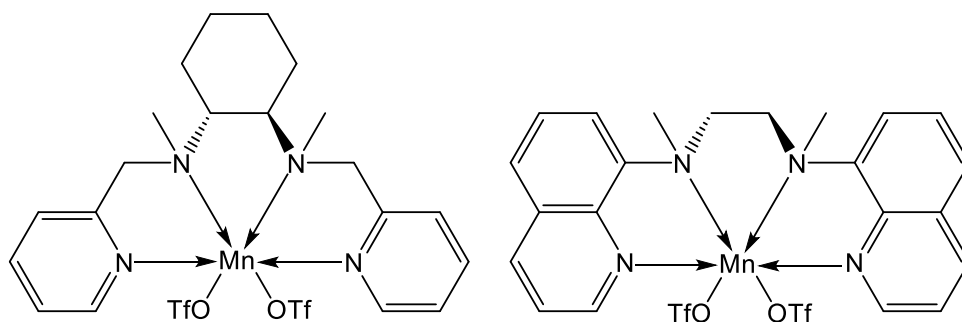


Figure 2.11:  $[(\text{BPMCn})\text{Mn}(\text{OTf})_2]$  and  $[(\text{BQEN})\text{Mn}(\text{OTf})_2]$  complexes used to catalyse the oxidation of alkanes, olefins and alcohols.<sup>65</sup>

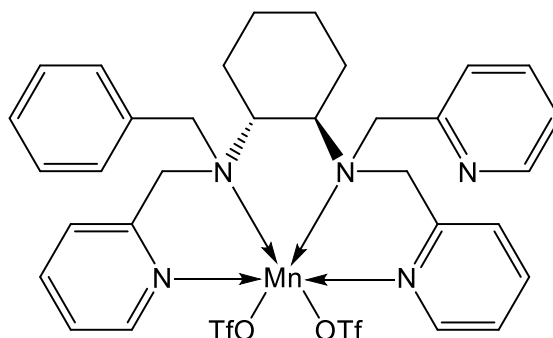


Figure 2.12:  $[(\text{Bn-TPEN})\text{Mn}(\text{OTf})_2]$  complex used to catalyse the oxidation of alkanes, olefins and alcohols.<sup>66</sup>

The utilisation of N,N',N''-trimethyl-1,4,7-triazacyclononane (TMTACN) ligated Mn(II)-complexes, as shown in Figure 2.13, has also been employed to catalytically oxidise alkanes. One study made use of an *in situ* prepared TMTACN ligated  $\text{MnSO}_4$  complex to oxidise cyclohexane, DMCH and hexane with  $\text{H}_2\text{O}_2$  (4.5 equivalents).<sup>67</sup> A catalyst concentration of 0.44 mole% was employed with sodium oxalate ( $\text{Na}_2\text{C}_2\text{O}_4$ ) as co-catalyst (1:1 with catalyst). Cyclohexane could be oxidised with 78% conversion in three hours at room temperature, while the other substrates showed much lower conversions. The high amount of oxidant needed illustrates the difficulty of activating C-H bonds.

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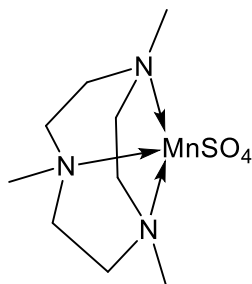


**Figure 2.13: [(TMTACN)MnSO<sub>4</sub>] complex used for catalytic oxidation of alkanes.<sup>67</sup>**

Other non-heme Mn(II) ligand systems used for alkane oxidation include derivatives of BPMEN and BPMCN. Insertion of a pyrrolidine backbone increased the percentage conversion during the oxidation of various alkane substrates.<sup>15</sup> Using a 0.1 mole% catalyst concentration with 1.3 to 2.5 equivalents of H<sub>2</sub>O<sub>2</sub> and AcOH (3.5 - 14 equivalents) as co-catalyst, high conversions of 87% for cyclohexane, 97% for DMCH and 71% for adamantane could be achieved in two to four hours at 0 °C. The ligand containing a pyrrolidine backbone instead of cyclohexane (BPMCN) performed better,<sup>68</sup> while the ligand with a bipyrrrolidine backbone performed the best. Another study confirmed the observation that the pyrrolidine backbone is better than its cyclohexane counterpart.<sup>12, 68</sup> Ethylbenzene was oxidised with 0.5 mole% catalyst concentration, 3.5 and 14 equivalents of H<sub>2</sub>O<sub>2</sub> and AcOH, respectively, over 30 minutes at room temperature, to produce the following percentage conversions: 6% for BPMCN and 15% for the pyrrolidine ligated complex.

Further investigation, using the same conditions, resulted in the observation that exchanging the pyridine donors with benzimidazole donors increased the percentage conversion even further to 68%. The increase in activity found from the change in ligand backbone and donors is illustrated in Figure 2.14. An analysis of these results indicates that an increase in the electron-donating properties of the backbone or ligand system towards the coordinated N-atom increases the activity of the complex.

From the abovementioned studies, it can be seen that rather high oxidant and catalyst concentrations are needed to activate C-H bonds. However, studies are still being conducted to find new ligand systems that can oxidise alkane substrates with even better efficiency. On the other hand, as will be seen below, the oxidation of alkene substrates is much easier due to their higher reactivity compared to alkane substrates.

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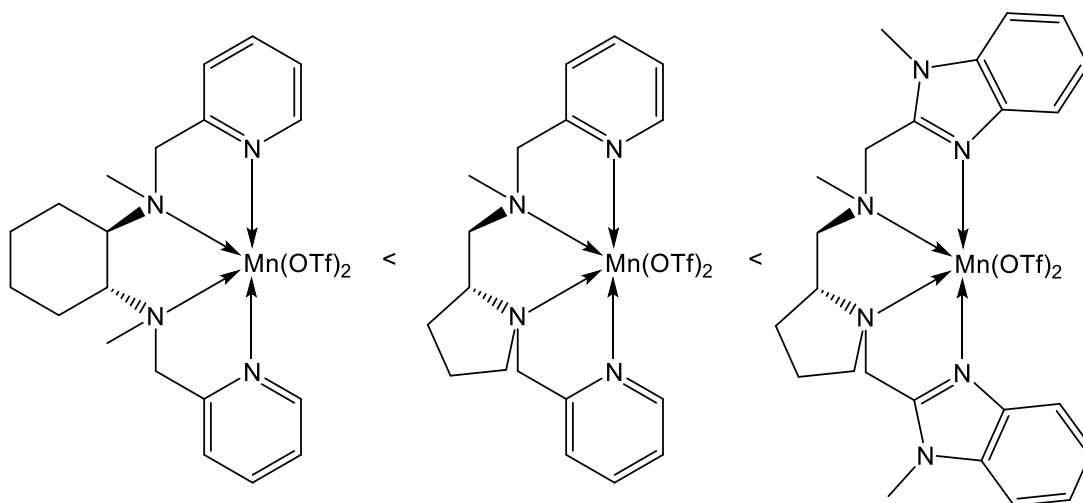


Figure 2.14: Increase in the activity of  $\text{Mn}(\text{OTf})_2$  complexes with a change in ligand system.<sup>12, 15, 68</sup>

### 2.3.2.3 Alkene oxidation

The catalytic oxidation of alkene substrates by non-heme  $\text{Mn}(\text{II})$ -complexes has been studied intensely due to the complexes' high activity and affinity towards these substrates. The use of TACN- and BPMCN-ligated  $\text{Mn}(\text{II})$ -complexes and derivatives thereof has been widely used for the oxidation of alkenes. A TMTACN ligand system was developed to study the oxidation of various aliphatic alkenes (terminal and internal).<sup>69</sup> Alkenes were oxidised with 0.15 mole% catalyst, 1.5 to three equivalents  $\text{H}_2\text{O}_2$  and 0.45 mole% oxalic acid as the co-catalyst. Reaction times varied between 20 minutes and two hours and excellent yields of up to 99% were obtained at 5 °C.

Results from Garcia-Bosch and co-workers illustrated that the introduction of a pyridyl substituent on one of the N-donors in TMTACN, resulting in PyTACN, also results in a complex with high activity when coordinated to  $\text{Mn}(\text{OTf})_2$ .<sup>70</sup> Only 0.1 to 0.15 mole% catalyst was needed with 1.4 equivalents of  $\text{AcOOH}$  to oxidise several aliphatic (linear and cyclic) and benzylic alkenes in percentage conversions above 89% in one hour at 0 °C.

In a follow-up study,  $\text{Mn}(\text{II})$ -complexes containing the following ligand systems: PyTACN, BPMCN and BPMEN, were used for the catalytic oxidation of several benzylic and aliphatic (linear and cyclic) alkenes.<sup>13</sup> Using 0.1 mole% complex with 1.1 to 1.4 and 14 equivalents of  $\text{H}_2\text{O}_2$  and  $\text{AcOH}$ , respectively, over 30 minutes at 0 °C, the following comparative results were obtained. Using  $[(\text{PyTACN})\text{Mn}(\text{OTf})_2]$  as the catalyst resulted in higher percentage conversions for all the substrates compared to  $[(\text{BPMCN})\text{Mn}(\text{OTf})_2]$ . Furthermore, it was seen that  $[(\text{BPMEN})\text{Mn}(\text{OTf})_2]$  resulted in the lowest activity. Murphy and his group earlier found that this

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observation is due to the [(BPMEN)Mn(OTf)<sub>2</sub>] complex being less thermodynamically and kinetically stable than the [(BPMCEN)Mn(OTf)<sub>2</sub>] complex when exposed to acids and air.<sup>71</sup> This is because the formation constant for [MnEDTA]<sup>2-</sup> is lower by a factor of four compared to that of [MnCDTA]<sup>2-</sup> where EDTA is trans-ethyl-1,2-diamine tetraacetic acid and CDTA the cyclohexyl derivative. During the latter study, it was found that using the [(BPMCEN)Mn(OTf)<sub>2</sub>] complex (0.1 mole%) with AcOOH (1.2 equivalents), instead of H<sub>2</sub>O<sub>2</sub> and AcOH, also results in excellent gas chromatography (GC) yields of up to 99% when various benzylic and aliphatic alkene substrates are oxidised.<sup>71</sup> However, reaction times, i.e. five minutes, were much shorter compared to previous studies.

Garcia-Bosch and co-workers extended epoxidation studies towards the use of Mn(II)-complexes containing different substituents and backbones.<sup>72</sup> A preliminary study on styrene oxidation with 0.1 mole% catalyst, 1.2 equivalent H<sub>2</sub>O<sub>2</sub> and 14 equivalents AcOH over a period of 30 minutes at 0 °C revealed that changing the cyclohexane backbone with bipyrrrolidine increased the conversion by ~ 10%. Exchanging the pyridine donors with pinene donors increased the conversion even further. It was then decided to use pinene donors along with a pyrrolidine backbone as the ligand system in a Mn(OTf)<sub>2</sub> complex and test its versatility towards various benzylic and cyclic alkenes. Excellent conversions of up to 100% could be achieved using the same conditions as mentioned above. Further studies found that the introduction of electron-donating groups (EDG), i.e. -OMe and -NH<sub>2</sub>, in the *para*-position of the bipyrrrolidine ligand system increases the activity of the Mn(II)-complex.<sup>73-74</sup> In some cases, the catalyst concentration could even be lowered to 0.01 mole%, while keeping the rest of the conditions constant, to achieve similar conversions. The difference in activity between the presence and absence of EDG on the N-donor is illustrated in Figure 2.15.

Changing the substituents on the ligand system does not only have an electronic effect, but also a steric effect. This effect has been seen in a previous study where epoxidation of 1-octene with peracetic acid was performed.<sup>75</sup> The study employed a [(BPMCEN)Mn(OTf)<sub>2</sub>] complex containing a methyl substituent on the C6 position of the pyridine donor and one without. The presence of a methyl group on the C6 position led to 6% substrate conversion, whereas the absence of a methyl group resulted in a 98% substrate conversion. The presence of the methyl therefore causes a more sterically hindered environment for the substrate and ultimately decreases the catalyst activity.

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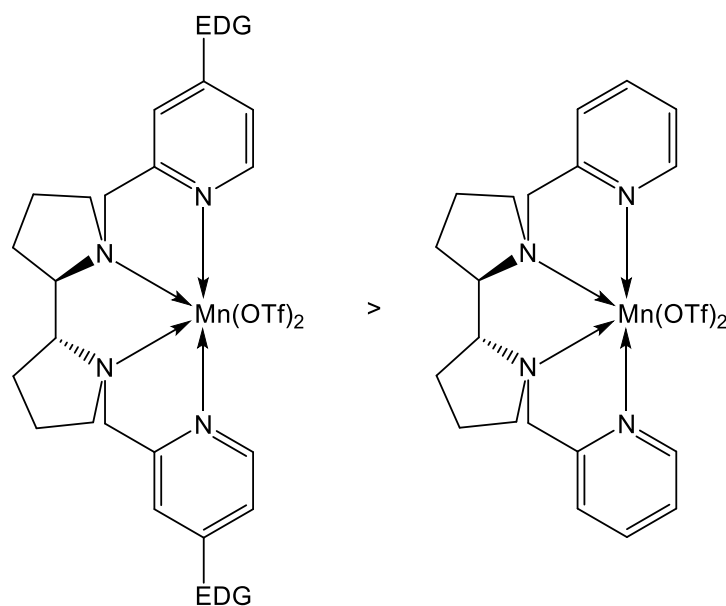


Figure 2.15: Difference in  $\text{Mn}(\text{OTf})_2$  complex activity due to the introduction of EDG.<sup>73-74</sup>

### 2.3.2.4 Alcohol oxidation

Research towards alcohol oxidation with the use of non-heme  $\text{Mn}(\text{II})$ -complexes has been limited and much is still to be discovered regarding optimal ligand systems and the mechanism by which it occurs. Some researchers have, however, achieved success in catalytically oxidising alcohol substrates with non-heme  $\text{Mn}(\text{II})$ -complexes, but there is a drawback, i.e. over-oxidation when primary alcohols are used as substrates. In an early study, the use of TMTACN-ligated  $\text{Mn}(\text{II})$ -complexes was found to be effective in the oxidation of various substrates, including 1-butanol and 2-pentanol.<sup>76</sup> A catalyst concentration of 0.04 mole% (for primary alcohol) and 0.5 mole% (for secondary alcohol) was used with 2.4 equivalents of  $\text{H}_2\text{O}_2$  as oxidant and ascorbic acid as co-catalyst (0.5:1 mole ratio of co-catalyst:Mn). Product yields determined by GC were very high (90% for secondary alcohol oxidation and 97% for primary alcohol oxidation), but it was found that the primary alcohol over-oxidised to the carboxylic acid as the major product. The secondary alcohol only produced the ketone product. Kani and Bolat found similar results when benzylic and aliphatic (linear and cyclic) alcohols were catalytically oxidised in the presence of a  $\text{Mn}(\text{II})$ -complex containing phenanthroline and phenylacetate ligands (Figure 2.16).<sup>4</sup>

Due to the phenylacetate ligand containing a carboxylic acid moiety, no co-catalyst was added. The oxidant  $t\text{-BuOOH}$  was utilised during oxidation in varying amounts (4-15 equivalents). Results indicated that benzyl alcohol was oxidised to benzaldehyde (52% conversion in 6 hours), but also over-oxidised to benzoic acid, which may have been caused by the high

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amount of oxidant used. An increase in the oxidant concentration led to higher conversions, but more benzoic acid formed. On the other hand, oxidation of the secondary alcohol, cyclohexanol, under the same conditions, selectively produced cyclohexanone as product.

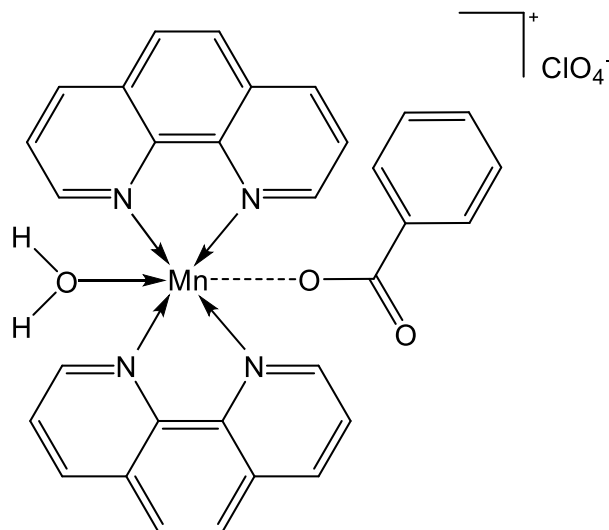


**Figure 2.16: Mn(II)-complex containing phenanthroline and phenylacetate ligands used for alcohol oxidation.<sup>4</sup>**

A previous study, already mentioned, also investigated the oxidation of benzyl alcohol, cyclohexanol and cyclooctanol with BQEN- and BPMCN-ligated Mn(II)-complexes.<sup>65</sup> Under oxidant limiting conditions, 100 equivalents AcOOH per Mn and 0.2 mole% catalyst concentration were utilised to produce the corresponding aldehyde and ketone products in 70 to 98% yield over a period of 30 minutes at 25 °C. It was found that the [(BQEN)Mn(OTf)<sub>2</sub>] complex performed better (16-28%) compared to the [(BPMCN)Mn(OTf)<sub>2</sub>] complex, which is contradictory to alkane and alkene oxidation studies. This may indicate a different mechanism being followed when alcohols are oxidised.

The best results thus far have been achieved by Shen and co-workers who utilised pyrrolidine-benzimidazole-ligated Mn(II)-complexes to oxidise secondary alcohols.<sup>16</sup> During this study, various secondary alcohols (benzylic and aliphatic) were oxidised with 1.5 and six to 14 equivalents of H<sub>2</sub>O<sub>2</sub> and AcOH, respectively. A 0.05 to 0.2 mole% catalyst concentration was used to achieve 55 to 99% conversion towards the ketone product in one hour at room temperature indicating the high activity of the catalyst. It was concluded that the strong electron-donating properties from the benzimidazole donor caused the high activity. This corresponds with previously mentioned studies where added EDG on the N-donor resulted in higher activity.<sup>73-74</sup>

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### **2.4 Conclusions**

This chapter aimed to describe how the importance of hydrocarbon oxidation led to the development of a greener alternative utilising non-heme Mn(II)-complexes. The oxidation of hydrocarbons was originally accomplished using oxidants such as  $\text{KMnO}_4$  and  $\text{H}_2\text{O}_2$ , but problems with regard to selectivity were encountered. Later on, various transition metals were introduced with the oxidants and it was found that much higher substrate conversions could be achieved during hydrocarbon oxidation reactions. Although greater activity was seen, selectivity problems in the form of over-oxidation still occurred.

Several decades later, a solution for the abovementioned problem was found, which was inspired by nature. It was discovered that some enzymes found in nature can catalyse the same hydrocarbon oxidation reactions, but with much greater selectivity, higher activity and utilising more benign conditions. The first was cytochrome P450, a class of heme monooxygenase enzymes capable of catalytically oxidising alkanes, alkenes and aromatic substrates. Later on, NDO, a non-heme Rieske dioxygenase enzyme capable of not only stereoselectively dihydroxylating aromatic substrates, but also various others, was discovered. It was concluded that the versatility of NDO is much greater than that of cytochrome P450, and this led to the development of non-heme Fe(II)-complexes.

Several studies were conducted with various non-heme ligand systems coordinated to a central Fe(II)-ion to catalyse the oxidation of alkanes, alkenes and alcohols. Ligand systems included BPMCN, PyTACN, BQCN, PDP and derivatives thereof. Although high activity could be achieved, it was found that the introduction of a Mn(II)-centre resulted in much greater activity. This is because the activation energy of Mn(II) towards an active high valent  $\text{Mn}^{\text{IV}}=\text{O}$  species is lower compared to that of Fe(II) activation towards  $\text{Fe}^{\text{III}}\text{-OOH}$ . The only drawback is the necessity of AcOH as a co-catalyst when non-heme Mn(II)-complexes are used to catalytically oxidise hydrocarbons.

Alkane and alkene oxidation with non-heme  $\text{N}_4$ -tetradentate Mn(II)-complexes has been studied intensely, as evidenced by the vast amounts of literature available. Several studies have illustrated the importance of the ligand system utilised in the Mn(II)-complexes and how it influences the reaction. Adding EDG onto the N-donor of the ligand system increases activity, but bulky groups in sterically more hindered positions on the N-donor decrease activity. Furthermore, it was found that the N-donor used in the ligand system also affects the activity of the complex. From these results, it is clear that the ligand system in the Mn(II)-complex can be varied to obtain the desired results during the oxidation reaction.

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The catalytic oxidation of alcohol substrates with non-heme  $N_4$ -tetradentate Mn(II)-complexes is much less studied, leaving a gap in the research field. This led to the instigation of the current study where novel non-heme  $N_4$ -tetradentate Mn(II)-complexes were developed and compared to already known examples for the oxidation of various alcohol substrates using  $H_2O_2$  as the oxidant and AcOH as the co-catalyst. In Chapter 3, the synthesis and characterisation of the novel non-heme  $N_4$ -tetradentate ligand systems with their corresponding Mn(II)-complexes that were used in the current study, will be discussed.

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## **Chapter 3**

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**The synthesis and characterisation of  
non-heme N<sub>4</sub>-tetradentate ligands and  
their manganese(II) complexes**

## Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

### 3.1 Introduction

The use of non-heme  $N_4$ -tetradentate ligated Mn(II)-complexes has been an interesting research area due to their ability to activate C-H bonds for the oxidation of hydrocarbons.<sup>1-4</sup> Previous oxidation studies have employed the use of various ligand systems, i.e. BPMCN, PDP and derivatives thereof, to determine their corresponding Mn(II)-complex's efficiency towards hydrocarbon oxidation.<sup>5</sup> The significance of these ligands is due to their contribution towards the stabilisation of high valent intermediates formed during hydrocarbon oxidation.<sup>5</sup>

Changing the ligand system and its substituents has a pronounced effect on the oxidation reaction. This effect has been seen in a previous study where epoxidation on 1-octene with AcOOH was performed.<sup>6</sup> The study employed a BPMCN-ligated Mn(OTf)<sub>2</sub> complex with the presence of a methyl substituent on the C6 position of the pyridine donor and one without. The presence of a methyl group on the C6 position led to a 6% substrate conversion, whereas the absence of a methyl group resulted in 98% substrate conversion. The presence of the methyl group therefore causes a sterically more hindered environment around the metal centre, which hinders substrate approach and ultimately decreases catalyst activity.

The substituents on the ligand can also play an electronic role during the reaction, thereby enhancing the substrate oxidation ability of the complex. This can be done through the introduction of electron-donating functional groups, which increase substrate conversion.<sup>7-8</sup> In two different epoxidation studies, a PDP ligand system was employed and exchange of the -H by a -OMe substituent in the *ortho* position with regard to the N on the pyridine increased conversion from 50% to 100% for methylstyrene and 61% to 80% for chalcone. This modification also led to a lowering of the required catalyst loading. In this way, the oxidation reactions can be manipulated to one's own advantage by altering the ligand system.

It has further been determined that the chirality, and ultimately the topology of the complex, might have an effect on the selectivity and activity during oxidation reactions.<sup>9-10</sup> Solid-state studies revealed that different topologies, i.e. *trans*, *cis*- $\alpha$  and *cis*- $\beta$ , are formed in the ensuing complexes, through the arrangement of the ligand around the metal centre. This may then lead to the creation of different reaction pockets, which can only accommodate a substrate in a certain way. It is, however, not clear whether the different topologies from the same ligand definitely affect the reaction, because a dynamic interchange between topologies occurs in solution.<sup>10</sup> Although it has not previously been investigated, it can be assumed that the effect of topology is negligible during alcohol oxidation, due to non-chiral  $sp^2$ -hybridised carbons formed in the oxidised product.

## Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

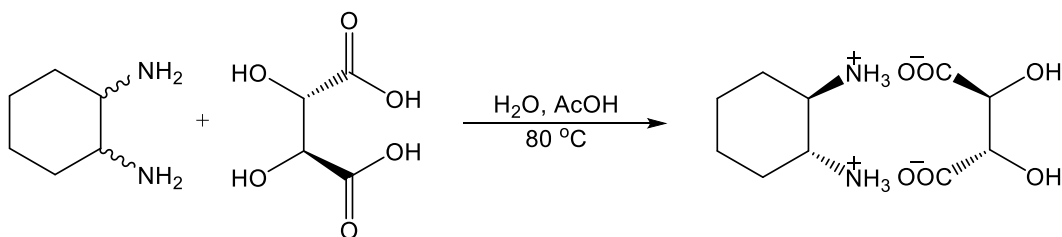
Taking the abovementioned factors into account, different aminopyridine and -imidazole ligands, ***R,R*-** and ***S,S*-L5 - L12**, have been developed to further synthesise non-heme  $N_4$ -tetradentate ligated  $Mn(OTf)_2$  complexes, ***R,R*-** and ***S,S*-C1 - C8**. The ligands have been selected in such a way to compare the effect of electron-donating and -withdrawing substituents, steric substituents, different N-donors, different degrees of amination and different ligand configurations (*R,R* and *S,S*) during catalytic alcohol oxidation. The synthesised ligands and complexes were characterised with various spectroscopic and analytical techniques to ensure that the correct complexes were made.

### 3.2 Results and discussion

#### 3.2.1 Synthesis of non-heme $N_4$ -tetradentate ligands

##### 3.2.1.1 Resolution of DACH tartrate salts

Before the synthesis of any ligands could commence, the 1,2-diaminocyclohexane *cis/trans* mixture needed to be resolved into its separate *R,R*- and *S,S*-enantiomers using different tartrate enantiomers. Resolution of the *R,R*-enantiomer is shown in Scheme 3.1. Although the 1,2-diaminocyclohexane (DACH) tartrate salts were isolated in low yields (up to 23%), confirmation of the salts was done using FT-IR spectroscopy.



**Scheme 3.1: Resolution of the *R,R*-DACH L-tartrate salt.**

The FT-IR spectrum illustrated in Figure 3.1 for the *R,R*-DACH L-tartrate salt showed a broad absorption band present from  $3100$  to  $2400\text{ cm}^{-1}$ , which corresponds with stretching vibrations originating from  $NH_3^+$  group. The wavenumber of the normal N-H stretch vibration is lowered due to the electronic interaction between the carboxylate ion and ammonium ion. The wavenumber for the O-H stretching vibration also decreases due to electron density moving towards the carboxylate group, thereby decreasing the O-H bond strength. The overtone band seen at  $2131\text{ cm}^{-1}$  is due to a combination of asymmetrical bending vibrations and torsional oscillations from the  $NH_3^+$ . The low intensity absorption band at  $1648\text{ cm}^{-1}$  is due to  $NH_3^+$  bending vibrations along with the strong absorption  $1561\text{ cm}^{-1}$ . The absorption band just left of

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1561  $\text{cm}^{-1}$  is due to asymmetrical carboxylate stretching. Similar observations were made when the *S,S*-DACH D-tartrate salt was characterised. All of the above observations serve as proof for the presence of the two DACH tartrate salts and correspond with the FT-IR spectrum of a previous study.<sup>11</sup>

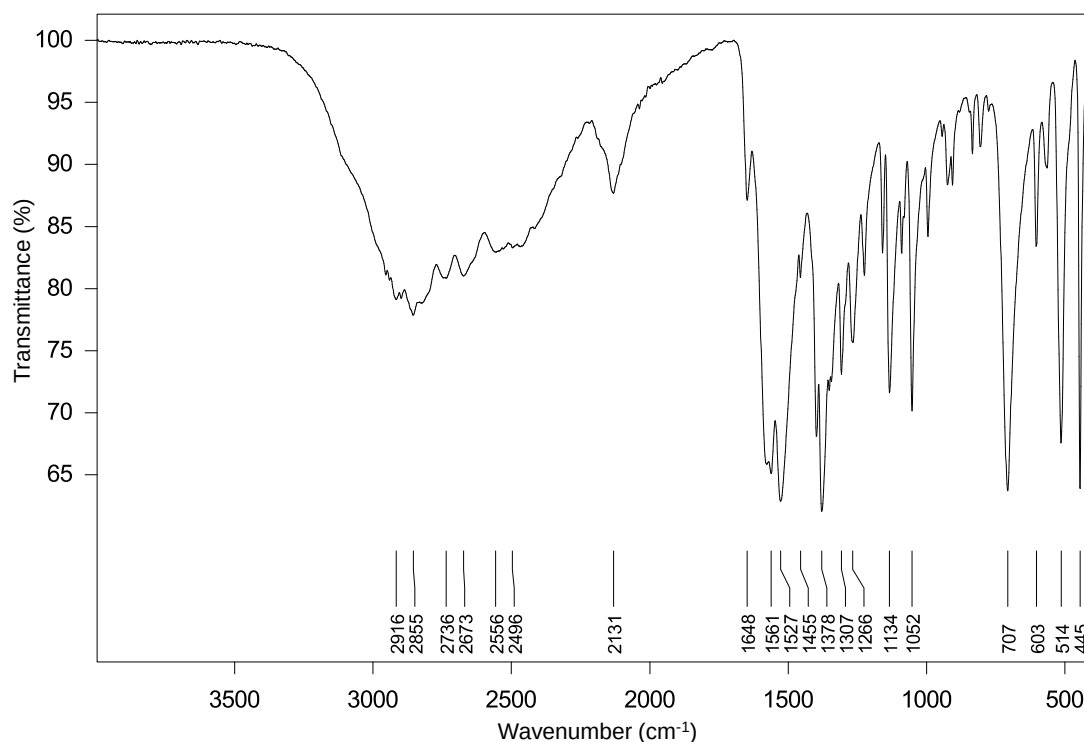
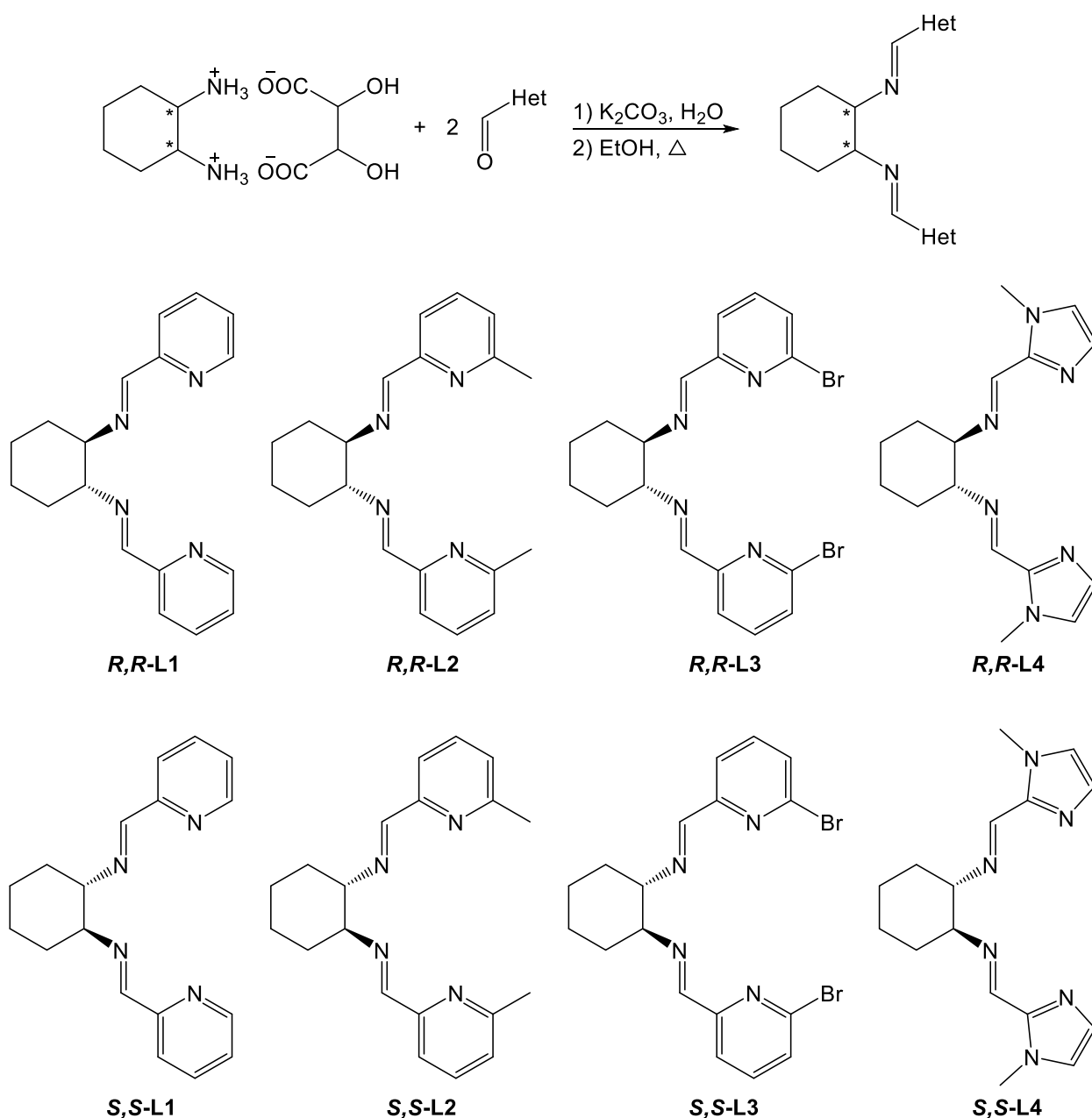


Figure 3.1: FT-IR spectrum of the *R,R*-DACH L-tartrate salt.

#### 3.2.1.2 Synthesis of non-heme $N_4$ -tetradentate diimine ligands *R,R*- and *S,S*-L1 - L4

The general synthesis route for the preparation of the  $N_4$ -tetradentate diimine ligands, *R,R*- and *S,S*-L1 - L4, proceeded via the condensation of the tartrate salt and different carboxaldehydes (varying in N-donor and type of substituents) as illustrated in Scheme 3.2. Moderate to good yields of 58 to 94% were achieved for the diimine ligands, all of which were isolated as solids, except *R,R*- and *S,S*-L4, which were isolated as oils. Solubility evaluation of the diimine ligands revealed that the *R,R*- and *S,S*-L1 ligands are soluble in polar organic solvents and insoluble in non-polar organic solvents, ethers and water. Ligands *R,R*- and *S,S*-L3 are also soluble in polar organic solvents (except EtOH, which requires heating) and insoluble in non-polar organic solvents and water. Ligands *R,R*- and *S,S*-L2 and L4 are soluble in polar organic solvents and insoluble in non-polar organic solvents and water. The formation of the produced diimine ligands and disappearance of the carboxaldehyde reagent were established by FT-IR and NMR ( $^1\text{H}$  and  $^{13}\text{C}$  { $^1\text{H}$ }) spectroscopy.

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**Scheme 3.2:** Synthetic route for the preparation of diimine ligands ***R,R*-** and ***S,S*-L1 - L4**.

The FT-IR spectra for all the diimine ligands, ***R,R*-** and ***S,S*-L1 - L4**, showed a sharp absorption band at 1643 to 1649  $\text{cm}^{-1}$  corresponding with the acyclic C=N stretch vibration. This serves as proof for the formation of the imine moiety in the ligands. The FT-IR spectrum for ***R,R*-L1** is shown in Figure 3.2, which illustrates the formation of the imine peak at 1643  $\text{cm}^{-1}$ . No difference regarding the position of the peak was seen when the *R,R*- and *S,S*-enantiomers were compared. When the 1700  $\text{cm}^{-1}$  region (characteristic of C=O stretch vibrations) of the FT-IR spectra for all the diimine ligands was evaluated, no peak was observed. This indicated that the carboxaldehyde reagent was fully consumed during diimine synthesis.

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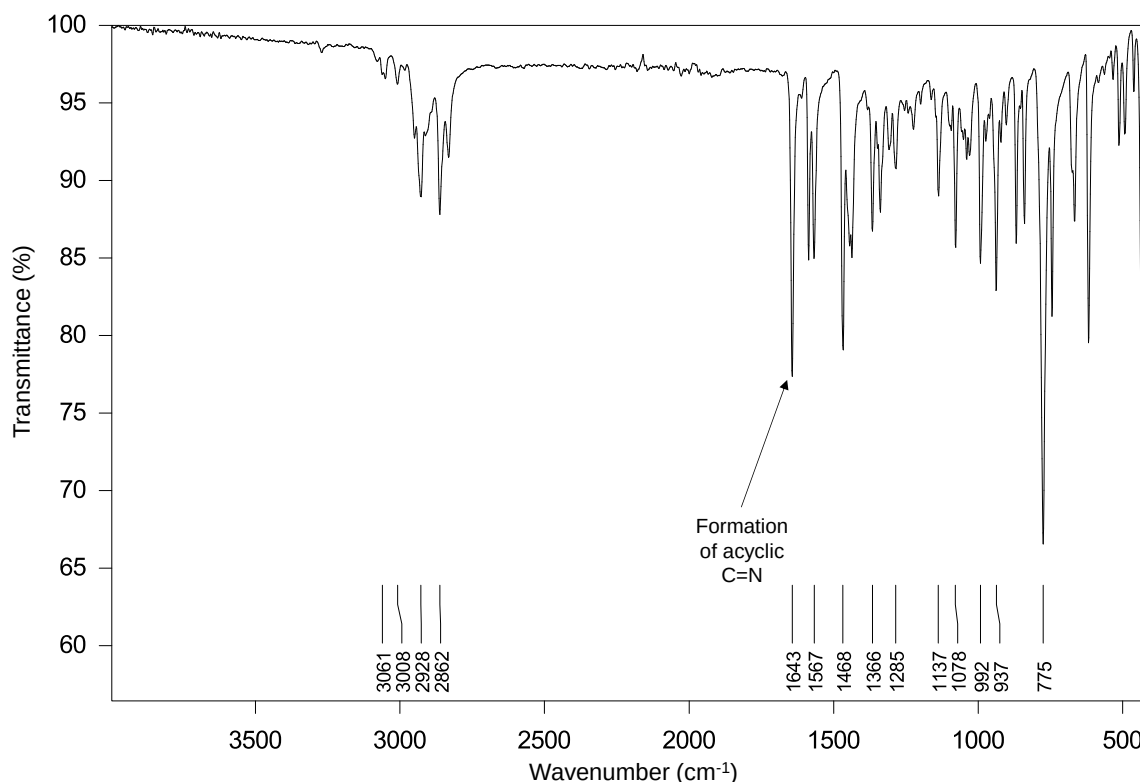


**Figure 3.2:** FT-IR spectrum of ligand **R,R-L1**.

The  $^1\text{H}$  NMR spectra of **R,R-** and **S,S-L1 - L4** showed the formation of a deshielded singlet in the range 8.15 to 8.32 ppm integrating for 2  $\text{H-C=N}$  protons (Figure 3.3). No singlet was seen around a chemical shift value of 10 ppm, indicating that  $\text{H-C=O}$  protons were not present. From this, it could be concluded that all the carboxaldehyde reagents had been consumed. Evaluation of the  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR spectra for **R,R-** and **S,S-L1 - L4** showed the presence of a deshielded resonance in the range 152 - 158 ppm indicating the presence of an imine carbon (Figure 3.4). The absence of a much more deshielded peak at  $\sim 200$  ppm (characteristic of a carbonyl carbon) indicated that the carboxaldehyde had been consumed during synthesis.

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Figure 3.3:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of ligand S,S-L1.

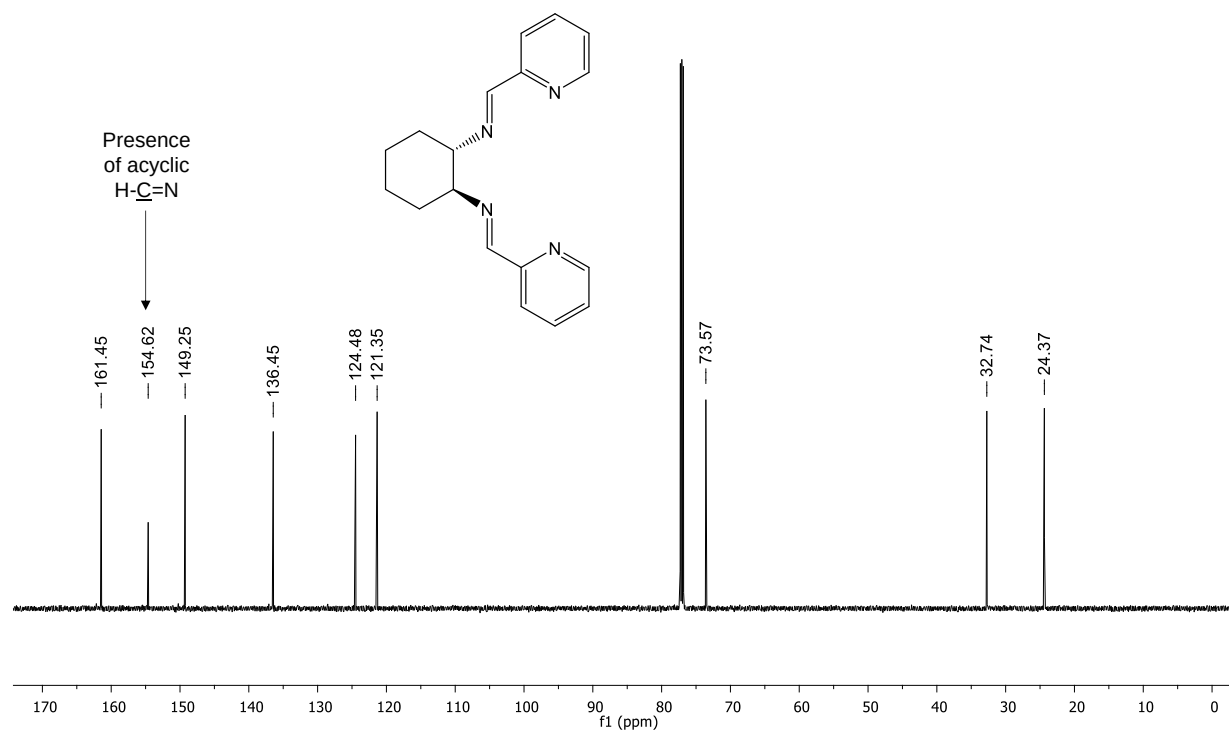


Figure 3.4:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of ligand S,S-L1.

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#### 3.2.1.3 Synthesis of non-heme $N_4$ -tetradentate secondary diamine ligands $R,R$ - and $S,S$ -L5 – L8

Synthesis of the secondary diamine ligands,  $R,R$ - and  $S,S$ -L5 - L8, was conducted by reducing the diimine ligands with  $\text{NaBH}_4$  in MeOH (Scheme 3.3). Good yields of 83 to 95% were achieved for the secondary diamine ligands, with L5 and L8 being isolated as oils and L6 and L7 as solids, respectively. Ligands  $R,R$ - and  $S,S$ -L5 - L8 show solubility in polar organic solvents, but are insoluble in non-polar organic solvents and water. Characterisation by FT-IR and NMR ( $^1\text{H}$  and  $^{13}\text{C}$   $\{^1\text{H}\}$ ) spectroscopy was done to evaluate the disappearance of the imine, and formation of a secondary amine.

All of the synthesised secondary diamine ligands,  $R,R$ - and  $S,S$ -L5 - L8, were seen to have a medium intensity peak in the 3278 to 3294  $\text{cm}^{-1}$  range, indicating the presence of N-H stretch vibrations typically seen for secondary amines. The FT-IR spectrum of  $S,S$ -L7 shown in Figure 3.5 illustrates the formation of the N-H stretch vibration seen at 3287  $\text{cm}^{-1}$ . The absence of a sharp peak at 1643 to 1649  $\text{cm}^{-1}$  previously identified as a C=N stretch vibration provided further evidence that successful reduction of the imine occurred.

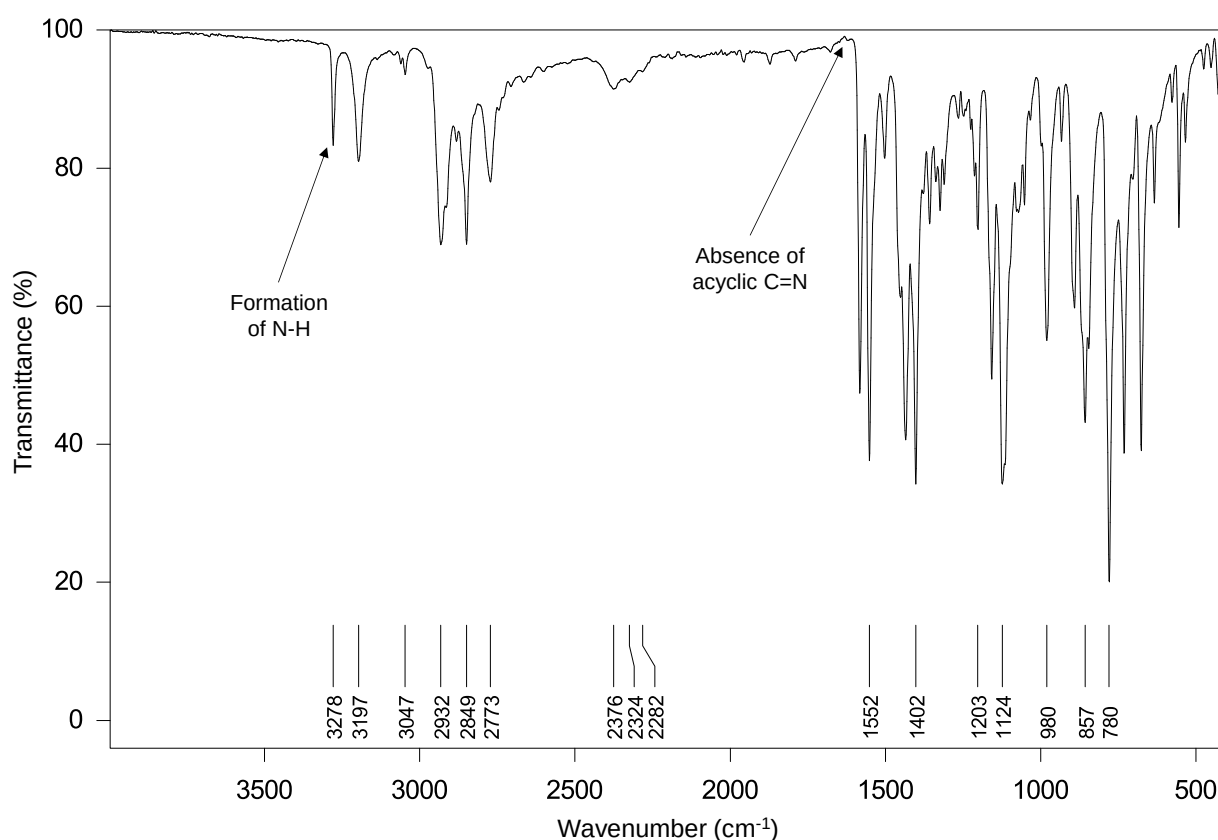
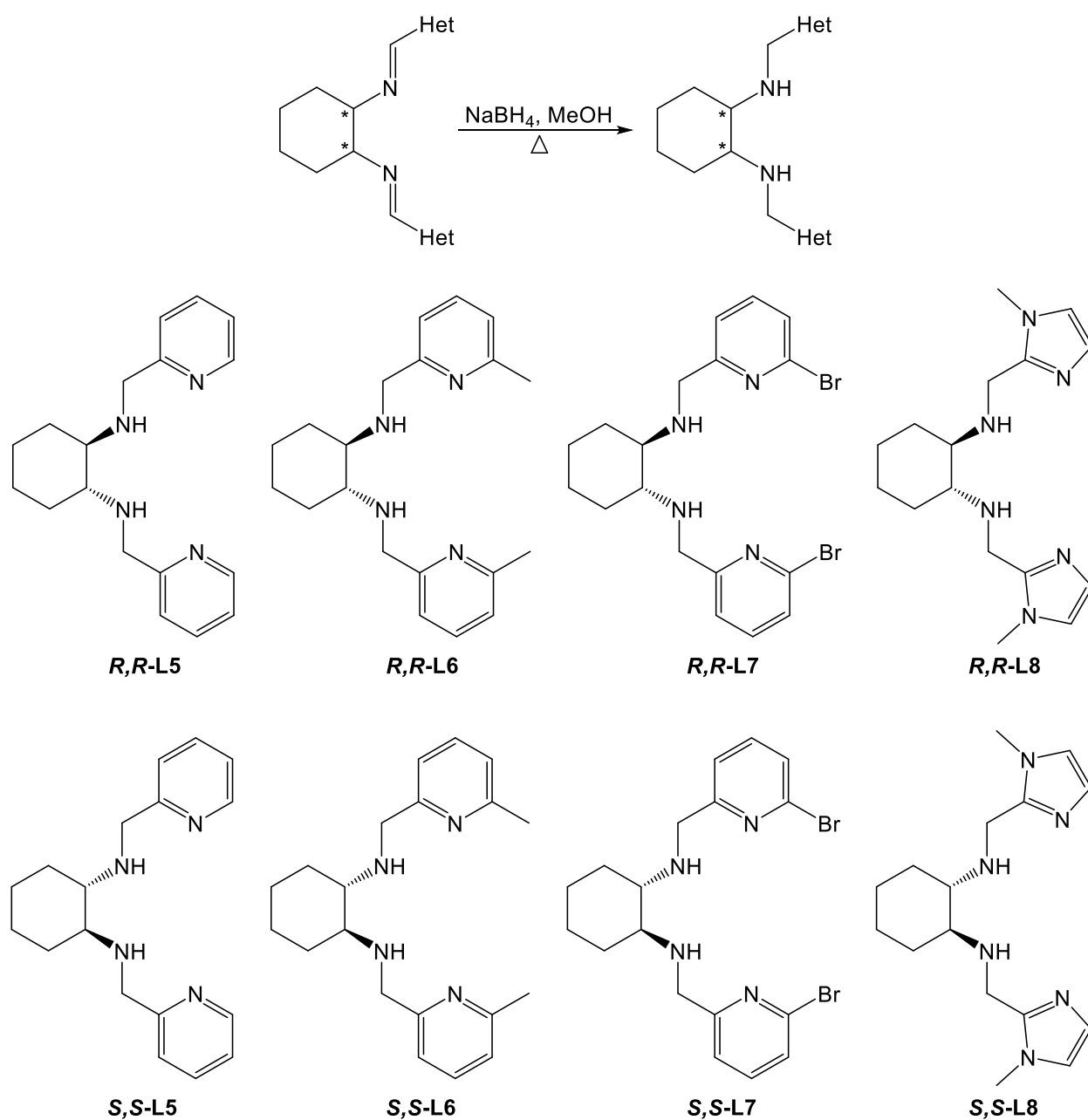


Figure 3.5: FT-IR spectrum of ligand  $S,S$ -L7.

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Scheme 3.3: Synthetic route for the preparation of the secondary diamine ligands *R,R*- and *S,S*-L9 - L12.

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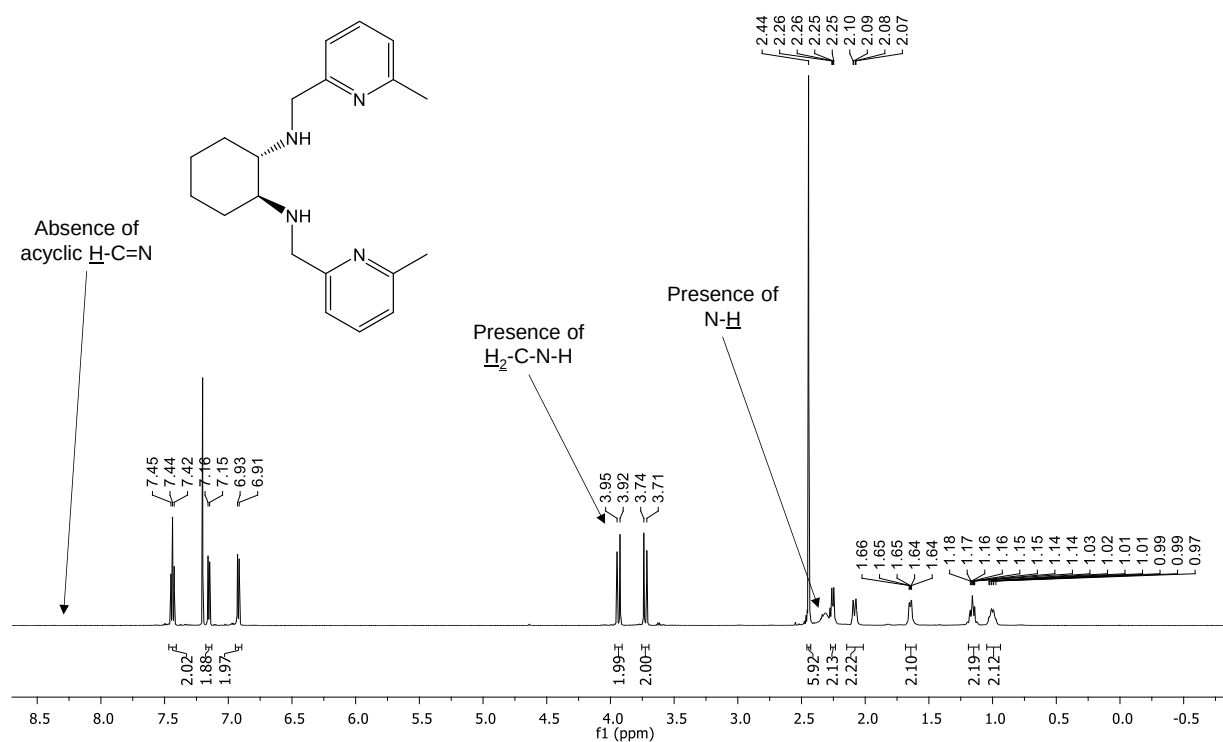


Figure 3.6:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of ligand  $S,S$ -L6.

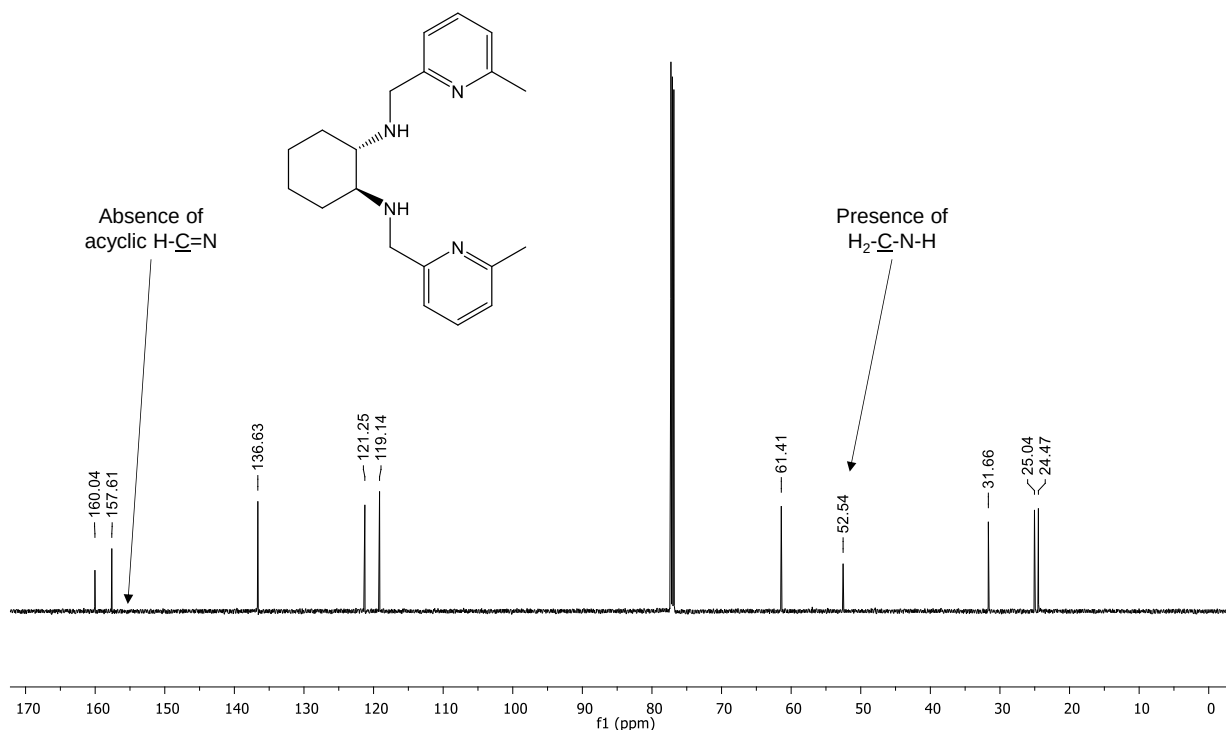


Figure 3.7:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of ligand  $S,S$ -L6.

### *Chapter 3: The synthesis and characterisation of non-heme N<sub>4</sub>-tetradentate ligands and their manganese(II) complexes*

Characterisation of all the secondary diamine ligands, **R,R-** and **S,S-L5 - L8**, by <sup>1</sup>H NMR spectroscopy showed the absence of the singlet previously seen in the range 8.15 to 8.32 ppm, which indicated the disappearance of the imine. The appearance of a doublet at a more shielded 3.61 to 4.05 ppm, for all the secondary diamine ligands, integrating for four methylene (-CH<sub>2</sub>-) protons, confirmed the successful reduction of the imine to the secondary amine. A broad resonance appearing at 2.3 ppm was also seen for all of the secondary diamine ligands, which corresponded with the proton bound to a secondary amine. The abovementioned observations are illustrated for **S,S-L6** in Figure 3.6.

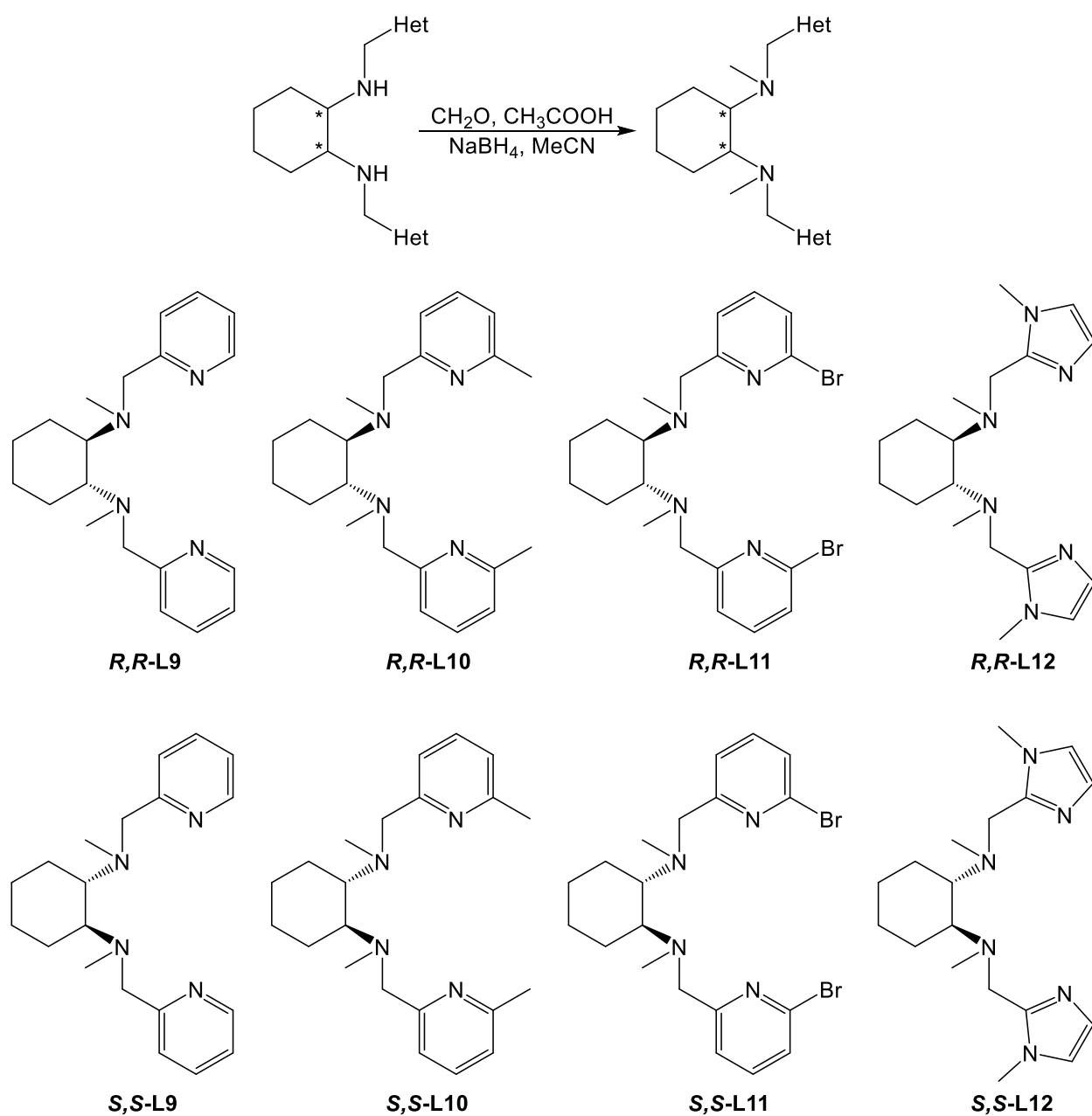
Evaluation of <sup>13</sup>C {<sup>1</sup>H} NMR spectra for **R,R-** and **S,S-L5 - L8** revealed the disappearance of a deshielded peak previously seen at 152 to 158 ppm (imine carbon) and introduction of a new shielded peak in the range 43 to 53 ppm. The new peak was attributed to a methylene (-CH<sub>2</sub>-) carbon, which illustrated the reduction of the imine. Both the abovementioned observations are illustrated in Figure 3.7 for **S,S-L6**. From these observations, it can be concluded that successful reduction from the diimine ligands to the secondary diamine ligands occurred.

#### **3.2.1.4 Synthesis of non-heme N<sub>4</sub>-tetradentate tertiary diamine ligands **R,R-** and **S,S-L9 - L12****

The secondary diamine ligands, **R,R-** and **S,S-L5 - L8**, were methylated to their tertiary diamine counterparts, **R,R-** and **S,S-L9 - L12**, using a method similar to the Eschweiler-Clarke method, except for the replacement of formic acid with formaldehyde and acetic acid (Scheme 3.4). Good yields between 68 and 88% were obtained with all of the tertiary diamine ligands isolated as oils. A similar solubility pattern for ligands **R,R-** and **S,S-L9 - L12** is observed when compared to ligands **R,R-** and **S,S-L5 - L8**. Confirmation of successful methylation was established by FT-IR and NMR (<sup>1</sup>H and <sup>13</sup>C {<sup>1</sup>H}) spectroscopy.

The FT-IR spectra for all the tertiary diamine ligands showed the absence of a N-H stretch vibration previously seen at 3278 to 3294 cm<sup>-1</sup> indicating successful methylation (Figure 3.8). Assessment of the <sup>1</sup>H NMR spectra for all the tertiary diamine ligands, **R,R-** and **S,S-L9 - L12**, revealed that an extra shielded singlet at 1.97 to 2.30 ppm integrating for six methyl (-CH<sub>3</sub>) protons was found (Figure 3.9). Characterisation with <sup>13</sup>C {<sup>1</sup>H} NMR showed the introduction of an extra shielded peak at 35 to 37 ppm for all the tertiary amine ligands indicating the presence of the added -CH<sub>3</sub> carbon (Figure 3.10). All of the abovementioned observations contributed to the confirmation of a successful methylation of the secondary to tertiary diamine ligands.

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Scheme 3.4: Synthetic route for the preparation of the tertiary diamine ligands *R,R*- and *S,S*-L9 - L12.

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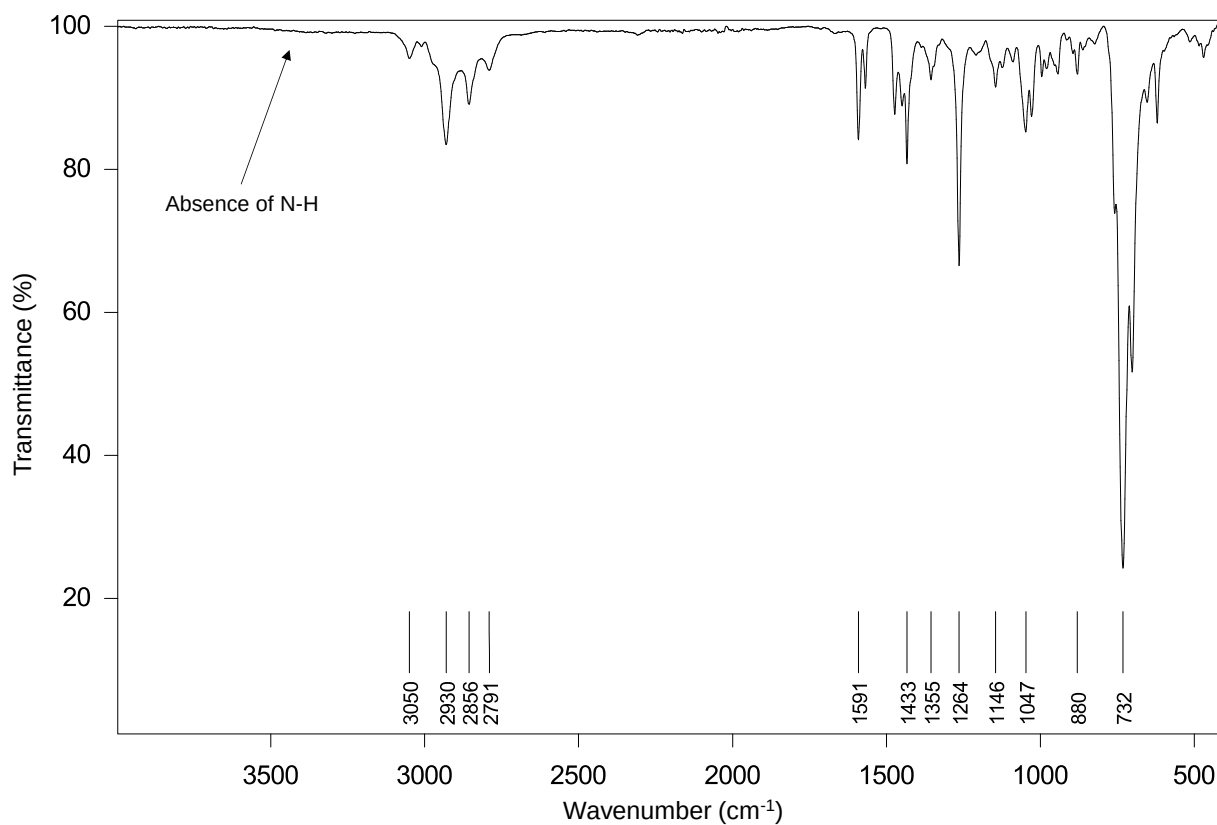


Figure 3.8: FT-IR spectrum of ligand *R,R*-L9.

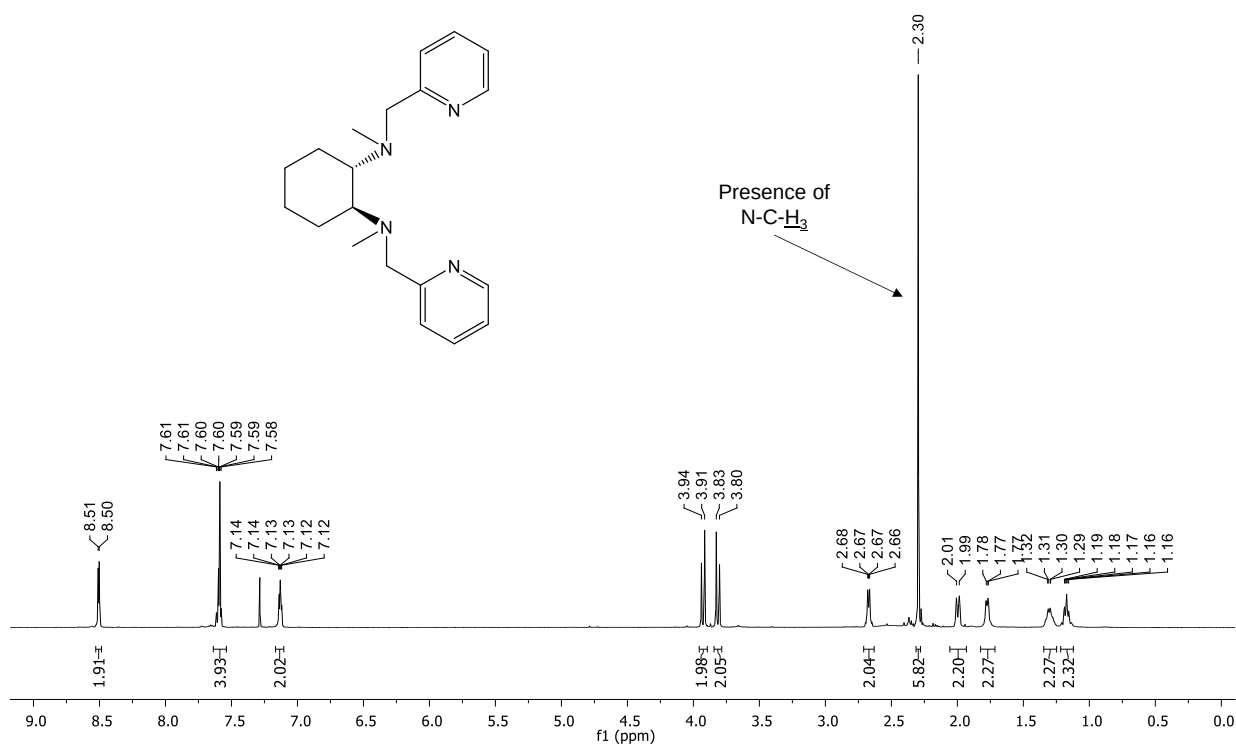


Figure 3.9:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of ligand *S,S*-L9.

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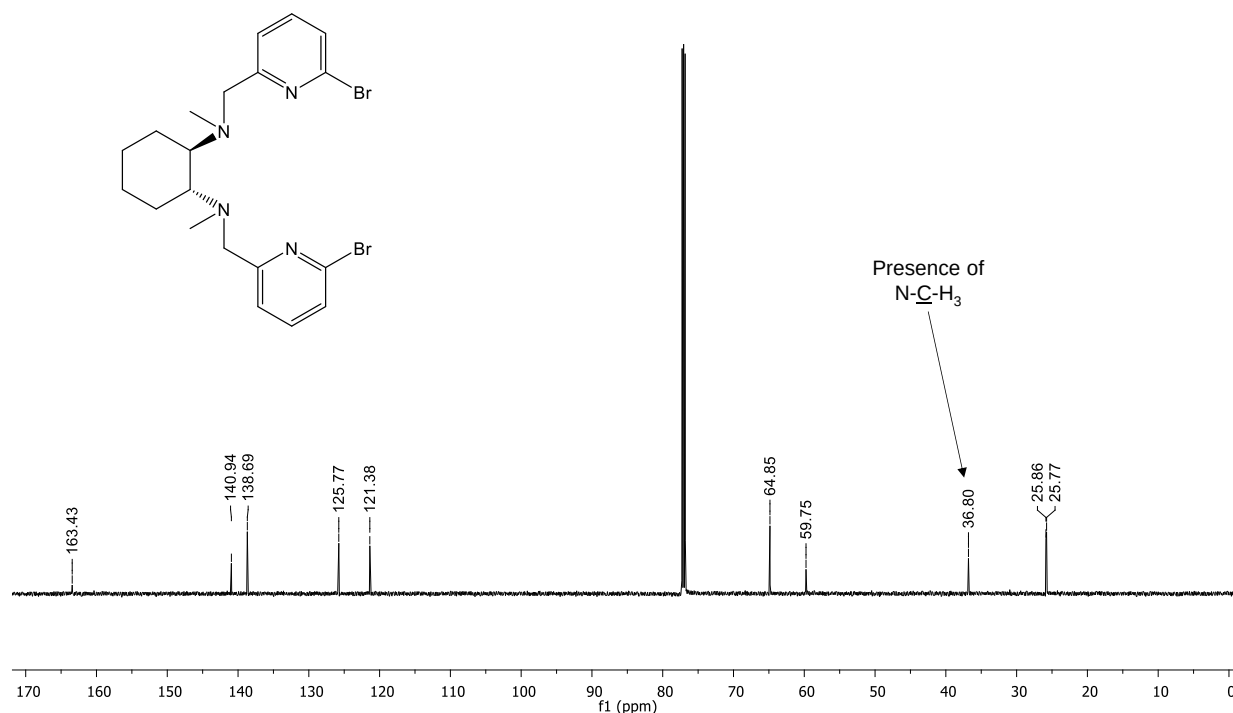


Figure 3.10:  $^{13}\text{C}$  { $^1\text{H}$ } NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of ligand **R,R-L11**.

### 3.2.2 Synthesis of non-heme $N_4$ -tetradentate $\text{Mn}(\text{OTf})_2$ complexes **R,R-** and **S,S-C1 - C8**

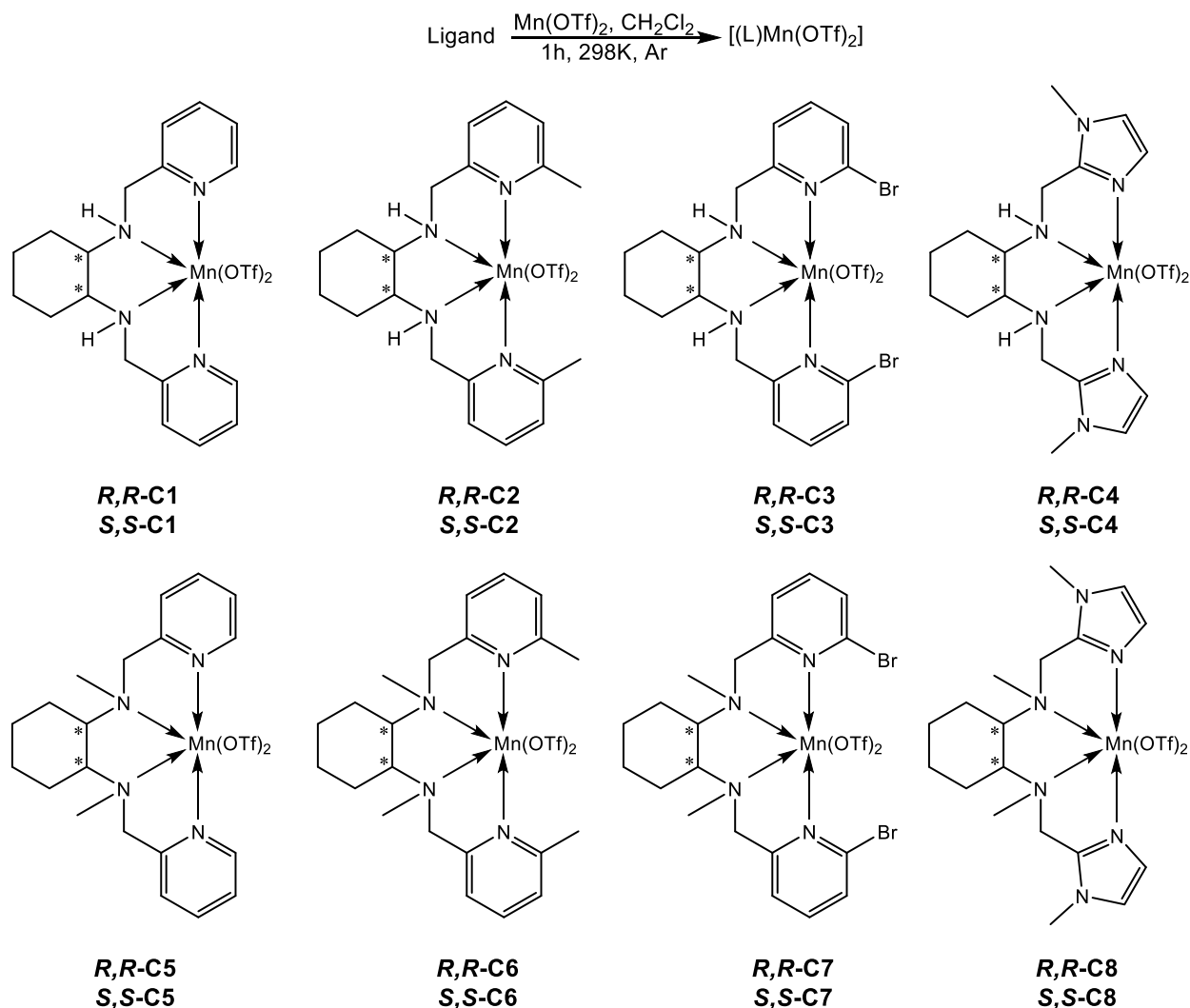
Synthesis of the non-heme  $N_4$ -tetradentate  $\text{Mn}(\text{II})$ -complexes, **R,R-** and **S,S-C1 - C8**, as shown in Scheme 3.5, was conducted by reacting the  $\text{Mn}(\text{OTf})_2$  precursor in a 1:1 ratio with each of the secondary and tertiary diamine ligands, **R,R-** and **S,S-L5 - C12**. The complexes were isolated after workup in moderate to good yields (29-87%) and displayed solubility in polar organic solvents (DCM, MeCN and acetone) while being insoluble in ethers, alkanes and water. The complexes were characterised by magnetic susceptibility, melting point analysis, APCI-MS, UV-visible spectroscopy, SC-XRD and elemental analysis to establish the atom connectivity, molecular structure and bulk purity of the synthesised complexes.

#### 3.2.2.1 Magnetic susceptibility and stability of complexes **R,R-** and **S,S-C1 - C8**

Magnetic susceptibility measurements were performed by making 50 mM MeCN solutions of the complexes at 298 K. The magnetic moments for all the complexes in this study, **R,R-** and **S,S-C1 - C8**, were found to be between 5.500 and 5.964 BM (Table 3.1). These values correlate well with theoretical and other experimental values indicating that the complexes synthesised correspond with manganese in its 2+ oxidation state. A theoretically calculated  $\mu_{\text{eff}}$  value for  $\text{Mn}(\text{II})$  is 5.9 BM,<sup>12</sup> whereas the observed magnetic moment of a high spin manganese

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species in its 2+ oxidation state at 298 K is observed in the range 5.6 to 6.1 BM.<sup>13-15</sup> Although this value corresponds with a spin-only value, dynamic interconversion between ligand enantiomers and solvent molecules may induce a fluctuation in the magnetic moment. This may lead to magnetic moment values, which are slightly different from theoretical values.



**Scheme 3.5: Synthetic route for the preparation of non-heme  $N_4$ -tetradentate Mn(II)-complexes *R,R*- and *S,S*-C1 - C8. Stars indicate *R,R*- and *S,S*-configurations.**

Evaluation of the melting temperatures indicated that all of the tertiary amine complexes, *R,R*- and *S,S*-C5 - C8, except *R,R*- and *S,S*-C7, had higher melting points than their secondary amine counterparts, *R,R*- and *S,S*-C1 - C4, did (Table 3.1). The extra methyl groups in the tertiary amine complexes may contribute to a more stable complex resulting in higher temperatures needed for their decomposition. Melting temperature ranges observed for all of the complexes were on average 2 to 3 °C, indicating that the complexes have little to none impurities.

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**Table 3.1:** Magnetic moment (in Bohr Magnetons) measured for complexes *R,R*- and *S,S*-C1 - C8.

| Complex   | Magnetic moment ( $\mu_{\text{eff}}$ = BM) |                           | Melting temperature (°C)  |                           |
|-----------|--------------------------------------------|---------------------------|---------------------------|---------------------------|
|           | <i>R,R</i> -configuration                  | <i>S,S</i> -configuration | <i>R,R</i> -configuration | <i>S,S</i> -configuration |
| <b>C1</b> | 5.780                                      | 5.710                     | 223 - 226                 | 221 - 224                 |
| <b>C2</b> | 5.500                                      | 5.928                     | 241 - 243                 | 250 - 253                 |
| <b>C3</b> | 5.845                                      | 5.659                     | 284 - 286                 | 283 - 285                 |
| <b>C4</b> | 5.655                                      | 5.658                     | 120 - 122                 | 120 - 122                 |
| <b>C5</b> | 5.553                                      | 5.909                     | 318 - 319                 | 322 - 324                 |
| <b>C6</b> | 5.964                                      | 5.798                     | 286 - 288                 | 284 - 287                 |
| <b>C7</b> | 5.761                                      | 5.775                     | 273 - 275                 | 270 - 273                 |
| <b>C8</b> | 5.713                                      | 5.650                     | 347 - 349                 | 344 - 347                 |

### 3.2.2.2 Mass spectrometry of complexes *R,R*- and *S,S*-C1 - C8

The isolated Mn(II)-complexes, *R,R*- and *S,S*-C1 - C8, were characterised by APCI-MS. Evaluation of the spectra illustrated that a high intensity peak with a *m/z* value corresponding with the loss of one -OTf group,  $[M - \text{OTf}]^+$ , was obtained for all of the complexes, as illustrated in Figure 3.11. This observation corresponds with results obtained from previous studies where the main peak observed originated from the loss of a -OTf group.<sup>8, 14, 16</sup> The original  $[M]^+$  ion, corresponding with the nominal mass of the complexes, was also seen for each complex, although it had a lower intensity.

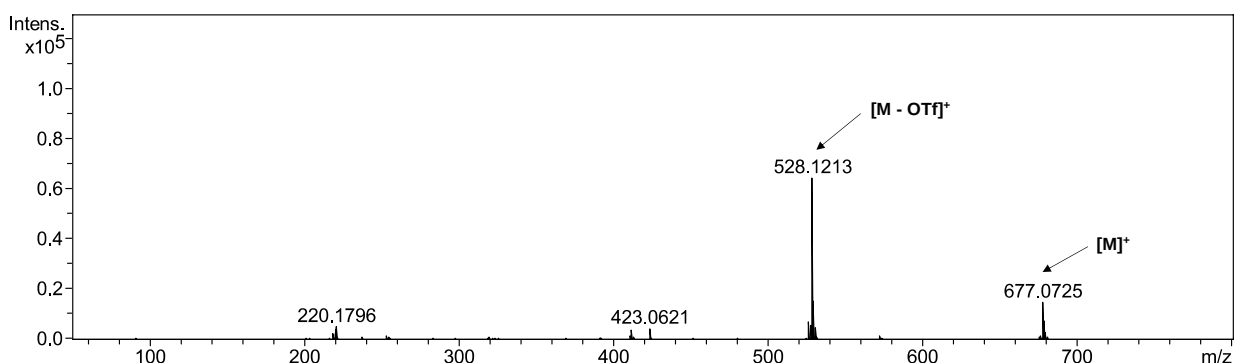


**Figure 3.11:** APCI-MS spectrum of *S,S*-C2.

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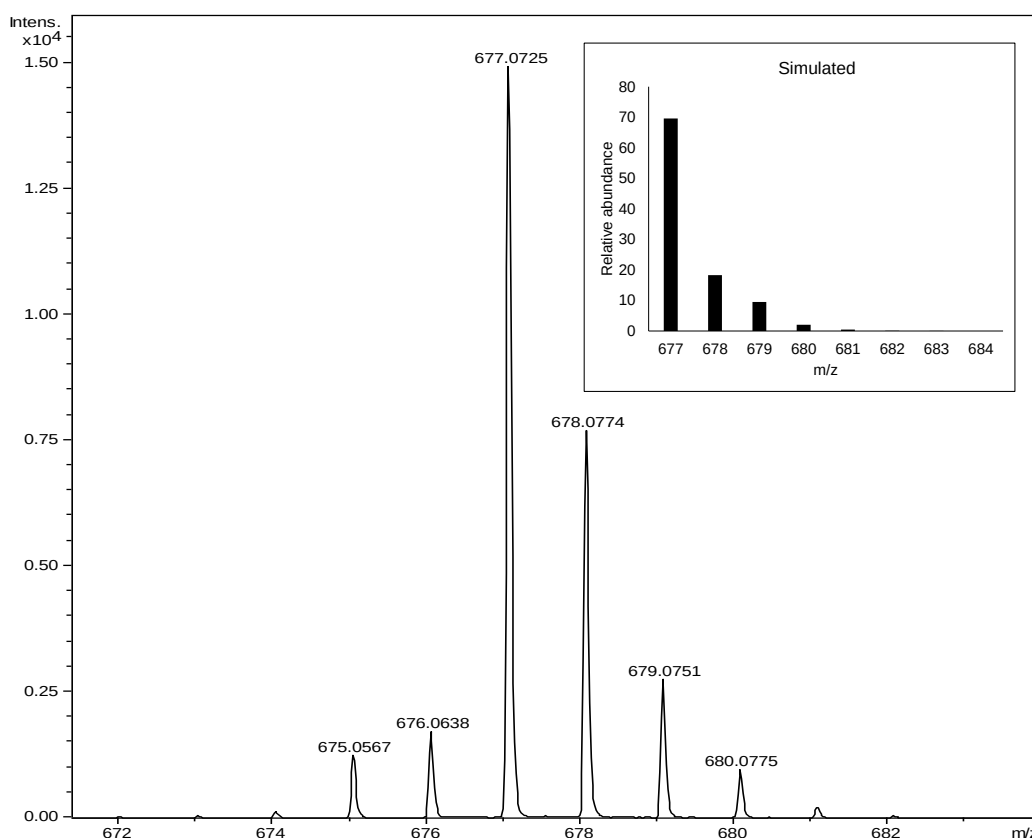


**Figure 3.12:** Zoomed-in APCI-MS spectrum of the  $[M]^+$  ion of **S,S-C2** and its simulated spectrum.

A simulated mass spectrum for **S,S-C2** was created to compare the experimental and theoretical spectrum seen for the  $[M]^+$  ion (Figure 3.12). Results illustrated that the theoretical and experimental spectra were similar, indicating that the correct complex was synthesised.

#### 3.2.2.3 UV-visible spectroscopy of complexes **R,R-** and **S,S-C1 - C8**

Evaluation of all the complexes, **R,R-** and **S,S-C1 - C9**, by UV-visible spectroscopy was performed by using 1 mM MeCN solutions at 298 K. All of the complexes showed strong absorption peaks in the 210 to 280 nm region. Peaks in this region are attributed to ligand  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions (Figure 3.13) and correlate with observations made during previous studies.<sup>17</sup>

All of the complexes containing pyridine donors, **R,R-** and **S,S-C1 - C3** and **C5 - C7**, showed strong absorption in the 250 to 280 nm range, but those with 1-methylimidazole donors **R,R-** and **S,S-C4** and **C8**, had low to no absorption in this range. This may be attributed to the reduced aromaticity of the imidazole ring compared to that of the pyridine. It could also be because the imidazole donor has a higher  $pK_a$  (higher electron donating ability) compared to

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pyridine<sup>18</sup>, which results in less electrons being available in the ring. Reduced electron flow in the ring causes decreased aromaticity and allows less UV light to be absorbed.

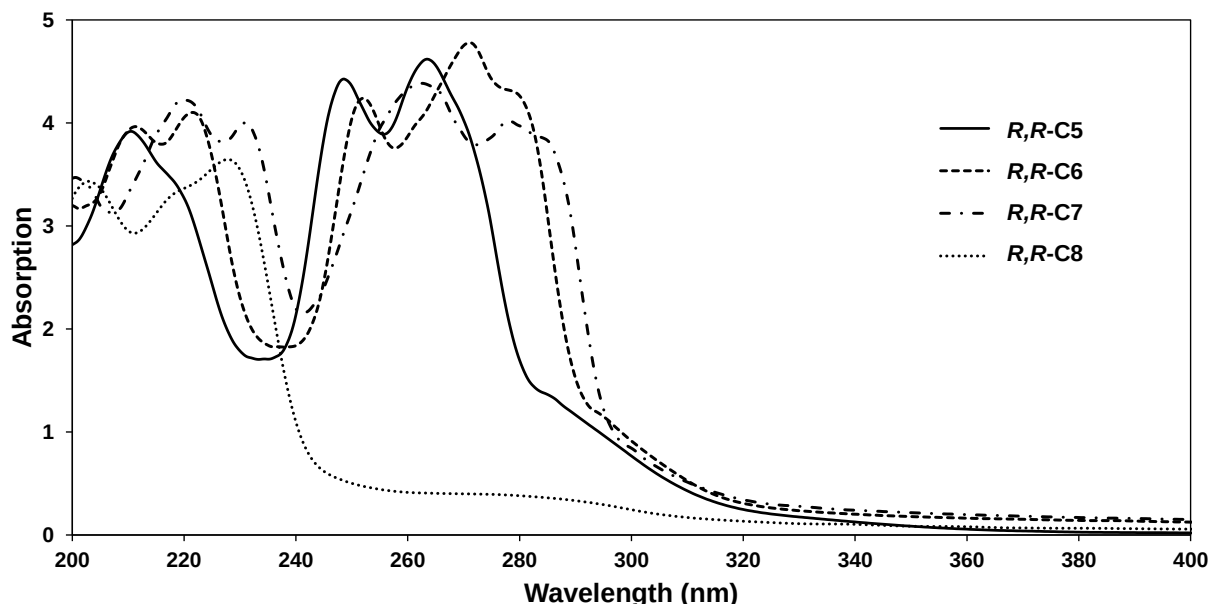


Figure 3.13: UV-visible spectrum of 1 mM of *R,R*-C5 - C8 in MeCN at 298 K.

No significant difference was observed when the UV-visible spectra of the secondary and tertiary amine complexes were compared. As is known, Mn(II)-complexes ( $d^5$ ) do not show any absorption peaks in the visible region due to no allowable transitions between electronic levels.<sup>17, 19</sup> This observation corresponds with the white and beige colours that were seen for the synthesised complexes.

#### 3.2.2.4 Single crystal x-ray diffraction analysis of complexes *R,R*- and *S,S*-C8

The solid-state structures of *R,R*- and *S,S*-C8 were unambiguously established by X-ray analysis. Suitable crystals were grown by slow diffusion of diethyl ether into concentrated acetonitrile solutions of the complexes. The ellipsoid diagrams for *R,R*- and *S,S*-C8 are shown in Figures 3.14(a) and 3.14(b), respectively, while crystallographic data and selected bond lengths and angles appear in Tables 3.2 and 3.3. For both complexes, the coordination geometry about the metal centre is distorted octahedral, in which the respective ligands adopt a *cis- $\alpha$*  topology. In the case of *R,R*-C8, this results in a  $\Delta$  helical chirality of the complex, whereas in the case of *S,S*-C8, it results in a  $\Lambda$  helical chirality of the complex. In both instances, the nitrogen atoms of the imidazole moieties (N1 and N1') are situated *trans* to each other, whereas the aliphatic nitrogen atoms (N3 and N3') are situated *cis* to each other. A comparison of the

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Mn-N bond lengths reflect the different chemical natures of the donor atoms. In both cases, the Mn-N1 bond lengths are significantly shorter [ $\sim 2.143(6)$  Å] than the corresponding Mn-N3 bond lengths [ $\sim 2.373(6)$  Å].

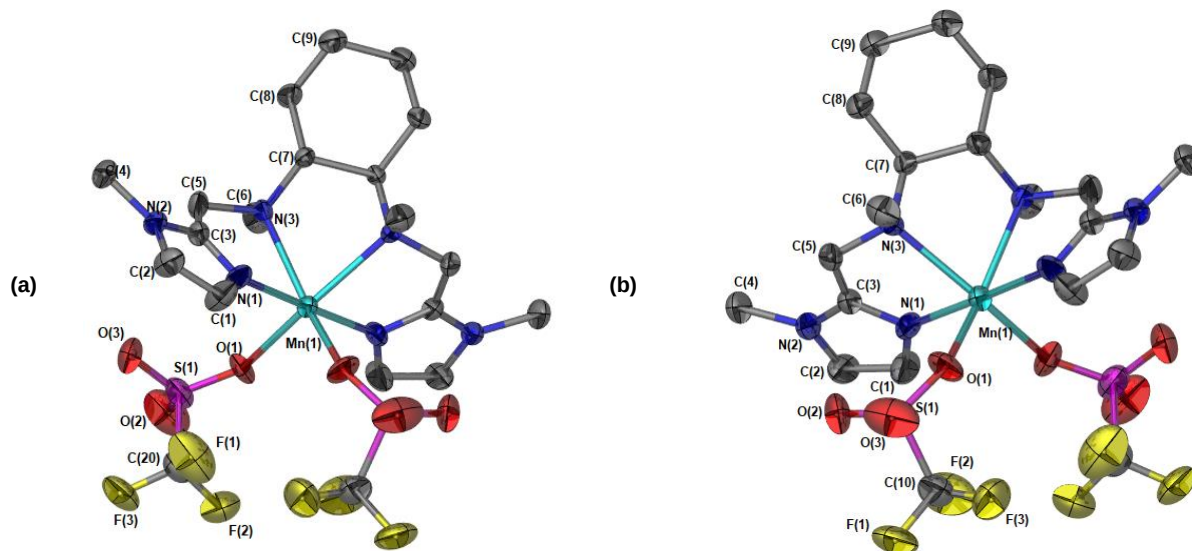


Figure 3.14: Ellipsoid diagrams of (a)  $R,R$ -C8 and (b)  $S,S$ -C8 drawn at 50% probability.

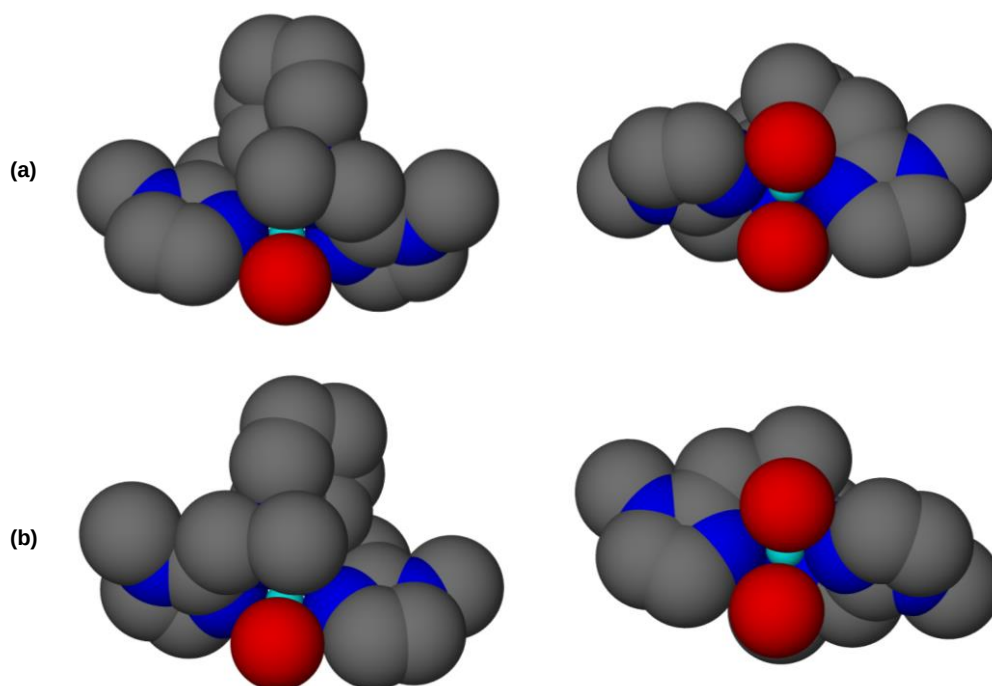


Figure 3.15: Space-filling diagrams of (a)  $R,R$ -C4 and (b)  $S,S$ -C4. The trifluoromethanesulphonate groups and hydrogen atoms have been omitted for clarity, but the O-atoms directly bound to the manganese centre have been retained. Colour code: grey (C), turquoise (Mn), blue (N) and red (O).

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**Table 3.2: Crystallographic data and structure refinement parameters for Mn(II)-triflate complexes *R,R*-C8 and *S,S*-C8.**

| Parameter                                                                                | Complex                                                                                       |                                                                                               |
|------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|
|                                                                                          | <i>R,R</i> -C4                                                                                | <i>S,S</i> -C4                                                                                |
| <b>Empirical formula</b>                                                                 | C <sub>20</sub> H <sub>30</sub> F <sub>6</sub> MnN <sub>6</sub> O <sub>6</sub> S <sub>2</sub> | C <sub>20</sub> H <sub>30</sub> F <sub>6</sub> MnN <sub>6</sub> O <sub>6</sub> S <sub>2</sub> |
| <b>Mr (g/mol)</b>                                                                        | 683.56                                                                                        | 683.56                                                                                        |
| <b>Crystal system</b>                                                                    | Tetragonal                                                                                    | Tetragonal                                                                                    |
| <b>Space group</b>                                                                       | P4(1)2(1)2                                                                                    | P4(3)2(1)2                                                                                    |
| <b><i>a</i> (Å)</b>                                                                      | 9.3461(3)                                                                                     | 9.3476(4)                                                                                     |
| <b><i>b</i> (Å)</b>                                                                      | 9.3461(3)                                                                                     | 9.348                                                                                         |
| <b><i>c</i> (Å)</b>                                                                      | 32.8191(12)                                                                                   | 32.8311(15)                                                                                   |
| <b><math>\alpha</math> (deg)</b>                                                         | 90.00                                                                                         | 90.00                                                                                         |
| <b><math>\beta</math> (deg)</b>                                                          | 90.00                                                                                         | 90.00                                                                                         |
| <b><math>\gamma</math> (deg)</b>                                                         | 90.00                                                                                         | 90.00                                                                                         |
| <b>Crystal dimension (mm)</b>                                                            | 0.17 x 0.21 x 0.29                                                                            | 0.087 x 0.180 x 0.314                                                                         |
| <b>Volume (Å<sup>3</sup>)</b>                                                            | 2866.7(2)                                                                                     | 2868.7(2)                                                                                     |
| <b>Z</b>                                                                                 | 4                                                                                             | 4                                                                                             |
| <b>D<sub>calc</sub> (g/cm<sup>3</sup>)</b>                                               | 1.584                                                                                         | 1.583                                                                                         |
| <b>F(000)</b>                                                                            | 1404                                                                                          | 1404                                                                                          |
| <b><math>\lambda</math> (MoK<math>\alpha</math>) (Å)</b>                                 | 0.71073                                                                                       | 0.71073                                                                                       |
| <b>Temperature (K)</b>                                                                   | 173(2)                                                                                        | 200(2)                                                                                        |
| <b>2<math>\theta</math> max (deg)</b>                                                    | 25.541                                                                                        | 25.038                                                                                        |
| <b>Absorption corrections applied (mm<sup>-1</sup>)</b>                                  | 0.691                                                                                         | 0.691                                                                                         |
| <b>Goodness-of-fit on F<sup>2</sup></b>                                                  | 1.078                                                                                         | 1.056                                                                                         |
| <b>Final <i>R</i><sub>1</sub> indices [<i>I</i> &gt; 2<math>\sigma</math>(<i>I</i>)]</b> | 0.0561                                                                                        | 0.0555                                                                                        |
| <b><i>wR</i><sub>2</sub> (all reflections)</b>                                           | 0.1523                                                                                        | 0.1380                                                                                        |
| <b>Flack x parameter</b>                                                                 | -0.007(9)                                                                                     | -0.0003(4)                                                                                    |

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**Table 3.3: Selected bond lengths (Å), bond angles (°) and torsion angle (°) as determined for Mn(II)-triflate complexes *R,R*-C8 and *S,S*-C8.**

|                                 | Complex        |                |
|---------------------------------|----------------|----------------|
|                                 | <i>R,R</i> -C8 | <i>S,S</i> -C8 |
| <b>Bond lengths<sup>a</sup></b> |                |                |
| <b>Mn-N1</b>                    | 2.143(6)       | 2.143(7)       |
| <b>Mn-N3</b>                    | 2.372(5)       | 2.373(6)       |
| <b>Mn-O1</b>                    | 2.212(6)       | 2.209(7)       |
| <b>Bond angles</b>              |                |                |
| <b>N1-Mn-N1'</b>                | 178.9(3)       | 179.0(4)       |
| <b>N1-Mn-O1</b>                 | 96.3(3)        | 96.3(3)        |
| <b>N1-Mn-O1'</b>                | 84.4(2)        | 84.3(3)        |
| <b>N1-Mn-N3</b>                 | 75.3(2)        | 75.3(2)        |
| <b>N1-Mn-N3'</b>                | 103.7(4)       | 103.9(3)       |
| <b>O1-Mn-O1'</b>                | 103.7(4)       | 103.5(4)       |
| <b>O1-Mn-N3</b>                 | 93.8(2)        | 93.9(3)        |
| <b>O1-Mn-N3'</b>                | 154.6(2)       | 154.6(3)       |
| <b>N3-Mn-N3'</b>                | 76.8(3)        | 76.7(3)        |

<sup>a</sup> Symmetry-generated atoms have equivalent bond lengths. Symmetry operator to generate equivalent atoms for *R,R*-C8 and *S,S*-C8: y, x, -z.

In general, the Mn-N distances for complexes *R,R*- and *S,S*-C8 are in the range observed for analogous high-spin Mn(II)-complexes with  $N_4$ -tetradentate ligands reported in literature.<sup>15, 20-24</sup> Comparative space-filling structural analysis shows the same degree of accessibility of the binding sites (represented by the triflate O-atoms) to the bulk (Figure 3.15a and b). This observation suggests that, all other factors being equal, both *R,R*- and *S,S*-C8 should display similar catalytic activity.

#### 3.2.2.5 Elemental analysis of complexes *R,R*- and *S,S*-C1 - C8

An investigation of the CHNS elemental analysis of all the complexes, *R,R*- and *S,S*-C1 - C8, illustrated that the experimental percentages found corresponded with the theoretically calculated values (Table 3.4). However, in some cases, it was found that small amounts of

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solvent, i.e. DCM, MeCN, Et<sub>2</sub>O or EtOH, used during ligand and complex synthesis, is included in the bulk sample. Taking the above variables into account, it was apparent that the bulk purity of each complex was sufficient.

**Table 3.4: Experimental and theoretical percentage CHNS in complexes *R,R*- and *S,S*-C1 - C8.**

| Complex                                | Experimental% (theoretical%) |             |               |             |
|----------------------------------------|------------------------------|-------------|---------------|-------------|
|                                        | C                            | H           | N             | S           |
| <b><i>R,R</i>-C1 + DCM</b>             | 34.46 (34.34)                | 3.21 (3.57) | 7.56 (7.63)   | 9.34 (8.73) |
| <b><i>S,S</i>-C1 + EtOH</b>            | 37.94 (37.99)                | 3.42 (4.35) | 8.18 (8.06)   | 8.54 (9.22) |
| <b><i>R,R</i>-C2 + 0.5 DCM</b>         | 37.52 (37.53)                | 3.68 (4.07) | 7.68 (7.78)   | 9.10 (8.91) |
| <b><i>S,S</i>-C2</b>                   | 38.95 (38.99)                | 3.85 (4.17) | 8.98 (8.27)   | 8.73 (9.47) |
| <b><i>R,R</i>-C3</b>                   | 30.07 (29.75)                | 2.72 (3.00) | 7.04 (6.94)   | 7.40 (7.94) |
| <b><i>S,S</i>-C3</b>                   | 29.95 (29.75)                | 2.79 (3.00) | 6.80 (6.94)   | 7.36 (7.94) |
| <b><i>R,R</i>-C4 + DCM</b>             | 30.67 (30.82)                | 3.76 (3.81) | 11.52 (11.35) | 9.09 (8.66) |
| <b><i>S,S</i>-C4 + DCM</b>             | 30.42 (30.82)                | 3.63 (3.81) | 11.66 (11.35) | 9.15 (8.66) |
| <b><i>R,R</i>-C5</b>                   | 39.45 (38.99)                | 3.84 (4.17) | 8.47 (8.27)   | 9.14 (9.47) |
| <b><i>S,S</i>-C5 + 0.5 MeCN</b>        | 39.33 (39.57)                | 4.16 (4.27) | 9.15 (9.03)   | 9.27 (9.19) |
| <b><i>R,R</i>-C6</b>                   | 41.15 (40.85)                | 4.46 (4.58) | 8.30 (7.94)   | 8.98 (9.09) |
| <b><i>S,S</i>-C6</b>                   | 40.66 (40.85)                | 4.54 (4.58) | 8.31 (7.94)   | 8.83 (9.09) |
| <b><i>R,R</i>-C7 + 0.25 DCM</b>        | 30.78 (31.20)                | 3.49 (3.36) | 6.86 (6.54)   | 7.89 (7.49) |
| <b><i>S,S</i>-C7 + Et<sub>2</sub>O</b> | 34.76 (34.34)                | 3.77 (3.99) | 6.92 (6.16)   | 7.28 (7.05) |
| <b><i>R,R</i>-C8</b>                   | 35.30 (35.14)                | 4.62 (4.43) | 12.20 (12.30) | 9.29 (9.38) |
| <b><i>S,S</i>-C8</b>                   | 35.10 (35.14)                | 4.50 (4.43) | 12.44 (12.30) | 9.29 (9.38) |

### 3.3 Conclusions

The objective for this part of the study was to synthesise non-heme  $N_4$ -tetradentate ligand systems that can be utilised for the development of Mn(II)-complexes, which can further be used for alcohol oxidation. The ligands, *R,R*- and *S,S*-L5 - L12, and corresponding complexes, *R,R*- and *S,S*-C1 - C8, were synthesised from established procedures. All the ligands and complexes were characterised by several characterisation and spectroscopic techniques, i.e. FT-IR,

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$^1\text{H}$  NMR,  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR, magnetic susceptibility, melting point, APCI-MS, UV-visible, SC-XRD and elemental analysis, which confirmed the preparation of the desired compounds.

After diamine ligand synthesis, the FT-IR spectra evaluation illustrated the formation of  $\text{C}=\text{N}$  stretch vibrations.  $^1\text{H}$  NMR and  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR also showed the appearance of a deshielded  $\text{HC}=\text{N}$  proton and carbon, respectively, indicating successful imine synthesis. Reduction to the secondary diamine ligands was confirmed by the disappearance of the  $\text{C}=\text{N}$  peak and evolution of a  $\text{N}-\text{H}$  stretch vibration on the FT-IR spectra.  $^1\text{H}$  NMR and  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR illustrated the disappearance of the deshielded  $\text{HC}=\text{N}$  and formation of a shielded  $\text{NHCH}_2$  functional group. Confirmation of methylation towards tertiary diamine ligands revealed the disappearance of the  $\text{N}-\text{H}$  stretch vibration on the FT-IR spectra and the formation of two extra  $-\text{CH}_3$  groups when  $^1\text{H}$  NMR and  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR spectra were evaluated. All of these observations contributed to the successful synthesis of the different ligands.

Magnetic susceptibility measurements revealed that the experimental values obtained correspond with theoretical values and those of previous studies where  $\text{Mn}(\text{II})$ -complexes were used. This indicated that all of the manganese complexes, ***R,R***- and ***S,S***-**C1 - C8**, synthesised were in their 2+ oxidation state. Melting point analysis revealed that the complexes bearing tertiary diamine ligands, ***R,R***- and ***S,S***-**C5 - C8**, were more stable than their secondary counterparts, ***R,R***- and ***S,S***-**C1 - C4**, due to the extra methyl groups.

Analysis of the solid state structures of complexes ***R,R***- and ***S,S***-**C8** by SC-XRD revealed that the complexes adopted a *cis*- $\alpha$  topology with a distorted octahedral coordination geometry. Comparing the space-filling diagrams of both complexes, ***R,R***- and ***S,S***-**C8**, indicates that the degree of accessibility to the metal centre is similar, suggesting that catalytic activity might also be similar. All of the synthesised complexes were evaluated with APCI-MS, which showed the presence of  $[\text{M}]^+$  and  $[\text{M}-\text{OTf}]^+$  ion peaks corresponding with the correct nominal masses of the corresponding complexes. UV-visible spectroscopic data revealed the presence of the pyridine and 1-methylimidazole donors in the complexes, which originated from ligand  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions seen at 210 to 280 nm.

Elemental analysis of all the complexes confirmed good overall bulk purity due to CHNS experimental values corresponding with calculated values. Some of the complexes did, however, reveal that traces of solvent, i.e. DCM, EtOH or MeCN were still present. To conclude, the synthesis of the  $N_4$ -tetradentate ligands and their respective  $\text{Mn}(\text{II})$ -complexes was successful.

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### 3.4 Experimental section

#### 3.4.1 General considerations

All chemicals and reagents were used without further purification and included 1,2-diaminocyclohexane cis/trans mixture (99%, Sigma-Aldrich), L-tartaric acid (99.5%, Sigma-Aldrich), D-tartaric acid (99%, Sigma-Aldrich), glacial acetic acid (99.8%, Rochelle Chemicals), methanol (99%, Minema), dichloromethane (99.5%, Rochelle Chemicals), ethanol (99.9%, Minema), 2-pyridinecarboxaldehyde (99%, Sigma-Aldrich), 6-methyl-2-pyridinecarboxaldehyde (98%, Sigma-Aldrich), 6-bromo-2-pyridinecarboxaldehyde (97%, Sigma-Aldrich), 1-methyl-2-imidazolecarboxaldehyde (98%, Sigma-Aldrich), sodium borohydride ( $\text{NaBH}_4$ ) (96%, Sigma-Aldrich), formaldehyde (35%, Merck) and acetonitrile (99.5%, Merck). Drying of the solvents for  $\text{Mn}(\text{OTf})_2$  complex synthesis commenced as follows:  $\text{Et}_2\text{O}$  was dried under a  $\text{N}_2$  atmosphere with Na-metal and benzophenone while DCM was dried with calcium hydride ( $\text{CaH}$ ) under a  $\text{N}_2$  atmosphere. The  $\text{Mn}(\text{OTf})_2$  (from Sigma-Aldrich) contained 5% metallic Mn.

FT-IR spectra were documented on a BrukerAlpha-P range infrared instrument equipped with an ATR accessory as neat samples in the range of  $400\text{ cm}^{-1}$  to  $4000\text{ cm}^{-1}$ .  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Ultrashield Plus (600 MHz and 151 MHz, respectively) in 5 mm cylindrical glass tubes. APCI-MS characterisation was done on a Bruker microTOF-Q II mass spectrometer. Magnetic susceptibility measurements were conducted using a Sherwood Scientific MK1 with 4 mm in diameter sample tubes containing 50 mM samples in acetonitrile. UV-vis characterisation was performed on a Specord® s600 from AnalyticJena at 298 K in 10 mm quartz cuvettes. Elemental analysis was carried out by the University of KwaZulu-Natal (UKZN) Mass Spectrometry Laboratory and the North-West University (NWU) Potchefstroom Laboratory for Analytical Services on a Perkin Elmer elemental analyser. Melting point analysis was performed on a Buchi Melting Point B-540.

For SC-XRD analysis, single crystals of complexes **R,R-** and **S,S-C8** were mounted on a nylon loop and centred in a stream of cold nitrogen at 173(2) and 200(2) K respectively. Crystal evaluation and data collection were performed on a Bruker D8 Quest Eco diffractometer with  $\text{Mo K}\alpha$  radiation ( $\lambda = 0.71073\text{ \AA}$ ). Data collection, reduction and refinement were performed using SAINT<sup>25</sup> and SADABS,<sup>26</sup> which forms part of the APEX3 software package.<sup>27</sup> The structures were solved by direct methods and refined by full-matrix least-squares on  $F^2$  using SHELX 2018<sup>28</sup> within the X-Seed graphic user interface.<sup>29-30</sup> All non-hydrogen atoms were refined anisotropically and all hydrogen atoms were placed using calculated positions and riding models.

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### 3.4.2 Synthesis of non-heme $N_4$ -tetradentate aminopyridyl ligands

#### 3.4.2.1 Resolution of DACH tartrate salts

Resolution of the 1,2-diaminocyclohexane tartrate salt was done using the same method as previously described.<sup>31-32</sup> Synthesis of the chiral ligands was carried out using a similar method than previously described in literature.<sup>33</sup> For *R,R*-ligands the L-tartrate salt was used and for *S,S*-ligands the D-tartrate salt was used.

##### 3.4.2.1.1 Resolution of *R,R*-DACH L-tartrate salt

L-tartaric acid (7.551 g, 50.310 mmol) was dissolved in water (20 ml) and heated close to boiling point. A *cis/trans* 1,2-diaminocyclohexane mixture (12 ml, 98.678 mmol) was added slowly to the solution. Adding glacial acetic acid (5 ml, 87.427 mmol) resulted in the formation of a yellow-white slurry. The solution was cooled to room temperature and put in an ice bath for 30 min. The solid was filtered with suction filtration and washed with ice water (3 x 5 ml) and methanol (3 x 5 ml). Recrystallisation was done by dissolving the crude product in boiling water and any residue filtered. The solution was allowed to cool down slowly to room temperature where after it was put in the freezer overnight. Filtration of the solution yielded a white salt (2.497 g, 19.0%).

##### 3.4.2.1.2 Resolution of *S,S*-DACH D-tartrate salt

The same procedure mentioned in 3.4.2.1.1 was followed except that D-tartaric acid (7.541 g, 50.243 mmol) was used. After filtration of the solution a white salt (3.103 g, 23.6%) was obtained with a slightly different crystalline structure compared to the *R,R*-DACH salt.

#### 3.4.2.2 Synthesis of *N,N'*-dimethyl-*N,N'*-bis(pyridyl-2-methyl)-1,2-cyclohexanediamine

##### 3.4.2.2.1 *R,R*-enantiomer

Diimine synthesis: In a beaker the *R,R*-DACH L-tartrate salt (0.346 g, 1.309 mmol) and  $K_2CO_3$  (0.360 g, 2.605 mmol) was dissolved in water (3 ml) which was added to a 100 ml round bottom flask. After everything dissolved, ethanol (5 ml) was added. The solution was heated almost to boiling point during which 2-pyridinecarboxaldehyde (0.275 g, 2.567 mmol), dissolved in ethanol (5 ml), was added to the solution. The reaction mixture was refluxed for 6 hours after which water (3 ml) was added. The solution was then cooled down in an ice bath for 30 min. The water layer was extracted with DCM (3 x 5 ml) where after the organic layer was washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic layer was dried with  $Na_2SO_4$  and the solvent removed. Diethyl ether ( $Et_2O$ ) was added until the entire product dissolved. The

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solvent was reduced until 10 ml and left overnight in the freezer to afford light yellow crystals (0.226 g, 60.2%) (**R,R-L1**).

- FT-IR (ATR,  $\text{cm}^{-1}$ ): 3061 (Pyr C-H), 3008 (Pyr C-H), 2928 (ring C-H), 2862 (ring C-H), 1643 (C=N), 1567 (Pyr C-N), 1468 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.49 - 8.45 (m, 2H, PyrH), 8.24 (s, 2H, HC=N), 7.81 (d,  $J = 7.9$  Hz, 2H, PyrH), 7.57 (td,  $J = 7.7, 1.5$  Hz, 2H, PyrH), 7.14 (ddd,  $J = 7.4, 4.8, 1.1$  Hz, 2H, PyrH), 3.46 (dd,  $J = 6.4, 3.4$  Hz, 2H, CycH), 1.78 (ddd,  $J = 18.9, 11.2, 2.2$  Hz, 6H, CycH), 1.49 - 1.39 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.45 (PyrC), 154.63 (C=N), 149.25 (PyrC), 136.45 (PyrC), 124.48 (PyrC), 121.35 (PyrC), 73.57 (CycC), 32.74 (CycC), 24.37 (CycC).

Secondary diamine synthesis: **R,R-L1** (0.206 g, 0.7045 mmol) was dissolved in MeOH (3 ml) and put in an ice bath for 30 min.  $\text{NaBH}_4$  (0.136 g, 3.595 mmol) was added portion wise over a period of 5 min whilst stirring the solution. The solution was then stirred for 1 hour at ambient temperature where after it was refluxed for another hour. After the solution cooled down to room temperature DCM (20 ml) was added and the organic layer washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic phase was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to yield a light yellow oil (0.196 g, 93.8%) (**R,R-L5**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3450 (N-H), 3292 (N-H), 3059 (Pyr C-H), 3008 (Pyr C-H), 2924 (Cyc C-H), 2853 (Cyc C-H), 1590 (Pyr C-N), 1432 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.50 - 8.40 (m, 2H, PyrH), 7.55 (td,  $J = 7.7, 1.7$  Hz, 2H, PyrH), 7.33 (d,  $J = 7.8$  Hz, 2H, PyrH), 7.07 (dd,  $J = 7.0, 5.2$  Hz, 2H, PyrH), 3.96 (d,  $J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 3.78 (d,  $J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 2.25 (dd,  $J = 5.4, 3.7$  Hz, 2H, CycH), 2.07 (dd,  $J = 10.9, 2.6$  Hz, 2H, CycH), 1.73 - 1.53 (m, 2H, CycH), 1.19 - 1.14 (m, 2H, CycH), 1.07 - 0.94 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.71 (PyrC), 149.08 (PyrC), 136.41 (PyrC), 122.32 (PyrC), 121.77 (PyrC), 61.38 (CycC), 52.53 ( $\text{NHCH}_2$ ), 31.60 (CycC), 25.02 (CycC).

Tertiary diamine synthesis: **R,R-L5** (0.136 g, 0.4587 mmol) was dissolved in MeCN (5 ml). Whilst stirring, 35% formaldehyde (0.436 g, 14.514 mmol) and glacial acetic acid (0.75 ml, 13.088 mmol) was added to the solution. The solution was stirred for 30 min after which  $\text{NaBH}_4$  (0.073 g, 1.923 mmol) of was added portion wise. The reaction mixture was stirred for 72 hours at ambient temperature where after the MeCN was removed under vacuum. KOH (2 M) was added to raise the pH of the solution above 10. The aqueous phase was treated with DCM (3 x 10 ml) where after the organic layer was washed with  $\text{H}_2\text{O}$  (2 x 10 ml) and a saturated NaCl

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solution (1 x 10 ml). The organic phase was dried over  $\text{Na}_2\text{SO}_4$  and the solvent removed under vacuum to obtain a brown oil (0.114 g, 76.6%) (**R,R-L9**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3050 (Pyr C-H), 2930 (Pyr C-H), 2856 (Cyc C-H), 2791 (Cyc C-H), 1591 (Pyr C-N), 1433 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.51 (d,  $J$  = 4.8 Hz, 2H, PyrH), 7.60 (dd,  $J$  = 6.2, 1.6 Hz, 2H, PyrH), 7.16 - 7.11 (m, 2H, PyrH), 3.94 (d,  $J$  = 14.5 Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.82 (d,  $J$  = 14.6 Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.68 (dd,  $J$  = 5.7, 3.2 Hz, 2H, CycH), 2.30 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 2.00 (dd,  $J$  = 10.6, 2.3 Hz, 2H, CycH), 1.85 - 1.70 (m, 2H, CycH), 1.34 - 1.27 (m, 2H, CycH), 1.23 - 1.12 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.29 (PyrC), 148.63 (PyrC), 136.32 (PyrC), 122.92 (PyrC), 121.63 (PyrC), 64.53 (CycC), 60.44 ( $\text{CH}_3\text{NCH}_2$ ), 36.68 ( $\text{CH}_3\text{NCH}_2$ ), 25.84 (CycC), 25.82 (CycC).

#### 3.4.2.2.2 S,S-enantiomer

Diimine synthesis: The synthesis was performed using the same method as described in 3.3.3.1 with S,S-DACH D-tartrate salt (0.346 g, 1.309 mmol),  $\text{K}_2\text{CO}_3$  (0.360 g, 2.605 mmol) and 2-pyridinecarboxaldehyde (0.283 g, 2.642 mmol) being used. A light yellow crystalline product (0.228 g, 59.0%) (**S,S-L1**) was obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3051 (Pyr C-H), 3009 (Pyr C-H), 2928 (ring C-H), 2862 (ring C-H), 1643 (C=N), 1468 (Pyr C-C), 1366.
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.56 (d,  $J$  = 4.7 Hz, 2H, PyrH), 8.32 (s, 2H, HC=N), 7.89 (d,  $J$  = 7.9 Hz, 2H, PyrH), 7.65 (t,  $J$  = 7.7 Hz, 2H, PyrH), 7.23 (dd,  $J$  = 7.3, 5.0 Hz, 2H, PyrH), 3.58 - 3.52 (m, 2H, CycH), 1.92 - 1.81 (m, 6H, CycH), 1.52 (t,  $J$  = 8.9 Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.45 (PyrC), 154.62 (C=N), 149.25 (PyrC), 136.45 (PyrC), 124.48 (PyrC), 121.35 (PyrC), 73.57 (CycC), 32.74 (CycC), 24.37 (CycC).

Secondary diamine synthesis: The synthesis was performed using the same method as described in 3.3.3.1 with **S,S-L1** (0.210 g, 0.7181 mmol) being used. A light yellow oil (0.187 g, 87.8%) (**S,S-L5**) was afforded.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3288 (N-H), 3063 (Pyr C-H), 3009 (Pyr C-H), 2925 (Cyc C-H), 2853 (Cyc C-H), 1591 (Pyr C-N), 1432 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.54 (d,  $J$  = 4.7 Hz, 2H, PyrH), 7.63 (td,  $J$  = 7.6, 1.7 Hz, 2H, PyrH), 7.41 (d,  $J$  = 7.8 Hz, 2H, PyrH), 7.15 (dd,  $J$  = 7.1, 5.2 Hz, 2H, PyrH), 4.04 (d,

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$J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 3.85 (d,  $J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 2.33 (dd,  $J = 5.4, 3.7$  Hz, 2H, CycH), 2.16 (dd,  $J = 11.0, 2.5$  Hz, 2H, CycH), 1.76 - 1.67 (m, 2H, CycH), 1.31 - 1.20 (m, 2H, CycH), 1.08 (dd,  $J = 9.9, 1.9$  Hz, 2H, CycH).

- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.67 (PyrC), 149.07 (PyrC), 136.43 (PyrC), 122.34 (PyrC), 121.78 (PyrC), 61.37 (CycC), 52.51 ( $\text{NHCH}_2$ ), 31.59 (CycC), 25.02 (CycC).

Tertiary diamine synthesis: The synthesis was performed using the same method as described in 3.3.3.1 with **S,S-L5** (0.312 g, 1.052 mmol) being used. A brown oil (0.235 g, 68.8%) (**S,S-L9**) was obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3048 (Pyr C-H), 2929 (Pyr C-H), 2855 (Cyc C-H), 2788 (Cyc C-H), 1590 (Pyr C-N), 1433 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.51 (d,  $J = 4.8$  Hz, 2H, PyrH), 7.64 - 7.54 (m, 4H, PyrH), 7.17 - 7.10 (m, 2H, PyrH), 3.93 (d,  $J = 14.6$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.81 (d,  $J = 14.6$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.67 (dd,  $J = 5.6, 3.2$  Hz, 2H, CycH), 2.30 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 2.00 (dd,  $J = 10.6, 2.3$  Hz, 2H, CycH), 1.82 - 1.72 (m, 2H, CycH), 1.30 (dd,  $J = 11.1, 2.5$  Hz, 2H, CycH), 1.22 - 1.12 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.41 (PyrC), 148.63 (PyrC), 136.29 (PyrC), 122.89 (PyrC), 121.60 (PyrC), 64.55 (CycC), 60.51 ( $\text{CH}_3\text{NCH}_2$ ), 36.66 ( $\text{CH}_3\text{NCH}_2$ ), 25.87 (CycC), 25.84 (CycC).

#### 3.4.2.3 Synthesis of N,N'-dimethyl-N,N'-bis(6-methyl-2-pyridylmethyl)-1,2-cyclohexanediamine

##### 3.4.2.3.1 *R,R*-enantiomer

Diimine synthesis: In a beaker the *R,R*-DACH L-tartrate salt (0.343 g, 1.298 mmol) and  $\text{K}_2\text{CO}_3$  (0.361 g, 2.612 mmol) was dissolved in water (3 ml) which was added to a 100 ml round bottom flask. After everything dissolved, ethanol (5 ml) was added. The solution was heated almost to boiling point during which 1-methyl-5-pyridinecarboxaldehyde (0.315 g, 2.600 mmol), dissolved in ethanol (4 ml), was added to the solution. The reaction mixture was refluxed for 3 hours after which water (3 ml) was added. The solution was then cooled down in an ice bath for 30 min. The water layer was extracted with DCM (3 x 5 ml) where after the organic layer was washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic layer was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to afford an orange solid (0.394 g, 94.7%) (**R,R-L2**).

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- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3060 (Pyr C-H), 2927 (Cyc C-H), 2857 (Cyc C-H), 1646 (C=N), 1572 (Pyr C-N), 1455 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.22 (s, 2H, HC=N), 7.64 (d,  $J = 7.8$  Hz, 2H, PyrH), 7.45 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.01 (d,  $J = 7.6$  Hz, 2H, PyrH), 3.46 - 3.40 (m, 2H, CycH), 2.44 (s, 6H, PyrCH<sub>3</sub>), 1.81 - 1.70 (m, 6H, CycH), 1.45 - 1.39 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.72 (PyrC), 157.78 (PyrC), 154.25 (C=N), 136.63 (PyrC), 124.08 (PyrC), 118.28 (PyrC), 73.63 (CycC), 32.74 (CycC), 24.40 (CycC), 24.30 (PyrCH<sub>3</sub>).

Secondary diamine synthesis: ***R,R*-L2** (0.373 g, 1.164 mmol) was dissolved in MeOH (3 ml) and put in an ice bath for 30 min.  $\text{NaBH}_4$  (0.222 g, 5.868 mmol) was added portion wise over a period of 5 min whilst stirring the solution. The solution was then stirred for 1 hour at ambient temperature where after it was refluxed for another hour. After the solution cooled down to room temperature DCM (20 ml) was added and the organic layer washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic phase was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to yield an orange solid (0.349 g, 92.4%) (***R,R*-L6**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3399 (N-H), 3291 (N-H), 3061 (Pyr C-H), 2924 (Cyc C-H), 2853 (Cyc C-H), 1577 (Pyr C-N), 1449 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.44 (t,  $J = 7.6$  Hz, 2H, PyrH), 7.16 (d,  $J = 7.7$  Hz, 2H, PyrH), 6.92 (d,  $J = 7.6$  Hz, 2H, PyrH), 3.94 (d,  $J = 14.2$  Hz, 2H, NHCH<sub>2</sub>), 3.73 (d,  $J = 14.2$  Hz, 2H, NHCH<sub>2</sub>), 2.44 (s, 6H, PyrCH<sub>3</sub>), 2.26 (dd,  $J = 5.3, 3.8$  Hz, 2H, CycH), 2.09 (dd,  $J = 10.9, 2.8$  Hz, 2H, CycH), 1.68 - 1.60 (m, 2H, CycH), 1.16 (dd,  $J = 8.7, 5.3$  Hz, 2H, CycH), 1.05 - 0.95 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.05 (PyrC), 157.60 (PyrC), 136.62 (PyrC), 121.24 (PyrC), 119.12 (PyrC), 61.42 (CycC), 52.54 (NHCH<sub>2</sub>), 31.67 (CycC), 25.04 (CycC), 24.48 (PyrCH<sub>3</sub>).

Tertiary diamine synthesis: ***R,R*-L6** (0.379 g, 1.168 mmol) was dissolved in MeCN (5 ml). Whilst stirring, 35% formaldehyde (1.128 g, 37.550 mmol) and glacial acetic acid (0.75 ml, 13.088 mmol) was added to the solution. The solution was stirred for 30 min after which  $\text{NaBH}_4$  (0.177 g, 4.679 mmol) was added portion wise. The reaction mixture was stirred for 72 hours at ambient temperature where after the MeCN was removed under vacuum. KOH (2 M) was added to raise the pH of the solution above 10. The aqueous phase was treated with DCM (3 x 10 ml) where after the organic layer was washed with  $\text{H}_2\text{O}$  (2 x 10 ml) and a saturated NaCl

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solution (1 x 10 ml). The organic phase was dried over  $\text{Na}_2\text{SO}_4$  and the solvent removed under vacuum to obtain a brown oil (0.324 g, 78.7%) (**R,R-L10**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3059 (Pyr C-H), 2926 (Pyr C-H), 2854 (Cyc C-H), 2782 (Cyc C-H), 1577 (Pyr C-N), 1452 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.49 (t,  $J = 7.6$  Hz, 2H, PyrH), 7.41 (d,  $J = 7.7$  Hz, 2H, PyrH), 6.99 (d,  $J = 7.5$  Hz, 2H, PyrH), 3.91 (d,  $J = 14.8$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.77 (d,  $J = 14.8$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.70 - 2.63 (m, 2H, CycH), 2.53 (s, 6H, PyrCH<sub>3</sub>), 2.30 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 1.99 (d,  $J = 12.8$  Hz, 2H, CycH), 1.84 - 1.70 (m, 2H, CycH), 1.34 - 1.26 (m, 2H, CycH), 1.17 (dd,  $J = 12.4, 6.4$  Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.80 (PyrC), 157.10 (PyrC), 136.52 (PyrC), 121.01 (PyrC), 119.63 (PyrC), 64.70 (CycC), 60.36 ( $\text{CH}_3\text{NCH}_2$ ), 36.70 ( $\text{CH}_3\text{NCH}_2$ ), 25.86 (CycC), 25.69 (CycC), 24.45 (PyrCH<sub>3</sub>).

#### 3.4.2.3.2 S,S-enantiomer

Diimine synthesis: The synthesis was performed using the same method as described in 3.3.4.1 with S,S-DACH D-tartrate salt (0.342 g, 1.294 mmol),  $\text{K}_2\text{CO}_3$  (0.358 g, 2.590 mmol) and 6-methyl-2-pyridinecarboxaldehyde (0.312 g, 2.576 mmol) being used. An orange solid (0.377 g, 91.3%) (**S,S-L2**) was obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3060 (Pyr C-H), 2927 (Cyc C-H), 2857 (Cyc C-H), 1646 (C=N), 1590 (Pyr C-N), 1455 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.31 (s, 2H, HC=N), 7.73 (d,  $J = 7.8$  Hz, 2H, PyrH), 7.53 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.09 (d,  $J = 7.6$  Hz, 2H, PyrH), 3.57 - 3.47 (m, 2H, CycH), 2.53 (s, 6H, CycH), 1.85 (ddd,  $J = 37.7, 15.2, 7.1$  Hz, 6H, CycH), 1.50 (dd,  $J = 14.3, 5.4$  Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 161.72 (PyrC), 157.78 (PyrC), 154.23 (C=N), 136.63 (PyrC), 124.09 (PyrC), 118.29 (PyrC), 73.63 (CycC), 32.74 (CycC), 24.40 (CycC), 24.30 (CycC).

Secondary diamine synthesis: The synthesis was performed using the same method as described in 3.3.4.1 with **S,S-L2** (0.359 g, 1.120 mmol) being used. The product was isolated as an orange solid (0.316 g, 86.9%) (**S,S-L6**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3563 (N-H), 3294 (N-H), 3061 (Pyr C-H), 2924 (Cyc C-H), 2853 (Cyc C-H), 1577 (Pyr C-N), 1449 (Pyr C-C).

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- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.44 (t,  $J = 7.6$  Hz, 2H, PyrH), 7.15 (d,  $J = 7.7$  Hz, 2H, PyrH), 6.92 (d,  $J = 7.6$  Hz, 2H, PyrH), 3.94 (d,  $J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 3.73 (d,  $J = 14.1$  Hz, 2H,  $\text{NHCH}_2$ ), 2.44 (s, 6H,  $\text{PyrCH}_3$ ), 2.25 (dd,  $J = 5.5, 3.6$  Hz, 2H, CycH), 2.08 (dd,  $J = 10.9, 2.7$  Hz, 2H, CycH), 1.68 - 1.60 (m, 2H, CycH), 1.16 (ddd,  $J = 7.2, 6.0, 2.4$  Hz, 2H, CycH), 1.05 - 0.94 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.04 (PyrC), 157.61 (PyrC), 136.63 (PyrC), 121.25 (PyrC), 119.14 (PyrC), 61.41 (CycC), 52.54 ( $\text{NHCH}_2$ ), 31.66 (CycC), 25.04 (CycC), 24.47 ( $\text{PyrCH}_3$ ).

Tertiary diamine synthesis: The synthesis was performed using the same method as described in 3.3.4.1 with **S,S-L6** (0.276 g, 0.8505 mmol) of being used. A brown oil (0.256 g, 85.4%) (**S,S-L10**) was afforded.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3059 (Pyr C-H), 2926 (Pyr C-H), 2854 (Cyc C-H), 2782 (Cyc C-H), 1577 (Pyr C-N), 1452 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.40 (t,  $J = 7.6$  Hz, 2H, PyrH), 7.33 (d,  $J = 7.7$  Hz, 2H, PyrH), 6.90 (d,  $J = 7.5$  Hz, 2H, PyrH), 3.82 (d,  $J = 14.8$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.68 (d,  $J = 14.8$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.58 (dd,  $J = 5.7, 3.2$  Hz, 2H, CycH), 2.45 (s, 6H,  $\text{PyrCH}_3$ ), 2.21 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 1.97 - 1.84 (m, 2H, CycH), 1.74 - 1.61 (m, 2H, CycH), 1.25 - 1.16 (m, 2H, CycH), 1.08 (t,  $J = 9.4$  Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.83 (PyrC), 157.10 (PyrC), 136.52 (PyrC), 121.00 (PyrC), 119.62 (PyrC), 64.71 (CycC), 60.38 ( $\text{CH}_3\text{NCH}_2$ ), 36.70 ( $\text{CH}_3\text{NCH}_2$ ), 25.87 (CycC), 25.69 (CycC), 24.45 ( $\text{PyrCH}_3$ ).

#### 3.4.2.4 Synthesis of N,N'-dimethyl-N,N'-bis(6-bromo-2-pyridylmethyl)-1,2-cyclohexanediamine

##### 3.4.2.4.1 R,R-enantiomer

Diimine synthesis: A round bottom flask was charged with 4-bromo-2-pyridinecarboxaldehyde (0.482 g, 2.591 mmol) and ethanol (3 ml) was added. In a separate beaker the R,R-DACH L-tartrate salt (0.343 g, 1.298 mmol) and  $\text{K}_2\text{CO}_3$  (0.359 g, 2.597 mmol) was dissolved in water (3 ml) after which ethanol (5 ml) was added. The solution was added to the round bottom flask and allowed to reflux for 3 hours after which water (3 ml) was added. The solution was cooled down in an ice bath for 30 min. The solid which formed was filtered and washed with ethanol after which recrystallisation was carried out using boiling ethanol. Cooling of the solution in a freezer overnight afforded a white crystalline product (0.394 g, 67.6%) (**R,R-L3**).

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- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 2930 (Pyr C-H), 2855 (Cyc C-H), 1649 (C=N), 1546 (Pyr C-N), 1439 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.15 (s, 2H, HC=N), 7.82 (dd,  $J$  = 7.6, 0.5 Hz, 2H, PyrH), 7.46 (t,  $J$  = 7.7 Hz, 2H, PyrH), 7.36 (dd,  $J$  = 7.8, 0.6 Hz, 2H, PyrH), 3.45 - 3.35 (m, 2H, CycH), 1.83 - 1.66 (m, 6H, CycH), 1.42 (dd,  $J$  = 15.2, 6.0 Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.09 (PyrC), 155.79 (C=N), 141.31 (PyrC), 138.84 (PyrC), 128.97 (PyrC), 119.77 (PyrC), 73.52 (CycC), 32.56 (CycC), 24.25 (CycC).

Secondary diamine synthesis: **R,R-L3** (0.371 g, 0.8241 mmol) was dissolved in MeOH (3 ml) and put in an ice bath for 30 min.  $\text{NaBH}_4$  (0.156 g, 4.124 mmol) was added portion wise over a period of 5 min whilst stirring the solution. The solution was then stirred for 1 hour at ambient temperature where after it was refluxed for another hour. After the solution cooled down to room temperature it was filtered. DCM (20 ml) was added to the filtrate and the organic layer washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic phase was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to yield a white solid (0.313 g, 83.6%) (**R,R-L7**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3291 (N-H), 3238 (N-H), 2927 (Pyr C-H), 2855 (Cyc C-H), 1553 (Pyr C-N), 1403 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.46 (t,  $J$  = 7.7 Hz, 2H, PyrH), 7.38 (d,  $J$  = 7.4 Hz, 2H, PyrH), 7.27 (d,  $J$  = 7.8 Hz, 2H, PyrH), 3.96 (d,  $J$  = 14.7 Hz, 2H,  $\text{NHCH}_2$ ), 3.74 (d,  $J$  = 14.7 Hz, 2H,  $\text{NHCH}_2$ ), 2.21 (dd,  $J$  = 5.5, 3.6 Hz, 2H, CycH), 2.07 (dd,  $J$  = 10.9, 2.8 Hz, 2H, CycH), 1.68 - 1.62 (m, 2H, CycH), 1.17 - 1.14 (m, 2H, CycH), 1.01 - 0.93 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 162.55 (PyrC), 141.40 (PyrC), 138.97 (PyrC), 126.09 (PyrC), 121.19 (PyrC), 61.40 (CycC), 51.88 ( $\text{NHCH}_2$ ), 31.67 (CycC), 24.96 (CycC).

Tertiary diamine synthesis: **R,R-L7** (0.491 g, 1.081 mmol) was dissolved in MeCN (5 ml). Whilst stirring, 35% formaldehyde (1.026 g, 34.154 mmol) and glacial acetic acid (0.75 ml, 13.088 mmol) was added to the solution. The solution was stirred for 30 min after which  $\text{NaBH}_4$  (0.164 g, 4.385 mmol) was added portion wise. The reaction mixture was stirred for 72 hours at ambient temperature where after the MeCN was removed under vacuum. KOH (2 M) was added to raise the pH of the solution above 10. The aqueous phase was treated with DCM (3 x 10 ml) where after the organic layer was washed with  $\text{H}_2\text{O}$  (2 x 10 ml) and a saturated NaCl solution (1 x 10 ml). The organic phase was dried over  $\text{Na}_2\text{SO}_4$  and the solvent removed under vacuum to obtain a yellow oil (0.461 g, 88.4%) (**R,R-L11**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3047 (Pyr C-H), 2927 (Pyr C-H), 2853 (Cyc C-H), 2784 (Cyc C-H), 1553 (Pyr C-N), 1402 (Pyr C-C).

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- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.45 (d,  $J = 7.5$  Hz, 2H, PyrH), 7.38 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.24 (d,  $J = 7.7$  Hz, 2H, PyrH), 3.81 (d,  $J = 15.3$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.68 (d,  $J = 15.3$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.65 - 2.47 (m, 2H, CycH), 2.20 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 1.88 (d,  $J = 12.8$  Hz, 2H, CycH), 1.73 - 1.66 (m, 2H, CycH), 1.23 - 1.16 (m, 2H, CycH), 1.12 - 1.04 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 163.43 (PyrC), 140.94 (PyrC), 138.69 (PyrC), 125.77 (PyrC), 121.38 (PyrC), 64.85 (CycC), 59.75 ( $\text{CH}_3\text{NCH}_2$ ), 36.80 ( $\text{CH}_3\text{NCH}_2$ ), 25.86 (CycC), 25.77 (CycC).

#### 3.4.2.4.2 S,S-enantiomer

Diimine synthesis: The synthesis was performed using the same method as described in 3.3.5.1 with S,S-DACH D-tartrate salt (0.344 g, 1.302 mmol),  $\text{K}_2\text{CO}_3$  (0.361 g, 2.612 mmol) and 4-bromo-2-pyridinecarboxaldehyde (0.481 g, 2.586 mmol) being used. White crystals (0.432 g, 74.2%) (**S,S-L3**) were obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 2982 (Pyr C-H), 2930 (Pyr C-H), 2854 (Cyc C-H), 1649 (C=N), 1546 (Pyr C-N), 1438 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.24 (s, 2H, HC=N), 7.91 (dd,  $J = 7.7, 0.7$  Hz, 2H, PyrH), 7.55 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.45 (dd,  $J = 7.8, 0.8$  Hz, 2H, PyrH), 3.55 - 3.44 (m, 2H, CycH), 1.97 - 1.86 (m, 2H, CycH), 1.85 - 1.75 (m, 4H, CycH), 1.56 - 1.45 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 160.09 (PyrC), 155.79 (C=N), 141.30 (PyrC), 138.84 (PyrC), 128.97 (PyrC), 119.77 (PyrC), 73.52 (CycC), 32.56 (CycC), 24.25 (CycC).

Secondary diamine synthesis: The synthesis was performed using the same method as described in 3.3.5.1 with **S,S-L3** (0.405 g, 0.8996 mmol) being used. A white solid (0.363 g, 88.8%) (**S,S-L7**) was obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3278 (N-H), 3197 (N-H), 3047 (Pyr C-H), 2932 (Pyr C-H), 2849 (Cyc C-H), 2773 (Cyc C-H), 1552 (Pyr C-N), 1402 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.46 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.38 (d,  $J = 7.5$  Hz, 2H, PyrH), 7.27 (d,  $J = 7.7$  Hz, 2H, PyrH), 3.96 (d,  $J = 14.7$  Hz, 2H,  $\text{NHCH}_2$ ), 3.74 (d,  $J = 14.7$  Hz, 2H,  $\text{NHCH}_2$ ), 2.21 (dd,  $J = 5.5, 3.6$  Hz, 2H, CycH), 2.07 (dd,  $J = 10.9, 2.7$  Hz, 2H, CycH), 1.72 - 1.57 (m, 2H, CycH), 1.16 (ddd,  $J = 11.1, 5.2, 1.7$  Hz, 2H, CycH), 0.97 (dd,  $J = 9.8, 1.8$  Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 162.53 (PyrC), 141.40 (PyrC), 138.97 (PyrC), 126.09 (PyrC), 121.19 (PyrC), 61.40 (CycC), 51.87 ( $\text{NHCH}_2$ ), 31.66 (CycC), 24.96 (CycC).

### Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

Tertiary diamine synthesis: The synthesis was performed using the same method as described in 3.3.5.1 with **S,S-L7** (0.543 g, 1.195 mmol) being used. A yellow oil (0.492 g, 85.3%) (**S,S-L11**) was afforded.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3064 (Pyr C-H), 2927 (Pyr C-H), 2853 (Cyc C-H), 2784 (Cyc C-H), 1553 (Pyr C-N), 1402 (Pyr C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 7.45 (d,  $J = 7.5$  Hz, 2H, PyrH), 7.38 (t,  $J = 7.7$  Hz, 2H, PyrH), 7.25 (d,  $J = 7.7$  Hz, 2H, PyrH), 3.81 (d,  $J = 15.3$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.68 (d,  $J = 15.3$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 2.56 (dd,  $J = 5.7, 3.2$  Hz, 2H, CycH), 2.20 (s, 6H,  $\text{CH}_3\text{NCH}_2$ ), 1.89 (d,  $J = 12.8$  Hz, 2H, CycH), 1.73 - 1.67 (m, 2H, CycH), 1.20 (d,  $J = 8.9$  Hz, 2H, CycH), 1.09 (t,  $J = 9.4$  Hz, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 163.40 (PyrC), 140.94 (PyrC), 138.69 (PyrC), 125.78 (PyrC), 121.39 (PyrC), 64.85 (CycC), 59.74 ( $\text{CH}_3\text{NCH}_2$ ), 36.81 ( $\text{CH}_3\text{NCH}_2$ ), 25.86 (CycC), 25.76 (CycC).

#### 3.4.2.5 Synthesis of N,N'-dimethyl-N,N'-bis(1-methylimidazole-2-methyl)-1,2-cyclohexanediamine

##### 3.4.2.5.1 *R,R*-enantiomer

Diimine synthesis: In a beaker the *R,R*-DACH L-tartrate salt (0.345 g, 1.305 mmol) and  $\text{K}_2\text{CO}_3$  (0.361 g, 2.612 mmol) was dissolved in water (3 ml) which was added to a 100 ml round bottom flask. After everything dissolved, ethanol (5 ml) was added. The solution was heated almost to boiling point during which 1-methyl-2-imidazolecarboxaldehyde (0.286 g, 2.597 mmol), dissolved in ethanol (3 ml), was added to the solution. The reaction mixture was refluxed for 3 hours after which water (3 ml) was added. The solution was then cooled down in an ice bath for 30 min. The water layer was extracted with DCM (3 x 5 ml) where after the organic layer was washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic layer was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to obtain a light yellow oil (0.348 g, 89.8%) (**R,R-L4**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3106 (Imid C-H), 2927 (Cyc C-H), 2857 (Cyc C-H), 1646 (C=N), 1518 (Imid C-N), 1438 (Imid C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.15 (s, 2H, HC=N), 6.96 (d,  $J = 0.8$  Hz, 2H, ImidH), 6.79 (s, 2H, ImidH), 3.82 (s, 6H, ImidCH<sub>3</sub>), 3.23 - 3.18 (m, 2H, CycH), 1.80 - 1.69 (m, 4H, CycH), 1.62 (dt,  $J = 9.7, 8.8$  Hz, 2H, CycH), 1.43 - 1.37 (m, 2H, CycH).

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- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 152.18 (**C=N**), 143.17 (Imid**C**), 128.88 (Imid**C**), 124.73 (Imid**C**), 74.80 (Cyc**C**), 35.51 (Imid**CH**<sub>3</sub>), 32.92 (Cyc**C**), 24.34 (Cyc**C**).

Secondary diamine synthesis: **R,R-L4** (0.324 g, 1.086 mmol) was dissolved in MeOH (3 ml) and put in an ice bath for 30 min.  $\text{NaBH}_4$  (0.206 g, 5.445 mmol) was added portion wise over a period of 5 min whilst stirring the solution. The solution was then stirred for 1 hour at ambient temperature where after it was refluxed for another hour. After the solution cooled down to room temperature DCM (20 ml) was added and the organic layer washed with water (2 x 5 ml) and a saturated NaCl solution (1 x 5 ml). The organic phase was dried with  $\text{Na}_2\text{SO}_4$  and the solvent removed to yield a yellow oil (0.279 g, 85.0%) (**R,R-L8**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3288 (N-H), 3109 (N-H), 2926 (Imid C-H), 2854 (Cyc C-H), 1520 (Imid C-N), 1449 (Imid C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 6.82 (d,  $J = 1.2$  Hz, 2H, Imid**H**), 6.71 (d,  $J = 1.1$  Hz, 2H, Imid**H**), 3.86 (d,  $J = 13.5$  Hz, 2H, **NHCH**<sub>2</sub>), 3.63 (d,  $J = 13.5$  Hz, 2H **NHCH**<sub>2</sub>), 3.56 (s, 6H, Imid**CH**<sub>3</sub>), 2.18 (dd,  $J = 5.5, 3.6$  Hz, 2H, Cyc**H**), 2.08 (dd,  $J = 11.0, 2.7$  Hz, 2H, Cyc**H**), 1.68 - 1.63 (m, 2H, Cyc**H**), 1.17 (dd,  $J = 15.1, 5.5$  Hz, 2H, Cyc**H**), 1.01 - 0.94 (m, 2H, Cyc**H**).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 146.84 (Imid**C**), 127.00 (Imid**C**), 121.14 (Imid**C**), 61.18 (Cyc**C**), 43.07 (**NHCH**<sub>2</sub>), 32.80 (Imid**CH**<sub>3</sub>), 31.27 (Cyc**C**), 24.90 (Cyc**C**).

Tertiary diamine synthesis: **R,R-L8** (0.295 g, 0.9753 mmol) was dissolved in MeCN (5 ml). Whilst stirring, 35% formaldehyde (0.932 g, 31.025 mmol) and glacial acetic acid (0.75 ml, 13.088 mmol) was added to the solution. The solution was stirred for 30 min after which  $\text{NaBH}_4$  (0.151 g, 3.992 mmol) was added portion wise. The reaction mixture was stirred for 72 hours at ambient temperature where after the MeCN was removed under vacuum. KOH (2 M) was added to raise the pH of the solution above 10. The aqueous phase was treated with DCM (3 x 10 ml) where after the organic layer was washed with  $\text{H}_2\text{O}$  (2 x 10 ml) and a saturated NaCl solution (1 x 10 ml). The organic phase was dried over  $\text{Na}_2\text{SO}_4$  and the solvent removed under vacuum to obtain a yellow oil (0.250 g, 77.6%) (**R,R-L12**).

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3105 (Imid C-H), 2928 (Imid C-H), 2855 (Cyc C-H), 2788 (Cyc C-H), 1499 (Imid C-N), 1449 (Imid C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 6.91 (d,  $J = 1.2$  Hz, 2H, Imid**H**), 6.82 (d,  $J = 1.1$  Hz, 2H, Imid**H**), 3.76 (d,  $J = 13.4$  Hz, 2H, **CH**<sub>3</sub>**NCH**<sub>2</sub>), 3.71 (d,  $J = 13.3$  Hz, 8H, **CH**<sub>3</sub>**NCH**<sub>2</sub> and **CH**<sub>3</sub>**NCH**<sub>2</sub>), 2.59 (dd,  $J = 5.2, 3.1$  Hz, 2H, Cyc**H**), 2.05 (s, 6H, **CH**<sub>3</sub>**NCH**<sub>2</sub>), 1.94 (dd,  $J = 8.0, 4.4$  Hz, 2H, Cyc**H**), 1.76 (dd,  $J = 6.4, 2.5$  Hz, 2H, Cyc**H**), 1.24 - 1.13 (m, 4H, Cyc**H**).

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- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 146.22 (ImidC), 126.89 (ImidC), 121.40 (ImidC), 62.01 (CycC), 50.94 ( $\text{CH}_3\text{NCH}_2$ ), 35.42 ( $\text{CH}_3\text{NCH}_2$ ), 32.72 (Imid $\text{CH}_3$ ), 25.64 (CycC), 24.44 (CycC).

#### 3.4.2.5.2 S,S-enantiomer

Diimine synthesis: The synthesis was performed using the same method as described in 3.3.6.1 with S,S-DACH D-tartrate salt (0.345 g, 1.305 mmol),  $\text{K}_2\text{CO}_3$  (0.361 g, 2.612 mmol) and 1-methyl-2-imidazolecarboxaldehyde (0.287 g, 2.606 mmol) being used. A light yellow oil (0.348 g, 89.5%) (**S,S-L4**) was obtained.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3106 (Imid C-H), 2927 (Cyc C-H), 2857 (Cyc C-H), 1646 (C=N), 1438 (Imid C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 8.24 (s, 2H, HC=N), 7.04 (s, 2H, ImidH), 6.87 (s, 2H, ImidH), 3.90 (s, 6H, Imid $\text{CH}_3$ ), 3.34 - 3.24 (m, 2H, CycH), 1.91 - 1.77 (m, 4H, CycH), 1.71 (dd,  $J$  = 16.5, 13.8 Hz, 2H, CycH), 1.53 - 1.43 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 152.17 (C=N), 143.16 (ImidC), 128.87 (ImidC), 124.73 (ImidC), 74.80 (CycC), 35.52 (Imid $\text{CH}_3$ ), 32.92 (CycC), 24.34 (CycC).

Secondary diamine synthesis: The synthesis was performed using the same method as described in 3.3.6.1 with **S,S-L4** (0.330 g, 1.106 mmol) being used. A light yellow oil (0.317 g, 94.8%) (**S,S-L8**) was afforded.

- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3292 (N-H), 3108 (N-H), 2926 (Imid C-H), 2854 (Cyc C-H), 1520 (Imid C-N), 1449 (Imid C-C).
- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 6.82 (d,  $J$  = 1.1 Hz, 2H, ImidH), 6.71 (d,  $J$  = 1.1 Hz, 2H, ImidH), 3.86 (d,  $J$  = 13.5 Hz, 2H,  $\text{NHCH}_2$ ), 3.63 (d,  $J$  = 13.5 Hz, 2H,  $\text{NHCH}_2$ ), 3.56 (s, 6H, Imid $\text{CH}_3$ ), 2.18 (dd,  $J$  = 5.4, 3.6 Hz, 2H, CycH), 2.11 - 2.05 (m, 2H, CycH), 1.70 - 1.63 (m, 2H, CycH), 1.18 (dd,  $J$  = 12.9, 6.3 Hz, 2H, CycH), 1.04 - 0.92 (m, 2H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 146.83 (ImidC), 126.99 (ImidC), 121.14 (ImidC), 61.17 (CycC), 43.05 ( $\text{NHCH}_2$ ), 32.80 (Imid $\text{CH}_3$ ), 31.26 (CycC), 24.89 (CycC).

Tertiary diamine synthesis: The synthesis was performed using the same method as described in 3.3.6.1 with **S,S-L8** (0.305 g, 1.008 mmol) being used. A yellow oil (0.233 g, 69.9%) (**S,S-L12**) was obtained.

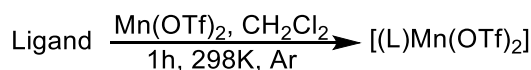
- FT-IR (ATR)  $\nu$ ,  $\text{cm}^{-1}$ : 3106 (Imid C-H), 2928 (Imid C-H), 2855 (Cyc C-H), 2790 (Cyc C-H), 1499 (Imid C-N), 1449 (Imid C-C).

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- $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 6.83 (d,  $J = 1.2$  Hz, 2H, ImidH), 6.74 (d,  $J = 1.1$  Hz, 2H, ImidH), 3.68 (d,  $J = 13.4$  Hz, 2H,  $\text{CH}_3\text{NCH}_2$ ), 3.62 (d,  $J = 13.1$  Hz, 8H,  $\text{CH}_3\text{NCH}_2$  and  $\text{CH}_3\text{NCH}_2$ ), 2.51 (dd,  $J = 5.2, 3.2$  Hz, 2H, CycH), 1.97 (s, 6H, ImidCH<sub>3</sub>), 1.86 (dd,  $J = 8.2, 4.1$  Hz, 2H, CycH), 1.68 (dd,  $J = 6.4, 2.5$  Hz, 2H, CycH), 1.18 - 1.04 (m, 4H, CycH).
- $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 146.21 (ImidC), 126.88 (ImidC), 121.40 (ImidC), 62.00 (CycC), 50.93 ( $\text{CH}_3\text{NCH}_2$ ), 35.42 ( $\text{CH}_3\text{NCH}_2$ ), 32.72 (ImidCH<sub>3</sub>), 25.63 (CycC), 24.44 (CycC).

#### 3.4.3 Synthesis of non-heme $N_4$ -tetradentate $\text{Mn}(\text{OTf})_2$ complexes $R,R$ - and $S,S$ -C1 - C8

Synthesis of non-heme  $N_4$ -tetradentate  $\text{Mn}(\text{II})$ -complexes were carried out in a similar manner than previously mentioned.<sup>15, 33</sup> All complex synthesis was done under an Ar atmosphere. Equal molar amounts of the ligand ( $R,R$ - or  $S,S$ -L5 - L12) and  $\text{Mn}(\text{OTf})_2$  were both dissolved in DCM (2 ml), added together and stirred for 1 hour in a cellulose extraction thimble inside a Schlenk tube. Reaction progress was monitored with thin-layer chromatography (TLC) using silica as the stationary and DCM as the mobile phase. After completion the thimble was washed with DCM (5 ml) and removed from the flask.  $\text{Et}_2\text{O}$  (2 x 20 ml) was added to the mixture and removed under vacuum to ensure precipitation, washing and drying of the complex. Only details regarding the amount of  $\text{Mn}(\text{OTf})_2$  and ligand used in the synthesis will be noted further in the methodology section.

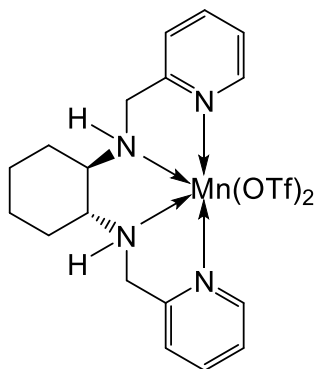


Scheme 3.6: Synthetic route of non-heme  $\text{Mn}(\text{II})(\text{OTf})_2$  complexes used in this study.

## Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

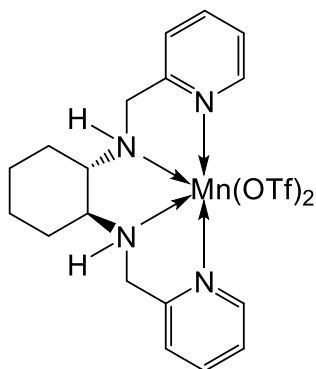
### 3.4.3.1 Complex 1 (*R,R*- and *S,S*-C1)

*R,R*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1071 g, 0.3033 mmol) and ***R,R*-L5** (0.093 g, 0.3137 mmol) afforded a beige solid (0.1569 g, 83.8%) (***R,R*-C1**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 218.0 (3662), 251.0 (4578).
- APCI-MS ( $m/z$ ): 500.0914  $[\text{M} - \text{OTf}]^+$ , 649.0428  $[\text{M}]^+$ .

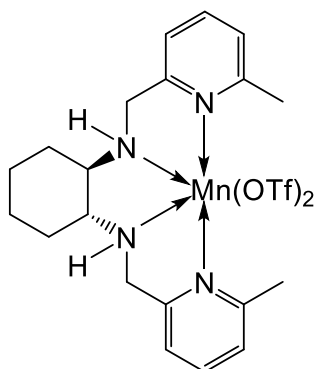
*S,S*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.0865 g, 0.2327 mmol) and ***S,S*-L5** (0.073 g, 0.2462 mmol) yielded a beige solid (0.0611 g; 40.4%) (***S,S*-C1**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 219.0 (3453), 267.5 (3971).
- APCI-MS ( $m/z$ ): 500.0896  $[\text{M} - \text{OTf}]^+$ , 649.0413  $[\text{M}]^+$ .

### 3.4.3.2 Complex 2 (*R,R*- and *S,S*-C2)

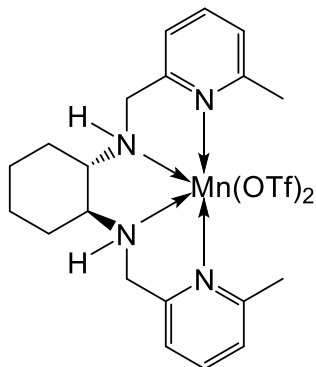
*R,R*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1385 g, 0.3923 mmol) and ***R,R*-L6** (0.131 g, 0.4037 mmol) ligand produced an off-white solid (0.0735 g, 29.1%) (***R,R*-C2**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 236 (4732), 277.5 (4673).
- APCI-MS ( $m/z$ ): 528.1214  $[\text{M} - \text{OTf}]^+$ , 677.0727  $[\text{M}]^+$ .

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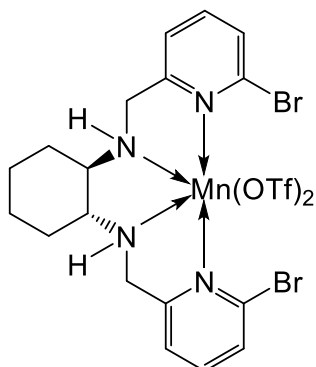
S,S-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1830 g, 0.4924 mmol) and **S,S-L6** (0.170 g, 0.5239 mmol) yielded an off-white solid (0.2893 g, 86.7%) (**S,S-C2**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 221.5 (3413), 261.0 (3686).
- APCI-MS ( $m/z$ ): 528.1213  $[\text{M} - \text{OTf}]^+$ , 677.0725  $[\text{M}]^+$ .

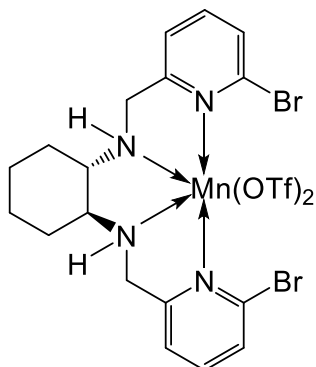
#### 3.4.3.3 Complex 3 (*R,R*- and *S,S*-C3)

R,R-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1296 g, 0.3487 mmol) and **R,R-L7** (0.166 g, 0.3654 mmol) produced an off-white solid (0.1423 g, 50.6%) (**R,R-C3**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 230.0 (4474), 265.0 (4604).
- APCI-MS ( $m/z$ ): 657.9070  $[\text{M} - \text{OTf}]^+$ , 806.8609  $[\text{M}]^+$ .

S,S-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1473 g, 0.3963 mmol) and **S,S-L7** (0.189 g, 0.4161 mmol) produced an off-white solid (0.1368 g, 42.8%) (**S,S-C3**) .

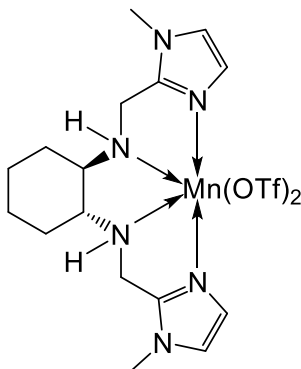


- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 225.5 (4944), 266.0 (5405).
- APCI-MS ( $m/z$ ): 657.9054  $[\text{M} - \text{OTf}]^+$ , 807.8653  $[\text{M}]^+$ .

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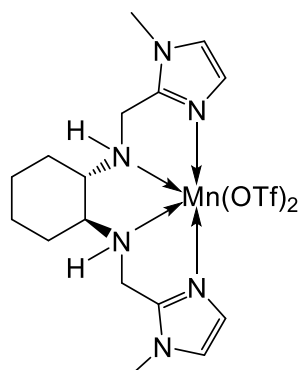
### 3.4.3.4 Complex 4 (*R,R*- and *S,S*-C4)

*R,R*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1170 g, 0.3148 mmol) and ***R,R*-L8** (0.099 g, 0.3273 mmol) ligand afforded a white solid (0.0950 g, 46.0%) (***R,R*-C4**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 220.0 (3260), 260.0 (272).
- APCI-MS ( $m/z$ ): 506.1111  $[\text{M} - \text{OTf}]^+$ , 655.0617  $[\text{M}]^+$ .

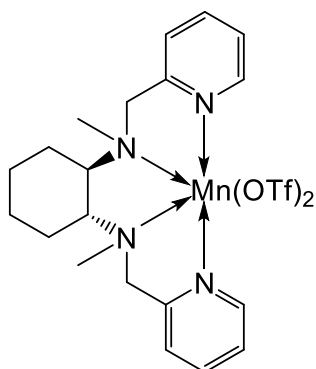
*S,S*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1362 g, 0.3665 mmol) and ***S,S*-L8** (0.115 g, 0.3802 mmol) yielded a white solid (0.1466 g, 61.0%) (***S,S*-C4**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 222.0 (3198), 270 (920).
- APCI-MS ( $m/z$ ): 506.1143  $[\text{M} - \text{OTf}]^+$ , 655.0656  $[\text{M}]^+$ .

### 3.4.3.5 Complex 5 (*R,R*- and *S,S*-C5)

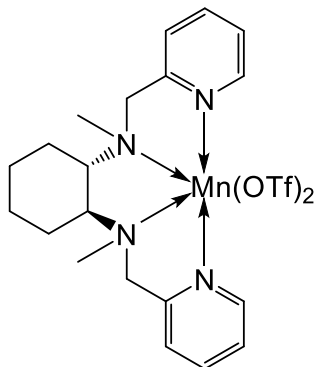
*R,R*-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1646 g, 0.4429 mmol) and ***R,R*-L9** (0.155 g, 0.4776 mmol) yielded a product that was isolated as a beige solid (0.1460 g, 46.2%) (***R,R*-C5**) .



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 210.5 (3463), 263.5 (4082).
- APCI-MS ( $m/z$ ): 528.1214  $[\text{M} - \text{OTf}]^+$ , 677.0722  $[\text{M}]^+$ .

### Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

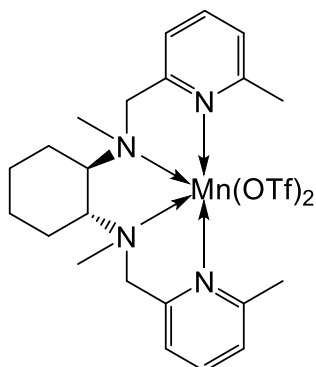
S,S-configuration:  $\text{Mn}(\text{OTf})_2$  (0.1308 g, 0.3519 mmol) and **S,S-L9** (0.120 g, 0.3698 mmol) afforded a beige solid (0.1371 g, 48.7%) (**S,S-C5**).



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 214.5 (3634), 265.5 (4141).
- APCI-MS ( $m/z$ ): 528.1244  $[\text{M} - \text{OTf}]^+$ , 677.0767  $[\text{M}]^+$ .

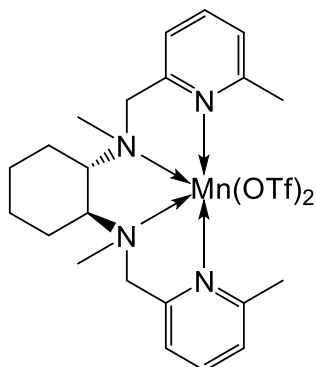
#### 3.4.3.6 Complex 6 (*R,R*- and *S,S*-C6)

R,R-configuration:  $\text{Mn}(\text{OTf})_2$  (0.2222 g, 0.5979 mmol) and **R,R-L10** (0.223 g, 0.6318 mmol) yielded a beige solid (0.2350 g, 55.7%) (**R,R-C6**).



- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 221.5 (3946), 271 (4598).
- APCI-MS ( $m/z$ ): 556.1512  $[\text{M} - \text{OTf}]^+$ , 705.1012  $[\text{M}]^+$ .

S,S-configuration:  $\text{Mn}(\text{OTf})_2$  (0.2436 g, 0.6554 mmol) and **S,S-L10** (0.243 g, 0.6892 mmol) afforded a beige solid (0.3603 g, 74.0%) (**S,S-C6**).

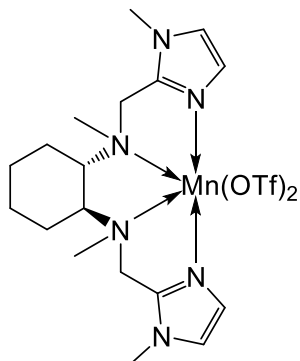


- UV-vis, nm ( $\epsilon$ ,  $\text{A/mol dm}^{-3}$ ): 219.5 (4215), 269.5 (4627).
- APCI-MS ( $m/z$ ): 556.1548  $[\text{M} - \text{OTf}]^+$ , 705.1051  $[\text{M}]^+$ .



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S,S-configuration: Mn(OTf)<sub>2</sub> (0.2203 g, 0.5927 mmol) and **S,S-L12** (0.206 g, 0.6232 mmol) afforded a white solid (0.2236 g, 52.4%) (**S,S-C8**) .



- UV-vis, nm ( $\epsilon$ , A/mol dm<sup>-3</sup>): 214.5 (3412), 274 (579).
- APCI-MS (m/z): 534.1429 [M - OTf]<sup>+</sup>, 683.0955 [M]<sup>+</sup>.

### Chapter 3: The synthesis and characterisation of non-heme $N_4$ -tetradentate ligands and their manganese(II) complexes

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## **Chapter 4**

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**Evaluating the catalytic performance of  
non-heme N<sub>4</sub>-tetradentate manganese(II)  
complexes during alcohol oxidation**

## *Chapter 4: Evaluating the catalytic performance of non-heme N<sub>4</sub>-tetradentate manganese(II) complexes during alcohol oxidation*

### **4.1 Introduction**

Aldehydes and ketones have become important feedstock materials over the last few decades, particularly for use in the perfume, pharmaceutical and fine chemicals industry.<sup>1-2</sup> To obtain these carbonyl compounds, several effective processes via the oxidation of alcohols have been developed, but severe oxidisers (HNO<sub>3</sub>, KMnO<sub>4</sub> and CrO<sub>3</sub>)<sup>3-4</sup> and expensive and toxic metals (Au, Pt and Cr)<sup>5-6</sup> are needed during their production. In an attempt to become more environmentally friendly and use benign conditions to catalyse the oxidation of alcohols, non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes have been developed utilising H<sub>2</sub>O<sub>2</sub> as terminal oxidant and AcOH as co-catalyst.

Many of these Mn(II)-complexes have previously been shown to oxidise hydrocarbons, i.e. alkenes and alkanes, with high activity and selectivity.<sup>7-10</sup> However, it was found that AcOH is a requirement during oxidation when Mn(II)-complexes are used. The reason for this requirement is still vague, but research has shown that it serves a co-catalytic function in aiding the activation<sup>8</sup> and suppressing the disproportionation of H<sub>2</sub>O<sub>2</sub>.<sup>11</sup> During the activation of H<sub>2</sub>O<sub>2</sub>, it promotes the fast heterolysis of the O-O bond in the intermediate Mn<sup>III</sup>-OOH species towards a more active high valent species, which is responsible for the oxidation of the hydrocarbon substrate.<sup>9</sup>

Although research on alkene and alkane oxidation with non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes is numerous, as previously mentioned, research with regard to alcohol oxidation is limited. Shen and co-workers have previously utilised a Mn(OTf)<sub>2</sub> complex bearing a pyrrolidine backbone and benzimidazole donors (Figure 2.14, Chapter 2) to catalyse the oxidation of various secondary alcohols using H<sub>2</sub>O<sub>2</sub> as oxidant along with AcOH as co-catalyst.<sup>12</sup> Excellent conversions exclusively to the corresponding ketones of up to 99% were achieved using a 0.05 mol % catalyst concentration with 1.5 and 6 equivalents of H<sub>2</sub>O<sub>2</sub> and AcOH, respectively.

Another study used a phenanthroline and phenylacetate ligated Mn(II)-complex (Figure 2.16, Chapter 2) to catalyse the oxidation of primary benzylic and aliphatic alcohols with t-BuOOH in the absence of an acid.<sup>3</sup> Conversions of up to 90% were achieved, but it was apparent that over-oxidation occurred. The oxidation of benzyl alcohol led to the formation of both benzaldehyde (47%) and benzoic acid (30%) after six hours of reaction time at 70 °C. In addition to the catalytic systems already mentioned, a [(TMTACN)Mn(SO<sub>4</sub>)] complex (Chapter 2, Figure 2.13) was also utilised to catalyse the oxidation of 1-octanol with H<sub>2</sub>O<sub>2</sub>

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(2.5 equivalents) and ascorbic acid.<sup>13</sup> Product analysis revealed that 1-octanoic acid (90%) was the major product produced, concluding that over-oxidation also occurred.

In an attempt to extend research in the field of alcohol oxidation with non-heme *N*<sub>4</sub>-tetradentate Mn(OTf)<sub>2</sub> complexes, it was decided to develop new complexes bearing different ligand substituents and N-donors to test their performance and to compare them to already known complexes. The 16 complexes synthesised and described in Chapter 3 (***R,R***- and ***S,S***-**C1 - C8**) were used for this purpose and H<sub>2</sub>O<sub>2</sub> served as the terminal oxidant along with AcOH as the co-catalyst during oxidation reactions.

### 4.2 Results and discussion

#### 4.2.1 Preliminary screening of reaction parameters

Before catalytic alcohol oxidation studies could be conducted, benchmark conditions needed to be obtained. Benzyl alcohol was chosen as the benchmark substrate due to its α-carbon being activated by the phenyl ring. The screening conditions that were tested are illustrated in Table 4.1. The time illustrated is an indication of the total reaction time, whereas the H<sub>2</sub>O<sub>2</sub> was added via a syringe pump over a period of 30 minutes to prevent its disproportionation. ***R,R***-**C5** was chosen as pre-catalyst for preliminary screening, because previous studies, as mentioned in Chapter 2, obtained good activity when it was used in alkane and alkene oxidation.<sup>7, 10, 14-15</sup> ***R,R***-**C6** was also used to see whether any preliminary differences are apparent due to the methyl groups in the C6 position of the pyridine donor.

A blank reaction showed that no reaction took place when the catalyst was absent from the reaction (Table 4.1, Entry 1). The introduction of 0.1 mol % of Mn(OTf)<sub>2</sub>, MnCl<sub>2</sub>·4H<sub>2</sub>O or ***R,R***-**C5** also had no effect on the percentage conversion (Table 4.1, Entries 2, 3 and 4). The addition of a carboxylic acid (AcOH) to the reaction mixture had no effect when Mn(OTf)<sub>2</sub> or MnCl<sub>2</sub>·4H<sub>2</sub>O was employed (Table 4.1, Entries 5 & 6). However, utilising ***R,R***-**C5** with AcOH resulted in a 19% conversion of the substrate (Table 4.1, Entry 7). This observation highlights the importance of the ligand system coordinated to the Mn(OTf)<sub>2</sub> precursor to facilitate oxidation of the substrate. The necessity of AcOH in the reaction mixture was to ensure conversion correlates with previously described studies where non-heme Mn(II)-complexes were used for hydrocarbon oxidation.<sup>8-9, 11</sup>

Further evaluation revealed that an increase in the amount of H<sub>2</sub>O<sub>2</sub> led to an increase in percentage conversion for both ***R,R***-**C5** and ***R,R***-**C6**, albeit not large (Table 4.1, Entry 8 and 12). The same phenomenon was noted with AcOH (Table 4.1, Entry 11). It was hypothesised that a

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decrease in temperature would lead to higher conversions due to the instability of the high valent Mn intermediates, but only a small increase was seen (Table 4.1, Entry 10).<sup>16</sup> Additional experiments (Table S.1 in supporting information) were also conducted to determine whether the reaction time had an effect, but no further conversion was seen even after 150 minutes. It was also found that the utilisation of **R,R-C6** led to a lower conversion compared to **R,R-C5** (Table 4.1, Entry 7 and 9), which illustrates the steric effect of the methyl groups.

**Table 4.1: Preliminary screening conditions for benzyl alcohol oxidation.<sup>a</sup>**

| Entry | Catalyst<br>mol %                             | H <sub>2</sub> O <sub>2</sub><br>(equivalents) | AcOH<br>(equivalents) | Temperature<br>(°C) | Conversion <sup>b</sup><br>(%) |
|-------|-----------------------------------------------|------------------------------------------------|-----------------------|---------------------|--------------------------------|
| 1     | -                                             | 1.2                                            | -                     | 25                  | 0.0                            |
| 2     | 0.1<br>(Mn(OTf) <sub>2</sub> )                | 1.2                                            | -                     | 25                  | 0.0                            |
| 3     | 0.1<br>(MnCl <sub>2</sub> ·4H <sub>2</sub> O) | 1.2                                            | -                     | 25                  | 0.0                            |
| 4     | 0.1<br>( <b>R,R-C5</b> )                      | 1.2                                            | -                     | 25                  | 0.0                            |
| 5     | 0.1<br>(Mn(OTf) <sub>2</sub> )                | 1.2                                            | 10                    | 25                  | 0.0                            |
| 6     | 0.1<br>(MnCl <sub>2</sub> ·4H <sub>2</sub> O) | 1.2                                            | 10                    | 25                  | 0.0                            |
| 7     | 0.1<br>( <b>R,R-C5</b> )                      | 1.2                                            | 10                    | 25                  | 19                             |
| 8     | 0.1<br>( <b>R,R-C5</b> )                      | 4.0                                            | 10                    | 25                  | 21                             |
| 9     | 0.1<br>( <b>R,R-C6</b> )                      | 1.2                                            | 10                    | 25                  | 8                              |
| 10    | 0.1<br>( <b>R,R-C6</b> )                      | 1.2                                            | 10                    | 0                   | 12                             |
| 11    | 0.1<br>( <b>R,R-C6</b> )                      | 1.2                                            | 14                    | 25                  | 12                             |
| 12    | 0.1<br>( <b>R,R-C6</b> )                      | 3.0                                            | 10                    | 25                  | 10                             |

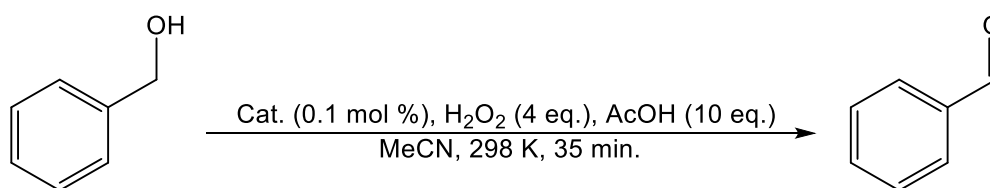
<sup>a</sup> Reaction conditions: The precursor or complex (2 μmol) was dissolved in acetonitrile with alcohol (2 mmol) and AcOH. H<sub>2</sub>O<sub>2</sub> was added by syringe pump over 30 min. at temperature indicated (total volume = 3.19 ml) and stirred for an additional 5 min. <sup>b</sup> Conversions were determined by GC against an internal standard (biphenyl).

In conclusion, the preliminary screening experiments revealed that the experimental conditions employed in Entry 8 had the highest percentage conversion. It was decided that these reaction conditions would be used to screen the rest of the synthesised complexes.

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**4.2.2 Screening of non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes *R,R*- and *S,S*-C1 - C8**

Benchmark conditions obtained during preliminary screening illustrated that 0.1 mol % complex, 10 equivalents AcOH, four equivalents H<sub>2</sub>O<sub>2</sub> and 35 minutes reaction times were the best conditions. These conditions were used to evaluate the non-heme Mn(II)-complexes synthesised (*R,R*- and *S,S*-C1 - C8), which varied according to their substituents and N-donors. They were screened against the oxidation of benzyl alcohol and in all cases the percentage conversion was determined as the average of two independent runs.



**Scheme 4.1: General procedure used for screening Mn(II)-complexes against benzyl alcohol oxidation.**

All the secondary diamine complexes (*R,R*- and *S,S*-C1 - C4) showed very low conversions (up to 11%), as illustrated in Figure 4.2. This may be attributed to the fact that the secondary amine moiety is susceptible to oxidation, especially when H<sub>2</sub>O<sub>2</sub> is used as the oxidant. This would then lead to oxidative degradation of the complex, which prevents further oxidation of the substrate. *R,R*-L5 was subjected to H<sub>2</sub>O<sub>2</sub> oxidation, and FT-IR results indicated the formation of an imine bond (Figure 4.1). Oxidation of the secondary amine to an imine can be followed by hydrolysis of the imine in the presence of a metal that degrades the ligand. No significant difference could be seen when the different secondary diamine complexes were compared.

From experiments where the tertiary diamine complexes, *R,R*- and *S,S*-C5 - C8, were evaluated (Figure 4.3), higher activity was only observed for the C5 and C8 complexes (up to 28% conversion) compared to their secondary counterparts (Figure 4.3). This higher activity can be attributed to the tertiary amine moiety being more stable towards oxidants compared to secondary amines, thereby preventing catalyst deactivation. This observation corresponds with the higher melting points seen for the tertiary diamine complexes compared to their secondary counterparts (Chapter 3, Table 3.1). Further evaluation of the magnetic susceptibility of complex *R,R*-C4 (secondary diamine) after 24 hours in an open atmosphere revealed a decrease in the magnetic moment of Mn from 5.655 to 4.880 BM, corresponding with an increase in the oxidation state of Mn from 2+ to 3+. For the tertiary amine complexes, this phenomenon was not seen.

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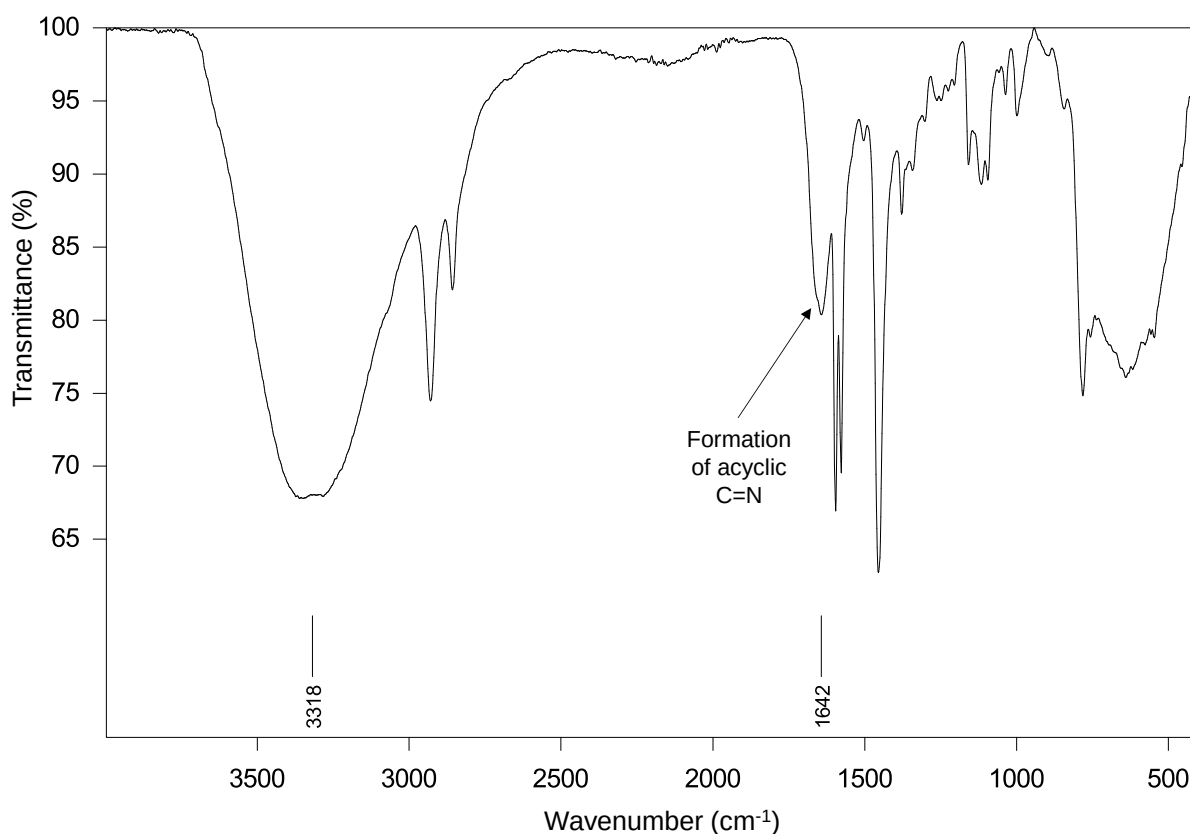


**Figure 4.1: Formation of an imine bond after *R,R*-L5 was subjected to H<sub>2</sub>O<sub>2</sub> treatment.**

Higher benzyl alcohol conversions were observed for ***R,R*-** and ***S,S*-C5** and **C8** compared to ***R,R*-** and ***S,S*-C6** and **C7**. This is attributed to the increased steric pressure exerted by the substituents (-CH<sub>3</sub> and -Br) in the C6 position of the pyridine donor. This observation correlates well with a previous alkene epoxidation study where a similar effect was seen when methyl substituents were added to the C6 position resulting in a decrease in alkene conversion.<sup>17</sup> It was assumed that the electronic properties of the -CH<sub>3</sub> and -Br substituents would affect the catalytic activity, but no significant difference was seen when ***R,R*-** and ***S,S*-C6** and ***R,R*-** and ***S,S*-C7** were compared. This phenomenon can be attributed to the fact that steric factors have a more pronounced effect than electronic effects do.

It was seen that ***R,R*-** and ***S,S*-C8** showed higher conversions compared to ***R,R*-** and ***S,S*-C5**, which may be attributed to the higher basicity (higher pK<sub>a</sub> value) of the 1-methylimidazole donor, resulting in a stronger electron donor.<sup>18</sup> This is advantageous to the stabilisation of high valent manganese intermediate species and in so doing increases its lifetime.<sup>16</sup> The higher conversion may also be attributed to an easier substrate approach by benzyl alcohol to the 1-methylimidazole ligated complex compared to the bulkier pyridine ligated complex. A previous

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study has also shown that exchanging the pyridine donor with a 1-methylbenzimidazole (similar to 1-methylimidazole) donor enhanced the activity of the complex during alkene oxidation.<sup>19</sup>

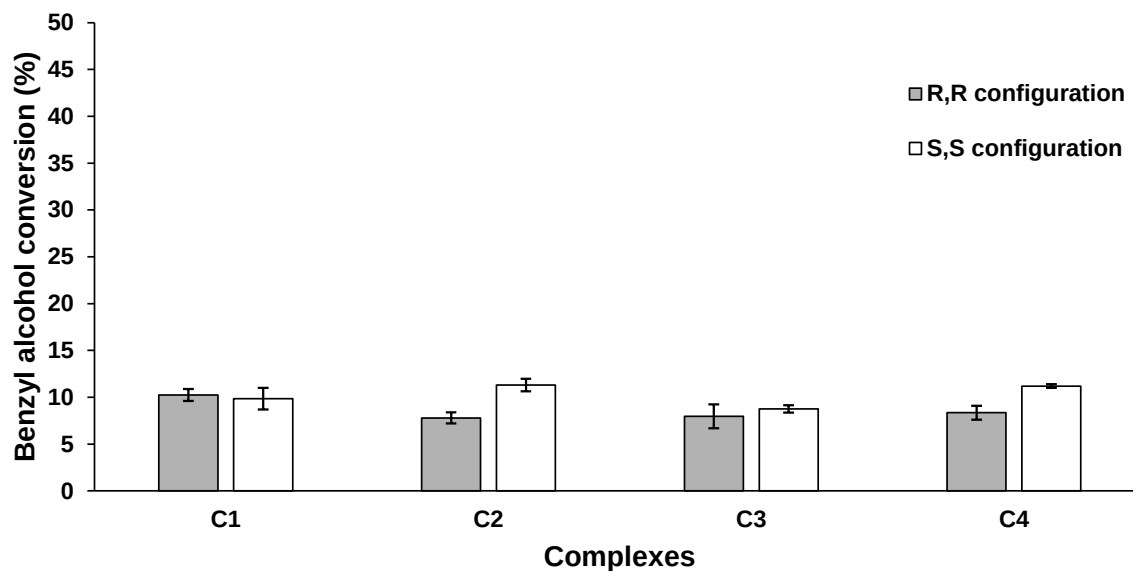


**Figure 4.2: Percentage benzyl alcohol conversion achieved with secondary diamine Mn(OTf)<sub>2</sub> complexes *R,R*- and *S,S*-C1 - C4.**

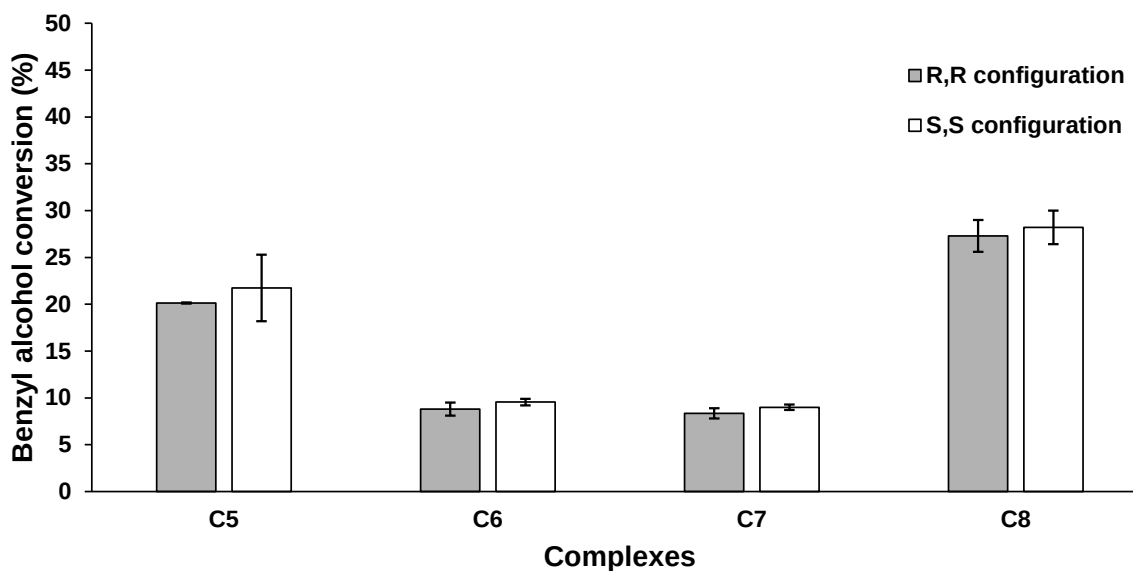


**Figure 4.3: Percentage benzyl alcohol conversion achieved with tertiary diamine Mn(OTf)<sub>2</sub> complexes *R,R*- and *S,S*-C5 - C8.**

The results shown in Figures 4.2 and 4.3 illustrate that the difference in benzyl alcohol conversion between the *R,R*- and *S,S*-configurations of each complex is very small. This is due

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to identical active site accessibility between the *R,R* and *S,S* configurations. This is illustrated by the space-filling diagrams of complexes *R,R*- and *S,S*-C8 in Figure 3.15, Chapter 3.

### 4.2.3 Optimisation of catalytic alcohol oxidation reaction parameters

Complex *S,S*-C8 showed the highest comparative conversion for benzyl alcohol oxidation (28%). It is for this reason that this complex was chosen for further investigations of reaction parameters, i.e. catalyst concentration, oxidant concentration and co-catalyst concentration.

#### 4.2.3.1 Optimisation of catalyst concentration

To determine the optimal catalyst concentration for benzyl alcohol oxidation, different catalyst concentrations ranging from 0.1 to 1 mol % were tested. Both the AcOH and H<sub>2</sub>O<sub>2</sub> were held constant at 10 and four equivalents with regard to the substrate, respectively. Variation of the catalyst concentration revealed that a 10-fold increase from 0.1 to 1 mol % increased the benzyl alcohol conversion two-fold from 28 to 56% (Figure 4.4). Increasing the catalyst concentration beyond 1 mol % had no increasing effect on conversion, indicating that catalyst deactivation occurs at higher catalyst concentrations.

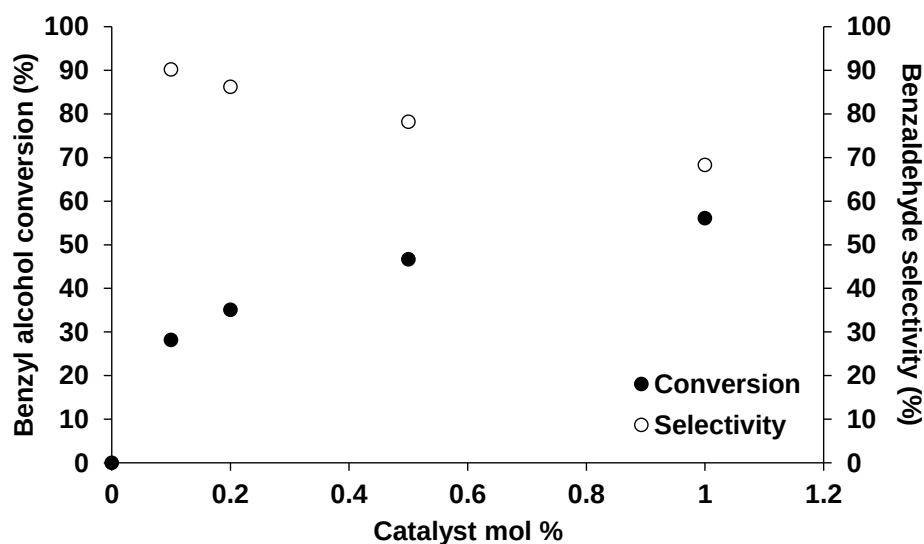


Figure 4.4: Optimisation of catalyst concentration. Reaction conditions: Complex *S,S*-C8 (0.1 - 1 mol %) in acetonitrile (1.225 ml) with BnOH (8 mmol), AcOH (8 mmol) and H<sub>2</sub>O<sub>2</sub> (3.2 mmol) at 298 K for 35 min. All values are the average of a duplicate set of runs.

In addition, an increase in catalyst concentration decreased the selectivity towards benzaldehyde. GC analysis showed that benzoic acid also starts to form in the reaction, suggesting that over-oxidation occurs during the oxidation of primary alcohols when non-heme

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Mn(II)-complexes are used. This corresponds with results from a previous study where it was seen that not only benzaldehyde is produced, but benzoic acid is also present in the product mixture when a primary alcohol is catalytically oxidised by a non-heme Mn(II)-complex utilising *t*-BuOOH as oxidant.<sup>3</sup>

### 4.2.3.2 Optimisation of oxidant concentration

Taking into account the highest percentage conversion and selectivity, it was decided to use 0.5 mol % as the optimal catalyst concentration to optimise the oxidant concentration. Varying amounts of H<sub>2</sub>O<sub>2</sub>, which ranged from 0.5 to 8 equivalents, were tested. The AcOH amount was held constant at 10 equivalents, with the catalyst concentration being 0.5 mol %. When the H<sub>2</sub>O<sub>2</sub> amount was increased from 0.5 to 8 equivalents, an increase in the percentage conversion from 19 to 43% was observed (Figure 4.5). This may be due to more hydroperoxo radicals ( $\bullet$ OOH) being produced to activate the Mn(II)-complex for alcohol oxidation resulting in an increased amount of active Mn-species.<sup>16</sup>

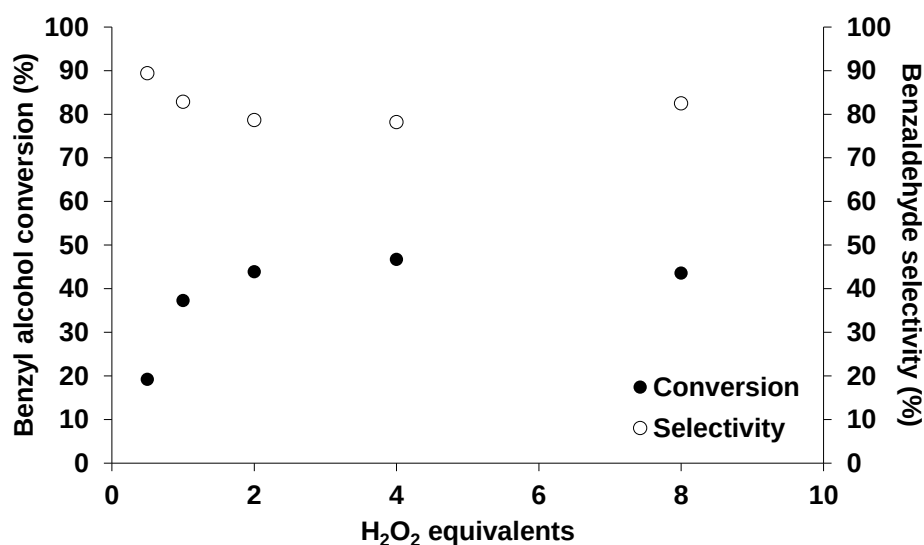


**Figure 4.5: Optimisation of H<sub>2</sub>O<sub>2</sub> concentration. Reaction conditions: Complex S,S-C8 (0.5 mol %) in acetonitrile with BnOH (0.8 mmol), AcOH (8 mmol) and H<sub>2</sub>O<sub>2</sub> (0.4 - 6.6 mmol) at 298 K for 35 min. All values are the average of a duplicate set of runs.**

Similar to what was seen during the optimisation of the catalyst concentration, increasing H<sub>2</sub>O<sub>2</sub> concentration beyond four equivalents had a negligible effect on conversion. This may be caused by oxidative degradation of the ligand system from the excess oxidant in solution, which leads to catalyst deactivation. Again, a decrease in the selectivity for benzaldehyde was observed as the H<sub>2</sub>O<sub>2</sub> concentration increased, with over-oxidation to benzoic acid.<sup>3</sup>

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### 4.2.3.3 Optimisation of co-catalyst concentration

From the preliminary screening experiments, it was determined that AcOH is necessary for oxidation to occur when non-heme *N*<sub>4</sub>-tetradentate Mn(II)-complexes are used as catalysts. However, it was still necessary to determine the optimal amount of AcOH needed to ensure high conversion. The amount of AcOH was varied from 0 to 15 equivalents, while the catalyst and H<sub>2</sub>O<sub>2</sub> concentration were kept constant at 0.5 mol % and four equivalents, respectively. Increasing the AcOH concentration incrementally to 10 equivalents led to an increase in percentage conversion (Figure 4.6). Increasing the concentration even further resulted in a negligible increase in conversion, attributed to decelerated conversion resulting from the excess AcOH.<sup>11</sup> As was observed for variations in catalyst and oxidant concentrations, an increasing AcOH concentration also led to a decrease in benzaldehyde selectivity.

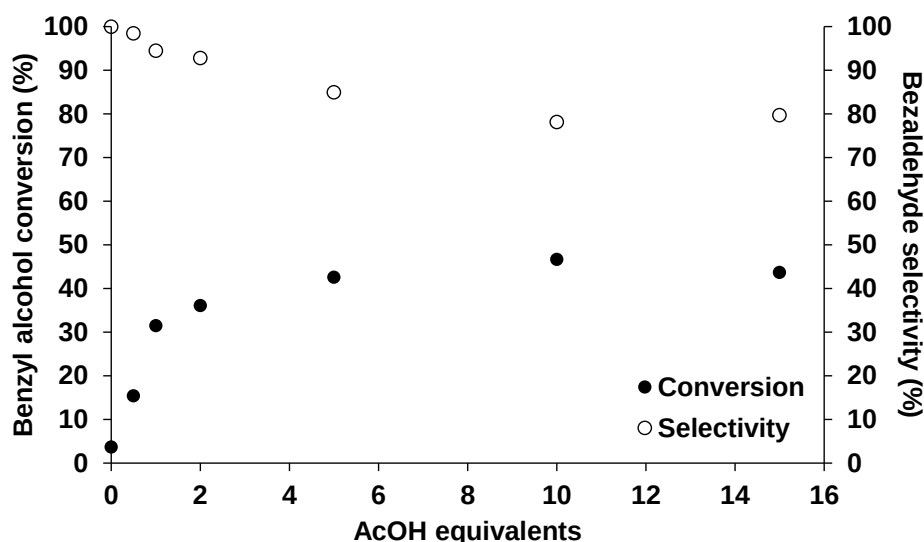


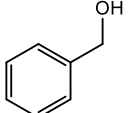
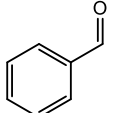
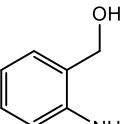
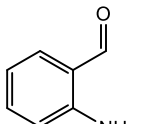
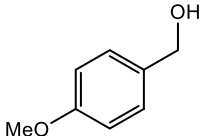
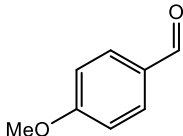
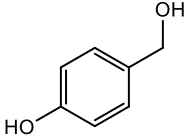
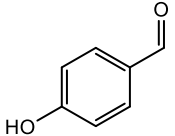
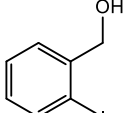
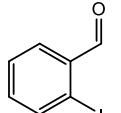
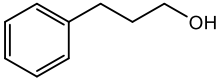
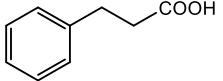
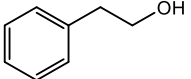
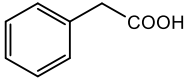
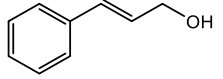
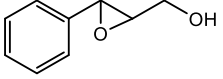
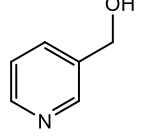
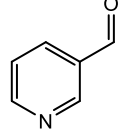
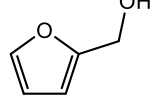
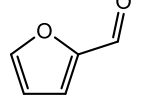
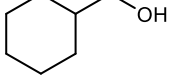
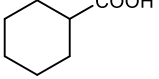
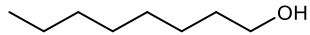
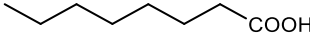
**Figure 4.6:** Optimisation of AcOH concentration. Reaction conditions: Complex **S,S-C8** (0.5 mol %) in acetonitrile with BnOH (0.8 mmol), AcOH (0 - 12 mmol) and H<sub>2</sub>O<sub>2</sub> (3.2 mmol) at 298 K for 35 min. All values are the average of a duplicate set of runs.

### 4.2.4 Evaluating primary alcohol oxidation with complex **S,S-C8**

After optimisation of reaction parameters, the following reaction conditions were chosen to achieve high conversion, but to minimise over-oxidation: 0.5 mol % **S,S-C8**, four equivalents of H<sub>2</sub>O<sub>2</sub> and 10 equivalents of AcOH. Under these conditions, various primary alcohol substrates were evaluated to establish the scope of Mn(II)-catalysed alcohol oxidation (Table 4.2).

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**Table 4.2: Catalytic oxidation of primary alcohols with complex **S,S-C8**.<sup>a</sup>**

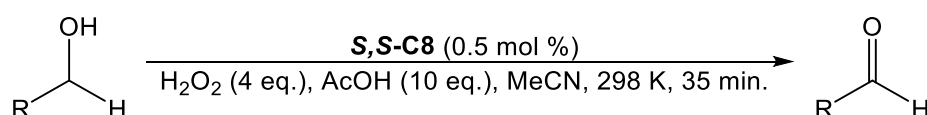
| Entry | Substrate                                                                           | Major product                                                                        | Conversion <sup>b</sup> /% | TON <sup>c</sup> |
|-------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------|------------------|
| 1     |    |     | 47                         | 97               |
| 2     |    |     | 77                         | 155              |
| 3     |    |     | 69                         | 140              |
| 4     |    |     | 22                         | 45               |
| 5     |   |    | 22                         | 45               |
| 6     |  |   | 67                         | 134              |
| 7     |  |   | 38                         | 76               |
| 8     |  |   | 82                         | 170              |
| 9     |  |   | 51                         | 105              |
| 10    |  |   | 97                         | 195              |
| 11    |  |   | 80                         | 163              |
| 12    |  |  | 72                         | 149              |

<sup>a</sup> Reaction conditions: Complex **S,S-C8** (0.5 mol %) in acetonitrile with alcohol (0.8 mmol), AcOH (8 mmol) and H<sub>2</sub>O<sub>2</sub> (3.2 mmol) at 298 K for 35 min. <sup>b</sup> Conversions were determined by GC against an internal standard (biphenyl) and are given as the average of two independent runs. <sup>c</sup> Turnover number (TON) = mol substrate converted/mol complex used.

The addition of electron-donating groups on the benzene ring, i.e. amino (Table 4.2, Entry 2), or methoxy (Table 4.2, Entry 3), resulted in increased conversion.<sup>12</sup> A drawback was the formation

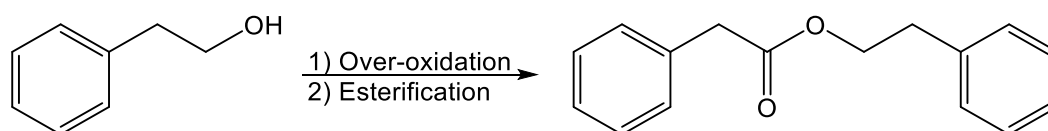
## Chapter 4: Evaluating the catalytic performance of non-heme *N*<sub>4</sub>-tetradentate manganese(II) complexes during alcohol oxidation

of dimers from 2-aminobenzaldehyde as soon as it formed, due to self-condensation in the presence of a Mn(II)-complex and diluted acidic solution.<sup>20</sup> The insertion of a para-hydroxy group (Table 4.2, Entry 4) resulted in a low conversion due to its lack of solubility in MeCN. The addition of an iodine group (Table 4.2, Entry 5) on the ortho-position decreased the conversion, again illustrating the influence that steric pressure has on catalytic activity.



**Scheme 4.2: General reaction conditions for catalytic oxidation of primary alcohols with R representing a benzylic, aliphatic or heteroaromatic functional group.**

Increasing the aliphatic chain length, by employing 3-phenyl-1-propanol as substrate, led to a 20% increase in conversion, albeit with over-oxidation to the carboxylic acid (Table 4.2, Entry 6 vs Entry 1). In contrast, employing 2-phenylethanol as substrate decreased the conversion (Table 4.2, Entry 7 vs Entry 1). The  $\alpha$  and  $\beta$  carbons in the alcohol are both activated and competition is experienced, which may cause a decrease in conversion.<sup>21</sup> Over-oxidation towards the carboxylic acid resulted in an esterification reaction with the alcohol substrate to produce phenethyl phenylacetate as the product (Scheme 4.3).



**Scheme 4.3: Formation of phenethyl phenylacetate caused by the over-oxidation and esterification of 2-phenylethanol.**

Evaluation of cinnamyl alcohol (Table 4.2, Entry 8) resulted in the epoxide as major product rather than an aldehyde or carboxylic acid, which is attributed to the higher reactivity of non-heme Mn(II)-complexes towards alkenes compared to alcohols.<sup>22</sup> The insertion of a heteroatom into the phenyl ring had no significant effect on the conversion compared to benzyl alcohol (Table 4.2, Entry 9 vs Entry 1). In contrast, a significant increase in conversion was observed when a furan ring was used as the heterocycle, due to the increased reactivity of furan (Table 4.2, Entry 10). Another problem was the rapid decomposition of furfural in the presence of an acid, transition metal and  $\text{H}_2\text{O}_2$ , which explains the high percentage conversion.<sup>23</sup> Maleic anhydride was observed as one of the decomposition products.

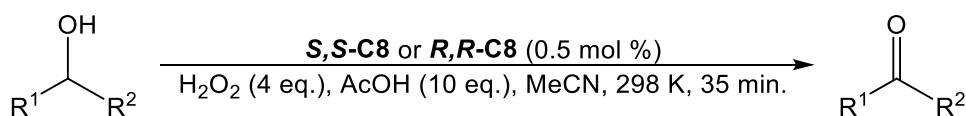
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High catalytic activity towards cyclic and linear aliphatic primary alcohols was observed, in which 80% of cyclohexanemethanol (Table 4.2, Entry 11) and 72% of 1-octanol (Table 4.2, Entry 12) were converted. Removing the aromaticity from the ring increases the electron density at the  $\alpha$ -carbon resulting in a higher conversion. This is in contrast with previous studies where benzylic alcohols were more reactive than their aliphatic counterparts.<sup>21, 24</sup> Both cyclohexanemethanol and 1-octanol, however, over-oxidise to the carboxylic acid; however, contrary to a previous study, a higher percentage 1-octanol was converted in our study using a lower substrate concentration and much shorter reaction time.<sup>13</sup>

The abovementioned results indicate that problems with regard to selectivity were experienced when primary alcohols are oxidised, often associated with over-oxidation to the carboxylic acid. In addition, side reactions due to the presence of AcOH in the reaction were also apparent and resulted in further reaction of carboxylic acid products with alcohol substrates forming esters (Scheme 4.3).

### 4.2.5 Evaluating secondary alcohol oxidation with complexes *R,R*- and *S,S*-C8

Due to the selectivity problems experienced with primary alcohol oxidation, the focus shifted to the oxidation of secondary alcohols, which can only oxidise to a ketone product resulting in no by-products (Scheme 4.4). The same conditions with regard to catalyst, oxidant and AcOH concentration, time and temperature were employed as before (section 4.2.4). Results obtained for the oxidation of secondary alcohols are illustrated in Table 4.3. In all cases, good to excellent conversions of up to 100% were obtained for the secondary alcohol substrates investigated, while isolated yields of up to 86% of the ketone products were obtained.

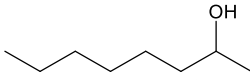
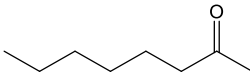
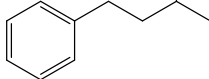
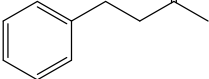
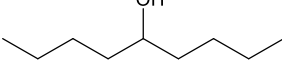
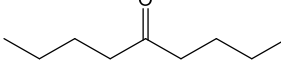
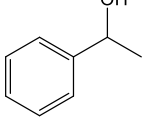
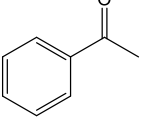
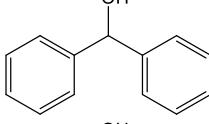
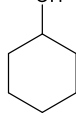
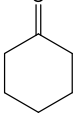
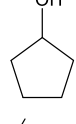
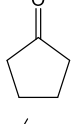
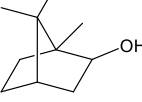
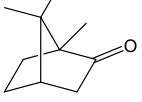


**Scheme 4.4:** General reaction conditions for catalytic oxidation of secondary alcohols with *R*<sup>1</sup> and *R*<sup>2</sup> representing a benzylic or aliphatic functional group.

The oxidation of 2-octanol and 4-phenyl-2-butanol (Table 4.3, Entries 1 and 2) was conducted with both *S,S*-C8 and *R,R*-C8 as catalysts with identical results being obtained, providing further evidence that the configuration and ultimately topology of the complex does not have an effect during alcohol oxidation. In general, excellent conversions and isolated yields were obtained for all the alcohols evaluated.

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**Table 4.3: Catalytic oxidation of secondary alcohols with complexes *R,R*- and *S,S*-C8.<sup>a</sup>**

| Entry | Substrate                                                                           | Major product                                                                       | Conversion <sup>b</sup> (%)  | Isolated yield (%) |
|-------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------|--------------------|
| 1     |    |    | <b>A:</b> 81<br><b>B:</b> 82 | 51                 |
| 2     |    |    | <b>A:</b> 68<br><b>B:</b> 68 | 64                 |
| 3     |    |    | <b>B:</b> 70                 | 67                 |
| 4     |    |    | <b>B:</b> 100                | 84                 |
| 5     |   | -                                                                                   | <b>B:</b> 0                  | -                  |
| 6     |  |  | <b>B:</b> 96                 | 10                 |
| 7     |  |  | <b>B:</b> 87                 | 7                  |
| 8     |  |  | <b>B:</b> 100                | 86                 |

<sup>a</sup> Reaction conditions: Complex ***S,S*-C8 (A)** or ***R,R*-C8 (B)** (0.5 mol %) in acetonitrile with alcohol (0.8 mmol), AcOH (8 mmol) and H<sub>2</sub>O<sub>2</sub> (3.2 mmol) at 298 K for 35 min. <sup>b</sup> Conversions were determined by GC against an internal standard (biphenyl) and are given as the average of two independent runs.

Specifically, the addition of a methyl group on the  $\alpha$ -carbon had no effect on catalytic activity, evident when comparing 4-phenyl-2-butanol (Table 4.3, Entry 1) and 4-phenyl-1-butanol (Table 4.2, Entry 3). In both instances, comparable conversions and isolated yields were obtained. Employing 1-phenylethanol as substrate resulted in 100% conversion and 84% isolated yield of acetophenone (Table 4.3, Entry 4). The addition of a methyl group, therefore, in this case, has an electron donating effect, increasing the oxidation activity.<sup>25-26</sup> In contrast, changing the methyl group on the  $\alpha$ -carbon to a phenyl substituent resulted in no conversion, attributed to increased steric bulk hindering substrate approach (Table 4.3, Entry 5).<sup>12</sup> In contrast, employing an aliphatic derivative, such as 5-nonanol, yielded the ketone product in 67% isolated yield. This is significantly higher to that reported in a previous study.<sup>24</sup>

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Cyclic aliphatic alcohols, cyclohexanol and cyclopentanol, were oxidised in good conversions of 96% and 87%, respectively (Table 4.3, Entries 6 and 7). Unfortunately, very low isolated yields were obtained for the cyclic ketones due to a higher distribution of the ketones in the water phase compared to the organic phase and high volatility.<sup>24</sup> Other solvents, i.e. CHCl<sub>3</sub> and Et<sub>2</sub>O, were also utilised for extraction and salting-out methods were employed, but no improvement was seen. Finally, a bicyclic aliphatic alcohol, i.e. isoborneol, was also oxidised near quantitative conversion with an 86% isolated yield (Table 4.3, Entry 8).

In the context of manganese(II)-catalysed secondary alcohol oxidation, the reported catalytic activity (conversions and isolated yields) for the substrates in Table 4.3 are comparable and in some cases better than literature precedent. Bhat and co-workers reported a terpyridine-ligated Mn(II)-complexes, which with a catalyst concentration of 0.5 mol % and 1 equivalent of TBHP (oxidant) was capable of oxidising 2-phenylethanol and cyclohexanol to the corresponding ketone in 11% and 38% GC yield, respectively, compared to the 10% and 84% isolated yield observed for our catalyst system.<sup>27</sup> Gao and co-workers reported a porphyrin-inspired Mn(II)-complex at a catalyst concentration of 1 mol %, 6 equivalents of H<sub>2</sub>O<sub>2</sub> and 50 mol % adamantane carboxylic acid.<sup>28</sup> Operating under these conditions cyclohexanol and 2-octanol was oxidised to the ketones in 38% and 25% GC yield, respectively. In comparison, isolated yields of 10% and 51% were obtained for the ketone products when employing our catalyst system. Nam and co-workers evaluated non-heme Mn(II)-complexes, operating at a catalyst concentration of 0.3 mol %, with 1.5 equivalents of H<sub>2</sub>O<sub>2</sub> and 1 mol % H<sub>2</sub>SO<sub>4</sub>, in the oxidation of secondary alcohols.<sup>29</sup> Under these conditions 2-phenylethanol and cyclohexanol were oxidised to the ketones in 95% and 86% isolated yield respectively. This example is the most efficient Mn(II) catalyst for alcohol oxidation reported to date.

Our catalyst system also outperforms analogous Fe(II) catalyst systems reported in literature. Sato and co-workers evaluated Fe(II)-picolinate complexes as alcohol oxidation catalysts, operating at 5 mol % Fe and 1.25 equivalents of H<sub>2</sub>O<sub>2</sub>.<sup>30</sup> Under these conditions, their catalyst oxidised 2-phenylethanol to acetophenone in 64% GC yield compared to the 84% isolated yield for our catalyst system. Olivo and co-workers applied an iron-base imine complex, with a catalyst concentration of 1 mol % and H<sub>2</sub>O<sub>2</sub> (2.5 equivalents) as oxidant, to the oxidation of alcohols.<sup>31</sup> Under their operating conditions, 2-phenylethanol was oxidised to the ketone in 9% GC yield. On the other hand, their catalyst system could oxidise cyclopentanol and cyclohexanol to the corresponding ketones in 54% and 70% GC yields respectively. Unfortunately, our Mn(II)-complexes are outperformed by the current state of the art in alcohol oxidation catalysis, i.e. a Cu(I)/ABNO (ABNO = 9-azabicyclo[3.3.1]nonane N-oxyl, a nitroxyl

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radical) catalyst system reported by Stahl and co-workers.<sup>32</sup> Operating at a copper concentration of 5 mol %, 2-octanol and 4-phenyl-1-butanol could be oxidised to the ketone products in isolated yields of 96% and 95%, respectively, compared to the 51% and 64% found for our system.

### **4.3 Conclusions**

Several non-heme N<sub>4</sub>-tetradentate Mn(OTf)<sub>2</sub> complexes, ***R,R***- and ***S,S***-**C1 - C8**, were developed to test their catalytic performance toward the oxidation of aliphatic and benzylic alcohols. These complexes differed according to their N-donors and substituents on the donor ligands. After benchmark conditions were established, all of the complexes were screened against benzyl alcohol oxidation. It was observed that the complexes containing tertiary diamine ligands, ***R,R***- and ***S,S***-**C5 - C8**, showed higher conversions due to lower susceptibility towards oxidative degradation. Furthermore, the results indicated that steric pressure exerted by the -Me and -Br substituents had a greater influence compared to their electronic effects, which led to low conversions. No significant difference was seen when *R,R*- and *S,S*-configurations were compared, indicating that the ligand topology in the complex does not have an influence on alcohol oxidation. The introduction of 1-methylimidazole donors possessing higher basicity resulted in higher benzyl alcohol oxidation compared to its pyridine counterpart.

The ***S,S***-**C8** complex showed the best conversion in benzyl alcohol oxidation and was further used to optimise the reaction parameters, i.e. catalyst, oxidant and co-catalyst concentration. For all of the reaction parameters evaluated, an increase thereof improved the percentage conversion of benzyl alcohol until a plateau was reached, indicative of catalyst deactivation. In addition, the increase of each reaction parameter led to lower benzaldehyde selectivity due to over-oxidation.

After the optimal conditions for each parameter were determined, they were used with ***S,S***-**C8** to evaluate the substrate scope for primary alcohol oxidation. Good conversions of up to 97% were achieved, although selectivity problems arose. Due to the excess H<sub>2</sub>O<sub>2</sub> and AcOH required in the reaction along with the high reactivity of the Mn(OTf)<sub>2</sub> complex, over-oxidation to the carboxylic acid was seen for most of the primary alcohols that were evaluated. To circumvent this issue, the focus was shifted to the oxidation of secondary alcohols to the corresponding ketone. Excellent conversions and isolated yields of up to 100% and 86%, respectively, were obtained. The isolated ketone products were characterised spectroscopically, confirming their purity.

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### **4.4 Experimental section**

#### **4.4.1 General considerations**

All chemicals and reagents were used without further purification and included acetonitrile (99.5%, Merck), glacial acetic acid (99.8%, Rochelle Chemicals), benzyl alcohol (99.5%, Associated Chemical Enterprises), 2-phenylethanol (99%, Sigma-Aldrich), 3-phenyl-1-propanol (98%, Sigma-Aldrich), cinnamyl alcohol (98%, Sigma-Aldrich), 2-iodobenzyl alcohol (99%, Sigma-Aldrich), 2-aminobenzyl alcohol (98%, Sigma-Aldrich), 4-methoxybenzyl alcohol (98%, Sigma-Aldrich), 4-hydroxybenzyl alcohol (99%, Sigma-Aldrich), 2-pyridinemethanol (98%, Sigma-Aldrich), furfuryl alcohol (98%, Sigma-Aldrich), cyclohexanemethanol (99%, Sigma-Aldrich), 1-octanol (99%, Merck), 4-phenyl-2-butanol (97%, Sigma-Aldrich), 2-octanol (97%, Sigma-Aldrich), 5-nonanol (95%, Sigma-Aldrich), 1-phenylethanol (98%, Sigma-Aldrich), diphenylmethanol (99%, Sigma-Aldrich), cyclohexanol (98%, Codex), cyclopentanol (99%, Merck) and isoborneol (95%, Sigma-Aldrich). Catalytic experiments were conducted with 30% H<sub>2</sub>O<sub>2</sub> (Sigma-Aldrich), containing an inhibitor to prevent disproportionation, and kept in a refrigerator when not in use. Confirmation of all catalytic reaction products were done on a GC and GC-MS whilst secondary alcohol oxidation products were confirmed with FT-IR, <sup>1</sup>H and <sup>13</sup>C {<sup>1</sup>H} NMR spectroscopy.

FT-IR spectra were documented on a BrukerAlpha-P range infrared instrument equipped with an ATR accessory as neat samples in the range of 400 cm<sup>-1</sup> to 4000 cm<sup>-1</sup>. Gas chromatographic analysis were performed on an Agilent 6890 Series GC System with a HP 5 column, 30 m in length, 0.320 mm internal diameter and 0.25 mm film thickness. Rinsing solutions included MeCN and DCM with N<sub>2</sub> serving as the carrier gas and biphenyl as an internal standard. <sup>1</sup>H and <sup>13</sup>C {<sup>1</sup>H} NMR spectra were recorded on a Bruker Ultrashield Plus (600 MHz and 151 MHz, respectively) in 5 mm cylindrical glass tubes.

#### **4.4.2 Screening of non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes *R,R*- and *S,S*-C1 - C8**

The Mn(II)-complex (2 μmol) was dissolved in MeCN (1.225 ml) along with BnOH (205 μl, 1.990 mmol) and AcOH (10 equivalents, 1.140 ml, 19.894 mmol). After everything was thoroughly mixed, 30% H<sub>2</sub>O<sub>2</sub> (4 equivalents, 0.620 ml, 7.929 mmol) was slowly added by syringe pump over a period of 30 minutes where after the reaction was stirred for an additional 5 minutes. Final concentrations: Mn(II)-complex (0.620 mM), BnOH (624 mM), AcOH (6.24 M) and H<sub>2</sub>O<sub>2</sub> (2.49 M). The mixture was filtered through a silica plug and analysed against an internal standard (biphenyl) by GC. All runs were done in duplicate.

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#### **4.4.3 Optimisation of catalytic alcohol oxidation reaction parameters**

##### **4.4.3.1 Optimisation of catalyst concentration**

Varying amounts of complex **S,S-C8** (0.1 mol % - 1 mol %) was dissolved in MeCN (1.225 ml) with BnOH (0.205 ml, 1.990 mmol) and AcOH (10 equivalents, 1.140 ml, 19.894 mmol). After everything was thoroughly mixed, 30% H<sub>2</sub>O<sub>2</sub> (4 equivalents, 0.620 ml, 7.929 mmol) was slowly added by syringe pump over a period of 30 minutes where after the reaction was stirred for an additional 5 minutes. Final concentrations = **S,S-C8** (0.25 - 2.50 mM), BnOH (624 mM), AcOH (6.24 M) and H<sub>2</sub>O<sub>2</sub> (2.49 M). The mixture was filtered through a silica plug and analysed against an internal standard (biphenyl) by GC. All runs were done in duplicate.

##### **4.4.3.2 Optimisation of oxidant concentration**

Complex **S,S-C8** (4 µmol) was dissolved in MeCN (varying amounts according to H<sub>2</sub>O<sub>2</sub> amount to make a finale volume of 3.19 ml) with BnOH (0.085 ml, 0.825 mmol) and AcOH (10 equivalents, 0.460 ml, 8.03 mmol). After everything was thoroughly mixed, varying amounts of 30% H<sub>2</sub>O<sub>2</sub> (0.5 - 8 equivalents, 0.030 - 0.520 ml, 0.384 - 6.65 mmol) was slowly added by syringe pump over a period of 30 minutes where after the reaction was stirred for an additional 5 minutes. Final concentrations = **S,S-C8** (0.125 mM), BnOH (0.259 mM), AcOH (2.52 M) and H<sub>2</sub>O<sub>2</sub> (0.120 - 2.08 M). The mixture was filtered through a silica plug and analysed against an internal standard (biphenyl) by GC. All runs were done in duplicate.

##### **4.4.3.3 Optimisation of co-catalyst concentration**

Complex **S,S-C8** (4 µmol) was dissolved in MeCN (varying amounts according to AcOH amount to make a finale volume of 3.19 ml) with BnOH (0.085 ml, 0.825 mmol) and varying amounts of AcOH (0 - 15 equivalents, 0 - 0.690 ml, 0 - 12.041 mmol). After everything was thoroughly mixed, 30% H<sub>2</sub>O<sub>2</sub> (4 equivalents, 0.250 ml, 3.197 mmol) was slowly added by syringe pump over a period of 30 minutes where after the reaction was stirred for an additional 5 minutes. Final concentrations = **S,S-C8** (0.125 mM), BnOH (0.259 mM), AcOH (0 - 3.77 M) and H<sub>2</sub>O<sub>2</sub> (1.00 M). The mixture was filtered through a silica plug and analysed against an internal standard (biphenyl) by GC. All runs were done in duplicate.

#### **4.4.4 Evaluating primary alcohol oxidation with complex S,S-C8**

Complex **S,S-C8** (4 µmol) was dissolved in MeCN (2.395 ml) with substrate (0.8 mmol) and AcOH (10 equivalents, 0.460 ml, 8.03 mmol). After everything was thoroughly mixed, 30% H<sub>2</sub>O<sub>2</sub>

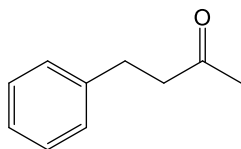
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(4 equivalents, 0.250 ml, 3.197 mmol) were slowly added via syringe pump over a period of 30 minutes after which the mixture was stirred for an additional 5 minutes. Final concentrations = complex (1.254 mM), alcohol (0.251 M), AcOH (2.52 M) and H<sub>2</sub>O<sub>2</sub> (1.00 M). After filtering through a silica plug, the mixture was analysed by GC and GC-MS. All runs were done in duplicate.

### 4.4.5 Evaluating secondary alcohol oxidation with complex *R,R*- and *S,S*-C8

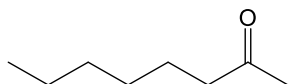
For oxidation of the secondary alcohol substrates, the same method as for the primary alcohol oxidation (section 4.4.4) was followed and all runs were again done in duplicate. To obtain the isolated products after the oxidation reaction, a saturated sodium hydrogen carbonate (NaHCO<sub>3</sub>) solution (3 ml) was slowly added to the reaction mixture until the bubbling ceased. DCM (10 ml) was added and separation of the aqueous and organic layers was done. Extraction of the remaining aqueous layer with DCM (2 x 10 ml) was performed where after all the organic layers were combined and dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration the solvent was allowed to dry in open air.

#### 4-Phenyl-2-butanone



Isolated as a yellow oil (79.5 mg; 63.9%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.37 (t, J = 7.5 Hz, 2H, PyrH), 7.30 – 7.25 (m, 3H, PyrH), 2.80 (dddd, J = 15.9, 13.8, 7.6, 4.9 Hz, 2H, CH<sub>2</sub>), 1.94 – 1.78 (m, 2H, CH<sub>2</sub>), 1.31 (d, J = 6.2 Hz, 3H, CH<sub>3</sub>). <sup>13</sup>C {<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>) δ (ppm): 208.13 (C=O), 142.07 (PyrC), 128.53 (PyrC), 128.43 (PyrC), 126.15 (PyrC), 32.17 (CH<sub>2</sub>), 29.76 (CH<sub>2</sub>), 23.65 (CH<sub>3</sub>). FT-IR (ATR) ν, cm<sup>-1</sup>: 1711 (C=O). Data corresponds to literature.<sup>33</sup>

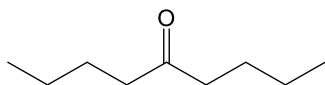
#### 2-Octanone



Isolated as a colourless oil (53.2 mg; 50.9%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 2.42 (ddd, J = 17.8, 14.9, 7.3 Hz, 4H, CH<sub>2</sub>), 2.09 (d, J = 28.9 Hz, 5H, CH<sub>2</sub> & CH<sub>3</sub>), 1.54 (t, J = 4.9 Hz, 2H, CH<sub>2</sub>), 1.31 – 1.20 (m, 2H, CH<sub>2</sub>), 1.08 – 0.77 (m, 3H, CH<sub>3</sub>). <sup>13</sup>C {<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>) δ (ppm): 208.94 (C=O), 43.43 (CH<sub>2</sub>), 31.60 (CH<sub>3</sub>), 29.94 (CH<sub>2</sub>), 28.85 (CH<sub>2</sub>), 23.16 (CH<sub>2</sub>), 22.50 (CH<sub>2</sub>), 14.04 (CH<sub>3</sub>). FT-IR (ATR) ν, cm<sup>-1</sup>: 1708 (C=O). Data corresponds to literature.<sup>34</sup>

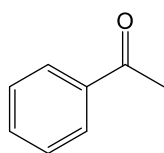
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**5-Nonanone**



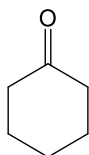
Isolated as a colourless oil (77.8 mg; 67.4%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 2.41 (dt, J = 35.6, 7.5 Hz, 5H, CH<sub>2</sub> & CH<sub>3</sub>), 1.53 (dt, J = 15.2, 7.6 Hz, 5H, CH<sub>2</sub> & CH<sub>3</sub>), 0.89 (t, J = 7.4 Hz, 8H, CH<sub>2</sub>). <sup>13</sup>C {<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>) δ (ppm): 212.09 (C=O), 42.66 (CH<sub>2</sub>), 22.50 (CH<sub>2</sub>), 22.42 (CH<sub>2</sub>), 13.99 (CH<sub>3</sub>). FT-IR (ATR) ν, cm<sup>-1</sup>: 1711 (C=O). Data corresponds to literature.<sup>24</sup>

**Acetophenone**



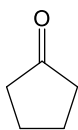
Isolated as a colourless oil (82.1 mg; 84.2%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 7.96 (dd, J = 8.3, 1.1 Hz, 2H, PyrH), 7.59 – 7.53 (m, 1H, PyrH), 7.46 (t, J = 7.8 Hz, 2H, PyrH), 2.60 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C {<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>) δ (ppm): 198.36 (C=O), 137.19 (PyrC), 133.24 (PyrC), 128.68 (PyrC), 128.42 (PyrC), 26.74 (CH<sub>3</sub>). FT-IR (ATR) ν, cm<sup>-1</sup>: 1680 (C=O). Data corresponds to literature.<sup>34</sup>

**Cyclohexanone**



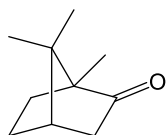
Isolated as a colourless oil (7.5 mg; 9.9%). Due to the high water solubility and volatility<sup>24</sup> of the compound resulting in a low yield, no usable NMR data could be obtained. FT-IR (ATR) ν, cm<sup>-1</sup>: 1696 (C=O).

**Cyclopentanone**



Isolated as a colourless oil (4.6 mg; 6.6%). Due to the high water solubility and volatility<sup>24</sup> of the compound resulting in a low yield, no usable NMR data could be obtained. FT-IR (ATR) ν, cm<sup>-1</sup>: 1703 (C=O).

**Camphor**



Isolated as a white solid (105.5 mg; 86.2%). <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) δ (ppm): 2.39 – 2.30 (m, 1H, HCH), 2.08 (t, J = 4.5 Hz, 1H, HCH), 1.94 (ddd, J = 15.8, 7.9, 3.8 Hz, 1H, HCH), 1.83 (d, J = 18.2 Hz, 1H, HCH), 1.67 (dd, J = 25.0, 3.7 Hz, 1H, HCH), 1.44 – 1.28 (m, 2H, CH<sub>2</sub>), 0.95 (s, 3H, CH<sub>3</sub>), 0.90 (s, 3H, CH<sub>3</sub>), 0.82 (s, 3H, CH<sub>3</sub>). <sup>13</sup>C {<sup>1</sup>H} NMR (151 MHz, CDCl<sub>3</sub>) δ (ppm): 220.01 (C=O), 57.86 (QC), 46.94 (QC), 43.44 (CH), 43.17 (CH<sub>2</sub>), 30.04 (CH<sub>2</sub>), 27.18 (CH<sub>2</sub>), 19.92 (CH<sub>3</sub>), 19.28 (CH<sub>3</sub>), 9.39 (CH<sub>3</sub>). FT-IR (ATR) ν, cm<sup>-1</sup>: 1738 (C=O). Data corresponds to literature.<sup>34</sup>

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## **Chapter 5**

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**Final conclusions and future  
recommendations**

## Chapter 5: Final conclusions and future recommendations

### 5.1 Final conclusions

This study focused on the synthesis, characterisation and catalytic application of various non-heme N<sub>4</sub>-tetradentate Mn(OTf)<sub>2</sub> complexes for alcohol oxidation. The target ligands, ***R,R***- and ***S,S***-**L5 - L12**, were those that differed according to their N-donors (pyridine, **L5** and **L9**, and 1-methylimidazole, **L8** and **L12**), substituents on the N-donors (methoxy, **L6** and **L10**, and bromo, **L7** and **L11**), configuration (*R,R* and *S,S*) and degree of amination. After ligand synthesis was completed, various characterisation techniques, including FT-IR, <sup>1</sup>H and <sup>13</sup>C {<sup>1</sup>H} NMR spectroscopy, established the bulk purity and molecular structure of the prepared ligands. Synthesis of the Mn(OTf)<sub>2</sub> complexes, ***R,R***- and ***S,S***-**C1 - C8**, commenced using the different ligands synthesised and was evaluated with several characterisation techniques, i.e. magnetic susceptibility, melting point analysis, UV-visible spectroscopy, APCI-MS, SC-XRD and CHNS elemental analysis, which confirmed the structure and purity of the isolated complexes.

Screening of complexes ***R,R***- and ***S,S***-**C1 - C8** against benzyl alcohol oxidation revealed that the tertiary diamine complexes, ***R,R***- and ***S,S***-**C5 - C8**, showed higher percentage conversion compared to their secondary amine counterparts, ***R,R***- and ***S,S***-**C1 - C4**. This was attributed to the higher stability of the tertiary diamine complexes. Substituents on the C6 position of the N-donor had a more steric rather than the expected electronic effect when benzyl alcohol was catalytically oxidised with the Mn(OTf)<sub>2</sub> complexes. It was further seen that substituting the pyridine donor with a 1-methylimidazole donor increased benzyl alcohol conversion due to the higher basicity and decreased steric environment of the 1-methylimidazole ring. When the *R,R*- and *S,S*-configurations of the complexes were compared, no significant difference in percentage conversion was seen. This was attributed to the similar *cis-α* topology adopted by the *R,R*- and *S,S*-configurations, resulting in an active site with the same accessibility.

Optimisation of reaction parameters, i.e. catalyst, H<sub>2</sub>O<sub>2</sub> and AcOH concentration revealed that an increase in each increased the conversion of benzyl alcohol, but also decreased the selectivity towards the aldehyde product. Furthermore, it was found that AcOH is necessary for the catalytic oxidation of alcohols using non-heme N<sub>4</sub>-tetradentate ligated Mn(OTf)<sub>2</sub> complexes. Optimal conditions were used to catalytically oxidise primary alcohol substrates and illustrated that the tertiary amine complexes containing a 1-methylimidazole N-donor, ***R,R***- and ***S,S***-**C8**, are versatile towards a wide range of linear, cyclic, bicyclic and benzylic alcohols. However, over-oxidation towards the carboxylic acid product was a drawback during primary alcohol oxidation due to the presence of excess AcOH and H<sub>2</sub>O<sub>2</sub>, but the oxidation of secondary alcohols revealed the production of a single ketone product. It was further seen that an increase

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in the electron density towards the C-OH carbon increased the percentage conversion due to the increased activation of the substrate and the nucleophilic nature of the active Mn-species in solution. Employing sterically bulky secondary alcohols led to lower conversion percentages. Research is currently underway to elucidate the mechanism of alcohol oxidation with non-heme N<sub>4</sub>-tetradentate Mn(OTf)<sub>2</sub> complexes and further identify the active Mn-species present during the oxidation reaction.

### **5.2 Future recommendations**

The biggest problem found during this study was the selectivity issues during the oxidation of primary alcohols. It would be interesting to further investigate this phenomenon and find a solution to overcome it. The introduction of other carboxylic acid additives with increased steric bulk could prevent the over-oxidation of the alcohol towards a carboxylic acid product. The increased steric bulk might hinder the formation of the more bulky RCOOH product and rather stop at the RCHO product. Investigating the use of a carboxylic acid co-catalyst containing substituents with different electronic properties during primary alcohol oxidation would also be interesting. It would also be of interest to explore the possibility of utilising H<sub>2</sub>SO<sub>4</sub> as an acid because it has been observed previously that the sulfate anion acts in a similar way to the COOH group.

Elucidation of the alcohol oxidation mechanism with non-heme N<sub>4</sub>-tetradentate Mn(II)-complexes would be valuable towards the research field of biomimetic catalysis. There has not yet been clear evidence as to the nature of the active Mn-species that contribute to the catalytic oxidation cycle of alcohols. Results obtained from the mechanism of alkane and alkene oxidation using similar Mn(II)-complexes can be used to facilitate the discovery of the active Mn-species during catalytic alcohol oxidation.

Lastly, it would also be interesting to incorporate amino-acids into the ligand system to determine whether they may be advantageous to increase the selectivity during the reaction. Enzymes contain amino acids as part of their ligand system and they show incredible selectivity towards certain substrates and products. The presence of a COOH group in the amino-acid would also potentially mitigate the need for a co-catalyst during the oxidation reaction.

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## **Supplementary information**

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**Additional reaction parameter  
optimisation and spectroscopic data of  
isolated ketone products**

# Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products

## S.1 Additional reaction parameter optimisation

Table S.1: Effect of variation of reaction time and temperature on the percentage benzyl alcohol conversion.<sup>a</sup>

| Entry | Catalyst<br>mol %        | H <sub>2</sub> O <sub>2</sub><br>(equivalents) | AcOH<br>(equivalents) | Temperature<br>(°C) | Time<br>(min.) | Conversion <sup>b</sup><br>(%) |
|-------|--------------------------|------------------------------------------------|-----------------------|---------------------|----------------|--------------------------------|
| 1     | 0.1<br>( <i>R,R</i> -C5) | 1.2                                            | 10                    | 25                  | 35             | 19                             |
| 2     | 0.1<br>( <i>R,R</i> -C6) | 1.2                                            | 10                    | - 5                 | 35             | 12                             |
| 3     | 0.1<br>( <i>R,R</i> -C6) | 3                                              | 10                    | 25                  | 60             | 9                              |
| 4     | 0.1<br>( <i>R,R</i> -C5) | 1.2                                            | 10                    | 25                  | 190            | 17                             |

<sup>a</sup> Reaction conditions: Complex *R,R*-C5 or *R,R*-C6 (2 μmol) was dissolved in acetonitrile with benzyl alcohol (2 mmol) and AcOH (0 or 1.140 ml). H<sub>2</sub>O<sub>2</sub> (0.19 or 0.620 ml) was added by syringe pump over 30 min. at temperature indicated (total volume = 3.19 ml) and stirred for an additional 5 min. <sup>b</sup> Conversions were determined by GC against an internal standard (biphenyl).

## S.2 Spectroscopic data of isolated ketone products

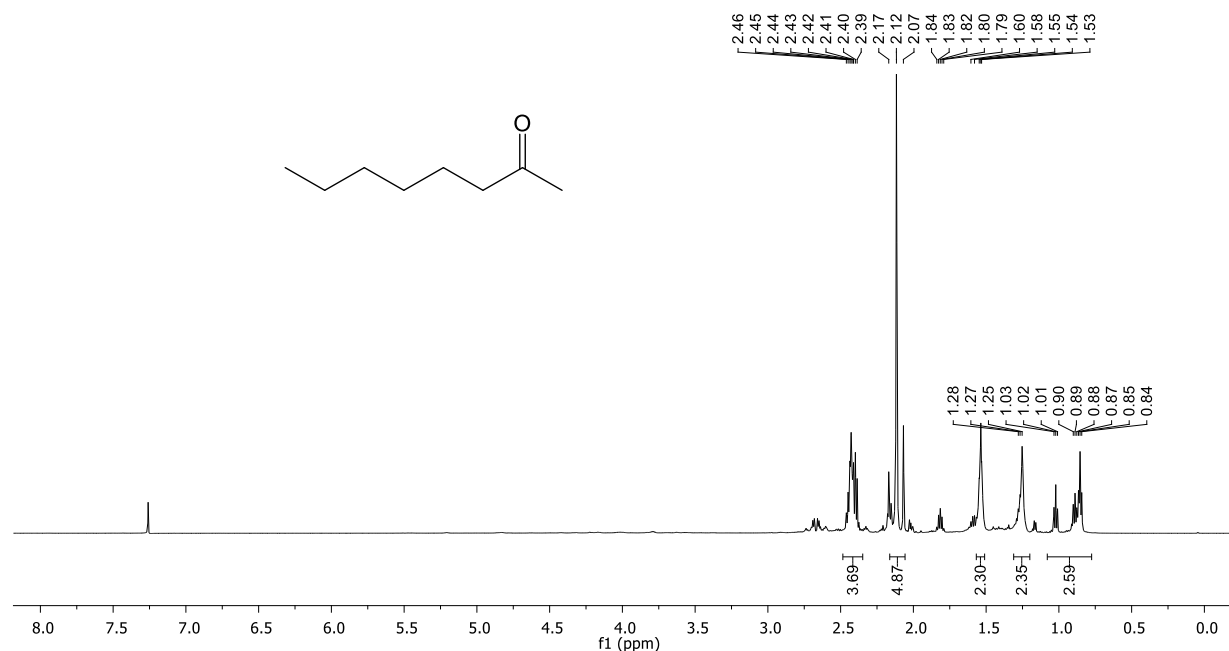


Figure S.1: <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>) spectrum of 2-octanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

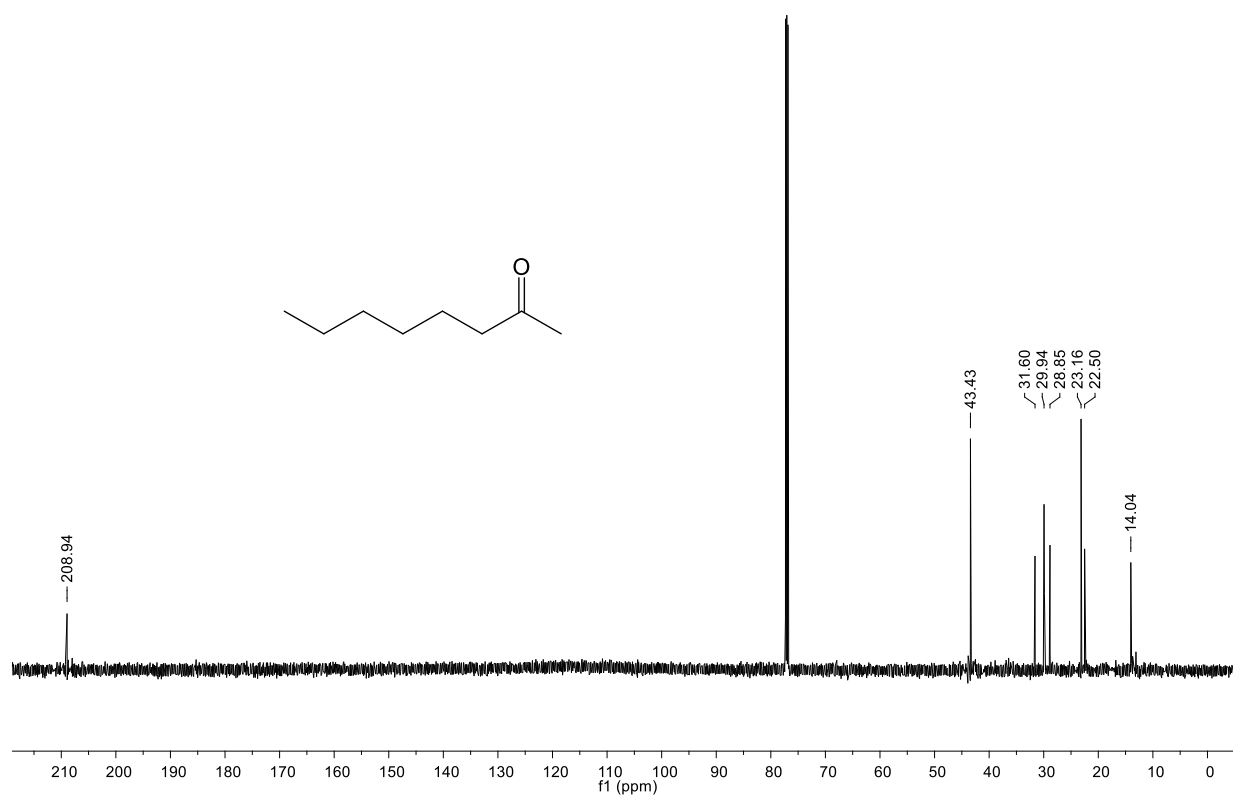


Figure S.2:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of 2-octanone.

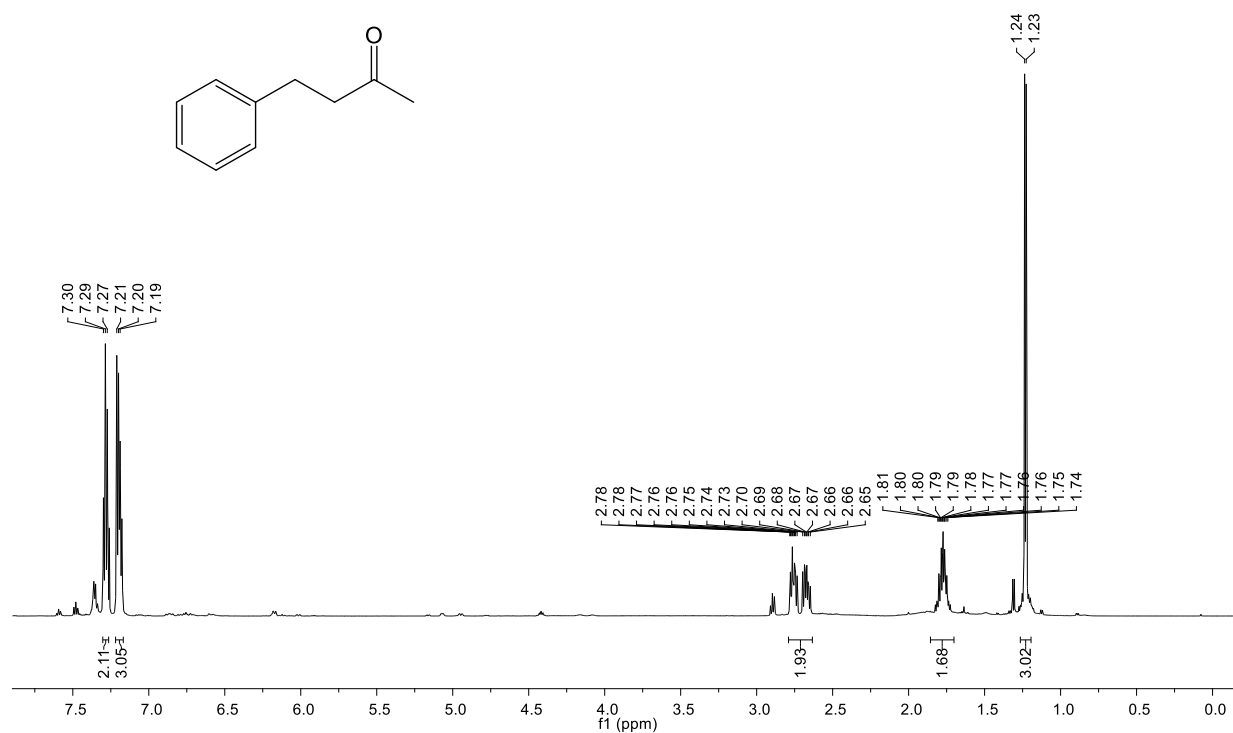


Figure S.3:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of 4-phenyl-2-butanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

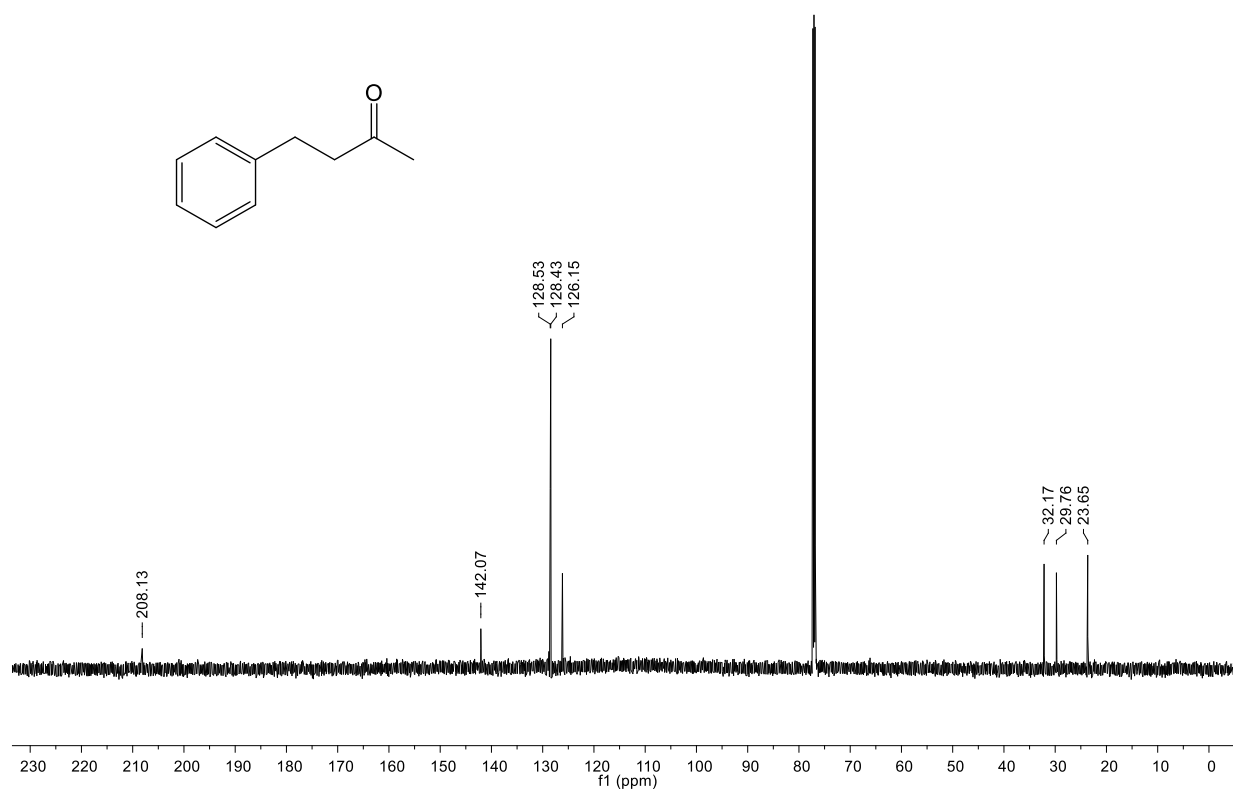


Figure S.4:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of 4-phenyl-2-butanone.

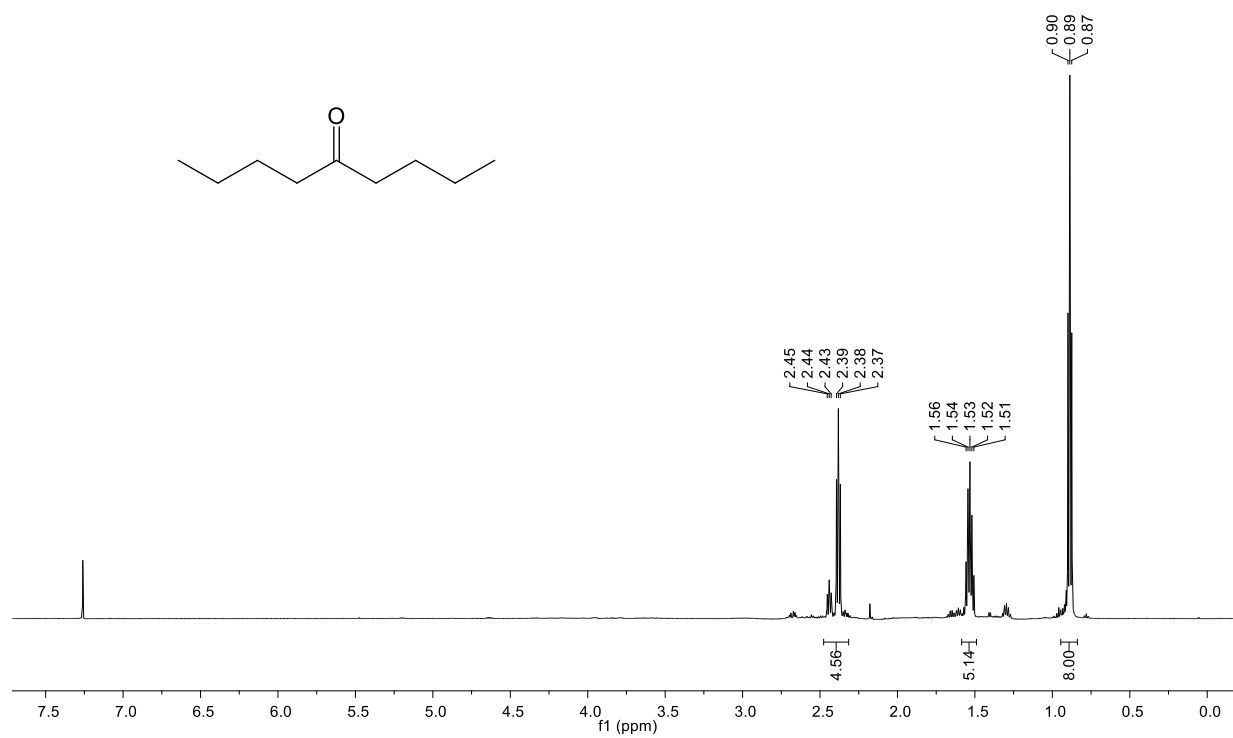


Figure S.5:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of 5-nonanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

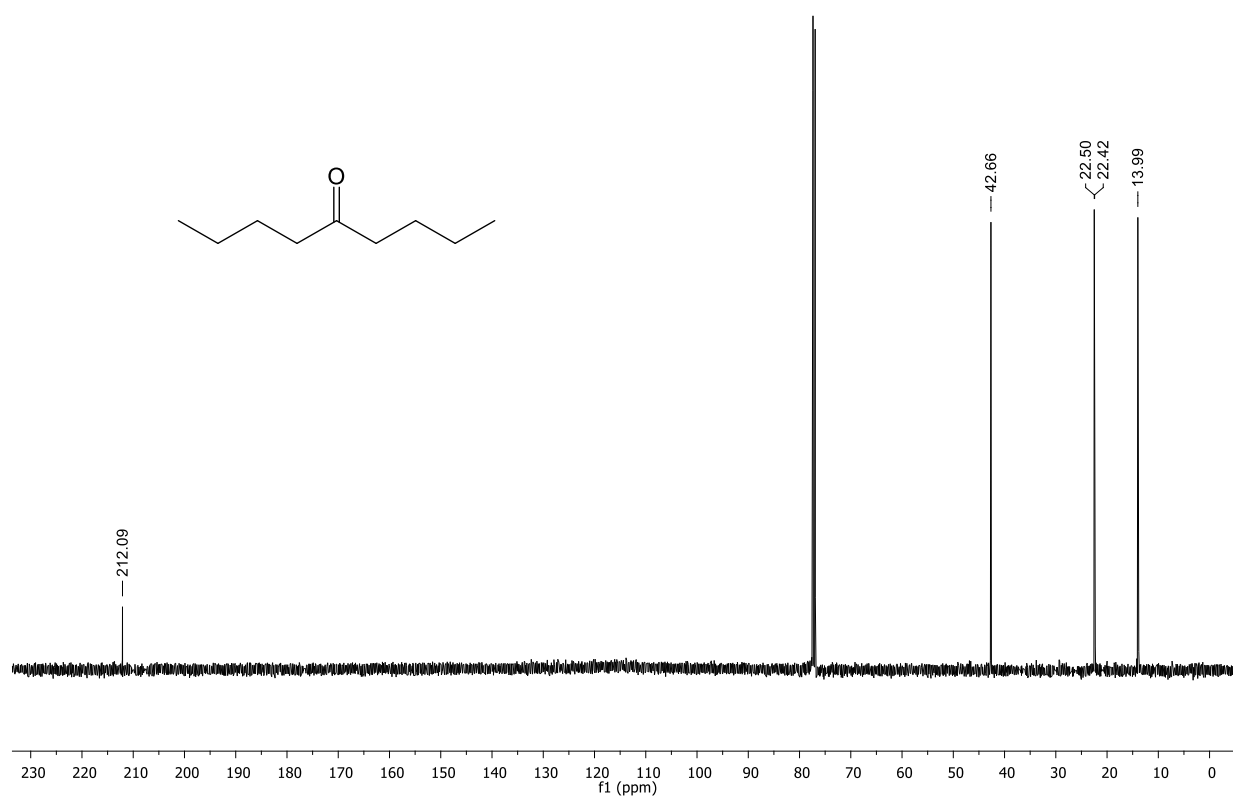


Figure S.6:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of 5-nonanone.

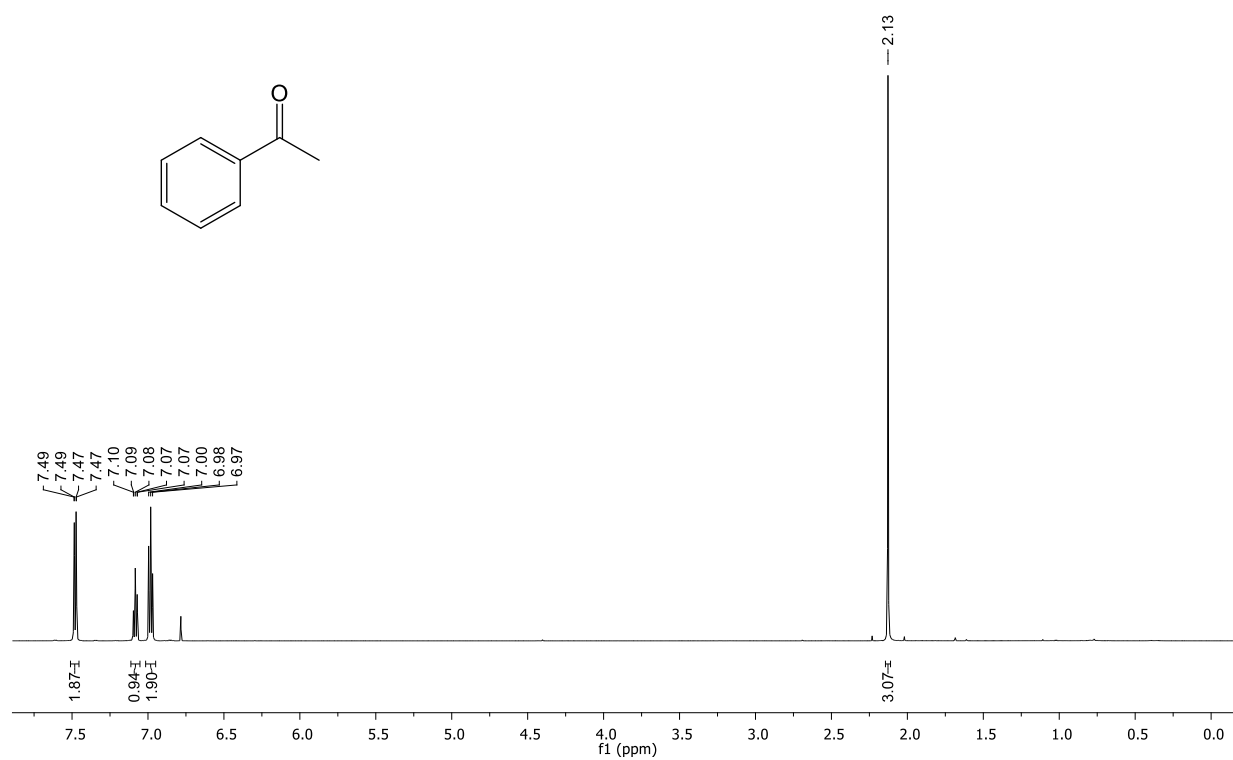


Figure S.7:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of acetophenone.

Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products



Figure S.8:  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of acetophenone.

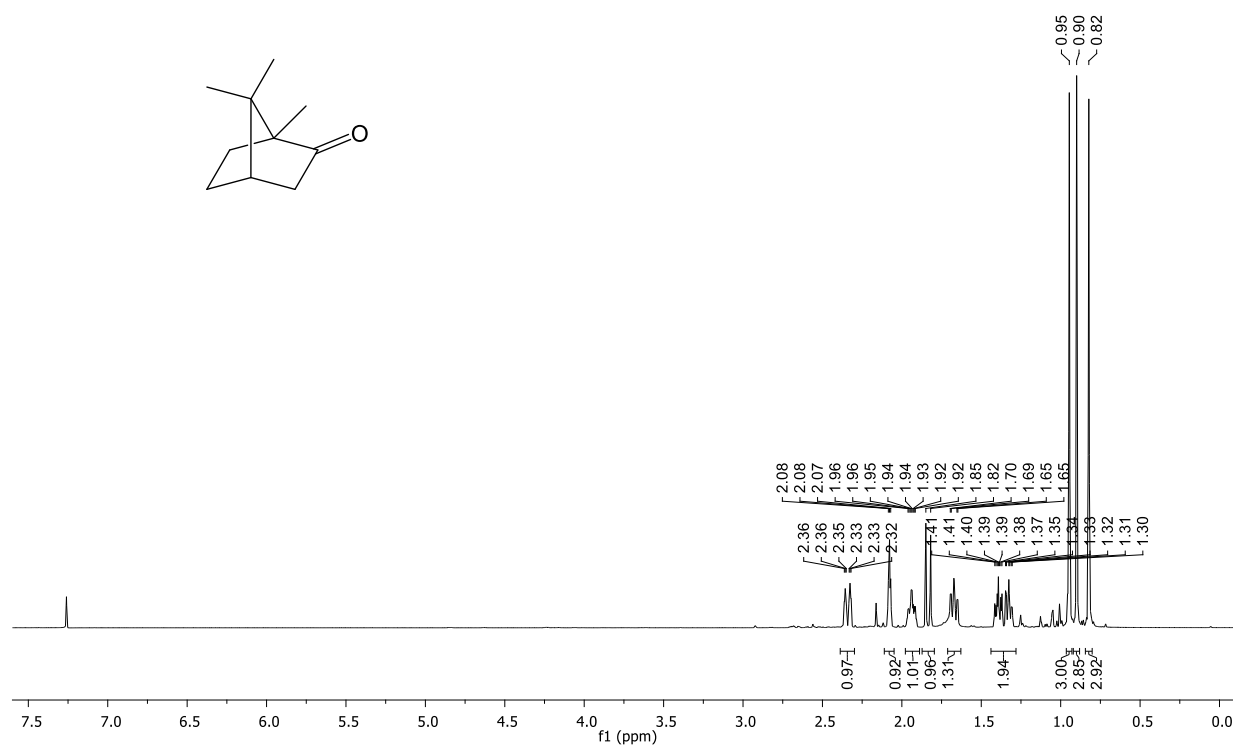


Figure S.9:  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ ) spectrum of camphor.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

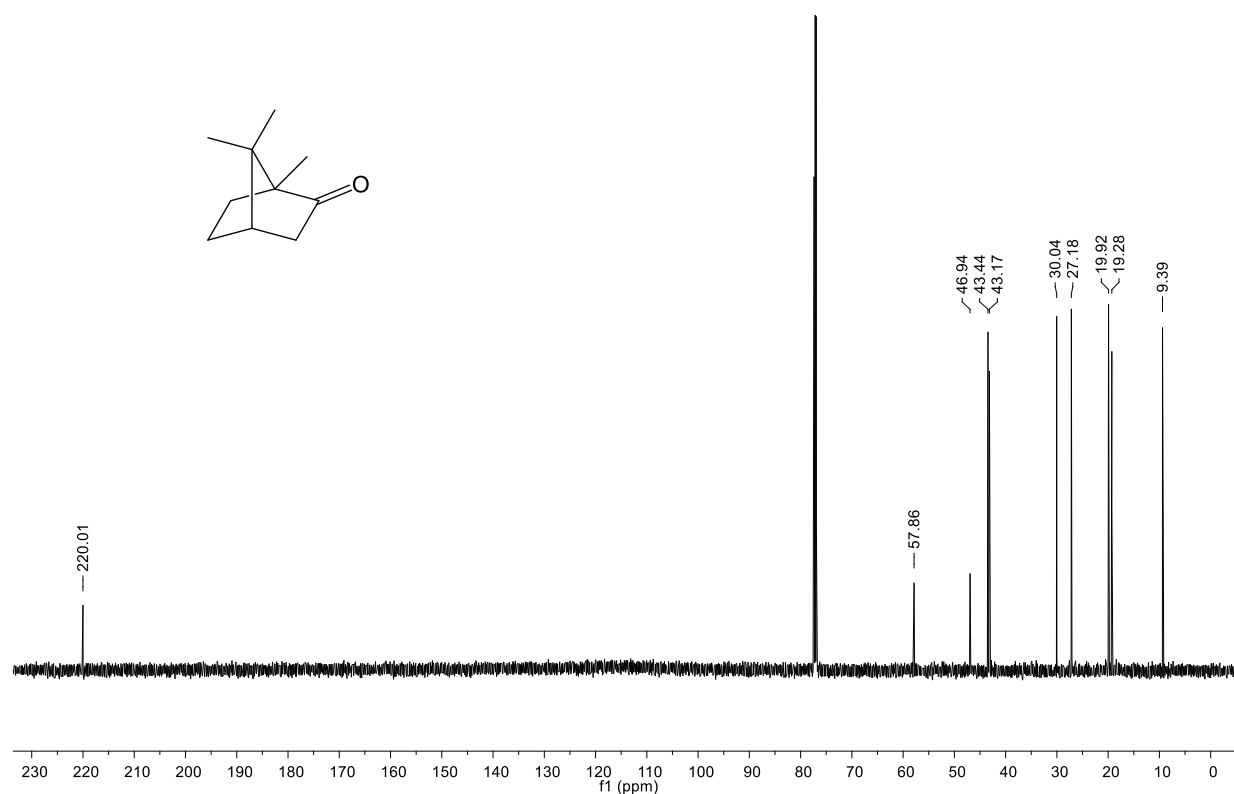


**Figure S.10:**  $^{13}\text{C}$   $\{^1\text{H}\}$  NMR (151 MHz,  $\text{CDCl}_3$ ) spectrum of camphor.

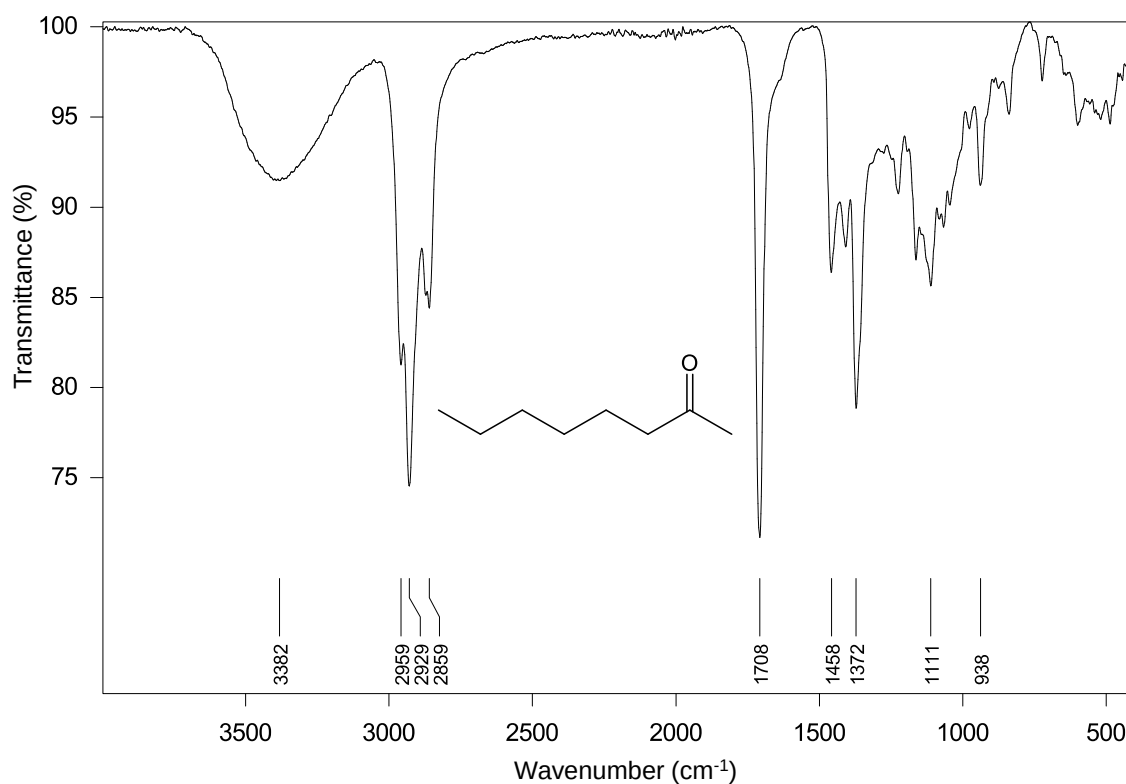


**Figure S.11:** FT-IR spectrum of isolated 2-octanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

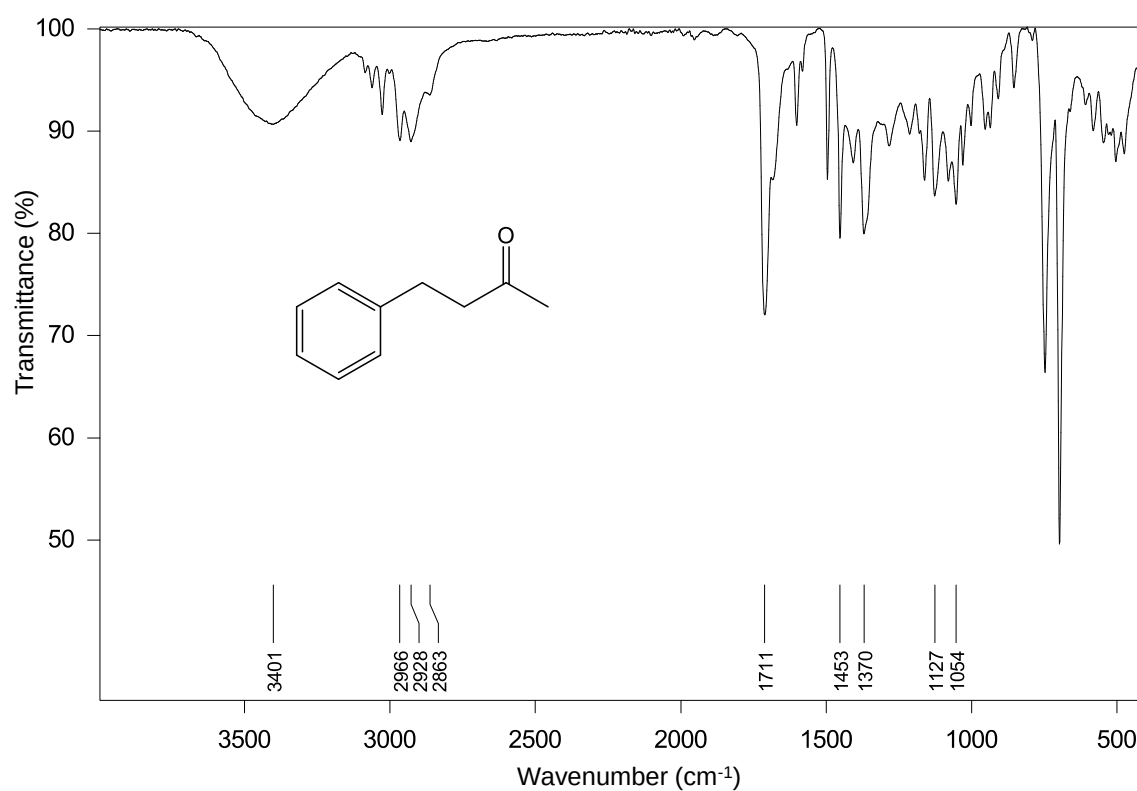


**Figure S.12:** FT-IR spectrum of isolated 4-phenyl-2-butanone.

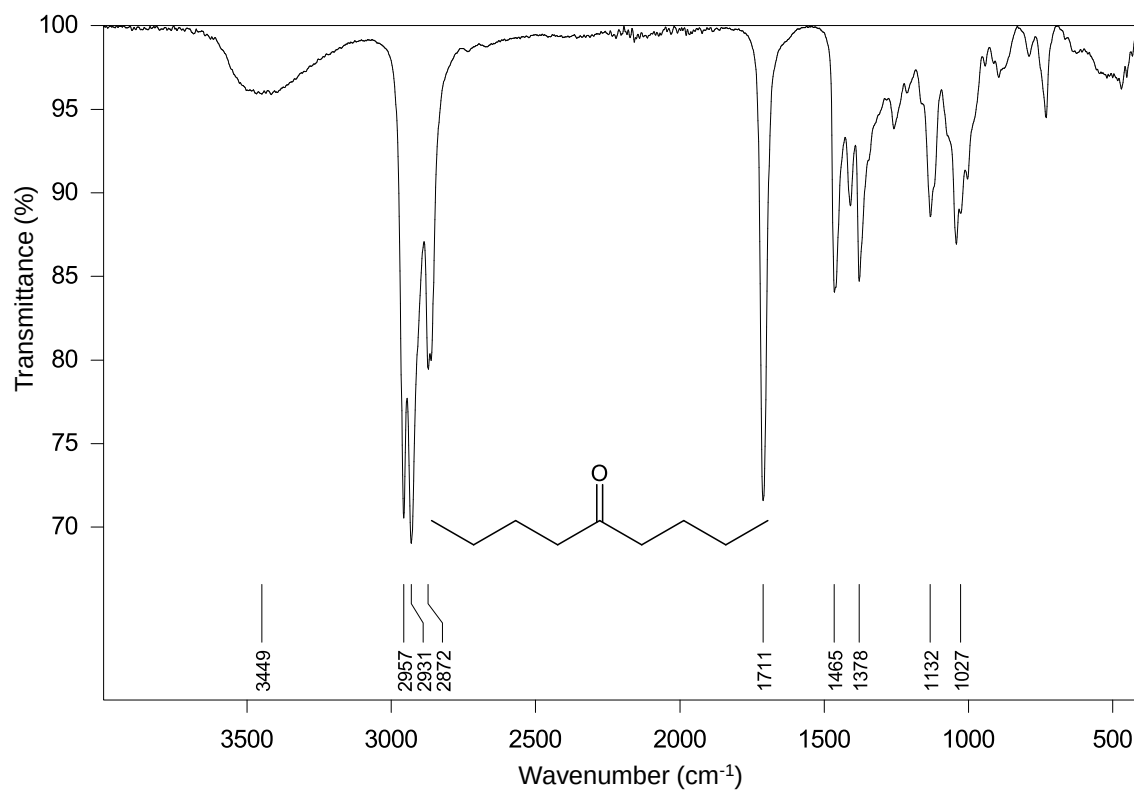


**Figure S.13:** FT-IR spectrum of isolated 5-nonanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

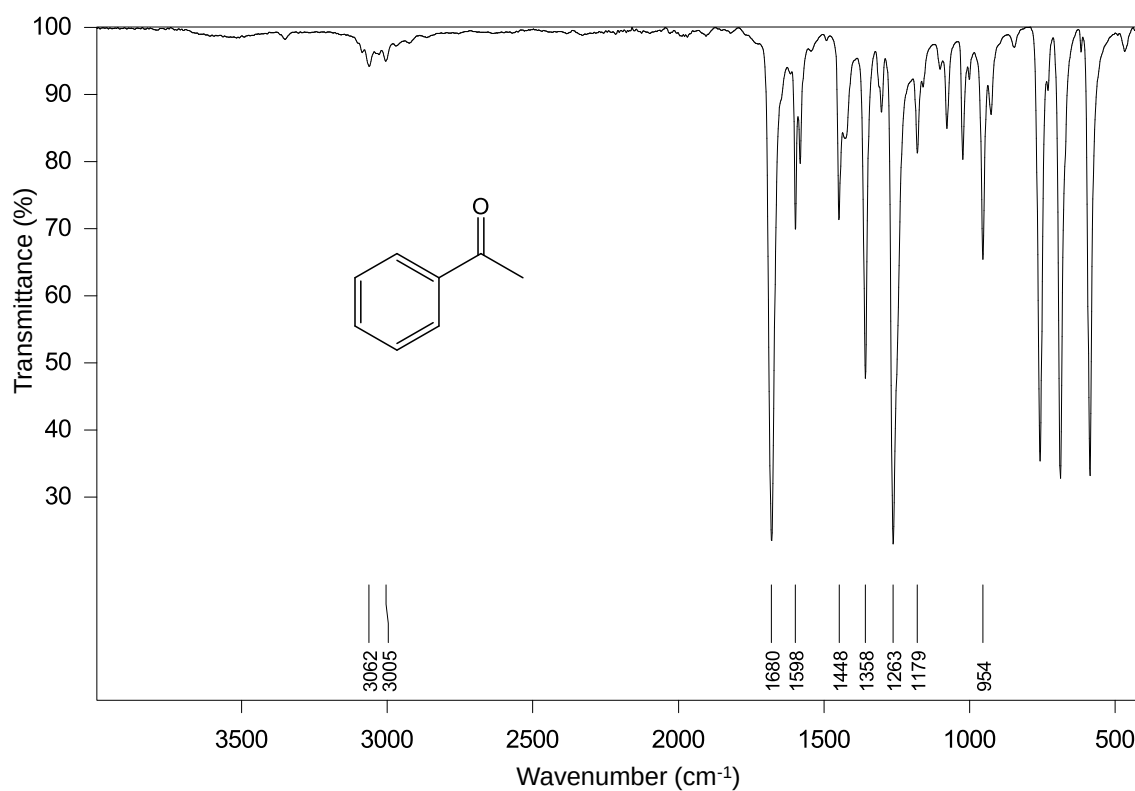


**Figure S.14:** FT-IR spectrum of isolated acetophenone.

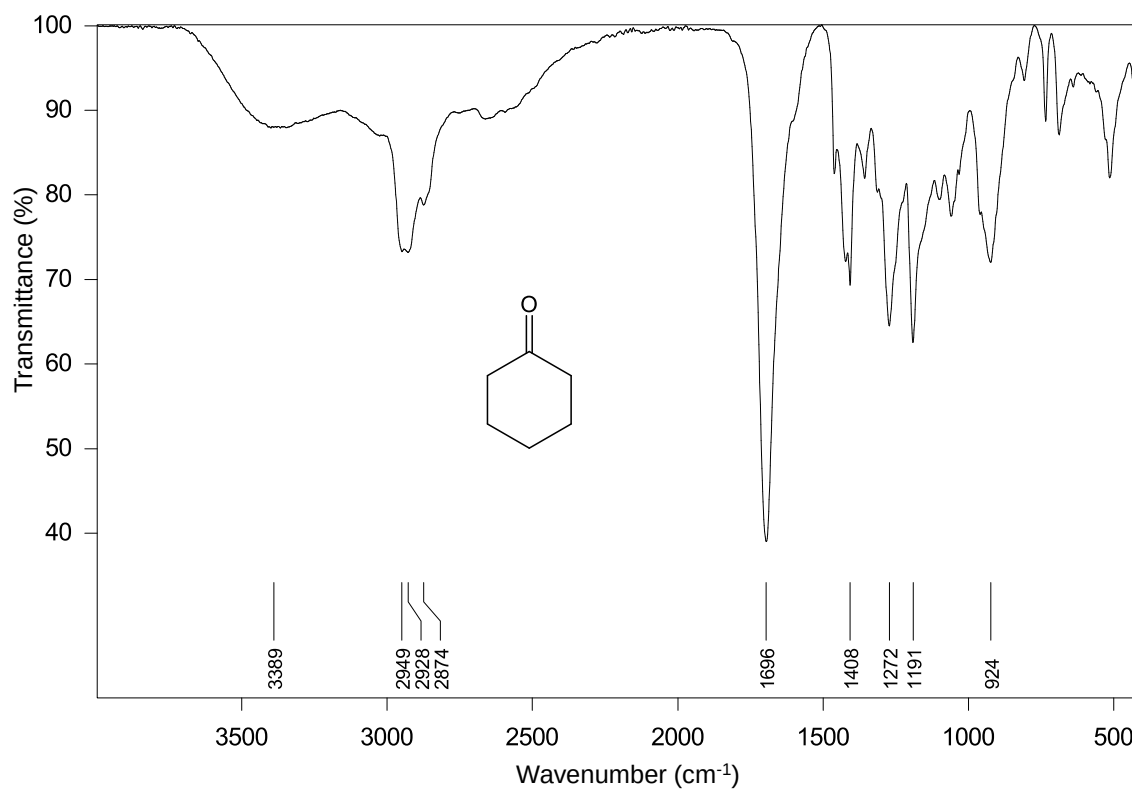


**Figure S.15:** FT-IR spectrum of isolated cyclohexanone.

*Supplementary information: Additional reaction parameter optimisation and spectroscopic data of isolated ketone products*

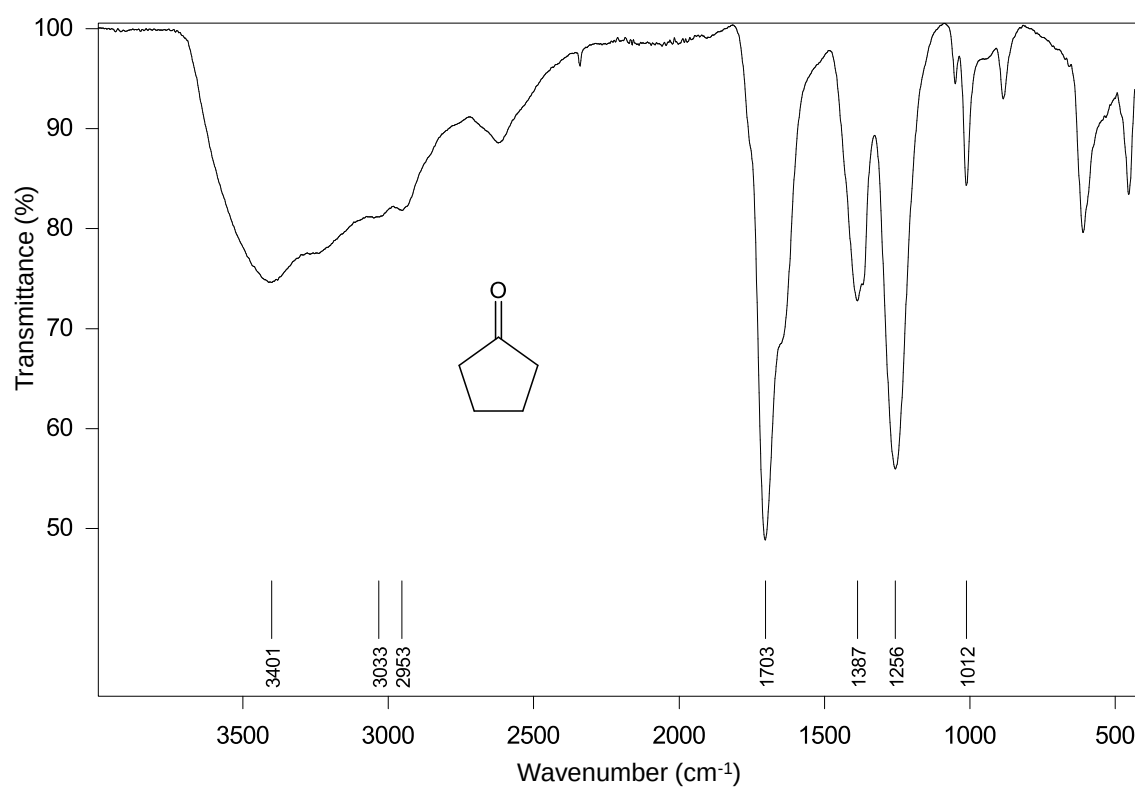


**Figure S.16: FT-IR spectrum of isolated cyclopentanone.**

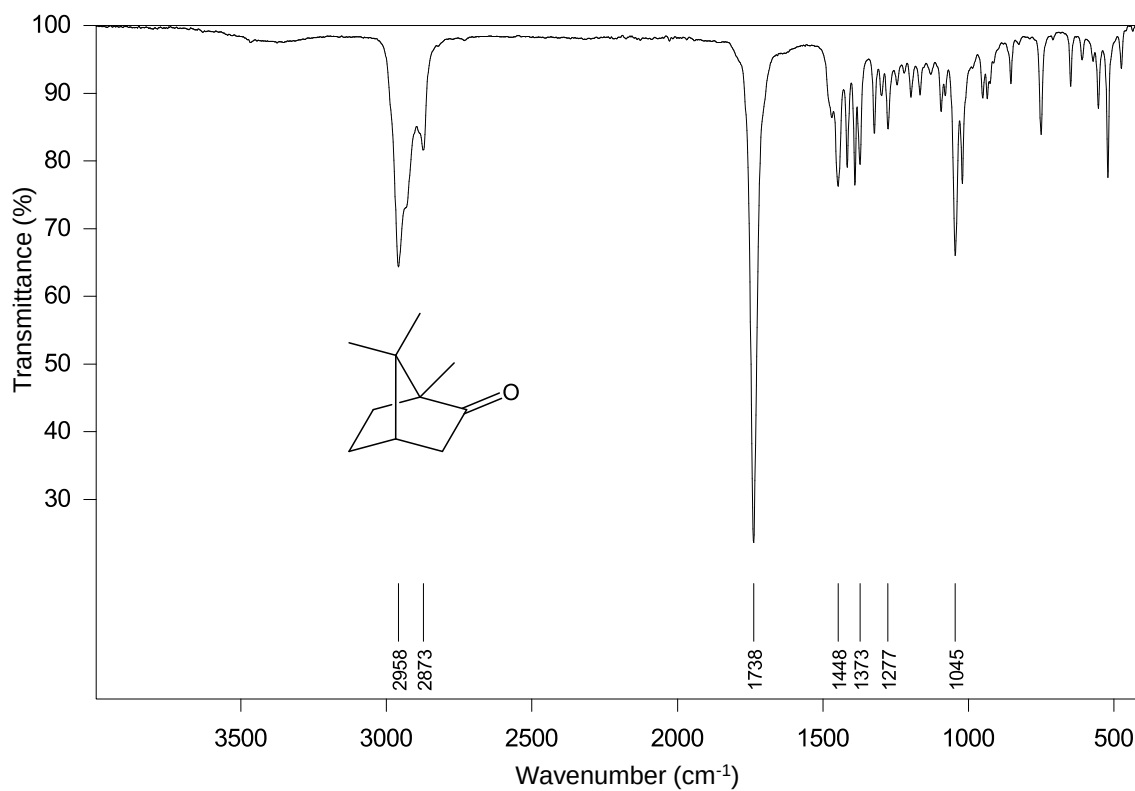


**Figure S.17: FT-IR spectrum of isolated camphor.**