SYNTHESIS, CHARACTERISATION AND CATALYTIC ACTIVITY OF GOLD, RHODIUM AND PALLADIUM COMPLEXES FEATURING FLUORINATED $N$-HETEROCYCLIC CARBENE LIGANDS

A thesis submitted to The University of Manchester for the degree of Doctor of Philosophy in the Faculty of Science and Engineering

2018

Mohamad Shazwan Shah Jamil

School of Chemistry
Contents

List of Figures ............................................................................................................ 7
List of Schemes ........................................................................................................... 12
List of Tables ............................................................................................................. 15
Abstract ....................................................................................................................... 17
Declaration .................................................................................................................. 18
Copyright Statement ................................................................................................. 19
Acknowledgements ..................................................................................................... 20
Abbreviations ............................................................................................................. 21
NHC Structures .......................................................................................................... 23

CHAPTER 1: INTRODUCTION .............................................................................. 24

1.1 N-Heterocyclic Carbenes .................................................................................. 25
1.1.1 Structure and general properties ................................................................. 25
1.1.2 Synthesis of NHC precursors and free NHCs .............................................. 28
1.1.3 Coordination of NHCs to transition metals .................................................. 29
1.1.4 Coordination of NHCs to p-block elements ............................................... 34
1.1.5 NHCs as organocatalysts ............................................................................ 35
1.2 Transition Metal Complexes featuring Fluorinated NHC Ligands ................. 39
1.2.1 Palladium complexes ................................................................................. 41
1.2.2 Ruthenium complexes ............................................................................... 46
1.2.3 Rhodium and Iridium complexes ................................................................. 56
1.3 Summary ............................................................................................................. 62
1.4 Thesis Structure ................................................................................................. 63
1.5 References ......................................................................................................... 64

CHAPTER 2: SYNTHESIS, CHARACTERISATION AND ELECTRONIC PROPERTIES OF FLUORINATED NHC LIGANDS .............................................................. 70

2.1 Introduction ........................................................................................................ 71
2.2 Synthesis and Characterisation ....................................................................... 72
2.3 Evaluation of the Electronic Properties of NHCs .......................................... 78
2.4 Summary ............................................................................................................ 90
2.5 Experimental .................................................................................................................. 90
2.5.1 General considerations .............................................................................................. 90
2.5.2 X-ray diffraction studies ......................................................................................... 91
2.5.3 Synthetic procedures ............................................................................................... 92
2.5.3.1 1,3-bis(4-fluorophenyl)imidazolium tetrafluoroborate: NHC-1 precursor .................. 92
2.5.3.2 1,3-bis(2,4-difluorophenyl)imidazolium tetrafluoroborate: NHC-2 precursor ................ 93
2.5.3.3 1,3-bis(2,6-difluorophenyl)imidazolium tetrafluoroborate: NHC-3 precursor .................. 94
2.5.3.4 1,3-bis(2,4,5-trifluorophenyl)imidazolium tetrafluoroborate: NHC-4 precursor .................. 95
2.5.3.5 1,3-bis(2,4,6-trifluorophenyl)imidazolium tetrafluoroborate: NHC-5 precursor .................. 96
2.5.3.6 1,3-bis(2,4,6-trimethylphenyl)imidazolium tetrafluoroborate: IMes precursor .................. 97
2.5.3.7 1,3-bis(phenyl)imidazolium tetrafluoroborate: IPh precursor .................. 98
2.5.3.8 1,3-bis(4-fluorophenyl)imidazol-2-selenone: Se(NHC-1) .................................................. 99
2.5.3.9 1,3-bis(2,4-difluorophenyl)imidazol-2-selenone: Se(NHC-2) ................................. 100
2.5.3.10 1,3-bis(2,6-difluorophenyl)imidazol-2-selenone: Se(NHC-3) ................................. 101
2.5.3.11 1,3-bis(2,4,5-trifluorophenyl)imidazol-2-selenone: Se(NHC-4) ................................. 102
2.5.3.12 1,3-bis(2,4,6-trifluorophenyl)imidazol-2-selenone: Se(NHC-5) ................................. 103
2.5.3.13 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-selenone: Se(IMes) ................................. 104
2.5.3.14 1,3-bis(phenyl)imidazol-2-selenone: Se(IPh) .................................................. 105
2.6 References .............................................................................................................. 106

CHAPTER 3: SYNTHESIS, CHARACTERISATION AND CATALYTIC ACTIVITY OF GOLD(I) COMPLEXES FEATURING FLUORINATED NHC LIGANDS .................................................. 109
3.1 Introduction .............................................................................................................. 110
3.2 Synthesis and Characterisation ............................................................................... 115
3.3 Steric Quantification ............................................................................................... 123
3.4 Catalytic Activity .................................................................................................. 133
3.5 Summary ............................................................................................................... 139
3.6 Experimental ........................................................................................................ 140
3.6.1 General considerations ..................................................................................... 140
3.6.2 X-ray diffraction studies .................................................................................. 141
3.6.3 Synthetic procedures ......................................................................................... 142
3.6.3.1 Chloro[1,3-bis(4-fluorophenyl)imidazol-2-ylidene]gold(I): Au-1 .............. 142
3.6.3.2 Chloro[1,3-bis(2,4-difluorophenyl)imidazol-2-ylidene]gold(I): Au-2 ....... 143
3.6.3.3 Chloro[1,3-bis(2,6-difluorophenyl)imidazol-2-ylidene]gold(I): Au-3 ........ 144
3.6.3.4 Chloro[1,3-bis(2,4,5-trifluorophenyl)imidazol-2-ylidene]gold(I): Au-4 ..... 145
3.6.3.5 Chloro[1,3-bis(2,4,6-trifluorophenyl)imidazol-2-ylidene]gold(I): Au-5 ..... 146
3.6.3.6 Chloro[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene]gold(I): AuCl(IMes) ........................................................................................................... 147
3.6.3.7 Chloro[1,3-bis(phenyl)imidazol-2-ylidene]gold(I): AuCl(IPh) ................. 148
3.6.4 A³ coupling catalytic testing procedure ............................................................... 149
3.7 References.............................................................................................................. 149

CHAPTER 4: SYNTHESIS, CHARACTERISATION AND CATALYTIC ACTIVITY
OF RHODIUM(I) COMPLEXES FEATURING FLUORINATED NHC LIGANDS ............. 153
4.1 Introduction .......................................................................................................... 154
4.2 Synthesis and Characterisation ............................................................................ 161
4.4 Catalytic Activity .................................................................................................. 178
4.5 Summary ............................................................................................................... 187
4.6 Experimental ........................................................................................................ 188
4.6.1 General considerations ..................................................................................... 188
4.6.2 X-ray diffraction studies .................................................................................. 189
4.6.3 Synthetic procedures ......................................................................................... 190
4.6.3.1 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(4-fluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-21 ................................................................. 190
4.6.3.2 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,4-difluorophenyl)imidazol-2- ylidene] rhodium(I): Rh-22 ............................................................................. 191
4.6.3.3 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,6-difluorophenyl)imidazol-2- ylidene] rhodium(I): Rh-23 ............................................................................. 192
4.6.3.4 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,4,5-trifluorophenyl)imidazol-2- ylidene] rhodium(I): Rh-24 ............................................................................. 193
4.6.3.5 Chloro(η^4-1,5-cyclooctadiene)[1,3-bis(2,4,6-trifluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-25 ............................................................... 194

4.6.3.6 Chloro(η^4-1,5-cyclooctadiene)[1,3-bis(phenyl)imidazol-2-ylidene] rhodium(I): Rh-26 ............................................................... 195

4.6.3.7 Chloro(η^4-1,5-cyclooctadiene)[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] rhodium(I): Rh-27 ............................................................... 196

4.6.4 Transfer hydrogenation catalytic testing procedure .................................................. 197

4.7 References .................................................................................................................. 197

CHAPTER 5: SYNTHESIS, CHARACTERISATION AND CATALYTIC ACTIVITY
OF PALLADIUM(II) COMPLEXES FEATURING FLUORINATED NHC LIGANDS .......... 201

5.1 Introduction .................................................................................................................. 202

5.2 Synthesis and Characterisation ................................................................................... 211

5.3 Unusual and Unique Structure of Pd-25 ................................................................... 218

5.4 Steric Quantification ................................................................................................... 227

5.5 Catalytic Activity ........................................................................................................ 231

5.6 Summary ..................................................................................................................... 238

5.7 Experimental ............................................................................................................... 239

5.7.1 General considerations ........................................................................................... 239

5.7.2 X-ray diffraction studies ......................................................................................... 240

5.7.3 Synthetic procedure ............................................................................................... 241

5.7.3.1 Dichloro(3-chloropyridyl)[1,3-bis(4-fluorophenyl)imidazol-2-ylidene] palladium(II): Pd-21 .................................................................................... 241

5.7.3.2 Dichloro(3-chloropyridyl)[1,3-bis(2,4-difluorophenyl)imidazol-2-ylidene] palladium(II): Pd-22 .................................................................................... 242

5.7.3.3 Dichloro(3-chloropyridyl)[1,3-bis(2,6-difluorophenyl)imidazol-2-ylidene] palladium(II): Pd-23 .................................................................................... 243

5.7.3.4 Dichloro(3-chloropyridyl)[1,3-bis(2,4,5-trifluorophenyl)imidazol-2-ylidene] palladium(II): Pd-24 .................................................................................... 244

5.7.3.5 (3-chloropyridyl)[1,3-bis(2,4,6-trifluorophenyl)imidazol-2-ylidene] palladium(0): Pd-25 ..................................................................................... 245

5.7.3.6 Dichloro(3-chloropyridyl)[1,3-bis(phenyl)imidazol-2-ylidene] palladium(II): Pd-26 ..................................................................................... 246
5.7.3.7 Dichloro(3-chloropyridyl)[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] palladium(II): \textbf{Pd-14} ................................................................. 247

5.7.4 Suzuki-Miyaura catalytic testing procedure ............................................... 248

5.8 References .................................................................................................. 248

\textbf{CHAPTER 6: CONCLUSION AND FUTURE WORK} .............................................. 252

Word count: 49,023
# List of Figures

## CHAPTER 1

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>General structure of an NHC</td>
<td>25</td>
</tr>
<tr>
<td>1.2</td>
<td>Structural diversity of NHCs</td>
<td>26</td>
</tr>
<tr>
<td>1.3</td>
<td>General structures of imidazole and imidazolidine-based NHCs</td>
<td>26</td>
</tr>
<tr>
<td>1.4</td>
<td>Features of IAd. Taken from reference</td>
<td>27</td>
</tr>
<tr>
<td>1.5</td>
<td>σ and π interactions between carbene and adjacent nitrogen atoms</td>
<td>27</td>
</tr>
<tr>
<td>1.6</td>
<td>σ and π interactions of NHC and a transition metal</td>
<td>30</td>
</tr>
<tr>
<td>1.7</td>
<td>Orientation of substituent groups, R on NHC and phosphine metal complexes. Figure taken from reference.</td>
<td>31</td>
</tr>
<tr>
<td>1.8</td>
<td>Structures of Grubbs I, Grubbs II, Hoveyda-Grubbs II and Grubbs III.</td>
<td>33</td>
</tr>
<tr>
<td>1.9</td>
<td>Examples of NHC-borane complexes. Taken from reference.</td>
<td>34</td>
</tr>
<tr>
<td>1.10</td>
<td>NHC-silicon complex in the zero oxidation state.</td>
<td>35</td>
</tr>
<tr>
<td>1.11</td>
<td>Frontier molecular orbital of singlet ground state of an NHC. Taken from reference.</td>
<td>39</td>
</tr>
<tr>
<td>1.12</td>
<td>Molecular orbital energy level diagrams of metal-NHC π bonding and antibonding for non-fluorinated NHC and fluorinated NHC.</td>
<td>40</td>
</tr>
<tr>
<td>1.13</td>
<td>Separation of fluorous catalyst and solvent in fluorous biphasic system. Re-drawn from Scheme 1 in reference</td>
<td>42</td>
</tr>
<tr>
<td>1.14</td>
<td>Structure of Pd-3, the analogue version of PEPPSI complex.</td>
<td>43</td>
</tr>
<tr>
<td>1.15</td>
<td>Grubbs II analogues containing non-fluorinated NHCs, Ru-2 to Ru-5.</td>
<td>47</td>
</tr>
<tr>
<td>1.16</td>
<td>Asymmetric NHC-ruthenium Grubbs second generation catalysts, Ru-10 to Ru-15.</td>
<td>52</td>
</tr>
<tr>
<td>1.17</td>
<td>Ruthenium complexes bearing asymmetric NHC ligands, Ru-18 to Ru-21.</td>
<td>55</td>
</tr>
<tr>
<td>1.18</td>
<td>Rhodium complexes featuring fluorinated NHC ligands, Rh-6, Rh-7, Rh-8 and non-fluorinated analogue, Rh-9.</td>
<td>60</td>
</tr>
</tbody>
</table>

## CHAPTER 2

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1</td>
<td>Structures of NHC precursors, NHC-1 - NHC-5</td>
<td>72</td>
</tr>
<tr>
<td>2.2</td>
<td>1H NMR spectrum of NHC-2 precursor recorded in deuterated DMSO</td>
<td>74</td>
</tr>
<tr>
<td>2.3</td>
<td>19F(1H) NMR spectrum of NHC-2 precursor recorded in deuterated DMSO</td>
<td>75</td>
</tr>
<tr>
<td>2.4</td>
<td>Non-fluorinated NHC precursors prepared in this work</td>
<td>76</td>
</tr>
<tr>
<td>2.5</td>
<td>ORTEP representation of the molecular structure of NHC-2 precursor. Thermal ellipsoids are drawn at 50% probability...</td>
<td>77</td>
</tr>
<tr>
<td>2.6</td>
<td>ORTEP representation of the molecular structure of NHC-4 precursor. Thermal ellipsoids are drawn at 50% probability...</td>
<td>77</td>
</tr>
<tr>
<td>2.7</td>
<td>ORTEP representation of the molecular structure of NHC-5 precursor. Thermal ellipsoids are drawn at 50% probability...</td>
<td>77</td>
</tr>
</tbody>
</table>
Figure 2.8 \(\sigma\)-donation from an NHC to the metal centre. Modified from reference.\(^7\) ................................................................. 79
Figure 2.9 \(\pi\)-back bonding donation from a metal to the NHC. Modified from reference.\(^7\) ................................................................. 79
Figure 2.10 \(\pi\)-donation from an NHC to the metal centre. Modified from reference.\(^7\) ................................................................. 79
Figure 2.11 Techniques developed to quantify the \(\pi\)-acceptor properties of NHCs. Taken from reference.\(^{15}\) ........................................... 82
Figure 2.12 Selenium-NHC adducts prepared in this study................................. 85
Figure 2.13 The \(^{77}\)Se NMR chemical shifts for various selenium-NHC adducts. 89

CHAPTER 3

Figure 3.1 Phosphine based gold(I) complex as an anticancer agent........... 110
Figure 3.2 Gold(I) complexes containing NHC ligands as new antitu\(_2\)mor agents................................................................. 110
Figure 3.3 The novel gold complexes containing fluorinated NHC ligands................................................................. 117
Figure 3.4 \(^1\)H NMR spectra (in the range of 7 to 11ppm) of NHC-1 precursor (top) and the corresponding Au-1 complex (bottom), recorded in deuterated DMSO. The carbene proton signal at 10.30 ppm (red mark) is not observed in the gold spectrum........................................................................ 118
Figure 3.5 \(^{19}\)F{\(^1\)H} NMR spectra comparison between the starting material, NHC-1 precursor (top) and the corresponding Au-1 complex (bottom), recorded in deuterated DMSO............. 119
Figure 3.6 ORTEP representation of the molecular structure of Au-1. Thermal ellipsoids are drawn at 50% probability................................. 120
Figure 3.7 ORTEP representation of the molecular structure of Au-2. Thermal ellipsoids are drawn at 50% probability................................. 121
Figure 3.8 ORTEP representation of the molecular structure of Au-4. Thermal ellipsoids are drawn at 50% probability................................. 121
Figure 3.9 Various methods for steric quantification of NHCs.\(^{24}\) ................. 124
Figure 3.10 Tolman cone angle for measuring the size of a ligand. Taken from reference.\(^{26}\) ................................................................. 124
Figure 3.11 Illustration of percent buried volume. Taken from reference.\(^{27}\) ................................................................. 125
Figure 3.12 Steric map visualisation of a gold complex bearing ITrop ligand. Taken from reference.\(^{24}\) ................................................................. 126
Figure 3.13 Summary of percent buried volumes for [AuCl(NHC)] type complexes........................................................................ 133
Figure 3.14 General mechanism of the A\(^3\) coupling reaction......................... 134
Figure 3.15 Gold catalysts employed in this reaction......................................... 135
Figure 3.16 Plot of percentage conversion of benzaldehyde in the A\(^3\) coupling reaction against \(^{77}\)Se NMR chemical shifts of NHC selenium adduct................................................................. 137
Figure 3.17 Plot of percentage conversion of benzaldehyde in A\(^3\) reaction against percent buried volume of [AuCl(NHC)] complexes........... 138
CHAPTER 4

Figure 4.1  Rhodium complexes employed in the hydroformylation reaction ......................................................... 154

Figure 4.2  Rhodium complexes bearing different NHC ligands prepared by Nolan and co-workers. Number 12 in the NHC-aromatic substituent groups of Rh-14 represents the 12-membered ring-cyclododecyl ............................................................ 155

Figure 4.3  Rhodium complexes bearing NHC ligands employed in the hydrogenation of 1-octene ........................................ 159

Figure 4.4  Rhodium complexes containing fluorinated NHC ligands in the form of [Rh(cod)Cl(NHC)] ................................................ 162

Figure 4.5  $^1$H NMR spectrum of Rh-22, recorded in deuterated chloroform. .............................................................. 163

Figure 4.6  $^{19}$F($^1$H) NMR spectrum of Rh-22, recorded in deuterated chloroform ............................................................. 164

Figure 4.7  $^{13}$C($^1$H) NMR spectrum of Rh-22, recorded in deuterated chloroform ........................................................................ 165

Figure 4.8  Rhodium complexes bearing non-fluorinated NHC ligands, Rh-26 and Rh-27 ............................................................. 166

Figure 4.9  ORTEP representation of the molecular structure of Rh-21. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity .......................................................... 168

Figure 4.10 ORTEP representation of the molecular structure of Rh-22. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity .......................................................... 168

Figure 4.11 ORTEP representation of the molecular structure of Rh-23. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity .......................................................... 168

Figure 4.12 ORTEP representation of the molecular structure of Rh-25. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity .......................................................... 169

Figure 4.13 ORTEP representation of the molecular structure of Rh-26. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity .......................................................... 169

Figure 4.14 Rhodium-carbene bond lengths of Rh-3 (2.022 Å), Rh-7 (2.027 Å) and Rh-8 (2.024 Å). 27 .................................................. 171

Figure 4.15 Summary of percent buried volumes for [Rh(cod)Cl(NHC)-type complexes .................................................................. 177

Figure 4.16 Time dependence of the catalytic transfer hydrogenation of acetophenone .................................................................. 180

Figure 4.17 Plot of percentage conversion of acetophenone against $^{77}$Se NMR chemical shifts of NHC selenium adduct. ............................. 183

Figure 4.18 Plot of percentage conversion against of acetophenone against the percent buried volume of [Rh(cod)Cl(NHC) complexes ............ 184

Figure 4.19 Plot of multiple linear regressions analysis of calculated % conversion of acetophenone versus observed % conversion of acetophenone catalysed by rhodium(I) complexes in this work ... 186
CHAPTER 5

Figure 5.1  Example of common palladium complexes containing NHC ligands ................................................................. 204
Figure 5.2  Palladium-PEPPSI complexes employed in the Suzuki-Miyaura and Negishi reactions ........................................... 205
Figure 5.3  Mechanism of cross-coupling reaction. Taken from reference.24 ........................................................................... 206
Figure 5.4  Palladium-PEPPSI complexes containing sterically demanding NHC ligands .......................................................... 207
Figure 5.5  Palladium-PEPPSI complexes employed in Buchwald-Hartwig amination between 4-chlorotoluene and morpholine ........... 208
Figure 5.6  Comparison of the catalytic activities of Pd-13, Pd-19 and Pd-20. Conversion to coupling product based on starting material determined by GC, average values over two-runs.33 ................................................................ 210
Figure 5.7  Comparison of the catalytic activities of Pd-13, Pd-19 and Pd-20 at low catalyst loading. Conversion to coupling product based on starting material determined by GC, average values over two-runs.33 ................................................................. 212
Figure 5.8  A series of new palladium-PEPPSI complexes prepared in this study ........................................................................ 214
Figure 5.9  1H NMR spectrum of Pd-21 complex, recorded in deuterated chloroform ................................................................. 215
Figure 5.10  19F{1H} NMR spectrum of Pd-21 complex, recorded in deuterated chloroform ............................................................ 216
Figure 5.11  13C{1H} NMR spectrum of Pd-21 complex, recorded in deuterated chloroform ............................................................ 217
Figure 5.12  ORTEP representation of the molecular structure of Pd-21. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity ................................................................. 218
Figure 5.13  ORTEP representation of the molecular structure of Pd-23. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity ................................................................. 218
Figure 5.14  ORTEP representation of the molecular structure of Pd-24. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity ................................................................. 219
Figure 5.15  The expected structure of Pd-25 versus the observed structure ................................................................................ 220
Figure 5.16  1H NMR spectrum of Pd-25. Both of meta-protons on each N- substituent group are unique (as indicated by the two distinct resonances at 2.02 and 2.06 ppm- blue stars). On the other hand, both meta-protons in the rhodium and gold complexes bearing the NHC-5 ligand are chemically equivalent to one another ........................................................................ 221
Figure 5.17  19F{1H} NMR spectrum of Pd-25. Both of ortho-fluorines on each N-substituent group are unique (as indicated by the blue and green indicators). In the case of the rhodium and gold complexes bearing the NHC-5 ligand, both ortho-fluorines are chemically equivalent to one another ........................................................................ 222
Figure 5.18  19F{1H} NMR spectrum of Au-5. Both of ortho-fluorines on each
$N$-phenyl substituent group are chemically equivalent to one another (indicated by the blue stars). Figure 5.19

$^{19}$F-$^{1}H$ NMR spectrum of Rh-25. Both of ortho-fluorines on each $N$-phenyl substituent group are chemically equivalent to one another (indicated by the blue stars). Figure 5.20

Figure 5.20 ORTEP representation of the molecular structure of complex Pd-25. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd1-C1 1.915(3), Pd1-N3 2.119(2), Pd1-F1 1.964(2), Pd1-F2 1.978(2), F1-C5 1.313(4), F2-C7 1.360(4), F3-C9 1.364(4), F4-C11 1.315(4), F5-C13 1.362(4), F6-C15 1.362(4), C1-Pd-N3 178.1(1) and Cl1-Pd-Cl2 175.07(9). Figure 5.21

Figure 5.21 ORTEP representation of the molecular structure of complex Ru-7. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Ruthenium-fluorine interaction is observed, with Ru-F distance around 3.231(1) Å, which is significantly longer than the Pd-F distance in Pd-25...... Figure 5.22

Figure 5.22 ORTEP representation of the molecular structure of complex Pd-28. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Pd1-F1 has a distance of 2.408(2) Å, which is well below the sum of the van der Waals radii of the two elements (3.10 Å). Th Pd1-F1 and F1-C1 distances (2.408(2) and 1.381(2) Å respectively) in Pd-28 are considerably longer than the Pd-F and F-C distances in Pd-25...... Figure 5.23

Figure 5.23 Summary of percent buried volumes for palladium-PEPPSI type complexes. Figure 5.24

Figure 5.24 The mechanism of Suzuki-Miyaura reaction between 4-iodotoluene and phenylboronic acid. Figure 5.25

Figure 5.25 Plot of percentage conversion of 4-iodotoluene against $^{77}$Se NMR chemical shifts of NHC-selenium adduct. Figure 5.26

Figure 5.26 Plot of percentage conversion of 4-iodotoluene against percent buried volume of various palladium-PEPPSI complexes. Figure 5.27

Figure 5.27 Plot of multiple linear regression analysis of calculated % conversion of 4-iodotoluene versus observed % conversion of 4-iodotoluene, catalyzed by palladium complexes. Chapter 6

Figure 6.1 Variation of fluorinated NHC ligands that can be prepared. Figure 6.2

Figure 6.2 Fluorinated and non-fluorinated NHCs involved in this work.
### List of Schemes

**CHAPTER 1**

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1</td>
<td>Synthetic routes to compounds a, b, c, and d.</td>
<td>28</td>
</tr>
<tr>
<td>1.2</td>
<td>Synthetic routes to compounds e and f.</td>
<td>29</td>
</tr>
<tr>
<td>1.3</td>
<td>Synthesis of free NHC from NHC precursor (azolium salt).</td>
<td>29</td>
</tr>
<tr>
<td>1.4</td>
<td>Common routes for synthesising NHC-metal complexes.</td>
<td>31</td>
</tr>
<tr>
<td>1.5</td>
<td>The NHC-palladium catalysed Heck reaction.</td>
<td>32</td>
</tr>
<tr>
<td>1.6</td>
<td>Mechanism of cross coupling reaction. Taken from reference.</td>
<td>32</td>
</tr>
<tr>
<td>1.7</td>
<td>Stabilisation of a carbonyl radical by pyrrolidinylidene.</td>
<td>35</td>
</tr>
<tr>
<td>1.8</td>
<td>Mechanism for the formation of a Breslow Intermediate.</td>
<td>36</td>
</tr>
<tr>
<td>1.9</td>
<td>Application of Breslow Intermediate.</td>
<td>37</td>
</tr>
<tr>
<td>1.10</td>
<td>Transesterification catalysed by an NHC.</td>
<td>37</td>
</tr>
<tr>
<td>1.11</td>
<td>Nguyen et al. reported that NHCs can promote the ring opening of epoxides by trialkylaluminum complexes. Taken from reference.</td>
<td>38</td>
</tr>
<tr>
<td>1.12</td>
<td>Wu et al. established that NHCs are efficient catalysts for the ring opening of aziridines by silylated nucleophiles. Taken from reference.</td>
<td>38</td>
</tr>
<tr>
<td>1.13</td>
<td>The role of an NHC as a catalyst for ester polymerisation.</td>
<td>38</td>
</tr>
<tr>
<td>1.14</td>
<td>Preparation of fluoroalkylated NHC, 1 and its palladium complex, Pd-1.</td>
<td>41</td>
</tr>
<tr>
<td>1.15</td>
<td>Preparation of a palladium complex containing fluorinated NHC ligand, Pd-2.</td>
<td>42</td>
</tr>
<tr>
<td>1.16</td>
<td>Synthetic route for a PEPPSI derivative complex containing a fluorinated NHC ligand, Pd-3.</td>
<td>43</td>
</tr>
<tr>
<td>1.17</td>
<td>Synthetic route to fluorinated NHC precursors, 4 to 7.</td>
<td>44</td>
</tr>
<tr>
<td>1.18</td>
<td>The Suzuki-Miyaura reaction of p-chloroanisole with phenylboronic acid with four different palladium NHC catalysts.</td>
<td>44</td>
</tr>
<tr>
<td>1.19</td>
<td>Preparation method of a palladium complex bearing fluorinated NHC, Pd-8.</td>
<td>46</td>
</tr>
<tr>
<td>1.20</td>
<td>Synthesis route of ruthenium complex containing fluorinated NHC, Ru-1.</td>
<td>47</td>
</tr>
<tr>
<td>1.21</td>
<td>Cyclisation of N-tosyldimethallylamine catalysed by Ru-1 to Ru-5.</td>
<td>47</td>
</tr>
<tr>
<td>1.22</td>
<td>Preparation of ruthenium complex bearing fluorinated NHC, Ru-6.</td>
<td>48</td>
</tr>
<tr>
<td>1.23</td>
<td>Conversion from Grubbs II analogue, Ru-6 to Hoveyda-Grubbs II analogue, Ru-7.</td>
<td>49</td>
</tr>
<tr>
<td>1.24</td>
<td>The scope of ring-closing olefin metathesis catalysed by ruthenium Catalysts.</td>
<td>49</td>
</tr>
<tr>
<td>1.25</td>
<td>Preparation of ruthenium complex bearing an asymmetric fluorinated NHC, Ru-8.</td>
<td>50</td>
</tr>
<tr>
<td>1.26</td>
<td>Conversion from Grubbs II analogue, Ru-8 to Hoveyda-Grubbs II analogue, Ru-9.</td>
<td>51</td>
</tr>
<tr>
<td>1.27</td>
<td>Preparation of fluorinated NHC precursors, 11 to 13.</td>
<td>54</td>
</tr>
</tbody>
</table>
Scheme 1.28 Preparation of bis-cyclometalated ruthenium complexes, Ru-16 and Ru-17................................................................. 54
Scheme 1.29 Preparation methods for rhodium and iridium complexes, Rh-1 and Ir-1 respectively..................................................... 57
Scheme 1.30 Preparation of rhodium complex containing a fluorinated NHC ligand, Rh-2................................................................. 57
Scheme 1.31 Preparation of rhodium complex bearing a fluorinated NHC, Rh-3.................................................................................. 58
Scheme 1.32 Synthesis of rhodium complexes containing fluorinated NHC, Rh-4 and Rh-5............................................................ 58
Scheme 1.33 Synthesis of Ir-2 from a fluorinated NHC precursor-14........... 59
Scheme 1.34 Preparation method for the iridium complex bearing two fluorinated NHCs, Ir-3......................................................... 59
Scheme 1.35 Reaction scheme of the hydrosilylation of propargylic alcohols, A and B................................................................. 60
Scheme 1.36 Preparation of bis-cyclometalated iridium complex containing fluorinated NHC, Ir-4...................................................... 62

CHAPTER 2
Scheme 2.1 Preparation of fluorinated NHC precursors.......................... 73
Scheme 2.2 Preparation of [Ni(CO)3(NHC)] for TEP measurement........... 80
Scheme 2.3 Preparation of [IrCl(CO)2(NHC)] from [IrCl(cod)(NHC)]........ 81
Scheme 2.4 Preparation of selenium-NHC adducts.................................. 84

CHAPTER 3
Scheme 3.1 A two-step ligand exchange reaction generating NHC-free gold complexes that were selectively harmful to breast cancer cells................................................................................ 111
Scheme 3.2 [AuCl(IMes)]-catalysed intermolecular bis-cyclopropanation of enynes with alkenes......................................................... 112
Scheme 3.3 [AuCl(IPr)]-catalysed intramolecular bis-cyclopropanation...... 113
Scheme 3.4 [AuCl(IPr)]-catalysed reaction of hydroamination of alkenes... 113
Scheme 3.5 Synthetic routes for [AuCl(NHC)] complexes : i) free carbene and ii) transmetallation via silver or copper transfer agent...... 116
Scheme 3.6 Preparation method for gold complexes featuring fluorinated NHC ligands........................................................................ 117
Scheme 3.7 General scheme of the A³ coupling........................................ 133
Scheme 3.8 The A³ coupling reaction benzaldehyde, dibenzylamine and phenylacetylene.............................................................. 135
Scheme 3.9 The A³ coupling reaction benzaldehyde, dibenzylamine and phenylacetylene.............................................................. 136

CHAPTER 4
Scheme 4.1 Hydroformylation reaction catalysed by Rh-10 and Rh-11...... 155
Scheme 4.2 Preparation of rhodium complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25..................................................... 161
Scheme 4.3 Transfer hydrogenation of acetophenone to 1-phenylethanol. 178
Scheme 4.4 Formation of dicarbonyl complex Rh-4 from Rh-3.............. 181
| Scheme 5.1 | Cross-coupling reactions catalysed by NHC-palladium complexes | 202 |
| Scheme 5.2 | The first catalytic application of a NHC-palladium complex | 203 |
| Scheme 5.3 | Preparation methods for palladium-PEPPSI complexes bearing fluorinated NHC ligands | 212 |
| Scheme 5.4 | Fluorine coordination to the palladium centre in Pd-28 | 222 |
| Scheme 5.5 | The fluorine-ruthenium interaction discovered in Ru-7, which was synthesised from Ru-6 | 225 |
| Scheme 5.6 | Palladium-catalysed Suzuki-Miyaura coupling reaction of 4-iodotoulene and phenylboronic acid | 231 |
### List of Tables

#### CHAPTER 1

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1.1</td>
<td>Percentage conversions for different NHC-palladium catalysts</td>
<td>45</td>
</tr>
<tr>
<td>Table 1.2</td>
<td>Comparison of the reactivity of Grubbs II analogues in cyclisation of N-tosylmethallylamine</td>
<td>48</td>
</tr>
<tr>
<td>Table 1.3</td>
<td>Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate</td>
<td>49</td>
</tr>
<tr>
<td>Table 1.4</td>
<td>Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate, catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane)</td>
<td>51</td>
</tr>
<tr>
<td>Table 1.5</td>
<td>Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate, catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane)</td>
<td>53</td>
</tr>
<tr>
<td>Table 1.6</td>
<td>Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate, catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane)</td>
<td>55</td>
</tr>
<tr>
<td>Table 1.7</td>
<td>Product ratio and yields obtained with different catalysts</td>
<td>61</td>
</tr>
</tbody>
</table>

#### CHAPTER 2

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 2.1</td>
<td>Elemental analysis of NHC-2 precursor, 1,3-Bis(2,4-difluorophenyl)imidazolium tetrafluoroborate</td>
<td>74</td>
</tr>
<tr>
<td>Table 2.2</td>
<td>Summary of the percentage yield and NMR data for NHC precursor prepared in this work</td>
<td>76</td>
</tr>
<tr>
<td>Table 2.3</td>
<td>Selected bond lengths and angles for NHC-2, NHC-4, NHC-5 and the previously reported IMes precursor</td>
<td>78</td>
</tr>
<tr>
<td>Table 2.4</td>
<td>IR carbonyl stretching frequencies of the carbonyl ligands in nickel(I) complexes for various NHC and phosphine based ligands, measured in CH$_2$Cl$_2$</td>
<td>81</td>
</tr>
<tr>
<td>Table 2.5</td>
<td>IR carbonyl stretching frequencies of the carbonyl ligands for various NHC and phosphine based ligands, measured in CH$_2$Cl$_2$.</td>
<td>82</td>
</tr>
<tr>
<td>Table 2.6</td>
<td>Percentage yields and $^{77}$Se NMR chemical shifts of selenium-NHC adducts</td>
<td>86</td>
</tr>
</tbody>
</table>

#### CHAPTER 3

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 3.1</td>
<td>Evaluation of various NHC-gold complexes in the allylic rearrangement of allylic acetates</td>
<td>114</td>
</tr>
<tr>
<td>Table 3.2</td>
<td>Summary of the percentage yield and NMR data for [AuCl(NHC)] complexes prepared in this work</td>
<td>120</td>
</tr>
<tr>
<td>Table 3.3</td>
<td>X-ray data comparison of Au-2 and the complex in the literature</td>
<td>121</td>
</tr>
<tr>
<td>Table 3.4</td>
<td>Selected bond lengths and angles for Au-1, Au-2, Au-4 and the previously reported [AuCl(IMes)] and [AuCl(IPr)]</td>
<td>122</td>
</tr>
<tr>
<td>Table 3.5</td>
<td>Summary of % $V_{bur}$ and steric maps for a series of gold complexes(I) bearing NHC ligands, measured by the SambVca web application tool</td>
<td>129</td>
</tr>
<tr>
<td>Table 3.6</td>
<td>Percentage conversion of the product for various gold catalysts</td>
<td>135</td>
</tr>
</tbody>
</table>
Table 3.7  A³ coupling reaction catalysed by various [AuCl(NHC)]
catalysts........................................................................................................ 137

CHAPTER 4
Table 4.1  Rhodium-catalysed hydrosilylation of 1-hexene.  a ............................. 156
Table 4.2  Rhodium-catalysed hydrosilylation of 1-hexene with high
catalyst loading at room temperature.  a .................................................. 156
Table 4.3  Steric and electronic characteristics of NHC ligands for Rh-12 to
Rh-15............................................................................................................. 157
Table 4.4  Steric parameters of NHC ligands for Rh-12 to Rh-15 and their
respective conversions.................................................................................. 158
Table 4.5  Rhodium-catalysed hydrogenation of 1-octene................................. 159
Table 4.6  The scope of [Rh(cod)Cl(NHC)] synthesis...................................... 166
Table 4.7  Selected bond lengths and angles for Rh-21, Rh-22, Rh-23, Rh-25,
Rh-26 and previously reported Rh-27....................................................... 169
Table 4.8  Summary of % V_bur and steric maps for a series of rhodium
complexes bearing different NHC ligands................................................. 172
Table 4.9  Catalytic activity of rhodium complexes in transfer
hydrogenation of acetophenone................................................................... 179
Table 4.10 Multiple linear regression analysis............................................... 186

CHAPTER 5
Table 5.1  Catalytic activity of the palladium-PEPPSI complexes in the
Suzuki-Miyaura coupling reaction................................................................. 206
Table 5.2  Catalytic activity of the palladium-PEPPSI complexes in the
Negishi coupling reaction............................................................................. 206
Table 5.3  Evaluation of palladium-PEPPSI complexes in the Suzuki-
Miyaura coupling reaction.......................................................................... 207
Table 5.4  Summary of the experimental data for palladium-PEPPSI
complexes prepared in this work................................................................. 215
Table 5.5  Comparison of selected bond lengths and angles of various
palladium-PEPPSI complexes.................................................................... 217
Table 5.6  Elemental analysis data for the expected and observed
structure of Pd-25.......................................................................................... 223
Table 5.7  Summary of % V_bur and steric maps for palladium complexes
bearing different NHC ligands.................................................................... 228
Table 5.8  Percentage conversion of 4-iodotoluene and phenylboronic acid
to 4-phenyltoluene, catalysed by various palladium-PEPPSI
complexes..................................................................................................... 233
Table 5.9  Multiple linear regression analysis............................................... 237

CHAPTER 6
Table 6.1  Summary of the key findings from this work............................... 261
Abstract
Synthesis, Characterisation and Catalytic Activity of Gold, Rhodium and Palladium Complexes featuring Fluorinated N-Heterocyclic Carbene Ligands
Mohamad Shazwan Shah Jamil, PhD in Chemistry, 2018

This thesis describes the development of gold, rhodium and palladium complexes incorporating a series of fluorinated N-heterocyclic carbene (NHC) ligands (NHC = 1,3-bis(fluorophenyl)imidazol-2-ylidene, fluorophenyl = 4-fluorophenyl (NHC-1), 2,4-difluorophenyl (NHC-2), 2,6-difluorophenyl (NHC-3), 2,4,5-trifluorophenyl (NHC-4) and 2,4,6-trifluorophenyl (NHC-5) and examines their steric and electronic properties and catalytic activities. The electronic properties have been evaluated by investigating the $^{77}$Se NMR chemical shifts of the corresponding selenium adducts, Se(NHC-1), Se(NHC-2), Se(NHC-3), Se(NHC-4) and Se(NHC-5). Comparative studies revealed that the fluorinated NHC ligands have stronger $\pi$-accepting abilities than the non-fluorinated NHC counterparts, 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) and 1,3-bis(phenyl)imidazol-2-ylidene (IPh).

The novel gold(I) complexes featuring fluorinated NHC ligands, [AuCl(NHC-1)] (Au-1), [AuCl(NHC-2)] (Au-2), [AuCl(NHC-3)] (Au-3), [AuCl(NHC-4)] (Au-4) and [AuCl(NHC-5)] (Au-5) have been synthesised and employed in the A³ coupling reaction of benzaldehyde, dibenzylamines and phenylacetylene. The catalytic activities of these complexes increased in the order of increasing steric bulk and $\pi$-accepting abilities of the NHC ligands.

The preparation of the rhodium(I) complexes bearing fluorinated NHC ligands, [Rh(cod)Cl(NHC-1)] (Rh-21), [Rh(cod)Cl(NHC-2)] (Rh-22), [Rh(cod)Cl(NHC-3)] (Rh-23), [Rh(cod)Cl(NHC-4)] (Rh-24) and [Rh(cod)Cl(NHC-5)] (Rh-25) is reported. The catalytic activities of Rh-21, Rh-22, Rh-23, Rh-24 and Rh-25 in the transfer hydrogenation of acetophenone to 1-phenylethanol were exceptionally higher than non-fluorinated derivatives, [Rh(cod)Cl(IPh)] (Rh-26) and [Rh(cod)Cl(IMes)] (Rh-27).


The findings from this work suggest that the presence of fluorine in NHC ligands affects the steric and electronic properties and enhances the metal complexes catalytic activities in various organic reactions. The link between the steric and electronic properties of the fluorinated NHCs and the outcome of the reactions in each catalytic system was investigated and reported in this thesis.
Declaration

I declare that no portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.
Copyright Statement

The author of this thesis (including any appendices and/or schedules to this thesis) owns certain copyright or related rights in it (the “Copyright”) and s/he has given The University of Manchester certain rights to use such Copyright, including for administrative purposes.

Copies of this thesis, either in full or in extracts and whether in hard or electronic copy, may be made only in accordance with the Copyright, Designs and Patents Act 1988 (as amended) and regulations issued under it or, where appropriate, in accordance with licensing agreements which the University has from time to time. This page must form part of any such copies made.

The ownership of certain Copyright, patents, designs, trademarks and other intellectual property (the “Intellectual Property”) and any reproductions of copyright works in the thesis, for example graphs and tables (“Reproductions”), which may be described in this thesis, may not be owned by the author and may be owned by third parties. Such Intellectual Property and Reproductions cannot and must not be made available for use without the prior written permission of the owner(s) of the relevant Intellectual Property and/or Reproductions.

Further information on the conditions under which disclosure, publication and commercialisation of this thesis, the Copyright and any Intellectual Property and/or Reproductions described in it may take place is available in the University IP Policy (http://documents.manchester.ac.uk/DocuInfo.aspx?DocID=24420), in any relevant Thesis restriction declarations deposited in the University Library, The University Library’s regulations (http://www.library.manchester.ac.uk/about/regulations/) and in The University’s policy on Presentation of Theses.
Acknowledgements

First and foremost, I would like to express my sincere gratitude to my supervisor, Dr Alan Brisdon for his advice, guidance and support during my time here and for giving me the opportunity to work in this interesting area.

I would like to thank the past and present members of Fluorine research group- Sultan, Dr Lulu, Jack E, Jack T, Joe, Rob, Hajar, Hind, Dr Amina, Dr Sanaa, Dr Arij, Dr Abeer, Kai, Emily, Fan, Sarah, Reece, Mathias, Inigo and Imogen whom have provided guidance, support and laugh throughout my studies here. My special thanks goes to Sultan Alkaabi for collecting and solving the X-ray crystallographic data. I would also like to thank all the staff in the School of Chemistry for their technical support and guidance, especially Dr Jenny Slaughter, Dr Neil Burton, Dr Robin Pritchard, Prof Mike Ingelson and Mr Martin Jennings.

I would like to acknowledge the Government of Malaysia and Majlis Amanah Raya (MARA) for their financial support through my studies at Manchester.

My deepest gratitude goes to my parents (Tuan Haji Jamil & Puan Hajah Seniah), my parents-in-law (Lt Kol. Osman & Puan Ramlah), my wife (Dr Nurul Amalina), my siblings (Shahril, Shamil & Shamim), sisters-in-law (Sakinah & Asma) relatives and friends, especially the members of IKRAM UKE (Waqi, Dr Munawar, Baharin, Dr Aslam, Dr Al-Amin, Dr Adlan, Muhsin, Faizal, Hilmi and many other) whom I regard as my own family members, for their support, advices, prayers and motivation which help me to strive towards my goal.

Finally, thank you to everyone who at some point has contributed any means of support during the course of my PhD.
Abbreviations

°   Degree
°C  Degree celcius
Å   Angstrom
Anal. Calcd  Elemental analysis calculated
Ar   Aromatic group
atm  Atmosphere
br   Broad
'Bu  Tertiary-butyl
cat  Catalytic
CDCl₃  Deuterated chloroform
cod  1.5-Cyclooctadiene
Cp   Cycopentadienyl
Cy   Cyclohexanyl
d   Doublet
DCE  Dichloroethane
DCM  Dichloromethane
dd  Doublet of doublet
Dipp  2,6-Diisopropylphenyl
DME  Dimethoxyethane
DMF  Dimethylformamide
DMS  Dimethylsulfide
DMSO  Dimethylsulfoxide
DFT  Density functional theory
dt  Doublet of triplet
δ   Chemical shift
EDG  Electron donating group
EWG  Electron withdrawing group
Equiv  Equivalent
Et   Ethyl
EtOAc  Ethyl acetate
EtOH  Ethanol
fac  Facial isomer
g   Gram
GC  Gas chromatography
h   Hour
HOMO  Highest occupied molecular orbital
Hz  Hertz
IR  Infrared
J  Coupling constant
LUMO  Lowest unoccupied molecular orbital
m   Multiplet
M   Molar
m.p.  Melting point
Me  Methyl
MeOH  Methanol
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mes</td>
<td>Mesityl</td>
</tr>
<tr>
<td>min</td>
<td>Minute</td>
</tr>
<tr>
<td>mL</td>
<td>Millilitre</td>
</tr>
<tr>
<td>mmol</td>
<td>Millimole</td>
</tr>
<tr>
<td>MS</td>
<td>Mass spectroscopy</td>
</tr>
<tr>
<td>MW</td>
<td>Molecular weight</td>
</tr>
<tr>
<td>NHC</td>
<td>N-heterocyclic carbene</td>
</tr>
<tr>
<td>NHT</td>
<td>N-heterocyclic thione</td>
</tr>
<tr>
<td>NMP</td>
<td>N-methyl-2-pyrrolidone</td>
</tr>
<tr>
<td>NMR</td>
<td>Nuclear magnetic resonance</td>
</tr>
<tr>
<td>OAc</td>
<td>Acetate</td>
</tr>
<tr>
<td>OTf</td>
<td>Triflate</td>
</tr>
<tr>
<td>ORTEP</td>
<td>Oak Ridge Thermal Ellipsoid Plot</td>
</tr>
<tr>
<td>PEPPSI</td>
<td>Pyridine-enhanced pre-catalyst preparation, stabilisation and initiation</td>
</tr>
<tr>
<td>Ph</td>
<td>Phenyl</td>
</tr>
<tr>
<td>PPh₃</td>
<td>Triphenylphosphine</td>
</tr>
<tr>
<td>ppm</td>
<td>Parts per million</td>
</tr>
<tr>
<td>Pr</td>
<td>Propyl</td>
</tr>
<tr>
<td>iPr</td>
<td>Iso-propyl</td>
</tr>
<tr>
<td>iPrOH</td>
<td>Iso-propanol</td>
</tr>
<tr>
<td>q</td>
<td>Quartet</td>
</tr>
<tr>
<td>RT</td>
<td>Room temperature</td>
</tr>
<tr>
<td>s</td>
<td>Singlet</td>
</tr>
<tr>
<td>t</td>
<td>Time</td>
</tr>
<tr>
<td>t</td>
<td>Triplet</td>
</tr>
<tr>
<td>T</td>
<td>Temperature</td>
</tr>
<tr>
<td>TDAE</td>
<td>Tetrakis(dimethylamino)ethylene</td>
</tr>
<tr>
<td>TEP</td>
<td>Tolman Electronic Parameter</td>
</tr>
<tr>
<td>THF</td>
<td>Tetrahydrofuran</td>
</tr>
<tr>
<td>TLC</td>
<td>Thin layer chromatography</td>
</tr>
<tr>
<td>TMS</td>
<td>Tetramethylsilane</td>
</tr>
<tr>
<td>% (V_{\text{bur}})</td>
<td>Percent buried volume</td>
</tr>
</tbody>
</table>

**NHC**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>IAd</td>
<td>1,3-Bis(adamantyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>i'Bu</td>
<td>1,3-Bis(tert-butyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IBu</td>
<td>1,3-Bis(2,6-diisobutylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>ICy</td>
<td>1,3-Bis(cyclohexyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IEt</td>
<td>1,3-Bis(2,6-diethylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IMe</td>
<td>1,3-Bis(methyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IMes</td>
<td>1,3-Bis(2,4,6-trimethylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IcPen</td>
<td>1,3-Bis(2,6-di-c-pentylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IPen</td>
<td>1,3-Bis(2,6-diisopentylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IPh</td>
<td>1,3-Bis(phenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IPr</td>
<td>1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>IPr*</td>
<td>1,3-bis(2,6-bis(diphenylmethyl)-4-methylphenyl)imidazol-2-ylidene</td>
</tr>
<tr>
<td>SIMes</td>
<td>1,3-Bis(2,4,6-trimethylphenyl)imidazolidin-2-ylidene</td>
</tr>
<tr>
<td>SIPr</td>
<td>1,3-Bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene</td>
</tr>
</tbody>
</table>
NHC Structures

IAd

IBu

ICy

IMes

IPh

ICop

IPen

IPr

IPr*
Chapter 1: Introduction
1.1 *N*-Heterocyclic Carbenes

1.1.1 Structure and general properties

*N*-Heterocyclic Carbenes (NHC) are neutral heterocyclic compounds containing a divalent carbon (a species with a valency of two and two unshared valence electrons) and at least one nitrogen atom in their ring structure.\(^1,2\) Pioneering work on NHCs began as early as 1835\(^3\) but attracted more attention in 1968 when Wanzlick and Ofele independently synthesised the first NHC-metal complexes, 1,3-bis(adamantyl)imidazol-2-ylidene bearing mercury(II) and chromium(0) species, respectively.\(^4,5\) Subsequently, research on NHCs was limited because carbenes were thought to be very reactive and unstable, due to their incomplete electron octet and coordinative unsaturation, hence they could not be isolated. A renaissance in this field occurred in 1991, when Arduengo *et al.*, reported the successful isolation and characterisation of an NHC,\(^6\) which opened up new experimental and theoretical studies with a range of NHCs being synthesised and analysed. Since this pioneering work, research on NHCs has been very active due to their practical applications in organic synthesis, catalysis and macromolecular chemistry.

![Figure 1.1 General structure of an NHC.](image)

Figure 1.1 illustrates the general structure of an NHC. There are many diverse structures of NHCs, ranging from 4-membered to 7-membered rings. The number of heteroatoms on the rings and the type of atoms give rise to considerable structural diversity of NHCs as exemplified in Figure 1.2.
The ring size and substitution patterns of the heterocycle affect the steric and electronic properties of the carbenes. Of all the possible NHCs, the most commonly encountered are those with two nitrogen atoms in the 5-membered imidazole and imidazolidine rings. The only difference between them is the nature of the carbon-carbon bond in the heterocyclic ring, one has a double bond and the other a single bond as illustrated in Figure 1.3.
The general features of NHCs can be exemplified with reference to the first reported compound, 1,3-bis(adamantyl)imidazol-2-ylidene, referred to as IAd, as shown in Figure 1.4 above. Unlike traditional carbenes, NHCs are electron rich due to the presence of nitrogen atoms in the ring which play a significant role by providing electronic stabilisation to the compound. Non-bonding electrons on the carbene can exist in paired (singlet) or unpaired (triplet) states. NHCs such as IAd exhibit a singlet ground-state electronic configuration with the highest occupied molecular orbital (HOMO) being a $sp^2$-hybridised lone pair of the carbene whilst the lowest unoccupied molecular orbital (LUMO) is described as an unoccupied $\pi$-orbital of the carbene. Nitrogen atoms provide both inductive and mesomeric stabilisation to the carbene through $\sigma$-electron withdrawing and $\pi$-electron donating by lowering the energy of the occupied $\sigma$-orbital and donating electron density into the empty $\pi$-orbital respectively.
The presence of nitrogen atoms, which are $\pi$-donors, increases the nucleophilicity of the carbene which favours the singlet state by forcing the carbene carbon into a bent, more $sp^2$-like arrangement as depicted in Figure 1.5. Another feature of NHCs is the ability to vary the substituents on nitrogen. Bulky substituents in particular, provide kinetic stabilisation sterically to the compound and these substituents can be varied to modify the steric properties of an NHC.

### 1.1.2 Synthesis of NHC precursors and free NHCs

To date, there are many reported methods for the synthesis of NHCs. In most cases, the first stage involves the production of NHC precursors in the form of azolium salts, followed by deprotonation of the cationic azolium salts to generate free NHCs. Generally, NHCs can be prepared from amines (such as anilines) and aldehydes (such as glyoxal and paraformaldehyde) via cyclisation of the carbon-carbon backbone of the imidazole ring and one carbon annulation with the desired diazabutadiene. Schemes 1.1 and 1.2 illustrate some of the known synthetic methods for preparing NHC precursors.

i) Through cyclisation of carbon-carbon backbone

![Scheme 1.1 Synthetics routes to compounds $a$, $b$, $c$, and $d$.](image-url)
ii) One carbon annulation with desired diazabutadiene

Scheme 1.2: Synthetic routes to compounds e and f.\textsuperscript{11}

Generation of free NHCS involves deprotonation of the corresponding azolium salts using a strong base. The presence of sterically bulky substituents on nitrogen helps isolation of free NHCS, as described by Arduengo et al., for the first reported stable NHC.

Scheme 1.3 Synthesis of free NHC from NHC precursor (azolium salt).

\subsection*{1.1.3 Coordination of NHCS to transition metals}

A number of applications of NHCS involve their coordination to transition metals. \textit{N}-heterocyclic carbenes are very good \textsigma-\textsigma-donors and readily bind to transition metals. This property has led to the most important application of NHCS as spectator ligands in homogenous transition metal catalysis, such as olefin metathesis,\textsuperscript{12,13} cross coupling\textsuperscript{14-17} and asymmetric catalysis.\textsuperscript{18} Besides that, NHCS also have extensive applications as organometallic compounds. This includes coordination polymers,\textsuperscript{19} metal-organic frameworks,\textsuperscript{20} photoactive materials\textsuperscript{21} and liquid crystals.\textsuperscript{22} NHCS have a formal \textit{sp}^2-hybridised lone pair in the carbene \textit{p}-orbital which is available for \textsigma-donation to an empty \textit{d}-orbital of a transition metal. In addition, \textpi back donation can occur from a filled metal orbital to the empty
orbital of $\pi$ symmetry on the carbene. Figure 1.6 displays these two interactions between an NHC and a transition metal.

![Figure 1.6](image)  
Figure 1.6 $\sigma$ and $\pi$ interactions of NHC and a transition metal.

Similar to phosphines, NHCs are most commonly spectator ligands that are used to alter the electronic and steric characters of a metal centre. However, there are many attractive features of NHCs that make them better spectator ligands than phosphines. Generally, NHCs are more electron donating than phosphines, which results in thermodynamically stronger metal-ligand bonds. This is proven by comparing the bond dissociation energies and metal-ligand bond length of NHC complexes and their phosphine analogues. Typically, NHC complexes have greater bond dissociation energies and shorter metal-ligand bonds than the corresponding phosphine-containing complexes, which make them more thermally and oxidatively stable.\(^{23}\)

Another advantage of NHCs is the ease of varying their steric and electronic properties by modifying the nitrogen substituents which gives a large effect on the steric environment at the metal centres. Bulky substituents on the nitrogen atoms adjacent to the carbene are oriented more towards the metal centre thus forming umbrella-shaped structures as illustrated in Figure 1.7. This allows rotation around the metal-carbene bond to occur in order to minimise clashing with other bulky ligands. In contrast to phosphines, changing the phosphorus substituents has less
effect on the steric properties of the phosphine metal complexes. This is because the phosphorus substituents are oriented away from the metal coordination sphere as shown below.

![Figure 1.7 Orientation of substituent groups, R on NHC and phosphine metal complexes. Figure taken from reference.](image)

There are many reported synthetic routes for making NHC-metal complexes. It is not always necessary to generate free NHCs before reacting them with metal complexes. Many common methods are based on *in situ* deprotonation of azolium salts in the presence of a suitable metal-base precursor or transmetallation of pre-formed NHC silver (I) or copper (I) complexes and through oxidative addition. Some common routes for synthesising NHC-metal complexes are illustrated below.

![Scheme 1.4 Common routes for synthesising NHC-metal complexes. Figure taken from reference.](image)
The fascinating features of NHC-metal coordination have contributed to a variety of different applications of these complexes, including the widest application as catalysts in homogeneous systems for organic transformations. This was first demonstrated in an NHC-palladium(II)-catalysed Heck reaction in 1995.

A huge number of NHC-palladium(II) catalysed reactions have since been studied including oxidation of alcohols and methane, allylic alkylation, Hiyama reactions, Stille reactions, Suzuki-Miyaura reactions, Negishi reactions, Buchwald-Hartwig reactions and dehalogenation. By far, the most extensively studied reactions are cross coupling reactions, which can be illustrated in a general way as shown below.

Scheme 1.5 The NHC-palladium catalysed Heck reaction.

Scheme 1.6 Mechanism of cross coupling reaction. Taken from reference.
Apart from NHC-palladium catalysed reactions, there are other reactions catalysed by different metal NHC complexes that have been reported. These include rhodium(I) and platinum(II)-catalysed hydrosilylation of acetophenone,\(^{36}\) gold(I) and gold(III)-catalysed activation of \(\pi\)-bonds\(^{37}\) and iridium(I) and ruthenium-catalysed hydrogenation and hydrogen transfer.\(^{38}\)

Another major contribution of NHC-metal complexes is their catalytic role in olefin metathesis, particularly for ruthenium complexes. Initially, a phosphine based complex, known as a first generation Grubbs catalyst (Grubbs I) was used for this metathesis reaction.\(^{35}\) However this type of catalyst was not efficient due to its low thermal stability and functional group intolerance. A modification was made to Grubbs I catalyst by replacing one phosphine ligand with an NHC, which is then known as a second generation Grubbs catalyst (Grubbs II). This new catalyst is more stable to air and has a higher reactivity than Grubbs I.\(^{39}\) Due to the benefits of this Grubbs II catalyst, different ranges of NHC-ruthenium complexes have been made, including the widely used second generation Hoveyda-Grubbs catalyst (Hoveyda-Grubbs II).\(^{40}\) More recently, Grubbs et al., prepared a third generation of Grubbs catalyst (Grubbs III) by replacing the remaining phosphine ligand in Grubbs II with a more labile pyridine ligand. This Grubbs III catalyst has increased the initiation rate of the cross-metathesis of acrylonitrile by a millionfold.\(^4\)

![Figure 1.8 Structures of Grubbs I, Grubbs II, Hoveyda-Grubbs II and Grubbs III.](image-url)
1.1.4 Coordination of NHCs to $p$-block elements

Beside their main applications as NHC-transition metal catalysts, there is also an expanding range of NHCs coordinated to $p$-block elements reported. Similar to NHC-metal complexes, NHCs coordinate strongly to $p$-block elements due to the $\sigma$-donation from the carbene into an empty $\sigma$-accepting orbital of the $p$-block element. This dative coordination bond is relatively stable, thus forming different properties and reactivity of NHCs adduct with a wide range of $p$-block elements. The following section describes some of the most useful applications of coordinated NHC-$p$-block compounds.

NHCs are Lewis base two–electron donors which can be combined with bulky Lewis acids, such as the borane $\text{B}(\text{C}_6\text{F}_3)$ to form frustrated Lewis pairs. These NHC-borane complexes are capable of splitting hydrogen and other small molecules.\(^4\)

![Figure 1.9](image)

Figure 1.9 Examples of NHC-borane complexes. Taken from reference\(^4\).

The electronic properties of NHCs find applications in the stabilisation of main-group radicals and activation of small molecules.\(^4\) The $\pi$-accepting capability of NHCs play a significant role by providing delocalisation of spin density of the highly reactive intermediates, which in turn makes them more stable. This is exemplified by the interaction of an NHC (pyrrolidinyldiene) with a carbonyl radical.\(^4\)
The ability of the $\sigma$-donor orbitals of NHCs to donate their lone pair of electrons into $\sigma$-accepting orbitals of $p$-block element has led to the stabilisation of $p$-block elements in their zero oxidation state, as reported by Robinson et al., in 2008.\textsuperscript{46} In this work, each NHC donates its electron pair into $\sigma$ orbital of silicon, as illustrated in Figure 1.10.

**1.1.5 NHCs as organocatalysts**

Another class of applications of NHCs is their role as organocatalysts. The chemistry behind this involves, for example, nucleophilic attack of the carbene at an electrophilic site, such as a carbonyl group, as explained earlier, the $\sigma$-donor capability of NHCs makes them good nucleophiles. This section will discuss three major types of reactions of NHCs, which are reactions with aldehydes, Michael acceptors and esters.
The most frequently reported NHC-organocatalysed reactions involve the nucleophilic attack of NHCs on aldehydes. The first report dates back to 1943 on the role of a thiazolium salt as a catalyst for transformation of an aldehyde to benzoin. Later in 1958, Breslow proposed a species that was generated from the reaction of an NHC with an aldehyde in the presence of a base. The mechanism for the formation of this species, known as a Breslow Intermediate, is outlined below.

This Breslow intermediate is unique in the sense that the electrophilic carbonyl acts as a temporary nucleophile, due to π-donation of the NHC compound. This phenomenon is referred as ‘umpolung’ where the polarity of the carbonyl group is inverted to allow a secondary reaction with another carbonyl/ electron deficient group. Hence, the Breslow intermediate can attack another aldehyde or imine in a benzoin condensation or Michael acceptor electron-deficient alkene in a Stetter reaction (an organic reaction to form carbon-carbon bonds through a 1,4-addition reaction utilising a nucleophilic catalyst).
Similar to the NHC-transition metal complexes reactions, it is not necessary to initially pre-form the free NHCs in these processes. As can be seen in Scheme 1.8, the catalyst is normally formed in situ through deprotonation of the thiazolium salt.

Another major reaction of NHCs is with esters. When an NHC is added to an ester, the nucleophilic carbene will attack the electrophilic carbonyl carbon, leading to the release of the alkoxy group and thus forming an acyl azolium salt. This type of salt is more electrophilic than the original ester, which has a significant advantage upon reaction with an alcohol in a transesterification reaction, as illustrated in Scheme 1.10. Two independently reported works by Hendrick and Nolan showed NHCs effectively catalysed transesterification reactions.
In addition to transesterification, other reactions efficiently promoted by NHCs are ring opening reactions, as demonstrated in Scheme 1.11 and Scheme 1.12.

Scheme 1.11  Nguyen et al., reported that NHCs can promote the ring opening of epoxides by trialkylaluminum complexes. Taken from reference.52

Scheme 1.12  Wu et al., established that NHCs are efficient catalysts for the ring opening of aziridines by silylated nucleophiles. Taken from reference.53

NHCs also play a role as nucleophilic catalysts for the ring-opening polymerisation of cyclic ester monomers.54 In this reaction, a propagating species is formed from the reaction between an NHC and a cyclic ester monomer, as shown in Scheme 1.13. The catalyst was employed in combination with an initiator, such as benzyl alcohol which generated an α-end group bearing the ester from the initiating alcohol upon ring-opening and a hydroxyl group functional ω-chain end that propagated the chain. The authors concluded that NHCs proved to be more efficient catalysts than tertiary amines and phosphine nucleophiles.

Scheme 1.13  The role of an NHC as a catalyst for ester polymerisation.55
1.2 Transition Metal Complexes featuring Fluorinated NHC Ligands

The discovery of N-heterocyclic carbenes undoubtedly resulted in great interest across many chemistry fields, especially in coordination and organometallic chemistry. Chemists around the Globe are working extensively to develop new NHCs with improved features, properties, and catalytic applications. One of the approaches for modifying NHC properties is by introducing fluorine into NHCs. Similar to phosphine ligands, introducing fluorine and fluorinated substituents on the NHCs may influence their steric and electronic properties.\textsuperscript{56}

NHCs coordinated to transition metals are excellent for catalysis due to their strong $\sigma$ electron donating properties. The inclusion of fluorine in an NHC is likely to reduce to some extent the electron donor ability. Experimental and computational (using density functional theory-DFT) studies have proven that $\pi$ interaction contributes a significant impact in the bonding between a carbene and transition metal.\textsuperscript{57,58} As the most electronegative element, the presence of a fluorinated group on the $N$-substituents can lower the energy of the LUMO hence improving their $\pi$-accepting ability from $\pi$-back bonding of metals. This results in a stronger NHC-metal bond and reducing the electron density on the metal of the NHC-metal complexes.\textsuperscript{59}

![Frontier molecular orbital of singlet ground state of an NHC.](image)
The \( \pi \)-back bonding interaction in the metal-NHC complexes involves \( \pi \)-donation from the metal centre into the \( \pi \)-accepting LUMO of NHC. Generally, the LUMOs of free NHCs are quite high in energy, relative to other kinds of carbenes. This is why NHCs are strong \( \sigma \)-donors but relatively weak \( \pi \)-acceptors. However, the substituents on nitrogen do influence the electronic properties of NHCs, particularly in the \( \pi \)-accepting LUMO of NHCs. By introducing fluorinated group on the \( N \)-substituents, it could lower the energy of the LUMO of NHCs resulting in better \( \pi \)-accepting ability from the metal \( \pi \)-back bonding orbital.

![Molecular orbital energy level diagrams of metal-NHC \( \pi \) bonding and antibonding for non-fluorinated NHC and fluorinated NHC.](image)

**Figure 1.12** Molecular orbital energy level diagrams of metal-NHC \( \pi \) bonding and antibonding for non-fluorinated NHC and fluorinated NHC.

It is very surprising that the number of transition metal complexes containing fluorinated NHC ligands is limited as compared to those bearing non-fluorinated NHC ligands. To date, various transition metal complexes containing fluorinated NHC ligands have been reported, with the first report in 2000. These complexes
consist of different transition metals and fluorine or fluorinated substituent groups of the imidazole and imidazolidine types of NHC ligands. Their synthetic routes and applications are discussed in the next section, according to the type of metal at which the fluorinated NHC ligand is coordinated.

1.2.1 Palladium complexes

The first fluorinated NHC metal complex was reported by Xu and co-workers in 2000.\(^{59}\) The authors described the synthesis and structure of a palladium(II) complex bearing a fluorinated NHC, Pd-1. The fluorinated NHC, compound 1, was prepared by alkylation of imidazole with fluoroctyl iodide, ICH\(_2\)CH\(_2\)C\(_6\)F\(_{13}\), followed by quaternisation of the resultant fluoroalkylimidazole with a second equivalent of the fluoroctyl iodide as shown in Scheme 1.14. Two equivalents of 1 were then reacted with a palladium source, Pd(OAc)\(_2\), in THF for 2 hours, generating Pd-1 in excellent yield. However, there was no report of the catalytic application of Pd-1 described in the work.

Scheme 1.14 Preparation of fluoroalkylated NHC, 1 and its palladium(II) complex, Pd-1.\(^{60}\)
Subsequently, Fukuyama et al., published a palladium(II) complex bearing a fluorinated NHC, Pd-2 which was employed in the Mizoroki-Heck arylation of α,β-unsaturated carboxylic acids and esters. Pd-2 was synthesised from Pd(OAc)$_2$, fluorinated NHC salt 2 and triphenylphosphine, PPh$_3$, in the presence of lithium chloride.$^{61}$ The catalytic reaction proceeded efficiently in a fluorous ether (C$_{14}$H$_{17}$F$_{13}$O), in an attempt to separate the catalyst from the organic product using a fluorous biphasic system. Their attempt was successful and they were able to separate the fluorinated NHC-palladium(II) catalyst and recycle it for further use. This is one of the potential applications of using fluorine-containing metal catalysts in fluorous biphasic catalysis.

Scheme 1.15  Preparation of a palladium complex containing a fluorous NHC ligand, Pd-2.

Figure 1.13  Separation of fluorous catalyst and solvent in fluorous biphasic system. Re-drawn from Scheme 1 in reference.$^{61}$
The pioneering work on fluorinated NHCs was expanded in 2009, by the preparation of another version of the palladium(II) complex. Skalicky and co-workers reported the synthesis of palladium(II) complex Pd-3, the analogue of the well-known palladium(II)-pyridine enhanced pre-catalyst preparation stabilisation (PEPPSI) complex. Pd-3 was synthesised by reacting 1 with palladium chloride and potassium carbonate in an excess of 3-chloropyridine as shown in Scheme 1.16.

![Scheme 1.16 Synthesis route for PEPPSI derivative complex containing a fluorinated NHC ligand, Pd-3.](image)

Pd-3 was tested in the Suzuki-Miyaura coupling of phenylboronic acid with 4-iodotoluene, and the Heck reaction of 4-iodotoluene with oct-1-ene. The results were compared with the original PEPPSI catalyst and it was found that the catalytic activity of Pd-3 was inferior to that of the original PEPPSI catalyst (50-60% yields after 24 hours reaction time with Pd-3, compared to 95-99% yield with the original PEPPSI catalyst in the same reaction time). However, there were no justifications made by the authors on the weaker performance of Pd-3 in these two catalytic
reactions. Theoretically, the presence of fluorine in the NHC ligands may influence its electronic and steric properties. As the most electronegative atom, fluorine in the alkylated chain of nitrogen substituents, $R_F$ can strongly pull the electron away from the aromatic heterocycle which can eventually reduce the overall donor strength of an NHC. This may affect the electronic properties of NHC and the catalytic activity of the resulting complex. However, in the case of Pd-3, the inclusion of $CH_2CH_2$ spacer means the electronic effect of fluoroalkylated chain, $R_F$ is minimal. Further studies are required to justify the impact of fluorinated NHC ligands in these catalytic reactions.

In 2012, Liu et al., reported highly efficient fluorinated NHC-based catalysts for the Suzuki-Miyaura reaction. The report suggested that fluorinated NHC-palladium catalysts are much more reactive for the Suzuki-Miyaura reaction than those catalysts from non-fluorinated counterparts. The scope of reactions involved the coupling between unactivated aryl chlorides with aryl boronic acids at room temperature. To compare the reactivity of fluorinated NHCs with non-fluorinated ones, the latter were also prepared and tested for their catalytic role.

![Scheme 1.17](image1)

Scheme 1.17  Synthetic route to fluorinated NHC precursors, 4 to 7.

![Scheme 1.18](image2)

Scheme 1.18  The Suzuki-Miyaura reaction of $p$-chloroanisole with phenylboronic acid with four different palladium NHC catalysts.
NHC-palladium catalysts were prepared in situ from 3 mol % of Pd(OAc)$_2$ and 6 mol % of NHC during the coupling reaction of $p$-chloroanisole (0.8 mmol) with phenyl boronic acid (1.2 mmol) in the presence of tripotassium phosphate in a THF/H$_2$O (5:1) solvent mixture at room temperature. The percentage conversions of the products are presented in Table 1.1.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-4</td>
<td>100</td>
</tr>
<tr>
<td>Pd-5</td>
<td>39</td>
</tr>
<tr>
<td>Pd-6</td>
<td>51</td>
</tr>
<tr>
<td>Pd-7</td>
<td>28</td>
</tr>
</tbody>
</table>

Table 1.1 shows that the palladium complex featuring a fluorinated NHC, Pd-4, is a much better catalyst than those bearing non-fluorinated NHC ligands, Pd-5, Pd-6 and Pd-7. The high reactivity of the Pd-4 complex was proposed to be due to the strong electron withdrawing group of the fluorinated N-substituent groups that reduces the electron density of the carbene, which favours the dissociation of one NHC ligand from the Pd(NHC)$_2$ complex. This in turn generates a less electron-rich monocarbene-palladium species for the reductive-elimination process in the catalytic cycle of the reaction to form the final product.

In the same year, another palladium complex bearing a fluorinated NHC was prepared and tested in the Suzuki-Miyaura reaction. This complex, Pd-8, was formed by deprotonation of fluorinated NHC salt 1 in the presence of a base, NaH, followed by reaction with a palladium precursor, [PdCl$_2$(PPh$_3$)$_2$] as demonstrated in Scheme 1.19.
**Scheme 1.19** Preparation method of palladium complex bearing fluorinated NHC, Pd-8.66

Pd-8 has proven to be an efficient catalyst for the Suzuki-Miyaura reaction with short reaction times, high yields and great reusability. However, there were no comparison studies between Pd-8 and the non-fluorinated analogues described in the work. The work can be extended by evaluating the catalytic activity of Pd-8 alongside the non-fluorinated counterparts to understand the effect of having fluorinated groups in the NHC ligands.

### 1.2.2 Ruthenium complexes

One of the great contributions of NHC-metal complexes is their catalytic role in olefin metathesis, particularly based on ruthenium(II) complexes. Olefin metathesis is a reaction that entails the redistribution of fragmented alkenes (olefins) by the scission and regeneration of the carbon-carbon double bond.66 The most common ruthenium complexes employed in these catalytic reactions are based on the Grubbs first, second and third generation catalysts. This is reflected by the increasing number of ruthenium complexes being prepared and studied since the discoveries of these Grubbs catalysts.

Fürstner et al., reported a comparative investigation of ruthenium(II)-based metathesis catalysts bearing NHC ligands in 2001.67 A series of ruthenium(II) NHC complexes have been prepared, including one with a fluorinated NHC ligand. The ruthenium complex containing a fluorinated NHC ligand, Ru-1, was prepared from
the fluorinated NHC precursor, \( \text{8} \), and the first generation Grubbs catalyst, as illustrated in Scheme 1.20.

![Scheme 1.20](image)

**Scheme 1.20** Synthesis route of ruthenium complex containing fluorinated NHC, Ru-1. 66

Substitution of one tricyclohexylphosphine (PC\(_3\)) ligand of the first generation Grubbs catalyst (Grubbs I) with the NHC ligand generates a second generation Grubbs catalyst (Grubbs II) with improved catalytic activity and greater stability. Ru-1 has been tested in the cyclisation of \( N \)-tosylmethallylamine alongside the non-fluorinated Grubbs II catalyst analogues, Ru-2, Ru-3, Ru-4, and Ru-5.

![Scheme 1.21](image)

**Scheme 1.21** Cyclisation of \( N \)-tosylmethallylamine catalysed by Ru-1 to Ru-5. 66

![Figure 1.15](image)

**Figure 1.15** Grubbs II analogues containing non-fluorinated NHCS, Ru-2 to Ru-5. 66
According to the results in Table 1.2, the catalytic activity of the fluorinated NHC analogue, Ru-1 was inferior compared to those of the non-fluorinated counterparts, Ru-2, Ru-3 and Ru-5. Amongst these complexes, Ru-2 that possessed the most similar structure to Grubbs II, was the most efficient catalyst giving nearly 100% yield of product in 24 hours.

In 2006, Grubbs’ group developed the fluorinated version of the Grubbs and Hoveyda-Grubbs second generation (II) catalysts, Ru-6 and Ru-7 respectively. The preparation of the Ru-6 complex involved reacting the fluorinated NHC precursor with silver(I) oxide, and then converting the silver complex into the ruthenium complex via transmetallation in the presence of a ruthenium(II) source, in the form of Grubbs first generation catalyst, as illustrated below.

The fluorinated analogue of the Grubbs II catalyst, Ru-6 was reacted with o-isopropoxy-β-methylstyrene to afford the fluorinated analogue of the Hoveyda-Grubbs second generation catalyst, Ru-7, as seen in Scheme 1.23.
These two fluorinated catalysts, \textbf{Ru-6} and \textbf{Ru-7}, have been tested in the ring-closing olefin metathesis of diethyl diallylmalonate, alongside the original Grubbs II and Hoveyda-Grubbs II catalysts in order to compare their catalytic performances.

According to the results from Table 1.3, the time taken for 100% conversion by \textbf{Ru-6} was only 15 minutes, shorter than any of the other catalysts. This indicates that \textbf{Ru-6} has the highest catalytic performance compared to the two standard second generation catalysts. Surprisingly, \textbf{Ru-7}, which also contains the same fluorinated NHC ligand as \textbf{Ru-6} has the lowest catalytic activity. To understand this, a detailed study of the structure of these two catalysts was undertaken in order to explain this contrary behaviour. X-ray single crystal structures of these two catalysts were determined.
fluorinated catalysts reveal that there is an additional fluorine-ruthenium interaction in \textbf{Ru-7} (as shown in Scheme 1.23), which is not seen in \textbf{Ru-6}. The absence of such interaction in the latter complex may be due to the steric congestion of the ligands around the metal centre.

The catalyst \textbf{Ru-6} contains one sterically demanding tricyclohexylphosphine ligand which causes the steric congestion. This effect will likely prevent the fluorine atom of the substituent groups of NHC ligand from making an interaction with the ruthenium centre. On the other hand, the isopropoxy group in the Hoveyda-Grubbs II catalyst is much smaller, leaving space for the fluorine atom to coordinate to the ruthenium centre. This is the first example of a fluorine-ruthenium interaction affecting the catalytic activity of ruthenium complexes in olefin metathesis.

The following year, the work was extended by the preparation of new ruthenium complexes bearing fluorinated NHCs, namely \textbf{Ru-8} and \textbf{Ru-9}, from an asymmetric NHC precursor, \textbf{10}.\textsuperscript{69} The combination of the asymmetric nature of the NHC and a possible fluorine-ruthenium interaction might have an impact on its stereo-selectivity in olefin metathesis reactions.

\begin{center}
\includegraphics[width=\textwidth]{Scheme1.25.png}
\end{center}

\textbf{Scheme 1.25} Preparation of ruthenium complex bearing an asymmetric fluorinated NHC, \textbf{Ru-8}.\textsuperscript{69}
Both Ru-8 and Ru-9 were tested in the ring-closing olefin metathesis of diethyl diallylmalonate, along with the original Grubbs and Hoveyda-Grubbs second generation catalysts. Table 1.4 below summarises the time taken for 100% conversion of the product for each catalyst.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time taken for 100% conversion (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grubbs II</td>
<td>27</td>
</tr>
<tr>
<td>Hoveyda-Grubbs II</td>
<td>30</td>
</tr>
<tr>
<td>Asymmetric fluorinated Grubbs II, Ru-8</td>
<td>10</td>
</tr>
<tr>
<td>Asymmetric fluorinated Hoveyda-Grubbs II, Ru-9</td>
<td>35</td>
</tr>
</tbody>
</table>

Based on Table 1.4, the results show similar findings to those previously detailed in Table 1.3. The asymmetric fluorinated Grubbs II analogue, Ru-8 behaves similarly like the symmetrical counterpart, Ru-6, as being the most active catalyst in each case. This finding shows that the activity of the fluorinated Grubbs II analogues, Ru-6 and Ru-8 in ring closing metathesis reaction under these conditions surpass that of the commercially available Grubbs II and Hoveyda-Grubbs II catalysts. According to this study and the one discussed previously, Hoveyda-Grubbs II and its analogue showed lower catalytic activity than Grubbs II and its analogue.

Subsequently, the work has been continued by developing a new series of ruthenium complexes bearing asymmetric NHC ligands and studying their catalytic
performance in the olefin metathesis reaction. These complexes, Ru-10, Ru-11, Ru-12, Ru-13, Ru-14 and Ru-15 are the analogues of Grubbs II and Hoveyda-Grubbs II catalysts and prepared in the same way as Ru-8 and Ru-9, as shown in Schemes 1.25 and 1.26 previously.

All of these complexes were tested in the ring-closing olefin metathesis of diethyl diallylmalonate (see Scheme 1.24), alongside the original Grubbs and Hoveyda-Grubbs second generation catalysts in order to study their catalytic performance. The time taken for 100% conversion of diethyl diallylmalonate catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane) was recorded for all the catalysts described above and tabulated in Table 1.5.
Table 1.5: Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate, catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane).\textsuperscript{70}

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Time taken for 100% conversion (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grubbs II</td>
<td>27</td>
</tr>
<tr>
<td>Hoveyda-Grubbs II</td>
<td>30</td>
</tr>
<tr>
<td>Ru-6</td>
<td>15</td>
</tr>
<tr>
<td>Ru-7</td>
<td>50</td>
</tr>
<tr>
<td>Ru-8</td>
<td>10</td>
</tr>
<tr>
<td>Ru-9</td>
<td>35</td>
</tr>
<tr>
<td>Ru-10</td>
<td>7</td>
</tr>
<tr>
<td>Ru-11</td>
<td>60</td>
</tr>
<tr>
<td>Ru-12</td>
<td>40</td>
</tr>
<tr>
<td>Ru-13</td>
<td>80</td>
</tr>
<tr>
<td>Ru-14</td>
<td>120</td>
</tr>
<tr>
<td>Ru-15</td>
<td>150</td>
</tr>
</tbody>
</table>

According to Table 1.5 above, these results show that fluorinated NHC analogues of Grubbs II catalysts Ru-6, Ru-8 and Ru-10 are the most efficient catalysts in this reaction. Surprisingly, the fully substituted penta-fluoro aryl analogue, Ru-12, has the lowest activity amongst these catalysts. Catalyst Ru-10 is the most active catalyst and contains an asymmetric NHC ligand with three fluorines in the ortho and para positions in one of the nitrogen aryl substituent groups. The second most active catalyst is Ru-8, which contains less fluorine in the NHC ligand than Ru-10. Catalyst Ru-6 with a symmetric NHC ligand appears to have a lower efficiency than the unsymmetric ones, Ru-8 and Ru-10.

The results of this study indicate that there is an effect of having fluorine in the NHC ligand towards the catalytic activity of these complexes. Generally, the phosphine-containing Grubbs II catalysts and its analogues show higher catalytic activity than the phosphine-free congener Hoveyda-Grubbs II catalysts. Based on these findings, the presence of fluorine in the NHC ligand has clearly influenced the catalytic performance of these ruthenium complexes in the ring-closing olefin metathesis of diethyl diallylmalonate.
In 2012, Harding et al., prepared a series of new fluorinated NHC precursors, 11 - 13 via one pot condensation of the desired fluorinated aniline with glyoxal and paraformaldehyde as shown in Scheme 1.27.

Isolation of free NHCs of 11, 12 and 13 was not possible, unlike the other common NHC precursors, such as IMes, IPr and IAd. Normally, the free NHCs can be formed by deprotonation of the carbene proton in the presence of an excess of strong base, for example NaH or KO\textsuperscript{t}Bu. However, this method was not successful in preparing the free NHCs of 11, 12 and 13. Subsequently, 11 and 12 were reacted directly with [RuF\textsubscript{2}(CO)\textsubscript{3}]\textsubscript{4}, to afford the ruthenium complexes Ru-16 and Ru-17 respectively. However, the catalytic activities of Ru-16 and Ru-17 were not described in the work.
More recently, Masoud et al., reported a new set of metathesis catalysts with fluorinated asymmetric NHC ligands. This work developed new fluorinated NHC-ruthenium (II) second-generation catalysts, based on the Grubbs and Hoveyda-Grubb second generation catalysts, **Ru-18, Ru-19, Ru-20 and Ru-21**.

![Figure 1.17 Ruthenium complexes bearing asymmetric NHC ligands, Ru-18 to Ru-21.](image)

These four complexes and the commercially available Grubbs II and Grubbs-Hoveyda II (refer to Figure 1.8) were examined in the ring closing metathesis of diethyl diallylmalonate in dichloromethane at 30°C (refer to Scheme 1.26). The time taken for 100% conversion for each complex is tabulated in Table 1.6.

**Table 1.6: Time taken for 100% conversion in ring closing metathesis of diethyl diallylmalonate, catalysed by various ruthenium(II) complexes (1 mol % catalyst loading in dichloromethane).**

<table>
<thead>
<tr>
<th>Complex</th>
<th>Time taken for 100% conversion / minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru-18</td>
<td>30</td>
</tr>
<tr>
<td>Ru-19</td>
<td>120</td>
</tr>
<tr>
<td>Ru-20</td>
<td>30</td>
</tr>
<tr>
<td>Ru-21</td>
<td>180</td>
</tr>
<tr>
<td>Grubbs II</td>
<td>30</td>
</tr>
<tr>
<td>Hoveyda-Grubbs II</td>
<td>30</td>
</tr>
</tbody>
</table>
According to Table 1.6, the times taken for 100% conversion of diethyl diallylmalonate catalysed by Ru-18 and Ru-20 are the same as that for the Grubbs II and Hoveyda-Grubbs II catalysts (30 min). However, the fluorinated NHC analogues of Hoveyda-Grubbs II catalysts, Ru-19 and Ru-21 were less active than the original Hoveyda-Grubbs II catalyst as reflected by their longer reaction times of 120 and 180 min respectively. The report concluded that the presence of fluorine in the NHC ligands influences the electronic properties of the metal complex and the activity of the complex in this reaction. These findings support the results from the previous works by Grubbs’ group which suggested that the phosphine-containing Grubbs II catalysts are more efficient than the phosphine-free Hoveyda-Grubbs II catalysts.

1.2.3 Rhodium and Iridium complexes

Rhodium and iridium NHC complexes have been synthesised and studied extensively, due to their excellent catalytic activities in transfer hydrogenation, hydrosilylation and hydroformylation. This is reflected by the large number of complexes that have been prepared and reported. Surprisingly, the number of reported rhodium and iridium incorporating fluorinated NHC complexes is considerably lower. A summary of the key developments of these complexes are described below, including their preparative methods and catalytic applications.

The first set of rhodium and iridium complexes bearing fluorinated NHC ligands was prepared in 2005. The rhodium and iridium complexes, namely Rh-1 and Ir-1, were synthesised from an asymmetric fluorinated NHC ligand, 14 via transmetallation of silver oxide in the presence of the corresponding metal precursor (see Scheme 1.29).
The asymmetric pentafluorobenzyl-substituted imidazolium bromide salt, 14 was prepared by treatment of N-methylimidazole with pentafluorobenzyl bromide in dichloromethane. NHC precursor 14 was then reacted with silver (I) oxide to afford the NHC-silver complex 15, an NHC transfer reagent. This silver complex was used in transmetallation of rhodium and iridium dimers, \([(\eta^5-C_5Me_5)RhCl(\mu-Cl)]_2\) and \([(\eta^5-C_5Me_5)IrCl(\mu-Cl)]_2\) to form rhodium and iridium complexes, Rh-1 and Ir-1 respectively. Rh-1 was then reacted with tert-butylisonitrile in an excess of sodium tetrafluoroborate to give a cationic rhodium complex, Rh-2. However, there were no descriptions of the catalytic activities of Ir-1, Rh-1 and Rh-2 reported in the work and the applications of these complexes remain unknown.
Subsequently, Burling et al., extended this work by preparing a series of neutral and cationic complexes of rhodium and iridium bearing fluorinated NHC ligands.\textsuperscript{73} The silver complex of NHC 15 was employed in a transmetallation reaction in the presence of [Rh(cod)Cl]$_2$ to afford Rh-3.

\begin{scheme}
\centering
\includegraphics[width=\textwidth]{Scheme1.31.png}
\caption{Preparation of rhodium complex bearing a fluorinated NHC, Rh-3.\textsuperscript{73}}
\end{scheme}

Reaction of carbon monoxide and AgOTf with Rh-3 gave Rh-4 and Rh-5 respectively. In Rh-4, the cyclooctadiene(cod) ligand has been replaced by two carbonyl ligands. This complex is very useful as it can be used to determine the electronic properties of the NHC by measuring the two $\nu$\textsubscript{CO} stretching frequencies of the carbonyls in the IR spectrum. The $\nu$\textsubscript{CO} bands of Rh-4 appear at 2003 and 2084 cm\textsuperscript{-1}, which are higher than the bands found in the non-fluorinated NHC analogues. Higher values of $\nu$\textsubscript{CO} indicate stronger CO bonds and lower electron density at the rhodium centre. This is presumably due to the weaker donating ability of the NHC in Rh-4. In the case of Rh-5, the chloride ligand in Rh-3 was replaced by a triflate, by a reaction with AgOTf, as shown in Scheme 1.32.

\begin{scheme}
\centering
\includegraphics[width=\textwidth]{Scheme1.32.png}
\caption{Synthesis of rhodium complexes containing fluorinated NHC, Rh-4 and Rh-5.\textsuperscript{73}}
\end{scheme}
Preparation of the iridium analogue of **Rh-3**, **Ir-2**, was carried out by reacting the fluorinated NHC precursor **14**, with [Ir(cod)OMe]₂ in dichloromethane. Interestingly, the reaction of silver NHC salt **15**, with [Ir(cod)Cl]₂ produced the cationic bis-carbene iridium complex **Ir-3**, instead of the standard mono-carbene in the form of [M(cod)Cl(NHC)] (where M= Rh or Ir) as seen in **Rh-3** (see Scheme 1.31).

![Scheme 1.33  Synthesis of Ir-2 from a fluorinated NHC precursor-14.](image)

The rhodium and iridium complexes, **Rh-3** and **Ir-2**, were tested in the intramolecular activation of the C₆F₅ ring, however, the reaction was unsuccessful. The explanation of these unfavourable results was due to the inability of the pentafluorobenzyl group to adopt the correct orientation for this intramolecular activation. However, they did not investigate this activation reaction using the less fluorinated NHCs such as di or tri-substituted fluorobenzyl groups to confirm whether favourable results can be achieved with those.
In 2012, a report appeared on the catalytic studies of rhodium complexes containing fluorinated NHCs in the hydrosilylation of propargylic alcohols. Three rhodium complexes bearing fluorinated NHCs, Rh-6, Rh-7, Rh-8 and one rhodium complex with a non-fluorinated NHC analogue, Rh-9, were prepared and tested for these studies.

These complexes were tested in the hydrosilylation of propargylic alcohols in dried THF under an inert atmosphere. The reaction scheme and the results are shown in Scheme 1.35 and Table 1.7.

Scheme 1.35 Reaction scheme of the hydrosilylation of propargylic alcohols, A and B.
Table 1.7: Product ratio and yields obtained with different catalysts.\textsuperscript{74}

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Substrate</th>
<th>Ratio E:Z:gem</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-6</td>
<td>A</td>
<td>2:0:1</td>
<td>85</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2:0:1</td>
<td>100</td>
</tr>
<tr>
<td>Rh-7</td>
<td>A</td>
<td>3:0:1</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2:0:1</td>
<td>75</td>
</tr>
<tr>
<td>Rh-8</td>
<td>A</td>
<td>2:0:1</td>
<td>70</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2:0:1</td>
<td>75</td>
</tr>
<tr>
<td>Rh-9</td>
<td>A</td>
<td>3:0:1</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2:0:1</td>
<td>100</td>
</tr>
</tbody>
</table>

(Reaction condition: 1 mol % catalyst loading in refluxing dried tetrahydrofuran over 48 hours).

As can be seen from Table 1.7, the isomer $E$ is formed preferentially and outweighs the other isomers. Generally, the yields of the reactions are relatively high (70% and above) for all the catalysts, however the catalyst bearing the non-fluorinated NHC, \textbf{Rh-9}, gives the best results for both substrates A (phenylprop-2-yn-1-ol) and B (2-propyn-1-ol). This report concluded that rhodium complexes containing the non-fluorinated NHC, \textbf{Rh-9}, has a higher catalytic activity than those of the fluorinated derivatives, \textbf{Rh-6}, \textbf{Rh-7} and \textbf{Rh-8}. However, the authors did not describe any comparison studies of the steric and electronic properties of these complexes. This piece of information may provide some explanations as to how the presence of fluorine in the substituent groups of the NHC affected their catalytic activities in this reaction.

Subsequently, Harding \textit{et al.}, reported the novel bis-cyclometallated iridium(III) complex featuring a fluorinated NHC, \textbf{Ir-4}.\textsuperscript{56} This complex was prepared from the fluorinated NHC precursor-\textbf{11} and \textit{fac}-[IrF$_3$(CO)$_3$] in the presence of potassium \textit{tert}-butoxide. Attempts to synthesise iridium complexes with a higher degree of fluorine content from the fluorinated NHC precursors \textbf{12} and \textbf{13} were unsuccessful. There were no catalytic studies described for \textbf{Ir-4} in the work.
1.3 Summary

This Chapter gives a general overview of NHCs and some of their coordination chemistry. A summary of the key developments of metal complexes incorporating fluorinated NHC ligand is given, involving palladium, ruthenium, iridium and rhodium complexes. According to some of the examples described in this Chapter, the presence of fluorine in the substituent groups of NHC ligands has influenced the catalytic activity of the corresponding metal complexes. However, there were no detailed comparison studies between the steric and electronic properties of these fluorinated NHCs and the non-fluorinated analogues and how these may affect the complex reactivity in any particular catalytic reaction.

Although there have been a large number of metal complexes bearing NHC ligands synthesised already, few contain fluorinated NHC ligands. Based on this review, ruthenium complexes bearing fluorinated NHC ligands are the most well studied metal complexes, but strictly in olefin metathesis reactions. The chemistry of other metal-fluorinated NHC complexes is underdeveloped and requires to be further explored. In order to fill this gap, we have concentrated on making new metal complexes incorporating fluorinated NHC ligands because such ligands may...
show a unique combination of steric and electronic properties, often along with enhanced thermal and oxidative stability.

Hence, this thesis describes systematic work undertaken to prepare, characterise and ultimately employ the novel gold, rhodium and palladium complexes featuring fluorinated NHC ligands in different catalytic systems. This will provide more information on how the presence of fluorine in NHCs can affect the electronic properties of a metal centre. In addition, the steric parameters of these fluorinated NHCs can also be investigated, to give an insight into how introducing fluorine may influence the steric environment of the corresponding metal complexes and their catalytic activity in organic reactions.

To select an NHC for a specific application, detailed knowledge of its properties is crucial. Hence, it is hoped that the findings from this work will enhance our understanding of the chemistry of fluorinated NHC ligands and contribute to a growing body of the development of NHC ligands containing fluorinated substituents and their corresponding metal complexes.

1.4 Thesis Structure

This thesis consists of six chapters and describes the synthesis, characterisation and catalytic activity of new gold, rhodium and palladium complexes featuring fluorinated NHC ligands.

Chapter 1 outlines a detailed background and literature review of the reported fluorinated NHCs and their transition metal complexes. This will help to portray the existing gap and the significance of this work.
Chapter 2 discusses the preparation and characterisation of a series of fluorinated NHC precursors. This chapter also examines the use of NHC selenium adducts to measure the \( \pi \)-accepting ability of these ligands and investigate the electronic properties of fluorinated NHC ligands.

Chapter 3 describes the synthesis of new gold(I) complexes featuring fluorinated NHCs and investigation of their catalytic activity in the \( \text{A}^3 \) coupling reaction. The steric properties of the fluorinated NHC ligands have been evaluated through the percent buried volume and steric maps.

Chapter 4 presents the preparation and characterisation of new rhodium(I) complexes containing fluorinated NHC ligands. Their catalytic performances have been determined in the transfer hydrogenation reaction of acetophenone to give 1-phenylethanol.

Chapter 5 describes the synthesis and characterisation of palladium(II) complexes bearing fluorinated NHCs. These complexes have been employed in the Suzuki Miyaura reaction and their catalytic efficiencies have been studied.

Chapter 6 draws some overall conclusions from the research work presented in this thesis and makes some recommendations for future works.

1.5 References


12496-12497.


33  M. S. Viciu, R. A. Kelly, E. D. Stevens, F. Naud, M. Studer and S. P. Nolan,


Chapter 2: Synthesis, Characterisation and Electronic Properties of Fluorinated NHC Ligands
2.1 Introduction

An important goal of coordination chemistry is to develop new ligand classes that possess desirable and adjustable characteristics for altering the electronic and steric properties of a metal centre. Since the successful isolation and characterisation of a free NHC, this area has experienced tremendous developments in making new NHCs and their corresponding metal complexes. This in turn has a great impact on the field of catalysis which is growing rapidly due to the production of new metal NHC catalysts employed in various catalytic systems.

NHCs are one of the most attractive ligands due to the excellent fine tuning and flexibility in their synthesis routes. Metal complexes containing NHC ligands have greater stability towards air, moisture and heat, as compared with phosphine analogues. Due to these appealing properties, various types of NHCs have been developed, in order to modify the electronic and steric parameters of the corresponding NHC metal complexes. These parameters can be altered through variation of the backbone and/or nitrogen substituents.

One of the approaches to modify the electronic and steric character of an NHC is by introducing fluorine and fluorinated groups on the nitrogen substituents. The incorporation of fluorinated substituents into NHC-containing metal complexes may lead to different properties and catalytic activities from their non-fluorinated analogues. This chapter describes the synthesis and characterisation of a series of fluorinated NHCs precursors, NHC-1 to NHC-5, which contain different nitrogen substituent aromatic groups. They differ from each other in terms of the number
and position of fluorine atoms in the aromatic ring. Figure 2.1 displays the structure of these NHC precursors and the number and position of fluorines in the nitrogen substituents.

![Structures of NHC precursors](image)

These NHC precursors were subsequently reacted with selenium, to generate the corresponding selenium NHC adducts. This has previously been shown to be very useful in determining the electronic properties of these ligands by analysing the $^{77}$Se NMR spectroscopy of their selenium adducts.

### 2.2 Synthesis and Characterisation

A series of fluorinated NHC precursors, **NHC-1** to **NHC-5** precursors were prepared via the one pot condensation of the appropriate fluoroaniline with glyoxal and para-formaldehyde in the presence of hydrochloric acid. This procedure was adopted from Harding *et al.*, with slight modifications,$^5$ and involved two steps. The
The first step was the reaction between the appropriate fluoroaniline, *para*-formaldehyde, glyoxal and hydrochloric acid in toluene at 100°C for 8 hours to form the NHC chloride salt. The second step was to replace the chloride ion with tetrafluoroborate by addition of tetrafluoroboric acid in water at room temperature, as shown in Scheme 2.1. These NHC precursors were collected as white solids in good yields (79 – 85%) and high purity.

The reason for generating the tetrafluoroborate salts is that although most procedures in the literature generate free NHCs from the imidazolium chloride salts, it has been shown that the deprotonation of the tetrafluoroborate salt is more efficient in term of time and yield. In addition, tetrafluoroborate salts are easier to handle and purify than the chloride salts.

The NHC-1 to NHC-5 precursors were characterised by multinuclear NMR spectroscopy and elemental analysis. The characterisation data of the NHC-1, NHC-2 and NHC-5 precursor salts are in good agreement with the data obtained from the literature, despite them having different counter ion, BF$_4^-$ rather than Cl$^-$ as reported in the literature. The carbene protons of these precursors appear around 10.2 – 10.3 ppm in the $^1$H NMR spectra. Experimental $^1$H and $^{19}$F[$^1$H] NMR spectra and elemental analysis of NHC-2 precursor are shown below as typical examples of the characterising data for these NHC precursors.
The $^1$H NMR data, shown in Figure 2.2 above displays seven proton resonances, where the five signals at higher chemical shifts (7 to 11 ppm) correspond to the resonances from the NHC-2 precursor, whilst the other two signals at 2.50 and 3.37 ppm are due to dimethylsulfoxide and water from the NMR solvents respectively. Reading the spectrum from left to right, the first signal (marked in red) is observed at 10.19 ppm and appeared as a singlet with an integration of one. This signal corresponds to the proton attached to the carbene. The second signal at 8.45 ppm (marked in green) is a singlet with a peak integration of two and belongs to the two protons attached to the carbons of the nitrogen heterocyclic ring backbone. The remaining three signals between 7.50 and 8.02 ppm (marked in blue) are multiplets (due to coupling with the neighbouring $^1$H and $^{19}$F nuclei), and belong to the six protons on the aromatic substituent groups of nitrogen.
The $^{19}\text{F}^{(1)}\text{H}$ NMR spectrum, Figure 2.3 above, shows three chemically different environments for fluorine in the NHC-2 precursor. The resonance at -103.36 ppm (marked in green) is a doublet with coupling constant, $^4J_{FF}$ of 8.8 Hz. The next resonance around -118.51 ppm (marked in blue) is also a doublet with coupling constant, $^4J_{FF}$ of 8.8 Hz. These two resonances belong to the fluorine nuclei in the ortho and para positions of the aromatic substituent groups of nitrogen. The most upfield signal at -148.22 ppm corresponds to the four fluorine nuclei of the tetrafluoroborate anion. This chemical shift value is in agreement with the previous reported NHC tetrafluoroborate salts/precursors.\textsuperscript{6,7} In addition, the elemental analysis data of NHC-2 precursor below shows that this compound is analytically pure.

Table 2.1 Elemental analysis of NHC-2 precursor, 1,3-Bis(2,4-difluorophenyl)imidazolium tetrafluoroborate.

<table>
<thead>
<tr>
<th>Element</th>
<th>Expected</th>
<th>Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>47.38</td>
<td>47.77</td>
</tr>
<tr>
<td>H</td>
<td>2.39</td>
<td>2.17</td>
</tr>
<tr>
<td>N</td>
<td>7.37</td>
<td>7.37</td>
</tr>
<tr>
<td>B</td>
<td>2.89</td>
<td>2.60</td>
</tr>
</tbody>
</table>
For comparative studies, the non-fluorinated NHC precursor analogues, 1,3-bis(2,4,6-trimethylphenyl)imidazolium tetrafluoroborate (IMes precursor) and 1,3-bis(phenyl)imidazolium tetrafluoroborate (IPh precursor) were also prepared. The structures of these NHC precursors are shown in Figure 2.4, whilst Table 2.2 summarises the yield and $^1$H and $^{19}$F NMR data for all the NHC precursors prepared in this work.

![IMes precursor and IPh precursor](image_url)

**Figure 2.4** Non-fluorinated NHC precursors prepared in this work.

**Table 2.2** Summary of the percentage yield and NMR data for tetrafluoroborate NHC precursors prepared in this work.

<table>
<thead>
<tr>
<th>NHC precursor</th>
<th>Yield (%)</th>
<th>$\delta_H$ (ppm)$^a$</th>
<th>$\delta_F$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHC-1</td>
<td>82</td>
<td>10.30</td>
<td>-111.00, -148.00</td>
</tr>
<tr>
<td>NHC-2</td>
<td>85</td>
<td>10.20</td>
<td>-105.36, -118.51, -148.22</td>
</tr>
<tr>
<td>NHC-3</td>
<td>78</td>
<td>10.33</td>
<td>-120.75, -148.27</td>
</tr>
<tr>
<td>NHC-4</td>
<td>75</td>
<td>10.23</td>
<td>-123.10, 129.57, -139.86, -148.00</td>
</tr>
<tr>
<td>NHC-5</td>
<td>79</td>
<td>10.27</td>
<td>-101.87, -117.17, -148.20</td>
</tr>
<tr>
<td>IMes</td>
<td>80</td>
<td>10.01</td>
<td>-148.00</td>
</tr>
<tr>
<td>IPh</td>
<td>78</td>
<td>10.34</td>
<td>-148.12</td>
</tr>
</tbody>
</table>

$^a$H NMR chemical shift of carbene protons (NCHCHN).

In order to investigate the molecular structure of these fluorinated NHC precursors, single crystals suitable for X-ray diffraction studies of NHC-2, NHC-4 and NHC-5 precursors were grown. This was achieved by slow diffusion of hexane into a saturated dichloromethane solution of the compounds. The molecular X-ray structures of these compounds further support the characterisation and identities of the fluorinated NHC precursors. Figures 2.5, 2.6 and 2.7 illustrate the ORTEP representation of the molecular structure of NHC-2, NHC-4 and NHC-5 precursors respectively.
Figure 2.5  ORTEP representation of the molecular structure of NHC-2 precursor. Thermal ellipsoids are drawn at 50% probability.

Figure 2.6  ORTEP representation of the molecular structure of NHC-4 precursor. Thermal ellipsoids are drawn at 50% probability.

Figure 2.7  ORTEP representation of the molecular structure of NHC-5 precursor. Thermal ellipsoids are drawn at 50% probability.
Some of the key atoms in these compounds are labelled for the bond length and bond angle comparison studies. The bond lengths and angles of fluorinated NHC precursors NHC-2, NHC-4 and NHC-5 are comparable to those of other reported non-fluorinated counterparts. According to the figures in Table 2.3 below, the bond lengths and angles of these compounds are quite similar and within close range. However, it would be interesting to investigate the metal-carbene bond once these NHCs are bonded to the metal and compare the length of the metal-carbene bond with those of non-fluorinated congeners. This will be described in the following Chapters.

<table>
<thead>
<tr>
<th>NHC precursor</th>
<th>Bond length (Å)</th>
<th>NHC-2</th>
<th>NHC-4</th>
<th>NHC-5</th>
<th>IMes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C3-N1</td>
<td>1.347(4)</td>
<td>1.328(8)</td>
<td>1.336(4)</td>
<td>1.329(6)</td>
</tr>
<tr>
<td></td>
<td>C3-N2</td>
<td>1.327(4)</td>
<td>1.328(8)</td>
<td>1.330(5)</td>
<td>1.324(6)</td>
</tr>
<tr>
<td></td>
<td>C1-N1</td>
<td>1.430(4)</td>
<td>1.430(7)</td>
<td>1.419(5)</td>
<td>1.444(6)</td>
</tr>
<tr>
<td></td>
<td>C2-N2</td>
<td>1.451(4)</td>
<td>1.430(7)</td>
<td>1.437(5)</td>
<td>1.462(7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bond angle (°)</th>
<th>N1-C3-N2</th>
<th>108.2(1)</th>
<th>108.0(7)</th>
<th>108.5(3)</th>
<th>109.2(4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C3-N1-C4</td>
<td>108.5(1)</td>
<td>109.1(5)</td>
<td>108.0(3)</td>
<td>107.5(4)</td>
</tr>
<tr>
<td></td>
<td>C3-N2-C5</td>
<td>109.3(1)</td>
<td>109.1(5)</td>
<td>109.1(3)</td>
<td>108.4(4)</td>
</tr>
<tr>
<td></td>
<td>C1-N1-C3</td>
<td>125.4(1)</td>
<td>124.6(5)</td>
<td>126.1(3)</td>
<td>125.9(4)</td>
</tr>
<tr>
<td></td>
<td>C2-N2-C3</td>
<td>125.7(1)</td>
<td>124.6(5)</td>
<td>126.1(3)</td>
<td>126.1(4)</td>
</tr>
</tbody>
</table>

*Taken from reference.8

2.3 Evaluation of the Electronic Properties of NHCs

Having synthesised and characterised all the NHC precursors, the next step was to study the effect of introducing fluorine into the NHC ligands. As mentioned previously in the first Chapter, σ and π interactions between the NHC and the metal centre are the key features determining their electronic properties. The NHC metal bond is composed of three possible interactions, i) σ-donation from the NHC to the metal, which is the major contribution to this bond, ii) π-back bonding from the
metal to the NHC and iii) π-donation from the NHC to the metal.\textsuperscript{9} Figures 2.8 to 2.10 below portray these interactions between the NHC and the metal.

Figure 2.8  σ-donation from an NHC to the metal centre. Modified from reference.\textsuperscript{9}

Figure 2.9  π-back bonding donation from a metal to the NHC. Modified from reference.\textsuperscript{9}

Figure 2.10  π-donation from an NHC to the metal centre. Modified from reference.\textsuperscript{9}
The importance of identifying the electronic and steric properties of the ligands was highlighted by pioneering work on phosphine ligands by Tolman.\textsuperscript{10} He developed a technique to study the properties of phosphines, including the Tolman Electronic Parameter (TEP) by measuring the IR-active stretching frequency ($\nu_{\text{CO}}$), of the carbonyl ligands in complexes of the type [Ni(CO)$_3$(phosphine-based ligand)].\textsuperscript{10} This technique can also be applied to NHC ligands by investigating the carbonyl stretching frequencies in [Ni(CO)$_3$(NHC)], which can be prepared from [Ni(CO)$_4$].

A strongly donating NHC increases the electron density at the nickel centre, which in turn improves $\pi$-back donation from the nickel to the carbonyl's antibonding orbital. As a result, the carbonyl (CO) bond is weakened and this leads to the CO stretching frequency being observed at a lower wavenumber in the IR spectrum. Contrarily, the good $\pi$-acceptor ability of NHCs would reduce the electron density at the nickel centre which strengthens the CO bond. The overall net effect of the ligand is then measured, by the frequency at which the CO stretching mode vibrates in the IR spectrum.

To understand the electronic and steric properties of the NHC ligand class using this technique, Nolan and co-workers have investigated the interaction between a series of NHC ligands with [Ni(CO)$_4$].\textsuperscript{11} IR-active carbonyl stretching...
frequencies of these [Ni(CO)\(_3\)(NHC)] complexes show that NHCs are better electron donors than the most basic tertiary phosphines, as shown in Table 2.4.

**Table 2.4**  IR carbonyl stretching frequencies of the carbonyl ligands in nickel(I) complexes for various NHC and phosphine based ligands, measured in CH\(_2\)Cl\(_2\).\(^{11}\)

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Complex</th>
<th>(\nu_{CO}/\text{cm}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMes</td>
<td>[Ni(CO)(_3)(IMes)]</td>
<td>2050.7</td>
</tr>
<tr>
<td>SIMes</td>
<td>[Ni(CO)(_3)(SIMes)]</td>
<td>2051.5</td>
</tr>
<tr>
<td>IPr</td>
<td>[Ni(CO)(_3)(IPr)]</td>
<td>2051.5</td>
</tr>
<tr>
<td>SIPr</td>
<td>[Ni(CO)(_3)(SIPr)]</td>
<td>2052.2</td>
</tr>
<tr>
<td>ICy</td>
<td>[Ni(CO)(_3)(ICy)]</td>
<td>2049.6</td>
</tr>
<tr>
<td>P(^{t})Bu(_3)</td>
<td>[Ni(CO)(_3)(P(^{t})Bu(_3))]</td>
<td>2056.1</td>
</tr>
<tr>
<td>PCy(_3)</td>
<td>[Ni(CO)(_3)(PCy(_3))]</td>
<td>2056.4</td>
</tr>
<tr>
<td>PPh(_3)</td>
<td>[Ni(CO)(_3)(PPh(_3))]</td>
<td>2068.9</td>
</tr>
</tbody>
</table>

A major disadvantage of this technique is the need to handle the extremely toxic [Ni(CO)\(_4\)]. Subsequently, this problem has been overcome by using less toxic iridium or rhodium complexes in the form of [MCl(CO)\(_2\)(NHC)] (M = Rh or Ir). Nolan and co-workers have prepared an extensive range of iridium complexes by bubbling carbon monoxide (CO) through a solution of the respective [IrCl(cod)(NHC)] to form [IrCl(CO)\(_2\)(NHC)].\(^{12}\) The average of the two CO stretching frequencies are measured, rather than a single frequency used in the [Ni(CO)\(_3\)(NHC)] system. Although this technique provides an excellent way to determine the overall donor properties of NHCs, it does not provide an insight into the relative contribution of the \(\sigma\)-donor and \(\pi\)-acceptor parameters of a particular NHC.

![Scheme 2.3](image-url)  Preparation of [IrCl(CO)\(_2\)(NHC)] from [IrCl(cod)(NHC)].\(^{12}\)
Table 2.5  IR carbonyl stretching frequencies of the carbonyl ligands for various NHC and phosphine based ligands, measured in CH₂Cl₂.¹²

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Complex</th>
<th>$\nu_{CO}$ / cm⁻¹</th>
<th>$\nu_{CO}^{av}$ / cm⁻¹</th>
<th>$\nu_{CO}^{a}$ / cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMes</td>
<td>[IrCl(CO)₂(IMes)]</td>
<td>2066.4, 1979.8</td>
<td>2022.6</td>
<td>2050.7</td>
</tr>
<tr>
<td>SIMes</td>
<td>[IrCl(CO)₂(SIMes)]</td>
<td>2068.0, 1981.2</td>
<td>2024.6</td>
<td>2051.5</td>
</tr>
<tr>
<td>IPr</td>
<td>[IrCl(CO)₂(IPr)]</td>
<td>2066.8, 1981.0</td>
<td>2023.9</td>
<td>2051.5</td>
</tr>
<tr>
<td>SIPr</td>
<td>[IrCl(CO)₂(SIPr)]</td>
<td>2068.0, 1981.8</td>
<td>2024.9</td>
<td>2052.2</td>
</tr>
<tr>
<td>ICy</td>
<td>[IrCl(CO)₂(ICy)]</td>
<td>2064.8, 1981.2</td>
<td>2023.0</td>
<td>2049.6</td>
</tr>
<tr>
<td>PCy₃</td>
<td>[IrCl(CO)₂(PCy₃)]</td>
<td>2072, 1984</td>
<td>2028.0</td>
<td>2056.4</td>
</tr>
<tr>
<td>PPh₃</td>
<td>[IrCl(CO)₂(PPh₃)]</td>
<td>2085, 2002</td>
<td>2043.5</td>
<td>2068.9</td>
</tr>
</tbody>
</table>

$^a$ $\nu_{CO}$ values are obtained from the [Ni(CO₂)L] system.¹¹

A number of alternative methods have been developed to assess the π-accepting ability of NHCs from the metal centre. Nolan proposed the analysis of $^1J_{Pt-C}$ coupling constants in [PtCl₂(DMSO)(NHC)] complexes,¹³ while Bertrand utilised the $^{31}P$ NMR chemical shifts of phosphinidene adducts.¹⁴ Subsequently, Ganter proposed a new method for assessing the π acceptor strength of NHCs, by analysing the $^{77}Se$ NMR chemical shift of selenium adducts, which were prepared from the NHC precursors and selenium powder in the presence of a base.¹⁵ Increasing π-acidity of NHCs would lead to a downfield shift of the selenium signal. Apart from these NMR methods, Belpassi reported a theoretical study of the $\nu_{CO}$ of the carbonyl ligand in [Au(CO)(NHC)]⁺ complexes, by DFT calculations.¹⁶

![Figure 2.11](image-url)  Techniques developed to quantify the π-acceptor properties of NHCs. Taken from reference.¹⁷

Amongst these techniques, the phosphinidene and selenium systems are the most well studied systems with considerable amounts of experimental data, compared to
the platinum and gold systems. These are probably due to more convenient ways and the inexpensive nature of preparing the phosphinidene and selenium adducts, rather than making the expensive metal complexes. Nolan et al., demonstrated a linear correlation between the $^{77}\text{Se}$ NMR chemical shifts of selenium adducts and $^{31}\text{P}$ NMR chemical shifts of phosphinidene adducts for several NHC ligands.\textsuperscript{17} The selenium system has more advantages over the phosphinidene system due to the more convenient route for preparing the adducts. Selenium adducts can be prepared in a one-step reaction from the moisture and air-stable NHC precursors whilst phosphinidene adducts require two step procedures from the air-sensitive free NHCs.

More recently, Ganter et al., extended the use of $^{77}\text{Se}$ NMR spectroscopy to assess the $\sigma$-donor strength of various NHC ligands, by measuring the coupling constant of the carbene and selenium, $^{1}J_{\text{CSe}}$.\textsuperscript{18} In NMR spectroscopy, it is understood that the coupling constants between directly bonded atoms are due to the interaction of the electron density in $s$ orbitals between the neighbouring atoms.\textsuperscript{18} Previous studies have shown that the coupling constant between phosphorus and selenium of the selenium-phosphine adducts arise from the basicity of the corresponding phosphine.\textsuperscript{19,20} Strong electron withdrawing substituents of a phosphine ligand would increase the $s$ character of the phosphorus orbital involved in bonding to the selenium atom, leading to a higher coupling constant between the phosphorus and selenium nuclei. Hence, decreasing basicity of NHC ligand would result in an increase in the coupling constant.
Taking advantage of this technique, Ganter and co-workers have attempted to obtain the coupling constants, $^1J_{\text{CSe}}$, from the selenium satellite signals in the $^{13}\text{C}^{(1)}\text{H}$ NMR spectra of various NHC ligands. However, most of the attempts were unsuccessful and only a few $^1J_{\text{CSe}}$ values for NHC ligands were obtained. This technique proved to be difficult and has some drawbacks. Firstly, due to the low natural abundances of $^{13}\text{C}$ and $^{77}\text{Se}$, which are only 1.1 and 7.5% respectively, the chance for both of these nuclei being spin-active in a single molecule is very slim, with just 0.08% probability of this occurring.

In order to investigate the electronic properties of the fluorinated NHC-1 to NHC-5 ligands, the corresponding selenium adducts were prepared according to the literature procedure with a slight modification. Instead of doing the preparation under argon as described previously, these selenium adducts containing fluorinated NHC ligands were readily prepared under ambient conditions. The appropriate NHC-1 to NHC-5 precursors and the non-fluorinated analogues, IMes and IPh precursors were reacted with excess selenium, in the presence of $\text{K}_2\text{CO}_3$. All the new compounds were air and moisture-stable and fully characterised by multinuclear NMR spectroscopies and elemental analysis.

Scheme 2.4  Preparation of selenium-NHC adducts.
For comparative studies, the selenium adducts of the non-fluorinated NHC precursors, IMes and IPh were also synthesised alongside the fluorinated NHC selenium adducts. The $^{77}$Se NMR chemical shifts of the selenium adducts were recorded to determine the π-accepting ability of the NHC ligands. Attempts to obtain the coupling constants $^1J_{CSe}$ from the selenium satellites in the $^{13}$C($^1$H) NMR spectra were unsuccessful. As described previously, this proved to be difficult due to the low abundance of the spin-active $^{13}$C and $^{77}$Se nuclei. Table 2.6 summarises the percentage yield and $^{77}$Se NMR chemical shift data of the selenium adducts prepared in this work.
Table 2.6  Percentage yields and $^{77}\text{Se}$ NMR chemical shift data of selenium-NHC adducts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>NHC precursor</th>
<th>Compound</th>
<th>Yield (%)</th>
<th>$\delta^{77}\text{Se}$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NHC-1</td>
<td>Se(NHC-1)</td>
<td>79</td>
<td>60.7</td>
</tr>
<tr>
<td>2</td>
<td>NHC-2</td>
<td>Se(NHC-2)</td>
<td>81</td>
<td>66.6</td>
</tr>
<tr>
<td>3</td>
<td>NHC-3</td>
<td>Se(NHC-3)</td>
<td>85</td>
<td>68.3</td>
</tr>
<tr>
<td>4</td>
<td>NHC-4</td>
<td>Se(NHC-4)</td>
<td>82</td>
<td>67.4</td>
</tr>
<tr>
<td>5</td>
<td>NHC-5</td>
<td>Se(NHC-5)</td>
<td>83</td>
<td>73.0</td>
</tr>
<tr>
<td>6$^a$</td>
<td>IMes</td>
<td>Se(IMes)</td>
<td>81</td>
<td>26.7</td>
</tr>
<tr>
<td>7</td>
<td>IPh</td>
<td>Se(IPh)</td>
<td>68</td>
<td>24.1</td>
</tr>
</tbody>
</table>

$^a$ The values obtained are consistent with a published literature data.$^{15}$

The $^{77}\text{Se}$ NMR chemical shifts were recorded in deuterated chloroform and covered a narrow range from 24 to 73 ppm. This is expected, given that these selenium adducts are structurally quite similar, with variations of the $N$-substituents of the NHC ligands. The compounds Se(NHC-1) to Se(NHC-5) feature fluorine substituents with different number and position of fluorine atoms whilst Se(IMes) possesses methyl substituents in the ortho and para positions of the phenyl rings. On the other hand, Se(IPh) does not have any substituents in the aromatic ring of the nitrogen substituents.

Higher $^{77}\text{Se}$ NMR chemical shifts values correlate to lower field resonances due to a less shielded selenium nucleus, which indicate stronger $\pi$-accepting ability of the NHC ligands. According to Table 2.5, selenium adducts containing fluorinated NHC ligands, Se(NHC-1) to Se(NHC-5) have higher $^{77}\text{Se}$ NMR chemical shifts values than the non-fluorinated analogues, Se(IMes) and Se(IPh). Based on this finding, the presence of fluorine atoms in the NHC ligands has increased the $\pi$-accepting ability of the NHC ligands. A possible explanation for this finding may be due to the strong electron withdrawing effect of the fluorine substituents in the NHC ligands. This in turn generates more electron deficient carbenes which increases the $\pi$-acceptor strength from the neighbouring selenium. The findings from this work are
consistent with a previous study which demonstrated that the presence of fluorine in the nitrogen substituent groups can lower the energy of the LUMO, hence improving the accepting ability of an NHC from π-back bonding of metal.\textsuperscript{22}

Amongst the fluorinated NHC selenium adducts \textit{Se(NHC-1)} to \textit{Se(NHC-5)}, those with the higher number of fluorine substituents, such as \textit{Se(NHC-4)} and \textit{Se(NHC-5)} possess the strongest π-acceptor strength compared with the lower fluorine-content analogues \textit{Se(NHC-1)} and \textit{Se(NHC-2)}. Surprisingly, \textit{Se(NHC-3)} that contains only two fluorine substituents has a higher π-accepting ability than its greater fluorine content counterpart, \textit{Se(NHC-4)}. Consideration of the structure of these three compounds reveal that the position of fluorine substituents in the aromatic ring of the nitrogen substituents also has an impact to the electronic properties of a particular NHC, apart from the number of fluorine substituents. \textit{Se(NHC-3)} possesses four fluorine substituents in the \textit{ortho} positions of the aromatic rings of the nitrogen substituents. This position is the closest to the nitrogen of the heterocycle ring and thus having fluorine substituents in this position appears to increase the π-accepting ability of the NHC ligands, as indicated by the $^{77}\text{Se}$ NMR chemical shift values.

Figure 2.13 displays the $^{77}\text{Se}$ NMR chemical shift range for selenium adducts containing various imidazole and imidazolidene NHC type ligands. Generally, saturated NHC ligands (imidazolidene) such as SIPr and SIMes are more π-accepting than the unsaturated (imidazole) NHCs ligands, IPr and IMes. This is reflected by the higher values of the $^{77}\text{Se}$ NMR chemical shift, 189.7 ppm for SIPr and 110.1 ppm for SIMes than their counterparts, 90.2 ppm and 26.7 ppm for IPr and IMes.
respectively. Surprisingly, there are no studies involving selenium adducts of the fluorinated NHC ligands reported so far. Therefore, the results obtained from this Chapter offer some important insights into the electronic parameters of the fluorinated NHC ligands and provide more information on how the presence of fluorines may influence the electronic properties of NHC ligands.

Although this concept provides a good measure of π-acceptor strength of the NHC ligands, however it must be taken into account that there is a limitation when it comes to very bulky ligands. The steric bulk of a ligand can always outweighs the electronic characters. For example, binding of a bulky ligand could be difficult due to steric hindrance despite favourable electronic interactions. This phenomenon can be exemplified by comparing the $^{77}$Se NMR chemical shifts of the Se(IAd) and Se(ICy) presented in Figure 2.13. Despite having similar structures, the $^{77}$Se NMR chemical shifts of Se(IAd) and Se(ICy) appear in the opposite extremes with the value of 196.9 and -22.1 ppm respectively. Initially, one might predict that their electronic properties should be similar, however the steric differences between the IAd and ICy ligands may cause variation in their electronic properties. Ultimately, both the electronic and steric properties are two important characteristics (hence the term stereoelectronic) in the interactions between the NHC ligands and the metal/selenium and these properties cannot be treated separately. Therefore, it is necessary to use this technique carefully and understand the scope and limitations of this technique for measuring the π-acceptor strength of the NHC ligands.
Figure 2.1. The $^{77}$Se NMR chemical shifts for various selenium-NHC adducts.

- $\text{Se}^{(i\text{Bu})}$: 183.2
- $\text{Se}^{(S\text{iPr})}$: 189.7
- $\text{Se}^{(i\text{Ad})}$: 196.9

$^{77}$Se δ (ppm) increasing π-acceptor strength

Figure 2.13. The $^{77}$Se NMR chemical shifts for various selenium-NHC adducts.\textsuperscript{15}
2.4 Summary

A series of fluorinated NHC precursors, NHC-1 to NHC-5 and their selenium adducts, Se(NHC-1) to Se(NHC-5) were successfully prepared and characterised. The electronic properties of NHC-1 to NHC-5 were assessed by $^{77}$Se NMR spectroscopy. Evaluation of the $^{77}$Se NMR chemical shifts of the selenium adducts reveal that these fluorinated NHCs have stronger π-accepting abilities than the non-fluorinated counterparts, IMes and IPh. Generally, the π-accepting ability of NHC ligands increases as the fluorine content in the nitrogen substituent groups increases. The compounds NHC-3 and NHC-5 that contain fluorines in the ortho position have the greatest influence on the $^{77}$Se NMR data, relative to the other fluorinated NHC ligands prepared in this work. The number and substitution pattern of fluorine atoms in the substituent groups have significant effects on the electronic properties of NHC ligands. The findings of this study suggest that the presence of fluorine atoms in the NHC ligands has increased the π-accepting ability of NHC ligands. This work contributes to existing knowledge by providing the measurement of the electronic properties of fluorinated NHC ligands and further supports the advantage of the $^{77}$NMR chemical shifts for assessing the electronic parameters of NHC ligands.

2.5 Experimental

2.5.1 General considerations

Unless otherwise stated all reactions were carried out in air. The IMes precursor and Se(IMes) have been reported previously.\textsuperscript{6,17} NHC precursors, NHC-1, NHC-2, NHC-3, NHC-4, NHC-5, IMes and IPh precursors and their selenium adducts were prepared as described below. 4-fluoroaniline, 2,4-difluoroaniline, 2,6-difluoroaniline, 2,4,5-trifluoroaniline and 2,4,6-trifluoroaniline were purchased
from Fluorochem; aniline, 2,4,6-trimethylaniline, para-formaldehyde and glyoxal were purchased from Sigma Aldrich and used without further purification. All other chemicals were obtained commercially from Sigma Aldrich or Alfa Aesar and were of analytical grade or higher and were used without further purification. $^1$H and $^{19}$F{$^1$H} NMR spectra were recorded using a Bruker Avance spectrometer at 400 and 376 MHz respectively, and were referenced to external TMS and CFCl$_3$ respectively. $^{13}$C{$^1$H} and $^{77}$Se{$^1$H} NMR spectra were recorded using a Bruker Avance spectrometer at 100 MHz and 95 MHz respectively, and were referenced to TMS and (CH$_3$)$_2$Se respectively. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The splitting patterns are labelled as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Elemental analyses were performed on a Perkin Elmer PE 2400 elemental analyser by Mr Martin Jennings at the School of Chemistry, The University of Manchester.

2.5.2 X-ray diffraction studies

Crystallographic data for NHC-2, NHC-4 and NHC-5 precursors were collected with an Agilent SuperNova diffractometer using Mo Kα radiation (λ = 0.71073 Å). All the raw data frames were reduced and corrections were applied for Lorentz, polarisation and absorption using the multi-scan methods with CrysAlisPro. The X-ray structural data were solved by direct methods, with full-matrix least-squares refinement of F2 using: Olex2, Shelx and Shelxtl programs. Ortep3 was used to generate the graphical representations and Mercury and Pluton were used to investigate and report the structures. All non-H atoms were modelled with anisotropic displacement parameters, H-atoms were placed in idealised positions and refined with isotropic thermal parameters.
2.5.3 Synthetic procedures

2.5.3.1 1,3-bis(4-fluorophenyl)imidazolium tetrafluoroborate: NHC-1 precursor

To a stirred solution of 4-fluoroaniline (4.30 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF$_4$ (1.2 mL of 40 wt. % in water, 19.3 mmol). The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined organic phases were dried with MgSO$_4$ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (5.45 g, 82%). The experimental data were consistent with the chloride analogue reported in reference 5. $^1$H NMR (DMSO-$d_6$) δ (ppm): 10.30 (s, 1H, NCHN), 8.54 (s, 2H, NCHCHN), 7.97 (m, 4H, H$_{phenyl}$), 7.62 (m, 4H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (DMSO-$d_6$) δ (ppm): 160.12, 155.53, 131.60, 125.10, 122.60, 117.60. $^{19}$F($^1$H) NMR (DMSO-$d_6$) δ (ppm): -111.00 (s, 2F, F$_{para}$), -148.00 (s, 4F, BF$_4$). Anal. Calcd for C$_{15}$H$_{11}$BF$_6$N$_2$ (%): C, 52.44, H, 3.22, N, 8.14, B, 3.20. Found: C, 52.76, H, 3.16, N, 8.15, B, 3.10.
To a stirred solution of 2,4-difluoroaniline (5.00 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF₄ (1.2 mL of 40 wt.% in water, 19.3 mmol). The aqueous phase was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic phases were dried with MgSO₄ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (6.23 g, 85%). The experimental data were consistent with the chloride analogue reported in reference 5. 

$^1$H NMR (DMSO-$d_6$) δ (ppm): 10.20 (s, 1H, NCHN), 8.45 (s, 2H, NCHCH), 8.00 (m, 2H, H_{phenyl}), 7.84 (m, 2H, H_{phenyl}), 7.52 (m, 2H, H_{phenyl}).

$^{13}$C$^1$H NMR (DMSO-$d_6$) δ (ppm): 162.11, 157.07, 154.40, 139.21, 129.19, 124.44, 122.50, 119.82. $^{19}$F$^1$H NMR (DMSO-$d_6$) δ (ppm): -105.36 (d, 2F, $^4$J_{FF} = 8.8 Hz, F_{para}), -118.51 (d, 2F, $^4$J_{FF} = 8.8 Hz, F_{ortho}), -148.22 (s, 4F, BF₄). Anal. Calcd for C₁₅H₉BF₈N₂ (%): C, 47.38, H, 2.39, N, 7.37, B, 2.89. Found: C, 47.77, H, 2.17, N, 7.37, B, 2.60.
To a stirred solution of 2,6-difluoroaniline (5.00 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF$_4$ (1.2 mL of 40 wt. % in water, 19.3 mmol). The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined organic phases were dried with MgSO$_4$ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (5.71 g, 78%). $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 10.33 (s, 1H, NCHN), 8.54 (s, 2H, NCHCHN), 7.84 (m, 2H, $H_{phenyl}$), 7.60 (t, 4H, $^3J_{HH} = 8.8$ Hz, $H_{phenyl}$). $^{13}$C($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): 164.66, 155.11, 141.61, 133.90, 125.44, 113.53. $^{19}$F($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): -120.75 (s, 4F, $F_{ortho}$), -148.27 (s, 4F, BF$_4$). Anal. Calcd for C$_{15}$H$_9$BF$_8$N$_2$ (%): C, 47.38, H, 2.39, N, 7.37, B, 2.89. Found: C, 47.34, H, 2.47, N, 7.08, B, 3.00.
To a stirred solution of 2,4,5-trifluoroaniline (5.70 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF₄ (1.2 mL of 40 wt. % in water, 19.3 mmol). The aqueous phase was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic phases were dried with MgSO₄ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (6.02 g, 75%). $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 10.23 (s, 1H, NCHN), 8.46 (s, 2H, NCHCHN), 8.25 (m, 2H, H$_{phenyl}$), 8.17 (m, 2H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): 163.10, 153.23, 152.75, 150.46, 139.57, 124.36, 119.54, 108.41. $^{19}$F($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): -123.10 (dd, 2F, $^3$J$_{FF}$ = 14.7 Hz, $^5$J$_{FF}$ = 5.2 Hz, F$_{ortho}$), -129.57 (dd, 2F, $^3$J$_{FF}$ = 23.2 Hz, $^5$J$_{FF}$ = 5.2 Hz, F$_{meta}$), -139.86 (dd, 2F, $^3$J$_{FF}$ = 23.2 Hz, $^4$J$_{FF}$ = 14.7 Hz, F$_{para}$), -148.00 (s, 4F, BF₄). Anal. Calcd for C$_{15}$H$_7$BF$_{10}$N$_2$ (%): C, 43.29, H, 1.69, N, 6.73, B, 2.64. Found: C, 43.93, H, 1.43, N, 6.76, B, 2.50.
To a stirred solution of 2,4,6-trifluoroaniline (5.70 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF$_4$ (1.2 mL of 40 wt. % in water, 19.3 mmol). The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined organic phases were dried with MgSO$_4$ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (6.32 g, 79%). The experimental data were consistent with the chloride analogue reported in reference 5. $^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 10.27 (s, 1H, NCHN), 8.49 (s, 2H, NCHCHN), 7.80 (m, 4H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): 165.71, 158.43, 141.83, 125.52, 110.10, 103.07. $^{19}$F($^1$H) NMR (DMSO-$d_6$) $\delta$ (ppm): -101.87 (t, 2F, $^4$J$_{FF}$ = 7.5 Hz, F$_{para}$), -117.17 (d, 4F, $^4$J$_{FF}$ = 7.5 Hz, F$_{ortho}$), -148.20 (s, 4F, BF$_4$). Anal. Calcd for C$_{15}$H$_7$BF$_{10}$N$_2$ (%): C, 43.29, H, 1.69, N, 6.73, B, 2.64. Found: C, 43.48, H, 1.43, N, 6.69, B, 2.64.
To a stirred solution of 2,4,6-trimethylaniline (5.23 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF$_4$ (1.2 mL of 40 wt. % in water, 19.3 mmol). The aqueous phase was extracted with CH$_2$Cl$_2$ (3 x 50 mL). The combined organic phases were dried with MgSO$_4$ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (6.06 g, 80%). The experimental data were consistent with the chloride analogue reported in reference 6. $^1$H NMR (DMSO-$d_6$) δ (ppm): 10.01 (s, 1H, NCHN), 8.25 (s, 2H, NCHCHN), 7.80 (s, 4H, H$_{phenyl}$), 2.45 (s, 6H, H$_{para-methyl}$), 2.18 (s, 12H, H$_{ortho-methyl}$). $^{13}$C($^1$H) NMR (DMSO-$d_6$) δ (ppm): 142.45, 138.19, 134.15, 130.22, 129.81, 125.52, 21.5, 17.3. $^{19}$F($^1$H) NMR (DMSO-$d_6$) δ (ppm): -148.20 (s, 4F, BF$_4$).

Anal. Calcd for C$_{21}$H$_{25}$BF$_4$N$_2$ (%): C, 64.25, H, 6.42, N, 7.14, B, 2.80. Found: C, 63.98, H, 6.43, N, 7.19, B, 2.64.
To a stirred solution of aniline (3.60 g, 38.7 mmol) in toluene (17 mL) was added paraformaldehyde (0.58 g, 19.3 mmol). The resulting mixture was heated to 100°C and then cooled to 40°C before glyoxal (2.20 mL of 40% aqueous solution, 19.3 mmol) was added. The mixture was stirred for 5 min, and then HCl (6.45 mL, 3 M) was added dropwise. The mixture was heated to 100°C for 12 hours. After cooling to room temperature, the solvents were removed on a vacuum rotary evaporator. The resulting compound was then dissolved in water (20 mL), followed by addition of tetrafluoroboric acid, HBF₄ (1.2 mL of 40 wt % in water, 19.3 mmol). The aqueous phase was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic phases were dried with MgSO₄ for 1 hour and placed under reduced pressure to remove any solvents. The final product was collected as a white solid (64.64 g, 78%).

$^1$H NMR (DMSO-$_d$₆) δ (ppm): 10.34 (s, 1H, NCHN), 8.55 (s, 2H, NCHCHN), 7.90 (d, 4H, $^3$J$_{HH}$ = 7.6 Hz, H$\text{phenyl}$), 7.72 (t, 4H, $^3$J$_{HH}$ = 7.8 Hz, H$\text{phenyl}$), 7.60 (t, 2H, $^3$J$_{HH}$ = 7.4 Hz, H$\text{phenyl}$).

$^{13}$C($^1$H) NMR (DMSO-$_d$₆) δ (ppm): 135.10, 134.55, 130.22, 130.10, 122.52, 121.95. $^{19}$F($^1$H) NMR (DMSO-$_d$₆) δ (ppm): -148.12 (s, 4F, BF$_4$). Anal. Calcd for C$_{16}$H$_{13}$BF$_4$N$_2$: C, 58.42, H, 4.25, N, 9.09, B, 3.57. Found: C, 58.58, H, 4.23, N, 9.19, B, 3.64.
2.5.3.8 1,3-bis(4-fluorophenyl)imidazol-2-selenone: Se(NHC-1)

![Chemical Structure of Se(NHC-1)](image)

In a 250 mL single neck round bottom flask, a mixture of NHC-1 precursor (0.580 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.450 g, 79%). ¹H NMR (CDCl₃) δ (ppm): 7.60 (s, 2H, NCHCHN), 7.20 (m, 4H, ³J_HH = 4.6 Hz, Hphenyl), 7.12 (m, 4H, ³J_HH = 8.9 Hz, Hphenyl). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 163.39, 134.87, 128.70, 123.90, 120.99, 116.30. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -111.60 (s, 2F, F). ⁷⁷Se{¹H} NMR (CDCl₃) δ (ppm): 60.7. Anal. Calcd for C₁₅H₁₀F₂N₂Se (%): C, 53.72, H, 3.01, N, 8.36. Found: C, 53.48, H, 3.43, N, 8.69.
2.5.3.9  1,3-bis(2,4-difluorophenyl)imidazol-2-selenone: \textbf{Se(NHC-2)}

\begin{center}
\includegraphics[width=0.4\textwidth]{structure}
\end{center}

In a 250 mL single neck round bottom flask, a mixture of \textbf{NHC-2} precursor (0.646 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) and filtered, to afford an off-white solid (0.511 g, 81%). $^1\text{H}$ NMR (CDCl$_3$) $\delta$ (ppm): 8.19 (s, 2H, NCHCHN), 7.71 (m, 2H, $H_{\text{phenyl}}$), 7.28 (s, 2H, $H_{\text{phenyl}}$), 7.20 (m, 2H, $H_{\text{phenyl}}$). $^{13}\text{C}^\{1\text{H}\}$ NMR (CDCl$_3$) $\delta$ (ppm): 163.39, 155.81, 149.91, 131.14, 129.85, 121.22, 112.19, 105.16. $^{19}\text{F}^\{1\text{H}\}$ NMR (CDCl$_3$) $\delta$ (ppm): -106.05 (d, 2F, $^4J_{\text{FF}} = 8.6$ Hz, $F_{\text{para}}$), -115.29 (d, 2F, $^4J_{\text{FF}} = 8.6$ Hz, $F_{\text{ortho}}$). $^{77}\text{Se}^\{1\text{H}\}$ NMR (CDCl$_3$) $\delta$ (ppm): 66.7. Anal. Calcd for C$_{15}$H$_8$F$_4$N$_2$Se (%): C, 48.51, H, 2.17, N, 7.55. Found: C, 48.48, H, 2.43, N, 7.69.
2.5.3.10 1,3-bis(2,6-difluorophenyl)imidazol-2-selenone: **Se(NHC-3)**

In a 250 mL single neck round bottom flask, a mixture of **NHC-3** precursor (0.646 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.536 g, 85%). $^1$H NMR (CDCl$_3$) δ (ppm) : 8.32 (s, 2H, NCHCHN), 7.55 (s, 2H, H$_{phenyl}$), 7.20 (t, 4H, $^3$J$_{HH}$ = 8.8 Hz, H$_{phenyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) δ (ppm): 163.68, 153.26, 140.19, 131.62, 122.26, 112.30. $^{19}$F($^1$H) NMR (CDCl$_3$) δ (ppm): -118.75 (s, 4F, F). $^{77}$Se($^1$H) NMR (CDCl$_3$) δ (ppm): 68.3. Anal. Calcd for C$_{15}$H$_8$F$_4$N$_2$Se (%): C, 48.51, H, 2.17, N, 7.55. Found: C, 48.71, H, 2.03, N, 7.39.
2.5.3.11  1,3-bis(2,4,5-trifluorophenyl)imidazol-2-selenone: Se(NHC-4)

In a 250 mL single neck round bottom flask, a mixture of NHC-5 precursor (0.707 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 ml) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.567 g, 82%). $^1$H NMR (CDCl$_3$) δ (ppm) : 8.19 (s, 2H, NCHCHN), 7.81 (m, 2H, H$_{phenyl}$), 7.68 (s, 2H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) δ (ppm): 151.68, 149.26, 146.19, 137.62, 122.26, 117.57, 114.59, 106.31. $^{19}$F($^1$H) NMR (CDCl$_3$) δ (ppm): -125.10 (dd, 2F, $^4$J$_{FF}$ = 14.7 Hz, $^5$J$_{FF}$ = 5.2 Hz, F$_{ortho}$), -127.30 (dd, 2F, $^3$J$_{FF}$ = 23.3 Hz, $^5$J$_{FF}$ = 5.2 Hz, F$_{meta}$), -137.66 (dd, 2F, $^3$J$_{FF}$ = 23.2 Hz, $^4$J$_{FF}$ = 14.7 Hz, F$_{para}$). $^{77}$Se($^1$H) NMR (CDCl$_3$) δ (ppm): 67.4. Anal. Calcd for C$_{15}$H$_6$F$_6$N$_2$Se (%): C, 44.23, H, 1.49, N, 6.88. Found: C, 44.25, H, 1.60, N, 6.85.
2.5.3.12 1,3-bis(2,4,6-trifluorophenyl)imidazol-2-selenone: Se(NHC-5)

In a 250 mL single neck round bottom flask, a mixture of NHC-6 precursor (0.707 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.574 g, 83%). $^1$H NMR (CDCl$_3$) δ (ppm) : 8.13 (s, 2H, NCHCHN), 7.28 (s, 2H, H$_{phenyl}$), 6.92 (m, 4H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) δ (ppm): 164.52, 161.90, 157.50, 121.33, 112.64, 101.79. $^{19}$F($^1$H) NMR (CDCl$_3$) δ (ppm): -102.84 (t, 2F, $^4$J$_{FF} = 7.5$ Hz, F$_{para}$), -112.68 (d, 4F, $^4$J$_{FF} = 7.5$ Hz, F$_{ortho}$). $^{77}$Se($^1$H) NMR (CDCl$_3$) δ (ppm) : 73.0. Anal. Calcd for C$_{15}$H$_6$F$_6$N$_2$Se (%): C, 44.23, H, 1.49, N, 6.88. Found: C, 44.71, H, 1.33, N, 6.89.
2.5.3.13 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-selenone: Se(IMes)

In a 250 mL single neck round bottom flask, a mixture of IMes precursor (0.671 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.528 g, 81%). $^1$H NMR (CDCl$_3$) δ (ppm) : 7.28 (s, 4H, H$_{phenyl}$), 6.97 (s, 2H, NCHCHN), 2.35 (s, 6H, H$_{para-methyl}$), 2.13 (s, 12H, H$_{ortho-methyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) δ (ppm): 157.52, 139.90, 135.62, 134.30, 129.11, 120.33, 21.15, 18.50. $^{77}$Se($^1$H) NMR (CDCl$_3$) δ (ppm) : 26.7. Anal. Calcd for C$_{21}$H$_{24}$N$_2$Se (%): C, 65.77, H, 6.31, N, 7.31. Found: C, 65.71, H, 6.33, N, 7.29.
2.5.3.14 1,3-bis(phenyl)imidazol-2-selenone: Se(ImPh)

In a 250 mL single neck round bottom flask, a mixture of IPh precursor (0.524 g, 1.70 mmol), selenium powder (0.135 g, 1.70 mmol) and potassium carbonate (0.290 g, 2.10 mmol) in methanol (50 mL) was heated at reflux for 24 hours after which the mixture was concentrated in a rotary evaporator. The remaining solid was dissolved in dichloromethane (30 mL), then the solution was filtered through celite and the solvent was evaporated. The resulting compound was recrystallized from dichloromethane (5 mL) and pentane (20 mL) mixture and filtered, to afford an off-white solid (0.346 g, 68%). $^1$H NMR (CDCl$_3$) δ (ppm): 8.05 (s, 2H, NCHCHN), 7.80 (d, 4H, $^3$J$_{HH}$ = 7.6 Hz, H$_{phenyl}$), 7.62 (t, 4H, $^3$J$_{HH}$ = 7.8 Hz, H$_{phenyl}$), 7.55 (t, 2H, $^3$J$_{HH}$ = 7.4 Hz, H$_{phenyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) δ (ppm): 154.60, 134.45, 130.22, 130.10, 122.12, 121.92. $^{77}$Se($^1$H) NMR (CDCl$_3$) δ (ppm): 24.1. Anal. Calcd for C$_{15}$H$_{12}$N$_2$Se (%): C, 60.19, H, 4.04, N, 9.36. Found: C, 60.31, H, 4.03, N, 9.29.
2.6 References


29 C. F. Macrea, P. R. Eddington, P. McCabe, E. Pidcock, G. P. Shields, R. Taylor,

Chapter 3: Synthesis, Characterisation and Catalytic Activity of Gold(I) Complexes featuring Fluorinated NHC Ligands
3.1 Introduction

Gold complexes have been studied for a number of potential applications, mainly in medicine, biology, material science and catalysis. They can exist in several oxidation states, $0, 1^-1, 2^+, 3^+, 4^+, 5^+$ but the most commonly encountered and well-studied are gold(I) and gold(III) complexes. In medicinal chemistry, gold complexes are known for their role as anti-arthritis and anticancer agents. Initial work on the anticancer activity of gold(I) complexes was reported by Mirabelli et al., in 1986. A range of gold(I) complexes were prepared and investigated for in vitro cytotoxic potency and in vivo antitumor activity against melanoma and leukaemia cells with phosphine-coordinated gold(I) thiosugar complexes demonstrating the greatest activities in both systems.

![Phosphine based gold(I) complex as an anticancer agent.](image1)

Following this discovery, a significant number of gold(I) complexes have been evaluated in various cancer cell studies, including those containing NHC ligands. For example, Hickey and co-workers designed a family of cationic linear gold(I) complexes of NHCs which can act as mitochondria-targeting antitumor agents.

![Gold(I) complexes containing NHC ligands as new antitumor agents.](image2)
A two-step ligand exchange of the NHCs with (H)E(Cys), where E = sulphur or selenium and Cys = cysteine, generated NHC-free gold complexes (see Scheme 3.1). These complexes were selectively toxic to breast cancer cells and did not affect normal breast cells. The degree of selectivity and potency can be tuned by altering the cationic and lipophilic character of the complexes. This was performed via modification of the substituent group on the NHC precursors. According to this study, the NHC ligand with isopropyl substituent groups (IPr), with intermediate lipophilicity, had better selectivity and cytotoxic potency than NHCs with propyl (n-Pr) and ethyl (Et) substituent groups.

![Scheme 3.1](image)

**Scheme 3.1** A two-step ligand exchange reaction generating NHC-free gold complexes that were selectively harmful to breast cancer cells.\(^\text{11}\)

Similar to other transition metal complexes, gold complexes also play a major role in catalysis, particularly gold(I) and gold(III) complexes. The first NHC-gold(I) and gold(III) complexes were isolated by Minghetti and Bonati in 1973.\(^\text{12}\) However, the chemistry of these NHC-gold complexes remained relatively unexplored until the last 10 years, upon discovery of straightforward synthesis routes to form NHC-gold complexes. Since then, various NHC-gold complexes have been prepared
and employed in homogenous and heterogenous catalysis. Generally, the most common gold catalysed reactions are nucleophilic additions to C-C multiple bonds, such as alkynes, alkenes and allenes. A brief summary of recent examples is described below.

In 2006, López and co-workers reported the efficient use of [AuCl(IMes)] and AgSbF$_6$ in the intermolecular bis-cyclopropanation of 1,6-enynes with alkenes. In this specific catalytic reaction, the NHC-gold(I) complex surpassed the phosphine analogues in terms of yield and selectivity.

![Scheme 3.2](image)

A year later, Chung et al., developed an intramolecular cycloisomerisation reaction catalysed by a NHC-gold(I) complex, [AuCl(IPr)]. This complex was employed in the intramolecular cyclopropanation of 1,6-enynes reaction forming tetracyclooctanes, as depicted in Scheme 3.3.
Gold complexes also display excellent catalytic activity in alkene activation reactions. This has been proven by Widenhoefer and Bender who utilised [AuCl(IPr)] in the hydroamination of unactivated alkenes, N-alkenyl ureas (refer to Scheme 3.4). The authors discovered that [AuCl(IPr)] demonstrated enhanced catalytic performance when compared to sterically hindered, electron-rich \( \sigma \)-biphenylphosphine gold complexes.

The mechanism proceeds via \( \pi \)-activation of the C=C bond which is susceptible to an intramolecular attack by the nucleophilic amines. This catalyst system is highly active for the exo-hydroamination of \( N \)-4-pentenyl and \( N \)-5-hexenyl ureas to produce the corresponding nitrogen heterocycles in excellent yields with good regioselectivity.
Subsequently, Nolan et al investigated the use of NHC-gold(I) complexes in the allylic rearrangement of allylic acetates. A series of gold(I) complexes featuring various NHC ligands were employed to study the effect of different ligands in this catalytic reaction. The reaction proceeded via the same mechanism as the previous example. The scope of the work is presented in Table 3.1.

Table 3.1 Evaluation of various NHC-gold complexes in the allylic rearrangement of allylic acetates.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[AuCl(NHC)]</th>
<th>NHC</th>
<th>%V_{bur}</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[AuCl(IPr)]</td>
<td>IPr</td>
<td>46.3</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>[AuCl(SIPr)]</td>
<td>SIPr</td>
<td>47.0</td>
<td>98</td>
</tr>
<tr>
<td>3</td>
<td>[AuCl(IMes)]</td>
<td>IMes</td>
<td>36.5</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>4</td>
<td>[AuCl(IAd)]</td>
<td>IAd</td>
<td>40.0</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>[AuCl(I^tBu)]</td>
<td>I^tBu</td>
<td>39.3</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>[AuCl(ICy)]</td>
<td>ICy</td>
<td>28.0</td>
<td>&lt; 5</td>
</tr>
</tbody>
</table>

As can be seen from the table above, sterically demanding NHC ligands bound to the gold centre, such as IPr, SIPr, IAd and I^tBu (high percent buried volume, %V_{bur} > 39) have significantly higher catalytic activities than those of the smaller ligands, IMes and ICy (%V_{bur} values of 36.5 and 28.0 respectively). The authors proposed that the steric hindrance was a key parameter to obtain full conversions to the isomerised product. This is because the sterically bulky ligands are prone to shield the cationic gold centre more efficiently than the smaller ligands.

Although extensive research has been carried out to evaluate a range of NHC ligands in various gold-catalysed organic reactions, little is known about fluorinated
NHC ligands. What is not yet clear is the impact of fluorinated NHC ligands on the catalytic activity of the corresponding gold complexes. Therefore, it is necessary to explore and understanding the chemistry of gold complexes bearing fluorinated NHC ligands. The main purpose of this research is to develop a series of gold complexes containing fluorinated NHC ligands and to assess their catalytic activity in the A³ coupling reaction. This research also examines the activity of gold complexes bearing non-fluorinated analogues, IMes and IPh for comparison.

3.2 Synthesis and Characterisation

For the purpose of designing a new series of metal complexes bearing fluorinated NHC ligands, it is important to take into account the practical aspects of the resulting metal complexes, such as their stability, reactivity and storage. In addition, the synthetic routes of preparing these metal complexes also play an important role, in terms of the relative ease, scalability, economic and environmental factors. These are the key parameters that have to be considered upon making the metal complexes. A close look at the literature reveals that the most common routes for preparing [AuCl(NHC)] type complexes involve the pre-generated free carbene or transmetallation via silver or copper carbene transfer agent in the presence of a suitable gold-based precursor, such as [AuCl(DMS)]. Although both preparation methods are efficient, there are some inconveniences associated. Moreover, these methods are indirect and require a two-step procedure as depicted in Scheme 3.5.
**Scheme 3.5** Synthetic routes for [AuCl(NHC)] complexes: i) free carbene and ii) transmetallation via silver or copper transfer agent.\(^{19,20,21}\)

In the case of the free carbene route, it must be performed under inert conditions such as the use of a glovebox and dried solvents. Deprotonation of the carbene proton requires the presence of an excess of strong base (NaH or KO\(^t\)Bu) which is relatively expensive.\(^{22}\) This can be avoided by utilising the transmetallation route which can be done in air and does not require the use of any base. However, the drawback of this route is the loss of one equivalent of metal (silver or copper) as waste during the transmetallation reactions. More recently, Collado and co-workers reported a versatile one-step synthesis under mild conditions, by direct treatment of NHC precursors with a weaker base, K\(_2\)CO\(_3\) in the presence of [AuCl(DMS)].\(^{23}\)

Inspired by this efficient protocol, the fluorinated NHC precursors \textbf{NHC-1} to \textbf{NHC-5} that were reported in Chapter 2 were reacted with [AuCl(DMS)] in the presence of K\(_2\)CO\(_3\). The resulting gold complexes containing fluorinated NHC ligands, [AuCl\(\text{NHC-1}\)] \textbf{Au-1}, [AuCl\(\text{NHC-2}\)] \textbf{Au-2}, [AuCl\(\text{NHC-3}\)] \textbf{Au-3}, [AuCl\(\text{NHC-4}\)] \textbf{Au-4}, and [AuCl\(\text{NHC-5}\)] \textbf{Au-5} were successfully synthesised in good yields (80 – 83%).
The identities of the complexes Au-1 to Au-5 were confirmed by multinuclear NMR spectroscopies and elemental analysis. The $^1$H NMR spectra of complexes Au-1 to Au-5 were characterised by a single resonance at low field for the two imidazole protons (8.07 – 8.22 ppm), as well as other signals corresponding to the phenyl substituent groups' protons. There were no signals observed above 10 ppm in these $^1$H NMR spectra indicating that all the NHC precursors have been transformed into...
the corresponding gold NHC complexes. Figure 3.4 below shows as an example of the $^1$H NMR spectra comparison between the NHC-1 precursor and the corresponding gold complex, Au-1.

Analysis of the $^1$H NMR spectrum of Au-1 reveals that there are three resonances at 8.07, 7.87 and 7.49 ppm. Integration of the singlet signal resonance at 8.07 ppm (marked in green) comes as two, which correspond to the two imidazole protons. The other resonances at 7.87 and 7.49 ppm each integrate to four protons, corresponding to the two chemically different proton environments of the phenyl substituent groups of the NHC (ortho and meta protons). The complete conversion from NHC-1 precursor to Au-1 can be further confirmed by analysing the $^{19}$F($^1$H) NMR spectra of the reactant and product. According to these spectra, the signal corresponding to the fluorine nuclei of the tetrafluoroborate anion, BF$_4^-$, of the

[Figure 3.4 $^1$H NMR spectra (in the range of 7 to 11ppm) of NHC-1 precursor (top) and the corresponding Au-1 complex (bottom), recorded in deuterated DMSO. The carbene proton signal at 10.30 ppm (red mark) is not observed in the gold spectrum.]
NHC-1 precursor, which typically appeared around -148 ppm was not observed. Figure 3.5 displays the $^{19}\text{F}^{(1)}\text{H}$ NMR spectra comparison between NHC-1 precursor and the corresponding gold complex bearing NHC-1, Au-1.

![Figure 3.5 $^{19}\text{F}^{(1)}\text{H}$ NMR spectra comparison between the starting material, NHC-1 precursor (top) and the corresponding Au-1 complex (bottom), recorded in deuterated DMSO.](image)

As can be seen from the $^{19}\text{F}^{(1)}\text{H}$ NMR spectrum of Au-1, there is an only one peak at -112.26 ppm, which corresponds to the single fluorine environment in this complex. Unfortunately, due to the poor solubility of the Au-1 to Au-5 complexes in deuterated solvents, the $^{13}\text{C}$ NMR spectra of these complexes were of poor quality making characterisation of these complexes by $^{13}\text{C}$ NMR spectroscopy impossible.

The gold complexes featuring the non-fluorinated NHC analogues, [AuCl(IMes)] and [AuCl(IPh)] were also prepared in a similar way for a comparative study. Table 3.2 below summarises the yield and multinuclear NMR data for the
[AuCl(NHC)] complexes prepared in this work. As can be seen from the table, the imidazole protons of the fluorinated analogues (Au-1 to Au-5) have higher chemical shifts than those of the non-fluorinated analogues, [AuCl(IMes)] and [AuCl(IPh)]. This is expected due to inductive effects as the presence of fluorines increases the electronegativity in the imidazole heterocycle, which causes the imidazole protons to be more deshielded and so appear at a higher chemical shift.

Table 3.2 Summary of the percentage yield and NMR data for [AuCl(NHC)] complexes prepared in this work.

<table>
<thead>
<tr>
<th>NHC</th>
<th>Complex</th>
<th>Yield (%)</th>
<th>( \delta_\text{H} ) (ppm)(^a)</th>
<th>( \delta_\text{F} ) (ppm)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHC-1</td>
<td>Au-1</td>
<td>81</td>
<td>8.07</td>
<td>-122.26</td>
</tr>
<tr>
<td>NHC-2</td>
<td>Au-2</td>
<td>80</td>
<td>8.17</td>
<td>-106.51, -117.66</td>
</tr>
<tr>
<td>NHC-3</td>
<td>Au-3</td>
<td>83</td>
<td>8.22</td>
<td>-119.67</td>
</tr>
<tr>
<td>NHC-4</td>
<td>Au-4</td>
<td>80</td>
<td>8.11</td>
<td>-122.17, -130.40, -140.26</td>
</tr>
<tr>
<td>NHC-5</td>
<td>Au-5</td>
<td>82</td>
<td>8.18</td>
<td>-102.69, -116.27</td>
</tr>
<tr>
<td>IMes</td>
<td>[AuCl(IMes)]</td>
<td>79</td>
<td>7.62</td>
<td>-</td>
</tr>
<tr>
<td>IPh</td>
<td>[AuCl(IPh)]</td>
<td>78</td>
<td>7.55</td>
<td>-</td>
</tr>
</tbody>
</table>

\( ^a \)\( \text{H NMR chemical shift of imidazole protons (NCHCHN).} \)
\( ^b \)\( \text{F}{^1}\text{H} \) NMR chemical shifts of fluorines in the substituent groups.

To investigate any structural differences between these new gold complexes containing various fluorinated NHC ligands, single crystals suitable for X-ray diffraction studies were grown by slow diffusion of hexane into saturated dichloromethane solutions of the complexes. Of the five complexes, Au-1 to Au-5, only three complexes namely Au-1, Au-2 and Au-4 produced good quality crystals. ORTEP representations of the structures are shown in Figure 3.6 (Au-1), Figure 3.7 (Au-2) and Figure 3.8 (Au-4).

![Figure 3.6 ORTEP representation of the molecular structure of Au-1. Thermal ellipsoids are drawn at 50% probability.](image-url)
Figure 3.7  ORTEP representation of the molecular structure of complex Au-2. Thermal ellipsoids are drawn at 50% probability. This complex is known and the X-ray crystal structure has been reported by Brisdon and Flower. 18

Figure 3.8  ORTEP representation of the molecular structure of complex Au-4. Thermal ellipsoids are drawn at 50% probability.

The complex Au-2 is known and has been reported by Brisdon and Flower in 2017. 18 The NMR spectroscopy and elemental analysis data of Au-2 are consistent with those in the literature. 18 However, there are slight differences in the X-ray structures between Au-2 and the published data. Table 3.3 below tabulates the X-ray structure data of Au-2 and the literature for comparison.

Table 3.3  X-ray data comparison of Au-2 and the complex in the literature. 18

<table>
<thead>
<tr>
<th>Properties/ Complex</th>
<th>Au-2</th>
<th>Literature 18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
<td>Monoclinic</td>
</tr>
<tr>
<td>Space group</td>
<td>P21/n</td>
<td>P 21/n</td>
</tr>
<tr>
<td>Temperature (K)</td>
<td>150</td>
<td>102</td>
</tr>
<tr>
<td>Cell angles (°)</td>
<td>90, 95.939(4), 90</td>
<td>90, 96.553(3), 90</td>
</tr>
<tr>
<td>Cell Volume (Å³)</td>
<td>1520.34 (13)</td>
<td>1505.2</td>
</tr>
<tr>
<td>R factor (%)</td>
<td>3.34</td>
<td>3.42</td>
</tr>
<tr>
<td>Au1-C1 (Å)</td>
<td>1.983(6)</td>
<td>1.971(7)</td>
</tr>
<tr>
<td>Au1-Cl1 (Å)</td>
<td>2.274(1)</td>
<td>2.2726(18)</td>
</tr>
<tr>
<td>N1-C1-N2 (°)</td>
<td>105.2(5)</td>
<td>104.0(6)</td>
</tr>
<tr>
<td>C1-Au1-Cl1 (°)</td>
<td>176.9(2)</td>
<td>176.8(2)</td>
</tr>
</tbody>
</table>
From Table 3.3, the bond lengths and bond angles are relatively similar and in good agreement. However, the unit cell dimensions appear slightly different. Notably, the crystals were analysed at different temperatures (Au-2 at 150 K whilst the literature at 102 K), which might affect the crystal structures. Normally, at higher temperature, the crystal will expand and this may result in larger cell dimensions. This is reflected by the slightly larger cell dimensions of Au-2 than those in the literature. For the purpose of comparative studies and steric measurements, the Au-2 data were used rather than those in the literature for consistency.

Table 3.4 presents a comparison of selected bond lengths and angles of these fluorinated NHC-gold(I) complexes and corresponding data for the published non-fluorinated analogue, [AuCl(IMes)]. The gold centre in the [AuCl(NHC)] complexes is coordinated to two ligands, the NHC and chloride ligands, in a linear geometry with NHC-Au-Cl bond angles around 180°. As can be seen from Table 3.4, the gold-carbene bonds (Au1-C1) of the fluorinated derivatives are significantly shorter than those of the non-fluorinated analogues. Generally, shorter bond lengths correspond to stronger bonds between the metal and carbene. This may suggest that the fluorinated NHCs have stronger bonds with the metal than the non-fluorinated...
analogue. As described in the previous chapter, the inclusion of fluorine in an NHC has been shown to increase the π-accepting ability of the ligand from the metal. Au-4 with the most number of fluorine atoms in the NHC ligand has the shortest Au1-C1 distance, 1.964(6) Å, followed by Au-2 and Au-1 with the values of 1.983(6) and 1.985(4) Å respectively. This systematic decrease of bond lengths is inversely proportional to the degree of fluorination, for example, the higher the number of fluorine atoms in the NHC ligand, the shorter the bond and the stronger the pull between the gold and carbene.

3.3 Steric Quantification

As described previously in the introduction section, the steric properties of NHC ligands play an important role to the structure and reactivity of the resulting complexes. This has been demonstrated by Nolan et al., who reported that gold complexes containing more sterically demanding NHCs displayed higher catalytic activities than less bulky derivatives. Inspired by this finding, it is appropriate to investigate the steric parameters of the fluorinated NHCs prepared in this work. Hence, this section aims to outline the general rules of quantifying the steric properties of an NHC and how we can utilise these techniques to measure the steric bulk of the new fluorinated NHCs and compare them with the non-fluorinated analogues.

To date, there are three methods that have been employed to quantify the steric properties of NHCs, which are Tolman cone angle (θ), percent buried volume (% \( V_{bur} \)) and steric maps as shown in Figure 3.9.
In early studies, Tolman proposed to quantify the size of a phosphine ligand by the cone angle ($\theta$), defined with the metal at the vertex and the atoms at the perimeter of the cone (see Figure 3.10). The distance between the phosphorus and metal is set to 2.28 Å, which is based on the phosphorus-nickel bond length in $[\text{Ni(CO)}_3(L)]$ complexes. This concept is commonly applied for symmetric ligands, for example tertiary phosphines with the same substituent groups (PR$_3$). For less symmetric ligands such as NHCs, using this concept has proven difficult and more complicated due to uneven distribution of the steric bulk.

To overcome this problem, Nolan and Cavallo introduced an alternative concept to determine the steric bulk, the percent buried volume ($V_{\text{bur}}$). A metal-ligand complex is considered as a sphere and the metal sits at the centre of the sphere as illustrated in Figure 3.11. The $V_{\text{bur}}$ can be defined as the percentage of the total volume of a sphere occupied by a ligand. Bulky ligands would occupy more...
space, hence the resulting $\% V_{\text{bur}}$ of these ligands would be higher than those of smaller ligands.

![Diagram of percent buried volume](image)

Figure 3.11 Illustration of percent buried volume. Taken from reference.\textsuperscript{27}

The $\% V_{\text{bur}}$ can be calculated using the SambVca (Salerno at the MoLNaC Buried Volume Calculation) web application tool,\textsuperscript{28} which was developed by Cavallo and co-workers.\textsuperscript{29} This tool only requires a CIF or XYZ file from X-ray crystal structures of any given NHC ligands or metal-NHC complexes to calculate the $\% V_{\text{bur}}$. In the case of metal-NHC complexes, the linear two-coordinate complexes such as $[\text{AuCl}(\text{NHC})]$ are ideal to measure the $\% V_{\text{bur}}$. This is because the ligand can adopt its preferred conformation without steric clashes between atoms of the ligand and those of other ligands bound to the metal centre. For higher coordination number complexes, the NHC ligand is more restricted to adopt its preferred conformation due to the steric hindrance from other ligands around the metal. However, it is still possible to compare $\% V_{\text{bur}}$ between high coordination number complexes, on the conditions that the complexes must contain the same metal, coordination number and geometry.

Although this concept can be applied to any ligand, it only gives a single number and does not provide detailed information on the steric environment of the ligand. Subsequently, Cavallo and co-workers proposed the use of steric maps, to represent and display the steric environment of a ligand.\textsuperscript{30} This concept
complements $\% V_{\text{bur}}$ and provides more detailed steric measurement of any particular ligand, especially for unsymmetrical NHC ligands as shown below.

![Steric map visualisation of a gold complex bearing ITrop ligand](image)

**Figure 3.12** Steric map visualisation of a gold complex bearing ITrop ligand. Taken from reference.\textsuperscript{24}

Figure 3.12 shows how the steric map visualises the steric environment of an ITrop ligand. The colour contours determine the steric bulk at the metal, with blue representing less bulky environments and red indicating more bulky environments. The steric map is divided into four quadrants, and each quadrant has its own $\% V_{\text{bur}}$. These features enable us to understand how the steric bulk of the ligand is distributed through space, especially for unsymmetrical ligands, as seen in the example above. As oppose to the $\% V_{\text{bur}}$ concept which only gives a single average number, the steric maps provide more information by giving $\% V_{\text{bur}}$ for each quadrant, hence the more and less bulky sites can be determined. This is very useful in catalysis, in order to understand the catalytic cycle and catalyst-substrate binding. For example, for [AuCl(ITrop)] shown in Figure 3.12, the ligand would allow substrates to approach the metal centre from the less bulky sites (North East and South West quadrants) as the more bulky sites (North West and South East quadrants) are hindered by the ligand. This phenomenon is described as catalytic pockets, the vacant or less bulky sites where the substrate would bind to the gold.
centre. Very recently, Cavallo and co-workers introduced an extended version of SambVca, SambVca 2.0 which provides both $\% V_{\text{bur}}$ and steric maps of a given ligand.\textsuperscript{31} This is a great tool and very easy to use without the need to handle any statistical methods.

Although these concepts provide more straight-forward ways to measure the steric parameters of a ligand, however there are some limitations associated which need to take into accounts. In order to use both concepts, a CIF or XYZ file of the desired NHC or NHC metal complex is required. Since the X-ray crystal structures or DFT calculations only provide one static representation or conformation of those particular ligands/complexes, it does not represent the whole nature or conformation of them. For instance, in the case of X-ray single crystal of NHC-metal complex, the metal-carbene bond length may vary due to some interactions in the crystal lattice but the CIF file only provides one single value which might not represent the actual length of metal-carbene. Moreover, poor quality X-ray data with a high R% factor or large thermal ellipsoids may not give a good estimate of the percent buried volume. In the case of DFT, calculations are usually generated for single gaseous phase molecules, which may lead to improper representation of the steric bulk of that given ligand. In addition, $\% V_{\text{bur}}$ and steric maps are measured from the solid-state crystal structures and do not necessarily reflect the behaviour in solution or at elevated temperature. Therefore, it is necessary to use these techniques carefully and understand the scope and limitations for steric quantification of NHCs.
Various NHCs have been studied and their steric parameters have been evaluated using these techniques. Surprisingly, there are no examples of fluorinated NHCs involved in any steric measurement studies. Due to this lack of information, it is therefore necessary to quantify the steric bulk of the fluorinated NHCs and understand how the presence of fluorine in the substituent groups may affect the steric environment of the metal centre. Having successfully synthesised the gold complexes containing fluorinated NHC ligands, Au-1 to Au-5, their steric bulk can be evaluated using $V_{bur}$ and steric maps measurements. As mentioned earlier, the measurement requires CIF or XYZ files of the desired NHC ligands or NHC-gold complexes. X-ray single crystal data of Au-1, Au-2 and Au-4 were used to obtain their $V_{bur}$ and steric maps. Table 3.5 presents the $V_{bur}$ and steric maps of the gold complexes bearing fluorinated NHC ligands, NHC-1, NHC-2 and NHC-4 and those containing non-fluorinated analogues, IMes, IPr, ICy, IAd and iBu ligands.
Table 3.5 Summary of $V_{\text{bur}}$ and steric maps for a series of gold(I) complexes, measured by the SambVca web application tool.\textsuperscript{28,29,31}

<table>
<thead>
<tr>
<th>Complex</th>
<th>$V_{\text{bur}}$</th>
<th>Steric map</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[\text{AuCl(NHC)}]$</td>
<td>31.9</td>
<td><img src="image1" alt="" /></td>
</tr>
<tr>
<td>$[\text{AuCl(NHC-1)}]$</td>
<td></td>
<td><img src="image2" alt="" /></td>
</tr>
<tr>
<td>$[\text{AuCl(NHC-2)}]$</td>
<td>32.9</td>
<td><img src="image3" alt="" /></td>
</tr>
<tr>
<td>$[\text{AuCl(NHC-4)}]$</td>
<td>33.4</td>
<td><img src="image4" alt="" /></td>
</tr>
<tr>
<td>$[\text{AuCl(IMes)}]$\textsuperscript{a}</td>
<td>36.5</td>
<td><img src="image5" alt="" /></td>
</tr>
<tr>
<td>[AuCl(NHC)]</td>
<td>% $V_{bur}$</td>
<td>Steric map</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
<td>------------</td>
</tr>
<tr>
<td>[AuCl(IPr)]$^a$</td>
<td>46.3</td>
<td>![Steric map for [AuCl(IPr)]$^a$]</td>
</tr>
<tr>
<td>[AuCl(ICy)]$^a$</td>
<td>28.0</td>
<td>![Steric map for [AuCl(ICy)]$^a$]</td>
</tr>
<tr>
<td>[AuCl(IAd)]$^a$</td>
<td>40.0</td>
<td>![Steric map for [AuCl(IAd)]$^a$]</td>
</tr>
<tr>
<td>[AuCl(i′Bu)]$^a$</td>
<td>39.3</td>
<td>![Steric map for [AuCl(i′Bu)]$^a$]</td>
</tr>
</tbody>
</table>

$^a$Published literature data.
According to Table 3.5, the gold(I) complexes featuring fluorinated NHC ligands are less bulky than most of the common non-fluorinated analogues. Amongst these fluorinated derivatives, **Au-4** with the highest number of fluorine atoms is the most sterically demanding (33.4%). This is followed by **Au-2** at 32.9%, which contains four fluorines in the NHC ligand. The complex containing the least number of fluorines, **Au-1** has the lowest % $V_{bur}$ at 31.9%. These results further support that the presence of fluorine in an NHC ligand affects the steric properties of the corresponding gold complexes. Generally, NHC ligands with higher number of fluorine are more bulky than those with lower number of fluorines. A summary of the steric parameters for [AuCl(NHC)] type complexes is displayed in Figure 3.13.
Figure 3.13  Summary of percent buried volumes for [AuCl(NHC)] type complexes.
3.4 Catalytic Activity

Gold complexes containing NHC ligands are known for their catalytic activity in a variety of organic transformations, such as hydroamination, cyclic isomerisation and allylic rearrangement. For a more detailed overview of catalytic uses of gold complexes bearing NHC ligands, the reader’s attention is directed towards the comprehensive reviews by Nolan et al. Another catalytic system that has attracted increased attention is \( A^3 \) coupling reaction. This reaction involves the synthesis of propargylamines from amines, aldehydes and terminal alkynes in a one-pot fashion as shown below.

\[
\begin{align*}
\text{aldehyde} + \text{amine} + \text{terminal alkyne} & \xrightarrow{\text{catalyst}} \text{propargylamine} \\
\end{align*}
\]

Scheme 3.7 General scheme of the \( A^3 \) coupling.

The first \( A^3 \) coupling reaction was reported in 1998 by Dax and co-workers using copper chloride as a catalyst. Since then, a range of transition metal catalysts have been employed, for example complexes of iridium, iron, cobalt, nickel, zinc, silver and gold. Previous studies have shown that \( A^3 \) coupling does not occur in the absence of a metal catalyst.

The general mechanism of the \( A^3 \) coupling reaction was proposed by Van der Eycken and co-workers as outlined in Figure 3.14. The rate determining step in this reaction is believed to be the \textit{in situ} formation of gold-alkyne species via C-H bond activation of the alkyne. The chemistry of gold-alkyne species is still not well-
understood, but it is proposed that the species may form through a $\pi$-interaction between the gold complex and the alkyne, which causes the alkyne’s proton to become more acidic and prone to deprotonation. The gold-alkyne intermediate reacts with an amine ion, resulting in the formation of the corresponding propargylamine and regeneration of the gold catalyst.

![Figure 3.14](Image)

Recently, our group prepared and utilised various gold complexes bearing different ligands, including one fluorinated NHC in the A$^3$ coupling reaction of benzaldehyde, dibenzylamine and phenylacetylene.$^{18}$ The gold catalysts involved in the study were gold complexes bearing various NHC ligands; a fluorinated NHC (Au-2), non-fluorinated NHCs (Au-6 and Au-7), and NHC-free gold complexes (Au-8, Au-9 and Au-10) (see Figure 3.15). The reaction was performed in water at 40°C for 24 hours with 1 mol % of gold catalyst as described in Scheme 3.8.
The A³ coupling reaction benzaldehyde, dibenzylamine and phenylacetylene.\textsuperscript{18}

Table 3.6  Percentage conversion of the product for various gold catalysts.\textsuperscript{18}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Au-2</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>Au-6</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>Au-7</td>
<td>10</td>
</tr>
<tr>
<td>4</td>
<td>Au-8</td>
<td>44</td>
</tr>
<tr>
<td>5</td>
<td>Au-9</td>
<td>97</td>
</tr>
<tr>
<td>6</td>
<td>Au-10</td>
<td>97</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Determined by \textsuperscript{1}H NMR analysis of crude reaction mixture based on benzaldehyde conversion.

According to the percentage conversions listed in Table 3.6, gold complexes with no NHC ligands, Au-9 and Au-10 were found to be more active than those containing NHC ligands (Au-2, Au-6, Au-7 and Au-8). The former complexes were further screened with a variety of substrates and reaction conditions and it turned out that these two complexes were excellent catalysts in a range of A³ coupling reactions.
The work described in the previous example has utilised and investigated the catalytic activity of several gold complexes, including one containing a fluorinated NHC ligand, Au-2. This work can be extended by investigating the catalytic activity of gold complexes bearing a series of fluorinated NHC ligands in the A³ coupling reaction and understanding how the presence of fluorine in an NHC ligand may influence the complex activity. Having prepared a range of gold complexes, Au-1 to Au-5 with systematic modification in term of the number and position of fluorines in the N-aryl substituent groups, their catalytic efficacy was investigated in the A³ coupling reaction of benzaldehyde, dibenzylamine and phenylacetylene, alongside those gold complexes containing the non-fluorinated NHC analogues, [AuCl(IMes)] and [AuCl(IPh)].

The scope of the reaction involved 1 mmol of benzaldehyde, 1.1 mmol of dibenzylamine and 1.5 mmol of phenylacetylene. All three substrates were reacted in methanol at reflux for 24 hours in the presence of 1 mol % catalyst, as illustrated in Scheme 3.9 below. The reaction progress was monitored by ¹H NMR spectroscopic analysis of the crude mixture based on benzaldehyde conversion. The percentage conversions were measured by comparing the aldehyde proton signal of benzaldehyde (s, δ 9.98 ppm) and that of the product (s, δ 5.22 ppm) averaged over three runs. Table 3.7 tabulates the results of this study.

Scheme 3.9 The A³ coupling reaction benzaldehyde, dibenzylamine and phenylacetylene.
Table 3.7  A$_3$ coupling reaction catalysed by various [AuCl(NHC)] catalysts. $^a$

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Au-1</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>Au-2</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>Au-3</td>
<td>82</td>
</tr>
<tr>
<td>4</td>
<td>Au-4</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>Au-5</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>[AuCl(IMes)]</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>[AuCl(IPh)]</td>
<td>60</td>
</tr>
</tbody>
</table>

$^a$ 1 mmol of benzaldehyde, 1.1 mmol of dibenzylamine and 1.5 mmol of phenylacetylene. All three substrates were reacted in methanol at reflux for 24 hours.

$^b$ Determined by $^1$H NMR analysis of crude reaction mixture based on benzaldehyde conversion.

According to the results in Table 3.7, Au-5 and [AuCl(IMes)] are the best catalysts, with 90% percentage conversion. Amongst the gold(I) complexes featuring fluorinated NHC ligands, Au-5 (90% conversion) has the highest catalytic activity, followed by Au-3 (82% conversion). It is interesting to note that both of these complexes possess fluorine in the ortho positions, which are those nearest to the nitrogen atoms in the NHC ligands. To investigate the electronic and steric effects of the NHC ligands in the catalytic activity of these complexes, a plot of percentage conversion against $^{77}$Se NMR chemical shifts and a plot of percentage conversion against the percent buried volume, $\% V_{bur}$ are drawn in Figures 3.16 and 3.17 respectively.

![Figure 3.16](image.png)

Figure 3.16  Plot of percentage conversion of benzaldehyde in the A$_3$ coupling reaction against $^{77}$Se NMR chemical shifts of NHC selenium adduct.
According to Figure 3.16, generally there is no direct correlation between the electronic properties of NHCs, measured by the $^{77}\text{Se}$ NMR chemical shift and the catalytic activity of these gold complexes. However, a closer look at the region of the fluorinated NHC derivatives (between 60 to 80 ppm), it appears that Au-5 with the strongest $\pi$-accepting ability (as indicated by the highest $^{77}\text{Se}$ NMR chemical shift) has the highest catalytic activity of the complexes. This is followed by Au-3, Au-4, Au-2 and Au-1 in the same order of decreasing $\pi$-accepting ability. So, in the case of gold complexes featuring fluorinated NHC ligands, those with stronger $\pi$-accepting ability have higher catalytic activities than those with weaker $\pi$-accepting ability. These findings may suggest that the presence of fluorine has influenced the electronic properties of the gold complexes and their catalytic activities.

To investigate the effect of changing the steric environment around the gold centre towards the catalytic activity of the gold complexes, a plot of percentage conversion in the $A^3$ coupling reaction against percent buried volume of [AuCl(NHC)] type complexes is depicted as shown below.

![Figure 3.17 Plot of percentage conversion of benzaldehyde in the $A^3$ coupling reaction against percent buried volume of [AuCl(NHC)] complexes.](image)
As can be seen from Figure 3.17, gold(I) complexes bearing more bulky NHC ligands have higher catalytic performances than those of less bulky NHCs. In this study, [AuCl(IMes)] is the bulkiest and has the highest catalytic activity (90%). On the other hand, the least sterically demanding, Au-1 has the lowest catalytic activity. Gold complexes bearing more bulky fluorinated NHC ligand, Au-2 and Au-4 both have higher catalytic activities than Au-1, which indicate that the presence of fluorine in the NHC ligand does affect the catalytic activity in this reaction. These findings are consistent with the previous work by Nolan, which reported that the sterically demanding NHC ligands bound to the gold centre, such as IPr, IAd and i^Bu performed better than the smaller ligands in the allylic rearrangement of allylic acetates.17

3.5 Summary

Gold(I) complexes featuring a series of fluorinated NHC ligands have been prepared and characterised successfully by multinuclear NMR spectroscopies, elemental analysis and X-ray diffraction studies. Comparison of X-ray crystal structures of these complexes reveal that the gold-carbene bond lengths are shorter than those found for complexes containing non-fluorinated NHC ligands, [AuCl(IMes)] and [AuCl(IPr)]. This may be due to the stronger \( \pi \)-accepting ability of fluorinated NHC ligands than the non-fluorinated congeners, which increases the strength of the gold-carbene bond, leading to shorter bond length. Computational studies using the SambVca tool reveal that gold complexes featuring fluorinated NHC ligands, Au-1, Au-2 and Au-4 are less bulky than those containing non-fluorinated NHC ligands, such as [AuCl(IMes)] and [AuCl(IPr)]. The catalytic activities
of Au-1 to Au-5 were investigated in the A$_3^3$ coupling reaction of benzaldehyde, dibenzylamine and phenylacetylene, alongside the non-fluorinated congeners, [AuCl(IMes)] and [AuCl(IPh)]. Amongst the gold(I) complexes bearing fluorinated NHC ligands, those with stronger π-accepting ability have higher catalytic activities than those with weaker π-accepting ability. In term of the steric properties, gold complexes containing more bulky NHC ligands are more efficient catalysts than those with less bulky NHC ligands. This work provides additional support that the inclusion of fluorine in the NHC ligands affects the steric and electronic properties of corresponding gold complexes and their catalytic activities in the A$_3^3$ coupling reaction.

3.6 Experimental

3.6.1 General considerations

Unless otherwise stated all reactions were carried out in air. The precursors to NHC-1, NHC-2, NHC-3, NHC-4, NHC-5, IMes and IPh were prepared according to the description in Chapter 2. [AuCl(DMS)] was purchased from Sigma Aldrich. [AuCl(IMes)] is known and prepared according to the published procedures. All other chemicals and solvents were obtained commercially from Sigma Aldrich or Alfa Aesar and were of analytical grade or higher and were used without further purification. $^1$H and $^{19}$F($^1$H) NMR spectra were recorded using a Bruker Avance spectrometer at 400 and 376 MHz respectively, and were referenced to external TMS and CFCl$_3$. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The splitting patterns are labelled as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet.
Elemental analyses of carbon, hydrogen and nitrogen were performed on a Perkin Elmer PE 2400 combustion elemental analyser. The elemental analysis of gold was performed by heating the complex in an acid solution at high temperature until the complex decomposed and analysed using the Thermo Scientific iCAP DUO 6300 ICP-OES instrument by Mr Martin Jennings at the School of Chemistry, The University of Manchester.

### 3.6.2 X-ray diffraction studies

Crystallographic data for Au-1, Au-2 and Au-5 were collected with an Agilent SuperNova diffractometer using Mo Kα radiation (λ = 0.71073 Å). All the raw data frames were reduced and corrections were applied for Lorentz, polarisation and absorption using the multi-scan methods with CrysAlisPro. The X-ray structural data were solved by direct methods, with full-matrix least-squares refinement of F2 using: Olex2, ShelX and ShelXTL programs. Ortep3 was used to generate the graphical representations and Mercury and Pluton were used to investigate and report the structures. All non-H atoms were modelled with anisotropic displacement parameters, H-atoms were placed in idealised positions and refined with isotropic thermal parameters.
3.6.3 Synthetic procedures

3.6.3.1 Chloro[1,3-bis(4-fluorophenyl)imidazol-2-ylidene]gold(I): Au-1

In a 100 mL single neck round bottom flask, a mixture of NHC-1 precursor (124 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K$_2$CO$_3$ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed in vacuo and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed in vacuo. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (118 mg, 81%).

$^1$H NMR (DMSO-d$_6$) δ (ppm): 8.07 (s, 2H, NCHCHN), 7.87 (m, 4H, H$_{\text{phenyl}}$), 7.49 (m, 4H, H$_{\text{phenyl}}$). $^{19}$F($^1$H) NMR (DMSO-d$_6$) δ (ppm): -112.26 (s, 2F, F). Anal. Calcd for C$_{15}$H$_{10}$N$_2$F$_2$ClAu (%): C, 36.85, H, 2.06, N, 5.73, Au, 40.32. Found: C, 36.79, H, 2.12, N, 5.43, Au, 40.45.
3.6.3.2 Chloro[1,3-bis(2,4-difluorophenyl)imidazol-2-ylidene]gold(I): \textbf{Au-2}

![Chemical structure of Au-2](image)

In a 100 mL single neck round bottom flask, a mixture of \textbf{NHC-2} precursor (137 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K$_2$CO$_3$ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed \textit{in vacuo} and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed \textit{in vacuo}. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (126 mg, 80%). The complex \textbf{Au-2} is known and has been reported by Brisdon and Flower in 2017.\textsuperscript{18} The NMR spectroscopy and elemental analysis data of \textbf{Au-2} are consistent with those in the literature.\textsuperscript{18} $^1$H NMR (DMSO-$d_6$) δ (ppm): 8.77 (s, 2H, NCHCHN), 8.05 (tt, 2H, H$_{\text{phenyl}}$), 7.79 (m, 2H, H$_{\text{phenyl}}$), 7.48 (m, 2H, H$_{\text{phenyl}}$). $^{19}$F\textsuperscript{1}H NMR (DMSO-$d_6$) δ (ppm): -106.51 (d, 2F, $^4$J$_{FF}$ = 8.8 Hz, F$_{\text{para}}$), -117.66 (d, 2F, $^4$J$_{FF}$ = 8.8 Hz, F$_{\text{ortho}}$). Anal. Calcd for C$_{15}$H$_8$N$_2$F$_4$ClAu (%): C, 34.32, H, 1.54, N, 5.34, Au, 37.55. Found: C, 34.62, H, 1.52, N, 5.43, Au, 37.45.
In a 100 mL single neck round bottom flask, a mixture of NHC-3 precursor (137 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K₂CO₃ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed *in vacuo* and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed *in vacuo*. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (131 mg, 83%).

¹H NMR (DMSO-ｄ₆) δ (ppm): 8.22 (s, 2H, NCHCHN), 7.80 (m, 2H, H phenyl), 7.52 (t, 4H, H phenyl). ¹⁹F{¹H} NMR (DMSO-ｄ₆) δ (ppm): -119.67 (s, 4F, F). Anal. Calcd for C₁₅H₈N₂F₄ClAu (%): C, 34.32, H, 1.54, N, 5.34, Au, 37.55. Found: C, 34.51, H, 1.51, N, 5.12, Au, 37.50.
In a 100 mL single neck round bottom flask, a mixture of NHC-4 precursor (150 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K$_2$CO$_3$ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed *in vacuo* and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed *in vacuo*. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (135 mg, 80%).

$^1$H NMR (DMSO-$d_6$) $\delta$ (ppm): 8.25 (m, 2H, H$_{\text{phenyl}}$), 8.11 (s, 2H, NCHCHN), 8.05 (m, 2H, H$_{\text{phenyl}}$). $^{19}$F$[^1$H] NMR (DMSO-$d_6$) $\delta$ (ppm): -122.17 (dd, 2F, $^4J_{FF} = 14.7$ Hz, $^5J_{FF} = 5.2$ Hz, F$_{\text{ortho}}$), -130.40 (dd, 2F, $^3J_{FF} = 23.2$ Hz, $^5J_{FF} = 5.2$ Hz, F$_{\text{meta}}$), -140.26 (dd, 2F, $^3J_{FF} = 23.2$ Hz, $^4J_{FF} = 14.7$ Hz, F$_{\text{para}}$). Anal. Calcd for C$_{15}$H$_6$N$_2$F$_6$ClAu (%): C, 32.12, H, 1.08, N, 5.00, Au, 35.14. Found: C, 31.96, H, 1.06, N, 4.89, Au, 35.34.
3.6.3.5 Chloro[1,3-bis(2,4,6-trifluorophenyl)imidazol-2-ylidene]gold(I): Au-5

In a 100 mL single neck round bottom flask, a mixture of NHC-5 precursor (150 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K$_2$CO$_3$ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed *in vacuo* and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed *in vacuo*. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (138 mg, 82%).

$^1$H NMR (DMSO-$d_6$) δ (ppm): 8.18 (s, 2H, NCH$_2$CHN), 7.70 (m, 4H, H$_{phenyl}$).

$^{19}$F($^1$H) NMR (DMSO-$d_6$) δ (ppm): -102.69 (t, 2F, $^4$J$_{FF}$ = 7.5 Hz, F$_{para}$), δ -116.27 (d, 4F, $^4$J$_{FF}$ = 7.5 Hz, F$_{ortho}$).

Anal. Calcd for C$_{15}$H$_6$N$_2$F$_6$ClAu (%): C, 32.12, H, 1.08, N, 5.00, Au, 35.14. Found: C, 32.47, H, 1.11, N, 4.99, Au, 35.44.
3.6.3.6 Chloro[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene]gold(I):AuCl(IMes)

In a 100 mL single neck round bottom flask, a mixture of IMes precursor (141 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K₂CO₃ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed in vacuo and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed in vacuo. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (127 mg, 79%). ¹H NMR (DMSO-d₆) δ (ppm): 7.62 (s, 2H, NCHCHN), 7.12 (s, 4H, Hphenyl), 2.38 (s, 6H, Hpara-methyl), 2.11 (s, 12H, Hortho-methyl). Anal. Calcd for C₂₁H₂₄N₂ClAu (%): C, 46.96, H, 4.51, N, 5.22, Au, 36.71 Found: C, 46.77, H, 4.57, N, 5.19, Au, 36.44.
3.6.3.7 Chloro[1,3-bis(phenyl)imidazol-2-ylidene]gold(I): AuCl(IPh)

In a 100 mL single neck round bottom flask, a mixture of IPh precursor (111 mg, 0.36 mmol), [AuCl(DMS)] (88 mg, 0.30 mmol) and K$_2$CO$_3$ (50 mg, 0.36 mmol) was refluxed at 60°C for 20 hours in acetone (10 mL). After this time, the solvent was removed in vacuo and dichloromethane (20 mL) was added. Subsequently, the mixture was filtered through celite and the solvent was removed in vacuo. A small amount of dichloromethane (3 mL) was added to the reaction mixture, followed by pentane (15 mL) which resulting in precipitation of a white solid. The solid was collected by vacuum filtration and further washed with pentane (106 mg, 78%).

$^1$H NMR (DMSO-$d_6$) δ (ppm): 7.55 (s, 2H, NCHCHN), 7.50 (d, 4H, $^3$$J_{HH}$ = 7.6 Hz, H$_{phenyl}$), 7.42 (t, 4H, $^3$$J_{HH}$ = 7.8 Hz, H$_{phenyl}$), 7.35 (t, 2H, $^3$$J_{HH}$ = 7.4 Hz, H$_{phenyl}$). Anal. Calcd for C$_{15}$H$_{12}$N$_2$ClAu (%): C, 39.78, H, 2.67, N, 6.19, Au, 43.53 Found: C, 39.67, H, 2.65, N, 6.10, Au, 43.44.
3.6.4 A³ coupling catalytic testing procedure

A mixture of benzaldehyde (0.1 mL, 1 mmol), dibenzylamine (0.210 mL, 1.1 mmol), phenylacetylene (0.162 mL, 1.5 mmol), and gold catalyst (1 mol %) in methanol (5 mL) was stirred at reflux for 24 hours. The solvent was removed in vacuo and the conversion determined by ¹H NMR spectroscopy. The experiments were repeated and the conversions were averaged over three runs. The product was purified by column chromatography on silica gel using hexane/EtOAc eluent.

¹H NMR (CDCl₃) δ (ppm): 8.01 (d, J = 8.0 Hz, 2H), 7.88 (dd, J = 8.0, 1.5 Hz, 2H), 7.70 (d, J = 7.5 Hz, 2H), 7.53 - 7.63 (m, 9H), 7.44 - 7.52 (m, 3H), 5.22 (s, 1H), 4.08 (d, J = 13.5 Hz, 2H), 3.82 (d, J=13.5 Hz, 2H). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 138.4, 138.1, 130.9, 127.8, 127.3, 127.2, 127.1, 127.0, 126.4, 125.9, 122.2, 87.6, 83.6, 55.0, 53.6.

3.7 References


23 A. Collado. A. Gómez-Suárez, A. R. Martin, A. M. Z. Slawin and S. P. Nolan, 


27 A. C. Hillier, W. J. Sommer, B. S. Yong, J. L. Petersen, L. Cavallo and 

28 https://www.molnac.unisa.it/OMtools/sambvca2.0/index.html

29 A. Poater, B. Cosenza, A. Correa, S. Giudice, F. Ragone, V. Scarano and 

16, 14348-14353.

31 L. Falivene, R. Credendino, A. Poater, A. Petta, L. Serra, R. Oliva, V. Scarano 

32 M. V. Baker, P. J. Barnard, S. K. Brayshaw, J. L. Hickey, B. W. Skelton and 


2534-2536.


Chapter 4: Synthesis, Characterisation and Catalytic Activity of Rhodium(I) Complexes featuring Fluorinated NHC Ligands
4.1 Introduction

The remarkable properties of NHCs as ancillary ligands coupled with the extensive use of rhodium complexes as organometallic catalysts have made their combination very important.\(^1\) Over the last ten years, numerous rhodium complexes containing NHC ligands have been developed,\(^2,3,4\) due to the ease of preparing the complexes, which normally proceed via the free NHC route\(^5\) or the corresponding NHC precursor in the presence of a base, such as potassium carbonate.\(^6\) Rhodium complexes have been employed in a variety of catalytic reactions, such as in transfer hydrogenation,\(^7,8\) hydrosilylation,\(^9,10,11,12,13\) hydroformylation\(^14,15,16\) and cyclisation of alkynes.\(^17\) A selection of rhodium complexes containing NHC ligands and their catalytic applications are given below. Whilst deliberately not exhaustive, the aim is to illustrate the breadth of applications that exist.

Cruden et al., reported the synthesis and catalytic application of two rhodium(I) carboxylate complexes bearing NHC ligands, \([\text{Rh(IPr)(CO)}_2(\text{OAc})]\) (Rh-10) and \([\text{Rh(IPr)}_2(\text{CO})(\text{OAc})]\) (Rh-11).\(^18\)

![Rh-10 and Rh-11](image)

Figure 4.1 Rhodium complexes employed in the hydroformylation reaction.\(^18\)
These two complexes were found to be efficient catalysts in the hydroformylation of both aryl and aliphatic alkenes, such as styrene, 4-phenyl-1-butene and 1-decene.\(^\text{18}\) Hydroformylation is one of the most investigated homogeneous catalysis reactions,\(^\text{19,20}\) which involves the production of aldehydes from alkenes.

![Scheme 4.1 Hydroformylation reaction catalysed by Rh-10 and Rh-11.](image)

Another major application of rhodium complexes is their catalytic role in the hydrosilylation of unsaturated compounds, such as carbonyls, alkenes and alkynes. This reaction involves the addition of silicon-hydrogen bonds across the unsaturated bonds of the substrate. In 2013, Nolan and co-workers published a comparative study of the catalytic activity and steric characteristics of four rhodium(I) complexes bearing different NHC ligands, \textbf{Rh-12} to \textbf{Rh-15}.\(^\text{19}\)

![Figure 4.2 Rhodium(I) complexes bearing different NHC ligands prepared by Nolan and co-workers. Number 12 in the NHC-aromatic substituent groups of \textbf{Rh-14} represents the 12-membered cyclododecyl ring.](image)
The catalytic activities of Rh-12 to Rh-15 were investigated in the hydrosilylation of 1-hexene. The scope of the reaction is depicted in Table 4.1 below.

Table 4.1  Rhodium(I)-catalysed hydrosilylation of 1-hexene.\(^{19}\)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion(^b)(%)</th>
<th>Yield A(^b)(%)</th>
<th>Yield B(^b)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-12</td>
<td>85</td>
<td>86</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td>Rh-13</td>
<td>94</td>
<td>83</td>
<td>17</td>
</tr>
<tr>
<td>3</td>
<td>Rh-14</td>
<td>93</td>
<td>84</td>
<td>16</td>
</tr>
<tr>
<td>4</td>
<td>Rh-15</td>
<td>93</td>
<td>86</td>
<td>14</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: HSi(Et)\(_3\) (0.3 mmol), 1-hexene (0.6 mmol), toluene (1 mL), catalyst (0.02 mol %) 60°C, 24 h. \(^b\) Product yields calculated from GC-MS (conversion relative to concentration of HSi(Et)\(_3\)) and confirmed by \(^1\)H NMR data.

According to the percentage conversions in Table 4.1, all four catalysts showed high catalytic activities, with conversions above 85% and similar selectivity for the products A and B. Since all catalysts produced similar results, the reaction was repeated under milder conditions (at room temperature) in order to obtain a clear comparison between the four catalysts.

Table 4.2  Rhodium-catalysed hydrosilylation of 1-hexene with high catalyst loading at room temperature.\(^{19}\)

<table>
<thead>
<tr>
<th>Entry(^a)</th>
<th>Catalyst</th>
<th>Conversion(^b)(%)</th>
<th>Yield A(^b)(%)</th>
<th>Yield B(^b)(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-12</td>
<td>42</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>2</td>
<td>Rh-13</td>
<td>82</td>
<td>75</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>Rh-14</td>
<td>89</td>
<td>71</td>
<td>29</td>
</tr>
<tr>
<td>4</td>
<td>Rh-15</td>
<td>&gt;99</td>
<td>93</td>
<td>7</td>
</tr>
</tbody>
</table>

\(^a\) Reaction conditions: HSi(Et)\(_3\) (0.3 mmol), 1-hexene (0.6 mmol), toluene (1 mL), catalyst (1.0 mol %) RT, 24 h. \(^b\) Product yields calculated from GC-MS (conversion relative to concentration of HSi(Et)\(_3\)) and confirmed by \(^1\)H NMR data.

Surprisingly, the reaction at room temperature showed considerable differences in the catalytic activity of these catalysts. Rh-12 experienced the greatest effect as the conversions dropped significantly from 85% to 42% when the reaction proceeded at lower temperature. Rh-13, Rh-14 and Rh-15 with similar conversions previously at
60°C (94, 93 and 93% respectively), behave differently at room temperature as indicated by their conversions (82, 89 and 99% respectively). To understand the variation of the catalytic activities between these catalysts, the steric and electronic properties of the NHC ligands were investigated. The steric parameters of these NHC ligands have been measured using the percent buried volumes (% $V_{\text{bur}}$), whilst the electronic properties of the ligands have been determined from the TEP values of the corresponding carbonyl stretching frequencies of [Ir(CO)$_2$Cl(NHC)] analogues. Table 4.3 below summarises the steric and electronic properties of various NHC ligands and their metal-carbene bond lengths.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>NHC</th>
<th>$V_{\text{bur}}$</th>
<th>TEP (cm$^{-1}$)</th>
<th>Rh-NHC (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-12</td>
<td>IPr</td>
<td>35.3</td>
<td>2051.5$^b$</td>
<td>2.046(6)</td>
</tr>
<tr>
<td>2</td>
<td>Rh-13</td>
<td>ICy</td>
<td>26.9</td>
<td>2049.6$^c$</td>
<td>2.022(3)</td>
</tr>
<tr>
<td>3</td>
<td>Rh-14</td>
<td>IDD</td>
<td>47.9</td>
<td>2049.0$^c$</td>
<td>2.054(8)</td>
</tr>
<tr>
<td>4</td>
<td>Rh-15</td>
<td>$t'$-PrMe</td>
<td>28.0</td>
<td>2049.6$^d$</td>
<td>2.044(3)</td>
</tr>
</tbody>
</table>

$^a$ Calculated using SambVca software (sphere radius = 3.5 Å, distance from centre of sphere = 2.00 Å, mesh spacing = 0.5, hydrogens omitted).$^{20}$ $^b$ Obtained from Nolan et al. 2008.$^{21}$ $^c$ Obtained from Nolan et al. 2010.$^{22}$ $^d$ DFT calculations from [Ni(CO)$_3$(NHC)].$^{23}$

As described previously in Chapter 2, a lower TEP value indicates stronger σ-donation from an NHC to a metal centre. From Table 4.3, the IPr ligand of Rh-12 has the highest TEP value amongst the four catalysts. This means that the IPr ligand has the weakest electron donating ability. Referring back to Table 4.2, the catalytic activity of Rh-12 in the hydrosilylation of 1-hexene at room temperature was lower than the other three catalysts. This observation may suggest that there is a correlation between the electron donor strength of an NHC and the catalytic activity of the corresponding rhodium catalyst.
Table 4.4  Steric parameters of NHC ligands for Rh-12 to Rh-15 and their respective conversions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>NHC</th>
<th>% V_{bur}</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-12</td>
<td>IPr</td>
<td>35.3</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>Rh-13</td>
<td>ICy</td>
<td>26.9</td>
<td>82</td>
</tr>
<tr>
<td>3</td>
<td>Rh-14</td>
<td>IDD</td>
<td>47.9</td>
<td>89</td>
</tr>
<tr>
<td>4</td>
<td>Rh-15</td>
<td>I'-PrMe</td>
<td>28.0</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

Based on the % $V_{bur}$ values in Table 4.4, there is no obvious link between the percentage conversion and the steric bulk of the NHC ligands. Compared with the IPr containing-complex (Rh-12), the other complexes give higher conversions, yet ICy and I'-PrMe are smaller and IDD is bigger. Previously, Nolan and co-workers have shown that the cyclododecyl rings in IDD ligand are flexible in solution, providing a variable steric environment and enabling lower energy-barriers between different conformations.\textsuperscript{22} According to this report, the high flexibility of the cyclododecyl rings is the key to achieve high catalytic activity and the % $V_{bur}$ measured from the solid-state crystal structure does not necessarily reflect the behaviour in solution or at elevated temperature. In summary, the authors concluded that the rhodium catalyst bearing a more-bulky NHC ligand (Rh-12) has a lower catalytic activity than those catalysts containing less-bulky NHC ligands (Rh-13 and Rh-15) due to steric hindrance that results in destabilisation of the catalytically active species during the hydrosilylation reaction. However, the rhodium catalyst bearing the more-bulky yet flexible NHC ligand (Rh-14) does not behave like the other catalysts bearing sterically demanding ligands due to the high flexibility of the cyclododecyl rings of the NHC ligand. These findings demonstrate that the stereo-electronic properties of the NHC ligand may inevitably affect the catalytic activity of the corresponding rhodium catalysts.
Rhodium(I) complexes bearing NHC ligands have also been employed in the hydrogenation of alkenes, as described by Hermann and co-workers. Five rhodium(I) complexes, Rh-16 to Rh-20 were prepared and their catalytic activity were screened in the hydrogenation reaction of 1-octene.

![Figure 4.3 Rhodium(I) complexes bearing NHC ligands employed in the hydrogenation of 1-octene.](image)

**Table 4.5 Rhodium(I)-catalysed hydrogenation of 1-octene.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh-16</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Rh-17</td>
<td>61</td>
</tr>
<tr>
<td>3</td>
<td>Rh-18</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>Rh-19</td>
<td>33</td>
</tr>
<tr>
<td>5</td>
<td>Rh-20</td>
<td>2</td>
</tr>
</tbody>
</table>

* Determined by $^1$H NMR spectroscopy.
Based on the percentage conversions listed in Table 4.5, Rh-18 was the best catalyst with the highest percentage conversion of the product (81%) whilst Rh-16 and Rh-20 were the worst catalysts with only 1 and 2% conversion respectively. Both Rh-16 and Rh-20 contain carbonyl ligands, unlike the other three complexes. The authors proposed that the combination of strong $\sigma$-donor (NHC) and strong $\pi$-acceptor (CO) ligands has deactivated the metal centre, with no oxidative addition of hydrogen occurring during the catalytic reaction. Based on this study, rhodium complexes bearing a carbonyl ligand were shown to be essentially inactive catalysts in the hydrogenation reaction. In this case, the electronic properties of the NHC ligands had drastically influenced the catalytic activity of the corresponding rhodium catalysts.

The two studies by Nolan (Rh-12 to Rh-15) and Hermann (Rh-16 to Rh-20) described above have shown how modifying the NHC ligand may affect the stereo-electronic characteristics of the ligands. This in turn will influence the catalytic activity of the corresponding rhodium complexes. Although there have been many rhodium complexes bearing NHC ligands in the literature, very few of them contain fluorinated NHC ligands. Introducing fluorine into NHC ligands is one of the ways to modify the electronic and steric properties of the NHC ligands. Hence, the work reported in this chapter is aimed at describing a method of preparing rhodium complexes containing fluorinated NHC ligands. Following successful preparation of these complexes, their electronic and steric properties were evaluated. Subsequently, the catalytic activity of these complexes was investigated in the transfer hydrogenation reaction, alongside the non-fluorinated analogues.
4.2 Synthesis and Characterisation

The most common routes for preparing NHC metal complexes are by the reaction of a pre-generated free carbene or from the in situ deprotonation of an NHC precursor in the presence of a suitable metal-base precursor. More recently, Savka and Plenio reported a facile one-step method for preparation of the [Rh(cod)Cl(NHC)]-type complexes, from a rhodium dimer, [Rh(cod)Cl]₂ and an NHC precursor.⁶ By using the same technique, fluorinated NHC precursors NHC-1 to NHC-5 were reacted with [Rh(cod)Cl]₂ in the presence of potassium carbonate, to afford a series of new rhodium(I) complexes bearing fluorinated NHC ligands, [Rh(cod)Cl(NHC-1)] Rh-21, [Rh(cod)Cl(NHC-2)] Rh-22, [Rh(cod)Cl(NHC-3)] Rh-23, [Rh(cod)Cl(NHC-4)] Rh-24, and [Rh(cod)Cl(NHC-5)] Rh-25 as air and moisture stable yellow crystalline solids in 75 – 85% yield.

![Scheme 4.2 Preparation of rhodium(I) complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25.](image)

The identities of the complexes Rh-21 to Rh-25 were confirmed by multinuclear NMR spectroscopies and elemental analysis. These complexes exhibit ¹³C NMR chemical shifts of the carbene carbon between 184 to 195 ppm that are comparable to those of other reported NHC-rhodium(I) complexes.²⁵ The elemental analyses of all the complexes were very close to the expected values suggesting that these complexes have been prepared in high purity.
Figures 4.4, 4.5, and 4.6 display the experimental $^1$H, $^{19}$F{$^1$H} and $^{13}$C{$^1$H} NMR spectra of Rh-22 as a typical example of the characterisation techniques used to characterise and identify these new complexes. The conversion of the NHC-2 precursor to Rh-22 was confirmed by the absence of a carbene proton resonance at ca. 10 ppm and the presence of additional proton peaks of the cod ligand at lower chemical shifts (between 1.58 to 4.80 ppm) in the $^1$H NMR spectrum of Rh-22 (refer Figure 4.5). There are eight signals observed, where the three multiplet signals at higher chemical shifts, 6.98, 7.11 and 8.88 ppm with integration of two each, arise from the three chemically different proton environments of the aryl substituent groups, labelled with blue stars in the figure below. The singlet resonance at 7.19
ppm corresponds to the protons of the NHC backbone. The remaining four signals (labelled with red dots) located between 1.58 to 4.80 ppm arise from the twelve protons of the cod ligand.

![Figure 4.5 $^1$H NMR spectrum of Rh-22, recorded in deuterated chloroform.](image)

The $^{19}$F($^1$H) NMR spectrum of Rh-22 (see Figure 4.6) displays two doublet signals at -107.52 and -119.67 ppm with peak integration ratios of one to one. These signals arise from the two inequivalent fluorines, where one fluorine sits in the *ortho* position and the other fluorine occupies the *para* position. Comparing the $^{19}$F($^1$H) NMR spectra of Rh-21, Rh-22, Rh-23, Rh-24 and Rh-25 complexes reveals that signals arising from the *meta* and *ortho*-fluorines normally appear at lower chemical shifts (more negative) whilst signals from the *para*-fluorine appear at higher chemical shifts (less negative). Based on this finding, the peak at -107.52 ppm is assigned to the *para*-fluorine (labelled as green) and the other peak around -119.67 ppm belongs to the *ortho*-fluorine (blue). These *ortho* and *para*-fluorine are coupled to each other with coupling constant $^4J_{FF} = 8.6$ Hz.
The $^{13}$C($^1$H) NMR spectrum of Rh-22 (refer Figure 4.7) shows thirteen signals, arising from eight chemically different carbon environments of the NHC ligand, four carbon environments of the COD ligand and one carbon environment of the solvent, chloroform (77.05 ppm). The peak at 187.60 ppm corresponds to the carbene carbon and appears as a doublet, with a coupling constant of 51.8 Hz. This is due to the coupling between the spin active $^{13}$C nucleus of the carbene and the $^{103}$Rh nucleus (100% abundance, $I = \frac{1}{2}$). The resonances at 161.31 and 154.96 ppm appear as doublets, with coupling constant values of 249.3 and 250.9 Hz respectively. These couplings are assigned to $^1J_{CF}$ allowing assignment of these signals to the carbons of the aryl substituent groups in the ortho and para positions. The signals at 132.20, 123.97, 123.27, 111.52 and 104.18 ppm correspond to the carbons of the NHC ligand whilst the other resonances at lower chemical shifts, 98.82, 68.35, 32.36 and 28.49 ppm belong to the carbon of cod ligand. The signals
at 98.82 and 68.35 ppm appear as doublets, due to the coupling between the cod carbons and rhodium centre, with coupling constants of 15.5 and 22.7 Hz respectively.

![13C NMR spectrum of Rh-22](image.png)

*Figure 4.7 13C(1H) NMR spectrum of Rh-22, recorded in deuterated chloroform.*

In addition to Rh-21 to Rh-25, rhodium complexes bearing non-fluorinated NHC ligands, Rh-26 and Rh-27, were also prepared for comparative studies. This will provide more information on how the introduction of fluorine into NHC ligands may affect their stereo-electronic properties and eventually the catalytic activity of the corresponding NHC-rhodium complexes. Some experimental data of Rh-21 to Rh-27 are presented in Table 4.6, which includes percentage yields, 13C NMR chemical shifts of the carbene bonded to the rhodium centre and the coupling constant between the spin active 13C carbene and 103Rh nuclei, J_{CRh}.
Table 4.6 The scope of [Rh(cod)Cl(NHC)] synthesis.

<table>
<thead>
<tr>
<th>NHC</th>
<th>Complex</th>
<th>Yield (%)</th>
<th>$\delta^{13}\text{C}_{\text{Rh}}$ (ppm)</th>
<th>$^{1}J_{\text{CRh}}$ (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHC-1</td>
<td>Rh-21</td>
<td>75</td>
<td>185.05</td>
<td>51.7</td>
</tr>
<tr>
<td>NHC-2</td>
<td>Rh-22</td>
<td>78</td>
<td>187.60</td>
<td>51.8</td>
</tr>
<tr>
<td>NHC-3</td>
<td>Rh-23</td>
<td>85</td>
<td>191.52</td>
<td>53.4</td>
</tr>
<tr>
<td>NHC-4</td>
<td>Rh-24</td>
<td>79</td>
<td>189.55</td>
<td>51.9</td>
</tr>
<tr>
<td>NHC-5</td>
<td>Rh-25</td>
<td>76</td>
<td>194.95</td>
<td>59.7</td>
</tr>
<tr>
<td>IPh</td>
<td>Rh-26</td>
<td>62</td>
<td>181.52</td>
<td>48.6</td>
</tr>
<tr>
<td>IMes</td>
<td>Rh-27</td>
<td>68</td>
<td>183.50</td>
<td>50.8</td>
</tr>
</tbody>
</table>

*Consistent with a published literature data.

Table 4.6 above summarises the scope of [Rh(cod)Cl(NHC)] synthesis in this study. The $^{13}\text{C}^{1}\text{H}$ NMR signal of the carbene carbon bonded to the rhodium centre, the complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25 have higher chemical shift values (> 185 ppm) than the non-fluorinated counterparts, Rh-26 and Rh-27 (180 – 184 ppm). A similar trend is also observed when comparing the $^{1}J_{\text{CRh}}$ coupling constant of these complexes. Those bearing fluorinated NHC ligands possess higher coupling constants than those of the non-fluorinated analogues. This may indicate that introducing fluorine to the NHC ligands has an impact on the electronic properties at the rhodium centre. In general, the $^{13}\text{C}$ carbene-rhodium chemical shifts increases in the systematic order of increasing fluorine-content of NHC ligands. Amongst this set of rhodium complexes, Rh-25, which possesses six fluorine atoms in the NHC ligand, has the highest $^{13}\text{C}$ carbene chemical shift value (194.95 ppm) and largest $^{1}J_{\text{CRh}}$ coupling constant (59.7 Hz). However, Rh-24 that also
contains six fluorine atoms like Rh-25 has lower $^{13}$C carbene chemical shift (189.55 ppm) and $^{1}J_{CRh}$ (51.9 Hz) values than those of Rh-25. Surprisingly, Rh-23 with four fluorine atoms in the ligand has a higher chemical shift (191.52 ppm) than Rh-24. However, Rh-23 and Rh-25 have fluorine atoms in both of the ortho positions of the aryl substituent groups, unlike Rh-24. This may explain why these two complexes have higher $^{13}$C carbene-rhodium chemical shifts and $^{1}J_{CRh}$ than the other complexes, since the fluorine atoms in the ortho positions of the substituent groups are closest to the NHC ring, hence providing stronger electronic effects than the more distant fluorines in the meta and para positions. According to the results from Table 4.6, both the number and position of fluorine atoms in the NHC ligand have an impact to the electronic properties of the rhodium centre.

Single crystals suitable for X-ray diffraction studies of Rh-21, Rh-22, Rh-23, Rh-25 and Rh-26 were grown by slow diffusion of hexane into saturated dichloromethane solutions of the complexes. The molecular structure for each complex comprises of a distorted square planar geometry with a chloride, the NHC and the two olefinic bonds of the COD ligand, coordinated to the rhodium centre. Figures 4.9, 4.10, 4.11, 4.12 and 4.13 represent the ORTEP molecular structures of Rh-21, Rh-22, Rh-23, Rh-25 and Rh-26 respectively.
Figure 4.9  ORTEP representation of the molecular structure of Rh-21. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.

Figure 4.10 ORTEP representation of the molecular structure of complex Rh-22. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.

Figure 4.11 ORTEP representation of the molecular structure of complex Rh-23. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.
Figure 4.12  ORTEP representation of the molecular structure of complex Rh-25. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.

Figure 4.13  ORTEP representation of the molecular structure of complex Rh-26. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.

Table 4.7  Selected bond lengths and angles for Rh-21, Rh-22, Rh-23, Rh-25, Rh-26 and previously reported Rh-27.

<table>
<thead>
<tr>
<th>Complex</th>
<th>NHC</th>
<th>Rh1-C1 length (Å)</th>
<th>Rh1-Cl1 length (Å)</th>
<th>C1-Rh1-Cl1 angle (°)</th>
<th>Rh1-C_{cod} \textsuperscript{trans-NHC} length (Å)</th>
<th>Rh1-C_{cod} \textsuperscript{trans-Cl} length (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-21</td>
<td>NHC-1</td>
<td>2.021(1)</td>
<td>2.414(3)</td>
<td>91.5(4)</td>
<td>2.102(1)</td>
<td>1.995(3)</td>
</tr>
<tr>
<td>Rh-22</td>
<td>NHC-2</td>
<td>2.000(8)</td>
<td>2.402(2)</td>
<td>88.9(2)</td>
<td>2.088(8)</td>
<td>1.979(2)</td>
</tr>
<tr>
<td>Rh-23</td>
<td>NHC-3</td>
<td>2.031(5)</td>
<td>2.389(2)</td>
<td>90.0(2)</td>
<td>2.087(5)</td>
<td>1.997(2)</td>
</tr>
<tr>
<td>Rh-25</td>
<td>NHC-5</td>
<td>2.005(4)</td>
<td>2.357(1)</td>
<td>89.0(1)</td>
<td>2.079(4)</td>
<td>1.997(1)</td>
</tr>
<tr>
<td>Rh-26</td>
<td>IPh</td>
<td>2.099(3)</td>
<td>2.408(9)</td>
<td>92.1(8)</td>
<td>2.088(3)</td>
<td>1.985(9)</td>
</tr>
<tr>
<td>Rh-27\textsuperscript{a}</td>
<td>IMes</td>
<td>2.049(2)</td>
<td>2.377(4)</td>
<td>89.0(1)</td>
<td>2.086(2)</td>
<td>1.985(4)</td>
</tr>
</tbody>
</table>

\textsuperscript{a} Taken from Evans \textit{et. al.}\textsuperscript{26}
Table 4.7 lists selected bond lengths and angles for complexes Rh-21, Rh-22, Rh-23, Rh-25 along with Rh-26 and Rh-27 for comparison. It is apparent from this table that the rhodium-carbene (Rh1-C1) distances of the fluorinated NHC ligands (Rh-21 to Rh-25) are shorter than those of the non-fluorinated analogues, Rh-26 and Rh-27. Generally, shorter bond distances correspond to stronger bond between the atoms. This is consistent with the findings from Chapter 3, where the gold-carbene bond distances of gold(I) complexes bearing fluorinated NHC ligands are shorter than those containing non-fluorinated NHC ligands.

As described previously in Chapter 2, the investigation of $^{77}$Se NMR chemical shifts revealed that the fluorinated NHC ligands, NHC-1 to NHC-5 have stronger π-accepting ability than the non-fluorinated counterparts, IMes and IPh. The stronger π-accepting ability of an NHC ligand from a metal centre may lead to a stronger metal-carbene bond, which results in shorter bond lengths. This could be a possible explanation for the observed shorter rhodium-carbene lengths of the fluorinated NHC complexes (Rh-21 to Rh-25), as compared to those of the non-fluorinated derivatives, Rh-26 and Rh-27. A closer look at the previously reported rhodium(I) complexes bearing unsymmetric fluorinated NHC ligands, Rh-3, Rh-7 and Rh-8 also revealed that their rhodium-carbene bond lengths (~2.02 Å) are shorter than those of non-fluorinated analogues (~2.10 Å).$^{27}$ Hence, the findings from this chapter are consistent with the previous work and further supports that the inclusion of fluorine in an NHC ligand affects the electronic properties of the resulting metal complex.
Figure 4.14  Rhodium-carbene bond lengths of Rh-3 (2.022 Å), Rh-7 (2.027 Å) and Rh-8 (2.024 Å).\textsuperscript{27}

4.3 Steric Quantification

The steric properties of various NHC ligands in their corresponding metal complexes can be evaluated using percent buried volume ($%V_{\text{bur}}$) and steric maps as described previously. Surprisingly, there are no steric measurement studies of rhodium complexes bearing fluorinated NHC ligands involved so far. Due to this lack of information, it is therefore necessary to quantify the steric bulk of the fluorinated NHCs and understand how the presence of fluorine in the substituent groups affects the steric environment around the rhodium centre.

Having successfully prepared a series of rhodium(I) complexes from various NHC ligands, Rh-21 to Rh-27, their steric parameters were investigated using $%V_{\text{bur}}$ and steric maps. These measurements were obtained using the SambVca 2.0 computational tool, developed by Cavallo and co-workers.\textsuperscript{28} The $%V_{\text{bur}}$ gives a
single average number, whilst the steric maps provide $\% \text{V}_{\text{bur}}$ values for each quadrant, which is very useful to portray a more detailed view of the steric environment around the rhodium centre. However, there are limitations of these techniques, such as the X-ray crystal structures only provide one static representation of these particular complexes, which may be influenced by packing forces as well as the steric hindrance of the NHCs. In addition, $\% \text{V}_{\text{bur}}$ and steric maps are measured from the solid-state crystal structures and do not necessarily reflect the behaviour in solution or at elevated temperature. Therefore, it is necessary to use these techniques carefully and understand the scope and limitations for steric quantification of NHCs. Table 4.8 summarises the $\% \text{V}_{\text{bur}}$ and steric maps of various [Rh(cod)Cl(NHC)] type complexes.

Table 4.8  Summary of $\% \text{V}_{\text{bur}}$ and steric maps for a series of rhodium(I) complexes bearing NHC ligands.

<table>
<thead>
<tr>
<th>Rhodium complexes</th>
<th>$% \text{V}_{\text{bur}}$</th>
<th>Steric map</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-21</td>
<td>32.1</td>
<td><img src="image" alt="Steric map" /></td>
</tr>
<tr>
<td>Rh-22</td>
<td>32.8</td>
<td><img src="image" alt="Steric map" /></td>
</tr>
<tr>
<td>Rhodium complexes</td>
<td>(% V_{\text{bur}})</td>
<td>Steric map</td>
</tr>
<tr>
<td>-------------------</td>
<td>---------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Rh-23</td>
<td>33.8</td>
<td><img src="image1" alt="Steric map" /></td>
</tr>
<tr>
<td>Rh-25</td>
<td>34.8</td>
<td><img src="image2" alt="Steric map" /></td>
</tr>
<tr>
<td>Rh-26</td>
<td>31.9</td>
<td><img src="image3" alt="Steric map" /></td>
</tr>
<tr>
<td>Rh-27(^a)</td>
<td>32.9</td>
<td><img src="image4" alt="Steric map" /></td>
</tr>
<tr>
<td>Rhodium complexes</td>
<td>% $V_{\text{bur}}$</td>
<td>Steric map</td>
</tr>
<tr>
<td>-------------------</td>
<td>------------------</td>
<td>------------</td>
</tr>
<tr>
<td><strong>Rh-3$^b$</strong></td>
<td>32.2</td>
<td><img src="image1" alt="Steric map" /></td>
</tr>
<tr>
<td><img src="image2" alt="Chemical structure" /></td>
<td><img src="image1" alt="Steric map" /></td>
<td></td>
</tr>
<tr>
<td><strong>Rh-7$^b$</strong></td>
<td>32.3</td>
<td><img src="image3" alt="Steric map" /></td>
</tr>
<tr>
<td><img src="image4" alt="Chemical structure" /></td>
<td><img src="image3" alt="Steric map" /></td>
<td></td>
</tr>
<tr>
<td><strong>Rh-8$^b$</strong></td>
<td>32.4</td>
<td><img src="image5" alt="Steric map" /></td>
</tr>
<tr>
<td><img src="image6" alt="Chemical structure" /></td>
<td><img src="image5" alt="Steric map" /></td>
<td></td>
</tr>
</tbody>
</table>

* Taken from Evans et al.*

$^b$ Taken from Burling et al.*
As can be seen from Table 4.8, Rh-25 contains the most bulky ligand NHC-5, as indicated by the highest % $V_{bur}$ (34.8%) value. It is interesting to note that amongst the complexes in the example above, Rh-25 possesses the highest number of fluorines in the NHC ligands. This could be the reason for the increased steric environment around the rhodium centre. The second most bulky ligand is NHC-3 in Rh-23 with % $V_{bur}$ of 33.8%. Similar to what has been observed in the gold complexes described in Chapter 3, NHC-2 in Rh-22 is less bulky than NHC-3 in Rh-23, although both NHCs contain the same number of fluorine atoms. Investigation of the molecular structures of these complexes revealed that both of the ortho-position of the substituents groups in NHC-5 and NHC-3 are occupied by fluorine atoms. Since fluorine atoms in the ortho-position are closer to the rhodium centre than those in the meta and para-position, having fluorine atoms at this position will have significant effect on the steric environment around the rhodium centre. These results indicate that both the number and position of fluorines have influenced the steric properties of NHC ligands and these are consistent with those observed in the previous chapter involving [AuCl(NHC)] complexes.

It is interesting to note that for the rhodium complexes bearing unsymmetric fluorinated NHC ligands, Rh-3, Rh-7 and Rh-8, their steric bulk are similar to each other, with % $V_{bur}$ values of 32.2, 32.3 and 32.4% respectively. All three complexes contain a pentafluoroaryl substituent group on one side of the NHC and a different substituent group on the other side. Since the % $V_{bur}$ values of these complexes are similar, this may suggest that the pentafluoroaryl substituent group of the nitrogen dominates the overall steric properties of the ligand. The presence of a CH$_2$ spacer
group between the nitrogen and the substituent groups of Rh-3, Rh-7 and Rh-8 may reduce the steric effect of changing the substituent groups. This is because the presence of a spacer would make the distance of the substituent groups further from the rhodium centre, hence changing the substituent group would make less effect to the steric properties of the NHC ligand. In the case of the rhodium complexes prepared in this work, Rh-21, Rh-22, Rh-23 and Rh-25, addition of fluorines and changing the position of fluorines in the substituent groups would influence the steric properties considerably, as indicated by variation of $V_{\text{bur}}$ values. Figure 4.15 illustrates the $V_{\text{bur}}$ scale of various [Rh(cod)Cl(NHC)] type complexes, including the new complexes prepared in this study. It is apparent from this Figure that both the number and position of fluorines have influenced the steric properties of NHC ligands, particularly for Rh-21 to Rh-25.
Figure 4.15 Summary of percent buried volumes for [Rh(cod)Cl(NHC)-type complexes.
4.4 Catalytic Activity

One of the applications of rhodium(I) complexes is their role as catalysts in transfer hydrogenation. Transfer hydrogenation is an efficient catalytic reaction which does not require handling of pressurised gaseous H\textsubscript{2} or hazardous reducing agents. This method is more preferable for large-scale industry than classical hydrogenation, due to the fact that the hydrogen donors such as isopropanol are readily available, relatively cheap and easy to handle. Having successfully synthesised rhodium complexes containing fluorinated NHC ligands Rh-21 to Rh-25, the next step of the work was to test the catalytic activities of these complexes in the transfer hydrogenation reaction of acetophenone. As described earlier, the presence of fluorine atoms in the NHC ligand has shown a significant effect, both electronically and sterically.

The scope of this transfer hydrogenation involved 1.0 mmol of acetophenone, 0.01 mmol (1% mol) of rhodium catalyst in 5 mL of isopropanol, with a catalyst:substrate ratio of 1:100. After the desired reaction time, the reaction aliquots was quenched with 1 M HCl (1 mL) and extracted with diethyl ether (10 mL). The organic phase was separated and collected. The solvents were removed under reduced pressure to afford a colourless liquid, 1-phenylethanol. The percentage conversion was measured by comparing the methyl proton signals of acetophenone (s, δ 2.60 ppm) and 1-phenylethanol (d, δ 1.50 ppm) in the \textsuperscript{1}H NMR spectrum of the crude product recorded in deuterated chloroform. Scheme 4.3 displays the catalytic reaction involved in this work.
Scheme 4.3 Transfer hydrogenation of acetophenone to 1-phenylethanol.

The catalyst was dissolved in a solution of isopropanol containing potassium hydroxide at 82°C for 30 min, followed by the addition of acetophenone. The progress of the reaction was monitored by $^1$H NMR spectroscopy and the results for each experiment are average over three runs. For comparative studies, rhodium(I) complexes containing non-fluorinated NHC analogues, Rh-26 and Rh-27 were also tested. Table 4.9 shows the percentage conversions for each catalyst employed in this catalytic reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>NHC</th>
<th>Catalyst</th>
<th>Conversion$^b$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NHC-1</td>
<td>Rh-21</td>
<td>80</td>
</tr>
<tr>
<td>2</td>
<td>NHC-2</td>
<td>Rh-22</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>NHC-3</td>
<td>Rh-23</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>NHC-4</td>
<td>Rh-24</td>
<td>87</td>
</tr>
<tr>
<td>5</td>
<td>NHC-5</td>
<td>Rh-25</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>IPh</td>
<td>Rh-26</td>
<td>48</td>
</tr>
<tr>
<td>7</td>
<td>IMes</td>
<td>Rh-27</td>
<td>67</td>
</tr>
</tbody>
</table>

$^a$1.0 mmol of acetophenone, 1% mol of catalyst in 5 mL of isopropanol at 82°C over 1 hour.

$^b$Determined by $^1$H NMR analysis of crude reaction mixture based on acetophenone conversion, averaged value over three runs.

As can be seen from Table 4.9, it is apparent that the rhodium(I) complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25 have higher catalytic activities than the non-fluorinated congeners, Rh-26 and Rh-27. Amongst the rhodium(I) complexes tested, Rh-25 in particular is the best catalyst with 96% conversion after one hour, whilst Rh-26 is the least catalytically active with only 45% conversion. To understand the catalytic behaviour of these complexes, the reaction progress was monitored periodically every 10 mins, up to one hour. After the desired reaction
time, the reaction aliquots was quenched with 1 M HCl (1 mL) and extracted with diethyl ether (10 mL). The product was isolated and analysed by the $^1$H NMR spectroscopy. The conversions obtained over this time for all rhodium(I) complexes are presented in Figure 4.16 as a time-dependence plot.

![Figure 4.16](image)

Figure 4.16  Time dependence of the catalytic transfer hydrogenation of acetophenone, as measured by the percentage conversion of acetophenone from the $^1$H NMR spectroscopy.

From the graph above we can see that the activation periods for Rh-21 to Rh-25 were very short compared to those of the non-fluorinated analogues, Rh-26 and Rh-27. For example, Rh-25 achieved 70% conversion after just 10 mins whilst Rh-26 only obtained 15% conversion within the same time. Variation in the catalytic performance of the rhodium complexes may be due to the electronic and steric properties of the NHC ligands. In the previous studies involving transfer hydrogenation of various ketones, Zinner and co-workers observed that the weaker donor strength of the NHC ligand seems to increase the catalytic activity of the iridium type complexes, by shortening the activation period and accelerating the
catalytic reaction.\textsuperscript{30} If we assume rhodium complexes in this study behave similarly to the iridium complexes in Zinner’s work, this may suggest that fluorinated NHCs, NHC-1 to NHC-5 are weaker donors than the non-fluorinated analogues, IMes and IPh. This explanation is consistent with the fact that the electron withdrawing nature of fluorine in the substituent groups pulls the electron density away from the carbene. This will eventually lower the electron density around the carbene and hence weaken the σ-donor strength of the carbene.

This justification can be further supported by one of the examples of rhodium complexes bearing a fluorinated NHC ligand, Rh-3 described previously in Chapter 1. Reaction of Rh-3 and carbon monoxide has afforded Rh-4 as shown in Scheme 4.4 below. During this process, the cod ligand has been replaced by two carbonyls.

![Scheme 4.4](image)

This complex is very useful as it was used to determine the electronic properties of the NHCs by measuring the two stretching frequencies, $\nu_{\text{CO}}$, of the carbonyls in the IR spectrum. The $\nu_{\text{CO}}$ bands of Rh-4 appear at 2084 and 2003 cm$^{-1}$, which are higher than the bands found in non-fluorinated NHC analogues, ca. 2068 and 1980 cm$^{-1}$.\textsuperscript{31} Higher $\nu_{\text{CO}}$ indicates a stronger CO bond and lower electron density at the rhodium centre. The presence of a fluorinated substituent group on the NHC ligand in Rh-4 has influenced the electronic properties by reducing the donating ability of the NHC.
ligand. Based on this finding, it can be proposed that the analogous complexes of fluorinated NHC ligands, NHC-1 to NHC-5 may have similar or higher $\nu_{\text{CO}}$ bands than Rh-4. This is because there is a spacer group between the nitrogen and the substituent group of the NHC ligand in Rh-4. The presence of this spacer may lower the electron withdrawing effect of fluorines as the distance between the fluorines in the substituent group and the carbene is greater, due to the extra bonds of the spacer group.

On the other hand, the fluorophenyl substituent groups in NHC-1 to NHC-5 are directly bonded to the nitrogen atoms, resulting in stronger electron withdrawing effects of the fluorines from the carbene. Based on this, it may suggest that fluorinated NHC ligands, NHC-1 to NHC-5 are weaker donors than the non-fluorinated derivatives, IMes and IPh. Hence, we might expect that the rhodium-carbene bond distances of the fluorinated analogues Rh-21 to Rh-25 to be longer, due to less electron density at the rhodium centre. However, the findings from the crystal structures contradict this proposal. Based on the rhodium-carbene bond distances of the complexes containing fluorinated NHC ligands, Rh-21 to Rh-25, have shorter lengths than those of the non-fluorinated counterparts, Rh-26 and Rh-27. In order to solve this contradiction, it is important to properly investigate the donor strength of these NHC ligands quantitatively.

Referring back to Chapter 2, one of the methods to quantify the electronic properties of NHCs is by measuring the IR-active carbonyl stretching frequencies of [Ni(CO)$_3$(NHC)] or [IrCl(CO)$_2$(NHC)] type complexes. A stronger donating NHC ligand increases the electron density at the metal centre, which in turn improves $\pi$-back
donation from the metal to the carbonyl’s anti-bonding orbital. As a result, the carbonyl (CO) bond is weakened and this leads to the CO stretching frequency being observed at a lower wavenumber in the IR spectrum. Contrarily, the good π-accepting ability of NHCs would reduce the electron density at the metal centre which strengthens the CO bond. The overall net effect of the ligand is then measured, by the frequency of the CO bond vibration in the IR spectrum. Due to the limitations and failures during preparation of the [IrCl(CO)₂(NHC)] and [RhCl(CO)₂(NHC)] complexes containing fluorinated NHC ligands, another technique was employed to measure the electronic properties on NHC ligands. The π-accepting ability of NHCs has been assessed using ⁷⁷Se NMR spectroscopy of their selenium adducts, which were prepared from the NHC precursors and selenium powder in the presence of base. Figure 4.17 below illustrates a plot of percentage conversion of acetophenone against the ⁷⁷Se NMR chemical shifts of NHC selenium adduct.

![Figure 4.17](image)
Higher $^{77}\text{Se}$ NMR chemical shifts indicate greater $\pi$-accepting ability of the NHC ligands. It can be seen from the plot above that the conversion generally increases as the $^{77}\text{Se}$ NMR chemical shift becomes higher. This indicates that there may be a link between the electronic properties of NHC ligands and the catalytic activity of the corresponding complexes. The NHC ligands with greater $\pi$-accepting ability, such as those in Rh-21 to Rh-25 have higher catalytic performances than those NHC ligands with weaker $\pi$-acceptor strengths (Rh-26 and Rh-27). Hence, the inclusion of fluorine atoms in NHC ligands has increased $\pi$-accepting ability of the ligands and influenced the catalytic activity of the corresponding complexes. These findings are consistent with those of other studies and suggest that $\pi$-interaction can also play a significant role in the bonding of these classical $\sigma$-donor from NHC ligands to transition metals.$^{32,33}$

On top of the electronic effects of NHC ligands described above, the steric properties of the NHC ligands may also influence the complex behaviour in this catalytic reaction. In order to investigate these effects, the steric parameters of rhodium complexes that have been quantified earlier were compared with the respective percentage conversions. A graph showing the relationship between the percent buried volume ($% V_{\text{bur}}$) and percentage conversion of acetophenone is depicted in Figure 4.18.
Based on the trend observed in the figure above, generally rhodium complexes bearing more bulky NHC ligands have higher catalytic activities than those containing less bulky NHC ligands. However, there is an anomaly in this trend where Rh-27 with a more bulky NHC ligand, IMes has a lower catalytic performance than the other two rhodium complexes bearing less bulky NHC ligands, Rh-21 and Rh-22. If there is a direct link between the steric environment around the rhodium metal and complex activity, there should follow a systematic order. These findings are consistent with the work described by Nolan and co-workers, in which the catalytic activity of rhodium complexes bearing NHC ligands does not follow any systematic order of increasing or decreasing steric bulk of NHC ligands. Some bulky NHC ligands may have low catalytic activity, whilst other bulky NHC ligands may have high catalytic activity due to the flexibility of the substituent groups to rearrange and avoid any steric clash.¹⁹
Interestingly, the plot from rhodium complexes containing fluorinated NHC ligands (Rh-21 to Rh-25) gives an approximately linear fit. Amongst these complexes, Rh-23 and Rh-25 exhibit the fastest rate of conversion. The similarity between Rh-23 and Rh-25 is that these complexes possess fluorine atoms in both of the ortho position of the substituent groups. These results are consistent with the findings from Chapter 3 involving gold complexes, in which Au-3 and Au-5 were found to be the best catalysts in the A3 coupling reaction and these two complexes also contain fluorine atoms in both of the ortho position of the nitrogen substituent groups. Hence, it is clear that the presence of fluorine atoms in NHC ligands has influenced the complex activity to some extent.

To determine whether a correlation exists between both steric and electronic effects of the NHC ligands on the catalytic activities of the rhodium complexes in the transfer hydrogenation of acetophenone, a multiple linear regression analysis was undertaken using Microsoft Excel, and the best fit is shown in Figure 4.19. Table 4.10 tabulates the data employed in this analysis. The best fit was given by the equation below:

\[
(\delta ^{77}\text{Se} \times a) + (% V_{\text{bur}} \times b) - 128.49 = \text{calculated }% \text{ conversion}
\]

where \(a = 0.5879\) and \(b = 5.2859\)

<table>
<thead>
<tr>
<th>Complex</th>
<th>NHC</th>
<th>(\delta ^{77}\text{Se})</th>
<th>% (V_{\text{bur}})</th>
<th>Observed % conversion</th>
<th>Calculated % conversion</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh-21</td>
<td>NHC-1</td>
<td>60.7</td>
<td>32.1</td>
<td>80</td>
<td>76.87</td>
<td>3.13</td>
</tr>
<tr>
<td>Rh-22</td>
<td>NHC-2</td>
<td>68.3</td>
<td>32.8</td>
<td>83</td>
<td>84.04</td>
<td>-1.04</td>
</tr>
<tr>
<td>Rh-23</td>
<td>NHC-3</td>
<td>67.4</td>
<td>33.8</td>
<td>91</td>
<td>90.32</td>
<td>0.68</td>
</tr>
<tr>
<td>Rh-25</td>
<td>NHC-5</td>
<td>73.0</td>
<td>34.8</td>
<td>96</td>
<td>98.38</td>
<td>-2.38</td>
</tr>
<tr>
<td>Rh-26</td>
<td>IPh</td>
<td>24.1</td>
<td>31.9</td>
<td>48</td>
<td>54.30</td>
<td>-6.30</td>
</tr>
<tr>
<td>Rh-27</td>
<td>IMes</td>
<td>26.7</td>
<td>32.9</td>
<td>67</td>
<td>61.11</td>
<td>5.89</td>
</tr>
</tbody>
</table>
Based on the plot in Figure 4.19, there is a linear correlation between the observed conversions and both the electronic and steric parameters and they model the observed catalytic activities of the rhodium complexes. These findings may suggest that the presence of fluorine influences both the electronic and steric properties of NHC ligands and therefore the catalytic activities of the corresponding complexes.

4.5 Summary

A series of rhodium(I) complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25 were successfully synthesised and structurally characterised. Comparison of X-ray crystal structures reveal that the rhodium-carbene bond lengths of these complexes are shorter than those containing non-fluorinated NHC ligands, Rh-26 and Rh-27. These findings are consistent with those found in the gold complexes described in Chapter 3 and the previously reported rhodium complexes bearing unsymmetrical NHC ligands. The shorter metal-carbene bond length of the
fluorinated NHC ligands may be due to the stronger $\pi$-accepting ability than those of the non-fluorinated congeners.

The percent buried volume ($% V_{\text{bur}}$) and steric maps were utilised to measure the steric parameters of these rhodium complexes. It was discovered that both the number and position of fluorine atoms in the substituent groups affected their steric properties, as indicated by the percent buried volume,$% V_{\text{bur}}$ calculations. **Rh-21 to Rh-25** were found to be excellent catalysts for the transfer hydrogenation of acetophenone to 1-phenylethanol. Both steric and electronic effects of these NHC ligands appear to influence the catalytic reaction to some extent. The weaker donor strength and stronger $\pi$-accepting ability of fluorinated NHC ligands are responsible for the high catalytic activity, by reducing the activation time and accelerating the catalytic reaction. This work contributes to existing knowledge by providing additional evidence on ligands effect in the catalytic transfer hydrogenation reaction.

**4.6 Experimental**

**4.6.1 General considerations**

Unless otherwise stated all reactions were carried out in air. The precursors to NHC-1, NHC-2, NHC-3, NHC-4, NHC-5, IPh and IMes were prepared according to the description in Chapter 2. $[\text{Rh(cod)}\text{Cl}]_2$ and **Rh-27** were prepared according to the published procedures.$^6$ Potassium hydroxide, potassium carbonate and isopropanol were purchased from Sigma Aldrich. All other chemicals were obtained commercially from Sigma Aldrich or Alfa Aesar and were of analytical grade or higher and were used without further purification.$^1$H and $^{19}$F{$^1$H} NMR spectra were
recorded using a Bruker Avance spectrometer at 400.1, and 376.5 MHz respectively, and were referenced to external TMS and CFCl$_3$ respectively. $^{13}$C($^1$H) NMR spectra were recorded using a Bruker Avance spectrometer at 100 MHz and referenced to TMS. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The splitting patterns are labelled as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Elemental analyses of carbon, hydrogen and nitrogen were performed on a Perkin Elmer PE 2400 combustion elemental analyser. The elemental analysis of rhodium was performed by heating the complex in an acid solution at high temperature until the complex decomposed and analysed using the Thermo Scientific iCAP DUO 6300 ICP-OES instrument by Mr Martin Jennings at the School of Chemistry, The University of Manchester.

### 4.6.2 X-ray diffraction studies

Crystallographic data for **Rh-21**, **Rh-22**, **Rh-23**, **Rh-25** and **Rh-26** were collected on an Agilent SuperNova diffractometer using Mo Kα radiation (λ = 0.71073 Å). All the raw data frames were reduced and corrections were applied for Lorentz, polarisation and absorption using the multi-scan methods with CrysAlisPro. The X-ray structural data were solved by direct methods, with full-matrix least-squares refinement of F2 using: Olex2, ShelX and ShelXTL programs. Ortep3 was used to generate the graphical representations and Mercury and Pluton were used to investigate and report the structures. All non-H atoms were modelled with anisotropic displacement parameters, H-atoms were placed in idealised positions and refined with isotropic thermal parameters.
4.6.3 Synthetic procedures

4.6.3.1 Chloro(\(\eta^1\)-1,5-cyclooctadiene)[1,3-bis(4-fluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-21

The complex was prepared from **NHC-1** precursor (69.5 mg, 0.202 mmol), [Rh(cod)Cl]_2 (50.0 mg, 0.101 mmol) and K_2CO_3 (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (76.1 mg, 75%). \(^1\)H NMR (CDCl\(_3\), δ (ppm)): 8.26 (s, 2H, NCH\(_2\)CHN), 7.28 (m, 4H, H\(_{\text{phenyl}}\)), 7.24 (m, 4H, H\(_{\text{phenyl}}\)), 4.92 (s, 2H, H\(_{\text{cod}}\)) 2.64 (s, 2H, H\(_{\text{cod}}\)), 2.01 – 1.92 (m, 4H, H\(_{\text{cod}}\)), 1.72 – 1.50 (m, 4H, H\(_{\text{cod}}\)). \(^{13}\)C\(^{\text{\(1\)}}\)H NMR (CDCl\(_3\), δ (ppm)): 184.82 (d, \(J_{C-Rh} = 51.7\) Hz, C\(_{\text{carbene}}\)), 163.36 (d, \(J_{C-F} = 245.3\) Hz, C\(_F\)), 160.89, 136.23, 129.07, 123.45, 97.80 (d, \(J_{C-Rh} = 15.1\) Hz, C\(_{\text{cod}}\)), 68.30 (d, \(J_{C-Rh} = 22.1\) Hz, C\(_{\text{cod}}\)), 32.41, 29.05. \(^{19}\)F\(^{\text{\(1\)}}\)H NMR (CDCl\(_3\), δ (ppm)): -113.11 (s, 2F, F\(_{\text{para}}\)). Anal. Calcd for C\(_{23}\)H\(_{22}\)F\(_2\)N\(_2\)ClRh (%): C, 54.92, H, 4.41, N, 5.57, Rh, 20.48. Found: C, 54.09, H, 4.32, N, 5.43, Rh, 20.45.
4.6.3.2 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,4-difluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-22

The complex was prepared from NHC-2 precursor (76.8 mg, 0.202 mmol), [Rh(cod)Cl]₂ (50.0 mg, 0.101 mmol) and K₂CO₃ (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (84.8 mg, 78%). ¹H NMR (CDCl₃) δ (ppm): 8.88 (s, 2H, H_phenyl), 7.19 (s, 2H, NCH₂CHN), 7.11 (m, 2H, H_phenyl), 6.98 (m, 2H, H_phenyl) 4.80 (br, 2H, H_cod) 2.69 (br, 2H, H_cod), 1.88 – 1.79 (m, 4H, H_cod), 1.65 – 1.50 (m, 4H, H_cod). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 187.60 (d, $J_{C-Rh} = 51.8$ Hz, C_carbene), 161.31 (d, $J_{C-F} = 249.3$ Hz, C_f), 154.96 (d, $J_{C-F} = 250.9$ Hz, C_f), 132.20, 123.97, 123.27, 111.48, 104.18, 98.82 (d, $J_{C-Rh} = 15.5$ Hz, C_cod), 68.35 (d, $J_{C-Rh} = 22.7$ Hz, C_cod), 32.36, 28.49. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -107.52 (d, 2F, $J_{F-F} = 8.6$ Hz, F_para), -119.69 (d, 2F, $J_{F-F} = 8.6$ Hz, F_ortho).

4.6.3.3 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,6-difluorophenyl)imidazol-2-ylidene] rhodium(II): Rh-23

The complex was prepared from NHC-3 precursor (76.8 mg, 0.202 mmol), [Rh(cod)Cl]₂ (50.0 mg, 0.101 mmol) and K₂CO₃ (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (92.5 mg, 85%). ¹H NMR (CDCl₃) δ (ppm): 7.72 (s, 2H, NCH₂CHN), 7.56 (m, 2H, H₆-phenyl), 7.22 (m, 4H, H₄-phenyl), 4.72 (br, 2H, H₄-cod) 3.29 (br, 2H, H₂-cod), 2.18 – 1.82 (m, 4H, H₄-cod), 1.73 – 1.45 (m, 4H, H₄-cod). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 191.52 (d, J_C-Rh = 53.4 Hz, C_carbene), 167.81 (d, J_C-F = 252.3 Hz, Cᵣ), 159.61, 128.71, 123.59, 111.04, 98.09 (d, J_C-Rhf = 16.5 Hz, C_cod), 68.14 (d, J_Rh-C = 22.7 Hz, C_cod), 32.71, 28.38. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -118.93 (s, 2F, F_ortho). Anal. Calcd for C₂₃H₂₀F₄N₂ClRh (%): C, 51.25, H, 3.74, N, 5.20, Rh, 19.11. Found: C, 50.99, H, 3.78, N, 5.05, Rh, 19.37.
4.6.3.4 Chloro(η₄-1,5-cyclooctadiene)[1,3-bis(2,4,5-trifluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-24

The complex was prepared from NHC-4 precursor (84.1 mg, 0.202 mmol), [Rh(cod)Cl]₂ (50.0 mg, 0.101 mmol) and K₂CO₃ (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (94.0 mg, 81%). ¹H NMR (CDCl₃) δ (ppm): 8.90 (s, 2H, NCH₂CHN), 7.51 (m, 2H, H₂phenyl), 7.32 (m, 2H, H₂phenyl), (4.72 (br, 2H, H₄cod) 2.56 (br, 2H, H₄cod), 1.80 – 1.71 (m, 4H, H₄cod), 1.57 – 1.45 (m, 4H, H₄cod). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 189.54 (d, J_CRh = 51.9 Hz, C_carbene), 152.41 (d, J_CF = 249.3 Hz, C_F₃), 145.82 (d, J_CF = 247.1 Hz, C_F₃), 144.11 (d, J_CF = 245.2 Hz, C_F₃), 139.89, 136.54, 123.33, 111.91, 98.28 (d, J_CRC = 15.8 Hz, C_cod), 71.14 (d, J_CRC = 21.4 Hz, C_cod), 31.40, 27.48. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -123.06 (dd, 2F, ⁴J₉F = 14.7 Hz, ⁵J₉F = 5.2 Hz, F_ortho), -129.46 (dd, 2F, ⁴J₉F = 23.3 Hz, ⁵J₉F = 5.2 Hz, F_meta), -139.73 (dd, 2F, ³J₉F = 23.2 Hz, ⁴J₉F = 14.7 Hz, F_para). Anal. Calcd for C₅₃H₄₈F₆N₂ClRh (%): C, 48.08, H, 3.16, N, 4.87, Rh, 17.91. Found: C, 48.68, H, 3.11, N, 4.71, Rh, 17.97.
4.6.3.5 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,4,6-trifluorophenyl)imidazol-2-ylidene] rhodium(I): Rh-25

The complex was prepared from NHC-5 precursor (84.1 mg, 0.202 mmol), [Rh(cod)Cl]₂ (50 mg, 0.101 mmol) and K₂CO₃ (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (88.2 mg, 76%). ¹H NMR (CDCl₃) δ (ppm): 7.83 (s, 2H, NCHCHN), 7.61 (m, 4H, Hphenyl), 4.55 (br, 2H, Hcod) 2.34 (br, 2H, Hcod), 1.85 – 1.74 (m, 4H, Hcod), 1.67 – 1.55 (m, 4H, Hcod). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 194.95 (d, J_C-Rh = 59.7 Hz, C carbene), 162.41 (d, J_C-F = 253.3 Hz, CF), 148.82 (d, J_C-F = 249.3 Hz, C₆F₅), 144.23, 139.51, 136.54, 125.33, 99.10 (d, J_C-Rh = 16.8 Hz, Ccod), 72.14 (d, J_C-Rh = 23.4 Hz, Ccod), 33.42, 27.53. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -115.39 (t, 2F, J_F-F = 7.5 Hz, Fpara), -122.93 (d, 4F, J_F-F = 7.5 Hz, Fortho). Anal. Calcd for C₂₃H₁₈F₆N₂ClRh (%): C, 48.07, H, 3.16, N, 4.87, Rh, 17.90. Found: C, 48.01, H, 3.22, N, 4.91, Rh, 17.93.
The complex was prepared from IPh precursor (62.2 mg, 0.202 mmol), [Rh(cod)Cl]_2 (50 mg, 0.101 mmol) and K_2CO_3 (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (58.4 mg, 62%). ^1H NMR (CDCl_3) δ (ppm): 7.73 (s, 2H, NCHCHN), 7.51 (d, 4H, ^3J_{HH} = 7.6 Hz, H_{phenyl}), 7.45 (t, 4H, ^3J_{HH} = 7.8 Hz, H_{phenyl}), 7.32 (t, 2H, ^3J_{HH} = 7.4 Hz, H_{phenyl}), 4.65 (br, 2H, H_{cod}) 2.31 (br, 2H, H_{cod}), 1.95 – 1.75 (m, 4H, H_{cod}), 1.65 – 1.45 (m, 4H, H_{cod}). ^13C(^1H) NMR (CDCl_3) δ (ppm): 181.52 (d, J_{C-Rh} = 48.6 Hz, C_{carbene}), 153.10, 150.65, 145.39, 143.55, 139.21, 96.11 (d, J_{C-Rh} = 7.2 Hz, C_{cod}), 67.44 (d, J_{C-Rh} = 13.3 Hz, C_{cod}), 32.21, 28.89. Anal. Calcd for C_{23}H_{24}N_2ClRh (%): C, 59.16, H, 5.18, N, 6.00, Rh, 22.06. Found: C, 59.01, H, 5.22, N, 5.91, Rh, 22.23.
4.6.3.7 Chloro(η⁴-1,5-cyclooctadiene)[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] rhodium(I): Rh-27

The complex was prepared from IMes precursor (79.2 mg, 0.202 mmol), [Rh(cod)Cl]₂ (50 mg, 0.101 mmol) and K₂CO₃ (83.6 mg, 0.606 mmol) in acetone (6.0 mL). The resulting mixture was refluxed for 20 hours at 60°C. After this time, the solvent was removed on a rotary evaporator and dichloromethane was added (6.0 mL). The mixture was filtered through silica and washed with dichloromethane until the filtrate turned colourless. Finally, the solvent was removed affording a yellow crystalline solid (88.2 mg, 76%). 

\(^1\)H NMR (CDCl₃) δ (ppm): 7.06 (s, 4H, Hphenyl), 6.97 (s, 2H, NCHCHN), 4.55 (br, 2H, Hcod), 3.29 (br, 2H, Hcod), 2.38 (s, 6H, Hmethyl), 2.31 (s, 6H, Hmethyl), 2.11 (s, 6H, Hmethyl), 1.93 – 1.76 (m, 4H, Hcod), 1.62 – 1.49 (m, 4H, Hcod). 

\(^{13}\)C\(^{1}\)H NMR (CDCl₃) δ (ppm): 183.50 (d, J_C-Rh = 50.8 Hz, Ccarbene), 139.21, 137.51, 137.00, 135.11, 129.75, 128.77, 124.33, 96.20 (d, J_C-Rh = 7.6 Hz, Ccod), 68.14 (d, J_C-Rh = 14.3 Hz, Ccod), 33.21, 28.89, 21.33, 20.11, 18.45. Anal. Calcd for C₂₉H₃₆N₂ClRh (%): C, 63.20, H, 6.59, N, 5.09, Rh, 18.69 Found: C, 63.01, H, 6.52, N, 5.11, Rh, 18.83.
4.6.4 Transfer hydrogenation catalytic testing procedure

The catalyst (Rh-21 to Rh-27) (0.01 mmol, 1 mol %) was dissolved in a solution of potassium hydroxide (5.61 mg, 0.1 mmol) and 2-propanol (5 mL) in a two-necked flask. The solution was heated at 80°C for 30 min under reflux conditions. Subsequently, acetophenone (0.12 mL, 1.0 mmol) was added. After the desired reaction time the reaction was quenched with 1 M HCl (1 mL) and extracted with diethyl ether (10 mL). The organic phase was separated and collected. The solvents were removed in vacuo to afford a colourless liquid, 1-phenylethanol. The reaction progress was monitored by $^1$H NMR spectroscopy and the results for each experiment were averaged over three runs. $^1$H NMR (CDCl$_3$) δ 7.36-7.39 (m, 4H), 7.25-7.30 (m, 1H), 4.90 (q, $J = 6.4$ Hz, 1H), 2.26 (br, 1H), 1.50 (d, $J = 6.4$ Hz, 3H). $^{13}$C($^1$H) NMR (CDCl$_3$) δ 145.8, 128.4, 127.4, 125.3, 70.3, 25.1.

4.7 References


2007, **349**, 1677-1691.


Chapter 5: Synthesis, Characterisation and Catalytic Activity of Palladium(II) Complexes featuring Fluorinated NHC Ligands
5.1 Introduction

Palladium is a transition metal and belongs to group 10 in the periodic table. It is one of the most widely used transition metals in the production of catalytic converters in the automobile industry,\textsuperscript{1} with other applications in electronics,\textsuperscript{2} dentistry\textsuperscript{3} and jewellery.\textsuperscript{4} In coordination chemistry, palladium complexes mainly exist in the 0 and +2 oxidation states. Other oxidation states are less commonly observed, such as +1,\textsuperscript{5} +3,\textsuperscript{6} +4\textsuperscript{7} and +6.\textsuperscript{8} Traditionally, palladium complexes bearing tertiary phosphine ligands have been extensively employed in organometallic chemistry and homogeneous catalysis.\textsuperscript{9} However, since the successful isolation of a free NHC by Arduengo et al., in 1991,\textsuperscript{10} NHCs and their palladium complexes have been explored intensively due to their many advantages over their phosphine analogues.\textsuperscript{11} In particular, NHC-palladium(II) complexes derived from imidazolium precursors have demonstrated excellent catalytic activities in cross-coupling reactions, such as Suzuki-Miyaura,\textsuperscript{12} Negishi,\textsuperscript{13} Mizoroki-Heck,\textsuperscript{14} and Sonogashira.\textsuperscript{15}

\begin{center}
\begin{tikzpicture}

\node (a) at (0,0) {\text{Suzuki-Miyaura}};
\node (b) at (-1,-1) {\text{Sonogashira}};
\node (c) at (1,-1) {\text{Negishi}};
\node (d) at (0,-2) {\text{Mizoroki-Heck}};

\draw[->] (a) -- (b);
\draw[->] (b) -- (c);
\draw[->] (c) -- (d);
\end{tikzpicture}
\end{center}

Scheme 5.1  Cross-coupling reactions catalysed by NHC-palladium complexes.\textsuperscript{12,13,14,15}
Historically, the first catalytic application of a NHC-palladium complex was reported by Hermann et al., in the Heck-Mizoroki coupling reaction of 4-chlorobenzaldehyde and n-butyl acrylate.\(^\text{14}\) This reaction was catalysed by a two-coordinated NHC-palladium(II) complex, **Pd-9**, as depicted in Scheme 5.2.

![Scheme 5.2 The first catalytic application of a NHC-palladium complex.\(^\text{14}\)](image)

Interestingly, **Pd-9** has a higher turnover numbers per hour (TOF = 15,000) than the classical phosphine analogues (TOF = 1,000 to 5,000).\(^\text{14}\) The authors concluded that the NHC ligand stabilised palladium(II) and palladium(0) complexes from degradation (such as phosphine dissociation), due to the strong donor properties of the NHC. In contrast to the common palladium-phosphine derivatives, where the phosphorus-carbon (P-C) bonds in the phosphine ligands are not stable at high temperature and prone to degradation by P-C bond cleavage, which leads to catalyst deactivation. In addition, phosphine ligands are more water and air-sensitive.\(^\text{16}\) The complex **Pd-9** was described as an excellent catalyst with high thermal stability, hydrolytic durability and better stabilising effects than most of the common phosphines.

Since this initial discovery, the development of palladium(II)-NHC catalysis has experienced a tremendous growth, with a huge number of palladium(II) complexes
containing NHC ligands being prepared and tested in various catalytic reactions.\textsuperscript{17} For a more detailed overview of palladium(II)-catalysed reactions using NHC ligands, the reader’s attention is directed towards the comprehensive review by Díez-González and Nolan.\textsuperscript{17} This review describes the use of both in situ-generated palladium(II)-NHC complexes and well-defined palladium(II)-NHC complexes in organic transformations. Of these two types, well-defined palladium(II)-NHC complexes are more favoured as they allow a strict control over the palladium and NHC ligand ratio. This is important to avoid the formation of inactive palladium metal which might influence the reaction. Comparative studies involving a number of cross-coupling systems reveal that the optimum palladium to NHC ratio was determined to be a one to one ratio. Following this finding, various palladium(II)-NHC complexes have been synthesised in different forms, ranging from a dimer with bridging chlorides, [Pd(IMes)Cl\textsubscript{2}]\textsubscript{2} \textbf{Pd-10},\textsuperscript{18} and those containing an auxiliary ligand, [Pd(IMes)(acac)Cl] \textbf{Pd-11},\textsuperscript{19} [Pd(IMes)(allyl)Cl] \textbf{Pd-12}\textsuperscript{20} and [Pd(IPr)(3-Cl-pyridyl)Cl\textsubscript{2}] \textbf{Pd-13}\textsuperscript{21} as shown in Figure 5.1 below.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Figure5.1}
\caption{Example of common palladium(II) complexes containing NHC ligands.\textsuperscript{18,19,20,21}}
\end{figure}
Previous studies have reported that the auxiliary ligand has a major impact on the catalytic activity of the corresponding palladium(II)-NHC complexes.\textsuperscript{17,22,23}

Amongst these palladium(II) complexes, the one containing the pyridine auxiliary ligand, \textbf{Pd-13} has received much attention over the past 10 years. Historically, it was first developed by Organ and co-workers in 2006 and later known as the palladium(II)-PEPPSI (pyridine-enhanced pre-catalyst preparation, stabilisation and initiation) complex.\textsuperscript{21} Unlike traditional palladium(II) complexes containing phosphine or NHC ligands, PEPPSI complexes have been proven to be air and moisture stable and can be stored out on the bench. Moreover, these complexes are relatively easy to synthesise and can be prepared outside an inert atmosphere. The presence of the auxiliary 3-chloropyridyl ligand acts as a ‘throw-away’ (easy to dissociate and get eliminated when required) ligand and provides extra stability to the complex.\textsuperscript{21} Three sets of palladium(II)-PEPPSI complexes containing different NHC ligands, namely [\textbf{Pd(IPr)}(3-Cl-pyridyl)\textbf{Cl}_2] \textbf{Pd-13}, [\textbf{Pd(IMes)}(3-Cl-pyridyl)\textbf{Cl}_2] \textbf{Pd-14} and [\textbf{Pd(IEt)}(3-Cl-pyridyl)\textbf{Cl}_2] \textbf{Pd-15} were prepared and evaluated in the Suzuki-Miyaura and Negishi coupling reactions.\textsuperscript{21} Tables 5.1 and 5.2 show the scope of the catalytic reactions and the percentage yields of products obtained in the Suzuki-Miyaura and Negishi coupling reactions respectively.

Figure 5.2 Palladium(II)-PEPPSI complexes employed in the Suzuki-Miyaura and Negishi reactions.\textsuperscript{21}
Table 5.1  Catalytic activity of the palladium(II)-PEPPSI complexes in the Suzuki-Miyaura coupling reaction.\textsuperscript{21}

<table>
<thead>
<tr>
<th>Entry</th>
<th>PEPPSI Complexes</th>
<th>% Yield\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd-13</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Pd-14</td>
<td>6.5</td>
</tr>
<tr>
<td>3</td>
<td>Pd-15</td>
<td>31</td>
</tr>
</tbody>
</table>

\textsuperscript{a} GC yield (internal standard-undecane), average values over two-runs.

Table 5.2  Catalytic activity of the palladium(II)-PEPPSI complexes in the Negishi coupling reaction.\textsuperscript{21}

<table>
<thead>
<tr>
<th>Entry</th>
<th>PEPPSI Complexes</th>
<th>% Yield\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd-13</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Pd-14</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>Pd-15</td>
<td>34</td>
</tr>
</tbody>
</table>

\textsuperscript{a} GC yield (internal standard-undecane), average values over two-runs.

From Tables 5.1 and 5.2 above, it can be seen that Pd-13 has the highest activity compared with the other two derivatives. The authors concluded that Pd-13 with a bulky NHC ligand, IPr, leads to a fast reductive elimination, which in turn generates the palladium(0) active species (see Figure 5.3)\textsuperscript{24}, in a similar manner to what has been reported previously with bulky phosphines.\textsuperscript{25,26}

![Figure 5.3](image-url)
Subsequently, a series of palladium(II)-PEPPSI derivatives containing more sterically demanding NHC ligands (Pd-16, Pd-17 and Pd-18) were developed by Organ and co-workers. These complexes contain IBu, IPen and IcPen type-NHC ligands respectively as shown in Figure 5.4.

![Figure 5.4 Palladium(II)-PEPPSI complexes containing sterically demanding NHC ligands.](image)

The catalytic activities of complexes Pd-16, Pd-17 and Pd-18, were evaluated in the Suzuki-Miyaura coupling reaction of 2,6-dimethylphenylboronic acid and 1-bromo-2-methoxynaphthalene, alongside Pd-13. The reactions were conducted in a KOH/1,4-dioxane solvent system at 65°C, and the percentage conversions were assessed by GC analysis after 24 hours. Table 5.3 illustrates the scope of this study.

<table>
<thead>
<tr>
<th>Entry</th>
<th>PEPPSI Complexes</th>
<th>% Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd-13</td>
<td>41</td>
</tr>
<tr>
<td>2</td>
<td>Pd-16</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Pd-17</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>Pd-18</td>
<td>9</td>
</tr>
</tbody>
</table>

* GC yield (internal standard-undecane), average values over two-runs.
* Control experiments with no catalyst showed no conversion.

The results, as shown in Table 5.3, indicate that Pd-17 has the highest catalytic activity with 91% conversion, followed by Pd-13 at 41% whilst Pd-16 and Pd-18
have the lowest conversions at 4 and 9% respectively. These results are consistent with the previous findings which stated that palladium(II) complexes bearing more bulky ligands have higher catalytic activities than those containing less bulky ligands.\textsuperscript{28,29,30} The catalytic activities of Pd-13 and Pd-17 were further investigated in other cross-coupling reactions, such as Negishi coupling of 2-mesitylzinc halides with 1,3-dimethyl-2-bromobenzene,\textsuperscript{31} and Buchwald-Hartwig amination of aryl halides with primary amines.\textsuperscript{32} In these reactions, Pd-17 outperformed Pd-13 consistently. In general, Pd-17 was found to demonstrate a higher catalytic performance than Pd-13.

Inspired by the positive influence of the steric bulk of an NHC ligand, Nolan and co-workers prepared a novel, well-defined palladium(II) PEPPSI analogue containing a more sterically demanding ligand, IPr* (Pd-19).\textsuperscript{33} The catalytic activity of Pd-19 was directly compared with the previously described and well established palladium-PEPPSI complexes, Pd-13 and its analogue, Pd-20 in the Buchwald-Hartwig amination between 4-chlorotoluene and morpholine.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{complexes}
\caption{Palladium(II)-PEPPSI complexes employed in Buchwald-Hartwig amination between 4-chlorotoluene and morpholine.\textsuperscript{33}}
\end{figure}
The percentage conversions were recorded over 6 hours. According to the results, **Pd-19** exhibited a slightly higher catalytic activity at room temperature (91% conversion) as compared to **Pd-13** and **Pd-20** with 81% and 80% conversions respectively. The comparison of these PEPPSI complexes was further evaluated at higher temperature with low catalyst loading. After optimisation screening of various base and solvent combinations, the authors discovered that using potassium tert-butoxide in toluene gave the best results (Figure 5.6). For the purpose of investigating the reactivity of the palladium-PEPPSI complexes at low catalyst loading, only 0.025 mol % of these complexes were utilised in the reaction, as opposed to a standard 1 mol % catalyst used in most cross-coupling reactions. Scheme 5.4 illustrates the scope of the reaction and the catalytic performance of **Pd-19**, alongside the other palladium-PEPPSI analogues, **Pd-13** and **Pd-20**.
With regards to the results above, the catalytic activity of **Pd-19** outperformed the other two analogues tremendously, as indicated by the short catalyst initiation time and the high percentage conversion. Remarkably, after just 1 hour, the conversion reached 100% whilst the other two complexes, **Pd-13** and **Pd-20** only gave poor conversions, 30%, after 6 hours. This finding has provided additional support that bulky NHC ligands can improve the reactivity of the corresponding palladium(II)-PEPPSI complexes by enhancing the reductive elimination step of the catalytic cycle.

As described above, the inclusion of sterically demanding NHC ligands is thought to enhance the activity of the palladium(II)-PEPPSI complexes by increasing the rate of the reductive elimination. An alternative method of enhancing the reductive elimination is to use a less donating NHC ligand. Thus, modification of the electronic properties of an NHC ligand may affect the reactivity of the corresponding palladium(II)-PEPPSI complexes.
One of the ways to modify the steric and electronic properties of an NHC is by introducing fluorine. As described in Chapter 4, the inclusion of fluorine in the NHC ligands resulted in enhanced catalytic activities of the rhodium(I) complexes in transfer hydrogenation of acetophenone. Based on these findings, it was decided to investigate whether fluorinated NHC ligands may also increase the catalytic activity of the corresponding palladium(II)-PEPPSI complexes. Hence, the major objective of this chapter is to describe the synthesis and characterisation of palladium(II)-PEPPSI complexes containing fluorinated NHC ligands and investigate their catalytic activities in the Suzuki-Miyaura reaction.

5.2 Synthesis and Characterisation

This work involves the preparation and evaluation of the fluorinated derivatives of the palladium(II)-PEPPSI complexes. These new complexes were prepared using the methodology developed by Organ and co-workers with slight modifications. Instead of 16 hours heating as described in their work, the reactions were carried out for 24 hours, in order to achieve full conversion of the products. The appropriate fluorinated NHC precursor, NHC-1 to NHC-5, was heated with palladium dichloride in the presence of an excess of potassium carbonate at 80°C for 24 hours in neat 3-chloropyridine, to afford Pd-21 to Pd-25 (Scheme 5.3 and Figure 5.8). For comparison studies, the non-fluorinated analogues were also prepared from IMes and IPh precursors to give Pd-14 and Pd-26 respectively. All these complexes were obtained as air- and moisture-stable yellow crystalline solids in good yields (75 – 85%).
Scheme 5.3  Preparation methods for palladium(II)-PEPPSI complexes bearing fluorinated NHC ligands.

Figure 5.8  A series of new palladium(II)-PEPPSI complexes prepared in this study.

The identities of the complexes were confirmed by multinuclear NMR spectroscopies and elemental analysis. Surprisingly, the characterisation data for Pd-25 indicate that this complex differs from the others and that shown in Figure 5.8. This interesting phenomenon will be discussed further in the next section.
The $^1$H NMR spectra of complexes **Pd-21** to **Pd-25** show no signals above 10 ppm, indicating that all the NHC precursors have been transformed into the corresponding palladium complexes. Moreover, this can be confirmed by analysing the $^{19}$F-$^1$H NMR spectra of these complexes, where the signals corresponding to the BF$_4^-$ anion in the NHC precursors, which typically appeared around -148 ppm, were not observed in any of these spectra. The $^1$H, $^{19}$F-$^1$H and $^{13}$C-$^1$H NMR spectra of **Pd-21** are shown below as a typical example.

![Figure 5.9 $^1$H NMR spectrum of Pd-21 complex, recorded in deuterated chloroform.](image)

Figure 5.9 displays the $^1$H NMR spectrum of **Pd-21** recorded in deuterated chloroform. There are nine signals observed in this spectrum; the seven signals at higher chemical shifts correspond to the **Pd-21** complex, while the other two signals at 7.28 and 1.58 ppm are due to chloroform and water respectively. The first four resonances of the spectrum (from left) at 8.75, 8.65, 8.62 and 8.53 ppm show the intensity ratio of 1:1:1:1, which correspond to the four different single proton environments in the 3-chloropyridyl ligand. Two multiplet signals at 8.05 and 7.33
ppm both have integration values of four, which belong to the two chemically inequivalent protons of the phenyl substituent groups of the NHC. A signal at 7.71 ppm with integration of two represents the two protons of the imidazole backbone (NCHCHN). Meanwhile, Figure 5.10 below shows the $^{19}$F{$^1$H} NMR spectrum of Pd-21 with one peak at -111.48 ppm, which corresponds to the single fluorine environment in this complex.

Figure 5.10 $^{19}$F{$^1$H} NMR spectrum of Pd-21 complex, recorded in deuterated chloroform.

Figure 5.11 on the next page displays the $^{13}$C{$^1$H} NMR spectrum of Pd-21. There are eleven signals for the carbon environments, of which six signals are from the NHC ligand whilst the other five signals are from the 3-chloropyridyl ligand. The resonance at 163.88 and 161.40 ppm appear as a doublet, which corresponds to the carbons in the para position of the aryl substituent groups of the NHC ligand. These carbons are coupled with the neighbouring fluorine spin active nuclei with $^1J_{CF}$ value of 245.0 Hz. This value is consistent with the data in the literature.$^{34,36}$
Figure 5.11 $^{13}\text{C}(\text{H})$ NMR spectrum of Pd-21 complex, recorded in deuterated chloroform(*)

Table 5.4 below summarises the experimental and characterisation data of the palladium complexes containing fluorinated NHCs, Pd-21 to Pd-25 and those bearing non-fluorinated NHC analogues, Pd-14 and Pd-26 for comparison.

Table 5.4 Summary of the experimental data for palladium(II)-PEPPSI complexes prepared in this work.

<table>
<thead>
<tr>
<th>NHC</th>
<th>Complex</th>
<th>Yield (%)</th>
<th>$\delta^{13}\text{C}_{\text{C-Pd}}$ (ppm)</th>
<th>$\delta^{19}\text{F}$ (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHC-1</td>
<td>Pd-21</td>
<td>80</td>
<td>163.88</td>
<td>-111.48</td>
</tr>
<tr>
<td>NHC-2</td>
<td>Pd-22</td>
<td>78</td>
<td>164.21</td>
<td>-106.06, -117.09</td>
</tr>
<tr>
<td>NHC-3</td>
<td>Pd-23</td>
<td>82</td>
<td>166.88</td>
<td>-118.67</td>
</tr>
<tr>
<td>NHC-4</td>
<td>Pd-24</td>
<td>85</td>
<td>165.10</td>
<td>-122.58, -129.04, -135.50</td>
</tr>
<tr>
<td>NHC-5</td>
<td>Pd-25</td>
<td>75</td>
<td>168.10</td>
<td>-106.09, -115.57, -138.50</td>
</tr>
<tr>
<td>IPh</td>
<td>Pd-26</td>
<td>78</td>
<td>151.10</td>
<td>-</td>
</tr>
<tr>
<td>IMes$^a$</td>
<td>Pd-14</td>
<td>75</td>
<td>151.20</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ Consistent with a published literature data.

From Table 5.4, it is interesting to note that the $\delta^{13}\text{C}_{\text{C-Pd}}$ of the complexes featuring fluorinated NHC ligands, Pd-21 to Pd-25 are higher than those of the non-fluorinated NHC counterparts, Pd-14 and Pd-26. This is consistent to what has been found in the previous Chapter where rhodium(I) complexes bearing fluorinated NHC ligands, Rh-21 to Rh-25, have higher $\delta^{13}\text{C}_{\text{C-Rh}}$ values (185 to 195.
ppm) than the non-fluorinated analogues, **Rh-26** and **Rh-27** (180 – 184 ppm). This may indicate that introducing fluorine to the NHC ligands has an impact on the electronic properties at the metal centre.

Crystals suitable for X-ray diffraction studies were grown by slow diffusion of hexane into saturated dichloromethane solutions of **Pd-21**, **Pd-23** and **Pd-24** complexes. These complexes adopt a slightly distorted square planar geometry, with two chlorides, an NHC ligand and a 3-chloropyridyl ligand as shown in Figures 5.12, 5.13 and 5.14.

![Figure 5.12 ORTEP representation of the molecular structure of Pd-21. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.](image1)

![Figure 5.13 ORTEP representation of the molecular structure of Pd-23. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity.](image2)
The bond angle between the carbene, palladium and nitrogen of the pyridine (C1-Pd- N3) and the bond angle between trans-chlorides and palladium (Cl1-Pd-Cl2) are observed around 180°. In general, the Pd1-C1 and Pd1-N3 bond lengths are comparable to the other palladium(II)-PEPPSI complexes.\textsuperscript{21,22,33}

Table 5.5 presents a comparison of selected bond lengths and angles of various palladium(II)-PEPPSI complexes.

Table 5.5  Comparison of selected bond lengths and angles of various palladium(II)-PEPPSI complexes.

<table>
<thead>
<tr>
<th>Complex</th>
<th>NHC</th>
<th>Pd1-C1\textsuperscript{a} length (Å)</th>
<th>Pd1-N3\textsuperscript{b} length (Å)</th>
<th>C1-Pd-N3 angle (°)</th>
<th>Cl1-Pd-Cl2 angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-13\textsuperscript{a}</td>
<td>IPr</td>
<td>1.969(3)</td>
<td>2.137(2)</td>
<td>178.1(1)</td>
<td>179.60(4)</td>
</tr>
<tr>
<td>Pd-14\textsuperscript{a}</td>
<td>IMes</td>
<td>1.962(3)</td>
<td>2.117(3)</td>
<td>176.4(1)</td>
<td>177.73(4)</td>
</tr>
<tr>
<td>Pd-15\textsuperscript{a}</td>
<td>IEt</td>
<td>1.969(3)</td>
<td>2.109(2)</td>
<td>176.0(1)</td>
<td>177.69(4)</td>
</tr>
<tr>
<td>Pd-19\textsuperscript{b}</td>
<td>IPr*</td>
<td>1.974(3)</td>
<td>2.132(2)</td>
<td>177.7(2)</td>
<td>176.57(7)</td>
</tr>
<tr>
<td>Pd-21</td>
<td>NHC-1</td>
<td>1.953(5)</td>
<td>2.089(5)</td>
<td>177.4(2)</td>
<td>176.64(6)</td>
</tr>
<tr>
<td>Pd-23</td>
<td>NHC-3</td>
<td>1.944(1)</td>
<td>2.131(1)</td>
<td>180.0(1)</td>
<td>174.5(3)</td>
</tr>
<tr>
<td>Pd-24</td>
<td>NHC-4</td>
<td>1.941(1)</td>
<td>2.121(1)</td>
<td>175.4(5)</td>
<td>174.0(1)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Taken from Organ et al.\textsuperscript{21}  \textsuperscript{b}Taken from Nolan et al.\textsuperscript{33}

Table 5.5 presents a comparison of selected bond lengths and angles of these fluorinated NHC palladium(II)-PEPPSI complexes and the previously published non-fluorinated analogues, Pd-13, Pd-14, Pd-15 and Pd-19. Interestingly, a closer look at the bond lengths of these complexes reveals that the fluorinated analogues (Pd-21 to Pd-24) have significantly shorter palladium-carbene distances than the non-
fluorinated congeners. This is consistent with the findings from Chapter 3 and 4, where both gold and rhodium complexes bearing fluorinated NHC ligands have shorter metal-carbene bond distances than those containing non-fluorinated NHC ligands. According to the results obtained from the investigation of the $^{77}$Se NMR chemical shift of selenium-NHC adducts in Chapter 2, the fluorinated NHC ligands have better $\pi$-accepting ability than the non-fluorinated derivatives. The stronger $\pi$-accepting ability of the NHC ligands may increase the bond strength between the metal and carbene, which eventually leads to a shorter metal-carbene bond. This finding provides additional evidence that the inclusion of fluorine in an NHC ligand may influence its electronic properties.

### 5.3 Unusual and Unique Structure of Pd-25

Characterisation data from multinuclear NMR spectroscopy, elemental analysis and X-ray crystallography have confirmed the identities of the new palladium(II)-PEPPSI complexes featuring fluorinated NHC ligands, Pd-21 to Pd-24. However, the characterisation data for Pd-25 reveal that this complex does not exist in its expected form, instead it has adopted an unusual structure as shown in Figure 5.15.

![Expected structure - Pd(II) and Observed structure - Pd(0)](image)

*Figure 5.15  The expected structure of Pd-25 versus the observed structure.*
Figure 5.16 displays the $^1$H NMR spectrum of Pd-25 recorded in deuterated chloroform. It can be seen that there are seven signals for Pd-25 whilst another signal at 7.27 ppm is due to the solvent, chloroform. The four signals marked with red dots, at 8.81, 8.73, 7.83 and 7.42 ppm have relative integrals of 1:1:1:1 and belong to the four chemically inequivalent protons of the 3-chloropyridyl ligand. The singlet resonance at 7.91 ppm corresponds to the proton of the imidazole backbone (NCHCHN) and the other two multiplet signals, both with integrations of two, at 6.50 and 6.21 ppm correspond to two chemically different proton environments of the meta-protons in the $N$-substituent groups of the NHC ligand. If Pd-25 adopts the expected structure, these meta-protons should be in the same chemical environment and only one signal would be observed, as seen in other complexes bearing the NHC-5 ligand, such as Au-5 and Rh-25.
The identity of **Pd-25** can be further supported by analysing the $^{19}$F($^1$H) NMR spectrum as shown in Figure 5.17. The spectrum in Figure 5.17 shows three signals at -106.09, -115.57 and -138.50 ppm with intensity ratio of 1:1:1 respectively, indicating three non-equivalent fluorine environments.

![Figure 5.17 $^{19}$F($^1$H) NMR spectrum of Pd-25 in deuterated chloroform. Both of ortho-fluorines on each N-substituent group are unique (as indicated by the blue and green indicators). In the case of the rhodium and gold complexes bearing the NHC-5 ligand, both ortho-fluorines are chemically equivalent to one another.](image-url)

However, $^{19}$F($^1$H) NMR spectra of the other metal complexes bearing the **NHC-5** ligand, **Au-5** (Figure 5.18) and **Rh-25** (Figure 5.19) only show two fluorine signals, in the ratio of 1:2 as expected. In the case of **Au-5** and **Rh-25**, the two signals arise due to the fluorine atoms in the para and ortho position of the nitrogen substituent groups. The two ortho-fluorines in each N-phenyl substituent group of **NHC-5** ligand in **Au-5** and **Rh-25** are in the same chemical environment and give rise to resonances at -116.27 and -113.86 ppm respectively.
Figure 5.18 $^{19}$F($^1$H) NMR spectrum of Au-5 in deuterated chloroform. Both of ortho-fluorines on each $N$-phenyl substituent group are chemically equivalent to one another (indicated by the blue stars).

Figure 5.19 $^{19}$F($^1$H) NMR spectrum of Rh-25 in deuterated chloroform. Both of ortho-fluorines on each $N$-phenyl substituent group are chemically equivalent to one another (indicated by the blue stars).

On the other hand, the two ortho-fluorines in Pd-25 are no longer chemically equivalent, as one of them is coordinated to the palladium centre. These coordinated ortho-fluorines (indicated by red dots in Figure 5.17) show a dramatic upfield shift of over 20 ppm relative to that of the non-coordinated ortho-fluorines.
(blue stars). An upfield chemical shift is expected for the fluorine atom coordinated to the palladium centre, as indicated by the previous reported palladium(II) PNF pincer complex, as shown in example below.\textsuperscript{34}

![Scheme 5.5 Fluorine coordination to the palladium centre in Pd-28.\textsuperscript{34}](image)

During the conversion from Pd-27 to Pd-28, the iodide ligand in Pd-27 was substituted by the fluorine of the quinoline ligand. Similar to Pd-25, the fluorine coordination to the palladium centre can be confirmed by the \(^{19}\text{F}[^{1}\text{H}]\) NMR chemical shifts. This fluorine experienced a drastic upfield shift from -110 ppm in Pd-27 to -144 ppm in Pd-28. Hence, these observations further support the upfield shift observed for Pd-25 with one of the fluorines coordinated to the palladium centre, as seen in Pd-28.

In addition to the NMR spectra, the elemental analysis of Pd-25 also provides additional support for this observation, as tabulated in Table 5.6. It is clear from the data that the analysis figures determined match with the values calculated for the alternative structure of Pd-25. The data from these characterisation techniques verify that Pd-25 adopts this unusual structure both in solid and solution states.
Table 5.6   Elemental analysis data for the expected and observed structure of Pd-25.

<table>
<thead>
<tr>
<th>Structure</th>
<th>Formula</th>
<th>C_{20}H_{10}N_{3}F_{6}Cl_{3}Pd</th>
<th>C_{20}H_{10}N_{3}F_{6}ClPd</th>
<th>Anal. Found (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Anal. Calculated (%)</td>
<td>Anal. Calculated (%)</td>
<td>Anal. Found (%)</td>
</tr>
<tr>
<td>C</td>
<td>38.78</td>
<td>43.80</td>
<td>43.57</td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>1.63</td>
<td>1.84</td>
<td>1.85</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>6.79</td>
<td>7.67</td>
<td>7.72</td>
<td></td>
</tr>
<tr>
<td>Cl</td>
<td>17.19</td>
<td>6.47</td>
<td>6.39</td>
<td></td>
</tr>
<tr>
<td>Pd</td>
<td>17.20</td>
<td>19.42</td>
<td>19.73</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5.20 displays the ORTEP representation of the structure of complex Pd-25. The crystal structure of Pd-25 differs from the other palladium(II)-PEPPSI complexes, in that the two chlorine atoms that are co-ordinated to the palladium centre in the other complexes are replaced by the ortho-fluorines of the N-substituent aromatic groups. It is noticeable that the palladium-carbene (Pd1-C1) bond length of Pd-25 (1.915 Å) is significantly shorter than those of the other palladium(II)-PEPPSI complexes. Typically, the palladium-carbene (Pd1-C1) bond lengths of other complexes are in the range of 1.944 to 1.974 Å.

The Pd-F bond distances in Pd-25, Pd1-F1 and Pd1-F4, have lengths of 1.964(2) and 1.978(2) Å respectively, which are the in the range of typical covalent Pd-F bonds, 1.947 – 2.090 Å. This suggests that the Pd-F bonds in Pd-25 are real covalent bonds, and not just weak interactions. In addition, the carbon-fluorine lengths of the coordinated fluorines (F1 and F4) are relatively shorter (1.314(4) Å) than those of the non-coordinated fluorines (F2, F3, F5 and F6) which have values around 1.360(4) Å.
Figure 5.20  ORTEP representation of the molecular structure of complex Pd-25. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Pd1-C1 1.915(3), Pd1-N3 2.119(2), Pd1-F1 1.964(2), Pd1-F2 1.978(2), F1-C5 1.313(4), F2-C7 1.360(4), F3-C9 1.364(4), F4-C11 1.315(4), F5-C13 1.362(4), F6-C15 1.362(4), C1-Pd-N3 178.1(1) and C11-Pd-C12 175.07(9).

It is very surprising to note that this phenomenon is rare and not seen in the other metal complexes featuring the NHC-5 ligand, such as the gold(I) (Au-5) and rhodium(I) complexes (Rh-25) described in the previous Chapters. A possible explanation for this might be due to the arrangement of the NHC-5 ligand in space. The NHC-5 ligand is flexible to move and rotate in its preferred position and at a certain time, one of the ortho-fluorines might come into close proximity to the palladium centre and make an interaction. Perhaps this conformer or geometry is the most favourable one for this complex and eventually it adopts this geometry. The preparation of Pd-25 has been repeated three times to test the reproducibility of this finding. Indeed, all the characterisation data each time show the same unusual and unique structure of Pd-25. At the time being, a current student in our group is continuing the work by modifying the synthetic route of making Pd-25. Interestingly, by shortening the reaction time from 24 hours to 12 hours resulting in
the formation of mixture between the expected Pd(II) complex of Pd-25 and the observed Pd(0) complex of Pd-25. Attempts to isolate and separate these two complexes are still underway.

A similar metal-fluorine interaction has been reported earlier in the ruthenium(II)-based Hoveyda-Grubbs second generation catalyst, Ru-7.36 It is interesting to note that one of the ortho-fluorines is coordinated to the ruthenium centre, in a similar fashion to what is observed in Pd-25. However, in the case of Ru-7, only one of the ortho-fluorine substituent groups is coordinated to the metal centre, unlike the two ortho-fluorine metal interactions from both substituent groups in Pd-25. This is probably due to the more coordinatively saturated nature of the ruthenium centre due to steric hindrance from the other bulky ligand in Ru-7, which makes the ortho-fluorines of the substituent group in the bulky system orient away from the ruthenium centre. Surprisingly, this ruthenium-fluorine interaction is not seen in the Grubbs second generation catalyst, Ru-6. The presence of bulky ligands, such as tricyclohexylphosphine (PCy₃) may prevent a ruthenium-fluorine interaction due to steric clashes.

Scheme 5.6 The fluorine-ruthenium interaction discovered in Ru-7, which was synthesised from Ru-6.36
Figures 5.21 and 5.22 represent the molecular structures of **Ru-7** and **Pd-28** respectively, showing the metal-fluorine interaction. These two examples are the closest comparison to **Pd-25**.

**Figure 5.21.** ORTEP representation of the molecular structure of complex **Ru-7**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Ruthenium-fluorine interaction is observed, with Ru-F distance around 3.231(1) Å, significantly longer than the Pd-F distance in **Pd-25**. Taken from reference.\(^3\)\(^6\)

**Figure 5.22.** ORTEP representation of the molecular structure of complex **Pd-28**. Thermal ellipsoids are drawn at 50% probability. Hydrogen atoms are omitted for clarity. Pd1-F1 has a distance of 2.408(2) Å, which is well below the sum of the van der Waals radii of the two elements (3.10 Å). The Pd1-F1 and F1-C1 distances (2.408(2) and 1.381(2) Å respectively) in **Pd-28** are considerably longer than the Pd-F and F-C distances in **Pd-25**. Taken from reference.\(^3\)\(^4\)
5.4 Steric Quantification

As described previously in Chapter 3, the steric properties of various NHC ligands and their corresponding metal complexes can be evaluated using percent buried volume (%$V_{\text{bur}}$) figures and steric maps. Surprisingly, there are no steric measurement studies of palladium complexes bearing fluorinated NHC ligands involved so far. Due to this lack of information, it is therefore sensible to quantify the steric bulk of fluorinated NHCs in these systems and understand how the presence of fluorine in the substituent groups affects the steric environment around the palladium centre.

Having successfully prepared a series of palladium-PEPPSI complexes from a series of fluorinated NHC ligands, **Pd-21** to **Pd-25**, their steric parameters were investigated using %$V_{\text{bur}}$ and steric maps. These measurements were obtained using SambVca 2.0 computational tool, developed by Cavallo and co-workers.\footnote{37} Table 5.7 summarises the %$V_{\text{bur}}$ and steric maps of the palladium complexes containing fluorinated NHC ligands, **Pd-21**, **Pd-23**, **Pd-24**, **Pd-25** and the non-fluorinated congeners, **Pd-13**, **Pd-14**, **Pd-15** and **Pd-19**.

According to the %$V_{\text{bur}}$ values in Table 5.7, **Pd-25** has the highest value, 46.4%, indicating that this complex is the most bulky as compared with the other complexes. However, it is inappropriate to compare **Pd-25**, since its structure is different due to the fluorine coordination to the palladium centre. Generally, the steric bulk of palladium complexes containing fluorinated NHC ligands are comparable with those of the non-fluorinated analogues. Figure 5.23 represents the %$V_{\text{bur}}$ values of some known palladium(II)-PEPPSI complexes and the new analogues prepared in this study.
Table 5.7 Summary of $\% V_{bur}$ and steric maps for palladium complexes bearing different NHC ligands.

<table>
<thead>
<tr>
<th>Palladium complex</th>
<th>$% V_{bur}$</th>
<th>Steric map</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-21</td>
<td>34.0</td>
<td><img src="image1" alt="Steric map Pd-21" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 47.3$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 19.8$</td>
</tr>
<tr>
<td>Pd-23</td>
<td>36.3</td>
<td><img src="image2" alt="Steric map Pd-23" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 48.7$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 24.0$</td>
</tr>
<tr>
<td>Pd-24</td>
<td>34.7</td>
<td><img src="image3" alt="Steric map Pd-24" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 47.5$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 20.5$</td>
</tr>
<tr>
<td>Pd-25</td>
<td>46.4</td>
<td><img src="image4" alt="Steric map Pd-25" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 29.0$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$% V_{bur} = 64.2$</td>
</tr>
<tr>
<td>Palladium complex</td>
<td>% $V_{\text{bur}}$</td>
<td>Steric map</td>
</tr>
<tr>
<td>-------------------</td>
<td>-------------------</td>
<td>------------</td>
</tr>
<tr>
<td><strong>Pd-13</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34.8</td>
<td><img src="image" alt="Steric map for Pd-13" /></td>
</tr>
<tr>
<td><img src="image" alt="Image of Pd-13" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pd-14</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34.9</td>
<td><img src="image" alt="Steric map for Pd-14" /></td>
</tr>
<tr>
<td><img src="image" alt="Image of Pd-14" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pd-15</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
<td>35.4</td>
<td><img src="image" alt="Steric map for Pd-15" /></td>
</tr>
<tr>
<td><img src="image" alt="Image of Pd-15" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pd-19</strong>&lt;sup&gt;b&lt;/sup&gt;</td>
<td>43.5</td>
<td><img src="image" alt="Steric map for Pd-19" /></td>
</tr>
<tr>
<td><img src="image" alt="Image of Pd-19" /></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Taken from Organ et al. <sup>21</sup>  
<sup>b</sup> Taken from Nolan et al. <sup>33</sup>
Figure 5.23  Summary of percent buried volumes for palladium-PEPPSI type complexes.
### 5.5 Catalytic Activity

As mentioned in the introduction section, modification of the steric and electronic properties of NHC ligands may influence the catalytic activity of the corresponding palladium-PEPPSI complexes. The current study has found that the number and position of fluorine atoms in the NHC ligands have an impact on the steric and electronic natures of the new palladium-PEPPSI complexes. These findings have important implications for investigating the catalytic activity of these complexes in various palladium-catalysed cross-coupling reactions.

The catalytic activity of the new palladium-PEPPSI complexes containing fluorinated NHC ligands, **Pd-21 to Pd-25** were investigated in the Suzuki-Miyaura coupling reaction between phenylboronic acid and 4-iodotoluene, alongside the non-fluorinated analogues, **Pd-14 and Pd-26** for comparison. A 1 mmol solution of 4-iodotoluene and 1.1 mmol of phenylboronic acid were reacted in dioxane at 80°C in the presence of 1 mol % catalyst, as illustrated in Scheme 5.6. The percentage conversion after 24 hours was monitored by \(^1\)H NMR analysis of the crude mixture based on 4-iodotoluene conversion. The percentage conversions were measured by comparing the methyl proton signal of 4-iodotoluene at 2.22 ppm with the methyl proton signal of the corresponding product, 4-methyl-biphenyl at 2.38 ppm and averaged over three runs.

![Scheme 5.6 Palladium-catalysed Suzuki-Miyaura coupling reaction of 4-iodotoluene and phenylboronic acid.](image)

**Scheme 5.6** Palladium-catalysed Suzuki-Miyaura coupling reaction of 4-iodotoluen and phenylboronic acid.
The proposed mechanism of this Suzuki-Miyaura reaction is illustrated in Figure 5.24. The active species in the catalytic cycle of most palladium-catalysed cross-coupling reaction is a Pd(0) species. Organ and co-workers proposed that the auxiliary ligand plays an important role in generating the Pd(0) active species, and 3-chloropyridine was proven to be an excellent ligand for this role. As described previously in the introduction section, electron donating NHC ligands aid the oxidative addition from species A to B, whilst bulky NHC ligands enhance the reductive elimination from species D to A. The rate of these processes would provide more information on the catalytic activities of the palladium complexes,
which can be reflected from the percentage conversions of 4-iodotoluene and phenylboronic acid to 4-phenyltoluene.

Table 5.8  Percentage conversion of 4-iodotoluene and phenylboronic acid to 4-phenyltoluene, catalysed by various palladium-PEPPSI complexes.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Conversion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Pd-21</td>
<td>75</td>
</tr>
<tr>
<td>2</td>
<td>Pd-22</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>Pd-23</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>Pd-24</td>
<td>82</td>
</tr>
<tr>
<td>5</td>
<td>Pd-25</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>Pd-26</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>Pd-14</td>
<td>45</td>
</tr>
</tbody>
</table>

\(^{a}\) Reaction conditions: 1 mmol solution of 4-iodotoluene, 1.1 mmol of phenylboronic acid and 1 mol % catalyst were reacted in dioxane at 80°C over 24 hours.

\(^{b}\) \(^{1}\)H NMR analysis of crude reaction mixture based on 4-iodotoluene conversion, averaged value over three runs.

According to the results in Table 5.8, the new palladium-PEPPSI complexes containing fluorinated NHC ligands (Pd-21 to Pd-25) gave higher conversions than those with the non-fluorinated analogues (Pd-26 and Pd-14). Complex Pd-25 is the best catalyst amongst the PEPPSI complexes employed in this specific reaction, with conversion of 90% under non-optimised conditions. The exceptional higher performance of Pd-25 may be due to its unique structure. As described previously, the active species in the catalytic cycle of Suzuki-Miyaura reaction is the Pd(0)-species A (refer to Figure 5.20). The activation of this species occurs when the 3-chloropyridyl ligand leaves the Pd(II) complex. All of the PEPPSI complexes need to undergo this activation process before taking part in the catalytic cycle, except Pd-25. This is because Pd-25 already exists as a Pd(0) complex, due to its unique cyclometallated structure, in which the two chlorides have been replaced by the ortho-fluorines of the NHC ligand. As a result, the initiation time for Pd-25 in this catalytic cycle is shortened and this may be the reason for higher conversion of product after 24 hours than those of other palladium(II)-PEPPSI complexes.
The second highest conversion at 85% is achieved by using Pd-23. It is interesting to note that both of the complexes Pd-23 and Pd-25 resulting in the highest conversions, possess fluorine in the ortho positions of the substituent groups of the NHC ligands, NHC-3 and NHC-5 respectively. These findings are consistent with those described in Chapters 3 and 4, in which gold and rhodium complexes bearing NHC-3 and NHC-5 ligands have higher catalytic activities than the other fluorinated NHC ligands, NHC-1, NHC-2 and NHC-4.

To determine whether there are electronic effects that influence the catalytic activity of these complexes, a plot of percentage conversion of 4-iodotoluene against $^{77}\text{Se} \text{NMR}$ chemical shifts of NHC selenium adduct is displayed in Figure 5.25.

![Figure 5.25](image.png)

Based on the graph above, the results suggest that there is a correlation between the π-accepting ability of the NHCs, as measured by the $^{77}\text{Se} \text{NMR}$ chemical shift, and the catalytic activity of these palladium-PEPPSI complexes. Higher $^{77}\text{Se} \text{NMR}$ chemical shifts of the selenium adducts indicates greater
π-accepting ability of the NHC ligands. The trend observed in Figure 5.21 illustrates that the stronger π-accepting ability of NHC ligands enhances the complex activity in the Suzuki-Miyaura coupling reaction between phenylboronic acid and 4-iodotoluene. A possible explanation for this might be that the presence of fluorine reduces the electron donating properties of NHC ligands, by pulling the electron density away from the carbene. As a result, a less donating NHC ligand enhances the reductive elimination step of the catalytic cycle, which leads to higher conversions of the product.

As previously mentioned in Chapter 2, the electronic donating properties of NHC ligands are based on the overall net contribution from σ and π components. Investigation of the 77Se NMR chemical shifts reveals that the fluorinated NHC ligands have stronger π-accepting abilities than the non-fluorinated derivatives, IMes and IPh. In addition, the inclusion of fluorine atoms in NHC ligands may also reduce to some extent the σ-donor strength of NHC ligands. Overall, the donating ability of NHC ligands is weakened and this in turn is expected to enhance the catalytic activity of the resulting complexes by increasing the rate of reductive elimination in the catalytic cycle.

In term of the steric properties, the inclusion of sterically demanding NHC ligands is thought to enhance the activity of the palladium-PEPPSI complexes by increasing the rate of the reductive elimination. In order to investigate these effects, the steric parameters of palladium complexes that have been quantified earlier were compared with the respective percentage conversions. A graph showing the relationship between the percent buried volume (% $V_{\text{bur}}$) and percentage conversion is depicted in Figure 5.26.
According to the Figure 5.26, palladium-PEPPSI complexes bearing more sterically demanding NHCs generally have higher observed catalytic activities than those of the less bulky NHCs. Pd-25 is the most bulky and has the highest catalytic activity of 90%. In this case, it would not be fair to compare Pd-25 with other complexes, since Pd-25 has a different structure from the other palladium(II)-PEPPSI complexes. In this study, there is a correlation observed for those palladium(II)-PEPPSI complexes containing fluorinated NHC ligands (Pd-21 to Pd-24), in which the percent buried volume ($V_{\text{bur}}$) is related to the percentage conversion. In the case of Pd-21, Pd-24 and Pd-23, as the steric bulk increases (34.0, 34.7 and 36.3% respectively), the percentage conversions also increase (75, 82 and 85% respectively). This may indicate that there is an effect of changing the steric bulk of NHC ligands on the catalytic activities of the corresponding palladium-PEPPSI complexes. Surprisingly, Pd-14 with a higher $V_{\text{bur}}$ than Pd-21 has a lower catalytic activity at just 30% conversion. A possible explanation for this might be that the
catalytic activities of the palladium-PEPPSI complexes described in this study were affected by both electronic and steric properties of NHC ligands. For example, although we might expect Pd-14 to perform better than Pd-21 based on their steric bulk, the electronic properties of the NHC ligands may contribute to enhance the catalytic activity of Pd-21 over Pd-14.

A multiple linear regression analysis was used to study the correlation between the steric and electronic effects of the NHC ligands on the catalytic activities of the palladium complexes involved in this work. The analysis was performed using Microsoft Excel and the data are tabulated in Table 5.9. The values of $\% V_{\text{bur}}$ and $\delta^{77}\text{Se}$ were used in the multiple linear regression analysis to fit the conversions using the equation below.

$$(\delta^{77}\text{Se} \times a) + (% V_{\text{bur}} \times b) - 14.2755 = \text{calculated } % \text{ conversion}$$

where $a = 0.8582$ and $b = 1.1044$

<table>
<thead>
<tr>
<th>Complex</th>
<th>NHC</th>
<th>$\delta^{77}\text{Se}$</th>
<th>$% V_{\text{bur}}$</th>
<th>Observed $%$ conversion</th>
<th>Calculated $%$ conversion</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pd-21</td>
<td>NHC-1</td>
<td>60.7</td>
<td>34.0</td>
<td>75</td>
<td>75.37</td>
<td>-0.37</td>
</tr>
<tr>
<td>Pd-23</td>
<td>NHC-3</td>
<td>68.3</td>
<td>36.3</td>
<td>85</td>
<td>84.43</td>
<td>0.57</td>
</tr>
<tr>
<td>Pd-24</td>
<td>NHC-4</td>
<td>67.4</td>
<td>34.7</td>
<td>82</td>
<td>81.89</td>
<td>0.11</td>
</tr>
<tr>
<td>Pd-25</td>
<td>NHC-5</td>
<td>73.0</td>
<td>38.0</td>
<td>90</td>
<td>90.34</td>
<td>-0.34</td>
</tr>
<tr>
<td>Pd-14</td>
<td>IMes</td>
<td>26.7</td>
<td>32.9</td>
<td>45</td>
<td>44.97</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Table 5.9 Multiple linear regression analysis calculated $\%$ conversion of 4-iodotoluene versus observed $\%$ conversion of 4-iodotoluene.
Based on the plot in Figure 5.27, there is a good correlation between the observed percentage conversions and a combination of steric and electronic factors. These findings suggest that the presence of fluorine influences the electronic and steric properties of NHC ligands and therefore the catalytic activities of the corresponding complexes.

5.6 Summary

A series of air and moisture-stable palladium(II)-PEPPSI complexes featuring fluorinated NHC ligands have been prepared and characterised. One of these complexes, Pd-25 features a unique structure with palladium-fluorine interactions, forming a cyclometallated complex which has never been seen before in the family of PEPPSI complexes. Comparison of X-ray crystal structures of these complexes reveal that the palladium-carbene bond lengths are shorter than those containing non-fluorinated NHC ligands, Pd-13, Pd-14, Pd-15 and Pd-19. These findings are consistent with those found in the gold(I) and rhodium(I) complexes incorporating
fluorinated NHC ligands described in Chapters 3 and 4. The shorter metal-carbene bond length of the fluorinated NHC ligands may be due to the stronger π-accepting ability than those of the non-fluorinated congeners. The percent buried volume (% $V_{\text{bur}}$) and steric maps were utilised to measure the steric parameters of these palladium complexes. It was discovered that both the number and position of fluorine atoms in the substituent groups affected their steric properties, as indicated by the percent buried volume (% $V_{\text{bur}}$). All of these new palladium(II)-PEPPSI complexes proved to be highly active in the Suzuki-Miyaura coupling reaction between phenylboronic acid and 4-iodotoluene and outperform the non-fluorinated congeners, Pd-14 and Pd-26. These results are similar to those found in the catalytic studies of rhodium(I) complexes described in the previous Chapter. This work provides additional evidence that the number and position of fluorine in the aromatic substituent group of NHC ligands have significant impacts on the catalytic activity of the corresponding metal complexes.

5.7 Experimental

5.7.1 General considerations

Unless otherwise stated all reactions were carried out in air. The precursors to NHC-1, NHC-2, NHC-3, NHC-4, NHC-5, IPh and IMes were prepared according to the description in Chapter 2. Palladium dichloride, potassium hydroxide, potassium carbonate, 3-chloropyridine, phenylboronic acid, 4-iodotoluene and 1,4-dioxane were purchased from Sigma Aldrich. $^1$H and $^{19}$F$\{^{1}$H$\}$ NMR spectra were recorded using a Bruker Avance spectrometer at 400 and 376 MHz respectively, and were referenced to external TMS and CFCl$_3$. $^{13}$C$\{^{1}$H$\}$ NMR spectra were recorded using a
Bruker Avance spectrometer at 100 MHz. Chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) are reported in Hertz (Hz). The splitting patterns are labelled as follows: s = singlet, d = doublet, t = triplet, q = quartet and m = multiplet. Elemental analyses of carbon, hydrogen and nitrogen were performed on a Perkin Elmer PE 2400 combustion elemental analyser. The elemental analysis of palladium was performed by heating the complex in an acid solution at high temperature until the complex decomposed and analysed using the Thermo Scientific iCAP DUO 6300 ICP-OES instrument by Mr Martin Jennings at the School of Chemistry, The University of Manchester.

5.7.2 X-ray diffraction studies

Crystallographic data for Pd-21, Pd-23, Pd-24 and Pd-25 were collected with an Agilent SuperNova diffractometer using Mo Kα radiation (λ = 0.71073 Å). All the raw data frames were reduced and corrections were applied for Lorentz, polarisation and absorption using the multi-scan methods with CrysAlisPro. The X-ray structural data were solved by direct methods, with full-matrix least-squares refinement of F2 using: Olex2, ShelX and ShelXTL programs. Ortep3 was used to generate the graphical representations and Mercury and Ploton were used to investigate and report the structures. All non-H atoms were modelled with anisotropic displacement parameters, H-atoms were placed in idealised positions and refined with isotropic thermal parameters.
5.7.3 Synthetic procedure

5.7.3.1 Dichloro(3-chloropyridyl)[1,3-bis(4-fluorophenyl)imidazol-2-ylidene] palladium(II): **Pd-21**

A mixture of **NHC-1** precursor (189 mg, 0.55 mmol), PdCl₂ (88 mg, 0.50 mmol) and K₂CO₃ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with vigorous stirring at 80°C for 24 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents by rotary evaporator, the crude product was recrystallized from a dichloromethane-pentane mixture (1 mL : 20 mL ratio) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was finally obtained after filtration and was collected as a yellow solid (219 mg, 80%). ¹H NMR (CDCl₃) δ (ppm): 8.75 (d, J = 2.3 Hz, 1H, Hₚyr), 8.65 (d, J = 5.6 Hz, 1H, Hₚyr), 8.62 (s, 1H, Hₚyr) 8.53 (d, J = 4.6 Hz, 1H, Hₚyr), 8.05 (m, 4H, Hₚhenyl), 7.71 (s, 2H, NCHCHN), 7.31 (m, 4H, Hₚhenyl). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 163.88 (d, J_C-F = 245.3 Hz, C_F), 161.40 155.38, 153.54, 149.86, 137.52, 135.77, 128.77, 124.41, 124.01, 116.16. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -111.48 (s, 2F, F). Anal. Calcd for C₂₀H₁₄N₃F₂Cl₃Pd (%): C, 43.88, H, 2.58, N, 7.68, Pd, 19.46. Found: C, 43.50, H, 2.50, N, 7.65, Pd, 19.49.
5.7.3.2 Dichloro(3-chloropyridyl)[1,3-bis(2,4-difluorophenyl)imidazol-2-ylidene] palladium(II): Pd-22

A mixture of NHC-2 precursor (209 mg, 0.55 mmol), PdCl\(_2\) (88 mg, 0.50 mmol) and K\(_2\)CO\(_3\) (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with stirring at 80°C for 24 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvent, the crude product was recrystallized from a dichloromethane-pentane mixture (1 mL : 20 mL ratio) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was finally obtained after filtration and was collected as a yellow solid (227 mg, 78%). \(^1\)H NMR (CDCl\(_3\)) δ (ppm): 8.73 (d, \(J = 2.3\) Hz, 1H, H\(_{Pyr}\)), 8.63 (d, \(J = 5.6\) Hz, 1H, H\(_{Pyr}\)), 8.43 - 8.53 (m, 3H overlapping of 1H, H\(_{Pyr}\) and 2H, H\(_{phenyl}\) ) 7.72 (d, \(J = 7.1\) Hz, 1H, H\(_{Pyr}\)), 7.36 (s, 2H, NCHCHN), 7.08-7.25 (m, 4H overlapping of 2H signals, H\(_{phenyl}\)). \(^{13}\)C\(^{1}\)H) NMR (CDCl\(_3\)) δ (ppm): 164.21 (d, \(J_{C-F} = 250.9\) Hz, C\(_f\)), 161.58 (d, \(J_{C-F} = 249.3\) Hz, C\(_f\)) 157.30, 155.18, 153.24, 148.86, 136.52, 134.77, 127.57, 126.53, 123.41, 123.01, 115.16. \(^{19}\)F\(^{1}\)H) NMR (CDCl\(_3\)) δ (ppm): -106.06 (d, 2F, \(4J_{FF} = 8.6\) Hz, F\(_{para}\)), -117.09 (d, 2F, \(4J_{FF} = 8.6\) Hz, F\(_{ortho}\)). Anal. Calcd for C\(_{20}\)H\(_{12}\)N\(_3\)F\(_4\)Cl\(_3\)Pd (%): C, 41.18, H, 2.07, N, 7.21, Pd, 18.26. Found: C, 41.50, H, 2.10, N, 7.35, Pd, 18.49.
A mixture of NHC-3 precursor (209 mg, 0.55 mmol), PdCl$_2$ (88 mg, 0.50 mmol) and K$_2$CO$_3$ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with vigorous stirring at 80°C for 24 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents by rotary evaporator, the crude product was recrystallized from a dichloromethane-pentane mixture (1 mL : 20 mL ratio) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was finally obtained after filtration and was collected as a yellow solid (239 mg, 82%). $^1$H NMR (CDCl$_3$) $\delta$ (ppm): 8.73 (d, $J$ = 2.3 Hz, 1H, H$_{Pyr}$), 8.63 (d, $J$ = 5.6 Hz, 1H, H$_{Pyr}$), 8.43 – 8.53 (m, 5H overlapping of 1H, H$_{Pyr}$ and 4H, H$_{phenyl}$) 7.72 (d, $J$ = 7.1 Hz, 1H, H$_{Pyr}$), 7.36 (s, 2H, NCHCHN), 7.25 (m, 2H, H$_{phenyl}$). $^{13}$C($^1$H) NMR (CDCl$_3$) $\delta$ (ppm): 166.88 (d, $J_{C-F} = 251.3$ Hz, C$_{t}$), 162.40, 157.38, 155.54, 149.96, 138.52, 136.71, 129.87, 124.51, 124.05, 117.16. $^{19}$F($^1$H) NMR (CDCl$_3$) $\delta$ (ppm): -118.67 (s, 4F, F). Anal. Calcd for C$_{20}$H$_{12}$N$_3$F$_4$Cl$_3$Pd (%): C, 41.18, H, 2.07, N, 7.21, Pd, 18.26. Found: C, 41.30, H, 2.11, N, 7.25, Pd, 18.39.
A mixture of NHC-4 precursor (229 mg, 0.55 mmol), PdCl₂ (88 mg, 0.50 mmol) and K₂CO₃ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was stirring at 80°C for 16 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents, the crude product was recrystallized from a dichloromethane/pentane mixture (1 mL/20 mL) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was finally obtained after filtration and was collected as a yellow solid (263 mg, 85%). ¹H NMR (CDCl₃) δ (ppm): 8.91 (d, J = 2.7 Hz, 1H, H_Pyr), 8.82 (d, J = 6.3 Hz, 1H, H_Pyr), 8.00 (s, 2H, NCHCHN), 7.93 (d, J = 8.1 Hz, 1H, H_Pyr), 7.51 (dd, J = 8.1 Hz, J = 6.3 Hz, 1H, H_Pyr), 6.62 (dt, J = 10.9 Hz, J = 2.3 Hz, 2H, H_phenyl), 6.31 (m, J = 10.9 Hz, J = 2.3 Hz 2H, H_phenyl). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 165.10 (d, J_{C-F} = 245.2 Hz, C_F), 159.61 (d, J_{C-F} = 249.3 Hz, C_F), 156.39 (d, J_{C-F} = 247.1 Hz, C_F), 153.94, 151.02, 147.08, 145.77, 138.64, 133.11, 125.17, 120.39, 103.58, 92.28. ¹⁹F{¹H} NMR (CDCl₃) δ (ppm): -122.58 (dd, J_{FF} = 14.3 Hz, J_{FF} = 4.3 Hz, 2F, F_{ortho}), -129.04 (dd, J_{FF} = 22.1 Hz, J_{FF} = 4.3 Hz, 2F, F_{meta}), -135.50 (dd, J_{FF} = 22.1 Hz, J_{FF} = 14.3 Hz, 2F, F_{para}).

A mixture of NHC-5 precursor (229 mg, 0.55 mmol), PdCl₂ (88 mg, 0.50 mmol) and K₂CO₃ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with vigorous stirring at 80°C for 24 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents by rotary evaporator, the crude product was recrystallized from a dichloromethane/pentane mixture (1 mL/20 mL) to remove completely unreacted 3-chloropyridine and precipitate out the product. The pure complex was finally obtained after filtration and was collected as a yellow solid (206 mg, 75%).

\(^1\)H NMR (CDCl₃) δ (ppm): 8.81 (s, 1H, H\textsubscript{Pyr}), 8.73 (d, \(J = 4.9\) Hz, 1H, H\textsubscript{Pyr}), 7.91 (s, 2H, NCHCHN), 7.83 (d, \(J = 8.5\) Hz, 1H, H\textsubscript{Pyr}), 7.42 (t, \(J = 6.2\) Hz, 1H, H\textsubscript{Pyr}), 6.50 (d, \(J = 10.5\) Hz, 2H, H\textsubscript{phenyl}), 6.21 (qq, \(J = 8.5\) Hz, \(J = 2.7\) Hz, 2H, H\textsubscript{phenyl}).

\(^{13}\)C\textsubscript{\textsubscript{\textsuperscript{1}H}} NMR (CDCl₃) δ (ppm): 168.10 (d, \(J_{C-F} = 248.5\) Hz, C\textsubscript{F}), 158.61 (d, \(J_{C-F} = 251.3\) Hz, C\textsubscript{F}), 156.35, 154.94, 151.06, 148.08, 145.67, 138.64, 132.11, 126.17, 120.35, 104.58, 92.18. \(^{19}\)F\textsubscript{\textsubscript{\textsuperscript{1}H}} NMR (CDCl₃) δ (ppm): -106.09 (s, 2F, F\textsubscript{para}), -115.57 (s, 2F, F\textsubscript{meta}), -138.50 (s, 2F, F\textsubscript{ortho}).

Anal. Calcd for C\textsubscript{20}H\textsubscript{10}N\textsubscript{3}F\textsubscript{6}ClPd (%): C, 43.80, H, 1.84, N, 7.67, Cl, 6.47, Pd, 19.42. Found: C, 43.57, H, 1.85, N, 7.72, Cl, 6.39, Pd, 19.73.
**5.7.3.6 Dichloro(3-chloropyridyl)[1,3-bis(phenyl)imidazol-2-ylidene] palladium(II): Pd-26**

A mixture of IPh precursor (169 mg, 0.55 mmol), PdCl₂ (88 mg, 0.50 mmol) and K₂CO₃ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with vigorous stirring at 80°C for 24 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents by rotary evaporator, the crude product was recrystallized from a dichloromethane-pentane mixture (1 mL : 20 mL ratio) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was obtained after filtration and was collected as a yellow solid (199 mg, 78%). ¹H NMR (CDCl₃) δ (ppm): 8.61 (s, 1H, H_Pyr), 8.53 (d, J = 1.9 Hz, 1H, H_Pyr), 7.81 (s, 2H, NCHCHN), 7.53 (d, J = 5.7 Hz, 1H, H_Pyr), 7.42 (d, J = 8.2 Hz, 1H, H_Pyr), 6.90 (m, 2H, H phenyl), 6.71 (m, 2H, H phenyl), 6.55 (m, 2H, H phenyl). ¹³C{¹H} NMR (CDCl₃) δ (ppm): 151.10, 150.61, 146.39, 143.94, 141.02, 137.08, 135.77, 133.11, 125.17, 125.33, 120.39. Anal. Calcd for C₂₀H₁₆N₃Cl₃Pd (%): C, 46.97, H, 3.16, N, 8.22, Pd, 20.83. Found: C, 46.77, H, 3.11, N, 8.20, Pd, 20.77.
5.7.3.7  Dichloro(3-chloropyridyl)[1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene] palladium(II): Pd-14

A mixture of IMes precursor (216 mg, 0.55 mmol), PdCl₂ (88 mg, 0.50 mmol) and K₂CO₃ (345 mg, 2.50 mmol) in 3-chloropyridine (5.0 mL) was heated with vigorous stirring at 80°C for 16 hours. After this time, the mixture was allowed to cool to room temperature and dichloromethane (20 mL) was added. Subsequently, the mixture was passed through a short pad of silica covered with a pad of celite eluting with dichloromethane until the product was completely extracted. After evaporation of the solvents by rotary evaporator, the crude product was recrystallized from a dichloromethane-pentane mixture (1 mL : 20 mL ratio) to remove unreacted 3-chloropyridine and precipitate out the product. The pure complex was obtained after filtration and was collected as a yellow solid (223 mg, 75%). The experimental data are consistent with those in the literature.²¹

¹H NMR (CDCl₃): δ (ppm): 8.60 (d, J = 1.9 Hz, 1H, H_Pyr), 8.52 (d, J = 5.8 Hz, 1H, H_Pyr), 7.58 (d, J = 8.2 Hz, 1H, H_Pyr), 7.10-7.08 (m, 7H), 2.40 (s, 6H, H_methyl), 2.38 (s, 12H, H_methyl). ¹³C(¹H) NMR (CDCl₃) δ (ppm): 151.2, 150.5, 149.5, 139.3, 137.5, 136.3, 135.0, 131.9, 129.4, 124.3, 124.3, 21.2, 19.1. Anal. Calcd. for C₂₆H₂₈N₃Cl₃Pd: C, 52.46, H, 4.74, N, 7.06, Pd, 17.89. Found: C, 52.70, H, 4.90, N, 7.19, Pd, 17.60.
5.7.4 **Suzuki-Miyaura catalytic testing procedure**

A mixture of phenylboronic acid (100 mg, 0.82 mmol, 1.2 equiv.) and 4-iodotoluene (149 mg, 0.68 mmol, 1.0 equiv.) were dissolved in dioxane (6 mL). Potassium hydroxide (114 mg, 2.03 mmol, 3 equiv.) and PEPPSI complex (1 mol %) were added and the reaction mixture was stirred at 80°C. After 24 hours, the reaction mixture was cooled to room temperature and subsequently diluted in diethyl ether (20 mL) and filtered through a short pad of silica. The solvent was removed *in vacuo* and the conversion determined by $^1$H NMR spectroscopy. The experiments were repeated and the conversions were averaged over three runs. The product was purified by column chromatography on silica gel using hexane/EtOAc eluent. The solvents were removed *in vacuo* to give a purified product, 4-methyl-biphenyl. $^1$H NMR (CDCl$_3$) $\delta$: 7.58 (d, $J = 7.3$ Hz, 2H), 7.48 (d, $J = 8.1$ Hz, 2H), 7.41 (t, $J = 7.6$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.23 (d, $J = 8.1$ Hz, 2H), 2.38 (s, 3H). $^{13}$C($^1$H) NMR (CDCl$_3$) $\delta$: 141.2, 138.4, 137.0, 129.5, 128.7, 127.0, 21.1.

5.8 **References**


Chapter 6: Conclusion and Future Work
This thesis describes the synthesis, characterisation and catalytic activity of new gold, rhodium and palladium complexes featuring fluorinated NHC ligands. A series of fluorinated NHC ligand precursors, \textbf{NHC-1, NHC-2, NHC-3, NHC-4} and \textbf{NHC-5} have been successfully prepared and characterised. The corresponding selenium adducts, \textbf{Se(NHC-1), Se(NHC-2), Se(NHC-3), Se(NHC-4) and Se(NHC-5)} have been synthesised in order to investigate the electronic properties of the fluorinated NHC ligands. Comparison studies of the $^{77}$SeNMR chemical shifts reveal that the fluorinated NHC ligands have stronger $\pi$-accepting abilities than the non-fluorinated counterparts IMes and IPh. Generally, the $\pi$-accepting ability of NHC ligands increases as the fluorine content of the aromatic substituent groups increase. Compounds \textbf{NHC-3} and \textbf{NHC-5} with fluorines in the \textit{ortho} position have the highest $\pi$-accepting ability amongst the fluorinated NHC ligands. These findings suggest that the number and the position of fluorines within the NHC ligands have profound effects on the electronic properties of the NHC ligands. The results from this work provide evidence that the inclusion of fluorine in the nitrogen substituent groups can improve the $\pi$-acceptor strength of NHC ligands.

Further work is required to assess the electronic properties of the fluorinated NHC ligands prepared in this work. As described in Chapter 2, the IR stretching frequencies of carbonyls, $\nu_{\text{CO}}$ in transition metal NHC carbonyl complexes can be utilised to determine the overall electron donating properties of NHC ligands. Hence, a series of [IrCl(CO)$_2$(NHC)] or [RhCl(CO)$_2$(NHC)] type complexes containing the fluorinated NHC ligands could be prepared for this purpose. The $\nu_{\text{CO}}$ values for dicarbonyl complexes of \textbf{NHC-1} to \textbf{NHC-5} can be compared with those of the non-fluorinated analogues, such as IMes, IPh and IPr and this will provide more
information concerning how the presence of fluorine affects the electronic character of the NHC ligands.

As shown by the $^{77}$SeNMR chemical shifts of NHC-1 to NHC-5, the substitution pattern of fluorines in the substituent groups contributes to variation of the $\pi$-acceptor strengths of these ligands. It would be interesting to vary the substitution pattern of the fluorinated groups in NHC ligands further. There are many ways to achieve this, such as preparing unsymmetric NHC ligands, introducing a spacer group between the nitrogen and the aromatic substituent groups or changing the substituent groups from aromatic rings to an alkyl group chain. In addition, substituent groups can be introduced to the heterocyclic backbone by replacing the hydrogens or adding hydrogens to the backbone to form the saturated NHC (imidazolidine) as these may affect the electronic properties of NHC more drastically. Some possibilities are shown in Figure 6.1 below.

Figure 6.1  Variation of fluorinated NHC ligands that can be prepared.
In Chapter 3, the preparation of gold(I) complexes of the fluorinated NHC ligands, Au-1, Au-2, Au-3, Au-4 and Au-5, has been achieved in good yields via transmetallation of the corresponding silver NHC transfer agent and chloro(dimethylsulfide)gold(I). The new complexes have been fully characterised by multinuclear NMR spectroscopy, elemental analysis and single crystal X-ray diffraction studies. The crystal structures of Au-1, Au-2 and Au-4 reveal that the gold-carbene bond lengths are shorter than those of the common non-fluorinated derivatives, [AuCl(IMes)] and [AuCl(IPr)]. This may be due to the stronger π-accepting ability of the fluorinated NHC ligands than the non-fluorinated congeners, which increases the strength of the gold-carbene bond, leading to shorter bond lengths. The steric bulk of the gold(I) complexes featuring fluorinated NHC ligands have been quantified using the percent buried volume, % $V_{bur}$ and steric map techniques. Comparative studies of these steric parameters have shown that the fluorinated NHC ligands are less sterically bulky than most of the common non-fluorinated analogues.

The gold(I) complexes Au-1, Au-2, Au-3, Au-4 and Au-5 were employed in the $A^3$ coupling reaction of benzaldehyde, dibenzylamine and phenylacetylene, alongside the non-fluorinated derivatives, [AuCl(IMes)] and [AuCl(IPh)] for comparison studies. Au-5 and [AuCl(IMes)] were found to be the best catalysts in this reaction. Amongst the gold(I) complexes bearing fluorinated NHC ligands, those with stronger π-accepting ability have higher catalytic activities than those with weaker π-accepting ability. Consideration of the steric properties reveal that gold complexes containing more bulky NHC ligands are more efficient catalysts than those with less bulky NHC ligands. Further work needs to be done to investigate the
catalytic activity of the gold(I) complexes bearing fluorinated NHC ligands in different catalytic reactions, such as hydroamination, cyclic isomerisation and allylic rearrangements. This will provide more evidence whether there are any steric or electronic effects of NHC ligands that may be associated with the catalytic activity of these complexes.

In Chapter 4, novel rhodium(I) complexes bearing a series of fluorinated NHC ligands, Rh-21, Rh-22, Rh-23, Rh-24 and Rh-25 that have been successfully prepared and characterised by multinuclear NMR spectroscopies, elemental analysis and single crystal X-ray diffraction studies are reported. The analysis of the crystal structures of Rh-21, Rh-22, Rh-23 and Rh-25 reveal that the rhodium-carbene bond lengths are shorter than those of the common non-fluorinated derivatives, Rh-26 and Rh-27. This may be due to the stronger π-accepting ability of the fluorinated NHC ligands which results in stronger and shorter rhodium-carbene bond. The steric parameters of the rhodium(I) complexes featuring fluorinated NHC ligands have been quantified using the percent buried volume, % \( V_{\text{bur}} \) and steric map techniques. Comparative studies of these steric parameters have shown that the fluorinated NHC ligands are more bulky than most of the common non-fluorinated analogues. Amongst Rh-21 to Rh-25, the steric bulk increases in the order of increasing fluorine content in the NHC ligands, similar to that which was observed in the gold complexes described in Chapter 3.

The catalytic activities of Rh-21, Rh-22, Rh-23, Rh-24 and Rh-25 in the transfer hydrogenation of acetophenone to 1-phenylethanol were superior to the non-fluorinated derivatives, Rh-26 and Rh-27. The weaker donor strength and
stronger π-accepting ability of the fluorinated NHC ligands may be responsible for the high catalytic activity, by reducing the activation time and accelerating the catalytic reaction. Both steric and electronic effects of these NHC ligands influence the catalytic reaction considerably. Further research is needed to determine whether fluorine containing NHC ligands and their metal complexes offer similar advantages in other catalytic systems, such as hydrosilylation, hydroformylation and cyclisation of alkynes.

Chapter 5 presents the synthesis of new palladium(II) complexes featuring fluorinated NHC ligands, Pd-21, Pd-22, Pd-23, Pd-24 and palladium(0) complex Pd-25. The complexes have been fully characterised by multinuclear NMR spectroscopies, elemental analysis and single crystal X-ray diffraction studies. Unexpectedly, the structure of Pd-25 is unique, where two of the fluorine atoms are coordinated to the palladium centre, forming a cyclometallated palladium(0) complex, which has not been seen before in the family of palladium(II)-PEPPSI complexes. X-ray diffraction studies of Pd-21, Pd-23, Pd-24 and Pd-25 reveal more conventional structures with palladium-carbene bond lengths that are shorter than those of the common non-fluorinated derivatives, Pd-13, Pd-14, Pd-15 and Pd-19. This is consistent with the findings from Chapters 3 and 4, where both gold and rhodium complexes bearing fluorinated NHC ligands have shorter metal-carbene bond distance than those containing non-fluorinated NHC ligands.

According to the results obtained from the investigation of the 77Se NMR chemical shifts of selenium-NHC adducts in Chapter 2, the fluorinated NHC ligands have better π-accepting abilities than the non-fluorinated derivatives. The stronger
π-accepting ability of the NHC ligands may increase the bond strengths between the carbene and the metal centre, which eventually leads to a shorter metal-carbene bond. This finding provides additional evidence that the inclusion of fluorine in an NHC ligand may influence its electronic properties. The steric bulk of the palladium complexes featuring fluorinated NHC ligands have been assessed using the percent buried volume, % $V_{\text{bur}}$ and steric map techniques. It is interesting to note that the steric bulk of palladium complexes prepared in this work decreases in the order NHC-5 $>$ NHC-3 $>$ IMes $>$ NHC-1, similar to the trend observed in the rhodium(I) complexes.

The catalytic activities of Pd-21, Pd-22, Pd-23, Pd-24 and Pd-25 in the Suzuki-Miyaura coupling between phenylboronic acid and 4-iodotoluene have been investigated, alongside the non-fluorinated derivatives, Pd-14 and Pd-26. Pd-25 was found to be the most effective catalyst in this reaction. The exceptionally high performance of Pd-25 may be due to its unique structure. The active species in the cross-coupling reaction is a Pd(0) complex. Pd(II) PEPPSI complexes undergo an activation process, by loss of the 3-chloropyridyl ligand and chloride to form a Pd(0) species. However, in the case of Pd-25, it already exists as a Pd(0) species. As a result, the initiation time for Pd-25 in this catalytic cycle is expected to be shortened and this may be the reason for higher conversion of product after 24 hours than those of other palladium(II)-PEPPSI complexes. In general, palladium(II) complexes containing fluorinated NHC ligands have better catalytic performance than those of the non-fluorinated counterparts. This work provides additional evidence that the number and position of fluorine in the aromatic substituent groups of NHC ligands
impacts in the catalytic activities of the corresponding metal complexes. More research is required to determine the efficacy of Pd-25 and the other palladium(II) complexes bearing fluorinated NHC ligands in other cross coupling reactions, for example Negishi, Mizoroki-Heck, Stille and Sonogashira.

Table 6.1 summarises the key results of this work. A series of NMR studies that are capable of providing information on the electronic properties of the NHCs all indicate the same order for the fluorinated and non-fluorinated NHCs. The $^{77}$Se NMR chemical shifts of the NHC selenium adducts, the position of $^{13}$C NMR resonances for the carbene in the [Rh(cod)Cl(NHC)] complexes, and the $^{1}J_{C-Rh}$ coupling constants between the spin active $^{13}$C carbene and $^{103}$Rh nuclei are all in the order of NHC-5 > NHC-3 > NHC-4 > NHC-2 > NHC-1 > IMes > IPh.

Steric measures of the NHCs were obtained from $V_{\text{bul}}$ calculations on the gold, rhodium and palladium complexes that crystallised. Although there are some gaps in the data since not all complexes crystallised, but a similar general trend was observed with NHC-5 and NHC-3 being larger than IMes followed by the other fluorinated NHCs.

The metal-carbene bond distance data showed that metal-carbene distances for the fluorinated NHCs are typically shorter than those for the non-fluorinated NHCs.

The results of the catalytic studies show that for the fluorinated NHC-containing complexes the trend in catalytic efficiency with the order being NHC-5 > NHC-3 > NHC-4 > NHC-2 > NHC-1. This order is the same as the electronic information which suggests that the presence of fluorine in NHC ligands has
influenced both electronic and steric properties of the corresponding metal complexes and their catalytic activity in various organic reactions. Those metal complexes containing NHC-5 ligand were found to be the most efficient catalysts within the scope of this study. Further development of the experimental studies as well as improved computational methods will help to assess the unique features associated with these fluorinated NHC ligands.
Table 6.1. Summary of the key findings from this work.

<table>
<thead>
<tr>
<th>NHC</th>
<th>δ^{77}Se (ppm)</th>
<th>δ^{13}C_{Rh} (ppm)</th>
<th>J_{Rh} (Hz)</th>
<th>Gold % V_{bur}</th>
<th>Rhodium % V_{bur}</th>
<th>Palladium % V_{bur}</th>
<th>Gold (Å)</th>
<th>Rhodium (Å)</th>
<th>Palladium (Å)</th>
<th>Gold (%)</th>
<th>Rhodium (%)</th>
<th>Palladium (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHC-1</td>
<td>60.7</td>
<td>185.05</td>
<td>51.7</td>
<td>31.9</td>
<td>32.1</td>
<td>34.0</td>
<td>1.985(4)</td>
<td>2.021(1)</td>
<td>1.953(5)</td>
<td>73</td>
<td>80</td>
<td>75</td>
</tr>
<tr>
<td>NHC-2</td>
<td>66.6</td>
<td>187.60</td>
<td>51.8</td>
<td>32.9</td>
<td>32.8</td>
<td>-</td>
<td>1.983(6)</td>
<td>2.000(8)</td>
<td>-</td>
<td>75</td>
<td>83</td>
<td>78</td>
</tr>
<tr>
<td>NHC-3</td>
<td>68.3</td>
<td>191.52</td>
<td>53.4</td>
<td>-</td>
<td>33.8</td>
<td>36.3</td>
<td>-</td>
<td>2.031(5)</td>
<td>1.944(1)</td>
<td>82</td>
<td>91</td>
<td>85</td>
</tr>
<tr>
<td>NHC-4</td>
<td>67.4</td>
<td>189.55</td>
<td>51.9</td>
<td>33.4</td>
<td>-</td>
<td>34.7</td>
<td>1.964(6)</td>
<td>-</td>
<td>1.941(1)</td>
<td>80</td>
<td>87</td>
<td>82</td>
</tr>
<tr>
<td>NHC-5</td>
<td>73.0</td>
<td>194.95</td>
<td>59.7</td>
<td>-</td>
<td>34.8</td>
<td>46.4</td>
<td>-</td>
<td>2.005(4)</td>
<td>1.915(3)</td>
<td>90</td>
<td>96</td>
<td>90</td>
</tr>
<tr>
<td>IMes</td>
<td>26.7</td>
<td>183.50</td>
<td>50.8</td>
<td>36.5</td>
<td>32.9</td>
<td>34.9</td>
<td>1.998(5)</td>
<td>2.377(4)</td>
<td>1.962(3)</td>
<td>90</td>
<td>67</td>
<td>45</td>
</tr>
<tr>
<td>IPh</td>
<td>24.1</td>
<td>181.52</td>
<td>48.6</td>
<td>-</td>
<td>31.9</td>
<td>-</td>
<td>-</td>
<td>2.408(9)</td>
<td>-</td>
<td>60</td>
<td>48</td>
<td>20</td>
</tr>
</tbody>
</table>

Figure 6.2. Fluorinated and non-fluorinated NHCs involved in this work.