Abstract

Density functional theory (DFT) calculations have been carried out to study the selective C–F bond activation of fluoroaromatics at rhodium and ruthenium complexes.

The C–F activation reaction of C₆F₅H with [Rh(SiR₃)(PMe₃)₃] (R₃ = Me₂Ph, Ph₃) to give [Rh(4-C₆F₄H)(PMe₃)₃] and FSiR₃, has been studied computationally. Using a model system, [Rh(SiMe₃)(PMe₃)₃], calculations show that the lowest energy process occurs via initial phosphine dissociation and subsequent C–F oxidative addition to give trans-[Rh(4-C₆F₄H)(F)(SiMe₃)(PMe₃)₂], with computed free energies of activation (ΔG‡) of +13.2 kcal/mol and +12.4 kcal/mol, respectively. Reductive elimination and phosphine association to give the final products [Rh(4-C₆F₄H)(PMe₃)₃] and FSiMe₃ are found to be facile. In addition, calculations show that C–F activation at trans-[Rh(SiMe₃)(PMe₃)₂] is more accessible kinetically and thermodynamically than C–H activation (ΔΔG‡ = 2.9 kcal/mol, ΔΔG = 51.3 kcal/mol).

DFT calculations have been used to model the reaction of C₅NF₃ at the 2-position with [Rh(X)(PEt₃)₃] (X = Si(OEt)₃, Bpin, where Bpin = pinacolate = –OCMe₂CMe₂O–). C–F activation at the computational models [Rh(X)(PMe₃)₃] (X = Si(OMe)₃ and Bpin) shows that the lowest pathways proceed via novel silyl- and boryl-assisted C–F activation in which short Rh⋯N contacts are computed in the transition states. These occur via modest barriers (ΔG‡ = +26.1 kcal/mol and +20.1 kcal/mol, respectively, relative to the two separated reactants) and also account for the experimental selectivity.

The hydrodefluorination (HDF) reaction of C₆F₅H at [Ru(H)₂(CO)(NHC)(PR₃)₂] (NHC = SIMes, SIPr, IMes, IPr; R = Ph) to give 1,2,3,4-C₆F₄H₂, has been investigated. Calculations on small (NHC = IMe, R = H) and full systems (NHC = IMes, R = Ph) have allowed a novel class of reaction mechanism to be defined involving a nucleophilic attack of one hydride ligand at C₆F₅H. The most accessible pathway has a computed transition state energy of +20.1 kcal/mol in THF (PCM, approach). In addition, calculations reveal that the use of a more sterically encumbered full model system is essential to explain the unusual ortho-regioselectivity observed experimentally.
To my parents, Françoise and Michel
and my brother, Maxime
Acknowledgements

Firstly, I would like to thank my supervisor, Professor Stuart Macgregor, for his guidance, enthusiasm and encouragement throughout my PhD. I would like also to thank my collaborators Professors Michael Whittlesey and Thomas Braun for their experimental contributions which form the basis for most of the work reported in this thesis. I am also grateful to Professor Odile Eisenstein and Doctors Christophe Raynaud and Eric Clot for their welcome during my internship in Montpellier.

I would also like to thank the previous and current members of the “Computational Inorganic Chemistry Group” for their help and the great atmosphere they created in the laboratory. Particularly, Abu, Andrés, Dave, Jenni, Jonas and Stefan for their friendship and their support during my Masters and PhD degrees.

I owe special thanks to Amalia for her love, advice and support during these last years. “Muchas gracias por todo y siempre estardés en mi corazón”.

I would also like to thanks my parents, Françoise and Michel, and my brother Maxime for being always present for me. I am also grateful for the support I received from all my friends, especially Bapt, Charis, Dom, Gauthier, Gerard, Jean-Jo, Loic, Lucia, Nico, Patricia, Santi, Stephen, Vins and Zincou.
Name: Julien Panetier

School/PGI: School of Engineering and Physical Sciences - Chemistry

Version: Final

Degree Sought: PhD

Declaration

In accordance with the appropriate regulations I hereby submit my thesis and I declare that:

1) the thesis embodies the results of my own work and has been composed by myself
2) where appropriate, I have made acknowledgement of the work of others and have made reference to work carried out in collaboration with other persons
3) the thesis is the correct version of the thesis for submission and is the same version as any electronic versions submitted*.
4) my thesis for the award referred to, deposited in the Heriot-Watt University Library, should be made available for loan or photocopying and be available via the Institutional Repository, subject to such conditions as the Librarian may require
5) I understand that as a student of the University I am required to abide by the Regulations of the University and to conform to its discipline.

* Please note that it is the responsibility of the candidate to ensure that the correct version of the thesis is submitted.

Signature of Candidate: [Signature]

Date: 17/04/2012

Submission

Submitted By (name in capitals):

Signature of Individual Submitting:

Date Submitted:

For Completion in the Student Service Centre (SSC)

Received in the SSC by (name in capitals):

Method of Submission

(Handed in to SSC; posted through internal/external mail):

E-thesis Submitted (mandatory for final theses)

Signature: [Signature]

Date: [Date]
# Table of Contents

**Chapter 1: Literature Introduction**

1. Background and Applications ................................................. 1

1.2 Survey of Experimental Studies of Intermolecular Aromatic C–F Bond Activation at Transition Metal Complexes ............................................. 5

1.2.1 Oxidative Addition at Group 10 Metals .................................. 5

1.2.2 Hydrodefluorination (HDF) Reactions ................................... 10

(i) At Group 4 Metals ............................................................ 10

(ii) At Group 8 Metals ........................................................... 13

(iii) At Group 9 Metals .......................................................... 14

(iv) At Group 10 Metals ......................................................... 16

1.2.3 Other Mechanisms ......................................................... 17

1.3 Survey of Computational Studies of Intermolecular Aromatic C–F Bond Activation at Transition Metal Complexes .................................... 19

1.3.1 Oxidative Addition ......................................................... 20

1.3.2 Ligand-Assisted C–F Activation ........................................ 24

1.3.3 Other Mechanisms ........................................................ 29

(i) Hydrodefluorination Reactions .............................................. 29

(ii) Nucleophilic Attack by a Ligand .......................................... 31

1.4 Thesis Overview ............................................................... 33

**Chapter 2: Computational Details**

(i) Method and Functionals ..................................................... 34

(ii) Pseudo-Potentials and Basis sets .......................................... 34

(iii) Optimisation Procedure .................................................... 34

(iv) Conformation Searching .................................................... 35

(v) Energies ............................................................................ 36

(vi) Physical Chemistry Background ......................................... 36
Chapter 3: Mechanistic Study of C‒F Bond Activation of Pentafluorobenzene at [Rh(SiR₃)(PMe₃)]₃ ................................................................. 39

3.1 Introduction .................................................................................. 44
  3.1.1 Comparison between Experimental and Calculated Structures .... 46
  3.1.2 Electron Transfer Pathway ......................................................... 47

3.2 Pathway 1: C‒F Oxidative Addition and Subsequent Si‒F Reductive Elimination ............................................................ 48
  3.2.1 C‒F Oxidative Addition ............................................................ 48
  3.2.2 Si‒F Reductive Elimination from mer-3, fac-3 and mer-3' ........ 53
  3.2.3 Summary of Pathway 1 ............................................................. 61

3.3 Pathway 2: Silyl-Assisted C‒F Bond Activation ................................. 63
  3.3.1 Summary of Pathway 2 ............................................................. 65
  3.3.2 Comparison of Pathway 1 and Pathway 2 ................................. 67

3.4 C‒H Oxidative Addition and HSiMe₃ Formation via Reductive Elimination ...... 69
  3.4.1 C‒H Oxidative Addition to form fac-8 ....................................... 69
  3.4.2 Si–H Reductive Elimination from fac-8 ................................. 70

3.5 Phosphine Substitution Followed by C‒F activation of C₆F₅H at trans-[Rh(SiMe₃)(PMe₃)]₃ (trans-1SiMe₃) .................................................. 73
  3.5.1 Phosphine Dissociation ............................................................ 73
  3.5.2 Pathway 3: C‒F Oxidative Addition of C₆F₅H at trans-1SiMe₃ .... 74
  3.5.3 Pathway 3: Si‒F Reductive Elimination ....................................... 78
  3.5.4 Pathway 4: Silyl-Assisted C‒F activation at trans-1SiMe₃ .......... 82

3.6 C‒H Oxidative Addition at trans-1SiMe₃ and HSiMe₃ Formation via Reductive Elimination ................................................................. 85
  3.6.1 C‒H Oxidative Addition at trans-1SiMe₃ to form cis-12 ............ 85
  3.6.2 Reductive Elimination from cis-12 .......................................... 86

3.7 Summary for C‒F and C‒H Activation of C₆F₅H at 1SiMe₃ ............ 89
3.8 Conclusions ................................................................................................................................. 91

Chapter 4: C–F Bond Activation at the 2- and 4-positions of Pentafluoropyridine at \([\text{Rh}(X)(\text{PEt}_3)_3] (X = \text{Si(OEt)}_3, \text{Bpin})\) ................................................................................................................................. 92

4.1 Introduction .................................................................................................................................. 92

4.2 Computational Studies on the Reactions of \([\text{Rh}\{\text{Si(OMe)}_3\}\text{PMe}_3)_3]\) with \(\text{C}_5\text{NF}_5\) ................................................................................................................................. 94

4.2.1 Pathway 1: C–F Oxidative Addition of \(\text{C}_5\text{NF}_5\) at the 2-Position................................. 94

4.2.2 Pathway 1: Phosphine Loss/Isomerisation and Subsequent Si–F Reductive Elimination from mer-15’ ................................................................................................................................. 99

4.2.3 Pathway 1: C–F Oxidative Addition of \(\text{C}_5\text{NF}_5\) at the 4-Position............................. 104

4.2.4 Pathway 1: Phosphine Loss/Isomerisation and Subsequent Si–F Reductive Elimination from mer-18’ ................................................................................................................................. 107

4.2.5 Pathway 2: Silyl-Assisted C–F Activation of \(\text{C}_5\text{NF}_5\) at the 2-Position....................... 111

4.2.6 Pathway 2: Silyl-Assisted C–F Activation of \(\text{C}_5\text{NF}_5\) at the 4-Position....................... 115

4.2.7 Summary for the C–F activation of \(\text{C}_5\text{NF}_5\) at the 2- and 4-positions at \(1_{\text{Si(OMe)}_3}\) ................................................................................................................................................. 117

4.3 Computational Studies on the Reactions of \([\text{Rh}(\text{Bpin})(\text{PMe}_3)_3]\) with Pentafluoropyridine ................................................................................................................................................ 119

4.3.1 Pathway 1: C–F Oxidative Addition of \(\text{C}_5\text{NF}_5\) at the 2-Position................................. 119

4.3.2 Pathway 1: Phosphine Loss/ Isomerisation and Subsequent B–F Reductive Elimination from mer-27’ ................................................................................................................................................. 121

4.3.3 Pathway 1: C–F Oxidative Addition of \(\text{C}_5\text{NF}_5\) at the 4-Position............................. 125

4.3.4 Pathway 1: Phosphine Loss/ Isomerisation and Subsequent B–F Reductive Elimination from mer-31’ ................................................................................................................................................. 126

4.3.5 Pathway 2: Boryl-Assisted C–F Addition of \(\text{C}_5\text{NF}_5\) at the 2- and 4-Positions .................................................................................................................................................................................. 130

4.4 Comparisons of Ligand-Assisted C–F Activation Processes at \([\text{Rh}(X)(\text{PMe}_3)_3]\) (\(X = \text{Si(OMe)}_3, \text{Bpin}\)) ........................................................................................................................................... 134

4.5 Conclusions .................................................................................................................................. 136
Chapter 5: Catalytic Hydrodefluorination of Pentafluorobenzene by [Ru(H)\textsubscript{2}(CO)(NHC)(PPh\textsubscript{3})\textsubscript{2}]: An Explanation for the Unusual Ortho-Regioselectivity

5.1 Introduction .................................................................................................................. 137

5.1.1 Proposed Mechanism for Catalytic HDF of C\textsubscript{6}F\textsubscript{5}H ......................... 138

5.1.2 Comparison between Experimental and Calculated Structures ...................... 139

5.2 Computational Studies on the Reaction of [Ru(H)\textsubscript{2}(CO)(IMe)(PH\textsubscript{3})]\textsubscript{2} with C\textsubscript{6}F\textsubscript{5}H: Identification of a Tetrafluorobenzyne Intermediate .................................................... 142

5.3 HDF of C\textsubscript{6}F\textsubscript{5}H at [Ru(H)\textsubscript{2}(CO)(IMe)(PH\textsubscript{3})]\textsubscript{2} via Initial Formation of an $\eta^2$-Arene Intermediate ........................................................................................................... 147

5.4 HDF of C\textsubscript{6}F\textsubscript{5}H at [Ru(H)\textsubscript{2}(CO)(IMe)(PH\textsubscript{3})]\textsubscript{2} without Initial Formation of an $\eta^2$-Arene Intermediate ........................................................................................................... 153

5.5 HDF of C\textsubscript{6}F\textsubscript{5}H at [Ru(H)\textsubscript{2}(CO)(IMes)(PPh\textsubscript{3})]\textsubscript{2} ..................................................... 156

5.5.1 Phosphine Dissociation ......................................................................................... 156

5.5.2 HDF via a Stepwise Mechanism ........................................................................ 156

5.5.3 HDF via a Concerted Mechanism ..................................................................... 161

5.5.4 Regioselectivity of HDF of C\textsubscript{6}F\textsubscript{5}H ......................................................... 161

5.6 Conclusions .................................................................................................................. 165

Chapter 6: Computational Background ......................................................................... 166

6.1 Introduction .................................................................................................................. 166

6.2 Background QM .......................................................................................................... 166

6.2.1 The Schrödinger Equation ................................................................................ 166

6.2.2 The Born-Oppenheimer Approximation ......................................................... 168

6.2.3 The Variational Principle .................................................................................... 169

6.2.4 The Hartree-Fock Approximation ..................................................................... 169

6.2.5 The Electron Correlation .................................................................................... 171

6.3 Density Functional Theory ......................................................................................... 172

6.3.1 The Electron Density ......................................................................................... 172
List of Publications


Chapter 1: Literature Introduction

This chapter deals with intermolecular C–F bond activation of fluoroaromatics at transition metal (TM) complexes. The discussion begins with a background to fluorine chemistry before reviewing experimental and computational studies. This chapter is based mainly on three topics, that are related to the studies in this thesis: 1) oxidative addition; 2) ligand-assisted C–F activation; and 3) hydrodefluorination reactions.

1.1 Background and Applications

The isolation of elemental fluorine was first reported in 1886 by Moissan, however, the practical use of fluorinated organic compounds started in the 1920s. One of the earliest examples (1927) is known as the Balz-Schiemann reaction which consists of introducing fluorine into specific positions of aromatic compounds. In the 1930s, fluorinated organic compounds were used in industry with the introduction of chlorofluorocarbons (CFCs) as refrigerants in cooling and air conditioning equipment, fire extinguishing chemicals and aerosol propellants. In 1938, Plunkett synthesised the first fluoropolymer, poly(tetrafluoroethylene), known as PTFE or Teflon. In the 1940s, Simons and co-workers developed the electrochemical fluorination (ECF) process used in the production of a variety of perfluorinated organic compounds. Industrial organofluorine chemistry was further developed with the Manhattan Project and the construction of the first nuclear weapon. At that time, fabrication of highly resistant materials (e.g. PTFE), lubricants and coolants was needed in order to handle the extremely aggressive uranium hexafluoride (UF₆).

In the 1950s, fluorinated organic compounds started to be used as potential drugs, mostly because of the properties of F (similar size to H, but much higher electronegativity), its propensity to hydrogen-bonding and the increased lipophilicity and physiochemical effects of fluorinated groups. In 1974, the industrial development of fluorinated compounds took a step back, however, after the prediction of the ozone-depleting effect of CFCs and the subsequent observation of the ozone hole over the Antarctic in 1980. In 1987, the Montreal Protocol initiated the phase-out of most CFCs. Since then, CFCs were mainly substituted by other fluorine-containing chemicals such as hydrofluorocarbons (HFCs) and fluorinated ethers. Nowadays, fluorinated organic compounds are widely used in the electronics, agrochemical and pharmaceutical
industries. In 2006, Thayer noted that “approximately 40% of all agrochemicals and 20% of all pharmaceuticals on the current market are organic molecules containing at least one fluorine atom”. In 2008, three of the top 10 drugs were fluorinated organic compounds: Lipitor, Seretide and Risperdal (see Figure 1.1).

Figure 1.1: Three of the top 10 drugs in 2008 containing at least one fluorine atom.

The synthesis of fluoroaromatics represents a significant challenge of modern synthetic chemistry. The most common synthetic methods are reductive aromatization, the fluoroformate process, the Halex process or the Balz-Schiemann reaction. This last reaction is actually one of the major industrial processes in the synthesis of monofluorinated arenes (see Figure 1.2). This consists of the fluorination of an arene diazonium tetrafluoroborate intermediate by heating up to 120 °C to yield the monofluorinated arene product. The reproducibility of the reaction yield is, however, quite poor and the arene diazonium tetrafluoroborate is potentially toxic, explosive and corrosive. Another variant of the Balz-Schiemann reaction has been reported by Yoneda and Fukuhara where, in this case, the arene diazonium tetrafluoroborate is not isolated but generated in situ, in the presence of 70% HF-pyridine with NaNO₂ at 0 °C. The resulting diazonium salt is then heated up to 160 °C. Despite the generation of large quantities of unwanted waste products such as NaBF₄, NaCl and HCl, this reaction is still performed on a large scale because of the lack of alternative methods.
Other environmental and cost efficient methods, however, have been and are being developed through the use of transition metal catalysis. This approach is similar in that they consist of selective fluorination into the aromatic compound. One example is the copper-catalysed oxidative fluorination developed at Dupont (see Figure 1.3).\textsuperscript{12} This is a “greener” alternative of the Balz-Schiemann reaction as the undesired chemical waste products, copper and HF, react at 400 °C in the presence of oxygen to regenerate the CuF\textsubscript{2} reactant and H\textsubscript{2}O.

In contrast, transition metal complexes can also be employed to prepare fluorinated organic compounds by selective defluorination, rather than by selective fluorination.\textsuperscript{13} The benefit of this approach is that it results in the synthesis of desired fluorinated organic compounds under mild conditions that are hard to access by conventional reactions. The use of fluoroaromatics in catalysis has therefore received much attention and several examples of catalytic cross-coupling\textsuperscript{13d,13e,14} and hydrodefluorination\textsuperscript{15} processes have emerged. Cross-coupling reactions are based on the activation of C–F bonds of fluorinated organic compounds and the subsequent formation of new C–C bonds, while hydrodefluorination (HDF) reactions consist of the substitution of fluorine by hydrogen (see Figure 1.4).
Figure 1.4: Examples of catalytic cross-coupling\textsuperscript{13j,14f} (top) and hydrodefluorination\textsuperscript{15a} (bottom, where $R' = \text{Ph, OEt}$) reactions.

The major challenge of these reactions is in the activation of the C–F bond. Indeed this bond is known to be one of the strongest single bonds to a heteroatom that carbon can form and results from the electrostatic interactions between the polarised C$\delta^+$ and F$\delta^-$ atoms (e.g. C\textsubscript{6}F\textsubscript{5}–F bond energies = +116 kcal/mol).\textsuperscript{13k,16} Several examples of stoichiometric intermolecular C–F bond activation are known and have been classified in four fundamentals patterns by Braun and Perutz: 1) oxidative addition; 2) M–C bond formation with E–F elimination, where E = H, Si; 3) hydrodefluorination with M–F bond formation, and 4) nucleophilic attack.\textsuperscript{13j,13k}

The following sections will mainly review reaction mechanisms of selective aromatic C–F activation in the presence of other bonds.
1.2 Survey of Experimental Studies of Intermolecular Aromatic C–F Bond Activation at Transition Metal Complexes

1.2.1 Oxidative Addition at Group 10 Metals

C–F oxidative addition of fluoroaromatics is mainly observed for complexes of group 10 metals and rarely otherwise. The use of nickel complexes to afford C–F activation is by far the most common. The first example in which C–F activation results in the formation of an oxidative product was studied experimentally by Fahey and Mahan.\(^\text{17}\) They reported the C–F activation of \(\text{C}_6\text{F}_6\) at \([\text{Ni(COD)}_2]\) (1, COD = 1,5-cyclooctadiene) in the presence of PEt\(_3\) to give trans-[\(\text{Ni}([\text{C}_6\text{F}_5])\text{(F)}\text{(PEt}_3\text{)}_2\)] (2, see Figure 1.5). In 1997, Yamamoto and Abla studied the C–F activation of \(\text{C}_6\text{F}_6\) at \([\text{Ni(Et)}_2\text{(bpy)}]\) (bpy = 2,2'-bipyridine) and reported the first example of cis-biaryl nickel (II) complex \([\text{Ni}([\text{C}_6\text{F}_5])\text{2(bpy)}]\).\(^\text{18}\) The same year, Perutz and co-workers fully characterised 2, formed upon C–F activation of \(\text{C}_6\text{F}_6\) at 1/PEt\(_3\), by X-ray crystallography and nuclear magnetic resonance (NMR) spectroscopy, and improved the yield of the reaction.\(^\text{19}\) The same group studied several examples of C–F activation of fluoroaromatics at \(\text{Ni}(0)\).\(^\text{13d,19-20}\) In one case, C–F bond activation of \(\text{C}_6\text{F}_5\text{H}\) at \([\text{Ni(PEt}_3\text{)}_4]\) gives a mixture of the three nickel fluoride isomers along with phosphoranes and the hydrodefluorination product \(1,2,4,5-\text{C}_6\text{F}_6\text{H}_2\). Moreover, partial fluoropyridine substrates undergo selective C–F activation over C–H activation (see 3 and 4 in Figure 1.5).\(^\text{19,21}\) In 1999, C–F activation of 2,4,6-trifluoropyrimidine in hexane in the presence of PEt\(_3\) at 1 was observed to give 5.\(^\text{22}\)

Mechanistic studies have permitted the isolation of key intermediates and allowed greater understanding of the reaction mechanism. Pörschke \textit{et al.}, for example, reported the initial formation of an \(\eta^2\)-arene intermediate \([\text{Ni}(\eta^2\text{-C}_6\text{F}_6)]\text{(Bu}_2\text{PCH}_2\text{CH}_2\text{P}^\text{Bu}_2\text{)}\]) for the C–F activation of \(\text{C}_6\text{F}_6\) at \([\{\text{Ni}\text{(Bu}_2\text{PCH}_2\text{CH}_2\text{P}^\text{Bu}_2\text{)}\}_{\text{2}}(\mu-\eta^2\eta^2\text{-C}_6\text{H}_{10})]\) prior to formation of \([\text{Ni}([\text{C}_6\text{F}_5])\text{(F)}\text{(Bu}_2\text{PCH}_2\text{CH}_2\text{P}^\text{Bu}_2\text{)}]\).\(^\text{23}\) A similar observation has been reported for the C–F activation of \(\text{C}_{10}\text{F}_8\) at 1/PEt\(_3\) to give trans-[\(\text{Ni}(2\text{-C}_{10}\text{F}_7)\text{(F)}\text{(PEt}_3\text{)}_2\)] (7) after initial formation of 6 (see Figure 1.6).\(^\text{24}\)

More recently, Johnson \textit{et al.} studied the C–F activation of \(\text{C}_6\text{F}_5\text{X}\) (X = F, H) at \([\text{Ni}(\eta^2\text{-C}_{14}\text{H}_{10})\text{(PEt}_3\text{)}_2]\) (8).\(^\text{25}\) With \(\text{C}_6\text{F}_5\text{H}\) C–F activation occurs at the 2-position to give trans-[\(\text{Ni}(2\text{-C}_6\text{F}_4\text{H})\text{(F)}\text{(PEt}_3\text{)}_2\)] with 97% selectivity. Moreover, the same group showed that
1,2,4,5-C₆F₄H₂ and 1,2,3,5-C₆F₄H₂ undergo C–H activation which then converts to the thermodynamic C–F products (see 9 and 10 in Figure 1.6).²⁶

Figure 1.5: Landscape of C–F activation of fluoroaromatics at 1/PEt₃.¹³,¹⁷,¹⁹,²²,²⁴

Figure 1.6: C-F activation of 1,2,4,5-C₆F₄H₂ and 1,2,3,5-C₆F₄H₂ at 8.²⁶
In contrast to the previous examples, Johnson and co-workers have shown that by using a different type of phosphine ligand, activation of 1,2,4,5-C₆F₄H₂ at [Ni(η²-C₁₀H₁₀)(P'Pr₃)₂] (11) resulted only in the C–H activation product [Ni(4-C₆F₄H)(H)(P'Pr₃)₂] (12). In addition, even after hours heating at 100 °C, no C–F activation products are observed suggesting that 12 is the kinetic and thermodynamic product. This contrasts with the general idea that C–H activation is kinetically more favourable while C–F activation is thermodynamically more accessible.

Braun and co-workers also showed that the outcome of the reaction between [Ni(COD)]₂ (1) and 5-chloro-2,4,6-trifluoropyrimidine depends on the phosphine ligand used. When the reaction is performed in the presence of PCy₃, P'Pr₃ or PPh₃ C–F activation took place to give 13, 14 and 15, respectively, while the C–Cl product is observed with PEt₃ (16, see Figure 1.7)

![Figure 1.7: Selective C–F activation and C–Cl activation of 5-chloro-2,4,6-trifluoropyrimidine at 1.](image)

On the other hand, substitution of excess of phosphine ligand by a nonaromatic imine has been showed to perform selective C–F activation over C–H activation of C₆F₅H and isomers of C₆F₄H₂ at 1 (see Figure 1.8).
Figure 1.8: Selective C–F activation over C–H activation of C₆F₅H and C₆F₄H₂ at 1 in the presence of a nonaromatic imine.

Since the isolation and characterisation of the first stable N-heterocyclic carbene (NHC) by Arduengo et al. in 1991, the use of these species as ligands for catalysis has emerged. Radius and co-workers reported a series of papers in which nickel(0)-NHC complexes, [Ni₂(Pr₂Im)₄(COD)] (21) and [Ni(Pr₂Im)₂(η²-C₄H₄)] (22, Pr₂Im = 1,3-bis(isopropyl)imidazol-2-ylidene), are used to afford C–F activation of fluoroaromatics. For instance, 22 performs C–F activation of C₅NF₅ at the 4-position while the reaction occurs at the 2-position at 1 in the presence of PEt₃ (see Figure 1.9).

Figure 1.9: C–F activation of C₅NF₅ at Ni(0).
Some examples are also known for selective C–F activation of fluoroaromatics at Pd metal centres. Perutz and co-workers, for instance, reported the C–F activation of C₅NF₅ at the 4-position with [Pd(PR₃)₂] (R = Cy, 'Pr) in toluene at 100 °C to give trans-[Pd(4-C₅NF₄)(F)(PR₃)₂] (see Figure 1.10). In the same study, the authors showed that formation of trans-[Pd(4-C₅NF₄)(F)(PR₃)₂] can be obtained in better yield by using a chelating palladium complex, [Pd(Me₂)(tmEDA)] (tmEDA = tetramethylethylenediamine) as starting point in the presence of C₅NF₅ and PR₃ (R = Cy, 'Pr). In contrast, [Pd(PR₃)₂] does not undergo C–F activation with 2,3,5,6-C₅NF₄H even at 100 °C. One year later, Grushin et al. reported the C–F activation of C₆F₆ at [Pd(PR₃)₂] (R = Cy, 'Pr) in THF at 70 °C and observed the formation of trans-[Pd(C₆F₅)(F)(PR₃)₂].

C–F activation at platinum metal centres has also been studied. The first example of oxidative addition was reported by Hofmann and Unfried, involving the C–F activation of C₆F₆ at room temperature at {Pt(dtbpm)} to give [Pt(C₆F₅)(F)(dtbpm)] (dtbpm = bis(di-t-butylphosphino)methane). In 2000, Perutz and co-workers also showed that trans-[Pt(H₂)(PCy₃)₂] undergoes C–F activation of C₆F₆ to give a mixture of trans-[Pt(H)(C₆F₅)(PCy₃)₂] and trans-[Pt(H)(FHF)(PCy₃)₂] in a 13:1 ratio. Later on, the same group studied the reaction of C₅NF₅ at [Pt(PR₃)₂] (R = Cy, 'Pr) in THF at room temperature. Unexpectedly, C–F activation occurs at the 4-position to form trans-[Pt(4-C₅NF₄)(R)(PR₃)(PR₂F)] in which F is displaced onto a phosphine ligand and one alkyl substituent transfers onto the metal centre (see Figure 1.10).

![Figure 1.10: C–F activation of C₅NF₅ at [Pd(PR₃)₂] (top) and C–F and P–C activation of C₅NF₅ at [Pt(PR₃)₂] (bottom).](image)
Grushin and co-workers observed similar results for the reaction of C₆F₆ at [Pt(PCy₃)₂] in THF at 70 °C which undergoes C–F and P–C activation to form trans-[Pt(C₆F₅)(Cy)(PCy₃)(PCy₂F)]. More recently, Perutz et al. reported the C–F activation of 2,3,5-trifluoro-4-(trifluoromethyl)pyridine at [Pt(PR₃)₂] (R = Cy, Pr, Cyp = cyclopentyl) to give cis-[Pt(F){2-C₅NF₂H(CF₃)}(PR₃)] which then converts to trans-[Pt(F){2-C₅NF₂H(CF₃)}(PR₃)] either thermally or photochemically (see Figure 1.11).

Figure 1.11: C–F activation of 2,3,5-trifluoro-4-(trifluoromethyl)pyridine at [Pt(PR₃)₂].

C–F activation of fluoroaromatics at group 10 metal centres has shown to be selective over activation of other bonds. The choice of the ligand and the metal is crucial for the outcome of the reaction. For example, C–F activation of C₅NF₅ at {Ni(PR₃)₂} occurs mostly at the 2-position in contrast to [M(PR₃)₂] (M = Pd, Pt) which proceeds at the 4-position.

1.2.2 Hydrodefluorination (HDF) Reactions

Hydrodefluorination reactions are another class of intermolecular C–F activation that results in the substitution of fluorine by hydrogen. In the following section, key experimental papers are reviewed by the transition metal groups involved.

(i) At Group 4 Metals

The first example of HDF at group 4 transition metal centres was reported by Kiplinger and Richmond. In this study, the authors showed that C₁₀F₈ can react at [Zr(η⁵-C₅H₅)₂(Cl)] in THF with Mg as terminal reductant to give 1,3,4,5,6,7,8-C₁₀F₇H (38, see Figure 1.12). To explain the C–F activation, an oxidative addition mechanism at the low-valent zirconocene fragment {Zr(η⁵-C₅H₅)₂} was proposed.
Figure 1.12: HDF of octafluoronaphthalene at \([\text{Zr}(\eta^2-\text{C}_5\text{H}_5)_2(\text{Cl})_2]\) to give 38.\(^{38}\)

The same group also reported the HDF and aromatization of cyclic perfluorocarbons at room temperature by using reduced titanocene and zirconocene complexes (see Figure 1.13).\(^{39}\)

Figure 1.13: HDF and aromatization of perfluorodecalin at titanocene and zirconocene complexes to give 38.\(^{39}\)

Since the first example of HDF reported by Kiplinger and Richmond at zirconocene complexes, Jones \textit{et al.} employed the related species, \([\text{Zr}(\eta^5-\text{C}_5\text{Me}_5)_2(\text{H})_2] (40)\), \([\text{Zr}(\eta^5-\text{C}_5\text{Me}_5)_2(\text{H})_2] (41)\) and \([\text{Zr}(\eta^5-\text{C}_5\text{H}_5)_3(\text{H})] (42)\) to perform HDF of other fluoroaromatics.\(^{13f,40}\) With 41, \(\text{C}_6\text{F}_6\) reacts at 85 °C in cyclohexane-\(d_{12}\) to give a mixture of \([\text{Zr}(\eta^5-\text{C}_5\text{Me}_5)_2(\text{F})(\text{H})] (43)\), \([\text{Zr}(\eta^5-\text{C}_5\text{Me}_5)_2(\text{C}_6\text{F}_5)(\text{H})] (44)\), and \(\text{C}_6\text{F}_3\text{H}\) in a 2:1:1 ratio (see Figure 1.14).\(^{40a,40b}\)

Figure 1.14: HDF reaction of \(\text{C}_6\text{F}_6\) at \([\text{Zr}(\eta^5-\text{C}_5\text{Me}_5)_2(\text{H})_2]\) and the postulated \(\sigma\)-bond metathesis transition state TS (41 – 43).\(^{13f,40a,40b}\)
To explain the formation of 43, a σ-bond metathesis transition state, TS (41 – 43), has been postulated as shown in Figure 1.14. In addition, 44 is thought to be formed by 1) initial migration of hydride to \( \eta^5\text{-C}_5\text{Me}_5 \); 2) attack of the Zr(II) on the arene ring to eliminate HF; and 3) reaction of HF with \([\text{Zr}(\eta^5\text{-C}_5\text{Me}_5)_2(\text{H})(\mu\text{-H})_2]\) to give 43 and \( \text{H}_2 \). In contrast, the reaction under similar conditions with \( \text{C}_6\text{F}_5\text{H} \) at 41 resulted in C–H activation rather than C–F activation. However, a mixture of hydrodefluorinated products, 1,2,3,4- and 1,2,4,5-C\( _6\)F\( _4\)H\( _2 \) in a 1.3:1 ratio, was also obtained.

HDF of fluorobenzene and 1-fluoronaphthalene has also been reported in the Jones group.\textsuperscript{13f,40c} C\( _6\)FH\( _5 \) reacts at 41 under 1.3 atm of \( \text{H}_2 \) in cyclohexane-\( d_{12} \) at 85 °C and results in a mixture of 43, \([\text{Zr}(\eta^5\text{-C}_5\text{Me}_5)_2(\text{C}_6\text{H}_5)(\text{H})]) \) (45), and \( \text{C}_6\text{H}_6 \) in a 1:0.75:1 ratio. Formation of \( \text{C}_6\text{H}_6 \) and 43 is postulated to go through a similar transition state to TS (41 – 43), while 45 is formed by ortho–C–H activation of C\( _6\)FH\( _5 \) and subsequent \( \beta \)-fluoride elimination to give a benzyne ligand which then inserts into the Zr–H. However, the main disadvantage of this reaction is that it is very slow, requiring up to 40 days. 1-fluoronaphtalene reacts faster than C\( _6\)FH\( _5 \) to give naphthalene and 43 at 85 °C, but it takes 4 days.\textsuperscript{13f,40c}

Therefore, development of new catalysts is needed for faster and better conversion. One way to quantify the efficiency of a catalytic HDF reaction is to use the turnover number (TON), defined by:\textsuperscript{15f}

\[
\text{TON} = \frac{\text{number of fluoroaromatic product(s)} \times \text{number of HDF steps}}{\text{moles of catalyst}} \quad (5.1)
\]

In 2007, Rosenthal and co-workers reported the catalytic HDF of C\( _5\)NF\( _5 \) at \([\text{rac-ebthi}(\text{Zr(H)}(\mu\text{-H}))_2], \) (46, ebthi = 1,2-ethylene-1,1′-bis(\( \eta^5 \)-tetrahydroindenyl), and \([\text{Zr}(\eta^5\text{-C}_5\text{Me}_5)_2(\text{H})(\mu\text{-H})_2] \) (47) in the presence of \( \text{iBu}_2\text{AlH} \) to give 2,3,5,6-C\( _5\)NF\( _4\)H and \( \text{iBu}_2\text{AlF} \).\textsuperscript{41} The best TON was obtained with 0.5 % of 46 at room temperature for 24 hours with a TON = 67, however, the conversion was relatively low (44 %). A better conversion (90 %) was seen with 10 % of 46 but the TON decreased considerably (TON = 7).
Lanthanides have also been used for HDF reactions. Andersen, Eisenstein and co-workers, for instance, reported a joint experimental and computational study on the HDF of C₆F₆ at [Ce(Cp’₂)₂H] [Cp’ = 1,3,4-(Me₃C)₃(C₅H₂)] to form [Ce(Cp’₂)F], H₂ and 1,2,4,5-C₆F₄H₂. [Ce(Cp’₂)F] and 1,2,4,5-C₆F₄H₂ are formed after decomposition of [Ce(Cp’₂)(C₆F₅)]. DFT calculations on the mechanism of this reaction have been performed and the results are discussed in Section 1.3.3.

(ii) At Group 8 Metals

Group 8 transition metals have also been employed to perform HDF of fluoroaromatics. In 2005, Holland et al. reported the HDF of C₆F₆, C₅F₅H and C₅NF₅ using β-diketiminate complexes of iron(II) in the presence of silanes as the reductant. In addition, the HDF of C₆F₅H occurred at the 4-position in the presence of HSiEt₃ to give 1,2,4,5-C₆F₄H₂ with a TON of 0.2 after 4 days at 45 °C (see Figure 1.16). With C₅NF₅, formation of 2,3,5,6-C₅NF₄H is observed with a TON of 3.6 under the same conditions.
This last result contrasts with that of Whittlesey and co-workers who reported HDF of C₆F₆, C₆F₅H and C₅NF₅ catalysed by [Ru(H₂)(CO)(NHC)(PPh₃)]₂ (50, NHC = SIMes, SIPr, IMes, IPr) in the presence of HSiEt₃ in THF at 70 °C (see Figure 1.17).¹⁵f With C₆F₅H and C₅NF₅ C–F activation occurs at the 2-position to yield 1,2,3,4-C₆F₄H₂ and 2,3,4,5-C₅NF₄H, respectively. HDF of C₆F₃H gave a TON up to 7.4 after 19.45 hours while with C₅NF₅ the TON is 13.6 under similar conditions. However, the TON for C₆F₅H could go up to 200 with 0.21 % of catalyst in neat fluoroaromatic, but still required 400 hours reaction time. DFT calculations have been performed to elucidate this unusual ortho-regioselectivity for HDF of C₆F₃H and the results are presented in Chapter 5 of this thesis.

Figure 1.17: HDF reaction of C₆F₃H catalysed by [Ru(H₂)(CO)(NHC)(PPh₃)]₂.¹⁵f

(iii) At Group 9 Metals

The first example of catalytic HDF of C₆F₆ and C₆F₅H at group 9 metal centres was reported by Milstein and Aizenberg in 1994, using [Rh(SiR₃)(PMe₃)]₃ (R₃ = Me₂Ph, Ph₃) in the presence of HSiR′₃ (R′ = Ph, OEt) to give C₆F₅H and 1,2,4,5-C₆F₄H₂, respectively (see Figure 1.18).¹⁵a The initial step for the reaction between C₆F₆ and [Rh(SiR₃)(PMe₃)]₃, corresponds to C–F activation to give [Rh(C₆F₅)(PMe₃)] (54) and FSiR₃. In the presence of HSi(OEt)₃, complex 56 was isolated and characterised by ³¹P,
\(^1\)H and \(^1\)9F NMR data and confirmed by an X-ray crystallographic study. From 56 subsequent C–H reductive elimination yields C\(_6\)F\(_5\)H and regenerates the original rhodium-silyl complex. In addition, Milstein and Aizenberg showed that C\(_6\)F\(_5\)H reacts at 54 in the presence of HSi(OEt)\(_3\) to give exclusively 1,2,4,5-C\(_6\)F\(_4\)H\(_2\) with a TON of 33 after 48 hours at 94 °C. This \textit{para} selectivity is similar to the one observed by Holland and co-workers, however, differs from that seen by Whittlesey \textit{et al.} \(^{15c,15f}\) Perutz and co-workers also studied the reaction of 2,3,5,6-C\(_5\)NF\(_4\)H at [Rh(SiPh\(_3\))(PMe\(_3\))\(_3\)] and obtained a mixture of C–F and C–H activation products, [Rh(2-C\(_5\)NF\(_3\)H)(PMe\(_3\))\(_3\)] and [Rh(4-C\(_5\)NF\(_4\))(PMe\(_3\))\(_3\)], respectively, in a 1.3:1 ratio, along with FSiPh\(_3\) and HSiPh\(_3\). \(^{43}\) Interestingly, C–F activation occurred at the 2-position and the product can further react with HSiPh\(_3\) to give 2,3,5-C\(_5\)NF\(_3\)H\(_2\) and an unidentified rhodium complex.

In 1995, Milstein and Aizenberg showed that H\(_2\) can be used as reductant instead of HSiR\(_3\) to perform HDF of C\(_6\)F\(_6\) and C\(_6\)F\(_5\)H in the presence of a base (e.g. NEt\(_3\)) at [Rh(C\(_6\)F\(_5\))(PMe\(_3\))\(_3\)] (54) and [Rh(H)(PMe\(_3\))\(_4\)] (58). \(^{15b}\) Species 54 is found to be more reactive than 58 with a TON up to 56 after 20 hours at 95-100 °C, corresponding to the conversion of C\(_6\)F\(_5\)H to 1,2,4,5-C\(_6\)F\(_4\)H\(_2\) in the presence of NEt\(_3\) and K\(_2\)CO\(_3\). In relation to that, Braun \textit{et al.} studied the C–F activation of C\(_5\)NF\(_5\) in the presence of NEt\(_3\) at [Rh(H)(PEt\(_3\))\(_3\)] to give [Rh(4-C\(_5\)NF\(_4\))(PEt\(_3\))\(_3\)] (59). \(^{14c}\) Later on, the same group showed that 59 could performed catalytic HDF of C\(_5\)NF\(_5\) with H\(_2\) in the presence of
NEt₃/Cs₂CO₃ to give 2,3,5,6-C₅NF₄H. After 2 days at atmospheric pressure and room temperature TONs up to 12 were obtained.

Grushin and Young also used a rhodium hydride complex, [Rh(Cl)₂(H)(PCy₃)₂], to perform the HDF of 1-fluoronaphthalene in the presence of H₂ and aqueous alkali at 95 °C. The same year, Angelici and co-workers reported the HDF of C₆F₅H and 1,2-C₆F₂H₄ under 4 atm of H₂ at 70 °C in the presence of NaOAc by using rhodium pyridylphosphine and bipyridyl complexes tethered to heterogeneous Pd-SiO₂.

(iv) At Group 10 Metals

A few examples of HDF at group 10 metal centres have also been reported. Fort and co-workers, for instance, studied the HDF of monofluoroaromatics by using Ni(0)/NHC complexes in the presence of chloride and Na(OPr or other β-hydrogen-containing alkoxides.

Braun and co-workers showed that trans-[Pd(4-C₅NF₄)(F)(PR₃)₂] (60) could react with HSiPh₃ for 2 hours at 70 °C in THF to give 2,3,5,6-C₅NF₄H in 52 % yield. More recently, a catalytic HDF reaction has been developed in which trans-[Pd(4-C₅NF₄)(F)(PR₃)₂] (R = iPr, Cy) reacts with C₅NF₅ and HBpin for 3 days at 60 °C in THF to yield 2,3,5,6-C₅NF₄H and [Pd(PR₃)₂] (see Figure 1.19).

![Figure 1.19: Catalytic HDF of C₅NF₄ at [Pd(PR₃)₂] to give 2,3,5,6-C₅NF₄H.](image-url)
However, the yields of the reaction for formation of 2,3,5,6-C₅NF₄H are lower than the previous study,⁴⁷ being 44 % (TON = 4 for R = iPr) and 30 % (TON = 3, for R = Cy).

1.2.3 Other Mechanisms

Other types of C–F activation are thought to occur experimentally, such as electron transfer and nucleophilic attack processes. Therefore, the following section will review some key examples of these two types of intermolecular C–F activation.

In 1992, Hintermann et al. reported the C–F activation of 4-XC₆F₄CN (X = F, H, CN) at trans-[Pt(H)₂(PCy₃)₂] (66) to yield trans-[Pt(H)(4-XC₆F₃CN)(PCy₃)₂] (67) and HF.⁴⁹ The authors proposed an electron transfer mechanism, in which one electron is transferred from 66 to the substrate to generate 4-XC₆F₃CN⁻ followed by the attack of F⁻ on H to give the products. In addition to 66, trans-[Pt(H)(F)(PCy₃)₂] and trans-[Pt(H)(FHF)(PCy₃)₂] were also observed. Several years later, Perutz and co-workers observed similar behaviour for the C–F activation of fluoroaromatics at cis-[Ru(H)₂(dmpe)₂] (dmpe = 1,2-bis(dimethylphosphino)ethane) which results in the formation of trans-[Ru(C₆F₅)(H)(dmpe)₂] and HF.⁵⁰ In addition, the authors obtained trans-[Ru(C₆F₅)(FHF)(dmpe)₂], as a side product. To explain the selective C–F activation at the 4-position of partial fluorinated substrates (C₆F₃H, 1,2,3,4-C₆F₄H₂ and 1,2,3-C₆F₃H₃), the authors also postulated an electron transfer pathway.

Intermolecular C–F activation via nucleophilic attack has also been observed experimentally. The first example of such process was reported by King and Bisnette in 1964. In this paper, the authors studied the nucleophilic substitution of C₆F₆ by the anion [Fe(η⁵-C₅H₅)(CO)₂]⁻ in THF to form [Fe(η⁵-C₅H₅)(C₆F₅)(CO)₂] and fluoride ion.⁵¹ Jones and co-workers proposed a nucleophilic attack pathway for the reaction of fluoroaromatics (ArF⁻) in pyridine or 1:1 pyridine/benzene at [Rh(η⁵-C₅Me₅)(H)] (68) to give the C–F cleavage products [Rh(η⁵-C₅Me₅)(ArF⁻)(PMe₃)] and HF.⁵² Interestingly, the authors showed that the reaction is autocatalysed by fluoride ion which deprotonates 68 to give 69, suitable to perform C–F cleavage.
In 1991, Milstein and co-workers reported the C–F activation of C₆F₆ at [Ir(Me)(PEt₃)₃] (70, see Figure 1.21). Upon heating the solution at 60 °C, C–F cleavage occurs but a fluorophosphine complex, trans-[Ir(C₆F₅)(PEt₃)₂(PEt₂F)] (71) was observed along with the elimination of ethane and methane. Although the authors postulated an electron transfer pathway, more recent DFT calculations discarded both this and an oxidative addition process. In reality, C–F activation proceeds via a nucleophilic attack in which the displaced F⁻ is trapped by the adjacent phosphine ligand to give a metallophosphorane intermediate. This so-called phosphine-assisted C–F activation will be discussed in Section 1.32.
1.3 Survey of Computational Studies of Intermolecular Aromatic C–F Bond Activation at Transition Metal Complexes

The last 20 years have seen the rapid growth of computational methods such as density functional theory (DFT) as a practical tool to study reaction mechanisms.\textsuperscript{55} Figure 1.22, which represents the number of publications containing the keyword “density functional theory” in chemistry and in all different fields, has been obtained by using the Web of Knowledge Database. This graph clearly shows by itself how DFT has emerged since 1990.

Nowadays, DFT is the main computational technique employed to understand the reactivity of transition metal (TM) complexes. The availability of more powerful computing hardware gives the possibility of modelling experimental problems and allows the location of reactive species along a potential energy surface (PES). However, challenges remain.\textsuperscript{56}

One of the earliest examples involving the reaction mechanism of intermolecular C–F activation at TM systems has been reported in 1997 by Su and Chu who studied the C–F activation of CH$_3$F at $trans$-[M(X)(PH$_3$)$_2$] (M = Rh, Ir; X = CH$_3$, H, Cl). Since then the field has diversified and several computational studies of intermolecular C–F activation of fluoroaromatics have been reported.
The following section will review key examples in this field and will also stress the point that a dialogue between experimentalists and theoreticians is essential. Indeed, most of the studies covered involve collaborations.

In the first section, oxidative addition from a computational perspective will be introduced before a discussion of the first reported examples of ligand-assisted C–F activation. Finally, studies of other mechanisms such as hydrodefluorination and nucleophilic attack processes will be covered.

1.3.1 Oxidative Addition

The first example in this area was reported in 1998 by Eisenstein, Caulton and Perutz on the oxidative addition of 1,4-C₆F₂H₄ at osmium and rhodium complexes.57 This work, which is also one of the earliest studies on intermolecular aromatic C–F activation in the presence of other bonds, highlights the thermodynamic preference for C–F activation over C–H activation. B3LYP calculations show that [Os(4-C₆FH₄)(F)(CO)(PH₃)₂], obtained after C–F activation, is 16.2 kcal/mol more stable than its C–H activated isomer, [Os(2-C₆F₂H₃)(H)(CO)(PH₃)₂]. Further calculations confirm that C–F activation is more accessible thermodynamically, with [Rh(η⁵-C₅Me₅)(4-C₆FH₄)(F)(PH₃)] being 2.7 kcal/mol more stable than [Rh(η⁵-C₅Me₅)(2-C₆F₂H₃)(H)(CO)(PH₃)₂]. However, C–H activation is observed experimentally which implies that this process must be kinetic in origin. This is confirmed by calculations in which the transition state for C–F activation is +23.9 kcal/mol above that of C–H activation.

In 2004, McGrady and Perutz studied computationally the oxidative addition of C₆X₆ (X = F, H) at [M(H₂PCH₂CH₂PH₂)] fragments (M = Ni, Pt; see Figure 1.23).58 C–F activation at [Ni(H₂PCH₂CH₂PH₂)] proceeds from an η²-C₆F₆ adduct (73, E = -25.0 kcal/mol), in which a 3-centred transition state TS (73 – 74) (E = -2.5 kcal/mol) is computed to give [Ni(C₆F₅)(F)(H₂PCH₂CH₂PH₂)] (74, E = -44.7 kcal/mol). Similar features are seen for M = Pt in which C–F activation occurs from 78 (E = -16.4 kcal/mol) via TS (78 – 79) (E = +12.9 kcal/mol) to give [Pt(C₆F₅)(F)(H₂PCH₂CH₂PH₂)] (79, E = -40.6 kcal/mol).
C–H activation of C₆H₆ has also been computed at [M(H₂PCH₂CH₂PH₂)] complexes. Both Ni and Pt showed formation of an η²-C₆H₆ adduct, 75 and 80, respectively, prior to C–H activation. The C–H cleavage step is found to be more accessible kinetically for Pt at 80 compared to Ni ($\Delta E^\ddagger_{\text{Pt}} = +15.5$ kcal/mol, $\Delta E^\ddagger_{\text{Ni}} = +21.3$ kcal/mol). In addition, the reaction at Pt is also more favourable thermodynamically than at Ni ($\Delta E_{\text{Ni}} = +20.4$ kcal/mol, $\Delta E_{\text{Pt}} = +0.1$ kcal/mol).

These differences in energies for C–F and C–H activation were explained by the nature of the M–F and M–H interactions for the two metal centres. For Pt, the greater radial extent of the 5d orbitals tends to strengthen the M–H interaction and therefore favours the C–H activation. In addition, the same feature destabilises the Pt–F interaction due to greater Pt(dπ)-F(pπ) repulsion. Overall, [Ni(H₂PCH₂CH₂PH₂)] is predicted to have...
enhanced selectivity for C–F activation, even in the presence of C–H bonds. With [Pt(H2PCH2CH2PH2)] both C–F and C–H activation are feasible and C–F activation is thermodynamically preferred. As with other oxidative additions at Group 10 [ML2] species59 a bent geometry imposed by a chelate ligand enhances reactivity. Indeed, calculations at [Ni(PH3)2] show a 10 kcal/mol destabilisation of both the η2-C6F6 adduct and the final oxidative addition product.

Since the work of McGrady and Perutz, several examples of computational studies on selective aromatic C–F activation at nickel complexes have emerged.32c,60 In 2008, Radius and co-workers reported a joint experimental and computational study on the selective C–F activation of a range of fluoroaromatics at [Ni2(Pr3Im)2(COD)] (21) and [Ni(Pr3Im)(η2-C2H4)] (22, Pr3Im = 1,3-bis(isopropyl)imidazol-2-ylidene).32d In all cases, C–F activation occurs after formation of an η2-adduct, as previously described by McGrady and Perutz. Therefore all energy barriers are relative to the lowest η2-species. C–F activation of C6F6 at {Ni(Pr3Im)2} occurs via a three-centred transition state with a computed energy of +24.3 kcal/mol (see Table 1.1). With C10F8, C–F activation at the 2-position is more accessible kinetically and thermodynamically than at the 1-position (ΔΔH‡ = 1.8 kcal/mol, ΔΔH = -7.8 kcal/mol) with a computed barrier of 25.5 kcal/mol. C–F activation of C6F3CF3 at {Ni(Pr2Im)2} has also been computed. Calculations show that activation of C6F3CF3 at the 4-position is kinetically and thermodynamically preferred.

Table 1.1: Computed energies (kcal/mol) for C–F activation of fluoroaromatics at [Ni(Pr2Im)2] relative to the most stable η2-adduct.32d

<table>
<thead>
<tr>
<th>ArF-F</th>
<th>TS</th>
<th>trans-[Ni(F)(ArF)(Pr2Im)2]</th>
<th>Selectivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6F6</td>
<td>+24.3</td>
<td>-31.3</td>
<td>-</td>
</tr>
<tr>
<td>C10F8</td>
<td>+27.3</td>
<td>-18.9</td>
<td>1-position</td>
</tr>
<tr>
<td></td>
<td>+25.5</td>
<td>-26.8</td>
<td>2-position</td>
</tr>
<tr>
<td>C6F3CF3</td>
<td>+24.6</td>
<td>+8.0a</td>
<td>2-position</td>
</tr>
<tr>
<td></td>
<td>+26.2</td>
<td>+0.5a</td>
<td>3-position</td>
</tr>
<tr>
<td></td>
<td>+21.7</td>
<td>0.0a</td>
<td>4-position</td>
</tr>
</tbody>
</table>

* Only relative energies were reported for these species.

Selective C–F activation over C–H activation is also seen for the activation of 1,2,4-C6F3H3 and 1,2,3-C6F3H3. With 1,2,4-C6F3H3, C–F activation occurs at the 2-position.
with a transition state located at 24.3 kcal/mol above the $\eta^2$-adduct. Activations at the 1- and 4-positions are 3.1 kcal/mol and 5.7 kcal/mol higher in energy, respectively. Finally, with 1,2,3-C$_6$F$_3$H$_3$ the calculations indicate a kinetic preference for reaction at the 2-position ($\Delta H^\ddagger = 20.8$ kcal/mol) although in this case this is not borne out experimentally where activation at the 1-position dominates. DFT calculations have also been employed to aid the spectroscopic characterisation of intermediates in the C–F activation process, including mononuclear [Ni(PEt$_3$)$_2$(C$_6$F$_6$-$\eta$H$_n$)$_n$] and dinuclear [Ni(PEt$_3$)$_2$]$_2$(C$_6$F$_6$-$\eta$H$_n$)$_n$ species ($n = 0$–2).$^{25,26b}$

Other examples of selective C–F activation in the presence of C–H bonds have also been studied computationally. In 2007, Harman et al. reported the reaction of [TpW(NO)(PMe$_3$)($\eta^2$-C$_6$H$_6$)] (82, Tp = trispyrazolyborate) with C$_6$FH$_5$ to give [TpW(C$_6$H$_5$)(F)(NO)(PMe$_3$)] (83, see Figure 1.24).$^{61}$ In contrast to the above studies, C$_6$FH$_5$ reacts through a $\kappa^1$-F (or a $\kappa^1$-H) intermediate. LSDA calculations showed that both C–F activation and ortho-C–H activation are facile but the reversibility of the C–H activation ($\Delta E^\ddagger = +12.5$ kcal/mol for the reverse reductive coupling) added to the irreversible C–F activation ($\Delta E = -52.0$ kcal/mol) account for formation of 83. It should be, however, noted that an $\eta^2$-adduct of C$_6$FH$_5$ has been located on the PES but it is found not to be on the pathway for either C–H or C–F bond cleavage.

![Figure 1.24: C–F activation of C$_6$FH$_5$ with 82.$^{61}$](image)

In 2002, Rzepa and co-workers also studied the C–F activation of monofluoroarenes and showed that the reaction is promoted by the choice of ring substituents.$^{62}$ Oxidative addition of C$_6$FH$_5$ at [Pd(PH$_3$)$_2$] has a computed barrier of 41.2 kcal/mol, however, this barrier is reduced by 5.7 kcal/mol for 4-C$_6$FH$_4$NO$_2$ and by 13.1 kcal/mol for 2-C$_6$FH$_4$NO$_2$. In addition, these effects appear to be additive as with 2,4-C$_6$FH$_3$(NO$_2$)$_2$ the activation barrier is reduced by 19.4 kcal/mol to +21.8 kcal/mol. The large effect of the
2-NO₂ group is linked to a short Pd⋯O contact in the transition state. Indeed, COSMO (H₂O) calculations showed formation of a stable Meisenheimer-type structure 84 (E = -7.4 kcal/mol, see Figure 1.25) in which the subsequent loss of F⁻ is facile.

Bahnanyar and co-workers reported similar results for the reaction of 2-fluoro-5-nitrobenzoate with [Pd(PH₃)₂] in which an even stronger Pd⋯O interaction of 2.13 Å is computed in the transition state.⁶³

1.3.2 Ligand-Assisted C–F Activation

More recently, a new type of mechanism for intermolecular aromatic C–F activation has emerged. In 2008, Macgregor and co-workers reported the first examples of ligand-assisted C–F activation, involving a “phosphine-assisted C–F bond activation”.³⁷,⁵⁴ This reaction pathway consists of a nucleophilic attack of an electron-rich metal-phosphine complex, [ML₉(PR₃)] (85), at electron deficient polyfluorinated aromatics to form a new M-ArF bond (see Figure 1.26).
However, the displaced F is trapped by a phosphine ligand such that the C–F bond adds over the M–PR\(_3\) bond to give a metallophosphorane intermediate, [L\(_n\)M(Ar\(^{5}\))(PR\(_3\)F)], \(^{86}\) This process, which involves a 4-centred transition state TS \((85 - 86)\), contrasts with the 3-centered structures associated with concerted oxidative addition. From \(^{86}\) subsequent transfer of an R group to the metal centre then generates a metal-alkyl complex, \(^{87}\), with a fluorophosphine co-ligand. Alternatively, F can transfer to generate a metal-fluoride, \(^{88}\), similar to a conventional oxidative addition product. Interestingly, species \(^{87}\) and \(^{88}\) are both oxidized products; however, the mechanism does not correspond to oxidative addition.

Phosphine-assisted C–F activation was first characterised for the reactions of C\(_6\)F\(_6\) at [Ir(Me)(P\(_\text{Et}_3\)\(_3\))]\(^{54}\) and of C\(_5\)F\(_5\)N at [Pt(P\(_\text{R}_3\))\(_2\)]\(^{37}\) which, in both cases, leads to fluorophosphine ligands being observed experimentally\(^{33,53}\) (see Figures 1.10 and 1.21). BP86 calculations on the C–F activation of C\(_6\)F\(_6\) at the model system trans-[Ir(Me)(PH\(_3\))\(_2\)(PH\(_2\)Et)] \(^{89}\) showed that the reaction proceeds from an encounter complex \((90)\) with a computed free energy of +5.1 kcal/mol in which the C\(_6\)F\(_6\) ring lies approximately parallel to the Ir coordination plane at a distance of about 3.5 Å (see Figure 1.27).

![Figure 1.27: Computed reaction profile for phosphine-assisted C-F activation of C\(_6\)F\(_6\) at trans-[Ir(Me)(PH\(_3\))\(_2\)(PH\(_2\)Et)] to give the metallophosphorane intermediate 91 followed by axial Et group transfer to Ir to form 92. \(^{54}\) Computed free energies are in kcal/mol and selected distances are in Å.](image-url)
Subsequent nucleophilic attack from 90 leads to the 4-centred transition state, TS (90 – 91) (G = +29.0 kcal/mol), with a short Ir–C contact (2.10 Å) and significant lengthening of the C–F bond (1.97 Å). TS (90 – 91) links to a metallophosphorane intermediate, trans-[Ir(C₆F₅)(Me)(PH₃)₂(PC₂H₅)] (91) with a computed energy of +19.8 kcal/mol from which the axial Et group transfers to Ir to form trans-[Ir(C₆F₅)(C₂H₅)(Me)(PH₃)₂(PC₂H₅)] (92, G = -13.7 kcal/mol). From 92, subsequent β–H elimination and CH₄ reductive elimination give the final model product trans-[Ir(C₆F₅)(C₃H₅)(Me)(PH₃)₂(PC₂H₅)] (93, G = -27.7 kcal/mol). In addition, the authors showed that phosphine-assisted C–F activation is promoted by more electron-rich metal centres and that the barrier to C–F activation is lowered by 4-5 kcal/mol for each ortho-F present in the substrate.

At the same time, BP86 calculations were performed for the C–F activation of C₅NF₅ at [Pt(PR₃)₂] (R = Ir, Cy) to give trans-[Pt(4-C₅NF₄)(R)(PR₃)(PR₂F)]. A computational model, [Pt(PH₃)(PH₂Me)] (94), was used leading to trans-[Pt(4-C₅NF₄)(Me)(PH₃)(PH₂F)] (97). Calculations have also characterised alternative routes to both trans- and cis-[Pt(4-C₅NF₄)(F)(PH₃)(PH₂Me)], 98 and 99, respectively, as shown in Figure 1.28. Complexes 98 and 99 are more favourable thermodynamically than 97, indicating that formation of the last of these must be kinetic in origin. Calculations showed that 97 can be formed directly from [Pt(PH₃)(PH₂Me)] via a phosphine-assisted transition state, TS (94 – 97) (E = +20.8 kcal/mol). In this case, the P–Pt–P angle is almost linear and the {PH₂MeF}⁻ phosphoranide moiety is cis to a vacant coordination site to which the Me group can transfer from P to Pt to give 97. This final product is therefore formed via a one step process and involves concerted C–F and P–C activation.
Alternatively, initial formation of an $\eta^2$-adduct is postulated ($95$, $E = -8.8$ kcal/mol) followed by phosphine-assisted C–F activation through $\text{TS (95 - 96)}$ ($E = +24.5$ kcal/mol) in which the P–Pt–P angle is now bent. In this case, a metallophosphorane intermediate is located ($96$, $E = -2.0$ kcal/mol) in which Me- or F-transfer can occur to give $97$ or $98$ respectively. Formation of the latter occurs through $\text{TS (96 - 98)}$ ($E = +3.6$ kcal/mol) and is found to be more accessible than formation of $97$ via $\text{TS (96 - 97)}$ ($E = +8.3$ kcal/mol). Finally, a conventional 3-centred transition state for oxidative addition have also been located, $\text{TS (95 - 99)}$, with a computed energy of 19.5 kcal/mol. This transition state is therefore close in energy to $\text{TS (94 - 97)}$ ($E = +20.8$ kcal/mol), suggesting that oxidative addition should be competitive with phosphine-assisted C–F activation. No oxidative addition product analogous to $99$ was seen experimentally, however. More recently, C–F activation of $C_6F_6$ at $[\text{Pt(PR}_3)_2]$ has been studied computationally and similar features have been observed.65
In 2010, a phosphine-assisted oxidative addition pathway has been computed for the reaction of C₅NF₅ at [Ni(PMe₃)]₂ (100) to give trans-[Ni(2-C₅NF₄)(F)(PMe₃)]₂ (103). This C–F activation at the 2-position contrasts with the previous example in which the reaction occurs at the 4-position. BP86 calculations showed initial formation an η²-arene intermediate [Ni(η²-C₅NF₅)(PMe₃)]₂ (101, E = -23.6 kcal/mol) from which C–F activation occurs via a phosphine-assisted transition state, TS (101 – 102) (E = -7.2 kcal/mol), to form a metallophosphorane intermediate (102, E = -15.6 kcal/mol, see Figure 1.29).

![Figure 1.29: Computed reaction profile for C–F activation of C₅NF₅ at 100. Computed energies are in kcal/mol and selected distances are in Å.](image)

The final product trans-[Ni(2-C₅NF₄)(F)(PMe₃)]₂ (103, E = -48.2 kcal/mol) is formed from 102 via TS (102 – 103) (E = -15.5 kcal/mol) in which F is transferred onto Ni. The key feature in this process is the short computed Ni···N contact (1.93 Å) in which the N lone-pair stabilises the transition state TS (101 – 102). This interaction is strong enough to alter the regioselectivity in favour of the 2-position. It should be, however, noted that for the C–F activation of C₅NF₅ at [Pt(PH₃)(PH₂Me)] a similar interaction was computed but in this case this was not strong enough to affect the outcome of the reaction which proceeds via C–F activation at the 4-position.
Another type of ligand-assisted C–F activation has been reported by Nakamura and co-workers in which the combination of mixed $P,O$-chelating ligands and the presence of Lewis acidic Mg$^{2+}$ centres promotes C–F activation of C$_6$FH$_5$ at Ni (see Figure 1.30).$^{66}$ The C$_6$FH$_5$ moiety can bind the Mg$^{2+}$ centre such that it introduces a stabilising Mg···F interaction in the $\eta^2$-adduct 105. C–F cleavage is postulated to occur via TS (105 -106) to give Ni-phenyl species 106 located at -40.8 kcal/mol. Attempts to optimise the $\eta^2$-adduct 105 showed spontaneous formation of 106 suggesting that the process is barrierless.

Figure 1.30: Spontaneous C–F activation of C–F activation of C$_6$FH$_5$ at Ni. Free energies are in kcal/mol.$^{46}$

1.3.3 Other Mechanisms

As discussed in the experimental section, other types of intermolecular aromatic C–F activation have been put forward. The following section will review examples of HDF and nucleophilic attack processes.

(i) Hydrodefluorination Reactions

Eisenstein and Andersen reported a joint computational and experimental study on the HDF of C$_6$F$_6$ at [Ce(Cp')$_2$(H)] $[\text{Cp}' = 1,3,4-(\text{Me}_3\text{C})_3(\text{C}_5\text{H}_2)]$.\textsuperscript{42} Using a [La($\eta^5$-C$_5$H$_5$)$_2$(H)] model, initial calculations ruled out processes based either a $\sigma$-bond metathesis transition state (see Figure 1.31) or initial hydride transfer onto the arene ring.
However, a mechanism involving initial formation of a σ-adduct (108, \(G = -8.2\) kcal/mol) has been computed in which one F substituent on the ring interacts with the La metal centre (see Figure 1.32).

This acts as a ‘hook’ and brings an ortho-C–F bond close to the hydride ligand. C–F activation from 108 proceeds via TS (108 – 109) (\(G = +29.8\) kcal/mol) in which F transfers onto hydride to generate \([\text{La(\(\eta^5\)-C\(_5\)H\(_5\))\(_2\)(HF)})\] (109, \(G = -61.8\) kcal/mol). The final products C\(_6\)F\(_5\)H and \([\text{La(\(\eta^5\)-C\(_5\)H\(_5\))\(_2\)(F)})\] (110, \(G = -90.5\) kcal/mol) are obtained via TS (109 – 110) (\(G = -60.2\) kcal/mol) corresponding to a proton transfer. In addition, the authors showed that this C–F activation process involves a significant redistribution
of charge with the negatively hydride becoming protonic and the originally positively charged *ortho*-carbon becoming carbanionic.

(ii) Nucleophilic Attack by a Ligand

Another type of intermolecular C–F activation of fluoroaromatics was reported by Lledós and co-workers, involving a nucleophilic attack by a bridging-S ligand in [Pt₂(μ-S)₂(R₂P(CH₂)₃PR₂)] (111, R = Ph; 114, R = H).⁶⁷ Experimentally, the reaction between 111 and C₆F₆ gives [Pt(o-S₂C₆F₄)(R₂P(CH₂)₃PR₂)] (112) and [Pt₃(μ₃-S)₂(R₂P(CH₂)₃PR₂)₃][F]₂ (113). DFT calculations (B3LYP, Toluene) with R = H showed that the bridging S ligand in [Pt₂(μ-S)₂(H₂P(CH₂)₃PH₂)₂] can attack the C₆F₆ ring in a conventional Sₐr process via TS (114 – 115) (E = +31.5 kcal/mol, see Figure 1.33) to give 115 (E = +0.5 kcal/mol).

![Diagram](attachment:image.png)

**Figure 1.33:** Computed mechanism for the reaction of [Pt₂(μ-S)₂(R₂P(CH₂)₃PR₂)] with C₆F₆⁶⁷ Computed energies are in kcal/mol and selected distances are in Å.

After rearrangement of 115, a second Sₐr step can occur at the 2-position of the SC₆F₅ ligand with a computed transition state energy of +31.7 kcal/mol, corresponding to TS (115 – 116) to give 116 (E = -8.4 kcal/mol) as an initial product. This species can then react to finally yield 117 and 118; however, these steps were not studied computationally. The high barriers for this double Sₐr process are consistent with the
slow reaction seen experimentally which occurs in toluene for 5 days. In contrast, reaction with C₅F₅N is rapid at room temperature, but results only in the first S_NAr step. Calculations in this case show a much reduced barrier for initial attack of the $\mu$-S ligand at the 4-position of the ring with a computed transition state energy of +20.5 kcal/mol, however, the second attack has a higher barrier of +34.1 kcal/mol.
1.4 Thesis Overview

The aim of the work presented in this thesis is to investigate the selective aromatic C–F activation. The main technique employed is density functional theory (DFT) and the computational details used are given in Chapter 2. In addition, a more detailed description of DFT is provided in Chapter 6.

Chapter 3 focuses on the C–F activation of C₆F₅H at [Rh(SiR₃)(PMe₃)₃] (R₃ = Me₂Ph, Ph₃), the first step of the catalytic HDF reaction reported by Milstein and Aizenberg.¹⁵a This chapter provides an explanation for the selective C–F activation, observed experimentally, in the presence of C–H bonds. In addition, a novel type of ligand-assisted C–F activation, involving the silyl ligand, is also described.

Chapter 4 presents a study of the C–F activation of C₅NF₅ at the 2- and 4- positions at [Rh(X)(PEt₃)₃] (X = Si(OEt)₃, Bpin, where Bpin = pinacolate = –OCMe₂CMe₂O–).⁶⁸ This chapter shows that C–F activation of C₅NF₅ at the 2-position occurs via a silyl-and boryl-assisted processes and therefore explains the experimental observations.

Chapter 5 details the investigation of possible reaction mechanism for the HDF reaction of C₆F₅H at [Ru(H)₂(CO)(NHC)(PPh₃)₂] (NHC = SIMes, SIPr, IMes, IPr) reported by Whittlesey and co-workers.¹⁵f Several pathways are considered to explain the formation of 1,2,3,4-C₆F₄H₂ seen experimentally, and the lowest process occurs via a novel nucleophilic attack of one hydride ligand at the fluoroarene moiety.
Chapter 2: Computational Details

This chapter deals with the practical aspects of the calculations that have been used in this thesis. A more comprehensive discussion of the methodologies involved can be found in Chapter 6.

(i) Method and Functionals

Density functional theory (DFT) calculations were performed with the Gaussian03 \(^69\) and Gaussian09 \(^70\) software packages. The BP86 functional, including the gradient corrected exchange functional of Becke \(^71\) and correlation functional of Perdew \(^72\), was used. BP86 belongs to the generalized gradient approximation (GGA) functionals. Other functionals (e.g. hybrid-GGA, meta-GGA) have also been tested. In this case, it has been found that the outcome of the reaction in Chapter 3 was similar to the one computed with BP86 (see Chapter 6). In addition, BP86 does not compute a percentage of exact exchange, known to increase the computational expensive of the calculations.

(ii) Pseudo-Potentials and Basis sets

The Stuttgart/Dresden (SDD) pseudo-potentials and the associated basis sets were employed to describe Ru, Rh, P and Si. \(^73\) P and Si were augmented by a set of d-orbital polarisation functions \(^74\) (\(\zeta = 0.387\) and 0.284, respectively), while 6-31G\(^**\) basis sets were employed for all other atoms. \(^75\) The use of different basis sets has also been tested, including triple-zeta polarised (6-311G\(^**\)), diffuse double-zeta polarised (6-31++G\(^**\)) and diffuse triple-zeta polarised (6-311++G\(^**\)) basis sets. \(^76\) Calculations showed that the use of more extended basis sets does not significantly affect the final results, therefore 6-31G\(^**\) basis sets were employed in this thesis.

(iii) Optimisation Procedure

Reactants and intermediates were optimised without symmetry constraints by using the default SCF convergence criterion (10\(^-8\) au) and the keyword “opt”. In this case, the optimisation procedure was run until a stationary point on the potential energy surface (PES) was found. From these geometries, frequency calculations were performed to confirm the location of minima (no imaginary frequency).
In order to locate a transition state, a stationary point thought to be connected to it is optimised. This intermediate can be obtained from an X-ray crystallographic structure (e.g. reactant) or built from chemical intuition. Once the structure is optimised a scan can be performed by varying one or several parameters (e.g. bond lengths, bond angles). The purpose of this step is to locate a maximum on the potential energy surface (PES) corresponding to a transition state. Before optimising this stationary point, a frequency calculation was performed in order to confirm the presence of the desired imaginary frequency. Identification of the proper imaginary frequency leads to the optimisation of the structure (without any constraint) and its characterisation by a frequency calculation. In some cases, the use of “opt=calcall” option (force constants are computed at every point) was required for example when the transition state was on a flat part of the PES.

After location of the transition state, intrinsic reaction coordinate (IRC) calculations were used in order to connect the stationary point to the adjacent intermediates, in the reverse and forward directions, on the PES.

(iv) Conformation Searching

The majority of the stationary points in this thesis were subjected to extensive conformational searching following the recently published protocol developed in our group. For each initial structure a molecular dynamics (MD) simulation was performed using the Tinker program and the MM3 force field. During the simulation, the metal-ligand bonds were fixed, due to a lack of parameters, in order to allow the movement of the substituents on the ligands. MD simulations were run for 1 nanosecond in an NVT ensemble, with coordinates being collected every picosecond to generate 1000 structures. The trajectories were propagated using the modified Beeman integration algorithm and a Berendsen thermostat was used to keep the temperature around 1000 K. This relatively high temperature was used in order to ensure that the conformational space was fully explored. The 1000 structures were then optimised with the MM3 force field with the same metal-ligand bond constraints as above. Up to 100 energetically reasonable structures were then selected for optimisation at the DFT level using the “opt=loose” option and SCF convergence of $10^{-6}$ au. Typically, the lowest 10 energy structures were then optimised as previously described without the “opt=loose” option.
As an example, the $\text{[Rh\{SiOMe}_3\}(\text{PMe}_3)_3]}$ complex in Chapter 4 was subjected to this conformational searching procedure. After optimisation of the 1000 structures at the molecular mechanics level, 39 different structures were collected. In this case, all the structures were optimised at the DFT (BP86) level using the “loose” option and the SCF convergence of $10^{-6}$ au. After optimisation, the difference in energies between the two extreme structures was 1.7 kcal/mol. The lowest 10 energy structures were then optimised and, in this case, the difference in energy between the less and most stable structure was around 0.5 kcal/mol. The most stable conformation is reported in this thesis.

(v) Energies

All reported energies in this thesis include a correction for zero-point energies at 0 K and free energies are at 298.15 K and 1 atm, unless otherwise stated. These energies have been obtained from the frequency calculations. In addition, the effect of solvation has been investigated using the polarisable continuum model (PCM, radii=UFF). This effect was found to be minimal in Chapters 3 and 4 but important in Chapter 5. Therefore, computed energies in THF have been reported in that case.

(vi) Physical Chemistry Background

The following sections include more detail on the background physical chemistry in order to understand the thermodynamic quantities such as enthalpy, entropy and Gibbs free energy which comes out of the Gaussian package software.

For all systems, the allowed energy states of molecules are quantified and can be found by solving the Schrödinger equation for a particle in a box defined by: \[^{78}\]

\[
-\frac{\hbar^2}{2m} \frac{d^2 \psi(x)}{dx^2} + V(x)\psi(x) = \varepsilon \psi(x)
\]  

(2.1)

where $\hbar$ is the reduced Planck constant, $m$ the mass of the particle, $x$ the position of the particle while $V(x)$, $\psi(x)$ and $\varepsilon$ are the potential energy, the wave function and the allowed energy of the particle, respectively. When the Schrödinger equation is solved, each wave function, $\psi(x)$, has an associated energy $\varepsilon_n$, where $n$ is the quantum number.
Also, the number of wave functions that have the same energy, \( \varepsilon_n \), corresponds to the degeneracy of that level, \( g_n \).

Molecules do not have only electronic energy (\( \varepsilon_{\text{elec}} = -D_e \)) but also kinetic translational energy. In the case of a particle of mass \( m \) in a one-dimensional interval \( 0 \leq x \leq a \), the allowed translational energy is given by:

\[
\varepsilon_{\text{trans}} = \frac{n^2 \hbar^2}{8ma^2} \quad n = 1, 2, ... \tag{2.2}
\]

However, for a particle in a three-dimensional volume such as a rectangular parallelepiped of sides \( a \), \( b \), and \( c \), the allowed energies in Equation 2.2 becomes:

\[
\varepsilon_{\text{trans}} = \frac{\hbar^2}{8ma^2} \left( \frac{n_x^2}{a^2} + \frac{n_y^2}{b^2} + \frac{n_z^2}{c^2} \right) \quad n_x = 1, 2, ... \quad n_y = 1, 2, ... \quad n_z = 1, 2, ... \tag{2.3}
\]

In addition to translational energy, molecules have vibrational and rotational motions. The vibrational motion of a diatomic molecule can be modelled by a harmonic oscillator. In a one-dimensional harmonic oscillator, the energy is restricted to the quantized values:

\[
\varepsilon_{\text{vib}} = \frac{\hbar}{2\pi} \left( k \frac{1}{\mu} \right)^{1/2} \left( v + \frac{1}{2} \right)
\]

\[
\varepsilon_{\text{vib}} = h \nu \left( v + \frac{1}{2} \right) \quad v = 0, 1, 2, ... \tag{2.4}
\]

with \( \nu \) being the vibrational frequency read as:

\[
\nu = \frac{1}{2\pi} \left( k \frac{1}{\mu} \right)^{1/2} \cdot \tag{2.5}
\]

\( k \) is the force constant of the string associated with the bond and \( \mu \) the reduced mass of the molecule given by:
\[ \mu = \frac{m_1 m_2}{m_1 + m_2}. \] (2.6)

One important feature of Equation 2.4 is that for \( v = 0 \), the energy of the ground state is not zero. This therefore corresponds to the lowest energy level called the zero-point energy of the harmonic oscillator.

In the case of polyatomic molecules, the vibrational motion decomposes into \( 3N - 5 \) (linear) or \( 3N - 6 \) (non-linear) normal modes in which each acts as independent harmonic oscillator:

\[ \varepsilon_{\text{vib}} = \sum_{j=1}^{n_{\text{vib}}} \hbar \nu_j \left( \nu_j + \frac{1}{2} \right) \quad \nu_j = 0,1,2, \ldots \] (2.7)

Also molecules rotate. The simplest model to describe these rotational motions is the rigid rotator model. In this case the distance between two atoms, \( R_e \), of masses \( m_1 \) and \( m_2 \), is fixed. Therefore the kinetic energy of the rigid rotator is:

\[ K = \frac{1}{2} I \omega^2 \] (2.8)

where \( \omega \) is the angular velocity and \( I \) the moment of inertia defined by:

\[ I = \mu R_e^2. \] (2.9)

In addition, when the Schrödinger equation is solved for a rigid rotator then the allowed energies is expressed as:

\[ \varepsilon_{\text{rot}} = \frac{\hbar^2}{2I} J(J + 1) \quad J = 0,1,2, \ldots \] (2.10)

and each energy level has a degeneracy, \( g_{\text{rot}} \), equal to:

\[ g_{\text{rot}} = 2J + 1 \quad J = 0,1,2, \ldots \] (2.11)
In summary, the energy of a molecule in the rigid rotator harmonic approximation is defined by:

\[ \varepsilon_{\text{total}} = \varepsilon_{\text{trans}} + \varepsilon_{\text{vib}} + \varepsilon_{\text{rot}} + \varepsilon_{\text{elec}} \]  \hfill (2.12)

**(vii) Thermodynamic Quantities**

Thermodynamic quantities such as enthalpy, entropy and Gibbs free energy are obtained from translational, vibrational, rotational and electronic energies. The starting point in each case is the *canonical* partition function \( Q(N, V, \beta) \) given by:

\[ Q(N, V, \beta) = \sum_j e^{-\beta E_j(N,V)} \]  \hfill (2.13)

in which \( E_j \) are the energies of the eigenvalues of the Schrödinger’s equation for a system of interest and \( \beta \) is the inverse of the temperature read as:

\[ \beta = \frac{1}{k_B T} \]  \hfill (2.14)

where \( k_B \) is the Boltzmann constant and \( T \) the temperature in kelvin.

Equation 2.13 can be however rewritten in terms of \( T \) to give:

\[ Q(N, V, T) = \sum_j e^{-E_j(N,V)/k_B T}. \]  \hfill (2.15)

This last partition function can be further reduced to molecular partition functions \( q(V, T) \) by dividing by \( N! \):

\[ Q(N, V, T) = \frac{[q(V, T)]^N}{N!}. \]  \hfill (2.16)
Finally the partition function of a molecular ideal gas can be deduced from Equation 2.16 to give:

\[ Q(N, V, T) = \frac{[q_{trans}q_{rot}q_{vib}q_{elec}]^N}{N!} \]  

(2.17)

In Equation 2.17, \( q_{trans} \) is defined by:

\[ q_{trans}(V, T) = \left( \frac{2\pi M k_B T}{h^2} \right)^{3/2} V \]  

(2.18)

where \( M \) is the total mass of the molecule and \( h \) is Planck’s constant.

In addition, the volume \( V \) for a specific system can be calculated for an ideal gas:

\[ PV = NRT. \]  

(2.19)

Knowing that \( N = n/N_A \) and \( k_B N_A = R \) it follows that \( V = k_B T/P \) and this can be substituted in Equation 2.18 to obtain:

\[ q_{trans}(V, T) = \left( \frac{2\pi M k_B T}{h^2} \right)^{3/2} \frac{k_B T}{P}. \]  

(2.20)

The electronic partition function can be written as a sum over levels read as:

\[ q_{elec}(T) = \sum_{i}^{\text{levels}} g_{ei} e^{-\epsilon_{ei}/k_B T} \]  

(2.21)

where \( g_{ei} \) is the degeneracy of the energy level and \( \epsilon_{ei} \) is the energy of the \( i \)th electronic level.

However as described previously the energy of the ground electronic state is \( \epsilon_{e1} = -D_e \) therefore the partition function in Equation 2.21 can be rewritten as:

\[ q_{elec}(T) = g_{e1} e^{D_e/k_B T} + g_{e2} e^{-\epsilon_{e2}/k_B T} + \ldots \]  

(2.22)
At this stage, it should be mentioned that in the Gaussian software package the first electronic excitation energy is considered to be much greater than $k_BT$. Therefore, the first and higher excited states are not taken into account at any temperature and the electronic partition function is simplified to:

$$q_{elec}(T) = g_{e1} e^{\frac{\epsilon_e}{k_BT}} \quad (2.23)$$

The rotational partition function is defined by:

$$q_{rot}(T) = \frac{\pi^{1/2}}{\sigma} \left( \frac{T^3}{\Theta_{rot,A} + \Theta_{rot,B} + \Theta_{rot,C}} \right)^{1/2} \quad (2.24)$$

where $\sigma$ is the symmetry number of the molecule and $\Theta_{rot,j}$ the characteristic rotational temperature given by:

$$\Theta_{rot,j} = \frac{\hbar}{2l_j k_B} \quad j = A, B, C. \quad (2.25)$$

Finally, the vibrational partition function is equal to:

$$q_{vib}(T) = \prod_{j=1}^{n_{vib}} \frac{e^{-\Theta_{vib,j}/2T}}{1 - e^{-\Theta_{vib,j}/T}} \quad (2.26)$$

with $\Theta_{vib,j}$ being a characteristic vibrational temperature read as:

$$\Theta_{vib,j} = \frac{h\nu_j}{k_B} \quad (2.27)$$

All these partition functions are important as they are needed to calculate the entropy contribution $S$ given by:

$$S = Nk_B \ln q + k_B \ln N! + Nk_B T \left[ \frac{\partial \ln q}{\partial T} \right]_V \quad (2.28)$$
In addition, to the entropy contribution, the different partition functions can be used to determine the internal thermal energy, $E$:

$$ E = N k_B T^2 \left[ \frac{\partial \ln q}{\partial T} \right]_V $$

(2.29)

and from the internal energy, the heat capacity, $C_V$:

$$ C_V = \left( \frac{\partial E}{\partial T} \right)_{N,V}. $$

(2.30)

In the Gaussian software package, the zero-point energy, $\varepsilon_{ZPE}$, is calculated using only the non-imaginary frequencies. In addition to that, the correction to the internal thermal energy, $E_{tot}$, is obtained by:

$$ E_{tot} = E_{trans} + E_{rot} + E_{vib} + E_{elec}. $$

(2.31)

Once $E_{tot}$ is known, the thermal correction to enthalpy can be deduced by:

$$ H_{corr} = E_{tot} + k_B T $$

(2.32)

and with Equations 2.28 and 2.32, the thermal correction to Gibbs free energy is obtained:

$$ G_{corr} = H_{corr} - TS_{tot} $$

(2.33)

where $S_{tot}$ is given by:

$$ S_{tot} = S_{trans} + S_{rot} + S_{vib} + S_{elec}. $$

(2.34)

It should also be mentioned that all previous energies include the zero-point energy.
Finally in the output file of the software, the following energies can be found:

\[
\begin{align*}
\text{Sum of eletronic and zero-point energies} &= \varepsilon_0 + \varepsilon_{ZPE} \\
\text{Sum of eletronic and thermal energies} &= \varepsilon_0 + E_{tot} \\
\text{Sum of eletronic and thermal enthalpies} &= \varepsilon_0 + H_{corr} \\
\text{Sum of eletronic and thermal free energies} &= \varepsilon_0 + G_{corr}
\end{align*}
\]

where \(\varepsilon_0\) is the total electronic energy.

In addition, if the Gibbs free energy of activation, \(\Delta G^\dagger\), is known therefore the rate constant of a specific reaction can be calculated by using the Eyring equation:

\[
k(T) = \kappa \frac{k_B T}{h} e^{-\Delta G^\dagger / RT}.
\]

(2.35)

where \(\kappa\) is the proportional constant. Equation 2.35 is widely used in transition state theory (TST) which assumes a special type of chemical equilibrium between reactants and activated transition state complexes.
Chapter 3: Mechanistic Study of C–F Bond Activation of Pentafluorobenzene at [Rh(SiR$_3$)(PMe$_3$)$_3$]

3.1 Introduction

This chapter describes computational studies aimed at modelling the C–F bond activation of pentafluorobenzene with [Rh(SiR$_3$)(PMe$_3$)$_3$] (R$_3$ = Me$_2$Ph, Ph$_3$), the first step of the catalytic hydrodefluorination reaction reported by Milstein and Aizenberg.$^{15a}$ Experimentally, the stoichiometric reaction between [Rh(SiMe$_2$Ph)(PMe$_3$)$_3$] and C$_6$F$_5$H occurs at 110 °C to yield quantitatively [Rh(4-C$_6$F$_4$H)(PMe$_3$)$_3$] and FSiMe$_2$Ph (Figure 3.1) while the same catalyst reacts with C$_6$F$_6$ at room temperature. Also, Milstein and co-workers showed that [Rh(SiMe$_2$Ph)(PMe$_3$)$_3$] is non-rigid at room temperature on the NMR time scale, giving rise to broad signals in $^{31}$P{${^1}$H} NMR spectrum.$^{79}$ This last feature is important as the fluxionality for 4-coordinate monovalent d$^8$ complexes is quite rare. This indicates that the high trans-influence of silyl ligands may facilitate phosphine dissociation resulting in intermolecular exchange of the phosphine ligands in the 16-electron complexes.

![Figure 3.1: C–F bond activation of C$_6$F$_5$H by [Rh(SiMe$_2$Ph)(PMe$_3$)$_3$] to form [Rh(4-C$_6$F$_4$H)(PMe$_3$)$_3$] and FSiMe$_2$Ph.$^{15a}$](image)

To explain the selectivity of C–F bond activation, Milstein and Aizenberg proposed two possible mechanisms. The first one is the C–F oxidative addition of C$_6$F$_5$H followed by Si–F reductive elimination. This mechanism was not favoured by the authors as, at that time, oxidative addition of partially fluorinated arenes resulted mostly in C–H rather than C–F bond activation. In addition, Milstein and Aizenberg proposed an electron transfer mechanism for the C–F cleavage step in which an electron can be transferred from the rhodium silyl complex to the substrate to generate C$_6$F$_3$H$^+$ and [Rh(SiR$_3$)(PMe$_3$)$_3$]$^{1+}$, followed by the attack of F$^-$ on silicon to yield [Rh(4-C$_6$F$_4$H)(PMe$_3$)$_3$] and FSiR$_3$. This type of mechanism had been postulated by Milstein.
and co-workers\textsuperscript{53} and subsequently by several other groups.\textsuperscript{49-50,52} In one case, Jones and Edelbach reported the C–F bond activation of fluoroaromatic species by [Rh(η\textsuperscript{5}-C\textsubscript{5}Me\textsubscript{5})(H)\textsubscript{2}(PMe\textsubscript{3})] in pyridine or 1:1 pyridine/benzene.\textsuperscript{52} To assess the possibility of an electron transfer reaction, a series of electrochemical measurements on the oxidation of [Rh(η\textsuperscript{5}-C\textsubscript{5}Me\textsubscript{5})(H)\textsubscript{2}(PMe\textsubscript{3})] and the reduction potential of the polyfluoroaromatics were performed. These experiments showed that the electron transfer of the overall process is uphill by more than 2 V which would require a minimum barrier of 45.0 kcal/mol.

Electron transfer therefore seems unlikely, although this pathway has been modelled and the results will be presented here. In addition, to assess the C–F activation of C\textsubscript{6}F\textsubscript{5}H with [Rh(SiR\textsubscript{3})(PMe\textsubscript{3})\textsubscript{3}] (1\textsubscript{SiMe\textsubscript{3}}), two other mechanisms have been computed (Figure 3.2). Pathway 1, is the formal C–F oxidative addition of C\textsubscript{6}F\textsubscript{5}H, to yield a 18-electron rhodium(III) silyl complex (e.g. \textit{fac}-3) followed by Si–F reductive elimination. Pathway 2 is a silyl-assisted C–F bond activation similar to the phosphine-assisted mechanism described in Chapter 1. In this case, C–F activation involves fluorine transfer directly onto silicon with simultaneous Rh–C\textsubscript{aryl} bond formation.

Figure 3.2: Possible reaction mechanisms for C–F activation of C\textsubscript{6}F\textsubscript{5}H at 1\textsubscript{SiMe\textsubscript{3}}.
3.1.1 Comparison between Experimental and Calculated Structures

This study started by computing three distinct rhodium(I) silyl complexes, [Rh(SiMe$_3$)(PMe$_3$)$_3$] (1$_{SiMe3}$), [Rh(SiMe$_2$Ph)(PMe$_3$)$_3$] (1$_{SiMe2Ph}$) and [Rh(SiPh$_3$)(PMe$_3$)$_3$] (1$_{SiPh3}$), to compare the calculated bond lengths and bond angles with the reported experimental data (see Table 3.1 and Figure 3.3).$^{79-80}$

Table 3.1: Experimental (Exp.) and calculated (Calc.) bond lengths (Å) and bond angles (degrees) in [Rh(SiR$_3$)(PMe$_3$)$_3$] ($R_3$ = Me$_3$, Me$_2$Ph, Ph$_3$).$^{79-80}$

<table>
<thead>
<tr>
<th></th>
<th>1$_{SiMe3}$</th>
<th>1$_{SiMe2Ph}$</th>
<th>1$_{SiPh3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rh–Si</td>
<td>2.402</td>
<td>2.408</td>
<td>2.387</td>
</tr>
<tr>
<td>Rh–P1</td>
<td>2.363</td>
<td>2.377</td>
<td>2.376</td>
</tr>
<tr>
<td>Rh–P2</td>
<td>2.283</td>
<td>2.314</td>
<td>2.322</td>
</tr>
<tr>
<td>Rh–P3</td>
<td>2.305</td>
<td>2.314</td>
<td>2.308</td>
</tr>
<tr>
<td>Si–Rh–P1</td>
<td>144.86</td>
<td>154.59</td>
<td>147.15</td>
</tr>
<tr>
<td>P2–Rh–P3</td>
<td>140.28</td>
<td>154.94</td>
<td>148.51</td>
</tr>
</tbody>
</table>

The first optimised structure was 1$_{SiMe3}$ which showed a distorted square-planar geometry in which the Si–Rh–P1 and P2–Rh–P3 angles are respectively 144.9° and 140.3°. The high trans-influence of the silyl ligand is also seen with an elongation of 0.07 Å of the Rh–P1 bond trans to SiMe$_3$, compared to the Rh–P2 and Rh–P3 distances cis to SiMe$_3$. These features are as well observed in the 1$_{SiMe2Ph}$ complex, studied experimentally by Milstein and Aizenberg.$^{79}$ In their crystallographic structure, the Si–Rh–P1 and P2–Rh–P3 angles of respectively 156.4° and 160.0°, are in good agreement with the computed bond angles in 1$_{SiMe2Ph}$ (Si–Rh–P1 = 154.6°; P2–Rh–P3 = 154.9°). Also, an elongation of the Rh–P1 bond by 0.04 Å was observed experimentally compared to the Rh–P2 and Rh–P3 distances, close to the computed value (0.06 Å). The major discrepancy between the experimental and computational structures is the Rh–P1 bond length which the calculations overestimate by 0.07 Å. In addition, the structure of 1$_{SiPh3}$ was studied experimentally by Thorn and Harlow.$^{80}$ The experimental and computed structures show a greater distortion compared to 1$_{SiMe3}$ and 1$_{SiMe2Ph}$ due to the presence of bulkier phenyl substituents. Also, the major difference in 1$_{SiPh3}$ between the two structures is seen in the Rh–Si bond length which is 0.07 Å shorter (cf. 2.32 Å experimental, 2.39 Å calculated).
Figure 3.3: Computed geometries (with selected key distances in Å) in $^{1}_{\text{SiMe}}$, $^{1}_{\text{SiMePh}}$ and $^{1}_{\text{SiPh}}$. Experimental bond lengths for $^{1}_{\text{SiMePh}}$ and $^{1}_{\text{SiPh}}$ are shown in italics. 

Hydrogen atoms are omitted for clarity. Overall, the computed bonds lengths and bond angles are in reasonable agreement with the reported experimental data. Therefore, the computational model $^{[\text{Rh}]}(\text{SiMe}_3)(\text{PMe}_3)_3$ ($^{1}_{\text{SiMe}}$) has been used to study the experimental reaction between $^{[\text{Rh}]}(\text{SiMe}_2\text{Ph})(\text{PMe}_3)_3$ ($^{1}_{\text{SiMePh}}$) and $\text{C}_6\text{F}_5\text{H}$.

### 3.1.2 Electron Transfer Pathway

In a first step, an electron transfer pathway from $^{1}_{\text{SiMe}}$ to $\text{C}_6\text{F}_3\text{H}$ to form the separated radicals, $^{[\text{Rh}]}(\text{SiMe}_3)(\text{PMe}_3)_3]^{+}$ and $\text{C}_6\text{F}_3\text{H}^{-}$, has been computed. Calculations show that this process is kinetically unfavoured with a change in energy of +120.2 kcal/mol in the gas phase. This decreases to +79.2 kcal/mol when hexafluorobenzene solvent is taken into account via a PCM approach. Therefore, this mechanism has been ruled out.
3.2 Pathway 1: C–F Oxidative Addition and Subsequent Si–F Reductive Elimination

3.2.1 C–F Oxidative Addition

Along Pathway 1, in addition to the \textit{fac}-isomer (\textit{fac}-3), illustrated in Figure 3.2, two further isomers can be formed, namely \textit{mer}-3, with 4-C$_6$H trans to SiMe$_3$, and \textit{mer}-3' with 4-C$_6$H trans to SiMe$_3$ (see Figure 3.4). In \textit{mer}-3, F is cis to SiMe$_3$ and can access reductive elimination directly, whereas in \textit{mer}-3' F is trans SiMe$_3$ and so a prior isomerisation step will be required.

![Diagram](image)

\textbf{Figure 3.4: Three possible isomers formed upon C–F activation of C$_6$F$_5$H to 1SiMe$_3$.}

In this chapter, all selected key distances are in Å while all energies are in kcal/mol, relative to the two separated reactants, 1SiMe$_3$ and C$_6$F$_5$H, denoted by 2. Also, figures show free energies in italics and non-participating hydrogen atoms are omitted for clarity. The stationary points involved for the C–F oxidative addition of C$_6$F$_5$H at 1SiMe$_3$ are shown in Figure 3.5.

The highest energy pathway corresponds to the formation of \textit{mer}-3 (H = -26.3 kcal/mol) via TS (2 – \textit{mer}-3) (H = +34.6 kcal/mol) in which the key C1…F1 bond distance is stretched to 1.58 Å. Short Rh⋯C1 and Rh⋯F1 contacts are also computed (Rh⋯C1 = 2.45 Å, Rh⋯F1 = 2.58 Å) and the Rh–Si bond increases to 2.53 Å (cf. 2.40 Å in 1SiMe$_3$), due to the approach of the 4-C$_6$F$_4$H moiety trans to the SiMe$_3$ ligand. Surprisingly, TS (2 – \textit{mer}-3) shows a contact between P2 and F1 with a distance of 2.83 Å. Related to this is the orientation of the C$_6$F$_5$H moiety, which is distorted away from the expected coplanar arrangement for a concerted oxidative addition. This distortion can be quantified, for an oxidative addition or reductive elimination process by $\alpha$, the angle between the L$_{eq}$–M–L$_{eq}$ and X–M–Y planes. In the current example, X corresponds to
the ipso carbon of 4-C₆F₄H, C1, while Y represents F1 (see Figure 3.6). L_{eq} are the ligands trans to these, here Si and P1. In this case, α = 20.5° and showed that the transition state is twisted away from normal oxidative addition probably due to the interaction with P2.

Figure 3.5: Computed geometries and energies to give mer-3, fac-3 and mer-3′.
The next most accessible pathway proceeds via TS (2 – fac-3) (H = +26.7 kcal/mol) to form fac-3 (H = -29.6 kcal/mol). Significant elongation of the breaking C1⋯F1 bond to 1.72 Å is also computed while the Rh⋯C1 and Rh⋯F1 interactions shorten to 2.18 Å and 2.65 Å, respectively. The Rh⋯F1 contact is slightly longer than the distance between P1 and F1 (P1⋯F1 = 2.59 Å), suggesting that P1 is more involved in the C–F cleavage step. Moreover the C1⋯F1 vector is more twisted relative to the P2–Rh–P3 plane (α = 54.3°) and thus again differs from the usual 3-centred concerted oxidative addition. A similar transition state has been reported for the C–F activation of C₆F₆ at [Ir(Me)(PEt₃)₃] (see Figure 3.7).⁵⁴

In this study, C–F activation of C₆F₆ at [Ir(Me)(PH₃)₂(PH₂Et)] occurs via a phosphine-assisted mechanism and in this case α is 58.1° (relative to the P5–Ir–P6 plane), close to the one in TS (2 – fac-3). However, to quantify this ligand-assisted process, the authors used the P4–Ir–C7–F7 angle which is therefore more suitable than using α, as the phosphine ligand is involved. For the iridium transition state, the P4–Ir–C7–F7 angle is
equal to +34.5° while in TS (2 – fac-3) the P1–Rh–C1–F1 angle is -32.3°. These similarities suggest that TS (2 – fac-3) differs from the traditional concerted oxidative addition in that a degree of phosphine-assistance is computed, in which Rh, C1, F1 and P1, all participate. Further characterisation of TS (2 – fac-3), via IRC calculations, confirmed that fluorine moves toward P1 and weakly interacts with the phosphine ligand, suggesting an anionic phosphoranide \{PFMe_3\}⁻ moiety, before transferring to the rhodium metal centre to yield fac-3 (H = -29.6 kcal/mol). Despite many attempts no metallophosphorane intermediates have been located.

Finally, the lowest C–F oxidative addition process occurs via TS (2 – mer-3') and has a computed barrier of only +17.8 kcal/mol. In the transition state, the C1⋯F1 bond increases to 1.60 Å while the Rh⋯F1 distance remains rather long (2.81 Å). As seen in TS (2 – fac-3), a short P2⋯F1 contact (2.55 Å) is also computed, suggesting that the phosphine ligand is more than a simple spectator and participates in the C–F activation. Indeed, this P2⋯F1 interaction is again shorter than the Rh⋯F1 distance and in this case α is 72.2° while the P2–Rh–C1–F1 angle is -20.7°. IRC calculations from TS (2 – mer-3') confirmed that fluorine weakly interacts with P2, before being transferred to Rh to form mer-3' (H = -31.4 kcal/mol).

The reaction profiles along Pathway 1 for the C–F activation to yield mer-3, fac-3 and mer-3' are shown in Figure 3.8. The stability of the three different isomers follows the trend: mer-3 (H = -26.3 kcal/mol) < fac-3 (H = -29.6 kcal/mol) < mer-3' (H = -31.4 kcal/mol). In mer-3', F is trans to SiMe₃ and therefore has the best arrangement of ligands, having the strongest electron donor ligand (SiMe₃) trans to the weakest donor (F). In addition, in mer-3 the Rh–Si bond trans to 4-C₆F₄H is slightly more elongated than in fac-3, in which 4-C₆F₄H is trans to PMe₃, suggesting that 4-C₆F₄H has a higher \textit{trans}-influence than PMe₃. Therefore, mer-3 is the least stable species because the high \textit{trans}-influence ligand SiMe₃ is trans to 4-C₆F₄H. From these observations, a final trend for the \textit{trans}-influence of the different ligands can be drawn: SiMe₃ > 4-C₆F₄H > PMe₃ > F.
Figure 3.8: Formation of mer-3, fac-3 and mer-3' via C‒F activation, along Pathway 1.

The above comparisons for the three different isomers in terms of energies and geometries can rationalise the difference in stability of the three different transition states: TS (2 – mer-3) (H = +34.6 kcal/mol) < TS (2 – fac-3) (H = +26.7 kcal/mol) < TS (2 – mer-3’) (H = +17.8 kcal/mol). TS (2 – mer-3’) is the most stable transition state as SiMe₃ is trans to vacant site while in TS (2 – fac-3) and TS (2 – mer-3) silyl is trans to PMe₃ and 4-C₆F₄H, respectively. In addition, TS (2 – fac-3) is more accessible than TS (2 – mer-3) because in the former SiMe₃ is trans to PMe₃ while in the latter silyl is trans to 4-C₆F₄H. The difference in energy between TS (2 – mer-3’) and TS (2 – fac-3) can be explained by the position of the phosphine ligand interacting with F1 as both transition states occurs with a degree of phosphine-assistance. In the latter, P1 which interacts with F1 is trans to SiMe₃ while in the former, P2 is trans to a weaker σ-donor ligand (PMe₃). This suggests that PMe₃ in TS (2 – mer-3’) is relatively more electron deficient and thus stronger stabilises F1, making the process more accessible.
As mentioned above, TS (2 – mer-3′) and TS (2 – fac-3) show a degree of phosphine-assistance and therefore differ from the traditional concerted oxidative addition process. During the C–F cleavage step, no metallophosphorane intermediates have been located and the final products are oxidative species. In comparison, Perutz et al. reported the C–F activation of C₅NF₅ at [Ni(PMe₃)₂] which occurs via a phosphine-assisted mechanism.⁶⁰ In this study, a metallophosphorane intermediate is located before F being transferred to Ni to give trans-[Ni(C₅NF₄)(F)(PMe₃)₂]. Therefore, the final species is an oxidative product; however the mechanism is not oxidative addition. This process has been described as “phosphine-assisted oxidative addition” and is similar to TS (2 – mer-3′) and TS (2 – fac-3) where a degree of phosphine-assistance is computed and the final products are Rh(III) species. The difference is the lack of a metallophosphorane intermediate.

3.2.2 Si–F Reductive Elimination from mer-3, fac-3 and mer-3′

The final product [Rh(4-C₆F₄H)(PMe₃)₃] (4) is observed experimentally after elimination of FSiMe₃.¹⁵a Therefore a Si–F reductive elimination step has to be considered from mer-3, fac-3 and mer-3′. For mer-3 and fac-3 this process can happen directly and the computed structures and relative energies involved in this process are shown in Figure 3.9.

The lower pathway for reductive elimination occurs from mer-3 and through the 3-centred transition state TS (mer-3 – 4) (H = -20.1 kcal/mol). In the transition state, the C1–Rh–P1 angle widens to 115.3° (cf. 97.9° in mer-3) and an elongation of the breaking Rh···Si and Rh···F1 bonds, to 2.65 Å and 2.28 Å, respectively, is computed. The Si···F1 contact decreases significantly to 1.87 Å and α which is, in this case, the angle between the Si–Rh–P1 and C1–Rh–F1 angles is 8.9°, consistent with the 3-centred nature of the process. This is in strong contrast with the previous C–F oxidative transition states. The final product 4 is obtained after release of FSiMe₃ and has a computed energy of -59.4 kcal/mol (G = -59.0 kcal/mol).
Figure 3.9: Computed geometries and energies for Si–F reductive elimination from mer-3 and fac-3.
The second reductive elimination pathway proceeds from \textit{fac-3} via the 3-centred transition state TS \((\text{fac-3 – 4})\) \((H = -14.4 \text{ kcal/mol})\). In TS \((\text{fac-3 – 4})\), the Rh···F1 and Rh···Si distances lengthen to 2.20 Å and 2.61 Å, respectively, while a short Si···F1 interaction is computed \((1.91 \text{ Å})\), all consistent with the Si–F reductive elimination process. As seen in TS \((\text{mer-3 – 4})\), the process is almost coplanar, with \(\alpha\) equal to 5.4°.

The reaction profiles for Si–F reductive elimination from \textit{mer-3} and \textit{fac-3} are shown in Figure 3.10. TS \((\text{mer-3 – 4})\) is more stable than TS \((\text{fac-3 – 4})\) by 5.7 kcal/mol. This difference in energy can be understood by looking at the Rh–Si bond. In \textit{mer-3}, the Rh–Si bond \((2.49 \text{ Å})\) is slightly weaker than in \textit{fac-3} \((2.47 \text{ Å})\), as in the former SiMe\(_3\) is trans to 4-C\(_6\)F\(_4\)H, which facilitates the process. Finally, computed free energies further favour formation 4 compared to the other stationary points, as two species are formed from one molecule.

![Figure 3.10: Formation of [Rh(4-C\(_6\)F\(_4\)H)(PMe\(_3\))]\(_3\), 4, and FSiMe\(_3\) via Si–F reductive elimination from \textit{mer-3} and \textit{fac-3}.](image)

The formation of FSiMe\(_3\) from \textit{mer-3’} has also been computed and two different approaches have been considered (Figure 3.11). One way to isomerise \textit{mer-3’} is to dissociate PMe\(_3\) either trans to trimethylphosphine \((\text{cis-5})\) or trans to 4-C\(_6\)F\(_4\)H \((\text{trans-5})\).
From these two putative rhodium(III) silyl complexes an isomerisation process can occur where F moves cis to SiMe$_3$ to give respectively cis-5′ and trans-5′. From these two species, the dissociated phosphine could bind the metal centre to form respectively fac-3 and mer-3″. Si–F reductive elimination from fac-3 has already been discussed and proceeds through a transition state at -14.4 kcal/mol (G = +2.1 kcal/mol).

![Diagram](image_url)

**Figure 3.11:** Possible pathways for the isomerisation of mer-3′ to afford Si–F reductive elimination.

In contrast to the sequence in Figure 3.11, attempts to optimise cis-5 and trans-5 resulted in isomerisation with F moving cis to SiMe$_3$ to give cis-5′ and trans-5′, respectively, while SiMe$_3$ ends up trans to the vacant site. This isomerisation process again reflects the high trans-influence of SiMe$_3$. After further calculations two transition states have been located, for direct formation of cis-5′ and trans-5′ from mer-3′, where the phosphine dissociates at the same time as the isomerisation occurs. The computed geometries and relative energies of the stationary points are shown in Figure 3.12.
Figure 3.12: Computed geometries and energies for the phosphine loss/isomerisation to give cis-5’ and trans-5’.

The higher transition state yields cis-5’ via TS (mer-3’ – cis-5’) (H = -15.5 kcal/mol). In the transition state, the Rh···P3 distance lengthens to 3.75 Å as phosphine is dissociated and the Si–Rh–F1 angle decreases to 169.9° (cf. 175.6° mer-3’). The second transition TS (mer-3’ – trans-5’) (H = -17.5 kcal/mol), gives trans-5’ in which the breaking Rh···P1 bond lengthens to 3.55 Å while the Si–Rh–F1 angle bends back to 150.8° (cf. 175.6° mer-3’).
Species cis-5' and trans-5' both have square pyramidal geometries and a distorted 4-C_{6}F_{4}H ligand. Cis-5' exhibits Rh–C1–C2 and Rh–C1–C6 angles of 110.2° and 134.9°, respectively, while the same angles are 112.5° and 134.4°, respectively, in trans-5'. These distortions are driven by some interactions between the metal centre and the C2–F2 bond. In cis-5', the Rh···C2 and Rh···F2 contacts are 2.89 Å and 2.88 Å, respectively, and the C2–F2 bond elongates to 1.39 Å. In addition, trans-5' shows similar features (Rh···C2 = 2.90 Å, Rh···F2 = 2.93 Å, C2–F2 = 1.39 Å). It should also be mentioned that experimentally these 5-coordinate complexes are known to have a fluxional behaviour as the energy barrier between trigonal bipyramid and square pyramidal is often quite low.

Overall, TS (mer-3' – trans-5') is 2.0 kcal/mol more stable than TS (mer-3' – cis-5'). This small difference in energy may come from the higher trans-influence of 4-C_{6}F_{4}H compared to PMe3 which promotes Rh···P1 dissociation in mer-3'. The stabilisation of trans-5' by 5.1 kcal/mol compared to cis-5' is explained by having 4-C_{6}F_{4}H trans to F while in the later 4-C_{6}F_{4}H is trans to PMe3. In addition, the phosphine loss/isomerisation step to form trans-5' from mer-3' is exothermic by 4.6 kcal/mol (ΔG = -20.7 kcal/mol). This stabilisation of trans-5' again confirms the high trans-influence of SiMe3 which prefers to be trans to a vacant site.

At this point, PMe3 addition to cis-5' and trans-5' gives fac-3 and mer-3", respectively (see Figure 3.11). It should be, however, mentioned that Si–F reductive elimination from both 5-coordinates species is also possible and will be considered in Section 3.5.3. Species mer-3" is found to be slightly less stable than fac-3 by 1.4 kcal/mol and has an unusual distorted octahedral geometry in which the Si–Rh–P1 and Si–Rh–F angles are 141.6° and 62.6°, respectively (Figure 3.13). These distortions appear to be driven by a weak Si···F1 interaction of 2.41 Å, as this contact is generally much longer in the other isomers (mer-3, Si···F1 = 3.25 Å; fac-3, Si···F1 = 2.91 Å).

Si–F reductive elimination from mer-3" occurs through the 3-centred transition state TS (mer-3" – 4) (H = -27.0 kcal/mol). This transition state has C1 symmetry, however a second negative eigenvalue has been found after the frequency calculations. This exhibits an imaginary frequency of -6.83 cm^{-1} corresponding to the rotation of the fluoroaryl ligand and could not be removed, despite many attempts, using very tight
optimisations. This discrepancy, however, should not significantly affect the energy of the transition state. In TS \textit{(mer-$3'' - 4$)}, the C1–Rh–Si angle widens to 129.8° (\textit{cf. 115.8° in mer-$3''$}). The Si···F1 distance shortens to 1.80 Å and the Si···F1 vector is coplanar with the C1–Rh–P1 plane ($\alpha = 0.0°$), as expected for a reductive elimination process. In addition, both Rh···Si and Rh···F1 distances lengthen to respectively 2.95 Å and 2.24 Å whereas the Rh–P1 bond remains rather long (2.63 Å), trans to the vacant site.

![Figure 3.13: Computed geometries and energies for Si–F reductive elimination from mer-$3''$.](image)

The reaction profiles for the Si–F reductive elimination from \textit{mer-$3'$} are shown in Figure 3.14. The most accessible process is through the transition state TS \textit{(mer-$3'$ – trans-$5'$)} with a computed enthalpy of -17.5 kcal/mol where PMe$_3$ dissociates trans to 4-C$_6$F$_4$H and F moves cis to SiMe$_3$. From \textit{trans-$5'$}, PMe$_3$ can bind trans to SiMe$_3$ to form \textit{mer-$3''$}. Reductive elimination from \textit{mer-$3''$} is then facile, with a barrier of 1.2 kcal/mol (H = -27.0 kcal/mol) to form 4 and FSiMe$_3$. Along this pathway the rate-limiting process is the phosphine loss/isomerisation step (H = -17.5 kcal/mol) to yield \textit{trans-$5'$}. 

59
Figure 3.14: Formation of \([\text{Rh}(4-C_6\text{F}_4\text{H})(\text{PMe}_3)_3]_3\), 4, and FSiMe$_3$ via Si–F reductive elimination from mer-3’.  

Reaction profiles comparing the formation of 4 and FSiMe$_3$ from mer-3, fac-3 and mer-3’ are given in Figure 3.15. The highest energy process goes via TS (fac-3 – 4) and has a computed enthalpy of -14.4 kcal/mol. The next most accessible pathway is from mer-3’ via TS (mer-3’ – trans-5’) (H = -17.5 kcal/mol) while the easiest process is from mer-3 through TS (mer-3 – 4) (H = -20.1 kcal/mol). The computed free energies show that the phosphine loss/isomerisation step from mer-3’ and the direct reductive
elimination from \textit{mer-3} become competitive (G = -3.5 kcal/mol) as the entropy favours the dissociation of the phosphine ligand in the former.

![Diagram of molecular structures](image)

Figure 3.15: Formation of \([\text{Rh}(4-C_6F_4H)(\text{PMe}_3)_3], 4, \) and \(\text{FSiMe}_3\) via \(\text{Si-F} \) reductive elimination from \textit{mer-3}, \textit{fac-3} and \textit{mer-3’}.

### 3.2.3 Summary of Pathway 1

The key stationary points for Pathway 1 are shown in Figure 3.16. The lowest lying process involves formation of \textit{mer-3’} with a barrier of +17.8 kcal/mol. Once \textit{mer-3’} is formed, isomerisation to \textit{mer-3’’} is required followed by \(\text{Si-F} \) reductive elimination. It should be noted that C–F activation is always the rate-limiting transition state and gives the three possible isomers, \textit{mer-3, fac-3} and \textit{mer-3’}. From these species, formation of 4 and \(\text{FSiMe}_3\) is then facile. The computed free energies increase the energies of the stationary points, which involve associative processes, by around 16.0 kcal/mol. Species \textit{trans-5’} and 4 are stabilised as they involve dissociation of one ligand. Finally, calculations showed that the C–F activation of \(\text{C}_6\text{F}_5\text{H}\) to form \textit{mer-3’} occurs with a certain degree of phosphine-assistance and therefore differs from the traditional 3-
centred concerted oxidative addition. Overall the process is highly exothermic by 59.4 kcal/mol ($G = -59.0$ kcal/mol).

Figure 3.16: Formation of $[\text{Rh}(4-\text{C}_4\text{F}_4\text{H})(\text{PMe}_3)_3]$, 4, and $\text{FSiMe}_3$ via $\text{C}–\text{F}$ activation of $\text{C}_4\text{F}_5\text{H}$ at $1_{\text{SiMe}_3}$.
3.3 Pathway 2: Silyl-Assisted C–F Bond Activation

This mechanism occurs with fluorine being transferred directly onto silicon with simultaneous Rh–C_Aryl bond formation to yield 4 and FSiMe₃ (Figure 3.2). Several transition states and stationary points have been computed for Pathway 2 but only the lowest energy mechanism for C–F activation will be discussed in detail. The first step is the formation of the η²-arene intermediate 6 which has a trigonal bipyramidal geometry in which the SiMe₃ ligand is in an equatorial position. In addition, the C1=C2 bond distance increases to 1.48 Å, consistent with the Dewar-Chatt-Duncanson model where the C1=C2 bond is weakened by the π-back donation from the metal centre to the π* antibonding orbital of the C₆F₅H moiety. A transition state, TS (2 → 6) (H = +16.1 kcal/mol) for formation of 6 has been computed by lengthening the Si–Rh–P₁ angle (in this case, Si–Rh–P₁ = 132.9°).

![Computed geometries and energies for formation of 6.](image)

From 6, a transition state has been located for C–F activation, TS (6 → 4) (H = +20.1 kcal/mol, see Figure 3.18), in which the C1…F1 is stretched to 1.72 Å. Moreover, the Si…F1 contact actually lengthens by 0.24 Å to 4.04 Å, implying little or no degree of silyl-assistance. Instead, it is the P₃…F1 interaction that shortens, by 0.61 Å to 2.61 Å, suggesting that the phosphine ligand again participates in the C–F activation similar to TS (2 → fac-3) and TS (2 → mer-3') (see Figure 3.19, for a comparison of all three). In addition this P₃…F1 interaction is shorter than the Rh…F1 contact (3.01 Å) and α is 64.3°. In this case, a better way to quantify this process is by using the torsion angles. In TS (6 → 4), the P₃–Rh–C₁–F₁ is -21.1°, very similar to the P₂–Rh–C₁–F₁ angle.
(-20.7°) in TS (2 – mer-3') and relatively close to the P2–Rh–C1–F1 angle (-32.3°) in TS (2 ‒ fac-3).

These three transition states exhibit similar geometries, suggesting that TS (6 ‒ 4) also proceeds via a degree of phosphine-assistance. However, unlike TS (2 ‒ fac-3) and TS (2 ‒ mer-3'), instead of having F transferred on the metal centre, IRC calculations show that F moves toward silicon to afford directly the fluorosilane elimination. These different outcomes can be understood by looking at the interactions between the metal centre and the 4-C₆F₄H moiety (see Figure 3.20).

Figure 3.18: Computed geometries and energies for C‒F activation to give 4 and FSiMe₃.

Figure 3.19: Computed geometries and energies for C‒F activation via TS (2 ‒ fac-3), TS (6 ‒ 4) and TS (2 ‒ mer-3'), respectively.
In all these cases, evidence is seen for interaction with the C2–F2 bond. However, these are weak in TS \(2 - \text{fac-3}\) and TS \(2 - \text{mer-3'}\) and so easily displaced, allowing F to move onto the metal centre. In contrast, a much stronger interaction is seen in TS \(6 - 4\) with short Rh⋯C2 and Rh⋯F2 contacts of 2.79 Å and 2.74 Å, respectively, while the C2–F2 distance lengthens to 1.41 Å. These block the vacant site at the metal and F therefore cannot be transferred onto Rh to form a 6-coordinate species. Instead F is moved onto silicon to yield 4 and FSiMe3 directly.

![Figure 3.20](image)

Figure 3.20: Computed geometries showing the interactions of the 4-C6F4H moiety with the rhodium metal centre in TS \(2 - \text{fac-3}\), TS \(6 - 4\) and TS \(2' - \text{mer-3'}\).

### 3.3.1 Summary of Pathway 2

The lowest reaction profile along Pathway 2 is shown in Figure 3.21. Computed enthalpies show that the rate-limiting transition state is associated with TS \(6 - 4\) \((H = +20.1 \text{ kcal/mol})\). The computed free energy of this transition state is +37.3 kcal/mol.
As TS (6 – 4) differs from the anticipated 4-centred transition state, attempts were made to characterise a silyl-assisted mechanism and two other transition states have been computed as shown in Figure 3.22. Both are higher in energy than TS (6 – 4) and show different binding modes of the C₆F₅H ring. The lower transition state is TSₕₐₗ₅-1 (H = +26.0 kcal/mol) in which the breaking C1···F1 bond is rather long (1.81 Å) and the Si–Rh–C1–F1 angle equal to +10.6°, consistent with the silyl-assisted nature of the process. Also, the Si···F1 distance of 2.13 Å shows that fluorine is moving toward silicon, consistent with a lengthening of the Rh···Si distance to 2.50 Å. IRC calculations confirm the formation of the Si···F1 bond. However, instead of FSiMe₃ formation, one methyl group from SiMe₃ is transferred onto the rhodium metal centre and PMe₃ trans to SiMe₃ dissociated.

An even higher energy process has been computed via TSₕₐₗ₅-2 (H = +31.7 kcal/mol). In the transition state, the P2–Rh–P3 bends back to 106.2° due to the η²-binding mode of C₆F₅H (Rh–C1 = 2.01 Å, Rh–C2 = 2.10 Å). The key C1···F1 distance lengthens to 1.63 Å and the Si–Rh–C1–F1 angle equal to +15.5°. In addition, the silyl ligand is completely dissociated from the rhodium metal centre (Rh···Si = 3.37 Å) and the Si···F1 distance is rather short (2.02 Å). IRC calculations showed that fluorine is transferred onto silicon to release FSiMe₃ and leads to a shallow intermediate in which the C2 is bound to Rh (Rh–C2 = 2.15 Å).
3.3.2 Comparison of Pathway 1 and Pathway 2

The reaction profiles for the lowest energy processes along Pathway 1 and Pathway 2 are shown in Figure 3.23. The rate-limiting transition state along Pathway 1 is the C‒F activation via TS (2 – mer-3') (H = +17.8 kcal/mol). This step is lower than the silyl-assisted pathway via TS (6 – 4) by 2.3 kcal/mol. The computed free energies increase this difference to 3.4 kcal/mol in favour of TS (2 – mer-3'). This suggests that C‒F activation at the 4-coordinate rhodium(I) silyl complex 1_{SiMe3} will involve the C‒F activation with a degree of phosphine-assistance to give the exothermic intermediate mer-3' (H = -31.4 kcal/mol).
Figure 3.23: Formation of [Rh(4-CF\textsubscript{6}H)(PMe\textsubscript{3})\textsubscript{3}], 4, and FSiMe\textsubscript{3} along Pathways 1 and 2.
3.4 C‒H Oxidative Addition and HSiMe₃ Formation via Reductive Elimination

3.4.1 C‒H Oxidative Addition to form fac-8

Experimentally, the reaction of C₆F₅H with 1SiMe₃ yields only C‒F activation, however, C‒H activation as a potential side reaction has also been considered.¹⁵a Calculations have been performed on the oxidative addition of C₆F₅H to form the three distinct isomers mer-8, mer-8’ and fac-8. Reaction via the last of these was found to be the most accessible and so will be discussed here. The computed geometries and energies of the stationary points involved in this process are shown in Figure 3.24.

Initially the approach of C₆F₅H toward the metal centre forms a loosely bound adduct 7 (H = -2.5 kcal/mol, G = +10.4 kcal/mol). Compound 7 exhibits an elongation of the C‒H bond to 1.12 Å due to a weak Rh···H contact (2.39 Å). Formation of fac-8 occurs via TS (7 – 8) in which the breaking C4···H4 bond lengthens to 1.39 Å and Rh···H4 interaction shortens to 1.63 Å. In addition, TS (7 – 8) has a late geometry in terms of the Rh···H4 contact with a distance of 1.63 Å (cf. 1.57 Å in fac-8). Also α is equal to +19.7° and confirms a near-coplanar arrangement in the transition state; however, the P2–Rh–C4–C5 dihedral angle of +151.4° is quite unusual. This suggests that C‒H oxidative addition is not conventional and so natural atomic charges were computed in order to understand the nature of this process (see Figure 3.25).
The computed natural atomic charges show that C4 becomes slightly less negative in 7 (-0.373 cf. -0.390 in free C₆F₅H) and H4 more positive (+0.295 cf. +0.286 in free C₆F₅H) while the C₆F₅H moiety becomes slightly more negative (total charge = -0.006 cf. +0.002 in free C₆F₅H). In addition, the rhodium metal bears a large negative charge (-0.621 cf. -0.590 in 1Me₃) and is more basic in the adduct 7. In the transition state TS (7 ‒ 8), some charge redistribution from the metal centre to the C₆F₅H moiety is also computed. The Rh metal centre is less negative (-0.451 cf. -0.621 in 7) as the C₆F₅H moiety becomes more negative (total charge = -0.130 cf. -0.06 in 7). In addition, C4 (-0.397 cf. -0.373 in 7) and H4 (+0.267 cf. +0.295 in 7) become less positively charged. These features suggest that this C‒H activation proceeds via an acid-base reaction where the rhodium complex deprotonates C₆F₅H.

3.4.2 Si‒H Reductive Elimination from fac-8

Computed geometries and energies for the Si‒H reductive elimination from fac-8 are shown in Figure 3.26. This process occurs through the transition state TS (fac-8 ‒ 9) with an activation barrier of +15.0 kcal/mol (H = +5.6 kcal/mol). In the transition state,
the P1–Rh–P2 angle widens to 121.0° (cf. +101.7° in fac-8) and the process is almost coplanar (α = 14.6°). Also, the Rh⋯Si contact increases to 2.99 Å as the bond breaks while the Si⋯H shortens by 1.04 Å to 1.63 Å. **TS (fac-8 – 9)** links to the final product 9 and HSiMe₃. Overall, the process is slightly exothermic by -8.2 kcal/mol (ΔG = -7.7 kcal/mol).

![Computed geometries and energies for Si–H reductive elimination from fac-8.](image)

Finally, the complete reaction profiles for C–F and C–H bond activation are compared in Figure 3.27. In both cases, the rate-limiting transition states for C–F and C–H activation correspond to the oxidative addition steps. C–H activation is kinetically preferred (ΔΔH‡ = 5.7 kcal/mol, ΔΔG‡ = 6.6 kcal/mol) however, C–F activation is thermodynamically more favourable (ΔΔH = 51.2 kcal/mol, ΔΔG = 51.3 kcal/mol). Experimentally, only C–F activation is observed, and so this implies that C–H activation may occur, but is reversible. An alternative interpretation is that C–F activation proceeds via a different pathway that is kinetically more favourable. It was therefore decided to study the C–F activation at 1SiMe₃ after an initial phosphine dissociation.
Figure 3.27: Complete reaction profiles for C-F and C-H bond activation.
3.5 Phosphine Substitution Followed by C–F activation of C₆F₃H at trans-[Rh(SiMe₃)(PMe₃)]₂ (trans-1SiMe₃)

3.5.1 Phosphine Dissociation

As discussed previously, species 1SiMe₃ showed an elongation of the Rh–P1 bond trans to SiMe₃ by 0.06 Å compared to the Rh–P2 and Rh–P3 distances. This elongation facilitates phosphine dissociation and a transition state for this step has been located as shown in Figure 3.28. As expected, TS (1 – trans-1)SiMe₃ shows an increase of the Rh⋯P1 distance to 3.97 Å and the Rh–Si bond shortens to 2.31 Å, as a vacant site is created trans to SiMe₃. The activation barrier for this step is +17.0 kcal/mol but computing the free energy decreases this barrier to +13.2 kcal/mol. The enthalpy of 3-coordinate trans-[Rh(SiMe₃)(PMe₃)]₂ (trans-1SiMe₃) is found to be +16.6 kcal/mol higher than the separated reactant but the free energy is only +2.3 kcal/mol. Phosphine dissociation cis to SiMe₃ was also computed and it was found that the 3-coordinate cis-1SiMe₃ has a computed enthalpy of +21.8 kcal/mol (G = +7.7 kcal/mol).

![Figure 3.28: Computed geometries and energies for phosphine dissociation to form trans-1SiMe₃.](image)

After formation of trans-1SiMe₃, two pathways, analogous to Pathways 1 and 2, have been considered (see Figure 3.29). Pathway 3, is the C–F oxidative addition of C₆F₃H at trans-1SiMe₃, to yield a 16-electron rhodium(III) silyl complex (e.g. trans-5') followed by Si–F reductive elimination. Pathway 4 is a silyl-assisted C–F bond activation at trans-1SiMe₃ where the Rh-Caryl bond is formed with the direct transfer of fluorine onto silicon.
3.5.2 Pathway 3: C‒F Oxidative Addition of C₆F₅H at trans-1₃Me₃₃

The first step along Pathway 3 is the approach of C₆F₅H toward the metal centre and this was found to form either an η²-intermediate (6b′) or a η¹-complex (6d′), as shown in Figure 3.30. The higher energy process goes through TS (6a′ – 6b′) (H = +12.9 kcal/mol) in which the C₆F₅H ring lies roughly parallel to the metal coordination plane and the P2–Rh–P3 angle slightly bends back to 147.6° (cf. 154.1° in 6a'). In the transition state, the Rh⋯C2 contact decreases to 3.00 Å and the Rh⋯C1 interaction shortens to 3.33 Å.

The lower energy pathway occurs via TS (6c′ – 6d′) (H = +10.8 kcal/mol) to form 6d' where the P2–Rh–P3 angle is barely perturbed (149.3° cf. 152.1° in 6c'). In TS (6c′ – 6d′), the Rh⋯C1 distance decreases to 2.94 Å while the Rh⋯C2 contact remains rather long at 3.44 Å.
Species $6b'$ ($H = -1.0 \text{ kcal/mol}$) adopts an unexpected trigonal bipyramid geometry with a vacant axial site trans to SiMe$_3$. The unusual structure of $6b'$ is due to the $\pi$-back donation of the Rh metal centre to the C$_6$F$_3$H ring as shown in Figure 3.31. The high trans-influence of SiMe$_3$ can also be important in stabilising this intermediate. A similar intermediate to $6b'$ has been reported by Grushin, Macgregor and co-workers where
[M(CF₃)(PR₃)₃] (M = Rh, Ir; R = H, Ph) adopted a trigonal bipyramid geometry with a vacant axial site trans to CF₃.⁸¹

In the second species 6d′ (H = +8.7 kcal/mol), the P2–Rh–P3 angle narrows to 141.6° and the fluoroaromatic ring is bound in an η¹-fashion (Rh–C1 = 2.22 Å). An interaction between Rh and F1 is also computed (Rh⋯F1 = 2.58 Å), as well as an elongation of the key C1–F1 bond to 1.43 Å.

After formation of 6b′ and 6d′, C–F oxidative addition occurs to give either cis-5′ or trans-5′, as shown in Figure 3.32. From 6b′ the rhodium metal centre migrates away from the aromatic π system along the C1–F1 bond, leading to the C–F oxidative addition transition state TS (6b′ – cis-5′) (H = +19.5 kcal/mol). In addition, the key C1⋯F1 bond distance lengthens to 1.52 Å. TS (6b′ – cis-5′) links to cis-5′ (H = -30.9 kcal/mol).

The lower lying C–F oxidative addition step along Pathway 3 proceeds via TS (6d′ – trans-5′) (H = +10.9 kcal/mol) in which the C1⋯F1 bond increases to 1.69 Å and the Rh⋯F1 distance shortens to 2.34 Å. TS (6d′ – trans-5′) links, after an isomerisation process to trans-5′ (H = -36.0 kcal/mol) in which F is trans to 4-C₆F₄H and SiMe₃ trans to a vacant site.
Figure 3.32: Computed geometries and energies for C–F oxidative addition to form cis-5′ and trans-5′.
3.5.3 Pathway 3: Si–F Reductive Elimination

After formation of the two isomers *cis*-5′ and *trans*-5′, Si–F reductive elimination is required to give, after phosphine association, [Rh(4-C₆F₄H)(PMe₃)]₃, 4, and FSiMe₃. The computed geometries and energies for this process from *cis*-5′ and *trans*-5′ are shown in Figure 3.33.

The less accessible reductive elimination pathway proceeds from *cis*-5′ via TS (*cis*-5′ – *cis*-5′″) and is associated with a computed energy of -25.7 kcal/mol. In the transition state, the Si–Rh–P2 angle increases to 114.1° (cf. 93.1° in *cis*-5′) and the Si···F1 contact significantly decreases to 2.19 Å. In contrast, both the Rh···Si and Rh···F1 bonds are almost unchanged.

Reductive elimination at 5-coordinate *trans*-5′ occurs via TS (*trans*-5′ – *trans*-5′″) (H = -28.4 kcal/mol). In the transition state, as seen in TS (*cis*-5′ – *cis*-5′″), the Si–Rh–C1 angle widens to 118.6° (cf. 101.7° in *trans*-5′″) and the major changes is the shortening of the Si···F distance to 2.20 Å.

Species *cis*-5″ and *trans*-5″ retain an interaction with the fluorosilane group (Rh–F1 = 2.35 Å in *cis*-5″, Rh–F1 = 2.39 Å in *trans*-5″). This is due to some electron transfer from one lone pair from F to Rh. The final product 4 can be formed by displacing FSiMe₃ by the dissociated phosphine ligand. A transition state has been located, TS (*trans*-5″ – 4), for the lowest energy profile from *trans*-5″ with a computed energy of -36.4 and a barrier of 1.3 kcal/mol (see Figure 3.34). Computed free energies increases the energy of TS (*trans*-5″ – 4) to -28.4 kcal/mol and the barrier to 10.6 kcal/mol, however, the process remains facile.
Figure 3.33 Computed geometries and energies for Si–F reductive elimination from cis-5' and trans-5'.
In TS (trans-5″ – 4), the Rh···F1 distance increases to 2.60 Å and Si–F1 bond is almost formed (1.69 Å cf. 1.66 in free FSiMe₃). The PMe₃ ligand approaches the metal centre (Rh···P1 = 3.53 Å) to give 4 and FSiMe₃.

The reaction profile for the lowest energy process along Pathway 3 is shown in Figure 3.35. The first step is the phosphine dissociation with a computed barrier of +17.0 kcal/mol. From trans-1′Me₃, formation of the η¹-species 6d′ occurs via TS (6c′ – 6d′) (H = +10.8 kcal/mol). Once 6d′ is formed, C–F activation process occurs through the 3-centred transition state TS (6d′ – trans-5′) (H = +10.9 kcal/mol) to form trans-5′. Si–F reductive elimination proceeds directly from this species and is found to be facile (TS (trans-5′ – trans-5″), H = -28.4 kcal/mol). The rate limiting-transition state along Pathway 3 is the phosphine dissociation, however, computed free energies show that phosphine dissociation and C–F oxidative addition are competitive with computed free energies of respectively +13.2 kcal/mol and +12.4 kcal/mol.
Figure 3.35: Formation of $[\text{Rh}(4-\text{C}_8\text{F}_5)(\text{PMe}_3)_3]$, 4, and $\text{FSiMe}_3$ via C–F activation at $1_{\text{SiMe}_3}$. 
3.5.4 Pathway 4: Silyl-Assisted C–F activation at trans-1$_{SiMe_3}$

Pathway 4 starts with the formation of $6b'$, previously described in Section 3.5.2, and two distinct transition states have been located for the silyl-assisted process (Figure 3.36).

Figure 3.36: Computed geometries and energies for silyl-assisted C–F activation from $6b'$. 
The first transition state $\text{TS (6b'} \rightarrow \text{cis-10)}$ is the higher energy process with a computed transition state at $+28.1 \text{ kcal/mol (G = +28.3 kcal/mol).}$ In $\text{TS (6b'} \rightarrow \text{cis-10)}$, the aromatic $\pi$ system remains bound to the metal centre with computed short Rh–C1 and Rh–C2 distances of 2.10 Å and 1.92 Å, respectively. The breaking C1⋯F1 distance lengthens to 1.83 Å and the Si–Rh–C1–F1 angle is $+3.5^\circ$ while the Si⋯F1 interaction decreases to 1.94 Å, consistent with a 4-centred transition state.

From 6b', a second transition state has been located $\text{TS (6b'} \rightarrow \text{trans-10)}$ (H = $+21.8 \text{ kcal/mol}$) in which the rhodium metal centre migrates away from the aromatic $\pi$ system along C1–F1 leading to the widening of the P2–Rh–P3 angle to 149.7°. In the transition state, the C1⋯F1 distance increases to 1.82 Å and the Si⋯F1 distance decreases to 2.47 Å (Si–Rh–C1–F1 = $+19.2^\circ$). $\text{TS (6b'} \rightarrow \text{trans-10)}$ has an early geometry compared to $\text{TS (6b'} \rightarrow \text{cis-10)}$ in terms of the Rh–Si and Si⋯F1 distances, being 2.38 Å and 2.47 Å, respectively ($\text{TS (6b'} \rightarrow \text{cis-10)}, \text{Rh⋯Si} = 2.62 \text{ Å, Si⋯F1} = 1.94 \text{ Å}).$ This last feature may explain the stabilisation of the former.

The transition state $\text{TS (6b'} \rightarrow \text{cis-10)}$ leads to the formation of cis-10 in which the fluorosilane group is fully dissociated, however, a relatively strong interaction between the rhodium metal centre and one ortho fluorine of the aryl ligand is computed (Rh⋯F6 = 2.47 Å). This contact explains the distortion of the P3–Rh–C1 angle to 161.4° and the elongation of the C6–F6 bond to 1.41 Å (Rh⋯C6 = 2.69 Å).

A related feature can be seen for trans-10 where one methyl group from SiMe$_3$ is interacting with the metal centre. The C–H bond lengthens to 1.17 Å while the Rh⋯C and Rh⋯H distances are 2.43 Å and 1.80 Å, respectively. The fluorosilane group can be fully dissociated by the incoming phosphine ligand to give 4 and FSiMe$_3$. This step is computed to be facile and involves a transition state similar to that in Figure 3.34.

The reaction profile for the lowest energy process along Pathway 4 is shown in Figure 3.37. The rate limiting-transition state is the silyl-assisted C–F activation through $\text{TS (6b'} \rightarrow \text{trans-10)}$ with a computed enthalpy of 21.8 kcal/mol (G = $+23.4 \text{ kcal/mol).}$ In addition, this transition state is found to be higher than C–F oxidative addition along pathway 3 through $\text{TS (6d'} \rightarrow \text{trans-5')}$ (H = $+10.9 \text{ kcal/mol, G = +12.4 kcal/mol})$ to
form *trans*-5', and so this indicates that C‒F activation at *trans*-1$_{\text{SiMe3}}$ would go via an oxidative addition pathway rather than a silyl-assisted mechanism.

Figure 3.37: Reaction profile for C‒F activation at 1$_{\text{SiMe3}}$ along Pathway 4.
3.6 C–H Oxidative Addition at \textit{trans-1}_{\text{SiMe}_3} and HSiMe$_3$ Formation via Reductive Elimination

3.6.1 C–H Oxidative Addition at \textit{trans-1}_{\text{SiMe}_3} to form cis-12

The C–H activation of C$_6$F$_5$H at \textit{trans-1}_{\text{SiMe}_3} has also been considered to form either cis-12 or \textit{trans-12}. Reaction via the former was found to be more accessible and so will be discussed here. The computed geometries and energies of the stationary points involved in this process are shown in Figures 3.38 and 3.39.

C–H activation proceeds via initial formation of a \( \eta^2 \)-coordinated arene complex 11, as shown in Figure 3.38. The approach of C$_6$F$_5$H results in adduct \textit{trans-7} (H = +10.1 kcal/mol) in which the C4–H4 bond elongates to 1.13 Å (cf. 1.09 Å in free C$_6$F$_5$H) due to a weak Rh···H4 contact (2.36 Å). From \textit{trans-7}, a transition state has been located, TS (\textit{trans-7} – 11) (H = +13.1 kcal/mol), in which the P2–Rh–P3 angles decreases to 153.6° to bind C$_6$F$_5$H in a \( \eta^2 \)-fashion via \( \pi \)-back donation and the C3=C4 bond lengthens to 1.41 Å. TS (\textit{trans-7} – 11) links to species 11 in which the C3=C4 bond increases to 1.47 Å and the C3–F3 distance lengthens to 1.40 Å. It should be noted that 11 is slightly higher in energy than 6b’ (H = -1.0 kcal/mol, G = +0.3 kcal/mol) in which the fluoroarene coordinates to the metal complex via a CF=CF bond.$^{13}$
After formation of the \( \eta^2 \)-complex 11, C–H occurs via TS (11 – cis-12) to form cis-12 as shown in Figure 3.39. In the transition state, the breaking C4⋯H4 bond elongates to 1.30 Å while the Rh⋯H4 contact decreases to 1.73 Å. The intermediate cis-12 is calculated to be slightly exothermic relative to the \( \eta^2 \)-adduct (\( \Delta H = -2.1 \text{ kcal/mol}, \Delta G = -1.2 \text{ kcal/mol} \)).

![Figure 3.39: Computed geometries and energies for C–H oxidative addition to give cis-12.](image)

### 3.6.2 Reductive Elimination from cis-12

The Si–H reductive elimination from cis-12 has also been considered in the present study. However, despite many attempts no transition state at the 5-coordinate cis-12 has been located. Moreover, by computing the 14-electron complex cis-[Rh(C\(_6\)F\(_5\))(PMe\(_3\))\(_2\)] and HSiMe\(_3\), calculations have showed that these species are +22.7 kcal/mol higher in energy than cis-12 (\( \Delta G = +7.4 \text{ kcal/mol} \)). Therefore, this represents a lower limit to the barrier of this process.

Finally, the reaction profiles for C–F activation (in black) and C–H activation (in blue) at 1\(_{\text{SiMe}_3}\) via initial phosphine dissociation are compared in Figure 3.40. Computed enthalpies show that the rate-limiting transition states correspond to the phosphine dissociation step (\( \Delta H^\ddagger = +17.0 \text{ kcal/mol} \)). However, calculations show that C–F activation is kinetically and thermodynamically more favourable than C–H activation (\( \Delta \Delta H^\ddagger = 3.0 \text{ kcal/mol}, \Delta \Delta H = 51.2 \text{ kcal/mol} \)). It should be also mentioned that the
lower limit computed for Si–H reductive elimination has an energy of +21.1 kcal/mol and is therefore higher than the C–H oxidative addition step (H = +13.9 kcal/mol). However, in reality some other species (PMe₃, solvent molecule) could come in and stabilise the unsaturated cis-12 species. Therefore, the Si–H reductive elimination can be considered to be more accessible kinetically than the C–H oxidative addition step.

With computed free energies, phosphine dissociation becomes competitive with the C–F activation oxidative addition with transition state energies located at +13.2 kcal/mol and +12.4 kcal/mol. Moreover, these two processes are both lower than C–H activation with a computed energy of +15.3 kcal/mol. Overall, C–F activation is computed to be more accessible kinetically and thermodynamically than C–H activation (ΔG ‡ = 2.9 kcal/mol, ΔG = 51.3 kcal/mol).
Figure 3.40: Reaction profiles for C–F activation (in black) and C–H activation (in blue) at $1^\text{SiMe}_3$. The energies for the reaction profiles are a) enthalpy energies and b) free energies.
3.7 Summary for C–F and C–H Activation of C₆F₅H at 1SiMe₃

The key stationary points for C–F activation and C–H activation of C₆F₅H at 1SiMe₃ are schematised in Figure 3.41. Computed enthalpies show that the rate-limiting transition states for the reaction of C₆F₅H at 1SiMe₃, without initial phosphine dissociation, are always the C–F and C–H oxidative addition steps. Direct C–H activation at 1SiMe₃ is preferred over C–F activation with a transition state located at +12.1 kcal/mol ($\Delta\Delta H^\ddagger = 5.7$ kcal/mol). However, C–F activation is much more favourable thermodynamically ($\Delta\Delta H = 51.2$ kcal/mol). In contrast, after initial phosphine dissociation, C–F activation becomes more accessible kinetically than C–H activation at trans-1SiMe₃ with a transition state located at +10.9 kcal/mol. Direct C–H activation at 1SiMe₃ and C–F activation at trans-1SiMe₃ are competitive ($\Delta\Delta H^\ddagger = 1.2$ kcal/mol in favour of C–H activation), however initial phosphine dissociation prior to C–F activation required a barrier of +17.0 kcal/mol and therefore C–H activation is preferred (H = +12.1 kcal/mol).

Computed free energies confirm that direct C–H activation at 1SiMe₃ (G = +27.3 kcal/mol) is more accessible kinetically than C–F activation (G = +33.9 kcal/mol) while the latter is more favourable thermodynamically ($\Delta\Delta G = 51.3$ kcal/mol). Reaction of C₆F₅H at trans-1SiMe₃ shows that C–H oxidative addition and C–F activation have computed energies located at +15.3 kcal/mol and +12.4 kcal/mol, respectively. This implies that the latter is again kinetically more accessible. In addition, computed free energies now favour the loss of PMe₃ with a computed transition state of +13.2 kcal/mol. In this case, phosphine dissociation and C–F activation at trans-1SiMe₃ are competitive. Moreover, this pathway now becomes lower in energy that direct C–H activation at 1SiMe₃ and thus account for the selectivity of C–F activation observed experimentally.
Figure 3.41: Computed enthalpies (plain) and free energies (italics) for C–F activation and C–H activation of C₆F₅H at 1₃SiMe₃.
3.8 Conclusions

Density functional theory calculations have been used to model the reaction between [Rh(SiR$_3$)(PMe$_3$)$_3$] and C$_6$F$_5$H. The most accessible process involves 1) phosphine substitution to form a η$^1$-arene species; 2) C–F activation of C$_6$F$_5$H; 3) Si–F reductive elimination; and 4) FSiMe$_3$ displacement by the incoming dissociated phosphine. This mechanism is consistent with the selectivity observed experimentally where only the C–F cleavage product is formed. Moreover, computed free energies show that C–F activation is more accessible kinetically and thermodynamically than C–H activation. It should also be mentioned that phosphine dissociation ($\Delta G^\ddagger$ = +13.2 kcal/mol) is competitive with C–F oxidative addition ($\Delta G^\ddagger$ = +12.4 kcal/mol). This last result contrasts with what is observed experimentally with C$_6$F$_6$ which occurs at room temperature while C–F activation of C$_6$F$_5$H proceeds at 110 °C. Indeed, if dissociation of PMe$_3$ is the rate-limiting transition state no difference should be seen experimentally between the two substrates. However, ligand dissociation is difficult to estimate computationally as the entropy contribution is not properly described and this affects the energy barrier. In addition, dissociation of PMe$_3$ is found to be functional dependent as shown in Chapter 6 (see Tables 6.2 and 6.3). One way to know if experimentally this pathway occurs will be to perform the reaction in excess of PMe$_3$ and to see if there is any effect on the rate of C–F activation of C$_6$F$_6$ and C$_6$F$_5$H. If the reaction is shut down this implies that dissociation of PMe$_3$ is important. Also, as mentioned previously the broad signals in the $^{31}$P{$^1$H} NMR spectrum may provide an evidence for dissociation of PMe$_3$ prior to C–F activation.

In addition, a transition state via a ligand-assisted C–F activation has been computed for direct elimination of FSiMe$_3$, involving the transfer of F onto one PMe$_3$ ligand before to bind silicon to form [Rh(4-C$_6$F$_4$H)(PMe$_3$)$_3$] after fluorosilane elimination. In this case, an initial trigonal bipyramidal precursor η$^2$-intermediate is formed. This last feature will be relevant for the discussion in Chapter 4.
Chapter 4: C–F Bond Activation at the 2- and 4-positions of Pentafluoropyridine at [Rh(X)(PEt₃)₃] (X = Si(OEt)₃, Bpin)

4.1 Introduction

The aim of this chapter is to study the C–F bond activation of C₅NF₅ at the 2- and 4-positions (i.e., the C–F bond *ortho* and *para* to the pyridyl nitrogen) at [Rh(X)(PEt₃)₃] (X = Si(OEt)₃, Bpin, where pin = pinacolate = –OCMe₂CMe₂O–). Experimentally, treatment of [Rh{Si(OEt)₃}(PEt₃)₃] at room temperature with one equivalent of C₅NF₅ in toluene yields [Rh(2-C₅NF₄)(PEt₃)₃] and [Rh(4-C₅NF₄)(PEt₃)₃] in a 9:1 ratio, while [Rh(Bpin)(PEt₃)₃] yields exclusively [Rh(2-C₅NF₄)(PEt₃)₃] under the same conditions (see Figure 4.1). In addition, [Rh(Bpin)(PEt₃)₃] was characterized in solution and the $^{31}$P{¹H} NMR spectrum at room temperature revealed only one broad signal. This indicates a dynamic behaviour which involves the exchange of the phosphine ligand. When the reaction between [Rh{Si(OEt)₃}(PEt₃)₃] and C₅NF₅ is conducted at -20 °C, only the selectivity at the 2-position is observed. In addition, both of these systems afford C–F activation without formation of fluorophosphoranes (e.g. F₂PEt₃) which are usually obtained between free phosphine and C₅NF₅. This indicates that phosphine dissociation does not occur and therefore the C–F activation of C₅NF₅ proceeds directly at the 4-coordinate [Rh(X)(PEt₃)₃]. This is in contrast with Chapter 3 where C–F activation of C₆F₅H happened after initial phosphine dissociation. In this case, only C–F activation at [Rh(X)(PEt₃)₃] will be discussed in this chapter.

![Figure 4.1: C–F bond activation of C₅NF₅ at [Rh(X)(PEt₃)₃] (X = Si(OEt)₃ or Bpin).](image)

These two rhodium(I) complexes show an unusual selectivity as C–F bond activation of C₅NF₅ most frequently involves reaction at the 4-position and such selectivity can be
associated with initial nucleophilic attack. Activation at the 2-position is less common, although it has been suggested that it might occur via a phosphine-assisted C–F activation process.\textsuperscript{60}

In order to assess the C–F activation of C\textsubscript{5}NF\textsubscript{5} at the 2- and 4-positions, two computational models, [Rh\{Si(O\textsubscript{Et})\textsubscript{3}\}(PMe\textsubscript{3})\textsubscript{3}], \textit{I}\textsubscript{Si}, and [Rh(Bpin)(PMe\textsubscript{3})\textsubscript{3}], \textit{I}\textsubscript{Bpin}, have been used to model the reaction between [Rh(X)(PMe\textsubscript{3})\textsubscript{3}] and C\textsubscript{5}NF\textsubscript{5}. In principle, C–F activation may occur via an oxidative addition process (Pathway 1) in which three isomers can be formed or via a ligand-assisted mechanism (Pathway 2), as shown in Figure 4.2.

Figure 4.2: Possible reaction mechanisms for C–F activation at the 2- and 4-positions of C\textsubscript{5}NF\textsubscript{5} at [Rh(X)(PMe\textsubscript{3})\textsubscript{3}] (X = Si(O\textsubscript{Et})\textsubscript{3} or Bpin) to yield [Rh(Ar\textsuperscript{F})(PMe\textsubscript{3})\textsubscript{3}] (Ar\textsuperscript{F} = 2-C\textsubscript{5}NF\textsubscript{4} or 4-C\textsubscript{5}NF\textsubscript{4}).
4.2 Computational Studies on the Reactions of [Rh{Si(OMe)₃}(PMe₃)₃] with C₅NF₅

4.2.1 Pathway 1: C–F Oxidative Addition of C₅NF₅ at the 2-Position

In this chapter, all selected key distances are in Å while all energies are in kcal/mol, relative to the two separated reactants, 1_{Si(OMe)₃} and C₅NF₅, denoted by 1₃. Also figures shown free energies in italics and hydrogen atoms are omitted for clarity. The stationary points involved in the C–F activation of C₅NF₅ at the 2-position to form mer-1₅, fac-1₅ and mer-1₅′ are shown in Figure 4.3.

The first isomer is mer-1₅ (H = -24.4 kcal/mol) which is formed via TS (1₃ – mer-1₅) (H = +23.9 kcal/mol), being the highest process for C–F activation at the 2-position. In the transition state, the key C₂–F₂ bond lengthens to 1.58 Å and the C₂–F₂ vector is slightly twisted relative to the Si–Rh–P₁ plane (α = 30.0°). Weak Rh···C₂ (2.31 Å) and Rh···F₂ (2.48 Å) interactions are also computed while the Rh···N₁ distance is 3.13 Å, which suggests that the nitrogen atom is not directly involved in the process. However, as seen in Chapter 3, F₂ weakly interacts with P₂ with a computed distance of 2.83 Å, although this remains rather long compared to the Rh···F₂ contact (2.48 Å).

The second most accessible C–F activation process occurs with the formation of fac-1₅ (H = -25.3 kcal/mol) via TS (1₃ – fac-1₅) (H = +20.4 kcal/mol). An elongation of the C₂···F₂ distance to 1.65 Å is computed and the C₂···F₂ vector is found to be coplanar to the P₂–Rh–P₃ plane (α = 7.2°), consistent with a concerted oxidative addition process. This feature differs from the previous transition state, TS (2 – fac-3) in Chapter 3, in which the fluorine atom interacted with one phosphine ligand (P₁···F₁ = 2.59 Å) before being transferred onto the rhodium metal centre. Instead of having a weak P₁···F₂ contact in TS (1₃ – fac-1₅), a Si···F₂ interaction is computed (2.88 Å). In addition, the Rh···N₁ interaction remains rather long (2.94 Å).

An alternative transition state with a weak degree of phosphine-assistance has also been located for formation of fac-1₅ but found to be higher in energy (TS’ (1₃ – fac-1₅), H = +22.5 kcal/mol, see Figure 4.4).
Figure 4.3: Computed geometries and energies for C–F oxidative addition at the 2-position of C$_2$NF$_3$. 
Figure 4.4: Computed transition state and energies for TS’ (13 – fac-15).

**TS’ (13 – fac-15)** has been obtained from the extensive conformation searching as described in Chapter 2. In the computed transition state **TS’ (13 – fac-15)**, the C2⋯F2 vector is more twisted relative to the P2–Rh–P3 plane ($\alpha = 40.2^\circ$) than in **TS (13 – fac-15)** ($\alpha = 7.2^\circ$), however the P1–Rh–C2–F2 angle is -43.8°. In addition, the P1⋯F2 interaction is computed to be 2.74 Å and remains long compared to the Rh⋯F2 distance (2.51 Å). These features show that the C–F activation through **TS’ (13 – fac-15)** has a weak degree of phosphine-assistance.

Finally, the lowest C–F oxidative addition pathway corresponds to the formation of **mer-15’** ($H = -27.1 \text{ kcal/mol}$) via **TS (14 – mer-15’)** and has a computed barrier of +17.3 kcal/mol. Significant elongation of the breaking C2⋯F2 bond to 1.76 Å is computed while the Rh–C2 bond is formed (2.08 Å). **TS (14 – mer-15’)** shows similar features to **TS (2 – mer-3’)** in that the P3⋯F2 interaction (2.46 Å) is shorter than the Rh⋯F2 contact (2.85 Å). Also, the C2⋯F2 vector is twisted relative to the Si–Rh–P1 plane ($\alpha = 71.5^\circ$) and the P3–Rh–C2–F2 angle is +23.3°. This suggests that **TS (14 – mer-15’)** clearly has a stronger degree of phosphine-assistance than **TS (13 – fac-15)**. In addition, a Rh⋯N1 interaction of 2.57 Å is also computed.

In contrast with **TS (13 – mer-15)** and **TS (13 – fac-15)** that link in the reverse direction to 13, **TS (14 – mer-15’)** leads to a $\eta^2$-arene intermediate 14 ($H = +0.4 \text{ kcal/mol}$, see Figure 4.5).
Figure 4.5: Computed geometries and energies for formation of the $\eta^2$-arene intermediate 14.

The $\eta^2$-arene intermediate 14 exhibits a trigonal bipyramidal geometry with the Si(OMe$_3$)$_3$ ligand in an equatorial position. Complex 14 shows an elongation of the C2=N1 bond to 1.39 Å, consistent with the Dewar-Chatt-Duncanson model. A transition state, TS (13 – 14) (H = +5.9 kcal/mol) for formation of this intermediate, has been located by increasing the Si–Rh–P1 angle (in this case, Si–Rh–P1 = 128.5° cf. 109.3° in 14).

The reaction profiles for the C–F oxidative addition of C$_5$NF$_5$ at the 2-position are shown in Figure 4.6. The stability of the three distinct isomers follows the trend: mer-15 (H = -24.4 kcal/mol) < fac-15 (H = -25.3 kcal/mol) < mer-15' (H = -27.1 kcal/mol). The mer'-isomer, in this case mer-15', has again the best arrangement of ligands, having the strongest electron donor ligand Si(OMe)$_3$ trans to the weakest donor (F). However, the difference in energy between mer-15 and mer-15' is only 2.7 kcal/mol, while in Chapter 3 the difference in energy between mer-3 and mer-3' was higher ($\Delta$H = 5.1 kcal/mol). This last point, can be explained by a weaker trans-influence of Si(OMe)$_3$ compared to SiMe$_3$. For instance, in fac-15 the Rh–P1 bond trans to Si(OMe)$_3$ is 2.55 Å while in fac-3 the same bond was 2.60 Å, trans to SiMe$_3$. In addition, 2-C$_5$NF$_4$ has a higher trans-influence than PMe$_3$. Indeed, in fac-15, the Rh–Si bond trans to PMe$_3$ is 2.37 Å while in mer-15 this bond is elongated to 2.44 Å, trans to 2-C$_5$NF$_4$. Therefore, mer-15 is the least stable isomer as both 2-C$_5$NF$_4$ and Si(OMe)$_3$ are trans to each other.

A final trend for the trans-influence of the different ligand can be drawn: Si(OMe)$_3$ > 2-C$_5$NF$_4$ > PMe$_3$ > F, similar to what has been observed in Chapter 3.
The stability of the three different transition states is the following: **TS (13 – mer-15)** (H = +23.9 kcal/mol) < **TS (13 – fac-15)** (H = +20.4 kcal/mol) < **TS (14 – mer-15')** (H = +17.3 kcal/mol). **TS (14 – mer-15')** is the lowest lying transition state as Si(OMe)₃ is computed to be trans to the vacant site while in **TS (13 – fac-15)** and **TS (14 – mer-15')**, the silyl ligand is trans to PMe₃ and 2-C₅NF₄, respectively. Comparing **TS (14 – mer-15')** and **TS (2 – mer-3')** shows that both transition states have similar energies with transition states located at +17.3 kcal/mol and +17.8 kcal/mol, respectively. This implies that the weak Rh···N1 contact of 2.57 Å computed in **TS (14 – mer-15')** does not contribute in the stabilisation of the transition state. In contrast, formation of mer- and fac-isomers is more accessible kinetically at 1Si(OMe)₃ than at 1SiMe₃ and may again reflect the weaker trans-influence of Si(OMe)₃. **TS (13 – mer-15)**, for instance, is 10.7 kcal/mol lower than **TS (2 – mer-3)** (ΔΔG‡ = 11.5 kcal/mol) and **TS (13 – fac-15)** is more favourable than **TS (2 – fac-3)** by 6.3 kcal/mol (ΔΔG‡ = 6.3 kcal/mol). Computed free energies increase all the energies of the stationary points by around 16.0 kcal/mol, as in Chapter 3, as the associative processes involved are equivalent.

**Figure 4.6: Formation of mer-15, fac-15 and mer-15' via C–F oxidative addition at the 2-position.**
4.2.2 Pathway 1: Phosphine Loss/Isomerisation and Subsequent Si–F Reductive Elimination from \textit{mer-15}'

As described in Chapter 3, the C–F oxidative addition step is the overall rate-limiting process, along Pathway 1. In this chapter, calculations have been performed on the Si–F reductive elimination from the three isomers and confirmed this argument. Therefore, Si–F reductive elimination step will only be discussed for the lowest lying C–F activation transition state which is derived from \textit{mer-15'}.

Species \textit{mer-15'} requires a phosphine loss/isomerisation step prior to Si–F reductive elimination. This process can occur via phosphine dissociation, either trans to 2-C$_5$N$_4$F$_4$ or trans to PMe$_3$ to give, after spontaneous isomerisation of F cis to Si(OMe)$_3$, \textit{trans-17'} and \textit{cis-17'}, respectively. Overall, as seen for the phosphine loss/isomerisation of \textit{mer-3'} in Chapter 3, reaction via the former was found to be more favourable and so will be discussed here (see Figure 4.7).

![Figure 4.7: Computed geometries and energies for the phosphine loss/isomerisation step to give \textit{trans-17'}](image)

From \textit{mer-15'}, a transition state has been located, \textbf{TS (mer-15' – trans-17')} (H = -12.5 kcal/mol), to give \textit{trans-17'} (H = -22.8 kcal/mol). The computed transition state shows that the Rh···P1 distance increases to 3.71 Å as the phosphine dissociates and at the same time, the Si–Rh–F$_2$ angle bends back to 157.6°, as F$_2$ begins to move cis to Si(OMe)$_3$. \textit{Trans-17'} has a square planar geometry and a distorted 2-C$_5$N$_4$F$_4$ ligand.
(Rh–C2–N1 = 109.2°, Rh–C2–C3 = 133.1°) and may come from the weak Rh···N1 interaction (2.77 Å). Interestingly, \textit{trans-17′} is slightly less stable than \textit{mer-15′} by 4.3 kcal/mol while in the previous chapter \textit{trans-5′} (H = -36.0 kcal/mol) was downhill compared to \textit{mer-3′} (H = -31.4 kcal/mol). This reflects again the weaker \textit{trans}-influence of Si(OMe)$_3$ compared to SiMe$_3$. However, computed free energies show that \textit{trans-17′} is lower in energy than \textit{mer-15′} by 10.6 kcal/mol, as it involves a dissociative process.

Si–F reductive elimination from \textit{trans-17′} proceeds via TS (\textit{trans-17′} – \textit{trans-17″}) (H = -15.7 kcal/mol) with the shortening of the Si···F2 distance by 1.01 Å to 2.38 Å (see Figure 4.8). TS (\textit{trans-17′} – \textit{trans-17″}) links to \textit{trans-17″} (H = -18.7 kcal/mol) in which the FSi(OMe)$_3$ group is loosely bound to the rhodium metal centre. The highly exothermic product [Rh(2-C$_5$NF$_4$)(PMe$_3$)$_3$] (16, H = -32.6 kcal/mol, see Figure 4.9) is then formed by displacing the FSi(OMe)$_3$ group by the dissociated phosphine. This process is expected to be facile (\textit{cf.} Figure 3.34 in Chapter 3).

![Figure 4.8: Computed geometries and energies for Si–F reductive elimination to give \textit{trans-17″}.

In addition, from \textit{trans-17′} PMe$_3$ can bind trans to Si(OMe)$_3$ to give \textit{mer-15″} (H = -24.4 kcal/mol) which shows an unusual distorted octahedral geometry (see Figure 4.9). This distortion was already observed in \textit{mer-3″} although there it was less pronounced. \textit{Mer-15″} has a similar Si–Rh–P1 angle (141.5° \textit{cf.} 141.6° in \textit{mer-3″}), however, the Si–Rh–F2 angle is more distorted (49.7° \textit{cf.} Si–Rh–F1 = 62.6° in \textit{mer-3″}). This difference
in the Si–Rh–F2/F1 angles can be explained by the stronger Si···F2 contact in mer-15″ (1.95 Å) compared to mer-3″ (Si···F1 = 2.41 Å).

From mer-15″, a transition state for Si–F reductive elimination has been found, TS (mer-15″ – 16) (H = -16.9 kcal/mol) by increasing the P1–Rh–C2 angle to 137.2°. This step is also characterised by a significant elongation of the Rh···F2 distance to 2.53 Å while the Rh···Si contact increases by only 0.07 Å to 2.50 Å. In contrast, TS (mer-3″ – 4) showed that both Rh···Si and Rh···F1 distances were elongated by 0.45 Å to 2.95 Å and by 0.15 Å to 2.24 Å, respectively. This difference again reflects the greater Lewis acidic character of SiOMe₃ where the Si···F2 bond is almost formed in mer-15″. Also, in TS (mer-15″ – 16), the Si···F2 distance shortens to 1.78 Å and α is 5.6°. Finally, TS (mer-15″ – 16) links to 16 and FSi(OMe)₃.

![Figure 4.9: Computed geometries and energies for Si–F reductive elimination to give 16 and FSi(OMe)₃.](image)

Overall, the lowest pathway for formation of [Rh(2-C₅NF₃)(PMe₃)₃], 16, and FSi(OMe)₃ is shown in Figure 4.10. The rate-limiting transition state, as seen in Chapter 3, is the C–F activation step which, in this case, has a computed barrier of +17.3 kcal/mol. After formation of mer-15′, the phosphine loss/isomerisation is facile and occurs via TS (mer-15’ – trans-17’) to yield the 5-coordinate intermediate trans-17’. The Si–F reductive elimination from trans-17’ and mer-15″ are relative close in energy, computed at -15.7 kcal/mol and -16.9 kcal/mol, respectively. Computed free
energies confirm the C–F oxidative addition step as rate-limiting transition state (\(G = +33.2\) kcal/mol). In addition, the phosphine loss/isomerisation step remains facile, however, the lowest pathway for Si–F reductive elimination now proceeds via TS (\(\text{trans-17}' \rightarrow \text{trans-17}''\)) which is more favourable kinetically than TS (\(\text{mer-15}'' \rightarrow 16\)) (\(\Delta \Delta G^\ddagger = 13.2\) kcal/mol). Overall the process is exothermic by 32.6 kcal/mol (\(\Delta G = -34.6\) kcal/mol).
Figure 4.10: Formation of [Rh(2-C$_5$NF$_2$)(PMe$_3$)$_3$], 16, and FSi(OMe)$_3$ via C-F activation of C$_5$NF$_2$ at the 2-position, along Pathway 1.
4.2.3 Pathway 1: C–F Oxidative Addition of C₅NF₅ at the 4-Position

To understand the formation of [Rh(4-C₅NF₄)(PEt₃)₃] observed experimentally, the C–F oxidative addition of C₅NF₅ at the 4-position has been computed. The stationary points and relative energies involved in this process are shown in Figure 4.11.

The highest process is again the formation of the mer-isomer, **mer-18** (H = -33.4 kcal/mol). The computed transition state, **TS (13 – mer-18)** (H = +22.7 kcal/mol), shows an elongation of the C4⋯F4 bond to 1.64 Å and α is 44.0°. **TS (13 – mer-18)** shows a weak P2⋯F4 interaction (2.74 Å) which is, however, longer than the Rh⋯F4 distance (2.55 Å). These features are similar to the ones computed in **TS (13 – mer-15)** (P2⋯F2 = 2.83 Å, Rh⋯F2 = 2.48 Å). Finally, oxidative addition at the 4-position is slightly lower than at the 2-position (ΔΔH‡ = 1.2 kcal/mol, ΔΔH‡ = 1.0 kcal/mol) for formation of the mer-isomer.

The second computed transition state is **TS (13 – fac-18)** (H = +20.6 kcal/mol) and corresponds to the formation of **fac-18** (H = -31.8 kcal/mol). This transition state is quite different to **TS (13 – fac-15)**, which was the lowest lying C–F activation transition state to give fac-15. In **TS (13 – fac-18)**, F4 clearly interacts with P1 (2.66 Å) while no similar interaction between P1 and F2 was found in **TS (13 – fac-15)**. In addition, in **TS (13 – fac-18)**, α is 47.9° while a coplanar arrangement was seen in **TS (13 – fac-15)** (α = 7.2°). All these differences can suggest that N1 played a role in the conformation of **TS (13 – fac-15)** and affects the energies of the transition states, as **TS (13 – fac-18)** and **TS (13 – fac-15)** have similar energies being +20.6 kcal/mol (G = +35.9 kcal/mol) and +20.4 kcal/mol (G = +36.1 kcal/mol), respectively.

Formation of the final computed species **mer-18′** (H = -34.9 kcal/mol) involves the lowest energy process. The C–F activation proceeds via **TS (13 – mer-18′)** (H = +13.2 kcal/mol) in which the key C4⋯F4 bond is stretched to 1.62 Å. The angle α is 64.0° (P2–Rh–C4–F4 = +29.2°) and therefore smaller than in **TS (14 – mer-15′)** (α = 71.5°, P3–Rh–C2–F2 = +23.2°). This suggests that **TS (14 – mer-15′)** proceeds with a higher degree of phosphine-assistance in which F2 interacts more strongly with the phosphine ligand (P3⋯F2 = 2.46 Å; **TS (13 – mer-18′)**, P2⋯F4 = 2.63 Å). This last feature implies that the short Rh⋯N1 contact in **TS (14 – mer-15′)** does not help to stabilise
the energy of the transition state as C–F activation at the 2-position is higher than at the 4-position (ΔΔH‡ = 4.1 kcal/mol, ΔΔG‡ = 3.9 kcal/mol) but may affect the geometry of the stationary points.

In contrast to C–F activation at the 2-position, all the three transition states link, in the reverse direction, to the two separated species 13 and therefore no η2-adduct, analogous to 14, has been located.

Figure 4.11: Computed geometries and energies for C–F oxidative addition at the 4-position of C₅NF₅.

The reaction profiles for C–F oxidative addition at the 4-position are shown in Figure 4.12. The most stable isomer again has silyl trans to F (e.g. **mer-18**). In contrast with
the previous C–F activation processes, **mer-18** (H = -33.4 kcal/mol) where Si(OMe)₃ is trans to 4-C₅NF₄ is actually more stable than **fac-18** (H = -31.8 kcal/mol). This difference is partially explained by the weaker *trans*-influence of Si(OMe)₃ compared to SiMe₃. A second contribution can be the weaker *trans*-influence of 4-C₅NF₄ compared to 2-C₅NF₄. Indeed, in **mer-15**, the Rh–Si bond trans to 2-C₅NF₄ is elongated to 2.44 Å while in **mer-18**, the same Rh–Si distance is 2.40 Å. Therefore this second argument can stabilise slightly more **mer-18** than **mer-15** which now becomes more stable than **fac-18**.

The lowest lying transition state for C–F activation has again Si(OMe)₃ trans to the vacant site and corresponds to **TS (13 – mer-18')** (H = +13.2 kcal/mol). Computed free energies increase the energy of **TS (13 – mer-18')** to +29.3 kcal/mol.

Experimentally, the final product [Rh(4-C₅NF₄)(PMe₃)₃], 19, is formed and so Si–F reductive elimination is required. This process again will be described for the lowest lying transition state for C–F activation and starts from **mer-18'**.
4.2.4 Pathway 1: Phosphine Loss/Isomerisation and Subsequent Si–F Reductive Elimination from **mer-18’**

**Mer-18’** requires a phosphine loss/isomerisation step prior to Si–F reductive elimination. The stationary points and energies involved in this process are shown in Figure 4.13.

![Computed geometries and energies for the phosphine loss/isomerisation to give trans-20’.](image)

The computed transition state for this process, **TS (mer-18’ – trans-20’)**, is very similar to the ones described previously where the Rh···P1 distance lengthens by 1.24 Å to 3.66 Å and the Si–Rh–F4 angle bends back to 155.1°. **TS (mer-18’ – trans-20’)** links to **trans-20’** (H = -32.2 kcal/mol) which has a square pyramidal geometry. As seen for **trans-5’** (see Section 3.2.2 in Chapter 3) this distorted geometry is due to some interaction between the metal centre and the fluoroaryl moiety. In **trans-20’**, short Rh···C3 and Rh···F3 contacts of 2.90 Å and 2.95 Å are computed, respectively. Another consequence of these interactions is the elongation of the C3–F3 bond to 1.38 Å (cf. C5–F5 =1.36 Å). **Trans-20’** is slightly less stable than **mer-18’** (ΔΔH = 2.7 kcal/mol), as already seen for **trans-17’** which was higher in energy than **mer-15’** (ΔΔH = 4.3 kcal/mol). However, computed free energies show that **trans-17’** is more stable than **mer-18’** by 13.5 kcal/mol.
Si–F reductive elimination from \textit{trans-20}', occurs via \textit{TS (trans-20' – trans-20'')} (H = -25.7 kcal/mol, see Figure 4.14). In the transition state, the major change is the shortening of the Si····F4 contact to 2.36 Å. \textit{TS (trans-20' – trans-20'')} links to \textit{trans-20''} (H = -28.6 kcal/mol) in which the FSi(OMe)₃ group is loosely bound to the rhodium metal centre. Formation of the highly exothermic product [Rh(4-C₅NF₄)(PMe₃)₃] (16, H = -45.6 kcal/mol, see Figure 4.15) is then obtained by substituting the FSi(OMe)₃ group by the dissociated phosphine.

![Figure 4.14: Computed geometries and energies for Si–F reductive elimination to give trans-20''.](image)

The 6-coordinate intermediate \textit{mer-18''} can be formed from \textit{trans-20'} by binding PMe₃ trans to Si(OMe)₃, as shown in Figure 4.15. \textit{Mer-18''} has again a distorted octahedral geometry (Si–Rh–P1 = 136.5°, Si–Rh–F4 = 50.0°). A short Si····F4 contact is also computed (1.95 Å) and reflects the Lewis acidic character of the Si(OMe)₃ ligand. The Si–F reductive elimination from \textit{mer-18''} is accessed via \textit{TS (mer-18'' – 19)} (H = -24.2 kcal/mol) by widening the P1–Rh–C₄ angle to 133.4°. This transition state shows again a significant elongation of the Rh····F4 distance by 0.39 Å to 2.54 Å. In addition, the Si····F4 contact shortens to 1.76 Å and is found to be coplanar to the P1–Rh–C₄ plane (\(\alpha = 3.1^\circ\)). Finally, the transition state \textit{TS (mer-18'' – 19)} links to 19 and FSi(OMe)₃.
The key stationary points for the lowest pathway to yield 19 and FSi(OMe)$_3$ are shown in Figure 4.16. Computed enthalpies confirms that the rate-limiting transition state corresponds to TS (13 – mer-18′) (H = +13.2 kcal/mol) and involves the oxidative addition step. The subsequent phosphine loss/isomerisation process and Si–F reductive elimination from trans-20′ are facile and involves transition states at -17.7 kcal/mol and -25.7 kcal/mol, respectively. In addition, computed free energies confirm the rate-limiting transition state as TS (13 – mer-18′) (G = +29.3 kcal/mol). Moreover, after the phosphine loss/isomerisation step, the lowest Si–F reductive elimination pathway remains via TS (trans-20′ – trans-20″). This final point is similar to the formation of [Rh(C$_6$F$_5$)(PMe$_3$)$_3$] and FSiMe$_3$, in which both computed enthalpies and free energies showed that the lowest pathway for Si–F reductive elimination occurred directly at the 5-coordinate trans-5′ (see Section 3.2.2 in Chapter 3).
In summary, calculations indicate a kinetic preference for reaction at the 4-position, via TS (13 – *mer-18*'), rather than at the 2-position, through TS (14 – *mer-15*') (ΔH‡ = 4.1 kcal/mol, ΔG‡ = 4.0 kcal/mol). This is odds with the experimental observations, therefore, another pathway must be considered in order to explain the experimental selectivity.
4.2.5 Pathway 2: Silyl-Assisted C–F Activation of C₅NF₅ at the 2-Position

This process shows the direct transfer of fluorine onto silicon with simultaneous Rh–C₅Arᵢ₁ bond formation (see Figure 4.2). The computed geometries and relative energies of the key stationary points for this process are shown in Figures 4.17-4.19. The first step is the formation of a η²-arene intermediate 21 (H = +5.0 kcal/mol), an isomer of 14 but now the Si is axial. Species 21 shows an elongation of the C2=N1 and C2–F2 bonds to 1.39 Å and 1.43 Å, respectively. A computed transition state for formation of 21, TS (13 – 21) (H = +9.6 kcal/mol) is accessed by widening the P2–Rh–P3 angle to 130.1°.

![Figure 4.17: Computed geometries and energies for formation of 21.](image)

From the η²-arene intermediate 21, a 4-centred transition state has been found, TS (21 – 22) (H = +10.2 kcal/mol), for silyl-assisted C–F activation (see Figure 4.18). In the transition state, significant elongation of the C2⋯F2 distance to 1.71 Å is computed while the Si⋯F2 contact shortens to 2.21 Å. Also, the Si–Rh–C2–F2 angle is -14.3, consistent with a silyl-assisted mechanism rather than a concerted oxidative addition. Moreover, TS (21 – 22) shows that the nitrogen of the pyridyl ring interacts with the metal centre (Rh–N1 = 2.17 Å) in which donation of electron density from the nitrogen atom lone pair serves to stabilise the rhodium metal centre.⁶⁰,⁶⁸b TS (21 – 22) links to a benzyne type complex 22 (H = -5.2 kcal/mol), similar to that previously reported by Perutz and co-workers at [Ni(PMe₃)₂].⁶⁰ Complex 22 shows that FSi(OMe)₃ weakly interacts with the rhodium metal centre (Rh⋯Si = 2.57 Å).
Formation of 16 and FSi(OMe)_3 happens from 22 via TS (22 – 16) (H = -4.1 kcal/mol). In the transition state, the Rh···N1 contact increases to 2.69 Å as the widening of the P1–Rh–P2 angle to 121.3° (cf. 97.9° in 22) does not permit the π-back donation from the metal centre to stabilise the benzyne like species 22. This process is relatively facile and has a computed barrier of 1.1 kcal/mol (ΔG‡ = +1.7 kcal/mol).

In addition to TS (21 ‒ 22), an alternative silyl-assisted transition state at the 2-position, TS (13 ‒ 23) (H = +14.6 kcal/mol) has been located but found to be higher in energy (see Figure 4.20). In both of these transition states the silyl ligand is involved in the process, with Si–Rh–C2–F2 angles of -14.3° and -11.2° in TS (21 ‒ 22) and TS (13 –
23), respectively. In addition, the Rh···N1 contact is rather long (2.85 Å) in TS (13 – 23) compared to TS (21 – 22) (2.17 Å). Knowing that TS (13 – 23) is higher in energy than TS (21 – 22) (ΔΔH‡ = 4.4 kcal/mol, ΔΔG‡ = 5.3 kcal/mol) confirms that the nitrogen atom is essential in stabilising the transition state through its lone pair. Finally, TS (13 – 23) links, in the reverse direction to the two separated reactants 13, and in the forward direction to the intermediate 23 (H = -27.6 kcal/mol) in which one oxygen from the Si(OMe)₃ group interacts with the metal centre (Rh···O = 2.20 Å, Rh···Si = 2.43 Å).

Figure 4.20: Computed geometries and energies for silyl-assisted C–F activation to give 23.

Formation 16 and FSi(OMe)₃ from 23 occurs by increasing the P1–Rh–C2 angle to 138.7° (cf. 96.9° in 23), as shown in Figure 4.21. In the transition state TS (23 – 16) (H = -17.4 kcal/mol), both Rh···O and Rh···Si contacts increase to 2.61 Å and 2.49 Å, respectively.
The key stationary points for the lowest silyl-assisted C–F activation process are shown in Figure 4.22. Computed enthalpies show that the rate-limiting transition state corresponds to the C–F activation step through TS (21 – 22), with a computed transition state located at +10.2 kcal/mol. From the benzyne-like complex 22, formation of [Rh(2-C₅NF₄)(PMe₃)₃] and FSi(OMe)₃ is facile (ΔH° = 1.1 kcal/mol). Computed free energies do not change the rate-limiting process which is now located at +26.1 kcal/mol. Formation of the final products proceeds with a computed free energy of 11.4 kcal/mol. Overall the process is exothermic by 32.6 kcal/mol (ΔG = -34.6 kcal/mol).
4.2.6 Pathway 2: Silyl-Assisted C–F Activation of $C_5NF_5$ at the 4-Position

In contrast with the silyl-assisted C–F activation at the 2-position, no $\eta^2$-arene species has been located for C–F activation at the 4-position. Instead the C–F cleavage occurs directly from the two separated species $13$ via $\text{TS (13} - \text{24)}$ ($H = +11.9 \text{ kcal/mol}$, see Figure 4.23). In the transition state, the C4···F4 distance lengthens to 1.70 Å and the Si–Rh–C4–F4 angle is $+14.6^\circ$. Also, both the Rh···C4 and Si···F4 distances shorten to 2.09 Å and 2.24 Å, respectively. $\text{TS (13} - \text{24)}$, links to the intermediate $24$ ($H = -33.2 \text{ kcal/mol}$) in which the FSi(OMe)$_3$ group interacts with the rhodium metal centre.
(Rh⋯O = 2.19 Å, Rh–Si = 2.42 Å), as previously seen for formation of 23 via TS (13 – 23). Formation of 19 and FSi(OMe)₃ from 24 proceeds via TS (24 – 19) (H = -24.4 kcal/mol, see Figure 4.24). This transition state shows the widening of the P1–Rh–C₄ angle to 134.0° (cf. +105.3 in 24) in order to break both Rh⋯O and Rh⋯Si interactions (Rh⋯O = 2.62 Å, Rh⋯Si = 2.52 Å).

The stationary points for silyl-assisted C–F activation at the 4-position are shown in Figure 4.25. As seen for the activation at the 2-position, the rate-limiting transition state
corresponds to the C–F activation via TS (13–24) with a computed enthalpy of +11.9 kcal/mol and free energy of +28.5 kcal/mol. Overall the process is exothermic by 45.6 kcal/mol (ΔG = -46.8 kcal/mol).

Figure 4.25: Formation of [Rh(4-C5NF4)(PMe3)3], 19, and FSi(OMe)3 via silyl-assisted C–F activation of C5NF5 at the 4-position.

4.2.7 Summary for the C–F activation of C5NF5 at the 2- and 4-positions at 1Si(OMe)3

The rate-limiting transition states for C–F activation of C5NF5 at the 2- and 4-positions at 1Si(OMe)3 are summarised in Figure 4.26.

With oxidative addition the most accessible process corresponds to the activation at the 4-position (ΔH‡ = +13.2 kcal/mol cf. ΔH‡ = +17.3 kcal/mol at the 2-position) which is at odds with experimental observations. In contrast, silyl-assisted C–F activation favours the 2-position (ΔH‡ = +10.2 kcal/mol cf. ΔH‡ = +11.9 kcal/mol at the 4-position). Moreover, both silyl-assisted C–F activation at the 2- and 4-positions are more accessible than oxidative addition at the 4-position. This pathway accounts for the experimentally observed selectivity where both [Rh(2-C5NF4)(PEt3)3] and [Rh(4-
C₅NF₅)(PEt₃)₃] are obtained in a 9:1 ratio in which phosphine dissociation is not required. In addition, computed free energies confirm that the lowest pathways for C–F activation at the 2- and 4-positions are via the silyl-assisted mechanism (ΔG‡ = +26.1 kcal/mol at the 2-position, ΔG‡ = +28.5 kcal/mol at the 4-position)

<table>
<thead>
<tr>
<th>2-Position</th>
<th>4-Position</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxidative Addition</strong></td>
<td><strong>Silyl-Assisted</strong></td>
</tr>
<tr>
<td>ΔH‡ = +17.3, ΔG‡ = +33.2</td>
<td>ΔH‡ = +10.2, ΔG‡ = +26.1</td>
</tr>
<tr>
<td>ΔH‡ = +13.2, ΔG‡ = +29.3</td>
<td>ΔH‡ = +11.9, ΔG‡ = +28.5</td>
</tr>
</tbody>
</table>

Figure 4.26: Rate-limiting transition states for C–F activation of C₅NF₅ at the 2- and 4-positions at 1Si(OMe)₃.
4.3 Computational Studies on the Reactions of [Rh(Bpin)(PMe$_3$)$_3$] with Pentafluoropyridine

4.3.1 Pathway 1: C‒F Oxidative Addition of C$_5$NF$_5$ at the 2-Position

Experimentally, the reaction between [Rh(Bpin)(PEt$_3$)$_3$] and C$_5$NF$_5$ undergoes C‒F activation at the 2-position to form [Rh(2-C$_5$NF$_4$)(PEt$_3$)$_3$] and FBpin (see Figure 4.1). Three distinct isomers can be formed upon oxidative addition at 1$_{Bpin}$: mer-27, fac-27 or mer-27' (see Figure 4.2), and reaction via the last of these was found to be more accessible and so will be discussed here. In this section, all reported energies are relative to the two separated reactants, 1$_{Bpin}$ and C$_5$NF$_5$, denoted by 25.

Initially, an η$^2$-arene species 26 (H = -0.9 kcal/mol) is formed which is analogous to 14 in which the X ligand, in this case Bpin, is in an equatorial position. Complex 26 is formed via TS (25‒26) (H = +1.5 kcal/mol) in which both B–Rh–P1 and P2–Rh–P3

Figure 4.27: Computed geometries and energies for formation of 26.
angles widen to 166.0° (cf. 151.7° in \textbf{1}_{\text{Bpin}}) and 159.3° (cf. 151.3° in \textbf{1}_{\text{Bpin}}). The $\eta^2$-arene species \textbf{26} exhibits a trigonal bipyramidal geometry and shows an elongation of the C2=N1 bond due to the $\pi$-back donation from the metal centre to the $\pi^*$ antibonding orbital of the C$_5$NF$_5$ moiety.

C–F oxidative addition step from the $\eta^2$-adduct \textbf{26} occurs via TS (\textbf{26} – \textit{mer-27'}) (H = +11.2 kcal/mol, see Figure 4.28). In the transition state, the rhodium metal centre migrates away from the aromatic $\pi$ system along the C2–F2 bond and therefore weakens the Rh···N1 interaction (2.73 Å). TS (\textbf{26} – \textit{mer-27'}) shows similar features to TS (\textbf{14} – \textit{mer-15'}) where the key C2···F2 distance increases to 1.70 Å and the C2···F2 vector is twisted away relative to the B–Rh–P1 angle ($\alpha = 66.4^\circ$, P3–Rh–C2–F2 = +27.2°). Also, F2 interacts with P3 (2.60 Å) and this interaction is shorter than the Rh···F2 distances (2.78 Å) which suggests a certain degree of phosphine-assistance in the process. TS (\textbf{26} – \textit{mer-27'}) links to the 6-coordinate species \textit{mer-27'} (H = -31.8 kcal/mol).

![Figure 4.28: Computed geometries and energies for C–F oxidative addition to give mer-27'.](image)

Species \textit{mer-27'} shows that the Rh–F2 bond trans to Bpin is 2.19 Å, and therefore longer than in \textit{mer-15'} (Rh–F2 = 2.15 Å, trans to Si(OMe)$_3$). This implies that Bpin has a stronger \textit{trans}-influence than SiOMe$_3$. In \textit{mer-27'}, however, the Rh–F2 distance is the same as the Rh–F1 bond (2.19 Å) in \textit{mer-3'} which is trans to SiMe$_3$. This implies that Bpin and SiMe$_3$ have similar \textit{trans}-influence and therefore the trend in terms of the \textit{trans}-influence for the X-ligand is the following SiMe$_3$ ≈ Bpin > Si(OMe)$_3$. 

120
4.3.2 Pathway 1: Phosphine Loss/Isomerisation and Subsequent B–F Reductive Elimination from mer-27′

Initial phosphine isomerisation step to a F/Bpin cis arrangement is achieved via TS (mer-27′ – trans-29′) (H = -20.1 kcal/mol) in which the phosphine ligand trans to the 2-C₅F₄N ligand dissociates (Rh⋯P1 = 3.45 Å, see Figure 4.29). The 5-coordinate structure undergoes spontaneous isomerisation to give trans-29′ (-30.1 kcal/mol) in which the C3–F3 bond is slightly elongated to 1.37 Å.

B–F reductive elimination can then proceed via TS (trans-29′ – trans-29″) (H = -25.7 kcal/mol) in which the B⋯F2 contact shortens by 1.04 Å to 2.14 Å (see Figure 4.30). Finally, TS (trans-29′ – trans-29″) links to trans-29″ (H = -34.6 kcal/mol) that can yield the final product 28 by displacing FBpin by the dissociated phosphine.

On the other hand, PMe₃ can bind trans-29′ trans to Bpin to give mer-27″, from which B–F reductive elimination can occur via TS (mer-27″ – 28) (H = -32.5 kcal/mol) to yield 28 and FBpin. The mer″-isomer again shows a distorted octahedral geometry, however, mer-27″ is less distorted (B–Rh–P1 = 151.7°, B–Rh–F2 = 76.1°) than mer-15″ (Si–Rh–P1 = 141.5°, Si–Rh–F2 = 49.7°). In addition, the B⋯F2 contact is longer in mer-27″ (2.57 Å) than the Si⋯F2 interaction in mer-15″ (1.95 Å).
B–F reductive elimination from \textit{mer-27''} occurs via \textbf{TS (mer-27'\textasciitilde 28)} by decreasing the B–F2 contact to 2.02 Å. In this case $\alpha$ is 1.0° and therefore consistent with a 3-centred transition state. In contrast to \textbf{TS (mer-15'\textasciitilde 16)} which is the Si–F reductive elimination at the 2-position, \textbf{TS (mer-27'\textasciitilde 28)} shows that the breaking Rh–F2 bond barely changes while in the former, the same bond was significantly elongated by 0.36 Å to 2.53 Å. Finally, \textbf{TS (mer-27'\textasciitilde 28)} links to the final product 28 and FBpin.
The stationary points involved in the C–F activation of C₅NF₅ at the 2-position are shown in Figure 4.31. Overall, the rate-limiting transition state is the C–F oxidative addition step which occurs through TS (26 – mer-27′) and has a computed enthalpy of +11.2 kcal/mol. Once mer-27′ is formed, subsequent phosphine loss/isomerisation and B–F reductive elimination from mer-27′ are facile and involve transition states at -20.1 kcal/mol and -31.1 kcal/mol, respectively. Computed free energies confirm the C–F oxidative addition step as the rate-limiting transition state (G = +26.9 kcal/mol), however, the B–F reductive elimination now proceeds at the 5-coordinate trans-29′ via TS (trans-29’ – trans-29′′) (G = -24.6 kcal/mol). This last point is similar to formation of [Rh(2-C₅NF₄)(PMe₃)]₃ and FSi(OMe)₃ where computed enthalpies showed that this process was more accessible at the 6-coordinate species mer-15′ while free energies suggested that Si–F reductive elimination at trans-17′ was easier. Overall, the process for formation of 28 and FBpin is exothermic by 45.8 kcal/mol (ΔG = -45.7 kcal/mol).
Figure 4.31: Formation of \( \text{Rh}(2\text{C-FNF})_2\text{PMe}_3 \) \( 28 \) and FBpin via C-F activation of C-F at the 2-position, along Pathway 1.
4.3.3 Pathway 1: C–F Oxidative Addition of C₅NF₅ at the 4-Position

The first step on the lowest energy pathway for C–F activation at the 4-position is the formation of the η¹-arene species 30 through TS (25 – 30) (H = -3.4 kcal/mol) in which the Bpin ligand is in an axial position (see Figure 4.32). In the transition state, the C₅NF₅ moiety approaches the rhodium metal centre forming a weak Rh⋯C4 contact (2.82 Å) while both the P₂–Rh–P₃ and B–Rh–P₁ angles widen to 158.7° (cf. 151.7° in 1Bpin) and 170.0° (cf. 159.3° in 1Bpin), respectively. TS (25 – 30) links to the η¹-arene species 30 in which the fluoroaromatic moiety is loosely bound to the complex (Rh⋯C4 = 2.32 Å).

Complex 30 shows an elongation of the C₄–F₄ bond to 1.41 Å and allows the location of TS (30 – mer-31′) (H = +5.8 kcal/mol, see Figure 4.32). In the transition state, the key C₄⋯F₄ distance increases to 1.61 Å while α and the P₃–Rh–C₄–F₄ angles are 66.4° and +27.1°, respectively. In addition, the Rh⋯F₄ contact remains rather long (2.77 Å) while a shorter P₃⋯F₄ interaction is computed (2.65 Å), which suggest a degree of phosphine-assistance during the C–F cleavage. TS (30 – mer-31′) links to the 6-coordinate species, mer-31′ (H = -41.6 kcal/mol) in which F is trans to B.
4.3.4 Pathway 1: Phosphine Loss/Isomerisation and Subsequent B–F Reductive Elimination from $\text{mer-31}'$

The stationary points involved in this process are shown in Figures 4.34 and 4.35.

The initial phosphine loss/isomerisation step prior to B–F reductive elimination proceeds via $\text{TS (mer-31’ – trans-33’)}$ (H = -27.0 kcal/mol) in which the Rh⋯P1 distance increases to 3.45 Å trans to 2-$\text{CsNF}_4$. $\text{TS (mer-31’ – trans-33’)}$ links to the square pyramidal structure $\text{trans-33’}$. An elongation of the C3–F3 bond to 1.38 Å is
also computed due to weak Rh···C3 and Rh···F3 contacts of 2.93 Å and 3.02 Å, respectively.

Figure 4.35: Computed geometries and energies for B–F reductive elimination from trans-33’ (top) and from mer-31” (bottom).

From the 5-coordinate structure trans-33’ (H = -41.3 kcal/mol) B–F reductive elimination happens through TS (trans-33’ – trans-33”) (H = -37.2 kcal/mol) with the shortening of the B···F4 contact to 2.11 Å (cf. 3.00 in trans-33’). IRC calculations showed that TS (trans-33’ – trans-33”) links to trans-33” (H = -45.1 kcal/mol) from which FBpin can be displaced by the dissociated phosphine to give 32.
B–F reductive elimination via TS (mer-31’’ – 32) \((H = -40.7 \text{ kcal/mol})\) starts with the formation of mer-31’’. In mer-31’’, the B–Rh–P1 and B–Rh–F4 angles are 148.3° and 76.0°, respectively, while the B···F4 contact is 2.55 Å. In the transition state, as seen for the B–F reductive elimination at the 2-position, the main change is the shortening of the B···F contact by 0.58 Å to 1.97 Å. In addition, \(\alpha\) is 0.3, coherent with a 3-centred transition state for reductive elimination.

The reaction profile for C–F activation at the 4-position is shown in Figure 4.36. Again, the rate-limiting transition state is the C–F oxidative addition step \((H = +5.8, G = +21.9 \text{ kcal/mol})\) which involves TS (30 – mer-31’). After formation of mer-31’, subsequent phosphine loss/isomerisation and B–F reductive elimination are facile. Computed enthalpies show that the lowest pathway for B–F reductive elimination occurs at the 6-coordinate species mer-31’’ (TS (mer-31’ – 32), \(H = -40.7 \text{ kcal/mol})\) while computed free energies suggest that the process happens at trans-33’ (TS (trans-33’ – trans-33’’), \(G = -35.9 \text{ kcal/mol})\). Overall, the process is exothermic by 58.8 kcal/mol \((G = -57.9 \text{ kcal/mol})\).
Figure 4.36: Formation of $[\text{Rh}(2\text{-C}_5\text{NF}_5)(\text{PMe}_3)_3]$, 32, and FBpin via C-F activation of C$_5$NF$_5$ at the 4-position, along Pathway 1.
4.3.5 Pathway 2: Boryl-Assisted C–F Addition of C₅NF₅ at the 2- and 4-Positions

The computed and relative energies of the stationary points for boryl-assisted C–F activation at the 2- and 4-positions are compared in Figure 4.37. C–F activation at the 2-position starts with formation of a trigonal bipyramidal η²-arene species 34 (H = -2.3 kcal/mol) in which both C2=N1 and C2–F2 bonds lengthen to 1.39 Å and 1.44 Å, respectively. In contrast, activation at the 4-position initially forms a square pyramidal η¹-intermediate 35 in which the C4–F4 increases to 1.40 Å due to a short Rh–C4 contact (2.27 Å). The η²-arene intermediate is formed via TS (25 – 34) (H = +3.8 kcal/mol) in which the P2–Rh–P3 angle widens to 149.1° (cf. 111.6° in 34) and the C2=N1 shorten to 1.35 Å. On the other hand, TS (25 – 35) (H = -0.8 kcal/mol) which gives 35 has been located by lengthening the Rh···C4 bond to 2.85 Å.

From 34 and 35, two transition states, TS (34 – 28) and TS (35 – 32), for boryl-assisted C–F activation at the 2- and 4-positions, respectively, have been located. The key feature of TS (34 – 28) is the short Rh–N1 interaction (2.22 Å) which stabilises the transition state as seen for the equivalent silyl-assisted process at the 2-position and previously reported. In addition, the B–Rh–C2–F2 angle is -13.1°, consistent with a boryl-assisted C–F activation mechanism. TS (34 – 28) leads to a shallow intermediate in which FBpin is weakly bound through boron, as seen for formation of 22 in which FSi(OMe)₃ interacts with Rh. Formation of the products 28 and FBpin then occurs by extension of the Rh–B distance and the barrier to this step was found to cost less than 0.2 kcal/mol.

In contrast, C–F activation at the 4-position proceeds via TS (35 – 32) (H = +10.0 kcal/mol). In the transition state, the Rh–C4 bond is fully formed (2.07 Å) while the breaking C4···F4 bond increases to 1.76 Å and the B–Rh–4–F4 angle is +22.8°. In terms of the C···F and B···F contacts, TS (35 – 32) has a late geometry compared to TS (34 – 28), consistent with its higher energy. TS (35 – 32) links as well to a shallow intermediate as described previously for TS (34 – 28) and the final product 32 and FBpin are formed by breaking the Rh–B interaction.
Figure 4.3: Computed geometries and energies for boryl-assisted C–F activation at the 2- (left) and 4-positions (right) to give 28 and 32, respectively, plus FBpin.
The reaction profiles for boryl-assisted C–F activation at the 2- and 4-positions are compared in Figure 4.38. In both cases the rate-limiting transition states correspond to the C–F activation. In addition, boron-assisted C–F activation favours the activation at the 2-position (ΔH‡ = +4.1 kcal/mol cf. ΔH‡ = +10.0 kcal/mol at the 4-position).

This contrasts with the C–F oxidative addition where activation at the 4-position was lower in energy (ΔH‡ = +5.8 kcal/mol cf. ΔH‡ = +11.2 kcal/mol at the 2-position), as shown in Figure 4.39. Moreover, boron-assisted C–F activation at the 2-position is now more accessible than oxidative addition at the 4-position and therefore accounts for the experimental selectivity. It should be, however, noted that the two transition states for boryl-assisted at the 2-position and oxidative addition at the 4-position are relatively close in energy. However, experimentally the [Rh(4-C₅NF₄)(PEt₃)₃] product is not observed.
**Oxidative Addition**

2-Position

\[ \Delta H^\ddagger = +11.2, \quad \Delta G^\ddagger = +26.9 \]

4-Position

\[ \Delta H^\ddagger = +5.8, \quad \Delta G^\ddagger = +21.9 \]

**Boryl-Assisted**

\[ \Delta H^\ddagger = +4.1, \quad \Delta G^\ddagger = +20.1 \]

\[ \Delta H^\ddagger = +10.0, \quad \Delta G^\ddagger = +26.7 \]

Figure 4.3: Rate-limiting transition states for C–F activation of C₅NF₂ at the 2- and 4-positions.
4.4 Comparisons of Ligand-Assisted C–F Activation Processes at [Rh(X)(PMe₃)₃] (X = Si(OMe)₃, Bpin)

The lowest pathways for C–F activation of C₅NF₅ at the 2-position, which occurs in both cases via a ligand-assisted C–F activation, are shown in Figure 4.40. All energies (kcal/mol) are related to the two separated reactants, [Rh(X)(PMe₃)₃] and C₅NF₅. Also, free energies are in italics and selected distances are given in Å.

Both silyl- and boryl-assisted C–F activation proceeds via initial formation of a trigonal bipyramidal η²-precursor, 21 and 34, respectively. In 21, the Rh–C2 bond (2.16 Å) is slightly longer than in 34 (Rh···C2 = 2.14 Å) and the Rh···N1 interaction is shorter in the former (2.20 Å cf. 2.22 Å in 34). More interestingly, the X···F2 contact is stronger...
in 34 than 21, being respectively 2.67 Å and 2.93 Å. This difference of 0.26 Å may be due to the better Lewis acidic character of the Bpin ligand. In addition, 34 is found to be 7.3 kcal/mol ($\Delta G = +7.0$ kcal/mol) more stable than 21.

In the transition states, TS (21 – 22) and TS (34 – 28), the Si···F2 and B···F2 interactions decrease by 0.72 Å and 0.69 Å, respectively, while both Rh–C2 bonds shorten by 0.09 Å. The major difference between the two transition states is found in the Rh···N1 contact which shortens by 0.03 Å in TS (21 – 22) whereas this interaction remains constant at 2.22 Å in TS (34 – 28). This last feature may suggest that the nitrogen lone pair in TS (21 – 22) needs to stabilise slightly more the transition state while for the boryl-assisted C–F activation this contact was already made in the trigonal bipyramidal $\eta^2$-precursor 34. In addition, the computed barriers for silyl- and boryl-assisted C–F activation are +5.2 kcal/mol and +6.4 kcal/mol, respectively, relative to the $\eta^2$-precursor. Computed free energies show that the computed barriers are again very similar, being +5.7 kcal/mol and +6.7 kcal/mol, respectively. Therefore, the transition state for boryl-assisted C–F activation (H = +4.1 kcal/mol) is lower than TS (21 – 22) (H = +10.2 kcal/mol) only because the $\eta^2$-precursor 34 prior to C–F activation is more stable.

It should be mentioned that experimentally C–F activation of C$_5$NF$_5$ at [Rh(Bpin)(PEt$_3$)$_3$] occurs at -25 °C while the reaction with [Rh(SiOEt)$_3$](PEt$_3$)$_3$] happens at room temperature. In addition, the lowest pathway for C–F activation proceeds via either silyl- or boryl-assisted C–F activation in which the activation barrier relative to the most stable precursor (see above) is similar. Therefore the temperature dependence of these catalysts is not well reproduced in the calculations. However, the important point in this chapter is to understand why C–F activation of C$_5$NF$_5$ is observed experimentally at the 2-position. In this case, DFT calculations reproduced properly this last feature.
4.5 Conclusions

Density functional theory calculations have been used to model the reaction between [Rh(X)(PEt$_3$)$_3$] (X = Si(OMe)$_3$ or Bpin) and C$_5$NF$_5$. Calculations showed that the unusual experimental selectivity at the 2-position (i.e. the C–F bond *ortho* to the pyridyl nitrogen) is obtained via novel ligand-assisted C–F activation mechanisms, silyl- or boron-assisted. Both of these processes involve direct transfer of fluorine onto either silicon or boron via a 4-centred transition state. In addition, these mechanisms show that the selective activation at the 2-position arises due to a stabilising Rh···N1 contact in the relevant transition state.
Chapter 5: Catalytic Hydrodefluorination of Pentafluorobenzene by
[Ru(H)$_2$(CO)(NHC)(PPh$_3$)$_2$]: An Explanation for the Unusual Ortho-
Regioselectivity

5.1 Introduction

The aim of this chapter is to model the hydrodefluorination (HDF) reaction reported by
Whittlesey and co-workers (see Figure 5.1). Experimentally, the HDF of C$_6$F$_5$H at
ruthenium N-heterocyclic carbene (NHC) complexes, [Ru(H)$_2$(CO)(NHC)(PPh$_3$)$_2$]
(36$_{NHC}$, NHC = SIMes, SIPr, IMes, IPr, see Figure 5.1) occurs at 70 °C in THF to give
in high selectivity (> 90 %) 1,2,3,4-C$_6$F$_4$H$_2$ and [Ru(F)(H)(CO)(NHC)(PPh$_3$)$_2$] (45$_{NHC}$,
see Figure 5.1). Isolation of 45$_{NHC}$ shows that it can react in the presence of	rialkylsilanes to release FSiR$_3$ and restart the catalytic cycle.

Experimentally, the reaction is shut down when 3 equivalents of PPh$_3$ are added, which
implies a phosphine dissociation step. In addition, kinetic studies showed a first-order
dependence with respect to the concentration of both C$_6$F$_5$H and the ruthenium
precursor, while a zero-order dependence is observed on the concentration of silane.
These last observations suggest that the rate-limiting step is contained within the HDF
of C₆F₅H. This is in contrast with Holland’s results which showed that the rate-determining is the reaction between the β-diketiminate iron(II) and silane.¹⁵c

5.1.1 Proposed Mechanism for Catalytic HDF of C₆F₅H

The most unusual feature of the Whittlesey system is that the HDF of C₆F₅H results in a high regioselectivity for the formation of 1,2,3,4-C₆F₄H₂ (see Figure 5.1) in complete contrast to the Milstein¹⁵a,¹⁵b and Holland¹⁵c systems in which 1,2,4,5-C₆F₄H₂ is formed experimentally. To account for this unusual ortho-regioselectivity, the involvement of a tetrafluorobenzyne intermediate (42_Ru) has been postulated that could be formed by successive C–H and ortho-C–F activation of C₆F₅H (see Figure 5.2). The first step of the catalytic cycle may result in phosphine dissociation to create a vacant site at the metal centre and give [Ru(H)₂(CO)(NHC)(PPh₃)] (38_Ru). C–H activation rather than C–F activation can occur from 38_Ru via oxidative addition/metathesis reactions in which H₂ is released to form [Ru(C₆F₅)(H)(CO)(NHC)(PPh₃)] (41_Ru). Subsequent ortho-C–F activation can happen at 41_Ru to form a tetrafluorobenzyne intermediate 42_Ru. This type of structure has already been observed experimentally⁸² and a computational⁸³ study by Hall and Wu showed this type of structure is accessible. Indeed, the authors studied the C–H and the C–Cl activation of C₆Cl₅ at {Ir(PNP)}⁺ (PNP = bis(Z-2-(dimethylphosphino)vinyl)amino) and showed that the lowest pathway for C–Cl activation proceeds via a benzyne intermediate (ΔG⁺ = +24.2 kcal/mol). Species 43_Ru can be formed from 42_Ru by subsequent hydrogen transfer from Ru to the ring. Then, H₂ can recoordinate the metal centre to give 44_Ru and subsequent σ-bond metathesis leads to the hydrodefluorinated product, 1,2,3,4-C₆F₄H₂ and 45_Ru. Finally, 45_Ru reacts with silane to restart the catalytic cycle.
5.1.2 Comparison between Experimental and Calculated Structures

The first step was to compute the model species [Ru(H)$_2$(CO)(IME)(PH$_3$)] (36$^\text{IMe}$ IMe = IMe = 1,3-dimethylimidazol-2-ylidene) and [Ru(F)(H)(CO)(IME)(PH$_3$)] (45$^\text{IMe}$) used to study the HDF of C$_6$F$_5$H. In addition, the X-ray crystallographic structures of [Ru(H)$_2$(CO)(IMes)(PPh$_3$)] (36$^{\text{IMes}}$) and [Ru(F)(H)(CO)(IMes)(PPh$_3$)] (45$^{\text{IMes}}$) have also been optimised. From these different structures, bond lengths and bond angles were compared with the reported experimental data (see Table 5.1 and Figure 5.3). It should be also mentioned that complexes 36$^{\text{IMes}}$ and 45$^{\text{IMes}}$ have been computed as they will be studied computationally in the HDF of C$_6$F$_5$H (see Section 5.5). In addition, bond lengths and bond angles for 36$^{\text{IMes}}$ and 45$^{\text{IMes}}$ in Table 5.1 are the ones computed from the X-ray crystallographic structures, however, lower conformations (< 0.5 kcal/mol) have been obtained from the extensive conformation searching. In contrast, in the mechanistic study the lowest conformation is always used.
Table 5.1: Experimental (Exp.) and calculated (Calc.) bond lengths (Å) and bond angles (degrees) in [Ru(H)_2(CO)(NHC)(PH_3)_2].

<table>
<thead>
<tr>
<th></th>
<th>36'</th>
<th>36IMes</th>
<th>45'</th>
<th>45IMes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ru–C8</td>
<td>2.063</td>
<td>2.0956 (17)</td>
<td>2.064</td>
<td>2.077 (2)</td>
</tr>
<tr>
<td>Ru–P1</td>
<td>2.365</td>
<td>2.3628 (4)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Ru–P2</td>
<td>2.326</td>
<td>2.2985 (5)</td>
<td>2.367</td>
<td>2.3403 (6)</td>
</tr>
<tr>
<td>Ru–C7</td>
<td>1.903</td>
<td>1.9145 (17)</td>
<td>1.826</td>
<td>1.820 (3)</td>
</tr>
<tr>
<td>Ru–F5</td>
<td>–</td>
<td>–</td>
<td>2.018</td>
<td>2.0315 (13)</td>
</tr>
<tr>
<td>P1–Ru–C8</td>
<td>96.18</td>
<td>104.94 (5)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>P2–Ru–C8</td>
<td>162.07</td>
<td>172.93</td>
<td>173.75</td>
<td>173.28 (6)</td>
</tr>
<tr>
<td>N1–C8–N2</td>
<td>102.87</td>
<td>103.45</td>
<td>103.59</td>
<td>103.61 (18)</td>
</tr>
<tr>
<td>C7–Ru–F5</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>165.30</td>
</tr>
</tbody>
</table>

Figure 5.3: Computed geometries (with selected key distances in Å) in 36', 36IMes, 45' and 45IMes. Experimental bond lengths for 36IMes and 45IMes are shown in italics while phosphine Ph groups are truncated at the ipso carbon centre and non-participating hydrogen atoms are omitted.
Complex 36’ shows an elongation of the Rh–P1 bond by 0.04 Å, trans to H1, compared to the Ru–P2 bond, trans to NHC, which implies a higher trans-influence of the hydride ligand. This last feature is seen in 36IMes as well, in which calculated and experimental structures show an elongation of the Ru–P1 bond by 0.05 Å and 0.06 Å, respectively. In addition, the X-ray crystallographic structure 36IMes has a slightly distorted octahedral geometry with P1–Ru–C8 and P2–Ru–C8 angles of 104.94° and 146.33°, respectively. The calculated species also show a distortion in the geometry, however, this is less pronounced (P2–Ru–C8 = 151.26°). This small distortion was not seen in 36’, probably due to the use of less bulky substituents on the NHC and phosphine ligands. The computed bond lengths and bond angles in 36IMes are in reasonable agreement with the reported experimental data. The major discrepancy results in the elongation of the Ru–P1 and Ru–P2 bond which are overestimated in the computed species 36IMes by 0.06 Å and 0.08 Å.

The calculated structure 45’ shows a small elongation of the Ru–P2 bond by 0.04 Å compared to the reactant 36’. In addition, the Ru–C7 bond is shorter in 45’ (1.826 Å), trans to F5, than in 36’ (Ru–C7 = 1.903 Å), trans to H5. This may be explained by a weaker trans-influence of fluorine ligand compared to hydride ligand or by a “push-pull” effect. Similar trends are observed in the calculated and experimental structures of 45IMes. In addition, the bond lengths and bond angles are relatively well represented in the calculated species 45IMes compared to the experimental data. Again, the major difference is the Ru–P2 bond which is slightly more elongated in the calculated structure with a bond length of 2.40 Å (cf. 2.34 Å in experimental species 45IMes).
5.2 Computational Studies on the Reaction of \([\text{Ru}(\text{H})_2(\text{CO})(\text{IMe})(\text{PH}_3)]\) with \(\text{C}_6\text{F}_5\text{H}\): Identification of a Tetrafluorobenzene Intermediate

DFT studies have been performed on the reaction of \(\text{C}_6\text{F}_5\text{H}\) at the computational model \([\text{Ru}(\text{H})_2(\text{CO})(\text{IMe})(\text{PH}_3)_2]\) (36', IMe = 1,3,-dimethylimidazol-2-ylidene) in order to test the presence of a tetrafluorobenzene intermediate (42') and therefore explain the unusual ortho-regioselectivity observed experimentally.

In this chapter, all selected key distances are in Å and all energies (kcal/mol) are self-consistent field (SCF) energies, in contrast to Chapters 3 and 4. This choice is useful as it highlights certain key intermediates essential to the discussion. Indeed, by considering enthalpy these intermediates were found to be higher than the preceding transition states. In addition, free energies will not be discussed as all reactions involve equivalent dissociative and associative processes. In Sections 5.2-5.4, all energies are quoted relative to the two separated reactants, 36' and \(\text{C}_6\text{F}_5\text{H}\), together denoted as 37'.

The first step is therefore dissociation of \(\text{PH}_3\) to yield the 5-coordinate species 38' (E = +25.8 kcal/mol), as shown in Figure 5.4. The major change in 38' is the shortening of the Ru−H1 bond to 1.56 Å, as a vacant site is created trans to H1.

C–H activation occurs from 38' via initial formation of a σ-complex (39', E = +18.2 kcal/mol) where the \(\text{C}_6\text{F}_5\text{H}\) moiety interacts with the metal centre through the C6–H6 bond (Ru···H6 = 2.03 Å, Ru···C6 = 2.67 Å) which therefore lengthens to 1.13 Å (see Figure 5.4: Computed geometries and energies for phosphine dissociation.)
A transition state for C–H activation from Figure 5.5 has been located, TS (39’ – 40’) (E = +27.9 kcal/mol) by decreasing the Ru···C6 contact. In the transition state therefore the Ru···C6 contact shortens to 2.32 Å while the C6···H6 distance lengthens to 1.49 Å. In addition, the computed transition state shows that the H5···H6 distance shortens to 1.19 Å and surprisingly the Ru–H5 bond lengthens slightly to 1.72 Å (cf. 1.68 in 39’). Moreover, ICR calculations showed that TS (39’ – 40’) leads to a η2-H2 complex 40’ (E = +15.6 kcal/mol), prior to H2 elimination. This C–H activation, therefore, proceeds via a σ-complex-assisted mechanism (σ-CAM) in which an intermediate is involved, 40’, before elimination of H2 (see a) in Figure 5.6). This is in contrast with a σ-bond metathesis mechanism which proceeds via a 4-centred transition state and where no intermediate is observed (see b) in Figure 5.6).
H₂ elimination at 40’ proceeds via TS (40’ – 41’) (E = +28.6 kcal/mol) which is competitive with the C–H activation TS (39’ – 40’) (E = +27.9 kcal/mol, see Figure 5.7). TS (40’ – 41’) has been located by widening of the C6–Ru–C7 angle in order to dissociate H₂. Therefore the C6–Ru–C7 angle increases to 119.81° (cf. 99.1 in 40’) while the Ru···H5 and Ru···H6 distances increase to 2.82 Å and 3.44 Å as H₂ dissociates. Finally, complex 41’ (E = +20.6 kcal/mol) is formed in which H₂ is fully dissociated and where the CO ligand is trans to the C₆F₅ moiety (C6–Ru–C7 = 175.9°). Also, the Ru–H1 bond decreases to 1.55 Å as a vacant site is created trans to H1.

The presence of this vacant site allows the ortho-C–F activation via TS (41’ – 42’) (E = +58.3 kcal/mol, see Figure 5.8). This transition state has been located by shortening the Ru···C5 distance. In the transition state, the breaking C5···F5 bond is stretched to 1.97 Å (cf. 1.39 Å in 38) as the Ru···C5 and Ru···F5 distances shorten to 2.21 Å and 2.24 Å.
respectively. TS (41′ – 42′) links to the tetrafluorobenzene intermediate 41′ which has an energy located at +43.0 kcal/mol.

Figure 5.8: Computed geometries and energies for ortho-C–F activation to form tetrafluorobenzene intermediate 42′.

The reaction profile for formation of 42′ is shown in Figure 5.9. The rate-limiting transition state corresponds to the ortho-C–F activation which has a computed energy of +58.3 kcal/mol. Therefore this step is kinetically unfeasible under the conditions used.
experimentally. In addition, the tetrafluorobenzyne intermediate is found to be more than 40.0 kcal/mol above the reactants, and so ruled out as a viable intermediate.
5.3 HDF of C₆F₅H at [Ru(H)₂(CO)(IMe)(PH₃)] via Initial Formation of an η²-Arene Intermediate

At this stage, another mechanism needed to be considered in order to explain the unusual ortho-regioselectivity observed experimentally. Since phosphine dissociation happens experimentally, initial formation of η²-arene intermediate was plausible. Therefore the η²-adduct 46’ (E = +16.7 kcal/mol) has been optimised and the computed geometry and energy are shown in Figure 5.10. Complex 46’ shows an elongation of the C₅–F₅ bonds to 1.39 Å (cf. 1.35 Å in free C₆F₅H) as well as a lengthening of the C₅–C₆ distance to 1.44 Å (cf. 1.40 Å). This last elongation is caused by π-back donation from the metal centre to the π* antibonding orbitals of C₆F₅H. Interestingly, 46’ is found to be slightly more stable than the σ-complex 39’ (E = +18.2 kcal/mol) computed prior to C–H activation.

![Figure 5.10: Computed geometry and energy for the η²-arene intermediate.](image)

The second step was to perform a scan from 46’ involving the shortening of the H₅···F₅ interaction as in principle HDF reaction results in the substitution of fluorine by hydrogen. In this case, HF could be eliminated to give a σ-aryl species [Ru(C₆F₅)(H)(CO)(NHC)(PH₃)] (48’) which could lead to the final products [Ru(F)(H)(CO)(NHC)(PH₃)] (45’) and 1,2,3,4-C₆F₄H₂ via a protonolysis step of HF (see Figure 5.11).
Therefore the shortening of the H5···F5 distance via a scan calculation has been performed and allowed the location of a transition state, TS (46' – 47') (E = +24.5 kcal/mol, see Figure 5.12). In the transition state, the H5···F5 contact shortens, as anticipated, to 2.07 Å, but more interestingly the C5···H5 distance decreases to 1.50 Å while the Ru···H5 and Ru···C5 bonds elongate to 1.72 Å and 2.34 Å, respectively. IRC calculations link to the species 47' which showed, unexpectedly, the formation of a new C5–H5 bond (1.25 Å) and therefore contrast with the expected HF formation.

At this point further characterisation of the structures involved in this process has been undertaken by comparing the bond lengths and computing the natural atomic charges of the different species (see Figure 5.13). During the process the C5–C6 distances becomes longer, from 1.44 Å in 46' to 1.49 Å in 47', suggesting a change in bond order. In addition, the C1–C6, C2–C3 and C4–C5 distances are slightly longer in 47' while the C1–C2 and C3–C4 becomes shorter. Computed natural atomic charges show that H5 becomes more positive, from -0.074 in 46' to +0.177 in 47', while C5 is less positive in 47' (+0.117) than in 46' (+0.261). Overall, the entire C₅F₅H moiety becomes more negative in 47' (total charge = -0.524) than in the η₂-arene intermediate 46' (total charge
while the metal centre is less negative in 47' (-0.454 cf. -0.536 in 46'). All these features suggest that the process occurs via a nucleophilic attack of H5 at C5 to lead the complex 47' in which the \{C_6F_5H_2\}^- moiety resembles a Meisenheimer intermediate. This last species is stabilised by interaction of the ortho position with the metal centre (Ru–C6 = 2.28 Å) as shown in Figure 5.12.

Since HF formation did not occur as expected, another approach has been considered. Intermediate 47' consists in the formation of a \{C_6F_5H_2\}^- moiety and the final product [Ru(F)(H)(CO)(NHC)(PH_3)] (45') and 1,2,3,4-C_6F_4H_2 can in principle be formed by transferring F5 onto the metal centre. A calculation involving the shortening of the Ru···F5 distance therefore was performed (see Figure 5.14). A transition state, TS (47' – 48') (E = +36.3 kcal/mol) was located in which the C5···F5 bond increases to 1.98 Å and the Ru···C5 contacts decreases to 2.29 Å (cf. 2.40 Å in 47'). However, another unexpected feature happens with the shortening of the H5···F5 distance to 1.71 Å (cf. 1.98 Å in 47'). In reality, IRC calculations showed that the highly fluoridic centre F5 (computed charge = -0.53) is able to abstract H5 to form HF and the σ-aryl species [Ru(C_6F_5H)(H)(CO)(NHC)(PH_3)] (48'). Also, calculations suggest that the HF
molecule weakly interacts within 48' with a H1···H5 contact of 1.47 Å (Ru···H5 = 2.37 Å, C5···H5 = 2.73 Å).

The final products [Ru(F)(H)(CO)(NHC)(PH₃)] (45') and 1,2,3,4-C₆F₄H₂ can then be formed from 48' via a protonolysis step. This process occurs via TS (48' – 45') (E = +3.8 kcal/mol) in which the breaking Ru···C5 bond lengthens to 2.26 Å (cf. 2.16 Å in 48', see Figure 5.15).

In addition, the Ru···F5 and C5···H5 interactions shorten to 2.89 Å (cf. 3.33 Å in 48’) and 1.81 Å (cf. 2.73 Å in 48’), respectively. IRC calculations showed that TS (48' –
45') links to an adduct of 45', 45'.C₆F₄H₂ (E = -24.7 kcal/mol), which is found to be more stable than the two separated products, 45' and 1,2,3,4-C₆F₄H₂ (E = -19.7 kcal/mol). This difference in energy may come from the H5···F5 contact of 1.95Å in 45'.C₆F₄H₂ and a basis set superposition error (BSSE).

The reaction profile for the HDF of C₆F₃H to give 45' and 1,2,3,4-C₆F₄H₂ is summarised in Figure 5.16. This mechanism involves initial phosphine dissociation in which the C₆F₃H can bind the metal centre to form an η²-arene intermediate 46' (E = +16.7 kcal/mol). A nucleophilic attack process happens from 46' to form a Meisenheimer intermediate 47' (E = +23.5 kcal/mol) via TS (46' – 47') (E = +24.5 kcal/mol). In this case, instead of transferring the fluorine atom directly onto the metal centre, a σ-aryl complex (48', E = -2.0 kcal/mol) is formed via HF loss. Finally, the protonolysis by HF with concomitant F transfer to the metal centre gives 45' and 1,2,3,4-C₆F₄H₂. The overall process can be described as a stepwise mechanism with the rate-limiting transition state being the HF elimination corresponding to TS (47' – 48') (E = +36.3 kcal/mol). This transition state is much lower than TS (41' – 42') for the formation of tetrafluorobenzyne intermediate 42' which had an energy of +58.3 kcal/mol.
Figure 5.16: Reaction profile for the HDF of C₆F₅H to give 45' and 1,2,3,4-C₆F₄H₂.
5.4 HDF of C₆F₅H at [Ru(H)₂(CO)(Im)(PH₃)] without Initial Formation of an η²-Arene Intermediate

When investigating this novel nucleophilic attack mechanism via initial PH₃/C₆F₅H substitution a second pathway has been identified, involving a direct transfer of the hydride ligand on the fluoroaromatic without initial formation of a η²-arene intermediate.

Initially, a loosely bound adduct is formed (49', E = +21.0 kcal/mol) in which the C₆F₅H moiety interacts with the ruthenium metal centre (see Figure 5.17). The C5–F5 bond lengthens to 1.36 Å due to a short Ru···F5 contact (2.67 Å). This adduct is actually higher in energy than the η²-arene species 46' (E = +16.7 kcal/mol) and the σ-complex 39' (E = +18.2 kcal/mol), formed prior C–H activation of C₆F₅H.

![Figure 5.17: Computed geometries for HDF of C₆F₅H at [Ru(H)₂(CO)(Im)(PH₃)] to give 45' and 1,2,3,4-C₆F₄H₂.](image)
A transition state, TS (49' – 45') (E = +37.5 kcal/mol) has been located from 49', by shortening the C5···H5 contact to transfer the hydride onto the C6F5H moiety. Therefore, in TS (49' – 45'), the C5···H5 distance decreases to 1.45 Å but at the same time the C5···F5 bond lengthens to 1.47 Å. In addition, due to the different orientation of the C6F5H moiety compared to the η²-arene species 46', the vacant site at the metal centre remains available. This implies that fluorine can be transferred to Ru, suggested by the shortening of the Ru···F5 distance to 2.48 Å. IRC calculations links to the separated products 45' and 1,2,3,4-C6F4H2.

Again to understand the nature of the transition state, the computed bond lengths and natural atomic charges have been compared between 49' and the transition state TS (49' – 45') (see Figure 5.18). The major changes in terms of the bond lengths results in the increase of the C4–C5 and C5–C6 distances to 1.43 Å in the transition state TS (49' – 45') (cf. 1.40 in 49'). In addition, computed natural atomic charges show that H5 becomes less negative in the transition state (-0.138 cf. -0.228 in 49') while the entire C6F5H moiety is more negative (total charge = -0.374 cf. +0.049 in 49'). Therefore, as seen in TS (46' – 47'), this process involves a nucleophilic attack of H5 at C5.

![Figure 5.18: Selected computed bond lengths and natural atomic charges for 49' and TS (49' – 45'), respectively. Non-participating atoms are omitted for clarity.](image)

In parallel, a similar example has been recently reported by Llusar and co-workers in the catalytic HDF of C5NF5 at [M3S4H3(dmpe)3]⁺ (M = Mo, W) clusters in the presence...
of HSiMe$_2$Ph to yield exclusively 2,3,5,6-C$_5$NF$_4$ (see Figure 5.19). DFT calculations have shown that initial phosphine dissociation is required to create a vacant site at the metal centre followed by a “$\sigma$-bond metathesis transition state”. The transition state for M = Mo is located at +38.6 kcal while for M = W the energy of the transition state is at +41.4 kcal/mol. This trend is in agreement with the experimental observations where faster conversion at Mo is observed.

![Diagram of HDF of C$_5$NF$_5$ at [M$_3$S$_4$H$_6$(dmpe)$_3$]$^+$ (M = Mo, W) in the presence of HSiMe$_2$Ph to give 2,3,5,6-C$_5$NF$_4$ with a schematic representation of the transition state proposed for this process.]

In summary, the concerted mechanism for the HDF of C$_6$F$_5$H proceeds via a nucleophilic attack of H$_5$ at C$_5$ with a computed transition state TS ($49'$ – $45'$) located at +37.5 kcal/mol. This is lower than formation of tetrafluorobenzyne intermediate 42' via TS ($41'$ – $42'$) (E = +58.3 kcal/mol), but this slightly higher than the stepwise mechanism in which the rate-limiting transition state, HF loss, is located at +36.3 kcal/mol. Therefore, from this point forward the proposed mechanism via initial phosphine dissociation followed by C–H and ortho-C–F activation to form tetrafluorobenzyne intermediate 42' will be discarded.
5.5 HDF of C₆F₂H at [Ru(H₂(CO))(IMes)(PPh₃)]

5.5.1 Phosphine Dissociation

In addition to the small computational model 36′, calculations have also been performed on the full experimental model by using IMes and PPh₃ ligands. In Section 5.5, all energies are quoted relative to the two separated reactants, 36(IMes) and C₆F₅H, denoted by 37IMes. In the figures, energies in italics include a solvent correction (PCM Approach, THF) and the energies that are underlined are those for the reaction of the small model 36′ with C₆F₅H. Also, for clarity, phosphine Ph groups are truncated at the ipso carbon centre and non-participating hydrogen atoms are omitted.

Because of the use of the more sterically encumbered full system, the Ru–P₁ bond (2.43 Å, see Figure 5.20) is weaker in the full model than in 36′ (Ru–P₁ = 2.37 Å). One direct consequence is that phosphine dissociation becomes more accessible than at 36′ by 14.7 kcal/mol with a computed energy of +11.1 kcal/mol. In addition, this step now costs only +7.8 kcal/mol in THF.

5.5.2 HDF via a Stepwise Mechanism

After phosphine dissociation, formation of the η²-arene intermediate 46(IMes) (E = +10.9 kcal/mol) is computed (see Figure 5.21). In 46(IMes), the Ru···C5 and Ru···C6 bonds are slightly longer than in 46′, being 2.30 Å (cf. 2.28 Å in 46′) and 2.38 Å (cf. 2.36 Å in...
46'), respectively. This reflects a more weakly bound arene in 46_{IMes} and the PPh_{3}/C_{6}F_{5}H substitution step has now a computed energy of +10.9 kcal/mol (+9.0 kcal/mol in THF) and is found to be 5.8 kcal/mol more accessible compared to 46'.

Figure 5.21: Computed geometry and energy for the η^2-arene intermediate.

A similar trend is observed for the nucleophilic attack (see Figure 5.22). In the transition state, TS (46 – 47)_{IMes} (E = +24.5), again the Ru···C5 and Ru···C6 distances are slightly longer than in TS (46' – 47') by 0.03 Å and 0.02 Å, respectively. With the full model, the nucleophilic attack is now more favourable kinetically by 4.0 kcal/mol than at 46' with a computed energy located at +20.5 kcal/mol (+18.0 kcal/mol in THF).

Figure 5.22: Computed geometries and relative energies for the nucleophilic attack of H5 at C5 to give 47_{IMes}.

The Meisenheimer intermediate 47_{IMes} shows shorter Ru···C5 and Ru···H5 contacts than in 47', however, the Ru···C6 bond (2.28 Å) is similar in 47_{IMes} and 47'. Species
47\textsubscript{IMes} is computed to be more stable by 4.3 kcal/mol than 47', with a computed energy of +19.2 kcal/mol (+16.0 kcal/mol in THF).

Figure 5.23: Computed geometries and relative energies for formation of 48\textsubscript{IMes}.

The effect of bulky substituents is particularly large for the HF elimination. TS (47 – 48)\textsubscript{IMes} (E = +25.1 kcal/mol) is computed to be 11.2 kcal/mol lower than with the small model (TS (47’ – 48’), E = +36.3 kcal/mol). This difference in energy can be explained by short contacts between the fluoride (computed charge = -0.54) and the NHC ligands. This last feature will be discussed later (see Section 5.5.4 and Figure 5.27). In addition, the HF molecule strongly interacts with the \{C\textsubscript{6}F\textsubscript{4}H\} moiety (C5…H5 = 1.97 Å) and shows the importance of the HF hydrogen bonding due to the difference in electronegativity between H5 and F5. Finally THF stabilises the energy of TS (47 – 48)\textsubscript{IMes} to +20.1 kcal/mol.

Intermediate 48\textsubscript{IMes} shows that the HF molecule strongly interacts with the C\textsubscript{6}F\textsubscript{4}H moiety (C5…H5 = 1.97 Å cf. 2.73 in 48’) which may explain the stabilisation of the former by 4.3 kcal/mol.

Finally, the protonolysis step shows similar behaviour in which the transition state, TS (47 – 48)\textsubscript{IMes}, is stabilised relative to the small model by 4.7 kcal/mol and the final products 45\textsubscript{IMes} and 1,2,3,4-C\textsubscript{6}F\textsubscript{4}H\textsubscript{2} by 15.7 kcal/mol (see Figure 5.24). It should also mentioned that TS (47 – 48)\textsubscript{IMes} links to an adduct, as seen with the small model, that is slightly lower in energy than the separated product (E = -39.6 kcal/mol; E = -42.1 kcal/mol in THF).
The reaction profiles for the HDF of $\text{C}_6\text{F}_5\text{H}$ at $[\text{Ru(H)}_2(\text{CO})(\text{NHC})(\text{PR}_3)]$ are shown in Figure 5.25. Calculations with the full model stabilised all the different stationary points along the stepwise mechanism compared to the HDF of $\text{C}_6\text{F}_5\text{H}$ at $[\text{Ru(H)}_2(\text{CO})(\text{Ime})(\text{PH}_3)]$. These differences in energies can be explained by the use of a more sterically encumbered full system which facilitates the initial phosphine dissociation. The rate-limiting transition state remains the HF elimination, $\text{TS (47 – 48)}_{\text{Imes}}$, with a computed barrier of +25.1 kcal/mol which drops to +20.1 kcal/mol in THF, qualitatively in agreement with the conditions used experimentally. Overall the reaction is exothermic by 35.4 kcal/mol ($\Delta E = -40.2$ kcal/mol in THF).
Figure 5.25: Reaction profiles for the HDF of C\textsubscript{6}F\textsubscript{5}H at [Ru(H\textsubscript{2})(CO)(NHC)(PR\textsubscript{3})\textsubscript{2}], to give [Ru(F)(H)(CO)(NHC)(PR\textsubscript{3})\textsubscript{2}] and 1,2,3,4-C\textsubscript{6}F\textsubscript{4}H\textsubscript{2}. Energies in italics include a solvent correction (PCM method, THF).
5.5.3 HDF via a Concerted Mechanism

A similar trend has been obtained for HDF via a concerted mechanism. The transition state, \( \text{TS (49 − 45)}_{\text{Mes}} \) shows an elongation of the Ru⋯H5 distance to 1.84 Å, 0.03 Å longer than in \( \text{TS (49′ − 45′)} \). The \( \text{C}_6\text{F}_5\text{H} \) moiety weakly interacts in the full model with computed Ru⋯C5 and Ru⋯F5 contacts of 2.96 Å and 2.57 Å, respectively (cf. \( \text{TS (49′ − 45′)} \), 2.88 Å and 2.48 Å). \( \text{TS (49 − 45)}_{\text{Mes}} \) is more accessible than \( \text{TS (49′ − 45′)} \) by 7.7 kcal/mol. In addition, no adduct has been located prior to the nucleophilic attack probably due to the steric bulk in the full model.

![Computed geometry and relative energy for TS (49 − 45)_{Mes} to give 45_{Mes} and 1,2,3,4-C_6F_4H_2.](image)

Finally, \( \text{TS (49 − 45)}_{\text{Mes}} \) has an energy of +29.8 kcal/mol (+27.1 kcal/mol in THF) and therefore remains higher in energy than the stepwise mechanism with a rate-limiting transition state energy located at +25.1 kcal/mol (+20.1 kcal/mol in THF), corresponding to \( \text{TS (47 − 48)}_{\text{Mes}} \).

5.5.4 Regioselectivity of HDF of \( \text{C}_6\text{F}_5\text{H} \)

The formation of the three different isomers of \( \text{C}_6\text{F}_4\text{H}_2 \) after HDF has also been considered and in all cases both transition states for concerted and stepwise mechanisms have been characterised. The energies of the rate-limiting transition states for the computational and full models involved in these processes are tabulated in Table 5.2. In the case of the stepwise mechanism the rate-limiting transition state always corresponds to the HF elimination step.
Table 5.2: Energies for the rate-limiting transition states for the concerted and stepwise mechanisms for the small and full models. The most stable transition states for each model are shown in bold. Energies in italics include a solvent correction (PCM method, THF).

<table>
<thead>
<tr>
<th></th>
<th>[Ru(H)(CO)(IMe)(PH₃)] (38')</th>
<th>[Ru(H)₂₂(CO)(IMes)(PPh₃)] (38IMes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concerted</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ortho</td>
<td>+37.5</td>
<td>+29.8/+27.1</td>
</tr>
<tr>
<td>meta</td>
<td>+34.9</td>
<td>+29.0/+26.2</td>
</tr>
<tr>
<td>para</td>
<td>+33.4</td>
<td>+27.2/+24.7</td>
</tr>
<tr>
<td>Stepwise</td>
<td></td>
<td>+25.1/+20.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+32.0/+23.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+31.9/+23.8</td>
</tr>
</tbody>
</table>

Interestingly, the concerted mechanism predicts that HDF of C₆F₅H at [Ru(H)₂₂(CO)(IMe)(PH₃)], would result in formation of the para-isomer (i.e. 1,2,4,5-C₆F₄H₂). This is in fact the idea of a nucleophilic attack pathway which usually shows selectivity for the 4-position. In contrast, the stepwise mechanism predicts the formation of 1,2,3,4-C₆F₄H₂ with a computed barrier +36.3 kcal/mol and this is consistent with the ortho-regioselectivity that is observed experimentally. However, by comparing the concerted and stepwise mechanisms for the small model, formation of the para-isomer is slightly more favourable (ΔΔE = 2.9 kcal/mol).

Some similarities are seen for the HDF of C₆F₅H at [Ru(H)₂₂(CO)(IMes)(PPh₃)]. The concerted mechanism predicts again formation of 1,2,4,5-C₆F₄H₂, now with a barrier of +27.2 kcal/mol, while the stepwise pathway forms 1,2,3,4-C₆F₄H₂ (ΔE = +25.1 kcal/mol). However, the stepwise mechanism becomes more accessible kinetically than the concerted nucleophilic attack and is now consistent with the unusual ortho-regioselectivity observed experimentally (ΔΔE = 2.2 kcal/mol). In addition, by including the solvent effect the stepwise mechanism remains lower in energy with a transition state located at +20.1 kcal/mol (ΔΔE = 4.6 kcal/mol). The stepwise mechanism corresponds, in fact, to the lowest energy barriers for the formation of 1,2,3,5- and 1,2,4,5-C₆F₄H₂ in THF with transition states located at +23.5 kcal/mol and +23.8 kcal/mol, respectively. It should be noted that the solvent effect is really significant as by not taking it into account then formation of 1,2,3,5- and 1,2,4,5-C₆F₄H₂ would be predicted to proceed via the concerted pathway.

This can be explained by looking at the three different transition states corresponding to the HF elimination step (see Figure 5.27). All these transition states, as all computed species with the full model, have been obtained after extensive conformation searching.
The two transition states \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \) correspond to the HDF of \( \text{C}_6\text{F}_5\text{H} \) to give \( \text{1,2,3,5-C}_6\text{F}_4\text{H}_{2} \) and \( \text{1,2,4,5-C}_6\text{F}_4\text{H}_{2} \), respectively. First of all, the stability of \( \text{TS (47 - 48)} \text{Mes} \) compared to \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \) can be explained by the interactions between the mesityl groups and the displaced fluoride. In \( \text{TS (47 - 48)} \text{Mes} \), two short \( \text{H} \cdots \text{F5} \) contacts of 1.91 Å and 1.92 Å are computed. In contrast, in \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \), the displaced fluorides, F4 and F3, respectively, interact only with one mesityl group (\( \text{H} \cdots \text{F4} = 1.80 \) Å, \( \text{H} \cdots \text{F3} = 1.81 \) Å). This difference is due to the orientation of the \( \text{C}_6\text{F}_5\text{H} \) moiety in the transition state which is twisted away from the NHC ligand. Indeed, in \( \text{TS (47 - 48)} \text{Mes} \), the presence of \( \text{H6} \) in the ortho-position permits an interaction between the hydrogen atom and the mesityl group. However, in the case of \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \), due to their high electronegativity, F2 and F1, respectively cannot interact with the mesityl group and the \( \text{C}_6\text{F}_5\text{H} \) twisted away from the NHC ligand. Therefore, the ortho-regioselectivity may be explained by the use of bulky NHC ligands.

Due to these different interactions between the displaced fluoride and the mesityl groups, the inclusion of the solvent effect is indispensable. Recomputation of \( \text{TS (47 - 48)} \text{Mes} \) in THF shows that the transition state is stabilised by 5.0 kcal/mol while the energies of \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \) decrease by around 8.0 kcal/mol. This difference of 3.0 kcal/mol can be explained by the higher total dipole moment \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \) than in \( \text{TS (47 - 48)} \text{Mes} \), these being +12.14 Debye, +11.19 Debye and +6.86 Debye, respectively. Therefore the use of polar aprotic solvent such as THF will stabilise the first two transition states more than the last one. Another contribution may result from the computed \( \text{H} \cdots \text{F} \) interactions between the displaced fluoride and the mesityl groups. Indeed, in \( \text{TS (47 - 48)} \text{Mes} \), as mentioned above, two short contacts are computed while in \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \) only one is seen. This implies that in \( \text{TS (47 - 48)} \text{Mes} \) the displaced fluoride is more stabilised and therefore the solvent effect affects less the energy of the transition state compared to \( \text{TS (47a - 48a)} \text{Mes} \) and \( \text{TS (47b - 48b)} \text{Mes} \).
Figure 5.27: Computed transition states corresponding to the HF elimination via TS (47 – 48)_{HMeiss}, TS (47a – 48a)_{HMeiss} and TS (47b – 48b)_{HMeiss}, respectively.
5.6 Conclusions

Density functional theory calculations have defined a novel class of reaction mechanism for the HDF of C₆F₅H catalysed by [Ru(H)₂(CO)(NHC)(PR₃)]. The key feature is the nucleophilic attack of one hydride ligand at the fluoroarene moiety. Two different pathways have been characterised, concerted or stepwise, in which the more accessible process for the full model is seen for the latter. In this case, formation of 1,2,3,4-C₆F₄H₂ involves 1) PPh₃/C₆F₅H substitution; 2) nucleophilic attack by the Ru hydride ligand at the ortho position on the ring; 3) HF loss and Ru fluoroaryl formation; and 4) protonolysis by HF with concomitant fluoride transfer to Ru to give the 1,2,3,4-C₆F₄H₂ and [Ru(F)(H)(CO)(IMes)(PPh₃)]. Overall, the rate-limiting transition state has a computed barrier of 20.1 kcal/mol in THF, which corresponds to the HF elimination, and is consistent with the unusual ortho-regioselectivity observed experimentally.
Chapter 6: Computational Background

6.1 Introduction

The following chapter deals with some fundamental aspects of density functional theory (DFT) which is the main computational method employed in this thesis. The discussion will begin with background quantum mechanics (QM) and continue with an overview of the Hartree-Fock approximation. In addition, the key concepts in the development of DFT will be reviewed. Finally, the results of benchmark calculations to compare different basis sets and functionals will be presented.

6.2 Background QM

6.2.1 The Schrödinger Equation

The main purpose of quantum chemical approaches is to solve, as far as possible, the time-independent Schrödinger equation:

\[ \hat{H} \Psi_i = E_i \Psi_i. \]  

(6.1)

In Equation (6.1), \( \hat{H} \) is the Hamiltonian operator for a system of \( M \) nuclei (with charges \( Z_i \) and mass \( m_i \), \( i = 1, \ldots, M \)) and \( N \) electrons. The Hamiltonian operator is described as:

\[ \hat{H} = \hat{T}_n + \hat{T}_e + \hat{V} \]  

(6.2)

where \( \hat{T}_n \) and \( \hat{T}_e \) represent the kinetic energy operators for the nuclei and electrons, respectively:

\[ \hat{T}_n = -\frac{1}{2} \sum_{i=1}^{M} \frac{1}{m_i} \nabla_i^2 \]  

(6.3)

\[ \hat{T}_e = -\frac{1}{2} \sum_{i=1}^{N} \nabla_i^2 \]  

(6.4)
In Equations 6.3 and 6.4, the Laplacians are respectively

\[ \nabla_i^2 = \frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2}, \]

\[ \nabla_i^2 = \frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2}, \]

where \( x, y, z \) are the Cartesian coordinates of the nuclei and electrons and correspond to \( R_i = (X_i, Y_i, Z_i) \) and \( r_i = (x_i, y_i, z_i) \), respectively.

\( \hat{V} \) represents the attractive electrostatic interaction between the nuclei and the electrons, and the repulsive potential due to the nucleus-nucleus and electron-electron interactions, respectively:

\[ \hat{V} = -\sum_{i=1}^{M} \sum_{i=1}^{N} \frac{Z_i}{r_{ii}} + \sum_{i=1}^{M} \sum_{j=1}^{M} \frac{Z_i Z_j}{R_{ij}} + \sum_{i=1}^{N} \sum_{j=1}^{N} \frac{1}{r_{ij}} \]  \hspace{1cm} (6.5)

or in a simplified form:

\[ \hat{V} = \hat{V}_{Ne} + \hat{V}_{NN} + \hat{V}_{ee}. \]  \hspace{1cm} (6.6)

In Equation (6.1), \( E \) is the energy of a specific system and \( \Psi \) is the wave function of this system. In addition, the square of the wave function:

\[ |\Psi(\tilde{x}_1, \tilde{x}_2, ..., \tilde{x}_N)|^2 \, d\tilde{x}_1 \, d\tilde{x}_2 \, ... \, d\tilde{x}_N \]  \hspace{1cm} (6.7)

corresponds to the probability that electrons 1, 2, ..., \( N \) are present in volume elements, \( d\tilde{x}_1 \, d\tilde{x}_2 \, ... \, d\tilde{x}_N \). Also, as electrons are indistinguishable, the probability must remain the same, even if two electrons are interchanged:

\[ |\Psi(\tilde{x}_1, \tilde{x}_2, ..., \tilde{x}_i, \tilde{x}_j, ..., \tilde{x}_N)|^2 = |\Psi(\tilde{x}_1, \tilde{x}_2, ..., \tilde{x}_j, \tilde{x}_i, ..., \tilde{x}_N)|^2. \]  \hspace{1cm} (6.8)
Moreover, as electrons are fermions, the wave function must be antisymmetric which means that $\Psi$ changes sign when two electrons are interchanged. This is described as:

$$|\Psi(\vec{x}_1, \vec{x}_2, ..., \vec{x}_i, \vec{x}_j, ..., \vec{x}_N)| = -|\Psi(\vec{x}_1, \vec{x}_2, ..., \vec{x}_j, \vec{x}_i, ..., \vec{x}_N)|.$$  \hspace{1cm} (6.9)

This last point is very important as it is a direct consequence of Pauli’s exclusion principle where two electrons cannot occupy the same state.

Finally, knowing that the square of the wave function is the probability of finding $N$ electrons in all space, the wave function must be normalised:

$$\int ... \int |\Psi(\vec{x}_1, \vec{x}_2, ..., \vec{x}_N)|^2 d\vec{x}_1 d\vec{x}_2 ... d\vec{x}_N = 1.$$  \hspace{1cm} (6.10)

### 6.2.2 The Born-Oppenheimer Approximation

The Born-Oppenheimer approximation is essential to simplify the Schrödinger equation. This approximation deals with the significant differences between the masses of nuclei and electrons. Indeed, the smallest nucleus, a proton, is approximately 1800 times heavier than an electron and therefore moves much more slowly. One direct consequence is that the nuclei can be considered as fixed and therefore their kinetic energy in Equation (6.3) is zero. Another key point is that the potential energy for the nucleus-nucleus repulsion in Equation (6.6), $\hat{V}_{NN}$, is a constant. Thus, the complete Hamiltonian is reduced to the so-called electronic Hamiltonian, read as:

$$\hat{H}_{elec} = -\frac{1}{2} \sum_{i=1}^{N} \nabla_{i}^2 - \sum_{l=1}^{M} \sum_{i=1}^{N} \frac{Z_{l}}{r_{li}} + \sum_{i=1}^{N} \sum_{j>i}^{N} \frac{1}{r_{ij}} = \hat{T}_{e} + \hat{V}_{Ne} + \hat{V}_{ee}.$$  \hspace{1cm} (6.11)

This implies that the electronic Schrödinger equation is therefore

$$\hat{H}_{elec} \Psi_{elec} = E_{elec} \Psi_{elec}$$  \hspace{1cm} (6.12)

where $\Psi_{elec}$ and $E_{elec}$ are the electronic wave function and energy, respectively.
6.2.3 The Variational Principle

The variational principle is important to many quantum mechanical applications as it provides a way for approaching the wave function of the ground state, \( \Psi_0 \), which is the state that delivers the lowest energy \( E_0 \). The variational principle states that all energies calculated from a trial wave function \( \Psi_{trial} \) will be always equal or higher to the actual ground state energy, \( E_0 \), described as:

\[
E_0 \leq \min_{\Psi \to N} E[\Psi] \leq \min_{\Psi \to N} \langle \Psi | \hat{T}_e + \hat{V}_{Ne} + \hat{V}_{ee} | \Psi \rangle \tag{6.13}
\]

It is therefore possible to assess the quality of trial wave functions, as the lower the energy, the better the trial wave function.

6.2.4 The Hartree-Fock Approximation

It is impossible to solve the Equation (6.13) by searching through all possible acceptable \( N \)-electron wave functions. Therefore a suitable subset has to be defined which incorporates a physically reasonable approximation to the exact wave function. A solution to this problem is the Hartree-Fock approximation where the \( N \)-electron wave function is considered through an antisymmetrized product of \( N \) one-electron wave functions called the Slater determinant, \( \Phi_{SD} \).

\[
\Psi_0 \approx \Phi_{SD} = \frac{1}{\sqrt{N!}} \begin{vmatrix}
\chi_1(\vec{x}_1) & \chi_2(\vec{x}_1) & \ldots & \chi_N(\vec{x}_1) \\
\chi_1(\vec{x}_2) & \chi_2(\vec{x}_2) & \ldots & \chi_N(\vec{x}_2) \\
\vdots & \vdots & \ddots & \vdots \\
\chi_1(\vec{x}_N) & \chi_2(\vec{x}_N) & \ldots & \chi_N(\vec{x}_N)
\end{vmatrix}
\tag{6.14}
\]

where \( \chi_i(\vec{x}_i) \) are the spin orbitals and are composed of a spatial orbital \( \phi_l(\vec{r}) \) and one of the two spin functions, \( \alpha(s) \) or \( \beta(s) \), spin up or down, respectively.

A Slater determinant is antisymmetric with respect to the interchange of any two electrons. This means that swapping two rows will result in a change in the sign of \( \Phi_{SD} \). In addition, if two columns are the same, \( \Phi_{SD} \) goes to zero, thus obeying the Pauli’s exclusion principle.
Hartree-Fock theory adopts a self-consistent field (SCF) approach. In this method, molecular orbitals are guessed before being introduced to the Fock operator, \( \hat{f}_i \), as shown in Equation (6.15), where \( \varepsilon_i \) corresponds to the orbital energies:

\[
\hat{f}_i \chi_i = \varepsilon_i \chi_i, \quad i = 1, 2, ..., N.
\]  

This eigenvalue problem is then solved and a new set of molecular orbitals is obtained. This process is repeated until the set of orbitals no longer change (i.e. the Fock equation is solved).

The Fock operator, \( \hat{f}_i \), is described as:

\[
\hat{f}_i = -\frac{1}{2} \nabla_i^2 - \sum_{l=1}^{M} \frac{Z_l}{r_{il}} + V_{HF}(i)
\]  

where the first two terms are the kinetic energy of the electrons and the potential energy due to the electron-nucleus attraction, respectively. \( V_{HF}(i) \) is the Hartree-Fock potential and is another key approximation that represents the average repulsive potential by an electron due to the remaining N-1 electrons. This simple electron operator \( V_{HF}(i) \) has two components, the Coulomb operator, \( \hat{J} \), and the exchange operator, \( \hat{R} \).

\[
V_{HF}(i) = \sum_{j=1}^{N} \left( \hat{J}_j(\vec{x}_1) - \hat{R}_j(\vec{x}_1) \right)
\]

The Coulomb operator represents the potential experienced by an electron at position \( \vec{x}_1 \) due to the charge distribution of another electron described by a spin orbital \( \chi_j \):

\[
\hat{J}_j(\vec{x}_1) = \int |\chi_j(\vec{x}_2)|^2 \frac{1}{r_{12}} \, d\vec{x}_2
\]

where the integration is over all space and spin coordinates, weighted by the probability that the other electron is at position \( \vec{x}_2 \).
The second term in Equation (6.17), \( \hat{R}_j(\vec{x}_1) \), corresponds to the exchange contribution. This operator does not have a classical interpretation and is defined by operating on a spin orbital, read as:

\[
\hat{R}_j(\vec{x}_1)\chi_i(\vec{x}_1) = \int \chi_j^*(\vec{x}_2) \frac{1}{r_{12}} \chi_i(\vec{x}_2) d\vec{x}_2 \chi_j(\vec{x}_1). \tag{6.19}
\]

\( \hat{R}_j(\vec{x}_1) \) leads to an exchange of the two electrons in the two spin orbitals \( \chi_i \) and \( \chi_j \). This implies that the integration depends on the value of \( \chi_i \) on all points in space, as \( \chi_i \) is related to \( \vec{x}_2 \), and for these reasons this operator is non-local. In addition, the exchange term resolves the artefact of self-interaction, generated by the Coulomb operator in equation (6.18), in which the result is non-zero for \( i = j \). In reality, there can be no electron-electron repulsion in a one electron system such as a hydrogen atom. \( \hat{R}_j(\vec{x}_1) \) removes this problem by producing an identical value to \( \hat{f}_j(\vec{x}_1) \) when \( i = j \), as shown in Equation 6.20, therefore the self-interaction is exactly cancelled and in this case the result is zero.

\[
\hat{R}_j(\vec{x}_1) = \hat{f}_j(\vec{x}_1) \text{ for } i = j \tag{6.20}
\]

### 6.2.5 The Electron Correlation

The Hartree-Fock method considers the electron-electron repulsion term as an average interaction. In reality, however, the motion of electrons is correlated, meaning that they do not move independently. One direct consequence is that the Hartree-Fock energy, \( E_{HF} \), is overestimated and lies above that of the ground state energy, \( E_0 \). This error between \( E_{HF} \) and \( E_0 \) is defined as the electron-correlation energy, \( E^{HF}_C \):

\[
E^{HF}_C = E_{HF} - E_0 \tag{6.21}
\]

The correlation energy connected to the movement of the individual electrons is called the dynamical electron correlation. This is a short range effect. A second contribution to \( E^{HF}_C \) is the static correlation, where a single ground state Slater determinant is not enough to describe a specific system. This implies that other Slater determinants have comparable energies.
For example, the Hartree-Fock approximation fails to model correctly infinitively separated particles, as more than one Slater determinant must be used. For example in the H₂ molecule, the Slater determinant will describe the wave function as being made up by the following contributions:

\[(H^1 \cdots H^1) + (H^1 \cdots H^1) + (H^{-1} \cdots H^1) + (H^+ \cdots H^{-1}).\]

The first two terms corresponds to the probability of each electron being distributed evenly over both nuclei. In contrast, the third and fourth terms represent the formation of a hydride and a proton. This description provides a reasonable approximation when the system is at its equilibrium geometry, however, when \( r \to \infty \) the ionic contribution should tend to zero which is not the case in the Hartree-Fock approximation. This results in an overestimation of the interaction energy as in reality H₂ dissociates to give two neutral atoms.

### 6.3 Density Functional Theory

#### 6.3.1 The Electron Density

The electron density, \( \rho(\vec{r}) \), is defined in quantum mechanics as the probability of finding any of the \( N \) electrons in a particular volume element. \( \rho(\vec{r}) \) is derived from Equation 6.10 and is read as:

\[
\rho(\vec{r}) = N \int \cdots \int |\Psi(\vec{x}_1, \vec{x}_2, ..., \vec{x}_N)|^2 d\vec{x}_1 d\vec{x}_2 ... d\vec{x}_N. \tag{6.22}
\]

The main advantage is that the electron density only has 3 spatial variables regardless of the size of the system. This is in contrast with wave function theory (WFT) methods in which 3N variables are taken into account for an N-electron system, which therefore increases considerably the size of the calculations.

#### 6.3.2 The Hohenberg-Kohn Theorems

The history of DFT started in 1927 with the Thomas-Fermi model in which the electron density was considered explicitly instead of a wave function. However, modern DFT
has seen its foundation in 1964 with the publication of two theorems of Hohenberg and Kohn that consider a non-degenerate ground state.

The first Hohenberg-Kohn theorem states that the ground state electron density, \( \rho_0 \), determines a unique external potential, \( \hat{V}_{\text{ext}} \), and thus all properties of the system. Therefore, the ground state electron density defines the ground state energy of a system:

\[
E_0[\rho_0] = E_{\text{Ne}}[\rho_0] + T[\rho_0] + E_{\text{ee}}[\rho_0]. \tag{6.23}
\]

Equation 6.23 can be separated into two parts and rewritten as:

\[
E_0[\rho_0] = \int \rho_0(\vec{r})V_{\text{Ne}}d\vec{r} + F_{\text{HK}}[\rho_0]. \tag{6.24}
\]

The first part involves the nuclei and the electron density. This term is therefore system dependent as it depends on the properties of the molecule or system studied. In contrast, the Hohenberg-Kohn functional, \( F_{\text{HK}}[\rho_0] \), is system independent and is described as:

\[
F_{\text{HK}}[\rho_0] = T[\rho_0] + E_{\text{ee}}[\rho_0]. \tag{6.25}
\]

\( F_{\text{HK}}[\rho_0] \) contains the functional for the kinetic energy, \( T[\rho_0] \), and the electron-electron interaction, \( E_{\text{ee}}[\rho_0] \). In addition, the latter is composed of a classical Coulomb part, \( J[\rho_0] \), and a non-classical contribution to the electron-electron interactions, \( E_{\text{ncl}}[\rho_0] \):

\[
E_{\text{ee}}[\rho_0] = \frac{1}{2} \int \int \frac{\rho(\vec{r}_1)\rho(\vec{r}_2)}{r_{12}}d\vec{r}_1d\vec{r}_2 + E_{\text{ncl}}[\rho_0] = J[\rho_0] + E_{\text{ncl}}[\rho_0]. \tag{6.26}
\]

The second Hohenberg-Kohn theorem is related to the variational principle (see Section 6.2.3). This theorem stipulates that the energy calculated from a trial density, \( \tilde{\rho}(\vec{r}) \), will give always an upper bound to the exact ground state energy, \( E_0 \):

\[
E_0 \leq E[\tilde{\rho}] = T[\tilde{\rho}] + E_{\text{Ne}}[\tilde{\rho}] + E_{\text{ee}}[\tilde{\rho}]. \tag{6.27}
\]
In addition, according to Equation 6.27, the minimum is bound to be the exact ground state energy, $E_0$, when $\rho_0$ is the exact ground-state density distribution.

### 6.3.3 The Kohn-Sham Approach

The practical breakthrough of DFT was made by Kohn and Sham in 1965. They realised that a large part of the kinetic energy of electrons could be calculated accurately. This is achieved by using a system of non-interacting electrons built from one-electron functions, in which electrons are uncharged fermions and therefore do not interact with each other via Coulomb repulsion.

The non-interacting reference is constructed from a Slater determinant:

$$
\Phi_S = \frac{1}{\sqrt{N!}} \begin{vmatrix}
\varphi_1(\vec{x}_1) & \varphi_2(\vec{x}_1) & \ldots & \varphi_N(\vec{x}_1) \\
\varphi_1(\vec{x}_2) & \varphi_2(\vec{x}_2) & \ldots & \varphi_N(\vec{x}_2) \\
\vdots & \vdots & \ddots & \vdots \\
\varphi_1(\vec{x}_N) & \varphi_2(\vec{x}_N) & \ldots & \varphi_N(\vec{x}_N)
\end{vmatrix}
$$

(6.28)

where $\varphi_i$ are the Kohn-Sham orbitals.

The large part of the kinetic energy is calculated by using the kinetic operator in Hartree-Fock theory and substituting the spin orbitals, $\chi_i$, by the Kohn-Sham orbitals, $\varphi_i$, to give:

$$
T_s = -\frac{1}{2} \sum_{i=1}^{N} \langle \varphi_i | \nabla^2 | \varphi_i \rangle.
$$

(6.29)

The rest of the kinetic energy can be included in the Hohenberg-Kohn functional $F[p]$:

$$
F[\rho(\vec{r})] = T_s[\rho(\vec{r})] + J[\rho(\vec{r})] + E_{XC}[\rho(\vec{r})]
$$

(6.30)

where the exchange-correlation energy, $E_{XC}$, is defined by

$$
E_{XC}[\rho] \equiv (T[\rho] - T_s[\rho]) + (E_{ee}[\rho] - J[\rho]) = T_c[\rho] + E_{ncl}
$$

(6.31)
in which \( T_c[\rho] \) is the residual part of the true kinetic energy.

At this stage, the best Kohn-Sham orbitals correspond to the lowest energy, expressed as:

\[
\hat{f}^{KS} \varphi_i = \epsilon_i \varphi_i
\]  

(6.32)

where \( \hat{f}^{KS} \) represents the one-electron Kohn-Sham operator, described as:

\[
\hat{f}^{KS} = -\frac{1}{2} \nabla^2 + V_{\text{eff}}(\vec{r}).
\]  

(6.33)

\( V_{\text{eff}}(\vec{r}) \) is the Kohn-Sham effective potential:

\[
V_{\text{eff}}(\vec{r}) = \int \frac{\rho(\vec{r}_2)}{r_{12}} d\vec{r}_2 + V_{XC}(\vec{r}_1) - \sum_{l=1}^{M} \frac{Z_A}{r_{1A}}
\]  

(6.34)

where \( V_{XC} \) is the potential due to the exchange-correlation \( E_{XC} \) and described as:

\[
V_{XC} \equiv \frac{\delta E_{XC}}{\delta \rho}.
\]  

(6.35)

Unfortunately, the exact function for \( E_{XC} \) is unknown and has to be approximated.

6.3.4 Jacob’s Ladder

The concept of the Jacob’s ladder has been introduced by Perdew in order to classify different density functionals.\(^{87}\) Jacob’s ladder leads from earth (Hartree-Fock Theory) to heaven (chemical accuracy), in which users are described as angels in order to climb or descend on it. Jacob’s ladder contains five rungs which represent the hierarchy of density approximations: the local density approximation (LDA), the generalized gradient approximations (GGA), the meta generalized gradient approximation (M-GGA), the hybrid and hybrid meta generalized approximations (H-GGA and MH-GGA, respectively) and finally the fully non-local description.
The local density approximation (LDA) provides a way of modelling the exchange-correlation energy, $E_{XC}$. LDA is based on the uniform electron gas (UEG) of density:

$$\rho = \frac{N}{V}$$

obtained when $N$ and $V$ approach infinity, where $N$ represents a set of uniformly distributed electrons and $V$ is the volume of the system. In addition, the UEG is set against a uniformly positively charged background potential, to neutralise the system and this is similar to an idealised metal, often called *jellium*.

This model is useful as both the exact exchange and correlation energies can be known accurately. In the local density approximation, $E_{XC}$ is expressed as:

$$E_{XC}^{LDA}[\rho] = \int \rho(\vec{r})\varepsilon_{XC}(\rho(\vec{r}))d\vec{r}$$

(6.37)

where $\varepsilon_{XC}(\rho(\vec{r}))$ represents the exchange-correlation energy per particle of a UEG of density $\rho(\vec{r})$. In addition, $\varepsilon_{XC}(\rho(\vec{r}))$ can be separated in two terms for the exchange and correlation contributions:

$$\varepsilon_{XC}(\rho(\vec{r})) = \varepsilon_{X}(\rho(\vec{r})) + \varepsilon_{C}(\rho(\vec{r})).$$

(6.38)

In addition, the exchange part, $\varepsilon_{X}(\rho(\vec{r}))$, is described exactly as:

$$\varepsilon_{X}(\rho(\vec{r})) = -\frac{3}{4}\left(\frac{3\rho(\vec{r})}{\pi}\right)^{\frac{1}{3}}.$$ 

(6.39)

In contrast, there is no known exact equation for the correlation energy, $\varepsilon_{C}(\rho(\vec{r}))$, however, values can be obtained based on fitting data from Monte-Carlo simulations for a UEG.
One major discrepancy with LDA is that it overestimates atomisation energies, resulting in overbinding.

(ii) The Generalized Gradient Approximation

Generalized gradient approximation (GGA) is one way to improve LDA by using not only the density $\rho(\vec{r})$ at a particular point $\vec{r}$, but by supplementing the density with the gradient of the charge density $\nabla \rho(\vec{r})$:

$$E_{XG}^{GGA}[\rho_\alpha, \rho_\beta] = \int f(\rho_\alpha, \rho_\beta, \nabla \rho_\alpha, \nabla \rho_\beta) d\vec{r}. \quad (6.40)$$

The exchange and correlation contributions of $E_{XG}^{GGA}$ can be, as well, separated:

$$E_{XG}^{GGA} = E_{XG}^{LDA} + E_{C}^{GGA} \quad (6.41)$$

where the exchange part, $E_{XG}^{GGA}$, is equal to:

$$E_{XG}^{GGA} = E_{XG}^{LDA} - \sum \int F(s_\sigma) \rho_\sigma^{4/3}(\vec{r}) \ d\vec{r}. \quad (6.42)$$

The term $s_\sigma$ corresponds to the local inhomogeneity parameter and described as:

$$s_\sigma(\vec{r}) = \frac{\left|\nabla \rho_\sigma(\vec{r})\right|}{\rho_\sigma^{4/3}(\vec{r})}. \quad (6.43)$$

There are several types of GGA exchange functionals. The first such functional has been published by Becke$^{71}$ in 1988 and is commonly abbreviated as B:

$$F^{B} = \frac{\beta s_\sigma^2}{1 + 6\beta s_\sigma \sin^{-1} s_\sigma}. \quad (6.44)$$

where $\beta$ is an empirical parameter (0.0042) which has been fitted to the exactly known exchange energies of the six nobles gases, He to Rn.
A second class of GGA exchange functionals have been developed with no empirical parameters. Instead, a rational function of the reduced density gradient is used. Examples of this approach include Becke, 1986 (B86), Perdew, 1986 (P86), Lacks and Gordon, 1993 (LG) and Perdew, Burke and Ernzerhof, 1996 (PBE).

There are as well several correlation functionals, such as the 1986 Perdew exchange functional (P86) which contains an empirical parameter fitted to the correlation energy of the neon atom. This correlation functional was then developed by Perdew and Wang in 1991 (PW91) which is free of any empirical parameters. In contrast, Lee, Yang and Parr created in 1988 a correlation functional (LYP) which is not based on the uniform electron gas but derived from a correlated wave function that reproduces the correlation energy for the helium atom. Therefore, this correlation functional contains one empirical parameter.

The exchange and correlation functionals can be paired together; for example BP86 includes the gradient corrected exchange functional of Becke and the correlation functional of Perdew.

(iii) Meta-GGA Functionals

The meta-GGA functionals are another improvement of the GGA functionals. They employ the kinetic energy density, $\tau_\sigma$, and the second derivative of the electron density (i.e. the Laplacian), in addition to the reduced gradient density. The kinetic energy density is described as:

$$\tau_\sigma = \sum_{\text{occ.}} \frac{1}{2} |\nabla \psi_i|^2. \quad (6.45)$$

One example of a meta-GGA is TPSS which employs the exchange and the $\tau$-dependent gradient-corrected functional of Tao, Perdew, Staroveroz and Scuseria.
(iv) Hybrid-GGA and Meta-Hybrid-GGA Functionals

The first idea of hybrid functionals was to compute an exact value of the Hartree-Fock exchange term, $E_X^{HF}$ and use the Kohn-Sham orbitals rather than Hartree-Fock orbitals:

$$E_{XC} = E_X^{HF} + E_C^{KS}$$  \hspace{1cm} (6.46)

However, this did not give the expected improvement and so instead, a part of the exchange and correlation contributions calculated using LDA was added. The first to use this approach was Becke\textsuperscript{95} in 1993 with the B3PW91\textsuperscript{92,95} functional:

$$E_{XC}^{B3PW91} = E_{XC}^{LSD} + a(E_{XC}^{\lambda=0} - E_{XC}^{LSD}) + bE_X^B + cE_C^{PW91}$$  \hspace{1cm} (6.47)

where a, b and c are semi-empirical parameters, used to determine the weight of each contribution and fitted to reproduce atomization and ionization energies, proton affinities and some total energies.

The most popular hybrid functional is B3LYP\textsuperscript{88,93} which was suggested by Stephen et al.\textsuperscript{96} and described as:

$$E_{XC}^{B3LYP} = (1 - a)E_{X}^{LSD} + aE_{XC}^{\lambda=0} + bE_X^{B88} + cE_C^{LYP} + (1 - c)E_C^{LSD}$$  \hspace{1cm} (6.48)

The meta-hybrid-GGA functionals are based on meta-GGA functionals and contain a percentage of exact exchange. TPSSh\textsuperscript{94} is one example as well as the highly parameterized Truhlar M06 suite of functionals (M06, M06-L, M06-2X and M06-HF).\textsuperscript{97} M06 has 27% exact exchange while in M06-2X this doubles to 54% and M06-HF has 100 % exact exchange. M06-L is actually a pure functional in which no exact exchange is computed, therefore this functional can be considered as a meta-GGA rather than a meta-hybrid-GGA.

(v) Double Hybrid Functionals

A final type of functionals has recently emerged called the double hybrid functionals. One of them has been introduced by Grimme (B2-PLYP)\textsuperscript{98} which includes a part of
Becke exchange (B) and the correlation reported by Lee, Yang and Parr (LYP) with a percentage of exact exchange and a contribution from MP2:

$$E_{XC}^{B2-PLYP} = (1 - a_x)E_X^B + a_xE_H^F + bE_C^{LYP} + cE_C^{MP2}$$  \hspace{1cm} (6.49)

The double hybrid functionals are, in a way, considered as the fifth rung of Jacob’s Ladder.

### 6.3.5 Dispersion-Corrected Functional

One of the biggest challenges in density functional theory is to account for weak non-covalent interactions or dispersion forces. The M06 functional has been parameterized (36 parameters) to consider non-covalent interactions, however, a new type of dispersion-corrected functional has also been recently developed. These are known as Grimme’s DFT-D functionals and use a semi-empirical dispersion correction.\(^99\) DFT-D functionals compute energies as:

$$E_{DFT-D} = E_{DFT} + E_{disp}$$  \hspace{1cm} (6.50)

where \(E_{DFT}\) is the DFT energy for a specific functional (e.g. BP86), and \(E_{disp}\) is semi-empirical dispersion correction given by:

$$E_{disp} = -s_6 \sum_{i=1}^{N_{at}-1} \sum_{j=i+1}^{N_{at}} \frac{C_{6}^{ij}}{R_{ij}^{6}} f_{dmp}(R_{ij})$$  \hspace{1cm} (6.51)

where, \(N_{at}\) is the number of atoms in the system, \(s_6\) is the global scaling factor, \(C_{6}^{ij}\) corresponds to the dispersion coefficient for atom pairs \(ij\) and \(R_{ij}\) is the interatomic distance. Also, \(f_{dmp}\) represents the damping function, used to avoid near-singularities for small \(R_{ij}\).

### 6.4 Basis Sets

Basis sets are employed to provide a number of predefined basis functions which are then used to describe the orbitals of an atom or molecule mathematically. The accuracy
of wave function calculations is maximised for an infinite number of basis functions, however, the calculation time increases rapidly and therefore becomes unpractical. On the other hand, in the Kohn-Sham scheme, the orbitals are used to construct the density:

$$\rho(\vec{r}) = \sum_{i=1}^{N} |\varphi_i(\vec{r})|^2$$  \hspace{1cm} (6.52)

and therefore the basis set requirements in Kohn-Sham calculations are less strong.

There are two types of basis functions commonly used for molecular calculations: Slater-type orbitals (STOs) and Gaussian-type orbitals (GTOs):

STO:

$$\chi_{\zeta,n,l,m}(r, \theta, \varphi) = NY_{l,m}(\Theta, \varphi) \ r^{n-1} \ exp[-\zeta r]$$  \hspace{1cm} (6.53)

GTO:

$$\chi_{\zeta,n,l,m}(r, \theta, \varphi) = NY_{l,m}(\Theta, \varphi) \ r^{(2n-2-l)} \ exp[-\zeta r^2]$$  \hspace{1cm} (6.54)

where N is a normalisation constant, while r, \theta, and \varphi are spherical coordinates. In addition, Y_{l,m} corresponds to the angular momentum and n, l, and m are quantum numbers. The GTOs depend on r^2 which makes them less accurate than the STOs. Indeed, at the nucleus (r = 0), the GTO has a slope that goes to zero and they also fail to model the wave function well as r \to \infty. However, this model can be improved by using linear combination of several primitive GTOs to model each STO.

The choice of the basis set is key as it needs to strike a balance between accuracy and the time of calculation. The minimal basis set only contains the number of basis functions which is required to accommodate all the electrons of the atom in the ground state. The most common minimal basis set is STO-3G in which 3 primitive GTOs are contracted to produce one STO.

These small basis sets can be improved by increasing the number of basis functions. For example, double-zeta basis sets can be used in which the number of basis functions will be double to describe each atomic orbital. These include the 3-21G and 6-31G basis sets developed by Pople and co-workers.\(^{76a}\) In 3-21G, the core electrons are represented by a contraction of 3 GTOs, while the valence electrons are described by 2
basis functions made up of 2 GTOs and 1 GTO, respectively. In 6-31G, the difference is that the core electrons are contracted by 6 GTOs, while the valence orbitals are contracted as 3 GTOs and 1 GTO.

The accuracy of the calculations can be further improved by addition of polarisation and diffuse functions. For example, 6-31G** adds d-orbital polarisation functions to the heavy atoms (e.g. carbon atoms) and p-orbital polarisation functions for light atoms (i.e. hydrogen and helium atoms). The use of diffuse basis sets (e.g. 6-31+G) will add a set of orbital functions with small exponents which decay slowly as the distance from the nucleus increases.

Finally, when the system contains atoms from the third row onwards, effective core potentials (ECPs) are generally employed to represent the electron core shells rather than modelling the core electrons explicitly. A set of associated basis sets is also used to model the valence electrons. In addition, ECPs can be designed to treat implicitly the scalar-relativistic effects for heavy atoms.

6.5 Benchmarking of Different Basis Sets and Exchange-Correlation Methods

Basis sets and DFT functionals were benchmarked for the rate-limiting transition states and key species involved in the reaction of C$_6$F$_5$H at [Rh(SiMe$_3$)(PMe$_3$)$_3$] (1$_{SiMe3}$, see Chapter 3). All reported energies are relative to 1$_{SiMe3}$ plus C$_6$F$_5$H.

The basis sets were tested by using the geometries optimised with the BP86 functional and 6-31G** basis sets for all atoms, except Rh, Si and P in which SDD pseudo-potentials and basis sets were employed. From these optimised structures, single point calculations were performed by using triple-zeta polarised (6-311G**), diffuse double-zeta polarised (6-31++G**) and diffuse triple-zeta polarised (6-311++G**) basis sets. The results are summarised in Table 6.1. As seen in Chapter 3, direct C–H activation is preferred over C–F activation at 1$_{SiMe3}$. Using 6-31G** basis sets, calculations showed indeed that C–H activation is more accessible by 3.5 kcal/mol, with 6-311G** by 3.2 kcal/mol, with 6-31++G** by 5.1 kcal/mol and finally with 6-311++G** basis sets by 4.4 kcal/mol. This implies that there is a relatively small energy difference by using richer basis sets for this pathway and therefore the use of 6-31G** is sufficient. In contrast, C–F activation was found to be kinetically and thermodynamically more
accessible at the 3-coordinate \textit{trans}-[Rh(SiMe_3)(PMe_3)_2] (\textit{trans}-1_{SiMe3}). C–F activation is lower than C–H activation by 4.0 kcal/mol (6-31G**), 3.4 kcal/mol (6-311G**), 1.4 kcal/mol (6-31++G**) and 1.6 kcal/mol (6-311G**), respectively. In this case, the same behaviour is seen and the key point is that C–F activation remains kinetically more accessible. In addition, phosphine dissociation to form \textit{trans}-1_{SiMe3} is computed to similar with all basis sets. Finally, the C–F activation product is much more favourable thermodynamically with relative energies of -53.1 kcal/mol, -51.5 kcal/mol, -52.5 kcal/mol and -50.9 kcal/mol, respectively. This is consistent with the experimental selectivity and again the use of 6-31G** basis sets represents properly this feature.
Table 6.1: Single point energies (kcal/mol) using BP86 functional with double-zeta polarised (6-31G**), triple-zeta polarised (6-311G**), diffuse double-zeta polarised (6-31++G**) and diffuse triple-zeta polarised (6-311++G**) basis sets.

<table>
<thead>
<tr>
<th></th>
<th>6-31G**</th>
<th>6-311G**</th>
<th>6-31++G**</th>
<th>6-311++G**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C–F and C–H activation at $1_{\text{SiMe}_3}$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+16.3</td>
<td>+18.1</td>
<td>+23.6</td>
<td>+22.3</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+12.8</td>
<td>+14.9</td>
<td>+18.5</td>
<td>+17.9</td>
</tr>
<tr>
<td><strong>Phosphine dissociation at $1_{\text{SiMe}_3}$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS</td>
<td>+17.9</td>
<td>+18.0</td>
<td>+17.9</td>
<td>+18.0</td>
</tr>
<tr>
<td>$\text{trans-[Rh(SiMe}_3)(\text{PMe}_3)_2]$</td>
<td>+17.9</td>
<td>+17.4</td>
<td>+17.3</td>
<td>+17.2</td>
</tr>
<tr>
<td><strong>C–F and C–H activation at $\text{trans-}1_{\text{SiMe}_3}$</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+12.1</td>
<td>+14.4</td>
<td>+19.5</td>
<td>+18.7</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+16.1</td>
<td>+17.8</td>
<td>+20.9</td>
<td>+20.3</td>
</tr>
<tr>
<td><strong>Final products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$[\text{Rh(4-C}_6\text{F}_4\text{H})(\text{PMe}_3)_3]$</td>
<td>-60.6</td>
<td>-58.4</td>
<td>-56.3</td>
<td>-55.6</td>
</tr>
<tr>
<td>$[\text{Rh(C}_6\text{F}_5)(\text{PMe}_3)_3]$</td>
<td>-7.5</td>
<td>-6.9</td>
<td>-3.8</td>
<td>-4.7</td>
</tr>
</tbody>
</table>
DFT functionals were as well benchmarked on the same species and the results are summarised in Tables 6.2 and 6.3. Before comparing the different functionals, it should be mentioned that no transition state for C–F activation of C₆F₅H at I₃SiMe₃ to form the mer'-isomer has been located using the BLYP functional. In all the cases, one phosphine ligand was fully dissociated (< 3.5 Å).

In general, the idea that C–F activation of C₆F₅H occurs at the three-coordinate trans-1₃SiMe₃ is confirmed. In the case of BLYP and B3LYP, phosphine dissociation is facile with computed enthalpies of +10.3 kcal/mol and +12.1 kcal/mol. For the remaining functionals this step can vary between +16.8 kcal/mol (B3PW91) to +18.1 kcal/mol (B3P86). TPSS and TPSSh show that phosphine dissociation is barrierless as the 3-coordinate trans-1₃SiMe₃ is slightly less stable. This may come from a basis set superposition error (BSSE) as in the transition state, the two fragments, [Rh(SiMe₃)(PMe₃)₂] and PMe₃ are computed together. From trans-1₃SiMe₃, most of the functionals confirm that C–F activation is kinetically more accessible. Only B3P86 shows that C–F and C–H activation are competitive, with computed energies located at +17.9 kcal/mol and +17.0 kcal/mol, respectively, while B3PW91 shows that C–H activation is more accessible by 1.9 kcal/mol. On the other hand, as described in Chapter 3, C–H activation at I₃SiMe₃ is preferred over both C–F activation and C–H activation at trans-1₃SiMe₃ as the initial phosphine dissociation is higher in energy. This hierarchy is respected with all the functionals except BLYP and B3LYP, which show that phosphine dissociation and subsequent C–F activation are more favourable than C–H activation at I₃SiMe₃.
Table 6.2: Enthalpies energies (kcal/mol) using a range of GGA (BP86, BLYP), hybrid GGA (B3P86, B3LYP, B3PW91), meta GGA (TPSS) and hybrid meta GGA (TPSSh) functionals with double-zeta polarised (6-31G**) basis sets.

<table>
<thead>
<tr>
<th></th>
<th>BP86</th>
<th>BLYP</th>
<th>B3P86</th>
<th>B3LYP</th>
<th>B3PW91</th>
<th>TPSS</th>
<th>TPSSh</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C–F and C–H activation at (I_{\text{SiMe3}})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+17.8</td>
<td>–</td>
<td>+20.0</td>
<td>+20.9</td>
<td>+25.3</td>
<td>+13.0</td>
<td>+15.9</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+12.1</td>
<td>+15.6</td>
<td>+12.1</td>
<td>+16.7</td>
<td>+16.0</td>
<td>+9.8</td>
<td>+11.1</td>
</tr>
<tr>
<td><strong>Phosphine dissociation at (I_{\text{SiMe3}})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS</td>
<td>+17.0</td>
<td>+10.3</td>
<td>+18.1</td>
<td>+12.1</td>
<td>+16.8</td>
<td>+17.2</td>
<td>+17.5</td>
</tr>
<tr>
<td>(\text{trans-}[\text{Rh(SiMe}_3\text{)(PMe}_3\text{)}_2\text{]})</td>
<td>+16.6</td>
<td>+9.0</td>
<td>+18.5</td>
<td>+11.4</td>
<td>+15.7</td>
<td>+17.8</td>
<td>+18.1</td>
</tr>
<tr>
<td><strong>C–F and C–H activation at (\text{trans-}I_{\text{SiMe3}})</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+10.9</td>
<td>+3.6</td>
<td>+17.9</td>
<td>+12.0</td>
<td>+18.8</td>
<td>+8.5</td>
<td>+12.4</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+13.9</td>
<td>+10.0</td>
<td>+17.0</td>
<td>+14.5</td>
<td>+16.9</td>
<td>+13.2</td>
<td>+15.2</td>
</tr>
<tr>
<td><strong>Final products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>([\text{Rh(4-C}_6\text{F}_4\text{H})(\text{PMe}_3\text{)}_3])]</td>
<td>-59.4</td>
<td>-65.7</td>
<td>-64.4</td>
<td>-69.2</td>
<td>-63.5</td>
<td>-63.7</td>
<td>-64.3</td>
</tr>
<tr>
<td>([\text{Rh(4-C}_6\text{F}_2\text{)(PMe}_3\text{)}_3])]</td>
<td>-8.2</td>
<td>-12.2</td>
<td>-10.3</td>
<td>-13.2</td>
<td>-9.8</td>
<td>-12.1</td>
<td>-12.4</td>
</tr>
</tbody>
</table>
Computed free energies are consistent with the experimental selectivity (see Table 6.3). First of all, the phosphine dissociation pathway becomes more favourable and in most cases subsequent C–F activation is kinetically more accessible than C–H activation. This is true with BP86, BLYP, B3LYP, TPSS and TPSSh functionals. B3P86 and B3PW91 functionals show the C–H activation is competitive. However, as mentioned in Chapter 3, C–H activation can be reversible and therefore the more favourable product, in this case through C–F activation, will be observed.

In conclusion, the use of different functionals does not change the outcome of the reaction in which the C–F activation product is observed experimentally. Indeed, all functionals confirm that this is the most stable thermodynamic product. Functionals such as BP86, BLYP, B3LYP, TPSS and TPSSh show that computed free energies for C–F activation are kinetically and thermodynamically more accessible while B3P86 and B3PW91 imply that C–F activation and C–H activation of C₆F₅H are competitive and thus the most stable product will be formed, [Rh(4-C₆F₄H)(PMe₃)₃], in agreement with the experiment.
Table 6.3: Free energies (kcal/mol) using a range of GGA (BP86, BLYP), hybrid GGA (B3P86, B3LYP, B3PW91), meta GGA (TPSS) and hybrid meta GGA (TPSSh) functionals with double-zeta polarised (6-31G**) basis sets.

<table>
<thead>
<tr>
<th></th>
<th>BP86</th>
<th>BLYP</th>
<th>B3P86</th>
<th>B3LYP</th>
<th>B3PW91</th>
<th>TPSS</th>
<th>TPSSh</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C–F and C–H activation at ¹SiMe₃</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+33.9</td>
<td>–</td>
<td>+36.2</td>
<td>+36.1</td>
<td>+41.4</td>
<td>+28.6</td>
<td>+31.7</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+27.3</td>
<td>+30.1</td>
<td>+26.9</td>
<td>+31.4</td>
<td>+31.0</td>
<td>+24.5</td>
<td>+25.9</td>
</tr>
<tr>
<td><strong>Phosphine dissociation at ¹SiMe₃</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TS</td>
<td>+13.2</td>
<td>+7.1</td>
<td>+13.8</td>
<td>+9.1</td>
<td>+13.2</td>
<td>+13.2</td>
<td>+13.8</td>
</tr>
<tr>
<td>trans-[Rh(SiMe₃)(PMe₃)₂]</td>
<td>+2.3</td>
<td>-5.0</td>
<td>+4.8</td>
<td>-2.5</td>
<td>+2.0</td>
<td>+4.3</td>
<td>+4.6</td>
</tr>
<tr>
<td><strong>C–F and C–H activation at trans-¹SiMe₃</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C–F Activation</td>
<td>+12.4</td>
<td>+4.9</td>
<td>+19.0</td>
<td>+13.3</td>
<td>+20.2</td>
<td>+9.8</td>
<td>+13.7</td>
</tr>
<tr>
<td>C–H Activation</td>
<td>+15.3</td>
<td>+10.1</td>
<td>+16.9</td>
<td>+14.6</td>
<td>+17.0</td>
<td>+13.3</td>
<td>+15.2</td>
</tr>
<tr>
<td><strong>Final products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[Rh(4-C₆F₄H)(PMe₃)₃]</td>
<td>-59.0</td>
<td>-66.0</td>
<td>-65.4</td>
<td>-69.7</td>
<td>-64.3</td>
<td>-64.0</td>
<td>-64.9</td>
</tr>
<tr>
<td>[Rh(C₆F₂)(PMe₃)₃]</td>
<td>-7.7</td>
<td>-12.1</td>
<td>-10.9</td>
<td>-13.4</td>
<td>-10.1</td>
<td>-12.3</td>
<td>-13.2</td>
</tr>
</tbody>
</table>
**Overall Conclusion**

Density functional theory calculations have been carried out in order to understand the selective C–F activation of fluoroaromatics at rhodium and ruthenium. Novel mechanisms such as silyl- and boryl-assisted C–F activation have been defined. This last idea could be a further step in the synthesis of catalysts containing atoms that may become hypervalent (e.g. silicon) or Lewis acidic ligands (e.g. BR₂) to activate inert C–F bonds of fluoroorganic molecules.

In addition, a novel nucleophilic attack of one hydride ligand at the fluoroarene moiety has been calculated. This type of mechanism could be taken into account to explain the selectivity for C–F activation of other systems previously described in the literature.¹⁵b,¹⁵c,⁴⁰,⁴⁹-⁵⁰
References

(1) (a) Moissan, H. C. R. Acad. Sci. 1886, 102, 1534; (b) Moissan, H. C. R. Acad. Sci. 1886, 103, 202; (c) Moissan, H. C. R. Acad. Sci. 1886, 103, 256.


(43) Lindup, R. J.; Marder, T. B.; Perutz, R. N.; Whitwood, A. C. Chem. Commun. 2007, 3664.
(44) Young, R. J.; Grushin, V. V. *Organometallics* 1999, 18, 294.
(45) Yang, H.; Gao, H.; Angelici, R. J. *Organometallics* 1999, 18, 2285.


Aspects of the work in this thesis have been published and are reproduced here on the following pages.
Transition-metal–boryl complexes are key intermediates in catalytic hydromediation and borylation reactions and find applications in boron-based materials.[1] Rhodium complexes can be applied in the rhodium-mediated hydromediation or dehydrogenative borylation reactions of olefins or even in the borylation of alkanes.[2,3] Rhodium and iridium boronates also play a crucial role in the borylation of arenes to give, for instance, Bpin derivatives.[4,5] Thus, it has been reported that rhodium complexes with boryl and phosphine ligands are intermediates in the catalytic borylation reactions of benzene, toluene, para-xylene, and mesitylene with HBpin (HBpin = 4,4,5,5-tetramethyl-1,3,2-dioxaborolane, pinacolborane).[3] Although it has been conceivably that the C–H activation step occurs at the 14-electron species [Rh(Bpin)(PPr3)2], density functional theory (DFT) calculations indicate that benzylic activation takes place at [Rh(H)(PPr3)].[4b] In this case, Rh(I)–Rh(V) cycles have been suggested, whereas iridium-based catalysts may operate through Ir(III)–Ir(V) cycles.[4,5]

Examples of C–F bond functionalization, i.e. where fluorine is replaced by a new group to access higher-value fluorinated compounds, are very limited,[6,7] and most examples involve hydrodefluorination.[6] Whereas rhodium complexes are almost without any precedent in the literature,[1,9] although [Rh(Bcat)(PMe3)4] has been synthesized by Marder and co-workers from the treatment of [Rh(Me)- (PMe3)4] with Bcat (Bcat = B[1,2-O,C6H4]).[10]

Herein, we report the identification of a unique 16-electron rhodium(I) species, [Rh(Bpin)(PEt3)3] (3). This complex is highly reactive and can effect the C–H activation of benzene, as well as the stoichiometric C–F activation and catalytic C–F borylation of fluorinated substrates.

We reasoned that a phenoxo complex might be an ideal starting compound for the formation of a rhodium(I)–boryl complex, partly because of the high stability of a boron-oxygen bond.[11,12] Treatment of the chloro complex [Rh(Cl)(PEt3)3] with NaOPh gave the rhodium phenoxide [Rh(OPh)(PEt3)3] (2; Scheme 1). The 1H and 31P NMR spectra of complex 2 showed the expected splitting patterns: the phosphorus–rhodium coupling constants in the 31P NMR spectrum of 169 and 142 Hz are characteristic of a rhodium(I) compound.[13] Reaction of 2 in benzene with excess B2pin2 (3 equiv) gave [Rh(Bpin)(PEt3)3] (3) after 16 hours, along with PhOBpin (Scheme 1). Moreover, we found that 3 can be generated in a comparable reaction, starting from the fluoro compound [Rh(F)(PEt3)3] (4).[14] The fluoroborane FBpin that was also formed can be removed in vacuo. Note that boryl complex 3 does not react with another equivalent of Bpin2 to give a RhIII complex that would be comparable to fac-[Rh(Bcat)(PMe3)4].[10]

Complex 3 was only characterized in solution: the 31P NMR spectrum at room temperature revealed only one broad signal at δ = 15.1 ppm. This indicates a dynamic behavior, which involves the exchange of the phosphine...
ligands, similar to the fluxionality which has been observed for [Rh(H)(PET$_3$)$_3$] (5).[13] Variable-temperature $^{31}$P NMR analysis shows that the free phosphine has no influence on the dynamic behavior, which suggests that the process is intramolecular. The $^{31}$P NMR spectrum at 203 K exhibits a signal at $\delta = 20.5$ ppm for the phosphine atoms that are in a mutually trans position. The resonance features characteristic couplings for a rhodium(I) compound, with doublet couplings to rhodium and to phosphorus of 166 Hz and 30 Hz, respectively.[12,13] A second resonance at $\delta = 9.1$ ppm, with a coupling to rhodium of 110 Hz, can be assigned to the phosphorus ligand that is in the position trans to the Bpin group. We could not resolve any couplings to the $^{11}$B nucleus. The $^{11}$B NMR spectrum of 3 shows one broad signal at $\delta = 46.5$ ppm ($\Delta v_p = 338$ Hz); this chemical shift is typical for a rhodium derivative of a 1,3,2-dioxaborolane.[10]

NMR spectroscopic investigations revealed that 3 is not very stable in benzene and converts slowly into the hydride [Rh(H)(PET$_3$)$_3$] (5) at room temperature, with concomitant formation of PhBpin (Scheme 2). In the presence of B$_2$pin$_2$, complex 5 reacts further to give the Rh$^{III}$ complex cis-fac-[Rh(H)(Bpin)$_2$(PET$_3$)$_3$] (6).

These observations indicate that C–H activation of benzene may occur at [Rh(Bpin)(PET$_3$)$_3$] (3), possibly via a Rh$^{II}$ intermediate, [Rh(H)(Ph)(Bpin)(PET$_3$)$_3$], although this could not be detected.[13] Reaction of 3 in C$_6$D$_6$ furnished (D$_5$C$_6$)Bpin and [Rh(H)(PET$_3$)$_3$] (5). $^1$H NMR EXSY spectra (400 MHz; EXSY = exchange spectroscopy) of 5 confirmed exchange between the hydrogen atom that is bound to the metal and the CH$_2$ and CH$_3$ hydrogen atoms of the cis phosphine ligands. It appears that intramolecular cyclometalation processes are occurring, which result in the transfer of deuterium atoms from being bound to the metal onto the phosphine alkyl groups.[17]

We have no indication for the generation of HBpin. It seems that reductive elimination from 6 to afford rhodium(I)–boryl complex 3 does not occur under the reaction conditions. This observation might explain why it was not possible to develop a catalytic process for the generation of PhBpin from benzene and B$_2$pin$_2$. Complex 6 can also be synthesized independently, starting from [Rh(Bpin)(PET$_3$)$_3$] (3; Scheme 2). A solution of 3 was treated with HBpin to give 6 plus considerable amounts of cis-fac-[Rh(H)$_2$(Bpin)(PET$_3$)$_3$] (7). The formation of 7 can be explained by the reductive elimination of B$_2$pin, from 6 to furnish the hydrido complex [Rh(H)(PET$_3$)$_3$] (5). It has been previously reported that treatment of 5 with HBpin affords 7.[8]

A signal at $\delta = -10.18$ ppm in the $^1$H NMR spectrum of 6 confirms the presence of the hydrid ligand. The $^{31}$P NMR spectrum shows rhodium–phosphorus coupling constants of 98 Hz and 75 Hz for the doublet of triplets at $\delta = 8.1$ ppm and the doublet of doublets at $\delta = 2.3$ ppm, respectively, reveal the presence of a Rh$^{III}$ compound.[12] The relatively small coupling constant of 75 Hz suggests that the two equivalent phosphine ligands are located trans to the boryl ligands. This arrangement is compatible with a fac configuration for 6; for complex 7, $J$(Rh,P$^\text{III}$) $\approx 78$ Hz for the phosphorus atom in the position trans to the boryl ligand has been observed.[8] The $^{11}$B NMR spectrum of 6 shows one broad signal at $\delta = 47.1$ ppm ($\Delta v_p = 633$ Hz), which confirms the presence of the boryl ligands.[8]

To avoid activation of the aromatic C–H bonds on 3, the phenoxy complex [Rh(OPh)(PET$_3$)$_3$] (2) and the fluoro compound [Rh(F)(PET$_3$)$_3$] (4) were treated stoichiometrically with B$_2$pin$_2$ in Me$_3$SiSiMe$_3$ as a solvent. Under these reaction conditions, boryl complex 3 was observed as the sole product (Scheme 1). The stability of 3 in Me$_3$SiSiMe$_3$ enabled us to perform further studies on the reactivity of 3 towards the activation of carbon–fluorine bonds.[8]

Treatment of 3 with perfluoropropene in Me$_3$SiSiMe$_3$ gave the propenyl compound [Rh(Z)(CF$_3$)=CF(CF$_3$)](PET$_3$)$_3$ (8a) and the isomeric complex [Rh(C=C$_3$)(CF$_3$)](PET$_3$)$_3$ (8b) in a ratio of 2:7 (Scheme 3). Therefore, compound 3 might indeed be an intermediate in the conversion of hexafluoropropene and HBpin into Bpin derivatives of trifluoropropane, as has been previously proposed.[9] The formation of complex 8a has been previously reported from the treatment of [Rh(H)(PET$_3$)$_3$] (5) with perfluoropropene.[14] The NMR spectra of 8b show the expected splitting pattern with a geminal fluorine–fluorine coupling constant of 61 Hz in the $^{19}$F NMR spectrum.[10]

Fluorinated pyridines are also interesting substrates for investigating C–F activation reactions with boryl complex 3.[19–23] For instance, the reaction of C$_5$NF$_5$ with [Rh(H)-(PET$_3$)$_3$] (5) gives [Rh(4-C$_5$NF$_5$)(PET$_3$)$_3$] (9a) and HF,[28] whilst reaction with [Rh(SiPh$_3$)(PMe$_3$)$_3$] revealed the isomeric compounds [Rh(2-C$_5$NF$_5$)(PMe$_3$)$_3$] and [Rh(4-C$_5$NF$_5$)-(PMe$_3$)$_3$] in a 3:1 ratio, along with $^{31}$P$^{19}$F spectra. When 2,3,5,6-tetrafluoropyridine was used as the substrate, a delicate balance between C–H and C–F activation was observed.[19,23] Thus, reaction with [Rh(H)(PET$_3$)$_3$] (5) furnished 9a by C–H activation,[19] whereas reaction with [Rh(SiPh$_3$)-(PMe$_3$)$_3$] gave a mixture of products that were derived from activation at the 2-(C–F) and 4-(C–H) positions.[19]

Reaction of 3 with 2,3,5,6-tetrafluoropyridine gave the C–H activation product [Rh(4-C$_5$NF$_5$)(PET$_3$)$_3$] (9a) and HBpin, with no observed C–F bond cleavage (Scheme 3).
However, treatment of in situ generated 3 with pentafluoropyridine selectively gave the C–F activation product [Rh(2-C,F5NF4)(PEt3)3] (9b), with FBpin by-product at room temperature. Thus, C–F activation at the boryl species 3 occurs exclusively at the 2-position of the fluorinated substrate. The 31P NMR spectrum of 9b showed a doublet of doublets at δ = 16.0 ppm and a resonance at δ = 19.7 ppm, with a complex splitting pattern arising from coupling with phosphorus, rhodium, and fluorine atoms. The four signals at δ = −87.7, −125.0, −155.4, and −175.9 ppm in the 19F NMR spectrum indicate the presence of the pyridyl ligand, with the metal at the 2-position.\[6,21,24\] Therefore, we wanted to investigate this unusual selectivity in the reaction of 3 with pentafluoropyridine.

Recently, a novel mechanism for aromatic C–F bond activation has been characterized at electron-rich iridium and platinum metal centers.\[25\] This process involves the addition of a C–F bond across a [M–PR3] moiety via a four-centered transition state, which can account for the selective activation at the 2-position of pentafluoropyridine and [Ni(PEt3)3] fragments.\[25,28\] Key to such phosphate-assisted processes is the Lewis acidity of the accepting phosphine ligand. By analogy, we reasoned that an equivalent boryl-assisted process may be possible for complex 3, wherein the formally sp3-hybridized boron atom may be a particularly effective Lewis acid.

The mechanism and selectivity of the reaction of pentafluoropyridine with 3 were investigated using DFT calculations on model complex [Rh(Bpin)(PMe3)3] (3').\[27\] Both concerted oxidative addition and boryl-assisted processes were considered, and the lowest energy C–F activation transition states for reaction at the 2- and 4-positions are shown schematically in Figure 1.

The most accessible oxidative addition process corresponds to activation at the 4-position (ΔE° = +24.2 kJ mol⁻¹ cf. +46.9 kJ mol⁻¹ at the 2-position). These processes give stable mer-[Rh(Bpin)(F)(4-C,F5NF4)(PMe3)3] and mer-[Rh(Bpin)(F)(2-C,F5NF4)(PMe3)3] complexes, in which the fluoride ligand is trans to the Bpin group. However, subsequent isomerization and reductive elimination of FBpin to give [Rh(4- or 2-C,F5NF4)(PMe3)3] (9a or 9b) is facile (see the Supporting Information). Therefore, oxidative addition of the C–F bond is the overall rate-determining step and, most importantly, indicates a kinetic preference for reaction at the 4-position, which is at odds with experimental observations.

In contrast, boryl-assisted C–F activation clearly favors the 2-position (ΔE° = +17.2 kJ mol⁻¹ cf. +74.9 kJ mol⁻¹ at the 4-position). Both processes lead directly to 9a or 9b and FBpin. Moreover, boryl-assisted C–F activation at the 2-position is now more accessible than oxidative addition at the 4-position, and so this pathway accounts for the experimentally observed selectivity. One factor that might contribute to the greater accessibility of the boryl-assisted process at the 2-position is the short Rh···N contact in the transition state (2.22 Å); donation of electron density from the nitrogen atom lone pair serves to stabilize the rhodium center (Figure 2).\[28\]

We also experimentally investigated the reactivity of 3 in catalytic borylation reactions of pentafluoropyridine. In Me3SiSiMe3 solvent, we anticipated a selective borylation reaction at the 2-position of pentafluoropyridine, because the formation of [Rh(PEt3)3](5) would not occur. As
mentioned above, the latter led to C–F bond cleavage at the 4-position.\textsuperscript{[20]} Indeed, perfluoropyridine was catalytically converted into its 2-boryl derivative 10 (45 % yield) in the presence of 2.5 mol % \textsuperscript{3} as the catalyst (based on equimolar amounts of C\textsubscript{5}NF\textsubscript{5} and B\textsubscript{pin}; Scheme 4). Borylation of the

\[
\begin{align*}
\text{C–F bond has also been reported by Marder, Perutz, and co-workers.} & \text{ The treatment of C–F activation products, such as [Rh(2-C\textsubscript{5}NF\textsubscript{4})(PMe\textsubscript{3})\textsubscript{3}] or [Rh(4-C\textsubscript{5}NF\textsubscript{4})(PMe\textsubscript{3})\textsubscript{3}], with B\textsubscript{cat}\textsuperscript{2} gave the pyridyl boronate esters and the Rh III complex fac- [Rh(Bcat)\textsubscript{2}(PMe\textsubscript{3})\textsubscript{3}]. However, in these examples the reactions were not catalytic.}
\end{align*}
\]

In conclusion, a 16-electron rhodium(I)–boryl complex (3) has been synthesized which undergoes C–H activation at room temperature with benzene to give PhBpin. Reaction with fluorinated substrates, such as perfluoropyridine and perfluoropropene, results in C–F activation products. DFT calculations suggest that C–F activation proceeds along a boryl-assisted pathway that involves direct transfer of fluorine onto the boron center via a four-membered transition state. This mechanism also shows that the selective activation at the 2-position arises because of a stabilizing Rh···N interaction in the transition state. Investigation of the catalytic borylation reaction led to the formation of tetrafluoropyridyl boronate esters, which can provide new fluorinated building blocks.\textsuperscript{[20]} Note that it is extremely difficult to access tetrafluoropyridines that are further functionalized at the 2-position.\textsuperscript{[6,21]}

Received: February 22, 2010  
Published online: April 23, 2010  

Keywords: boryl ligands · borylation · C–F activation · C–H activation · rhodium

Catalytic Hydrodefluorination of Pentafluorobenzene by [Ru(NHC)-(PPh₃)₂(CO)H₂]: A Nucleophilic Attack by a Metal-Bound Hydride Ligand Explains an Unusual ortho-Regioselectivity

Julien A. Panetier, Stuart A. Macgregor,* and Michael K. Whittlesey*

The selective synthesis of fluoroarene compounds is a subject of intense current interest, driven by the prominent role such species play in many pharmaceuticals, agrochemicals, and other industrially important products.[1] One attractive route to selectively substituted fluoroarenes involves the activation and functionalization of aromatic C–F bonds derived from readily available perfluoroarenes.[2] The simplest example of such a process is the hydrodefluorination reaction (HDF), in which fluorine is substituted for hydrogen. Catalytic HDF of C₆F₆ and C₆F₅H has been reported by Milstein et al.[3] and Holland et al.[4] using Rh and Fe catalysts.[5] However, both these systems exhibit practical problems that limit the mechanistic understanding of the HDF cycle. For example, the Rh system requires high pressures of H₂ as well as a sacrificial amine to remove HF, while with Fe no C–F activation is observed in the absence of a reductant. As a consequence, the development of more active Rh or Fe catalysts has not been forthcoming.

We recently reported[6] the HDF of C₆F₆ and C₆F₅H using the ruthenium N-heterocyclic carbene (NHC) dihydride complex 1 (NHC = IMes, SIMes, IPr, SIPr,[7] see Scheme 1a) in the presence of trialkylsilanes at 70 °C in THF. Isolation and characterization of 1 allowed detailed kinetic studies to be undertaken, and these supported a mechanism involving initial phosphine dissociation to form 2 followed by HDF of the substrate to give the Ru–F species, 3. Isolation of this 16e complex allowed us to demonstrate its reaction with trialkylsilane in the presence of PPh₃ to regenerate catalyst 1. The most unusual feature of this system was the high regioselectivity for the formation of 1,2,3,4-C₆F₄H₂ upon HDF of C₆F₅H, in contrast to the Milstein and Holland systems[3,4] where the 1,2,4,5-isomer is dominant.

To account for the unusual ortho-regioselectivity we postulated the involvement of a tetrafluorobenzyne intermediate (Scheme 1b). Such species have been reported previously[8] and could be formed here from 2 by successive C–H and ortho-C–F activation of C₆F₅H. However, density functional theory (DFT) calculations[9] (with NHC = IMes) have now shown that this species lies more than 200 kJ mol⁻¹ above the reactants, effectively ruling it out as a viable intermediate under the conditions used experimentally.

Further calculations, however, have now allowed us to define a series of alternative pathways which are based on a novel nucleophilic attack mechanism whereby a hydride ligand reacts directly with C₆F₅H.[10] These processes produced significantly lower barriers and, moreover, the lowest-energy pathway was found to be consistent with the unusual ortho-regioselectivity observed experimentally. Our calculations have shown that, after initial phosphine loss from 1, nucleophilic attack of hydride at C₆F₅H can occur through two different pathways (Scheme 2). In the concerted pathway I, the hydride is transferred from the metal onto the arene ring and the displaced fluorine migrates directly onto the metal center. In the alternative stepwise pathway II, an n²-arene adduct, 4, is formed prior to the hydride attack. In this case the different orientation of the arene precludes direct transfer of fluorine onto the metal. Instead an intermediate is formed, 5, from which HF can be lost to form a α-aryl species, 6. Protonolysis by HF with concomitant F⁻ transfer to metal then yields 1,2,3,4-C₆F₄H₂ and the M–F species 3.

The lowest-energy reaction profile for the HDF of C₆F₅H by 1 to give 1,2,3,4-C₆F₄H₂ is computed to proceed through pathway II, and full details are shown in Figure 1.[11] Initial

Scheme 1. a) Catalytic hydrodefluorination (HDF) of C₆F₅H to 1,2,3,4-C₆F₄H₂ by 1; b) postulated tetrafluorobenzyne intermediate.
PPh₃/C₆F₅H substitution gives 4 \((E = +37.7 \text{ kJ mol}^{-1})\) in THF\(^{(9)}\), in which the \(η^2\)-arene binds through the C₅/C₆ bond. Attack of H₅ at C₅ occurs through TS\((4\rightarrow 5)\) \((E = +75.3 \text{ kJ mol}^{-1})\) and gives 5 \((E = +69.5 \text{ kJ mol}^{-1})\), in which the \(\{\text{C}_6\text{F}_5\text{H}\}_2\) moiety resembles a Meisenheimer intermediate (C₅–H₅ 1.24 Å, C₅–F₅ 1.45 Å). This structure is also stabilized by interaction of the \textit{ortho} position with the metal center (Ru–C₆ 2.28 Å). The subsequent step through TS\((5\rightarrow 6)\) \((E = +84.1 \text{ kJ mol}^{-1})\) involves elongation of the C₅–F₅ bond to 1.95 Å. To this point the reaction parallels nucleophilic aromatic substitution, however, rather than acting as a simple leaving group the highly fluoridic center F₅ (computed charge 0.54) is able to abstract H₅ to form HF. As this occurs, the remaining \[\text{C}_6\text{F}_5\text{H}\]− moiety is trapped by Ru to give 6 \((E = -40.2 \text{ kJ mol}^{-1})\). The calculations suggest that HF remains loosely associated with the aryl ligand in 6 (H₅–C₅ 1.97 Å), and so it is ideally placed to effect protonolysis of the Ru–C₅ bond with concomitant F transfer to Ru. This step occurs through TS\((6\rightarrow 3)\) \((E = -18.4 \text{ kJ mol}^{-1})\) and gives \([\text{Ru(IMes)}(\text{PPh}_3)(\text{CO})\text{HF}]\) (3) and 1,2,3,4-C\(_6\)F\(_4\)H\(_2\). Overall, HDF of C\(_6\)F\(_5\)H is a highly favorable process \((\Delta E = -168.1 \text{ kJ mol}^{-1})\) and proceeds with a barrier of 84.1 kJ mol\(^{-1}\) corresponding to TS\((5\rightarrow 6)\).

A transition state for the concerted HDF process through pathway I was also located (Figure 2). This process involves the direct reaction of C\(_6\)F\(_5\)H with five-coordinate \([\text{Ru(IMes)}(\text{PPh}_3)(\text{CO})\text{H}_2]\) (2) to give 1,2,3,4-C\(_6\)F\(_4\)H\(_2\) and 3 and proceeds through TS\((2\rightarrow 3)\) \((E = +113.4 \text{ kJ mol}^{-1})\). The structure of TS\((2\rightarrow 3)\) features a side-on orientation of C\(_6\)F\(_5\)H, and this means that the vacant site at Ru is now readily available to accept the displaced F₅ substituent directly. In contrast, in TS\((5\rightarrow 6)\) this site is blocked by interaction with the \textit{ortho} C₆ position. Overall, the barrier computed in THF for the concerted reaction through TS\((2\rightarrow 3)\) is 29.3 kJ mol\(^{-1}\) above that for the stepwise process through TS\((5\rightarrow 6)\).

**Scheme 2.** Mechanisms of nucleophilic attack by a metal hydride ligand at C\(_6\)F\(_5\)H to give 1,2,3,4-C\(_6\)F\(_4\)H\(_2\); \(L_nM = [\text{Ru(NHC)}(\text{PPh}_3)(\text{CO})\text{H}]\).
We have also considered the formation of different isomers of C₆F₄H₂, and in all cases were able to characterize both the stepwise and concerted pathways. The lowest energy barriers computed for the formation of 1,2,3,5- and 1,2,4,5-C₆F₄H₂ through pathway I were 98.3 kJ mol⁻¹ and 99.5 kJ mol⁻¹, respectively, and in both cases corresponded to the stepwise mechanism. The formation of 1,2,3,4-C₆F₄H₂ with a barrier of 84.1 kJ mol⁻¹ therefore remains the most accessible reaction, and this kinetic preference is consistent with the ortho-selectivity that is observed experimentally.[12,13]

The factors promoting these unusual hydride ligand nucleophilic attack reactions have been probed by calculations with a small model system featuring an N-methyl substituted carbene and PH₃ ligands. Thus, [Ru(IMes)(PH₃)₂(CO)H₂] (I)[10] yields barriers that are between 20 and 45 kJ mol⁻¹ higher than those computed with the full model. One reason for this difference is that the initial phosphine/C₆F₄H substitution step is more accessible for the more sterically encumbered full system. Reduced barriers for the nucleophilic attack/C–F bond cleavage steps are also seen in the full model system, and these may again reflect a more weakly bound arene. These steric effects are particularly large for the formation of the 1,2,3,4-C₆F₄H₂ isomer, where calculations with I give a barrier 45 kJ mol⁻¹ higher than that computed for the full system.

In summary, DFT calculations have defined a novel class of reaction mechanism for the HDF of C₆F₄H catalyzed by [Ru(IMes)(PPh₃)₂(CO)H₂]. The key feature is the direct nucleophilic attack of a Ru hydride ligand at the fluoroarene substrate. The overall HDF process may occur either through a stepwise or a concerted pathway. The most accessible reaction, and this kinetic preference is consistent with the unusual ortho-regioselectivity that is observed experimentally. We believe that these results will provide a starting point for further experimental studies on transition metal hydride induced HDF and may allow the development of systems that display higher activity and additional control of regioselectivity.

Received: October 28, 2010
Revised: December 7, 2010
Published online: February 18, 2011

Keywords: C–F activation · density functional calculations · fluoroarenes · hydrodefluorination · ruthenium


All key stationary points were the subject of extensive conformational searching according to the protocol described in the Supporting Information.

1,2,3,4-C₆F₄H₂ can also be formed from an isomer of 4 in which the arene binds through the C1–C2 bond and H5 attacks C1. This process entailed a barrier of +125.5 kJ mol⁻¹ in THF, significantly higher than the reaction shown in Figure 1.

The lowest-energy pathway computed for HDF of C₆F₆ was also found to involve nucleophilic attack of the hydride ligand and had a barrier of 91.2 kJ mol⁻¹ corresponding to the stepwise pathway. This therefore supersedes the σ-bond metathesis mechanism proposed previously.[⁶]

[10] 1,2,3,4-C₆F₄H₂ can also be formed from an isomer of 4 in which the arene binds through the C1–C2 bond and H5 attacks C1. This process entailed a barrier of +125.5 kJ mol⁻¹ in THF, significantly higher than the reaction shown in Figure 1.

[12] The lowest-energy pathway computed for HDF of C₆F₆ was also found to involve nucleophilic attack of the hydride ligand and had a barrier of 91.2 kJ mol⁻¹ corresponding to the stepwise pathway. This therefore supersedes the σ-bond metathesis mechanism proposed previously.[⁶]