SYNTHESIS, CATALYSIS AND RECYCLING STUDIES

OF PERFLUOROALKYLATED PALLADIUM

COMPLEXES

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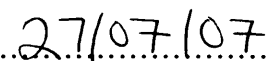
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The experimental work in this thesis has been carried out by the author in the department of chemistry at the University of Leicester between September 2003 and October 2006. The work has not been submitted, and is not presently submitted, for any other degrees at this or any other university.

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SYNTHESIS, CATALYSIS AND RECYCLING STUDIES OF PERFLUOROALKYLATED PALLADIUM COMPLEXES

Daniel Duncan

Abstract

Palladium catalysis has emerged to be a fundamental tool for organic chemists in the synthesis of carbon-carbon bonds offering a range of versatile reactions. Fluorous catalysis has evolved over 10 years now and the aim of this research was to synthesise a range of perfluoroalkylated palladium catalysts and evaluate fluorous solid phase extraction as a 'separation technique' for recycling homogeneous palladium catalysts which can be used in conventional organic solvents.

A range of fluorous monodentate triarylphosphines were synthesised using novel chemistry and modified literature methods. The corresponding complexes were shown to be more active in the Suzuki reaction, compared with the non-fluorous derivative, triphenylphosphine. However, the catalysts simply decomposed under the reaction conditions to form palladium black making it impossible for these fluorous catalysts to be recycled.

The synthesis and coordination chemistry of fluorous and non-fluorous pincer phosphines has been investigated. Both palladium pincer catalysts successfully catalyse a range of Heck and Suzuki reactions. However, recovery and reuse was only possible with the fluorous pincer catalyst, which could be successfully recovered and reused three times in the Heck reaction with no loss in activity. In the Suzuki reaction, recovery and reuse of the fluorous pincer catalyst was possible, however, decomposition of the catalyst was detected under the reaction conditions leading to an inevitable loss in activity.

A range of fluorous and non-fluorous monodentate, bidentate and pincer NHC ligands and palladium complexes were synthesised using novel chemistry and modified literature methods. The monodentate NHC complexes were evaluated in Heck reactions. The recovery and reuse of the fluorous carbene complexes were evaluated with differing success. Under homogenous reaction conditions, decomposition of the light fluorous catalyst was detected upon recovery of the catalyst. Conversely, when supporting the heavily fluorinated carbene complex on Fluorous Reverse Phase Silica Gel (FRPSG), the catalyst was successfully used three times. However, due to poor recovery of the support, inevitable loss in product conversion was observed.

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Chapter One

Chapter One - Introduction

1.1 Heterogeneous and Homogeneous Catalysis

Catalysis is an extremely important area of chemistry. There are two different classes of catalysis; heterogeneous and homogeneous. Heterogeneous catalysis is where the catalyst is in a different physical state to the reagents. The catalyst is usually in the solid state and the reagents are in the liquid or gaseous phase. The catalysis takes place at the interface between the phases, so small particles of solid catalyst are used to maximise the surface area. Homogeneous catalysis is where both the catalysts and reagents are in the same physical state. This generally takes place in the liquid phase, with solid catalysts being dissolved in the reaction solution. The catalyst is a discrete entity, as opposed to heterogeneous catalysis where the catalyst is a number of sites grouped together.

Both types of catalysis have their own advantages and disadvantages that either makes them desirable or undesirable. Heterogeneous catalysis is usually preferred in industry due to the ease of separation of the product from the catalyst. The solid-state nature of the catalyst means high reaction temperatures and pressures can be endured, which increase the rates of reactions. Catalyst poisoning can occur from by-products being formed in the reaction and sticking to the surface of the catalyst. Regeneration of the catalyst can be achieved by simply burning off such by-products.

An example of heterogeneous catalysis is the Haber process, which has been used on an industrial scale since 1914. The process involves the reaction between nitrogen and hydrogen over an iron catalyst, at 450 °C and ~200 bar, to produce ammonia. Nitrogen and hydrogen are adsorbed on to the iron surface. They undergo surface diffusion and the reaction takes place to form ammonia on the surface. Desorption of the product occurs, where the ammonia-catalyst bond is broken and the product returns to the gas phase.

Industry has used heterogeneous catalysis to promote palladium catalysed reactions. Palladium on carbon is used to catalysed Suzuki reactions.[1] At the end of the reaction, the mixture is poured through a column of silica gel, the catalyst is retained on the column to give the organic product free from the catalyst.

The main drawback with heterogeneous catalysis is the lack of selectivity. In solid-state catalysts, not all the sites are active towards the synthesis of the desired product; some sites may be inactive or, worse, catalyse the synthesis of an undesired by-product.[2] Even in the pure metallic state, the individual metal ions can be in numerous different environments, with possibly only one of these catalysing the desired reaction.

Homogeneous catalysis operates under much milder conditions. It offers higher selectivity, activity and ease of study and modification. Each catalyst entity catalyses the desired reaction so a higher activity per metal centre can be obtained. Studies such as NMR

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and Infrared spectroscopy have allowed more in-depth mechanistic details of catalytic cycles to be investigated and determined. The catalyst can also be optimised by ligand modification. All of these advantages show why homogeneous catalysis is a powerful tool in synthesis.

Hydroformylation reactions can be successfully carried out under homogeneous conditions. This was first carried out in 1938 by Roelen[3] and is now the largest homogeneous catalytic process. The first hydroformylation reactions were between alkenes with hydrogen and carbon monoxide using a cobalt catalyst. The cobalt catalyst was later replaced with a rhodium version as it produced high n/i ratios of aldehydes, which are synthetically more useful.

The major drawback with a homogeneous approach is the inability to separate the catalyst from the product and possibly reuse the catalyst. These are qualities which heterogeneous reactions possess. Therefore, it would be desirable if the 'heterogenisation' of a homogeneous reaction were possible. This would supply the best of both worlds; high yields and selectivities with facile separation and reuse of the catalyst.

1.2 Palladium Catalysed Reactions

Transition metals have been used as catalysts due to their variable oxidation states. In particular, palladium is one the most versatile transition metals. It offers a number of different reactions, and some of the most important are the C-C bond forming reactions. Palladium can catalyse a wide range of C-C coupling reactions (Scheme 1.1).
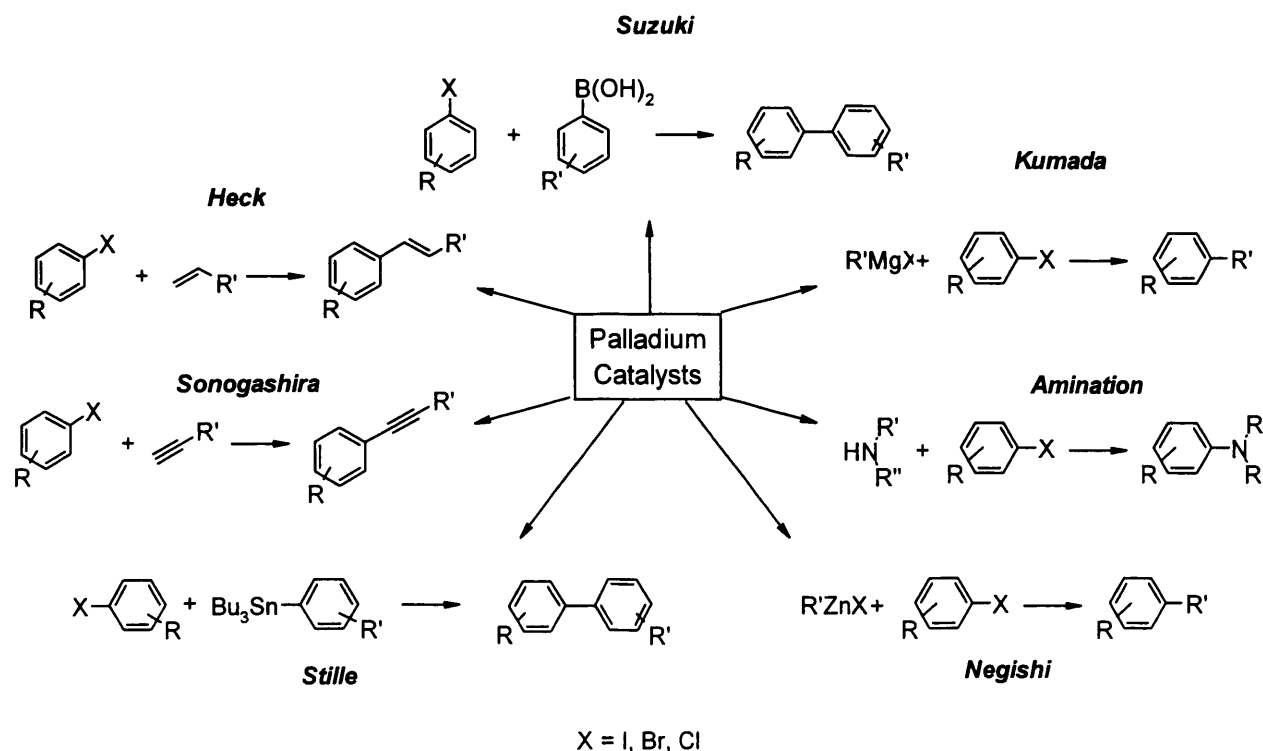
Scheme 1.1. *Examples of reactions catalysed by palladium.*

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1.2.1 General Catalytic Cycle
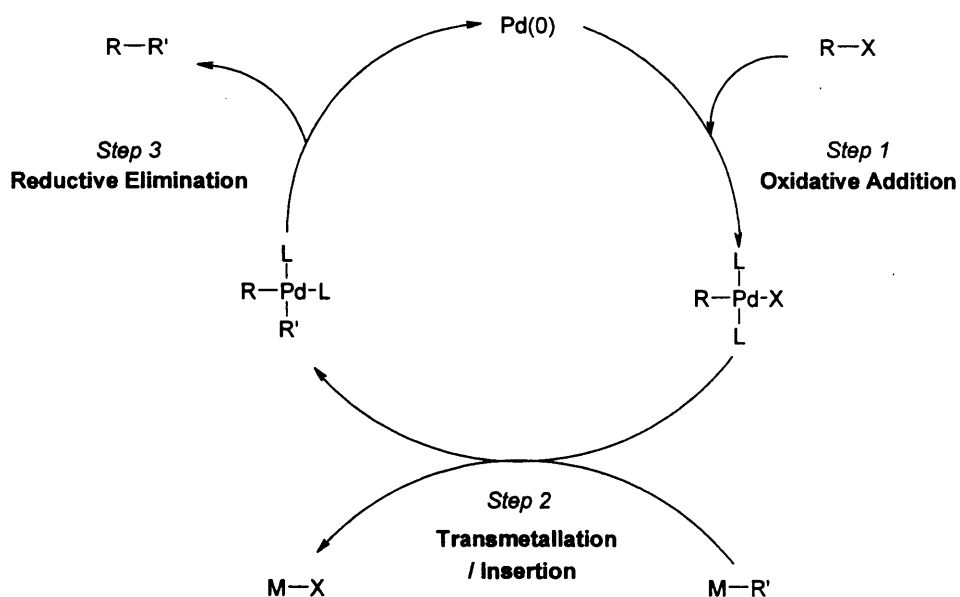
Figure 1.1. *General catalytic cycle for palladium catalysed reactions.*

The general catalytic cycle for palladium catalysed reactions goes in three main steps; oxidative addition, transmetallation/insertion and reductive elimination (Figure 1.1). The mechanism for the oxidative addition and reductive elimination steps are quite well understood with different mechanisms occurring in *Step 2* dependent on the catalytic reaction. The aryl halide adds across the palladium and oxidises the palladium centre from palladium(0) to palladium(II) to form a stable *trans* isomer.[4] This organopalladium(II) halide then undergoes a transmetallation reaction. After this, the two organic substituents must be *cis* to one another in order for reductive elimination to take place. If the two organic substituents are *trans*, isomerisation must take place to form the *cis* isomer first (Scheme 1.2).
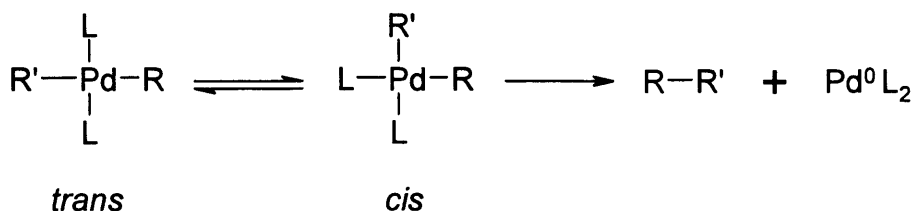
Scheme 1.2. *The equilibrium from trans to cis for reductive elimination.*

The oxidative addition of aryl electrophiles is generally the rate-determining step (RDS) in the catalytic cycle of the palladium catalysed reactions. Aryl halides are the most common substrates used, however, aryl triflates and diazonium salts are becoming ever more

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popular alternatives. The relative reactivities for aryl halides usually decrease in the order of I > Br >> Cl. This is not surprising as the relative bond enthalpies for carbon-halogen bonds decrease as you descend down the group, i.e. C-Cl > C-Br > C-I (Table 1.1).[5]

C-X	Bond Enthalpy / kJ mol^{-1}
C-Cl	397
C-Br	280
C-I	209

Table 1.1. *Bond enthalpy for the different C-X bonds.*

In 1971, Fitton and Rick studied the mechanism of oxidative addition.[6] They compared the oxidative addition of halobenzenes to [Pd(PPh₃)₄]. The order of reactivity was found to be PhI > PhBr > PhCl. The mechanism was found to be similar to that of Nucleophilic Aromatic Substitution (NAS), however, a different rate-determining step has been observed; the rate determining step associated with oxidative addition is the breaking of the C-X bond (Scheme 1.3). Conversely, with NAS, the rate determining step is the formation of the intermediate and is also dependent on the electronegativity of the halide leaving group, not the breaking of the C-X bond (Scheme 1.4). This is reflected in the opposite rates of reactivity for each aromatic halide for both reactions (Figure 1.2).

X = I, Br, Cl
L = PPh₃
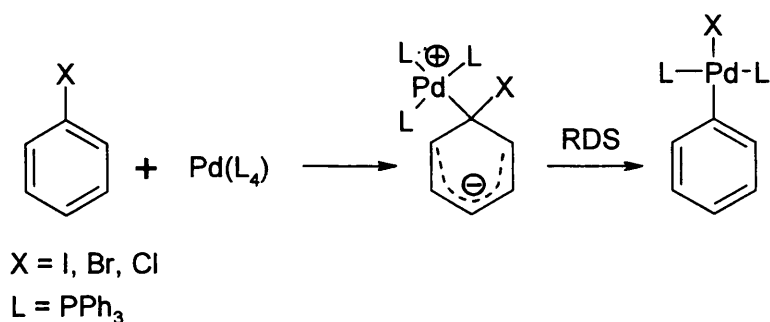
Scheme 1.3. *Mechanism for Oxidative Addition of aryl halides*

X = I, Br, Cl
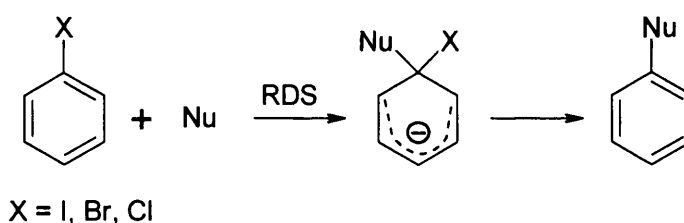
Scheme 1.4. *Mechanism for Nucleophilic Aromatic Substitution of aryl halides*
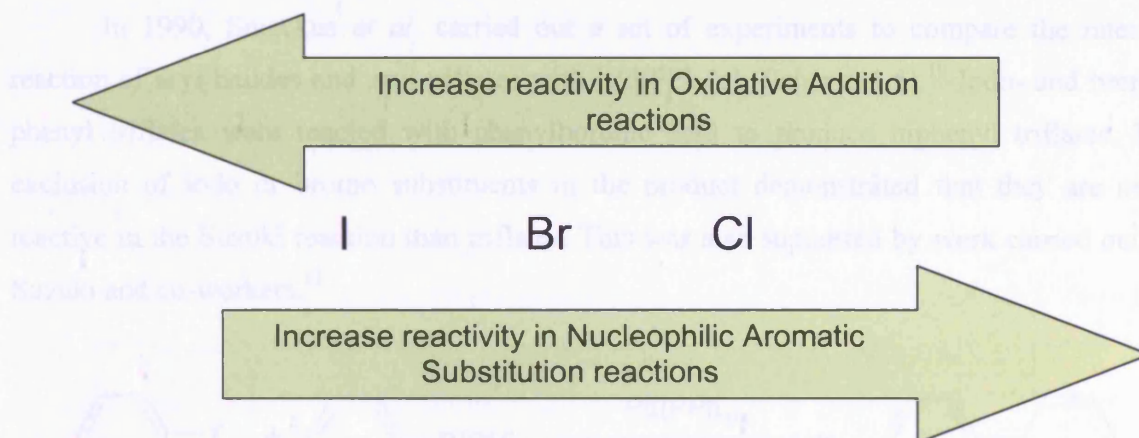
Figure 1.2. *The reactivity for aromatic halides in Oxidative Addition and Nucleophilic Aromatic Substitution reactions.*

The relative reactivities of the halobenzenes in oxidative additions are dependent on the electronic effects of the different substituents on the aromatic ring. The reactivity decreases in order of electron withdrawing > electron neutral > electron donating substituents. This is attributed to the electron-withdrawing substituent removing electron density from the aromatic ring making the breaking of carbon-halide bond easier.

The palladium catalysed reactions do have one major drawback; aryl chlorides often do not react[7] or react very slowly.[8] Aryl chlorides are more desirable for industrial use since they are cheaper and more widely available than their iodide and bromide counterparts. Aryl chlorides do not react particularly quickly in the Suzuki reaction due to the strength of the C-Cl bond. In order to overcome this problem the catalyst metal centre must possess a sufficient degree of electron density to be able to break this bond in the oxidation step. The electronic properties of a metal are governed by the donor ligands that are coordinated to it. The ligand must possess enough electron donating character to push electron density onto the metal centre to facilitate the oxidative addition of the aryl chloride. In recent years, catalysts have been developed with sufficient ability to facilitate the oxidative addition of aryl chlorides and hence, catalyse the Suzuki reaction. Examples of these include palladacycles and palladium complexes containing pincer ligands.

1.2.2 Alternative leaving groups

The use of triflates instead of halides as leaving groups in the Suzuki reaction was first introduced by Huth *et al.* in 1989.[9] The triflate group is an exceptional leaving group and can easily be prepared from readily available phenols. However, triflates are expensive to prepare, thermally labile, and may undergo hydrolysis.

In 1990, Snieckus *et al.* carried out a set of experiments to compare the rates of reaction of aryl halides and aryl triflates with [Pd(PPh₃)₄] (Scheme 1.5).[10] Iodo- and bromo-phenyl triflates were reacted with phenylboronic acid to produce biphenyl triflates. The exclusion of iodo or bromo substituents in the product demonstrated that they are more reactive in the Suzuki reaction than triflates. This was also supported by work carried out by Suzuki and co-workers.[11]

X= I, Br
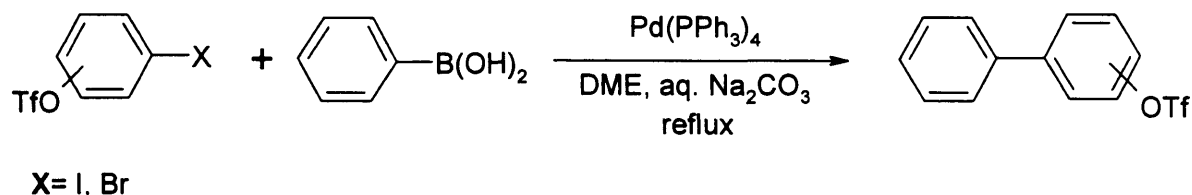
Scheme 1.5. *A selective Suzuki reaction using triflates.*

However, in 1995, Jutand and Mosleh carried out a set of experiments to compare the rates of oxidative addition of aryl halides and aryl triflates.[12] They compared the oxidative addition rates of PhI, PhBr and PhOTf with [Pd(PPh₃)₄]. They found that the relative reactivity decreased in the order PhI >>PhOTf > PhBr, concluding that aryl triflates were more reactive than aryl bromides, but less reactive than aryl iodides in oxidative addition reactions. This seems to contradict the previous work.

Reactions using triflates as substrates have often proved to be unsuccessful, with palladium black being formed in the initial stages of the reaction due to catalyst decomposition.[12, 13] It is thought that phosphine ligands from the catalyst can react with the aryl group reducing the palladium(II) centre to palladium(0) and forming a phosphonium salt with the triflate (Scheme 1.6). This can be overcome by the addition of potassium or lithium bromide, or lithium chloride. This converts the reactive cationic palladium(II) species into a more stable organopalladiumhalide. However, some biaryl coupling reactions with triflates give high yields without the need for an additive.[12]
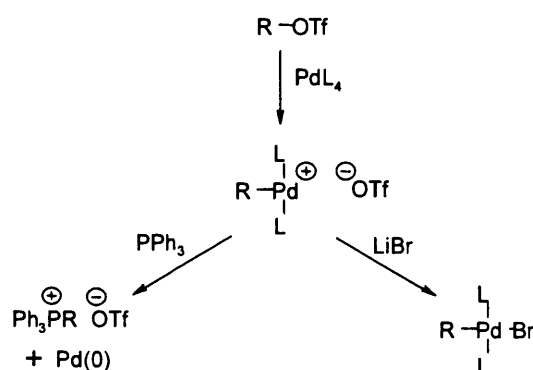
Scheme 1.6. *Decomposition of palladium catalysts with triflates and stabilisation using LiBr.*

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Since 1996 diazonium salts have been used as alternative substrates to aryl halides in the Suzuki[14] and Heck reactions, as they can be easily prepared from the corresponding, readily available anilines. Their high reactivity means that reactions can be carried out using extremely mild conditions, without the need for any base or phosphine ligands.

Diazonium salts have been used successfully in a number of Heck reactions. Sengupta et al. demonstrated diazonium salts are highly reactive leaving groups, more so than iodide. The iodobenzene diazonium tetrafluoroborate 1 was found to preferentially react with the diazonium group enabling the stepwise assembly of complex molecules (Scheme 1.7).

R = Ph, CO₂Et   R' = CO₂Et, CN
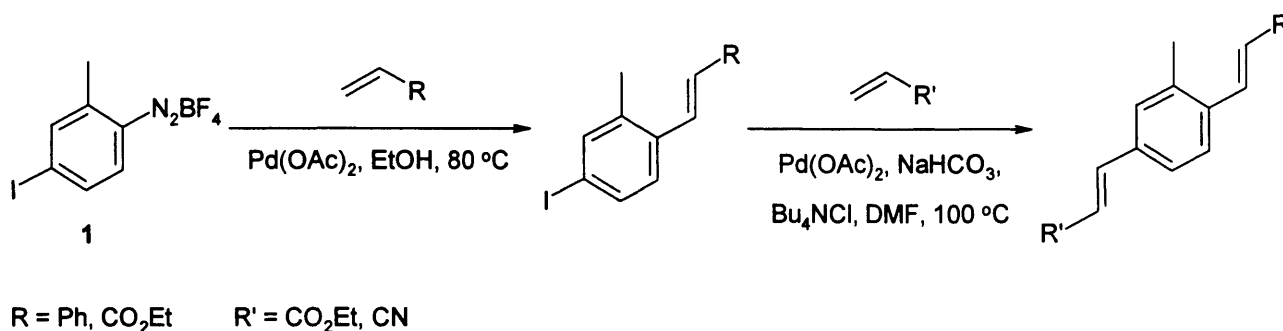
Scheme 1.7. *Use of a diazonium salt in a Heck reaction.*

Genet *et al* demonstrated that a variety of arenediazonium tetrafluoroborate salts containing different electron withdrawing and electron donating groups could be reacted in the Suzuki reaction. Optimised reaction conditions gave isolated yields ranging from 52–95% (Scheme 1.8). [14] It was reported that when 4-bromobenzene diazonium tetrafluoroborate was reacted with phenylboronic acid the product was found to be 4-bromobiphenyl. This shows that the diazonium salt was more reactive than the aryl bromide and a selective Suzuki reaction could take place.

R = Me, OMe, CO₂Et, COPh, Br
R' = H, OMe, Cl, F
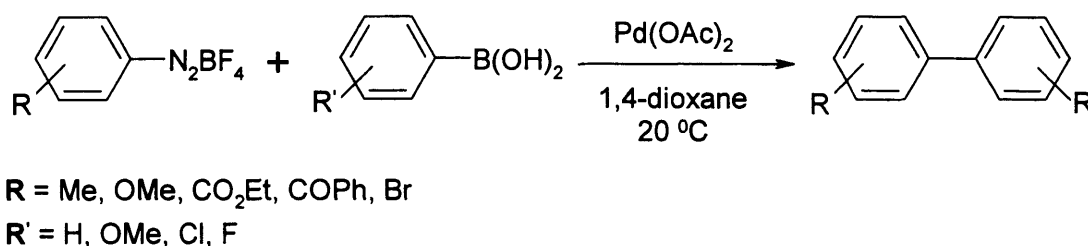
Scheme 1.8. *The use of arenediazonium tetrafluoroborate salts in the Suzuki reaction.*

Shortly after, Genet *et al.* reported the use of arenediazonium salts with potassium aryl- and alkenyl-trifluoroborates in Suzuki coupling reactions.[15] This work again demonstrated the use of mild conditions and no base. Selective Suzuki reactions using

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arenediazonium salts with bromide, triflate and iodide substituents were coupled with aryl- and alkenyl-trifluoroborates. The diazonium functionality reacted in the coupling step leaving the unreacted halide or triflate groups as substituents on the biphenyl ring (Scheme 1.9). This shows that the arenediazonium salts are more reactive than the iodide leaving group, making it the most reactive leaving group.

R = Br, OTf, I
R' = aryl, alkenyl
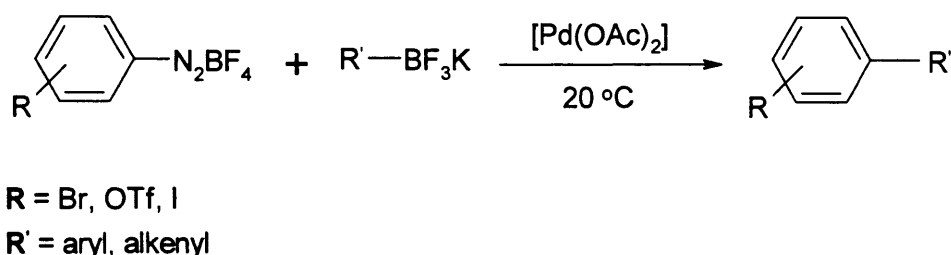
Scheme 1.9. *Reaction of bromide, triflate and iodide substituted arenediazonium salts with aryl- and alkenyltrifluoroborates in Suzuki coupling reactions.*

1.3 Heck Reaction

The Heck reaction has emerged to be a fundamental tool for organic chemists in the synthesis of carbon-carbon bonds. Mizoroki[16] and Heck[17] both independently reported examples in the early 1970's, however, the reaction was further developed by Heck. The reaction couples aryl halides with olefins in the presence of a palladium catalyst to generate substituted olefins with excellent chemoselectively (Scheme 1.10). Although aryl halides are often used as substrates, there are now a variety of aryl compounds bearing alternative leaving groups such as triflates and diazonium salts. The Heck reaction has been used to synthesis a range of substituted olefins, dienes and unsaturated compounds for use as dyes, UV screens and pharmaceuticals.

X = I, Br, Cl, OTf, N$_2$ EWG = CO$_2$R, CN, Ph
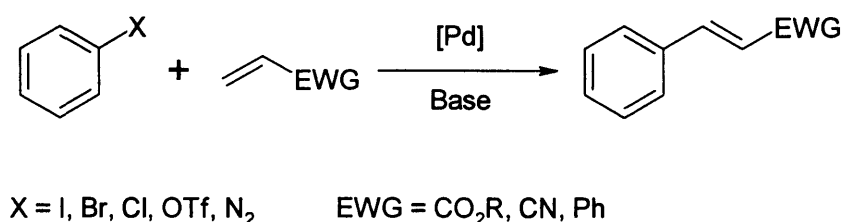
Scheme 1.10. *General scheme for Heck reaction.*

1.3.1 Mechanism of the Heck reaction

The general mechanism for the Heck reaction consists of oxidative addition, migratory insertion and reductive elimination steps, with the re-generation of the palladium catalyst (Figure 1.3). The processes that make the Heck reaction different from other palladium catalysed reaction mechanism are the migratory insertion and β-hydride elimination steps.

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After the alkene association to the palladium centre, migratory insertion takes place. The C-C bond is formed when the alkene inserts into the Pd-Aryl bond forming an unstable σ-bond (Scheme 1.11).
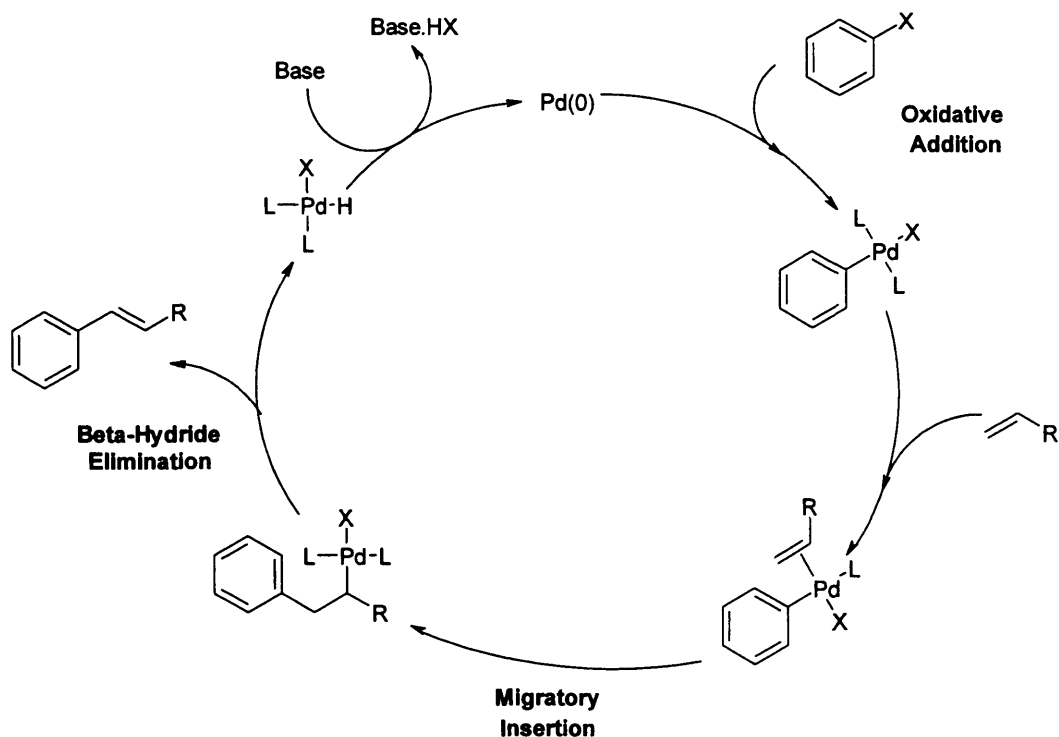
Figure 1.3. *General catalytic cycle for the Heck reaction.*
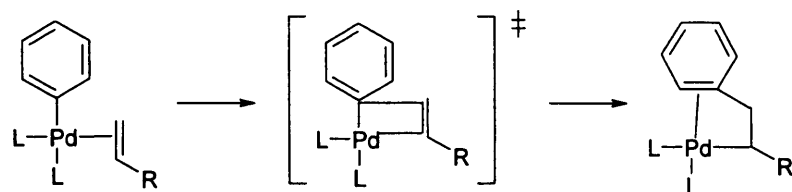
Scheme 1.11. *Migratory insertion step in Heck reaction.*

The catalyst generally goes through *syn*-elimination, which defines the stereochemistry of Heck product to be the *trans*-isomer (Scheme 1.12). In the majority of cases, the *trans*-isomer dominates, with most reactions being highly stereospecific. The relative ratios of the isomers can be explained by the Curtin-Hammett kinetic control principle, where the transition state for the hydride elimination that gives the *trans*-isomer requires less energy and, therefore, is more favourable than the transition state that produces the *cis*-isomer. The palladium catalyst is finally regenerated by the loss of HX using a base, before the catalytic cycle can be resumed.
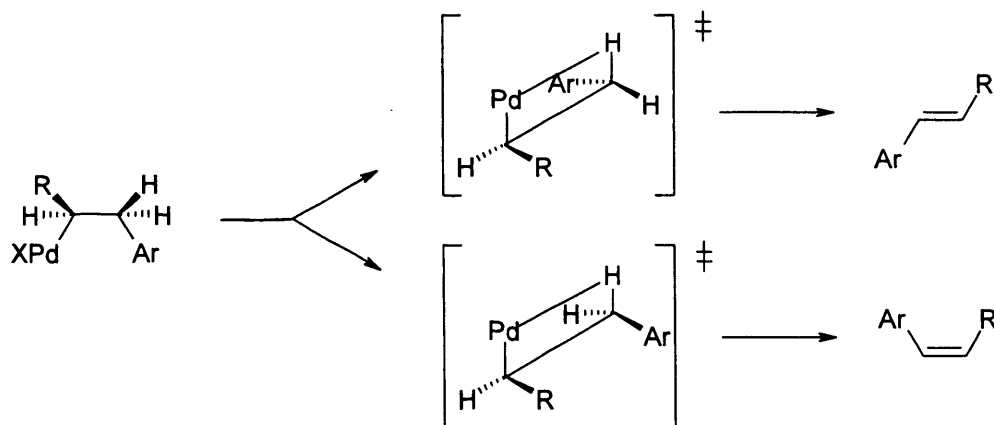
Scheme 1.12. *Transition states for the formation regio-isomers.*

1.4 Suzuki Reaction

The Suzuki reaction has proven to be a very powerful tool for the synthesis of carbon-carbon bonds.[7] The reaction was first reported in 1979 and involves the coupling of an aromatic halide or triflate (R-X) to an organoboron derivative (R'-BY$_2$) mediated by a palladium catalyst (Scheme 1.13).

$$R{-}X \quad + \quad R'{-}BY_2 \quad \xrightarrow{\text{[Pd]}} \quad R{-}R'$$

$$X = I, Br, Cl, OTf$$

$$Y = OH, O\text{-alkyl}$$
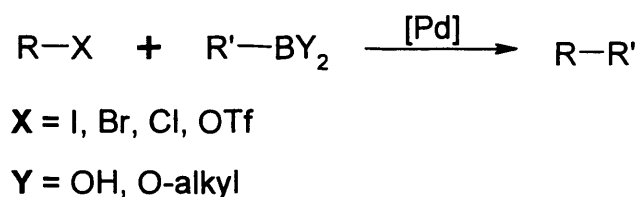
Scheme 1.13. *A general Suzuki cross-coupling reaction.*

Over the past 25 years the Suzuki reaction has been one of the most widely used carbon-carbon coupling reactions.[8, 18-22] This is mainly due to the reaction offering many advantages over other organometallic reactions, such as a high level of regio- and stereo-selectivity, tolerance of a large number of functional groups, no major side-effects in the presence of water and, most importantly, non-toxic by-products which can be removed easily. All of these features have led to the Suzuki reaction becoming popular in industry as well as in academia.

The versatility of the reaction is shown by the many different substrates which can be used. Examples range from electrophiles with aryl,[9, 23] alkenyl,[7, 24] alkynyl,[7] porphyrins,[25] heterocycles,[26] to even alkyl substrates[27] and boron derivatives bearing aryl,[7, 9, 13] alkenyl,[13, 24] alkynyl[13, 28] and alkyl substituents.[27]

The synthesis of biaryl compounds is the most widely used application for the Suzuki reaction. The first biaryl Suzuki coupling was reported in 1981,[23] (Scheme 1.14). Biaryl

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products are important as they can be found in many pharmaceutical compounds. One example is the drug trityl losartan 2,[29] which is an angiotensin II receptor antagonist used for the treatment of high blood pressure and heart failure (Figure 1.4).

X = I, Br
R = Me, OMe, Cl, CO₂Me, Br
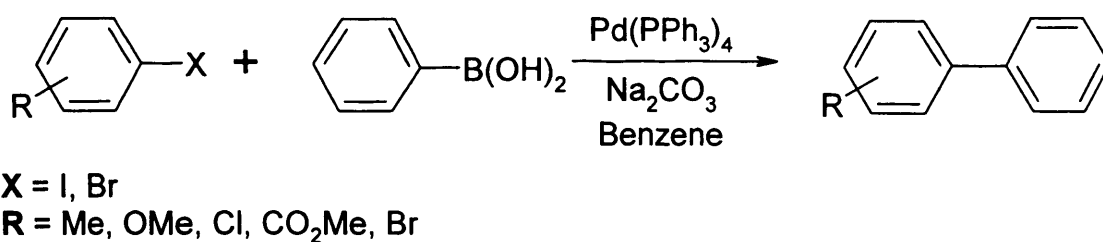
Scheme 1.14. *An example of a Suzuki cross-coupling reaction to form biaryls.*

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━━ Bond made in Suzuki reaction
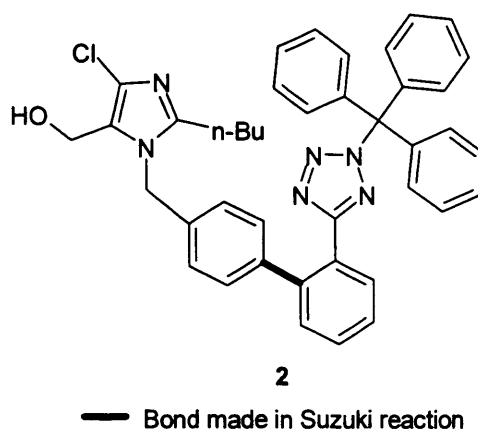
Figure 1.4. *Trityl losartan, an example of a biphenyl in a pharmaceutical product.*

1.4.1 Mechanism for the Suzuki Reaction

The standard catalytic cycle for an organometallic cross-coupling reaction involves oxidative addition, transmetallation and reductive elimination steps, with the re-generation of the palladium catalyst (Scheme 1.15). The classical mechanism for the reaction goes through a Pd(0)/Pd(II) species. However, speculation is now growing that a different mechanism involving Pd(II)/Pd(IV) species can also be adopted in certain situations.[30]

As the boron atom is not as electropositive as other organometallic species, the organic group attached to the boron has a lower nucleophilicity and, therefore, does not undergo transmetallation readily.[23] This can be improved by the addition of base, which quarternises the boron atom to form an anionic tetravalent boron atom or "ate" complex. This has been detected by ¹¹B NMR spectroscopy.[31]

There are three possible mechanisms which have been proposed for the transmetallation step. Smith *et al.* conducted a set of experiments which concluded that two equivalents of base and water are needed for the reaction to proceed; one equivalent to form

the "ate" complex and the other to mop up the boron species after transmetallation has occurred (Scheme 1.16 & 1.17).
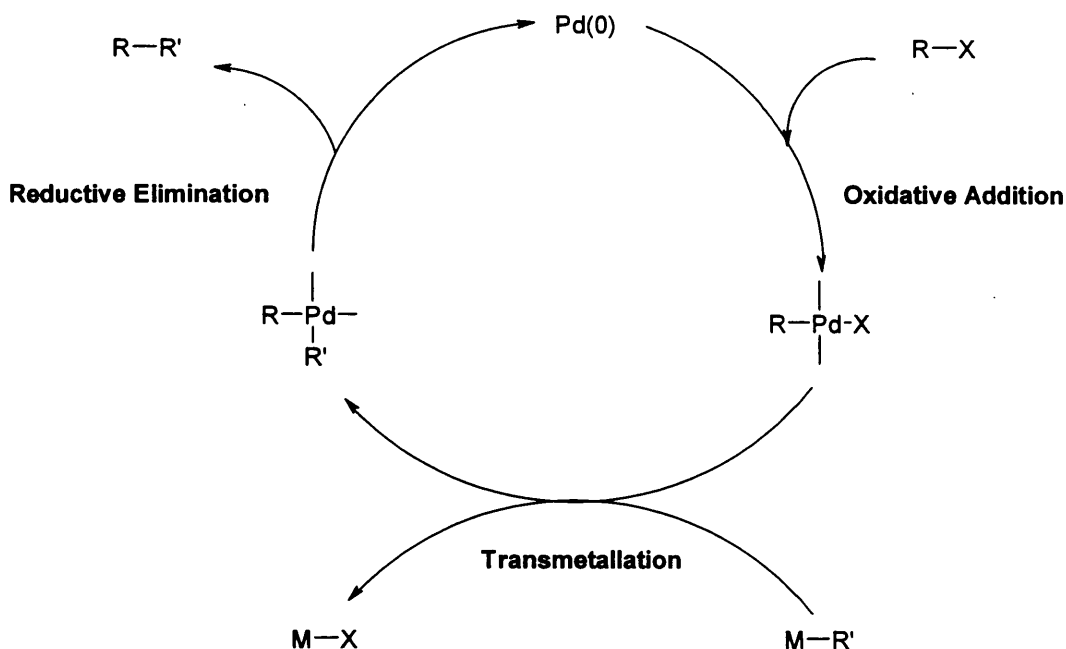
Scheme 1.15. *The general catalytic cycle for the Suzuki reaction.*

(1) $ArB(OH)_2$ + K_2CO_3 + H_2O ⟶ $ArB(OH)_3^- K^+$ + $KHCO_3$

(2) $B(OH)_3$ + K_2CO_3 + H_2O ⟶ $B(OH)_4^- K^+$ + $KHCO_3$
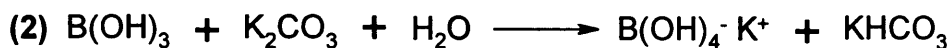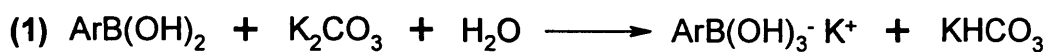
Scheme 1.16. *Effects of base on the boron derivative before and after transmetallation.*
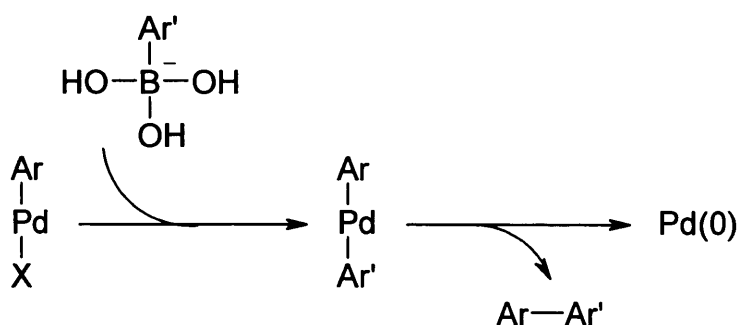
Scheme 1.17. *The boronate species in the transmetallation step.*

The second mechanism involves a metathesis reaction between sodium hydroxide or sodium methoxide and the arylpalladium(II) halide. In this mechanism, the hydroxide or methoxide ions do not act as a base, coordinating to boron centre to form the "ate" complex but, undergo an ion exchange with the halide on the palladium centre (Scheme 1.18).

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$$\text{OH}$$
$$\text{Ar'}\!\!-\!\!\overset{|}{\underset{\text{OH}}{B}}$$
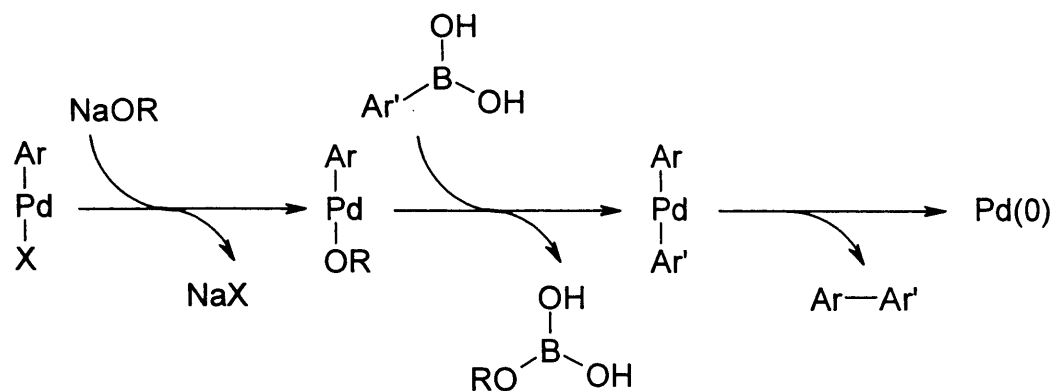
Scheme 1.18. *The metathesis in the transmetallation step.*

A reaction has been carried out with PhBr and [Pd(PPh₃)₄] to form the phenylpalladium(II) bromide. Upon addition of KOAc the bromide is substituted and phenylpalladium(II) acetate is formed.[32] This species is thought to undergo the transmetallation step as the Pd-OR bond is more reactive than the Pd-Br bond. This is because the oxygen atom is more electronegative than bromide atom, creating a greater dipole.

The third mechanism involves the addition of a fluoride additive. Addition of three equivalents of the fluoride is found to lead to an aryl(trifluoro)borate complex which undergoes the transmetallation step (Scheme 1.19).[33, 34]
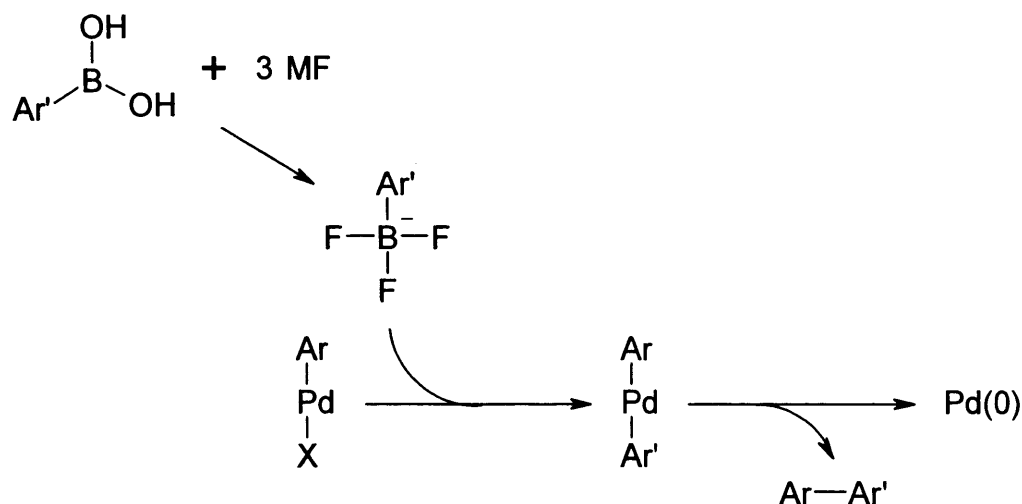
Scheme 1.19. *The effect of a fluoride additive on the transmetallation step.*

1.4.2 Palladium Catalysts

There are a wide range of palladium(0) catalysts or precursors that can be used in palladium catalysed reactions. The first catalyst used in the Suzuki reaction was [Pd(PPh₃)₄],[7] and it is still the most commonly used catalyst today. However, this catalyst is not ideal as possible scrambling can occur, with the integration of one of the phenyl groups from PPh₃ into the product. [8]

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Numerous alternative catalysts have been synthesised, however [PdCl$_2$(PPh$_3$)$_2$] and [Pd(OAc)$_2$] with phosphine ligands, are among the most commonly used. These are efficient precursors for Pd(0) as they are air-stable and are readily reduced from Pd(II) (Scheme 1.20).[29, 35, 36]
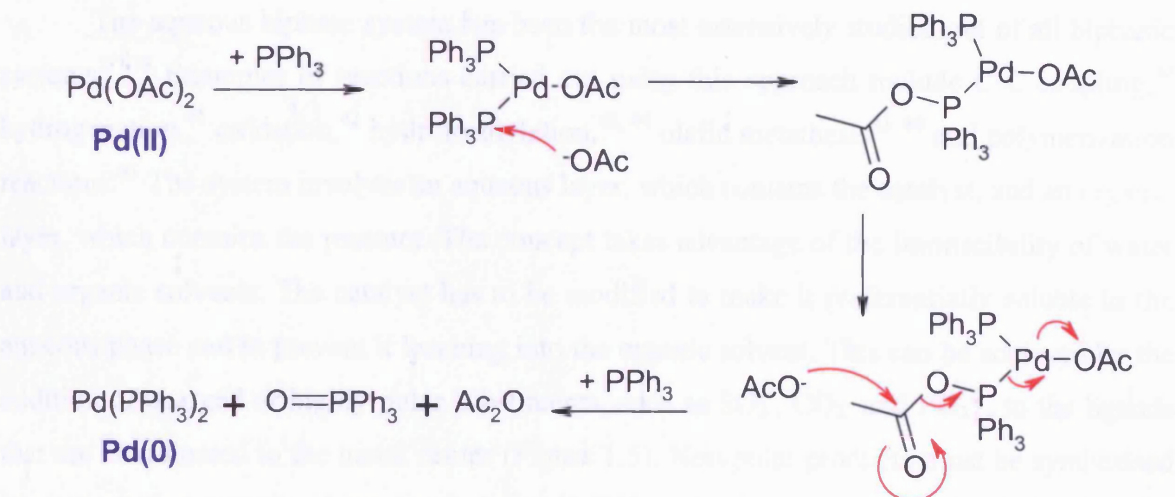
Scheme 1.20. *Mechanism for the reduction of palladium acetate with phosphine ligand.*

1.4.3 Conclusions for Palladium Reactions

The Heck and Suzuki reactions have proven to be valuable tools in carbon-carbon coupling reactions. They have been used extensively to synthesise natural and synthetic products due to their diversity and ease of application. More substrates have become available as alternatives to the traditional aryl bromides and iodides. For instance triflates and diazonium salts, both offering a broad range of functional groups for use in Heck and Suzuki reactions, can be used. The order of reactivity for these leaving groups has been determined as N$_2$ > I > Br ~ OTf >> Cl. Reactions are now also available using aryl chlorides, which are desirable for use in industry as they are relatively cheap compared to the aryl iodides and bromides.

There is no set formula for the combination of catalyst, substrate, base or solvent, for obtaining good yields. However, as the success of Heck and Suzuki reactions continues to grow and more studies into reaction conditions and parameters are carried out, the answers may become clearer.

1.5 Techniques for Facile Separation

1.5.1 Biphase Catalysis

The use of biphase catalysis has been studied as a solution to the separation problem associated with homogeneous catalysis. The concept manipulates the immiscibilities of two

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solvent mediums, which will allow facile separation by liquid-liquid extraction. The catalyst must be modified to make it sufficiently soluble in one solvent over the other. Two systems will be looked at in detail: the aqueous biphase and the fluorous biphase system.

1.5.1.1 Aqueous Biphase Catalysis

The aqueous biphase system has been the most extensively studied out of all biphasic systems.[37-39] Examples of reactions carried out using this approach include C-C coupling,[40] hydrogenation,[41] oxidation,[42] hydroformylation,[43, 44] olefin metathesis[43, 44] and polymerization reactions.[45] The system involves an aqueous layer, which contains the catalyst, and an organic layer, which contains the reactant. The concept takes advantage of the immiscibility of water and organic solvents. The catalyst has to be modified to make it preferentially soluble in the aqueous phase and to prevent it leaching into the organic solvent. This can be achieved by the addition of charged or highly polar substituents, such as SO_3^-, CO_2^- and PO_3^{2-}, to the ligands that are coordinated to the metal centre (Figure 1.5). Non-polar products must be synthesised to prevent the organic phase becoming miscible with the aqueous phase, destroying the biphase. Polar organic reagents may be used at the start of the reaction, as long as the polarity is not present in the product.
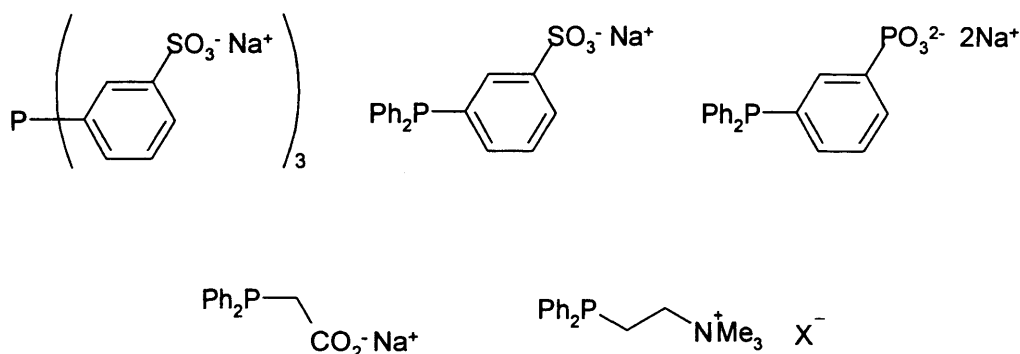
Figure 1.5. *Examples of modified ligands for use in aqueous biphase catalysis.*

The immiscibility of the solvents is an advantage as far as purification is concerned, but is a disadvantage in terms of the rate of the reaction. The reaction can only occur at the interface, therefore, limiting the interactions between catalyst and reactants. Usually, increasing the temperature can aid solubility of organic substrates in the aqueous phase but, sometimes, the extremely low solubility of the substrate in the aqueous phase inhibits the reaction. Many protocols have been designed to aid this problem; the use of ultrasound or rapid stirring to increase the surface area of the interface, co-solvents, phase transfer catalysts, detergents and surfactants.

An example of the use of aqueous biphase catalysis was demonstrated by Paetzold and Oehme, who performed a Suzuki reaction between 4-iodomethoxybenzene and phenyl boronic acid (Scheme 1.21).[46] The organic substrate was dissolved in toluene and the catalyst was dissolved in water. Ethanol was used as a co-solvent. A surfactant was used to help increase reaction yields and decrease the formation of by-products. At the end of the reaction liquid-liquid separation took place and the product was isolated, generally in high yields.
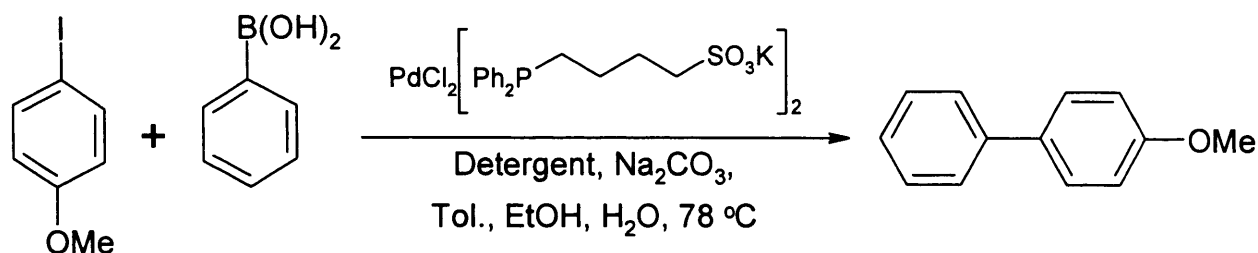
Scheme 1.21. *A Suzuki reaction carried out using aqueous biphase catalysis.*

1.5.1.2 Fluorous Biphase Catalysis

Fluorous biphase catalysis was first reported in 1994 by Horváth and Rábai[47] and has attracted a high level of interest ever since.[48-53] The concept takes advantage of the temperature dependent miscibility of perfluorocarbon (fluorous) solvents with organic solvents. The fluorous phase contains a modified fluorous-derivatised catalyst. This is a conventional catalyst which has been modified by the addition of perfluoroalkyl chains commonly known as 'fluorous ponytails', such as $-C_6F_{13}$, $-C_7F_{15}$, $-C_8F_{17}$ or $-C_{10}F_{21}$, to make it soluble in the fluorous phase. Hydrocarbon spacer groups are normally inserted between the fluorous ponytail and the donor atom in order to insulate the donor atom from the electron-withdrawing effects of the fluorous ponytails. These can be in the form of alkyl (C_2H_4 or C_3H_6), aryl (phenyl ring), a heteroatom with an alkyl component (OCH_2) or a mixture of aryl and alkyl ($C_6H_4C_2H_4$).

The organic phase contains the reagents of the reaction. At room temperature the two phases are immiscible and, therefore, two separate layers persist. At elevated temperatures, the phases become miscible and a homogeneous reaction can take place. The reaction mixture is then cooled and the two phases separate again to contain the product in the organic phase and the fluorous catalyst in the fluorous phase (Scheme 1.22). A simple liquid-liquid separation results in the separation of the organic product from the fluorous catalyst contained in the fluorous phase which can be used in another reaction.
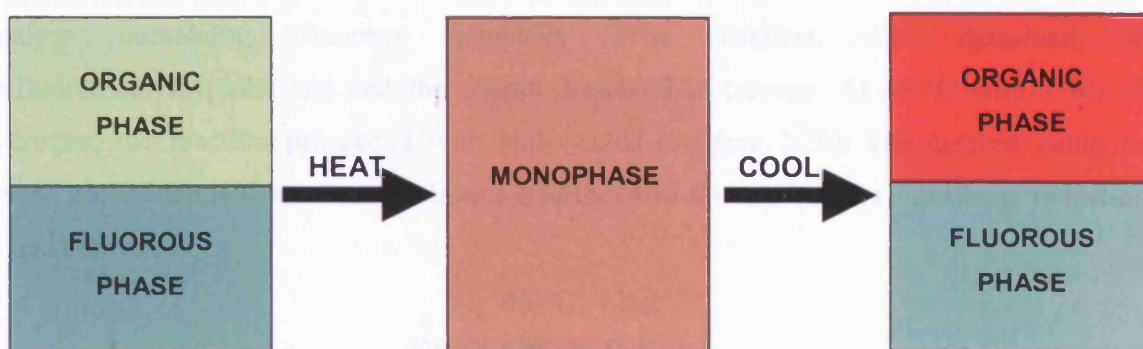
Scheme 1.22. *The concept of fluorous biphase catalysis.*

The advantages of this reaction methodology are that the reaction proceeds in a homogeneous fashion, so high yields and high selectivity can be achieved, as well as utilising the easy separation of the products from the catalyst that is normally achieved with heterogeneous reactions. Water sensitive compounds can also be used and synthesised. The final advantage is the attribute associated with the perfluorocarbon solvents. They are extremely stable, non-toxic and are excellent solvents for dissolving gases. They are able to dissolve large quantities of hydrogen, carbon monoxide, oxygen and nitrogen, which can become extremely important when the rates of the reaction are dependent on gas diffusion.

The first reported example of fluorous biphase catalysis was the hydroformylation of 1-alkenes.[47, 54] The alkene, either 1-octene or 1-decene, was dissolved in a toluene organic phase and the catalyst, formed *in situ*, was dissolved in the fluorous phase, perfluoromethylcyclohexane. The reaction was carried out at 100 °C at 10 bar pressure of CO/H_2 and, under these conditions, a homogeneous reaction took place (Scheme 1.23). Separation of the products from the catalyst, using phase separation, gave high purity organic products with high *n/i* ratios. The catalyst was reused a further eight consecutive times with a total turnover number of more than 35,000. The levels of rhodium leaching into the organic phase were determined to be 1.18 ppm per mole of product.

$$RCH=CH_2 \xrightarrow[\substack{HRh(CO)[P(C_2H_4C_6F_{13})_3]_3 \\ Toluene\ /\ CF_3C_6F_{11} \\ 100\ ^oC}]{CO\ /\ H_2,\ 10\ bar} RCH_2CH_2CHO \quad + \quad R(CH_3)CHCHO$$

$$\phantom{RCH=CH_2 \xrightarrow{xxxxxxx}} \textit{normal} \qquad\qquad \textit{iso}$$
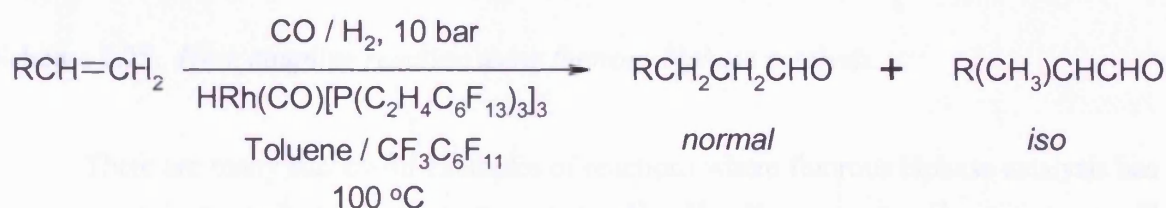
Scheme 1.23. *Hydroformylation in the fluorous biphase system.*

Horváth and co-workers have also demonstrated the hydrogenation of alkenes under fluorous biphase conditions.[55] The modified catalyst was an aliphatic version of Wilkinson's

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catalyst containing fluorous ponytails. The catalyst was dissolved in perfluoromethylcyclohexane and the alkene dissolved in toluene. At 45 °C with 1 bar of hydrogen, the reaction proceeded with high yields (Scheme 1.24). The catalyst could be reused under identical reaction conditions a further two times without a significant reduction in reaction yield.

$$RCH{=}CH_2 \xrightarrow[\text{Toluene, } CF_3C_6F_{11}]{\overset{\text{H}_2,\ 45\ ^\circ\text{C, 1 bar}}{Rh(Cl)[P(C_2H_4C_6F_{13})_3]_3}} RCH_2CH_3$$
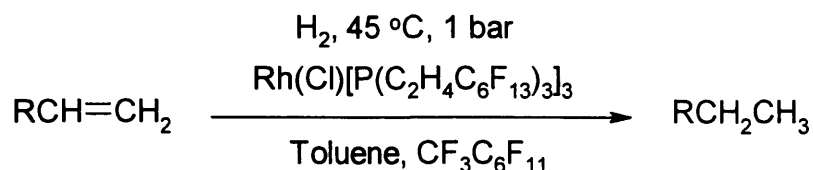
Scheme 1.24. *Hydrogenation reaction carried out using fluorous biphase catalysis.*

Moineau and co-workers have demonstrated Heck reactions using fluorous biphase catalysis.[56] The palladium(II) catalysts were prepared *in situ* from fluorous phosphines with [Pd(dba)$_2$] or [Pd(OAc)$_2$] and a variety of aryl iodides were coupled with methyl acrylate (Scheme 1.25). A solvent mix of acetonitrile and DC-100 (mainly *n*-perfluorooctane) was used as the organic and fluorous phase respectively. At 80 °C a homogeneous phase was achieved and the reaction occurred with quantitative yields for the first run. At room temperature, a liquid-liquid extraction was carried out and the fluorous phase was then reused in catalysis. In the second run, yields fell to between 95 – 85 % and dropped further to between 70 – 40 % in the third run. The authors did not give an explanation for the drop in activity, but it is likely that there was leaching of the fluorous catalyst into the organic phase.

R = H, NO$_2$, OMe   R' = OCH$_2$C$_7$F$_{15}$, C$_6$F$_{13}$
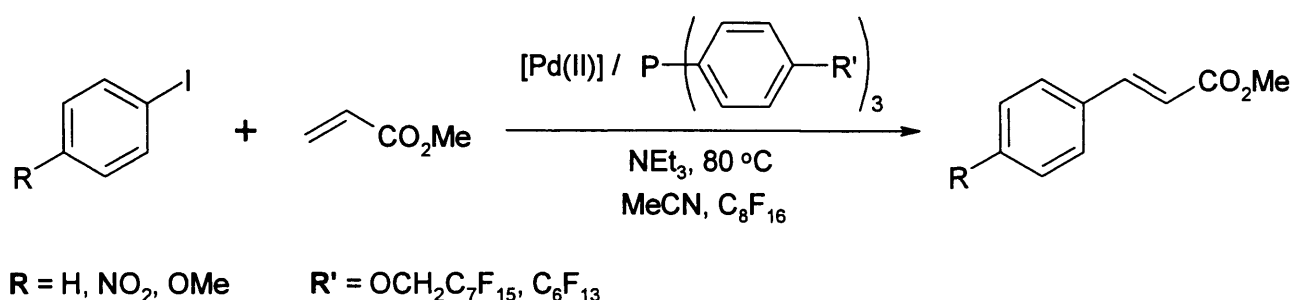
Scheme 1.25. *Heck coupling reaction using fluorous biphase catalysis.*

There are many successful examples of reactions where fluorous biphase catalysis has been employed including hydroformylation,[47, 48, 54] oxidation,[57] epoxidation,[57] hydrogenation,[55] hydroboration,[58] hydrosilylation,[59] hydride reduction[60] and C-C coupling reactions.[56, 61] However, despite the wide number of applications, this approach is not perfect and has disadvantages associated with it. Firstly, the perfluorocarbon solvents are expensive and environmentally persistent. Secondly, a high percentage of fluorine is needed within the fluorous-derivatised catalysts to allow them to be preferentially soluble in the fluorous phase.

Although no exact figure has been set, it has been agreed that a molecule needs to contain approximately 60 % of fluorine by weight to be preferentially fluorous soluble. Finally, there is also a possibility for the catalyst to leach into the organic phase. Over time, this will lead to lower turnover frequencies and is particularly a problem with regards to unwanted, toxic heavy metals in pharmaceutical compounds.

1.5.1.3 Conclusions for Biphase Catalysis

Both biphase systems discussed offer a simple method for the separation of products from their catalysts but both come with their own drawbacks. The aqueous biphase system is limited to reagents, products and catalysts that are not moisture sensitive. The immiscibility of organic substrates with an aqueous media leads to lower reaction rates being achieved in aqueous biphase catalysis. Many protocols have been developed in an attempt to overcome this problem.

Fluorous biphase catalysis offers higher rates of reactions due to the ability of the system to homogenise with an increase in temperature. Perfluorocarbon solvents have the ability to dissolve high volumes of gases, which may also increase yields, as well as tolerating moisture-sensitive compounds. They are also extremely stable solvents, which is an advantage in terms of reactions, but a disadvantage from an environmental perspective, combined with their high cost makes them unattractive for large-scale industrial applications.

Both systems pose two major drawbacks; the first being catalyst leaching in certain systems and the second being the extensive ligand modification which is required in order to achieve the desired solubility characteristics. The ligand modification can often be expensive, time consuming and create great difficulty.

1.5.2 Thermomorphic Catalysis

An alternative approach to fluorous biphase catalysis is to use thermomorphic fluorous-derivatised catalysts.[62] In this method, a solid fluorous-derivatised catalyst is suspended in a conventional organic solvent, containing reactants. At low temperatures the fluorous catalyst shows very little or no solubility in the organic solvent. However, at elevated temperatures the catalyst becomes soluble, creating a monophase, allowing a homogeneous reaction to proceed. Upon cooling, the catalyst precipitates out of solution and a simple filtration recovers the catalyst, which can be used in further reactions (Scheme 1.26).

| Reactants | Heat → | Monophasic | Cool → | Product |

Insoluble thermomorphic fluorous catalyst with reactants | Fluorous-tagged catalyst and reactants in same phase | Insoluble thermomorphic fluorous catalyst with product
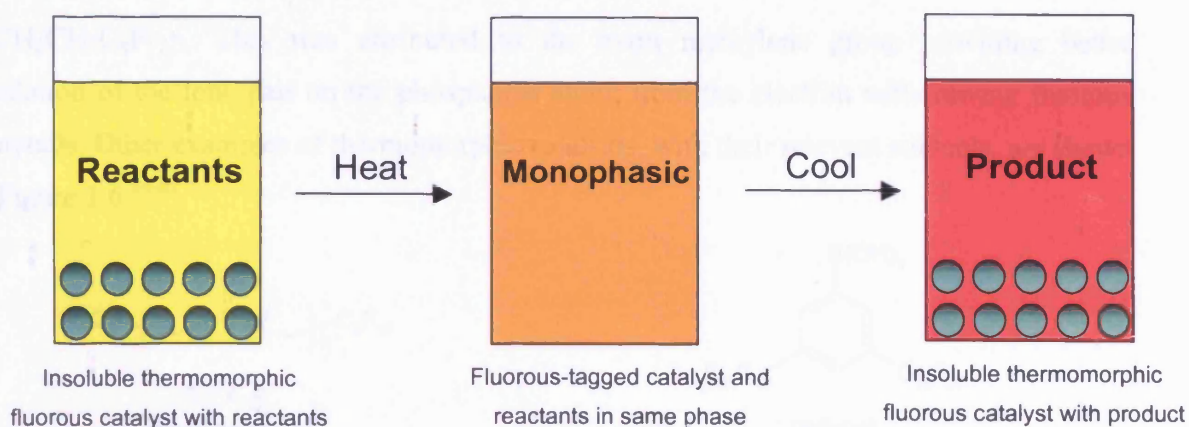
Scheme 1.26. *Thermomorphic catalysis.*

The use of a highly fluorinated catalyst is advantageous due to their temperature dependent solubilities in organic solvents. The reaction proceeds *via* a homogeneous reaction phase, so high yields and levels of selectivities can be achieved. The thermomorphic properties of the catalyst allow facile separation of the product from the catalyst with the potential to reuse the catalyst in further reactions.

Gladysz *et al.* have demonstrated the use of a thermomorphic fluorous-derivatised phosphine to catalyse the conjugate addition of alcohols to methyl propiolate in *n*-octane (Scheme 1.27).[62, 63] At -30 °C there are two phases, but at 65 °C homogeneous conditions are achieved. The catalyst is recovered by cooling the reaction mixture to -30 °C, which causes it to precipitate out of solution. The catalyst can then be reused in further reactions with no significant reduction in yields.

$$\text{propiolate} + \text{R'OH} \xrightarrow[\text{n-octane, 65 °C}]{\text{10 mol. \% cat.}} \text{R'O} \text{---} \text{ester}$$

cat. = P(CH$_2$CH$_2$C$_8$F$_{17}$)$_3$
or
P(CH$_2$CH$_2$CH$_2$C$_8$F$_{17}$)$_3$
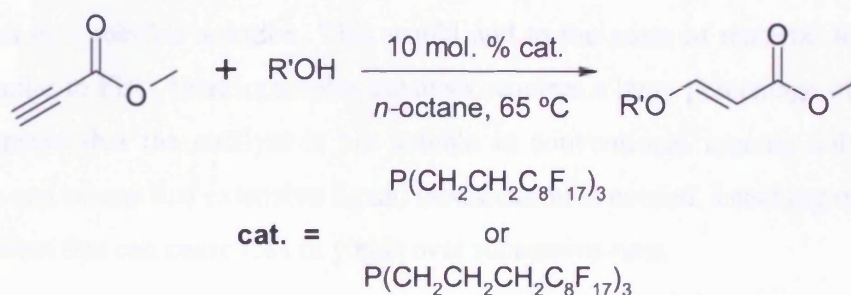
Scheme 1.27. *Thermomorphic catalysis using a fluorous-derivatised phosphine catalyst.*

Leaching levels of the catalyst, P(CH$_2$CH$_2$C$_8$F$_{17}$)$_3$, were determined, by ^{19}F NMR spectroscopy to be 2.3% per cycle. Teflon shavings were also used as a solid support, anchoring the catalyst around the surface of the support. Lower leaching levels, which can be attributed to the affinity of the catalyst for the support and higher yields were achieved using

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$P(CH_2CH_2C_8F_{17})_3$. This was attributed to the extra methylene group providing better insulation of the lone pair on the phosphorus atom, from the electron withdrawing fluorous ponytails. Other examples of thermomorphic catalysts, with their relevant solvents, are shown in Figure 1.6.[64-67]
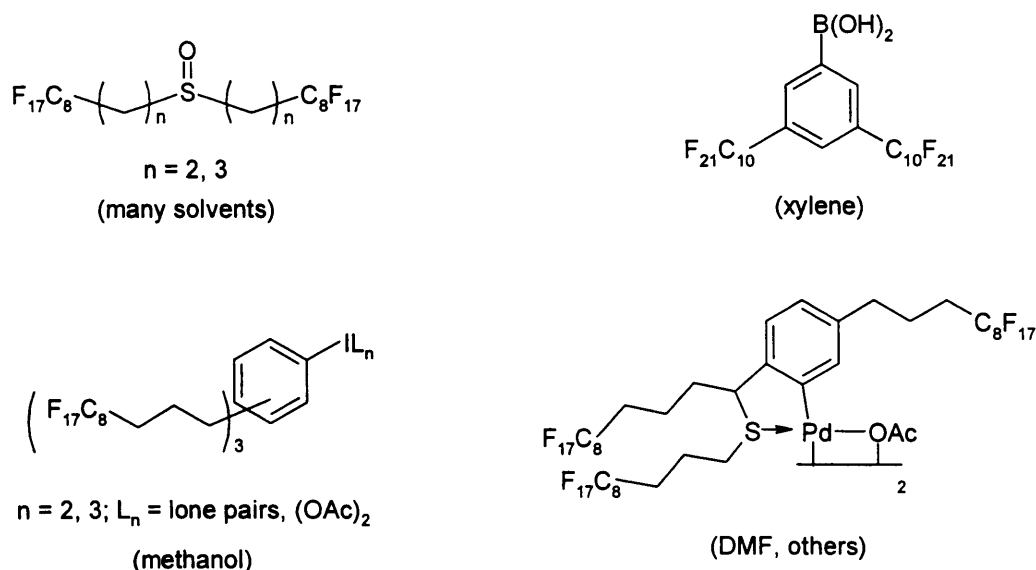
Figure 1.6. *Thermomorphic fluorous-derivatised catalysts and their relevant solvents.*

Thermomorphic catalysis has illustrated a major advantage over the fluorous biphase system; there is no need for perfluorocarbon solvents. However, there are still some disadvantages associated with thermomorphic catalysis. Insoluble by-products can cause problems with catalyst recovery, which can add extra steps to isolate the catalyst. The requirement for elevated temperatures to achieve a homogeneous phase means that this technique is only appropriate for high temperature reactions. The use of low catalyst loadings can lead to such small quantities of catalyst that it may be difficult to manipulate. The use of solid supports is a possible solution. This would add to the mass of material that would be recycled. Similar to FBC, thermomorphic catalysis requires a large percentage of fluorine, by weight, to ensure that the catalyst is not soluble in conventional organic solvents at low temperatures and means that extensive ligand modification is needed. Leaching of the catalyst is also a problem that can cause loss in yields over successive runs.

1.5.3 Polymer Supports for Catalysis

The most commonly used organic supports are polystyrene and styrene-divinylbenzene copolymer beads that are modified with different functional groups that can bind to metal centres, such as diphenylphosphine,[68] tertiary amino,[69] thiol[70] and carbene[71] groups. The level of cross linking in the polymer can affect the reactivity of the metal bound catalyst; a low level can lead to a flexible polymer that results in unfavourable interactions

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catalyst; a low level can lead to a flexible polymer that results in unfavourable interactions between functional groups, whereas, a high level prevents the substrate from entering the polymer matrix.

Polymer-supported catalysis has been successful in a number of different systems including hydroformylation,[72] hydrogenation,[72] oligomerisation,[73] Suzuki,[74] Heck[75] and metathesis[76] reactions. Although the polymer-supported catalyst can be recovered over several cycles, lower reaction rates are generally observed in polymer supported systems in comparison to homogeneous analogues. This is attributed to diffusion rates of the reactants into the polymer core. The low mechanical strength and thermal stability of the polymer-supports limit the number of times the supports can be recovered and reused.

1.5.4 Supported Aqueous Phase Catalysis

Supported Aqueous Phase Catalysis (SAPC) was first introduced by Arhancet *et al.* in 1989 and is a combination of aqueous biphase catalysis and catalysts covalently-bound to supports.[77] A water-soluble catalyst is dissolved in an aqueous solvent and distributed over a hydrophilic support, such as silica or glass beads, before the support is dried. The support is then hydrated with a specific amount of water, anchoring the catalyst to the support without the covalent bonds. Reactions are carried out in non-polar hydrophobic solvents and the catalytic reactions occur at the interface of the two solvents (Figure 1.7). The catalyst is still mobile in the supported hydrophilic solvent and product/catalyst separation can be achieved by simple filtration.
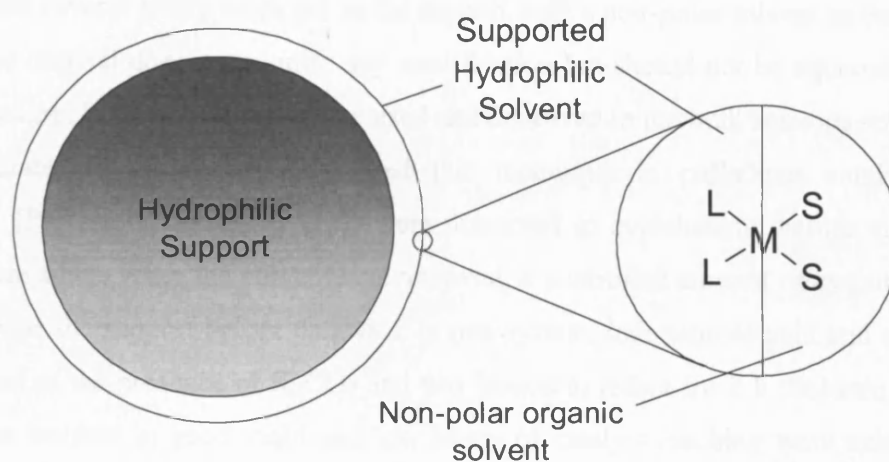
M = Catalyst Metal Centre, L = Hydrophilic Ligand, S = Substrate

Figure 1.7. *Supported Aqueous Phase Catalysis.*

Williams *et al.* used this technique in the hydrofomylation of oleyl alcohol,[78] a water insoluble substrate, which does not react under biphasic conditions.[79] The water-soluble

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controlled pore glass support (CPG-240). Using the supported catalyst, conversions of 97 % were achieved (Scheme 1.28).
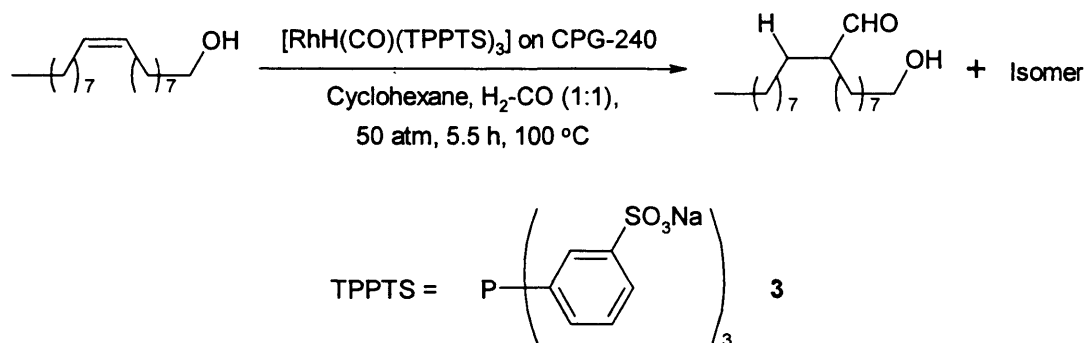
Scheme 1.28. *Hydroformylation using SAPC.*

This technique has all of the advantages associated with ABC, however, due to the large surface area the solvent interface is extremely large and, therefore, significantly higher reaction rates are achieved in SAPC. As there are no covalent bonds, the catalyst has the mobility to adopt structural changes during the catalytic cycle. However, the systems are limited to organic substrates that are not soluble in polar solvents and are not water sensitive. The catalyst also has to be modified to ensure it is preferentially soluble in the aqueous phase.

1.5.5 Supported Organic Phase Catalysis

Supported Organic Phase Catalysis (SOPC) uses the same principles as SAPC, however, a hydrophobic support and catalyst is used in an aqueous solvent system. This approach uses reverse phase silica gel as the support with a non-polar solvent as the supported solvent. The catalyst does not require any modification but should not be aqueous soluble to prevent leaching. Polar substrates can be used and dissolved in the bulk aqueous solvent.

Williams *et al.* successfully used this technique in palladium catalysed Heck reactions.[80] [Pd(OAc)$_2$] and PPh$_3$ (1:4) were dissolved in cyclohexane before stirring with reverse phase silica. After the solvent was removed, a controlled amount of cyclohexane was used to solvate the support before catalysis. In one system, iodobenzoic acid and acrylic acid were coupled in the presence of K$_2$CO$_3$ and was heated to reflux for 2 h (Scheme 1.29). The product was isolated in good yield and low levels of catalyst leaching were achieved. The reverse phase beads were recovered and reused seven times with no apparent loss in activity.

Scheme 1.29 reaction conditions:

$$\text{2 mol-\% [Pd(OAc)}_2]$$
$$\text{8 mol-\% PPh}_3$$
$$\text{Supported on RPSG beads}$$
$$\xrightarrow{\quad\quad\quad}$$
$$\text{1.5 eq K}_2\text{CO}_3, \text{H}_2\text{O},$$
$$\text{100 °C, 2 h}$$

HO$_2$C–(aryl iodide) + CH$_2$=CH–CO$_2$H → (aryl)–CH=CH–CO$_2$H (HO$_2$C substituted)

Yield = 90 %
0.18 % Pd leaching
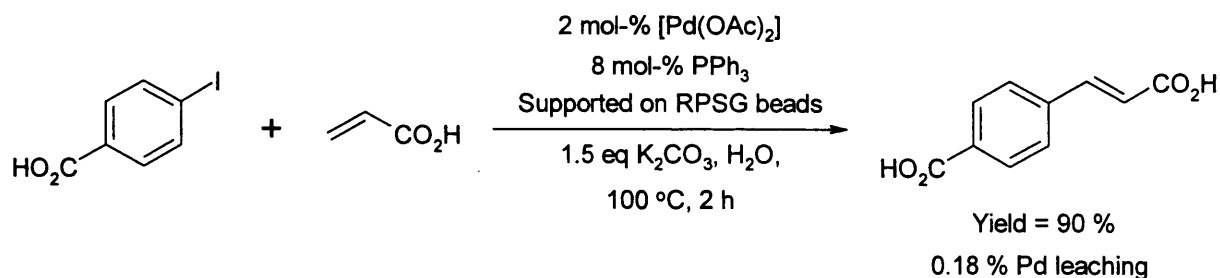
Scheme 1.29. *Heck reaction using SOPC.*

SOPC offers some advantages as SAPC, such as no ligand modification but still suffers from incompatibilities with water-sensitive compounds.

1.5.6 Fluorous Reverse Phase Silica Gel

Fluorous Reverse Phase Silica Gel (FRPSG) was first reported in 1978 by Berendsen, Pikaart and de Galan[81] and was used in analytical chemistry as a substitute for standard reverse phase columns in the separation of organic molecules. Its use in preparative solid phase extraction is a relatively new area of research.[82] FRPSG has been used in examples of:

- column chromatography of fluorous compounds;[83]

- solid phase extraction of fluorous catalysts;[84, 85]

- solid phase extraction as an alternative to column chromatography of fluorinated compounds;[86]

- fluorous mixture synthesis. [87]

The synthesis of FRPSG is similar to the synthesis of reverse phase silica gel (RPSG).[88] In RPSG synthesis, silica gel is reacted with a chlorosilane in the presence of base (Scheme 1.30). Silica gel elutes products in order of increasing polarity, whereas RPSG elutes products in order of decreasing polarity. In the synthesis of FRPSG, silica gel is reacted with a fluorous-derivatised chlorosilane (Scheme 1.31). FRPSG has shown unique properties, with a low retention for organic molecules. Molecules containing only a low amount of fluorine (w/w <60 %) can be retained on the column.[83] This makes FRPSG a suitable candidate for solid phase extraction of organic and light fluorous molecules.

$$\text{Silica}-\text{OH} \quad + \quad \underset{\underset{\text{Me}}{|}}{\overset{\overset{\text{Me}}{|}}{\text{Cl}-\text{Si}-\text{C}_{18}\text{H}_{37}}} \quad \xrightarrow{\text{Base}} \quad \underset{\underset{\text{Me}}{|}}{\overset{\overset{\text{Me}}{|}}{\text{Silica}-\text{Si}-\text{C}_{18}\text{H}_{37}}}$$

Silica Gel   **Reverse Phase Silica Gel**
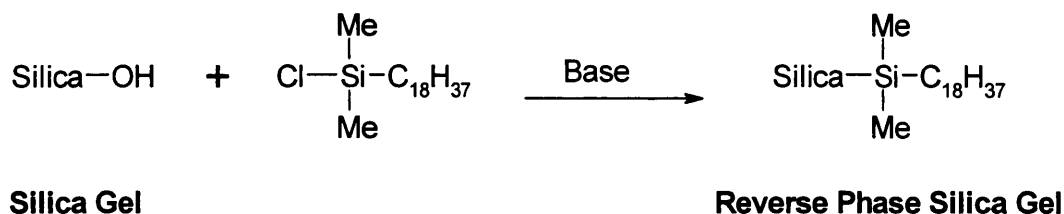
Scheme 1.30. *The synthesis of Reverse Phase Silica Gel.*

Me
|
Silica—OH + Cl—Si—CH$_2$CH$_2$C$_8$F$_{17}$ Base   Silica—Si—CH$_2$CH$_2$C$_8$F$_{17}$
| |
Me   Me

Silica Gel   **Fluorous Reverse Phase Silica Gel**
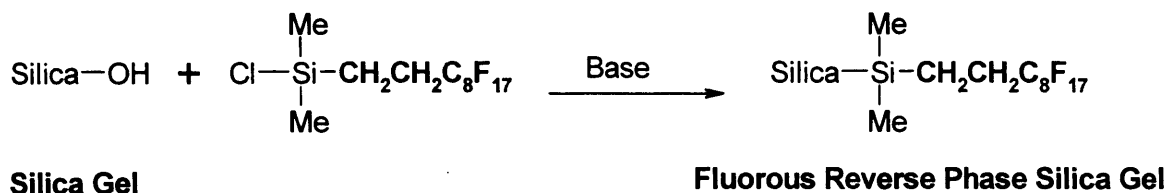
Scheme 1.31. *The synthesis of Fluorous Reverse Phase Silica Gel.*

FRPSG has been used in the separation of fluorinated molecules by preparative HPLC. The greater the fluorine content in a molecule the better the retention on the surface of the FRPSG. An example is the separation of fluorinated amides **4** (Figure 1.8). The mobile phase gradient was methanol/water (80:20), increasing to methanol (100%) over 30 mins. The non-fluorinated amide was eluted first with a short retention time and the fluorinated amides were then eluted in order of increasing fluorine content.

Rf	C$_7$H$_{15}$	C$_4$F$_9$	C$_6$F$_{13}$	C$_7$F$_{15}$	C$_8$F$_{17}$	C$_9$F$_{19}$	C$_{10}$F$_{21}$
R$_t$ (min)	2.6	4.6	9.7	13.5	17.7	22.0	26.0

4
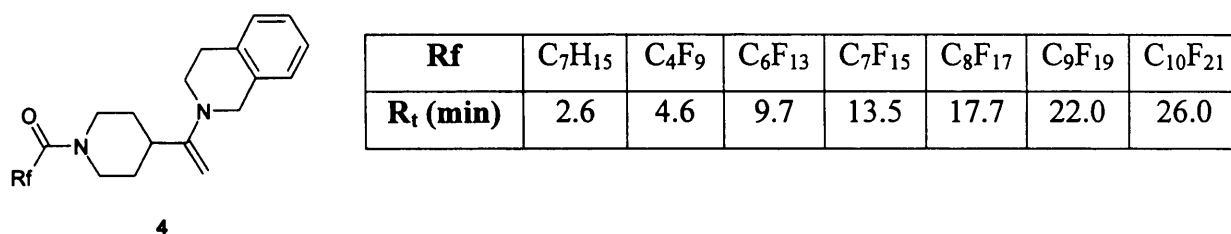
Figure 1.8. *HPLC separation of a mixture of amides using a FRPSG column.*

FRPSG has been used in solid phase extraction, where an organic molecule has been modified with fluorous ponytails and used in an organic reaction with organic solvents. At the end of the reaction the solvent is removed and the residue is loaded onto a short column of FRPSG. The organic product can be eluted with a fluorophobic solvent (e.g. acetonitrile or methanol) leaving the fluorous-derivatised reagent still bound to the column. This can then be eluted with a fluorophilic solvent (e.g. diethyl ether or THF) giving facile separation of the fluorinated and non-fluorinated products (Scheme 1.33).

Curran *et al.* have demonstrated the application of solid phase extraction, using FRPSG, to separate fluorous metal compounds from organic products.[89-91] In these reactions a range of aldehydes were reacted with fluorous-derivatised tin compounds (Scheme 1.32). At the end of the reaction, the residues were loaded onto a short column of FRPSG and eluted with acetonitrile to produce the corresponding alcohols in good yields and purity. The fluorous-derivatised tin by-product was retained on the column.

25
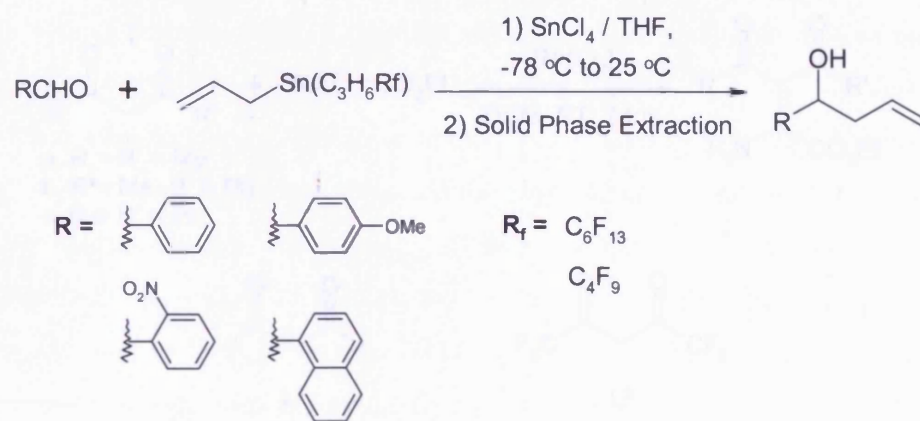
Scheme 1.32. *The use of FRPSG in solid phase extraction.*
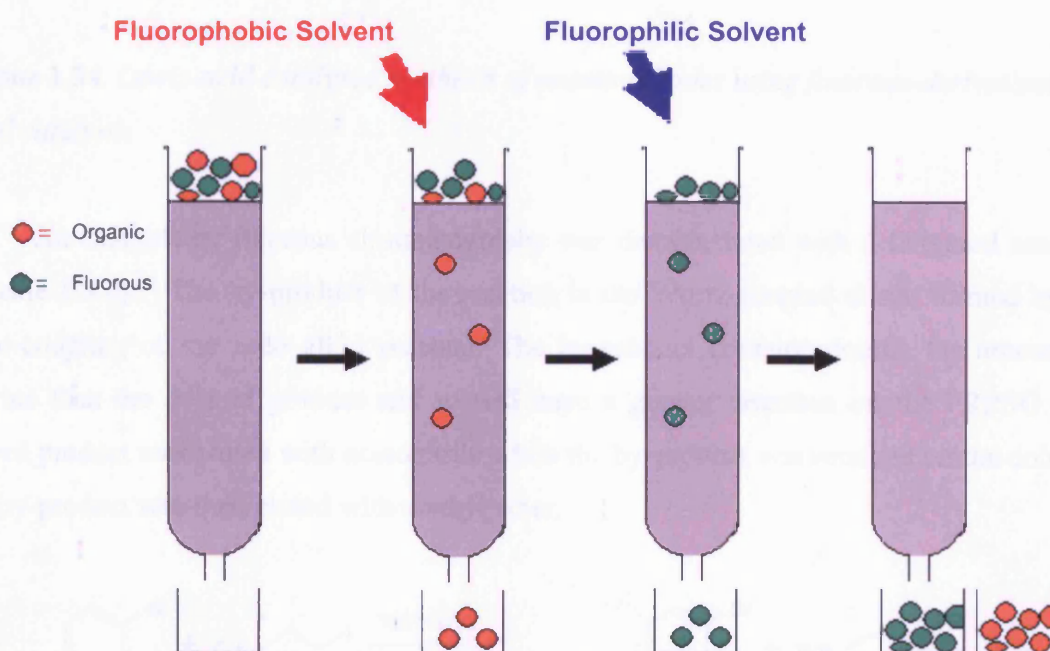
Scheme 1.33. *Solid phase extraction using FRPSG.*

An example of solid phase extraction of fluorous catalysts was shown by Stuart *et al.* in the Lewis-acid catalysed synthesis of enaminodiones (Scheme 1.34).[84] A nickel catalyst was derivatised with fluorous ponytails and could be used in conventional organic solvents. At the end of the reaction the crude reaction mixture was loaded onto a short column of FRPSG and the organic product was eluted with dichloromethane leaving the fluorous catalyst still bound to the column. This was then eluted with diethyl ether and reused in further reactions. There were four different catalysts tested which all showed different selectivities in the reaction. However, only the catalyst, [Ni(L^4)$_2$] was successfully recycled using FRPSG.
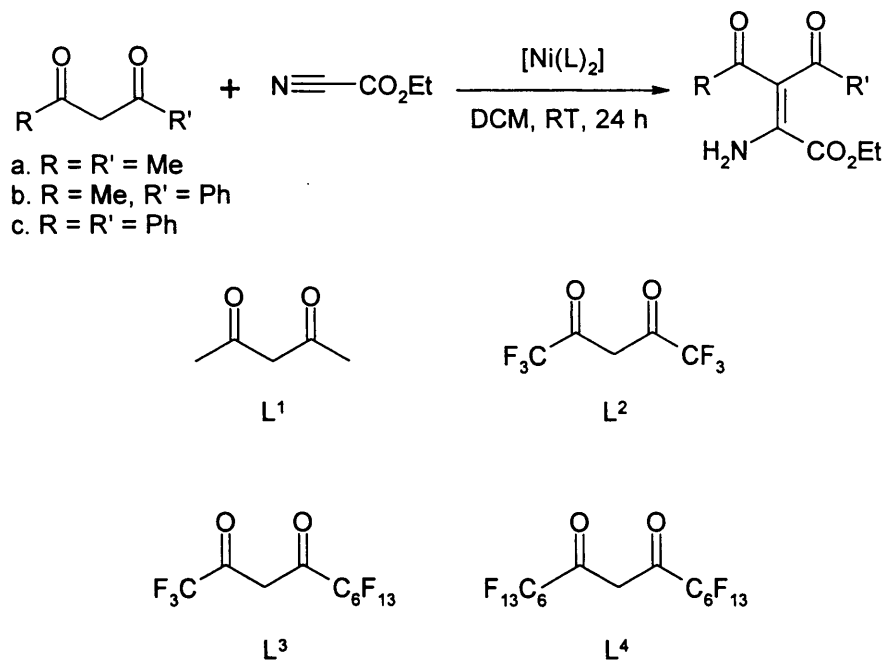
Scheme 1.34. *Lewis-acid catalysed synthesis of enaminodiones using fluorous-derivatised nickel catalysts.*

An example of fluorous chromatography was demonstrated with a Grignard reaction (Scheme 1.35.).[86] The by-product of the reaction is the Wurtz-coupled dimer formed by the homo-coupling of the iodo alkyl reactant. The by-product contains double the amount of fluorine than the desired product and so will have a greater retention on the FRPSG. The desired product was eluted with acetonitrile while the by-product was retained on the column. The by-product was then eluted with diethyl ether.
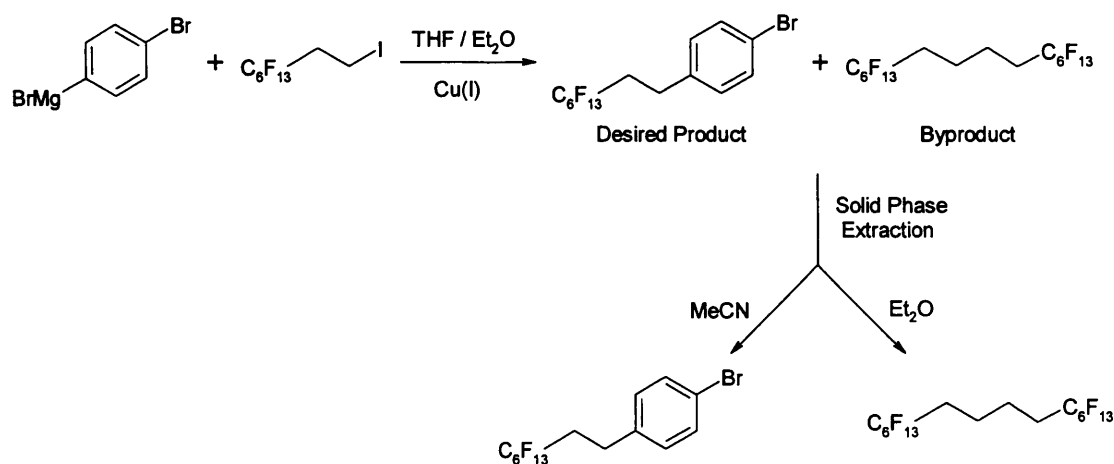
Scheme 1.35. *Reaction purified by fluorous solid phase extraction.*

This separation technique is extremely useful as the desired product and by-product are difficult to separate using standard techniques. Both products have similar retention

values, on standard silica, and similar boiling points so separation by normal column chromatography or distillation would be extremely difficult.

Another application of FRPSG columns is in Fluorous Mixture Synthesis (FMS) (Scheme 1.36).[87] A set of substrates are each tagged with a different fluorous domain containing an increase in the fluorine content (CF_3, C_2F_5, C_3F_7, etc). The tagged substrates are mixed together and taken through a multistep synthesis. The mixture of tagged products can be separated (or *demixed*) using fluorous-HPLC to give the individually pure tagged products. These can then be detagged to give the final pure products.

$F_1Tag + A \longrightarrow F_1Tag—A$
$F_2Tag + B \longrightarrow F_2Tag—B$
$F_3Tag + C \longrightarrow F_3Tag—C$

$\xrightarrow{D}$

$F_1Tag—A—D$
$F_2Tag—B—D \xrightarrow{E}$ F
$F_3Tag—C—D$

$F_1Tag—A—D—E—F$
$F_2Tag—B—D—E—F$
$F_3Tag—C—D—E—F$

F-HPLC

$F_1Tag—A—D—E—F \longrightarrow A—D—E—F$
$F_2Tag—B—D—E—F \longrightarrow B—D—E—F$
$F_3Tag—C—D—E—F \longrightarrow C—D—E—F$

TAGGED   SYNTHESIS   DEMIXED   DETAGGED
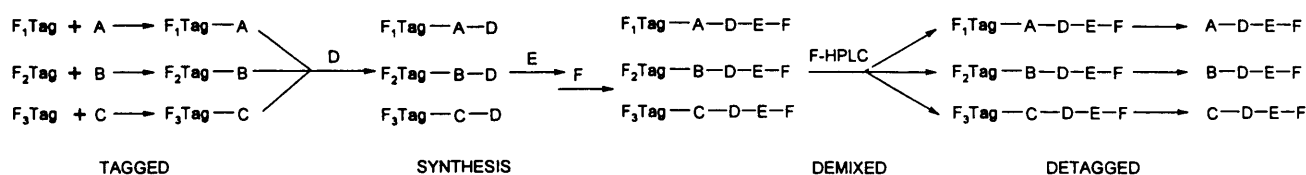
Scheme 1.36. *Concept of Fluorous Mixture Synthesis*

1.6 Outline of Research

Palladium catalysed reactions have been demonstrated to be a fundamental tool for organic chemists. A variety of methods have been investigated in order to recover and reuse the catalyst with different levels of success.

Systems using FBC achieve good activities as the reactions are homogeneous. However, this approach has problems associated with leaching of the catalyst into the organic phase leading to a drop in yields in subsequent catalytic runs. A large percentage of fluorine is required in the catalyst for it to be preferentially soluble in the fluorous phase. With this in mind, as well the cost and the environmental persistence associated with fluorous solvents, research groups have started to move away from FBS to other fluorous methods. Supported catalysis using FRPSG omits the use of perfluorocarbon solvents, however, the heterogeneous reaction conditions decrease catalytic activity, resulting in longer reaction times, and have demonstrated poor recycling results.

Solid phase extraction (SPE) can be used as a simple and efficient method to separate catalysts from organic products. Using the idea of incorporating a fluorous domain to create a fluorous-derivatised catalyst would serve as an immense advantage; not only could the organic product be isolated with minimum contamination from the catalyst, but the catalyst could be reused in further catalysis.

It is envisaged that by using a 'light' fluorous approach, reactions with fluorous catalysts could be carried out homogeneously in conventional organic solvents and fluorous SPE could be used to recover the catalyst.

The work presented in this thesis describes the investigation of a range of fluorous catalysts in palladium catalysed reactions. Chapter 2 focuses on the synthesis of monodentate fluorous triarylphosphine palladium complexes. The electron-withdrawing effects of perfluoroalkyl groups are evaluated using different positions around the aryl ring along with different spacer groups. Chapter 3 focuses on the synthesis of a fluorous pincer palladium complex. Optimum reaction conditions are investigated through solvent/base screens. Chapter 4 focuses on the synthesis of a range of fluorous monodentate, bidentate and pincer NHC ligands and complexes. In all of the chapters, the activities of the catalysts were evaluated in Heck and Suzuki reactions and compared to the parent, non-fluorous catalysts. Separation studies were conducted with fluorous pre-catalysts and post reaction fluorous solid phase extraction was carried out to evaluate catalyst recovery and recycling.

1.7 References for Chapter One

1   M. W. Urquhart, *Personal Communation*.

2   C. Masters, 'Homogeneous Transition-Metal Catalysis - A Gentle Art.' Chapman and Hall, London, 1981.

3   O. Roelen, *Angew. Chem.*, 1948, **60**, 62.

4   A. O. Aliprantis and J. W. Canary, *J. Am. Chem. Soc.*, 1994, **116**, 6985.

5   J. A. Kerr, 'CRC Handbook of Chemistry and Physics 1999-2000: A Ready-Reference Book of Chemical and Physical Data (CRC Handbook of Chemistry and Physics)', CRC Press, 2000.

6   P. Fitton and E. A. Rick, *J. Organometal. Chem.*, 1971, **28**, 287.

7   N. Miyaura, K. Yamada, and A. Suzuki, *Tetrahedron Lett.*, 1979, **36**, 3437.

8   S. Kotha, K. Lahiri, and D. Kashinath, *Tetrahedron*, 2002, **58**, 9633.

9   A. Huth, I. Beez, and I. Schumann, *Tetrahedron*, 1989, **45**, 6679.

10   J.-M. Fu and V. Snieckus, *Tetrahedron Lett.*, 1990, **31**, 1665.

11   T. Oh-e, N. Miyaura, and A. Suzuki, *Synlett*, 1990, 221.

12   A. Jutand and A. Mosleh, *Organometallics*, 1995, **14**, 1810.

13   T. Oh-e, N. Miyaura, and A. Suzuki, *J. Org. Chem.*, 1993, **58**, 2201.

14   S. Darses, J. Tuyet, and J.-P. Genet, *Tetrahedron Lett.*, 1996, **37**, 3857.

15   S. Darses and J.-P. Genet, *Tetrahedron Lett.*, 1997, **38**, 4393.

16   T. Mizoroki, K. Mori, and A. Ozaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 581.

17   R. F. Heck and J. P. Nolley, *J. Org. Chem.*, 1972, **14**, 2320.

18   N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457.

19   A. Suzuki, *J. Organometal. Chem.*, 1999, **576**, 147.

20   J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, and M. Lemaire, *Chem. Rev.*, 2002, **102**, 1359.

21   S. P. Stanforth, *Tetrahedron*, 1998, **54**, 263.

22   A. R. Martin and Y. Yang, *Acta Chem. Scand.*, 1993, **47**, 221.

23   N. Miyaura, T. Yanagi, and A. Suzuki, *Synth. Commun.*, 1981, **11**, 513.

24   N. Miyaura, K. Yamada, H. Suginome, and A. Suzuki, *J. Am. Chem. Soc.*, 1985, **107**, 972.

25   K. S. Chan, X. Zhou, M. T. Au, and C. Y. Tam, *Tetrahedron*, 1995, **51**, 3129.

26   C. K. Chang and N. Bag, *J. Org. Chem.*, 1995, **60**, 7030.

27   T. Ishiyama, S. Abe, N. Miyaura, and A. Suzuki, *Chem. Lett.*, 1992, 691.

28   A.-S. Castanet, F. Colobert, and T. Schlama, *Org. Letts.*, 2000, **2**, 3359.

29   G. B. Smith, G. C. Dezeny, D. L. Hughes, A. O. King, and T. R. Verhoeven, *J. Org. Chem.*, 1994, **59**, 8151.

30   B. Shaw, *New J. Chem*, 1998, 77.

31   M. J. S. Dewar and R. Jones, *J. Am. Chem. Soc.*, 1967, **89**, 2408.

32   T. Ishiyama, M. Murata, and N. Miyaura, *J. Org. Chem.*, 1995, **60**, 7508.

33   S. W. Wright, D. L. Hageman, and L. D. McClure, *J. Org. Chem.*, 1994, **59**, 6095.

34   J. W. Benbow and B. L. Martinez, *Tetrahedron Lett.*, 1996, **37**, 8829.

35   C. Amatore, A. Jutand, and M. A. M'Barki, *Organometallics*, 1992, **11**, 3009.

36   C. Amatore and A. Jutand, *Acc. Chem. Res.*, 2000, **33**, 314.

37   B. Cornils, *Organic Process Research & Development*, 1998, **2**, 121.

38   B. Cornils, *J. Mol. Catal. A: Chem.*, 1999, **143**, 1.

39   D. J. Adams, P. J. Dyson, and S. J. Tavener, 'Chemistry in alternative reaction media', John Wiley & Sons Ltd, Chichester, UK, 2003.

40   C. Mercier and P. Chabardes, *Pure Appl. Chem.*, 1994, **66**, 1509.

41   A. M. Tafesh and M. Beller, *Tetrahedron Lett.*, 1995, **36**, 9305.

42   S. J. H. F. Arts, E. J. M. Mombarg, H. van Bekkum, and R. A. Sheldon, *Synthesis*, 1997, **6**, 597.

43   W. A. Herrman and C. W. Kohlpaintner, *Angew. Chem. Int. Ed. Engl.*, 1993, **32**, 1524.

44   C. W. Kohlpaintner, R. W. Fischer, and B. Cornils, *Appl. Catal.*, 2001, **221**, 219.

45   B. M. Novak and R. H. Grubbs, *J. Am. Chem. Soc.*, 1988, **110**, 7542.

46   E. Paetzold and G. Oehme, *J. Mol. Catal. A: Chem.*, 2000, **152**, 69.

47   I. T. Horváth and J. Rábai, *Science*, 1994, **266**, 72.

48   I. T. Horváth, *Acc. Chem. Res.*, 1998, **31**, 641.

49   E. G. Hope and A. M. Stuart, *J. Fluorine Chem.*, 1999, **100**, 75.

50   M. Cavazzini, F. Montanari, G. Pozzi, and S. Quici, *J. Fluorine Chem.*, 1999, **94**, 183.

51   E. deWolf, G. van Koten, and B.-J. Deelman, *Chem. Soc. Rev.*, 1999, **28**, 37.

52   R. Fish, *Chem. Eur. J.*, 1999, **5**, 1677.

53   T. Kitazume, *J. Fluorine Chem.*, 2000, **105**, 265.

54   I. T. Horváth, G. Kiss, R. A. Cook, J. E. Bond, P. A. Stevens, and J. Rábai, *J. Am. Chem. Soc.*, 1998, **120**, 3133.

55   D. Rutherford, J. J. J. Juliette, C. Rocaboy, I. T. Horváth, and J. A. Gladysz, *Catal. Today*, 1998, **42**, 381.

56   J. Moineau, G. Pozzi, S. Quici, and D. Sinou, *Tetrahedron Lett.*, 1999, **40**, 7683.

57   I. Klement, H. Lütjens, and P. Knochel, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1454.

58   J. J. J. Juliette, I. T. Horváth, and J. A. Gladysz, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1610.

59   J. A. Gladysz and L. V. Dinh, *Tetrahedron Lett.*, 1999, **40**, 8995.

60   D. P. Curran and S. Hadida, *J. Am. Chem. Soc.*, 1996, **118**, 5312.

61   B. Betzemeier and P. Knochel, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2623.

62   M. Wende and J. A. Gladysz, *J. Am. Chem. Soc.*, 2003, **125**, 5861.

63   M. Wende, R. Meier, and J. A. Gladysz, *J. Am. Chem. Soc.*, 2001, **123**, 11490.

64   C. Rocaboy and J. A. Gladysz, *Chem. Eur. J.*, 2003, **9**, 88.

65   C. Rocaboy and J. A. Gladysz, *New. J. Chem.*, 2003, **27**, 39.

66   C. Rocaboy and J. A. Gladysz, *Tetrahedron*, 2002, **58**, 4007.

67   K. Ishihara, S. Kondo, and H. Yamamoto, *Synlett*, 2001, 1371.

68   Y. M. A. Yamada, K. Takeda, H. Takahashi, and S. Ikegami, *Tetrahedron Lett.*, 2003, **44**, 2379.

69   K. Oono and M. Sato, *International Patent WO 2004011140*, 2004.

70   L. D. Rollmann, *Inorg. Chim. Acta*, 1972, **6**, 137.

71   P. G. Steel and C. W. T. Teasdale, *Tetrahedron Lett.*, 2004, **45**, 8977.

72   M. M. Mdleleni, R. G. Rinker, and P. C. Ford, *Inorg. Chim. Acta*, 1998, **270**, 345.

73   U. Schuchardt, E. N. d. Santos, and F. S. Dias, *J. Mol. Cat.*, 1989, **55**, 340.

74   K. Glegola, E. Framery, and K. M. Pietrusiewicz, *Adv. Synth. Catal.*, 2006, **348**, 1728.

75   J. Schwarz, V. P. W. Bohm, M. G. Gardiner, M. Grosche, W. A. Herrmann, W. Hieringer, and G. Raudaschl-Sieber, *Chem. Eur. J.*, 2000, **6**, 1773.

76   M. Ahmed, T. Arnauld, A. G. M. Barrett, D. C. Braddock, and P. A. Procopiou, *Synlett*, 2000, 1007.

77   J. P. Arhancet, M. E. Davis, J. S. Merola, and B. E. Hanson, *Nature*, 1989, **339**, 454.

78   M. S. Anson, M. P. Leese, L. Tonks, and J. M. J. Williams, *J. Chem. Soc.; Dalton Trans.*, 1998, 3529.

79   J. P. Arhancet, M. E. Davis, J. S. Merola, and B. E. Hanson, *J. Catal.*, 1990, **121**, 327.

80   M. S. Anson, L. Tonks, A. R. Mirza, and J. M. J. Williams, *Tetrahedron Lett.*, 1999, **40**, 7147.

81   G. E. Berendsen and L. de Galan, *J. Liquid Chromatogr.*, 1978, **1**, 403.

82   D. P. Curran, *Angew. Chem. Int. Ed. Engl.*, 1998, **37**, 1174.

83   D. P. Curran, *Synlett*, 2001, **9**, 1488.

84   B. Croxtall, E. G. Hope, and A. M. Stuart, *Chem. Commun.*, 2003, 2430.

85   E. G. Hope, A. M. Stuart, and A. J. West, *Green Chem.*, 2004, **6**, 345.

86   S. Kainz, Z. Y. Luo, D. P. Curran, and W. Leitner, *Synthesis*, 1998, 1425.

87   W. Zhang, *Tetrahedron*, 2003, **59**, 4475.

88   D. P. Curran, S. Hadida, and M. He, *J. Org. Chem.*, 1997, **62**, 6714.

89   D. P. Curran and Z. Y. Luo, *Med. Chem. Res.*, 1998, **8**, 261.

90   D. P. Curran, Z. Y. Luo, and P. Degenkolb, *Bioorg. Med. Lett*, 1998, **8**, 2403.

91   I. Ryu, T. Niguma, S. Minakata, M. Komatsu, Z. Y. Luo, and D. P. Curran, *Tetrahedron Lett.*, 1999, **40**, 2367.

Chapter Two

2. Investigation into Triarylphosphines

2.1. Introduction

2.1.1. Synthesis of Fluorous Triarylphosphines

Much of the work in FBC has concentrated on fluorous phosphines due to the abundance of hydrocarbyl phosphines in homogeneous catalysis. A phenyl spacer group, as an alternative to alkyl spacer groups, is advantageous as aromatic phosphines are less air sensitive than their alkyl-derivatives.[1] The first synthesis of a fluorous triarylphosphine was reported in 1970 in a patent for perfluorocarbon-soluble phosphorus(III) antioxidant oil additives, however their use as ligands in FBC was originally overlooked.

In 1997, Hope and Knochel both independently prepared $tris$(4-tridecafluorohexylphenyl)phosphine.[2, 3] The synthesis involved a copper-mediated cross-coupling reaction to attach the perfluoroalkyl group to the aromatic ring, followed by a lithium-bromine exchange and then reaction with phosphorus trichloride. This methodology has been applied to the synthesis of $meta$-derivatised ligands, as well as ligands with longer perfluoroalkyl chains (Scheme 2.1).[4-6]

(i) $C_6F_{13}I$, Cu, bipy, DMSO, C_6H_5F, 70 °C, 72 h; (ii) n-BuLi, Et_2O, -78 °C; (iii) PCl_3, Et_2O, -78 °C to RT.
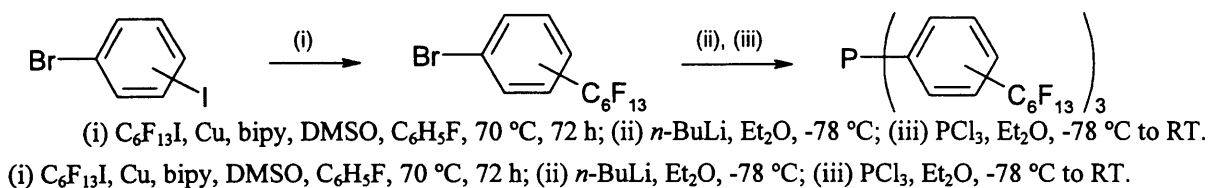
Scheme 2.1. *Synthesis of triarylphosphines containing perfluoroalkyl groups attached directly to the aryl ring.*

Fluorous triarylphosphines have also been synthesised that contain fluorous substituents in a mixture of different positions on the aryl rings such as $P(2-C_6H_4C_6F_{13})(4-C_6H_4C_6F_{13})_2$ which was synthesised from $P(2-C_6H_4C_6F_{13})Cl_2$.[4]

Bannwarth *et al.*[7] reported the synthesis of $tris$(3- and 4-heptadecafluorooctylphenyl)phosphines using a procedure modified from previous work by Knochel.[3] Starting from iodoanilines, a copper-mediated cross-coupling reaction with perfluorooctyl iodide, followed by diazotisation, gave the corresponding heptadecafluorooctylbromobenzene. Lithiation and reaction with phosphorus trichloride gave the corresponding $tris$(heptadecafluorooctylphenyl)-phosphines. The first step for the *para*- and *meta*-derivatives gave yields of 53 % and 51 % respectively. The phosphination step gave a poor yield of 25 % for the *para*-derivative but a more respectable 59 % yield for the *meta*-derivative. The authors did not explain the low yield for the *para*-derivatised phosphine, but it is thought that the poor solubility of the corresponding bromobenzene in diethyl ether at low temperature is a contributing factor.

Chen and Xiao reported an alternative synthesis of triarylphosphines.[8] *Tris*(4-bromophenyl)phosphine oxides undergo a copper-mediated cross-coupling reaction with perfluoroalkyl iodides (Scheme 2.2). Reduction of the phosphine oxide with trichlorosilane gives the corresponding triarylphosphine. The authors report yields between 91 – 95 % for the first step and ≥95 % for the second step.

n = 1, 2, 3
$R_f = C_6F_{13}, C_8F_{17}$
(i) R_fI, Cu, DMSO; (ii) $HSiCl_3$, Tol.
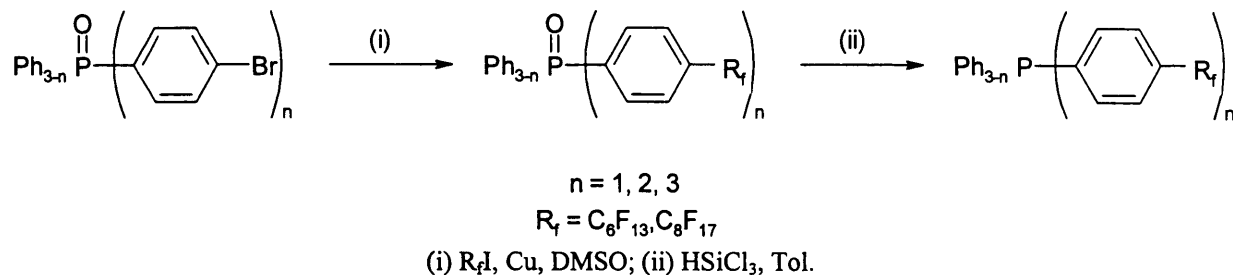
Scheme 2.2. *An alternative preparation of triarylphosphines.*

Although the phenyl spacer group acts as a better insulator from the electron-withdrawing effects of the perfluoroalkyl chains than the traditional alkyl spacer groups, spectroscopic data and catalytic studies have shown that the donor atom is not completely shielded.[1] Alternative spacer groups have been investigated, incorporating the phenyl spacer group with the addition of extra alkyl units. Leitner *et al.* have investigated aryl spacer groups with an additional ethylene group between the aromatic ring and the perfluoroalkyl chain (Scheme 2.3).[9]

(i) Mg; (ii) $C_6F_{13}C_2H_4I$, [Cu]; (iii) *n*-BuLi; (iv) PCl_3.
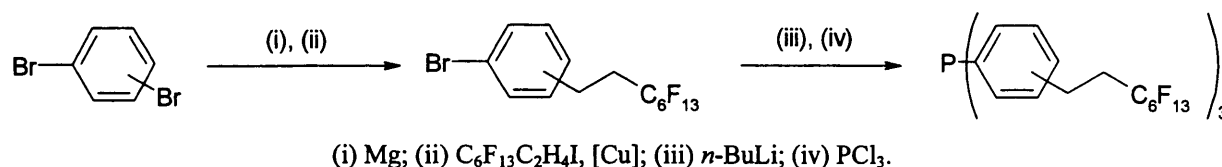
Scheme 2.3. *Synthesis of triarylphosphines with an additional ethylene spacer group.*

Curran *et al.* have synthesised triarylphosphines with the same ethylene spacer groups, by employing a selective Negishi-type reaction for the synthesis of the corresponding bromobenzene.[10] Genêt and co-workers have adopted a different approach to synthesise similar triarylphosphines.[11] They employed a selective Heck reaction to couple bromoaryldiazonium salts with perfluoroalkenes. The Heck product was hydrogenated, lithiated and subsequently reacted with phosphorus trichloride to form the triarylphosphine.

Chen and Xiao have also reported the synthesis of triarylphosphines with similar spacer units (Scheme 2.4).[12] Again, they start from (4-bromophenyl)phosphine oxides, but this time they use a Heck reaction to attach perfluoroalkenes. The Heck product was hydrogenated and the phosphine oxide reduced to the corresponding phosphine. The authors report high yields for the overall synthesis of the phosphines, with ≥ 90 % yield for each step.

n = 1, 2, 3

$R_f = C_6F_{13}, C_8F_{17}$
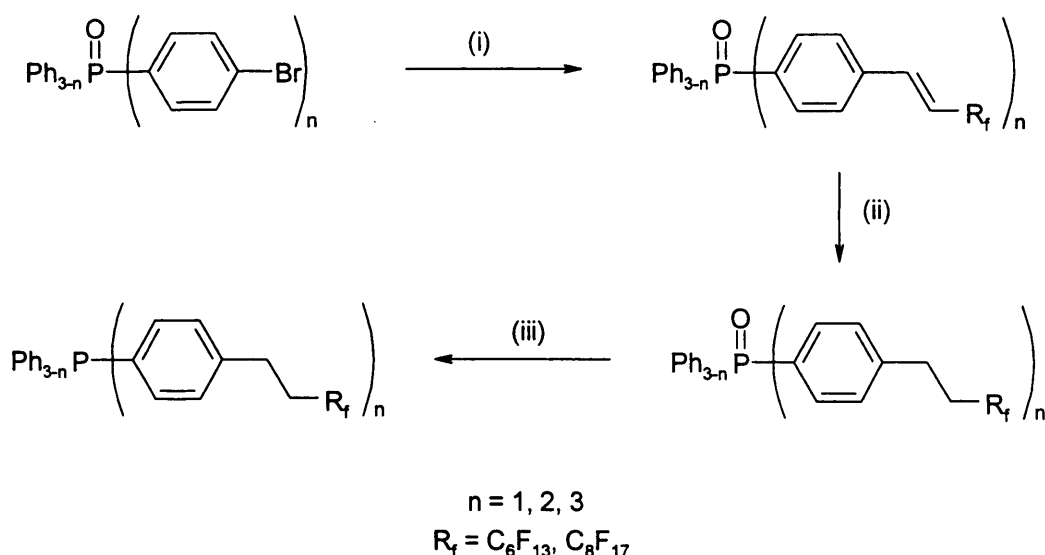
(i) $CH_2=CHR_f$, [Pd]; (ii) H_2, Pd/C; (iii) $HSiCl_3$, Et_3N.

Scheme 2.4. *An alternative synthesis of triarylphosphines with an additional ethylene spacer group.*

Hope *et al.* have employed the use of an additional oxymethylene group between the aryl ring and the fluorous ponytail.[13] The synthesis converts *tris*(4-methoxyphenyl)phosphine to the corresponding oxide using hydrogen peroxide. The product can then be demethylated, functionalised with perfluoroalkyl substituents and then reduced to give the free phosphine (Scheme 2.5). The oxymethylene spacer group has been shown to be extremely effective in minimising the electron-withdrawing effects of the perfluoroalkyl chains.

n = 1, 3   Y = Ts, Tf $R_f = C_7F_{15}, C_8F_{17}$
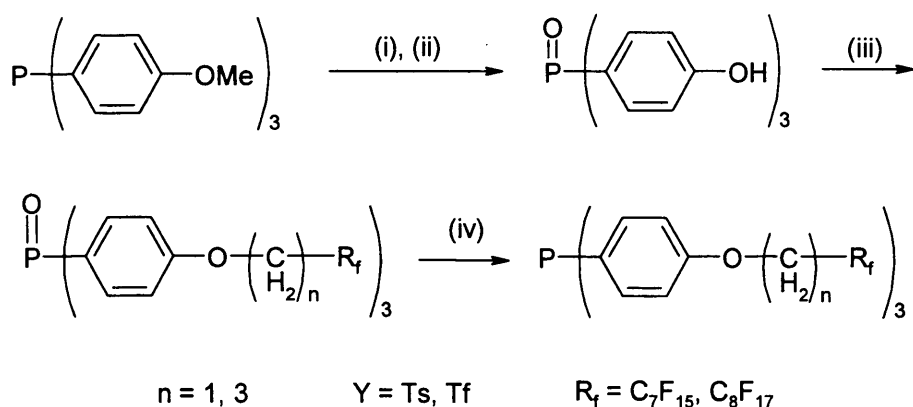
(i) H_2O_2; (ii) BBr_3; (iii) R_f-$(CH_2)_n$-OY, Cs_2CO_3; (iv) $HSiCl_3$.

Scheme 2.5. *Synthesis of triarylphosphines with an additional oxymethylene spacer group.*

Van Koten has employed the use of arylsilanes as spacer groups to attempt to reduce the electron-withdrawing effects of the perfluoroalkyl chains.[14] Fluorous-derivatised chlorosilanes are coupled with 1,4-dibromobenzene and then reacted with trialkylphosphite to form the corresponding triarylphosphine (Scheme 2.6).

36

$R_f = C_2H_4C_6F_{13}, C_2H_4C_8F_{17}$
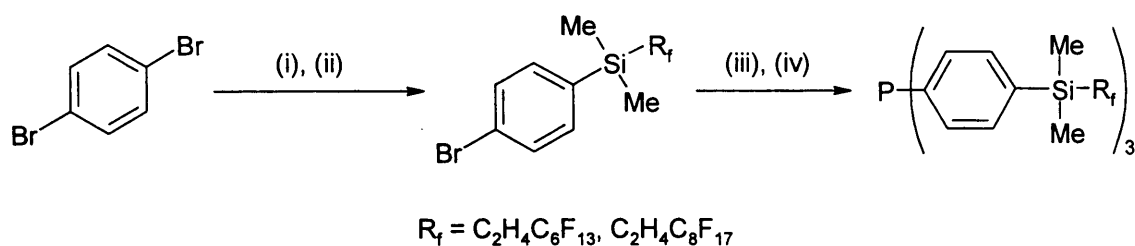
(i) n-BuLi; (ii) $R_f(Me)_2SiCl$; (iii) n-BuLi; (iv) $P(OMe)_3$

Scheme 2.6. *Synthesis of triarylphosphines with silyl spacer groups.*

Clearly, there are a large selection of spacer units that have been designed to insulate the donor atom from the electronic influence of the perfluoroalkyl chains. Larger spacers groups are more effective, however, the increase in overall mass decreases the percentage fluorine, by weight. This in turn will reduce the solubility of the fluorous ligand/catalyst in perfluorocarbon solvents and subsequently decrease the bias of partition coefficient in FBS. However, not all of the spacer units are efficient and the ponytails will, therefore, have some effect on the properties of the ligand and the catalytic ability of subsequently prepared catalysts.

2.1.2 Palladium Catalysis with Fluorous Triarylphosphines

Sinou *et al.* reported the use of fluorous ligands **5-7** in Heck reactions in FBC. The fluorous palladium catalysts were generated *in situ* from either [Pd(OAc)$_2$] or [Pd$_2$(dba)$_3$] in D-100 (mainly n-perfluorooctane) before an acetonitrile solution containing the iodobenzene and methyl acrylate were added (Scheme 2.7).[15] The reaction mixture was heated at 80 °C for 4 h and system remained biphasic. After cooling the reaction mixture to 0 °C, the organic phase was separated and the fluorous phase was reused under the same conditions. Although it was possible to recycle the catalyst, a decrease in catalytic activity was observed when all three fluorous ligands were used (Table 2.1).
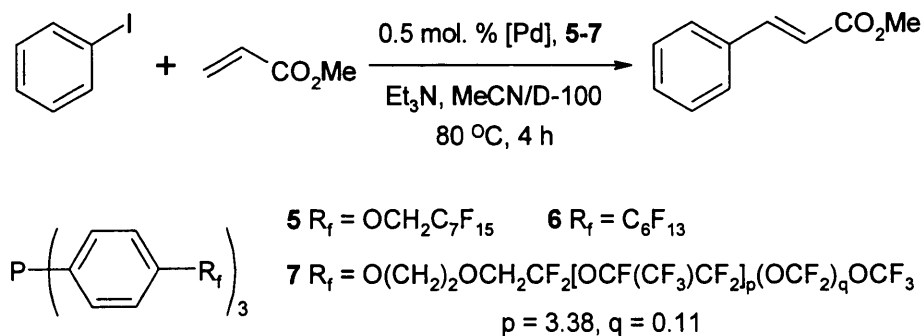
Scheme 2.7. *The application of the Heck reaction in fluorous biphase catalysis.*

Run	Ligand	Conversion/%
1	5	100
2	5	85^a
3	5	60^a
1	6	100
2	6	92^a
3	6	70^a
1	7	100
2	7	60^a
3	7	40^a

Data from Ref 15. ^{a}Catalysis carried out using fluorous phase from the previous run.

Table 2.1. *Selected recycling results from Heck reaction with fluorous phosphines.*

Knochel *et al.* reported successful Negeshi reactions using fluorous phosphine **6** under fluorous biphase conditions (Scheme 2.8). The fluorous palladium catalyst, [Pd{P(C$_6$H$_4$C$_6$F$_{13}$)$_3$}$_4$], was formed *in situ* before coupling a range aryl iodides and arylzinc bromides in excellent yields (89 - 99 %). At 60 °C the reaction mixture was homogeneous and upon cooling to 0 °C the system becomes biphasic, allowing facile separation. Recycling results from the cross-coupling reaction between phenylzinc bromide and 4-iodophenyl acetate, with an increased catalyst loading of 1.5 mol-% %, allowed the fluorous phase to reused four times without any significant loss in activity. However, the increase in catalyst loading could disguise any catalyst leaching that might have occurred.

$$ArZnBr \quad + \quad Ar'—I \quad \xrightarrow[\text{Tol. / C}_8\text{F}_{17}\text{Br, 60 °C, 0.2-0.5 h}]{\text{0.6 mol. \% 6, 0.15 mol. \% [Pd(dba)}_2]} \quad Ar—Ar'$$
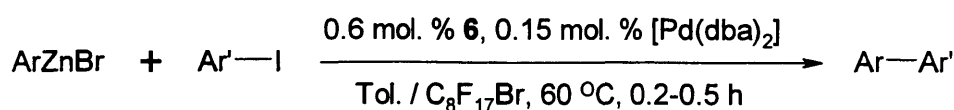
Ar = Ph, 4-ClC$_6$H$_4$, 3-CF$_3$C$_6$H$_4$, 2-thienyl, 4-TIPS-OC$_6$H$_4$
Ar' = 4-AcOC$_6$H$_4$, 4-NO$_2$C$_6$H$_4$, 3-EtO$_2$CC$_6$H$_4$, 4-MeOC$_6$H$_4$, 4-BrC$_6$H$_4$

Scheme 2.8. *Negeshi Coupling in Fluorous Biphase System.*

Bannwarth and co-workers demonstrated the use of a range of fluorous triarylphosphines as ligands for Pd-catalysed Stille, Suzuki and Sonogashira reactions in a fluorous biphase system. In the Stille reaction,[7] a selection of aryl bromides and aromatic tin reagents were dissolved in DMF whilst the fluorous-tagged Pd(II) catalysts **8-10** were dissolved in perfluoromethylcyclohexane. The reaction proceeded homogeneously at 80 °C, generally with high yields. When the reaction had cooled, liquid-liquid separation gave the

palladium catalyst in the fluorous phase, which could be reused in further reactions. In the reaction between methyl 4-bromobenzoate and 2-(tributylstannyl)furan, the catalyst could be reused up to six times without a significant reduction in reaction yields (Scheme 2.9). However, there was no analysis of the organic products for palladium leaching that may have occurred.
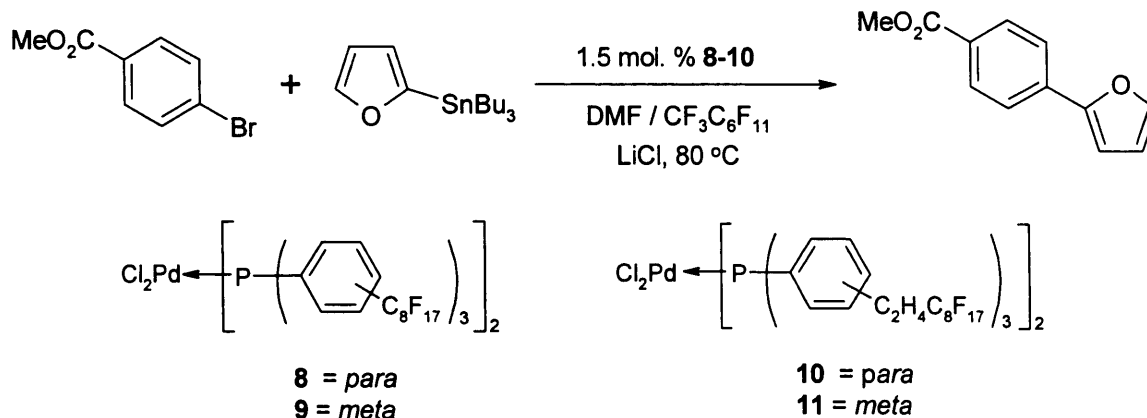
Scheme 2.9. *The application of the Stille reaction in fluorous biphase catalysis.*

In the Suzuki reaction,[16] electron-deficient and electron-rich bromobenzenes were reacted with phenylboronic acid in 1,2-dimethoxyethane (DME). The catalysts **8-11** were each dissolved in the fluorous layer, perfluoromethylcyclohexane, and the reaction was carried out in the presence of 2 M sodium carbonate (Scheme 2.10). At room temperature two separate layers were formed, but at 75 °C the system was almost homogeneous. After 2 hours, the reaction mixture was cooled, resulting in phase separation, and the organic and fluorous layers were separated. The fluorous layer, containing the fluorous catalysts, was used in six consecutive reactions without loss of activity for each catalyst.

The yields of product from reactions between phenylboronic acid with electron-deficient and electron-rich aryl bromides were approximately the same (Table 2.2). The authors report that there is virtually no difference in the activity of the catalysts **8-11**.
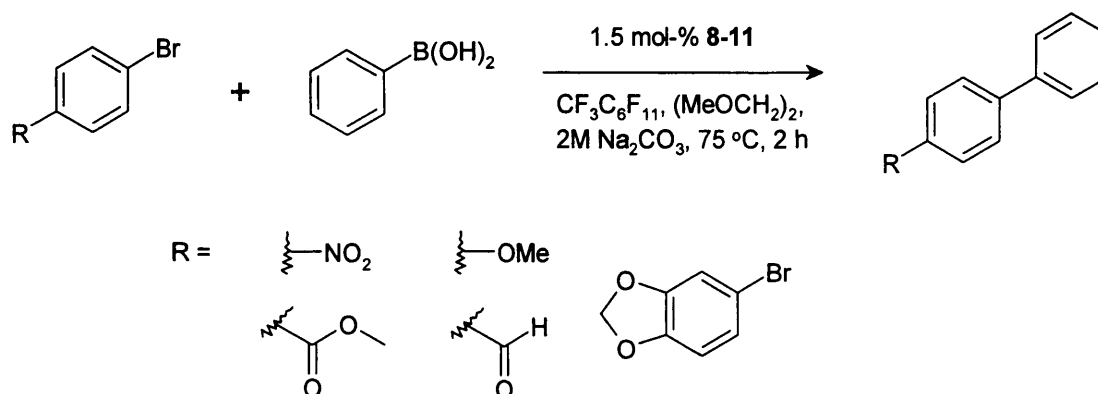
Scheme 2.10. *Suzuki reaction between a range of aryl bromides and phenylboronic acid with catalysts 8-11 in FBC*

R	Catalyst	Yield/%^{a}
NO$_2$	8	95, 99, 85, 84, 79, 78
NO$_2$	9	85, 94, 92, 90, 92, 91
NO$_2$	10	91, 97, 93, 89, 91, 90
NO$_2$	11	95, 94, 93, 93, 92, 93
MeO	8	95, 93, 91, 90, 91, 88
MeO	9	99, 96, 90, 86, 83, 88
MeO	10	87, 90, 92, 89, 86, 90
MeO	11	95, 95, 93, 92, 94, 89

Data from Ref 16. ^{a}Isolated yield from runs 1 to 6 using the same catalyst.

Table 2.2. *Selected results from Suzuki recycle.*

A Suzuki reaction was also carried out with only 0.1 mole % of the catalysts **8-11** with an aryl bromide and 4-methoxyphenylboronic acid (Scheme 2.11). After two hours the reaction mixture was cooled and a liquid-liquid separation was carried out. The catalyst in the fluorous layer was reused in a further three identical reactions. However, unlike previously, reaction conversions and yields dropped after each run, from 100 % conversion in the first run down to < 20 % conversion in the fourth run. Catalyst **10** and **11** had the highest catalytic activities over the four runs. The authors did not explain why the yields had dropped, but it is thought that the catalyst may have been decomposing, therefore, a drop in yield would be inevitable. There was no analysis carried out on the organic product for any palladium leaching, which would have given an indication of the efficiency of the biphase system.
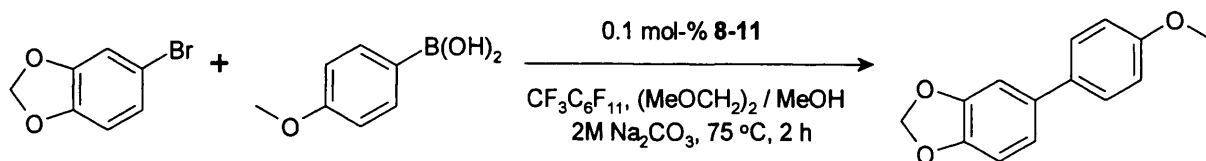
Scheme 2.11 *Suzuki coupling using 0.1 mol-% % of catalysts 8-11 in FBC.*

Bannwarth and co-workers demonstrated the use of the fluorous-tagged catalysts **10-12** in Sonogashira reactions using FBC.[17] Catalyst **12**, has an aryl oxymethylene spacer group, to help insulate against the electron withdrawing effects from the fluorous ponytails (Figure 2.1). Catalysts **8** and **9** were not used in these reactions, as preliminary experiments had shown the formation of palladium black occurred when these palladium complexes with no additional spacer groups between the aryl ring and the fluorous ponytail were employed.

12
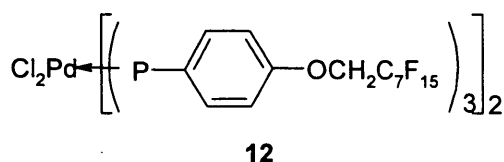
Figure 2.1. *Trans-dichlorobis[tris(4-1H,1H,-perfluorooctyloxyphenyl)phosphine]palladium 12.*

A range of aryl bromides and alkynes were dissolved in the organic phase, which was DMF, and the catalysts **10-12** were each dissolved in the fluorous phase, perfluoro-1,3-dimethylcyclohexane. The reaction was carried out in the presence of copper(I) iodide as a co-catalyst, and dibutylamine as the base with a catalyst loading of 2 mole %. At 100 °C, the system remained biphasic, but the miscibility of the phases was increased. Upon cooling to 0 °C, liquid-liquid separation of the reaction mixture gave the product in the organic layer and the catalyst in the fluorous layer. The catalyst was reused in identical reactions a further two times. For electron-deficient aryl bromides and non-aliphatic alkynes reaction yields were high, ranging between 80 and 99 % for the first run. When 4-bromonitrobenzene was used, the second and third runs gave virtually the same yield. However, when other electron-deficient aryl bromides were used, the second run gave similar results but a drop in the yield was observed in the third run. The electron-rich aryl bromide, 4-bromoanisole, only gave good yields with (triisopropylsilyl)ethyne when **10** and **12** were used as the catalysts. The recycled catalysts gave disappointing yields of between 10 and 16 %, and in the third run there was hardly any activity. Overall, catalysts **10-12** showed similar activities, with reaction yields only varying by a few percent for most reactions.

The difference in activity between electron-rich and electron-deficient aryl halides can be attributed to the different electronic environments for the halide leaving group. The electron-deficient aryl halides undergo oxidative addition reactions with palladium catalysts more easily than electron-rich aryl halides as the electron-withdrawing groups on the aryl ring extract electron density from the aromatic ring making the C-X bond weaker and, therefore, easier to cleave. These reactions would be faster resulting in a higher turnover of starting material to product.

Bannwarth and co-workers have also immobilised fluorous catalysts **10-12** on FRPSG (Figure 2.2).[18] FRPSG was added to a solution of the palladium complex in diethyl ether and hexafluorobenzene. The solvent was evaporated to give the catalyst supported on the FRPSG. Different catalyst loadings on the FRPSG were evaluated in the Suzuki reaction between 4-nitrobromobenzene and phenylboronic acid (Scheme 2.12). Catalyst loadings from 1.5 mole % down to 0.001 mole % were tested and the results are shown in Table 2.3. Reaction times

increased from 2 hours, using FBC, to 15 hours. This decrease in activity may be accounted for by the change in the system from 'homogeneous' to heterogeneous reaction conditions.
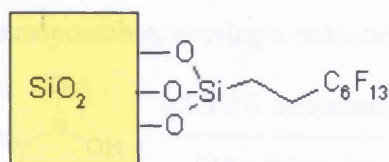
Figure 2.2. *Fluorous Reverse Phase Silica Gel used as a solid support.*
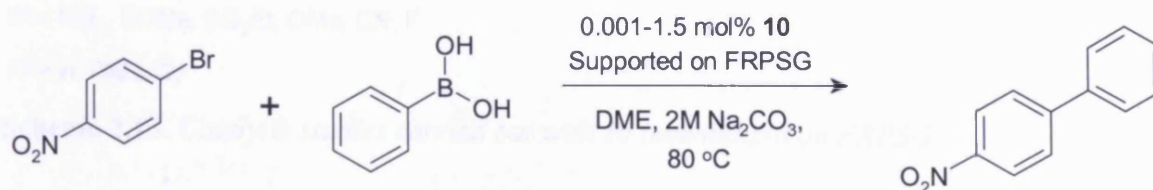
Scheme 2.12. *Suzuki coupling using **10** immobilised on FRPSG.*

Catalyst loading on FRPSG (mg g^{-1})	Catalyst loading [10] (mol %)	Yield (%)^a
100	1.5	>98, >98, 92
10	0.1	>98, >98
1	0.01	>98, >98
0.1	0.001	86, 45

Data from Ref 18. ^{a}The first yields are for the initial catalyst and then the second (and third) are from the recycled catalyst.

Table 2.3. *Results from Suzuki coupling between 4-nitrobromobenzene and phenylboronic acid using **10** immobilised on FRPSG.*

Catalyst loadings of 0.01 mole % could be used to produce yields of >98 % for the first and second runs using the recycled catalyst. Catalyst leaching from the solid support was determined by inductively coupled plasma mass spectrometry (ICP-MS) using 0.1 mole % of **10**. Only 5.4 ppm of palladium was reported to have leached into the crude product, corresponding to 1.8 % of the total palladium. The palladium content in the inorganic residue was determined to be 0.2 ppm and so, a total of <1.9 % of the palladium leached from the FRPSG. However, the product was subjected to further purification before it was analysed and, therefore, may have removed some palladium that had been present.

Catalyst **10** immobilised on FRPSG was evaluated with a range of different substrates (Scheme 2.13 and Table 2.4). Yields for the first run were generally high for electron-deficient aryl bromides (>90 %), but for the electron-rich 4-bromomethoxybenzene only a 48 % conversion was achieved. Reactions using phenylboronic with the recycled catalyst were

successful with 4-nitrobromobenzene achieving constant yields for the three runs. All of the other substrates showed a significant decrease in catalytic activity. The authors did not explain why this had occurred, but it is thought that decomposition of the palladium catalyst to form palladium black may be responsible, causing a reduction in catalytic activity.
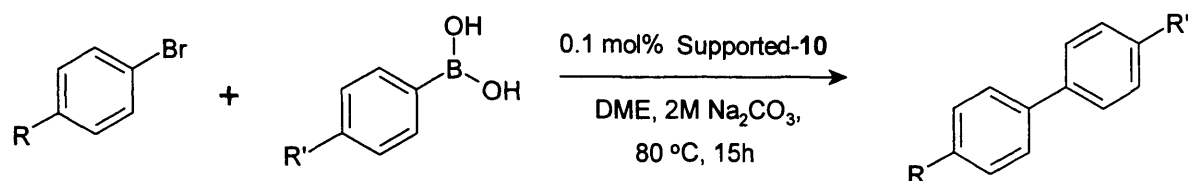
$R^1 = NO_2$, COMe, CO_2Et, OMe, CN, F

$R^2 = H$, OMe, Cy

Scheme 2.13. *Catalytic studies carried out with 10 immobilised on FRPSG.*

R	R'	Yield/%^{a}
NO$_2$	H	95, 97, 97
CH$_3$CO	H	>98, 85, 14
CO$_2$Et	H	93, 69, 4
3,4-F	H	78, 6, 0
MeO	H	48, 2

Data from Ref 18.^{a}The first yields are for the initial catalyst and then the second (and third) are from the recycled catalyst.

Table 2.4. *Selected recycling results from Suzuki reaction with 10 immobilised on FRPSG.*

A range of fluorous triarylphosphines have been previously synthesised and coordinated to palladium(II) metal centres. A range of palladium coupling reactions have been successfully investigated and attempts to recycle the fluorous catalyst have been successful but limited by a decrease in catalyst activity. Systems using FBC achieve good activities as the reactions are homogeneous. However, this approach has problems associated with leaching of the catalyst into the organic phase leading to a drop in yield in subsequent catalytic runs. A large percentage of fluorine is required in the catalyst for it to be preferentially soluble in the fluorous phase. With this in mind, as well as the cost and the environmental persistence associated research groups have started to move away from FBS to other fluorous methods. Supported catalysis using FRPSG omits the use of perfluorocarbon

solvents, however, the heterogeneous reaction conditions decrease catalytic activity, resulting in longer reaction times, and have demonstrated poor recycling results.

It is envisaged that by using fluorous solid phase extraction (SPE), reactions can be conducted in conventional organic solvents whilst homogeneously. Post reaction fluorous SPE can be used for facile product/catalyst separation with minimal leaching of the catalyst into the organic product. The catalyst and fluorous column can then be used in further reactions. This approach should offer good activities without the need for perfluorocarbon solvents or to support the catalyst.

2.2 Results and Discussion
2.2.1 Synthesis of Triarylphosphines

There are a number of synthetic routes that have been established for the synthesis of fluorous phosphines **15** & **16**. Chen's method has been repeated within the group, however, it was not possible to reproduce the high yields reported by the author. The alternative method, used by Bannwarth, had a number of synthetic steps to reach the fluorous bromobenzene. This route was not chosen as there was an established method within the Leicester group for a one-step synthesis of the fluorous bromobenzenes.

A synthetic route has already been established for the synthesis of *tris*(4-tridecafluorohexylphenyl)phosphine and *tris*(3-tridecafluorohexylphenyl)phosphine and both have been previously prepared within the group.[2] This method was followed with some modification, incorporating the C_8F_{17} chain instead of the previously used C_6F_{13} chain (Scheme 2.14). The first step (i) achieves the addition of fluorous ponytails to an aryl ring by a copper-mediated cross-coupling reaction. This type of reaction was first investigated by McLoughlin and Thrower, who reported the coupling of a range of perfluoroalkyl iodides with aryl iodides and bromides.[19]

13 = *para*
14 = *meta*

15 = *para*
16 = *meta*
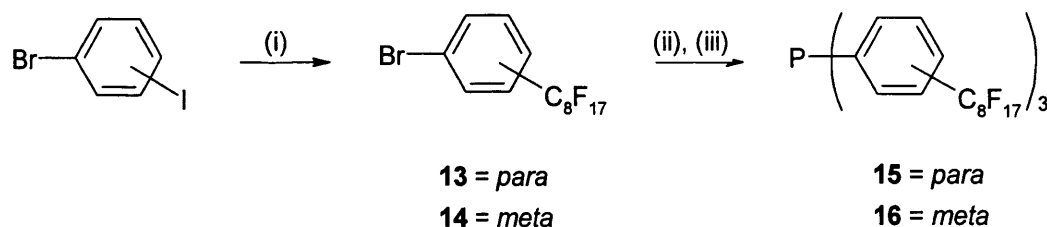
(i) $C_8F_{17}I$, Cu, bipy, DMSO, C_6H_5F, 70 °C, 72 h; (ii) *n*-BuLi, Et_2O, -78 °C; (iii) PCl_3, Et_2O, -78 °C to RT.
Scheme 2.14. *Synthesis of 15 and 16.*

The C-I bond has reversed polarity in perfluoroalkyl iodides since the electron-withdrawing effects of the fluorine atoms in the perfluoroalkyl chain creates a partial negative charge on the carbon atom and partial positive charge on the iodine atom. The perfluoroalkyl

iodide can form a perfluoroalkyl copper species in polar aprotic solvents and subsequently react with an aryl iodide to form the desired cross-coupled product (Scheme 2.15).

$$R_f\!-\!I \xrightarrow[L]{Cu} \quad \overset{I\!-\!CuL_3}{\diagup}\quad R_f\!-\!CuL_3 \xrightarrow[\quad I\!-\!CuL_3 \quad]{Ar\!-\!I} R_f\!-\!Ar$$

L = 2,2'-bipyridine
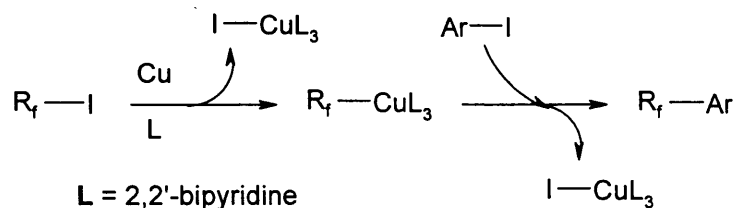
Scheme 2.15. *Proposed mechanism for the copper-mediated cross-coupling reaction between perfluoroalkyl iodides and aryl iodides.*

In the synthesis of **15** and **16**, a selective copper coupling reaction was employed using the *para-* or *meta*-substituted bromoiodobenzene to form the corresponding perfluoroalkyl-bromobenzene **13** and **14**. The reaction was carried out using DMSO as the polar aprotic solvent, with fluorobenzene acting as a co-solvent to solubilise the perfluorooctyl iodide. A catalytic amount of 2,2'-bipyridine was used to stabilise the perfluorooctyl copper intermediate formed in the reaction. The reaction mixture was heated at 70 °C with slow addition of the perfluorooctyl iodide over several hours. At this temperature, the perfluoroalkyl chain reacts at the iodo-substituent only, but at temperatures above 70 °C, the perfluoroalkyl chain also reacts at the bromo-substituent, potentially forming a *bis*-substituted byproduct. Therefore, it is important to maintain the temperature at 70 °C to ensure that a high yield of the desired product is obtained.

After working-up the reaction mixture, the crude product was obtained as a brown/orange solid due to the longer perfluorooctyl chain whereas oils were obtained in the case of the perfluorohexyl chain. Recrystallisation from methanol gave the pure products as white solids in yields which were better than those reported in the literature using an alternative synthesis.[7]

In step (ii), the synthesis of the corresponding phosphines proved to be more difficult, as the bromo-perfluorooctyl-benzenes only have a low solubility in organic solvents at low temperatures. Previous work had shown that this led to a dramatic drop in yields to only 25 % for the preparation of **15**.[7] The low solubility is thought to lead to a partial heterogeneous reaction and was improved by increasing the amount of solvent. When 400 mL of diethyl ether was used at -78 °C, instead of 30 mL, the reaction yield increased dramatically to 49 % **15**. An alternative approach to using large volumes of diethyl ether to dissolve the perfluorooctyl bromobenzene was to use a solvent mixture. When a 1:1 diethyl ether and THF solvent mixture (120 mL) was used at an increased temperature of -30 °C the yield of **16**

increased to 68 %, which is higher than that reported in the literature using an alternative method (Scheme 2.16).[7]

Br—⟨ ⟩—C_8F_{17} (ii), (iii) →   P—(⟨ ⟩—C_8F_{17})$_3$

(ii) n-BuLi, Et$_2$O/THF, -30 °C; (iii) PCl$_3$, Et$_2$O/THF, -30 °C to RT.
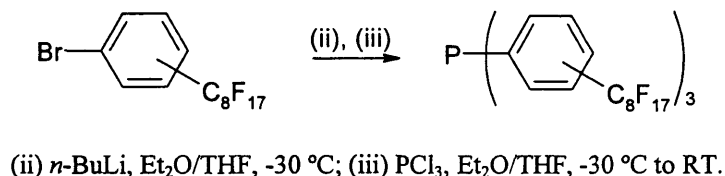
Scheme 2.16. *Alternative conditions for the preparation of 15 and 16.*

The overall yield for the complete synthesis of **15** is 27 % and for **16** is 52 %. This was due to the moderate yields obtained by both the copper coupling and phosphination steps.

A synthetic route has already been established for the synthesis of tris(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine **23**.[11] This method was followed with a slight modification as it offered straightforward, high yielding reactions with very little purification. This method was also used for the synthesis of tris(3-1H,1H,2H,2H-perfluorodecylphenyl)phosphine **24** (Scheme 2.17).

Br—⟨ ⟩—NH$_2$ (i) →   Br—⟨ ⟩—N≡N$^+$ BF$_4^-$ (ii) →   Br—⟨ ⟩—CH=CH–C_8F_{17}

17 = para
18 = meta

19 = para
20 = meta

(iii) ↙

P—(⟨ ⟩—$C_2H_4C_8F_{17}$)$_3$ (iv), (v) ←   Br—⟨ ⟩—C_8F_{17}

23 = para
24 = meta

21 = para
22 = meta
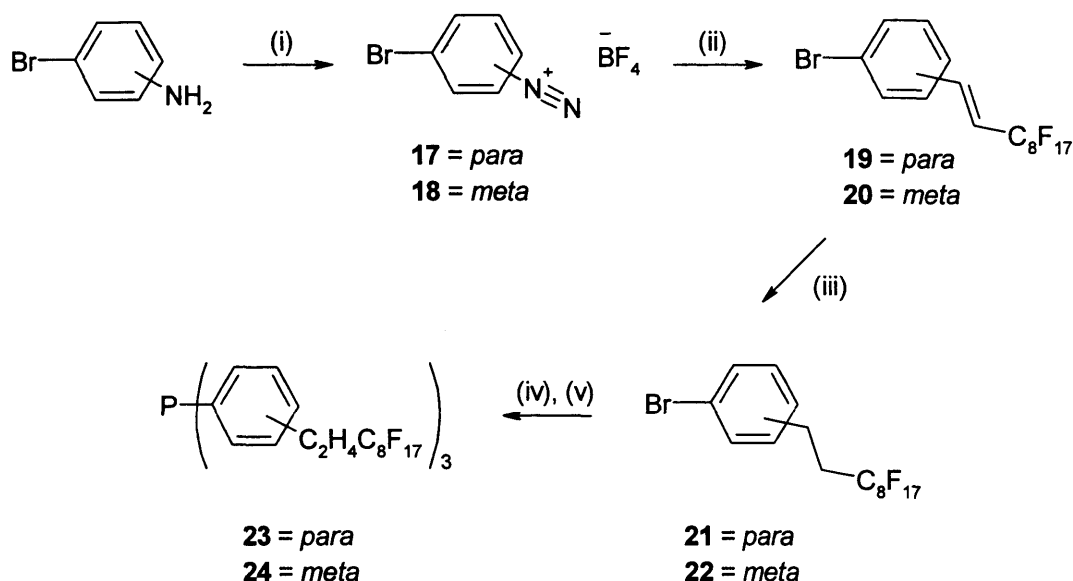
(i) HBF$_4$, NaNO$_2$, H$_2$O, 0 °C; (ii) CH$_2$=CHC$_8$F$_{17}$, Pd(OAc)$_2$, MeOH; (iii) H$_2$, 50 bar, Rh/C, MeOH, 20 °C; (iv) n-BuLi, Et$_2$O, -30 °C; (v) PCl$_3$, Et$_2$O, -30 °C to RT.

Scheme 2.17. *Synthesis of 23 and 24.*

The corresponding diazonium salts **17** and **18** were synthesised and reacted, without characterisation, in a selective Heck reaction with 1H,1H,2H-perfluorodec-1-ene. Hydrogenation of the alkenes **19** and **20**, using rhodium on carbon as the catalyst, led to the formation of the desired product **21** and **22**. The use of rhodium, instead of palladium, was

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imperative, as this suppressed the formation of the debrominated byproduct that is difficult to separate from the desired product.[11]

Initially, the final step (iv) of the synthesis of phosphine **23** was carried out using a large volume of diethyl ether and a higher temperature of -40 °C. The desired product was isolated in a 55% yield. However, as noted earlier, the use of a significant amount of diethyl ether to dissolve the bromobenzene is undesirable and an alternative solvent or solvent mixture was required.

Phosphine **23** was then synthesised using a 1:1 diethyl ether and THF mixture at -30 °C, as this combination dramatically increased the solubility of the bromobenzene. The work-up of the reaction was carried out in air, rather than under nitrogen, as previous work had suggested that **23** was not as air-sensitive as the other phosphines, **15** and **16**. A low yield of only 22 % was obtained, which was disappointing. Working up the reaction in air had led to the formation of a significant amount of the corresponding phosphine oxide. Higher yields were obtained by carrying out the reaction work-up under nitrogen, isolating the phosphine in a 46 % yield.

The synthesis of phosphine **24** was carried out using a 1:1 diethyl ether and THF mixture at -30 °C, the reaction was worked-up under nitrogen to give 34 % yield. The overall yield for the complete synthesis of **23** was 38 % and for **24** was 24 %. This is due to the low yields obtained in the phosphination step.

2.3 Coordination Chemistry

The formation of the Pd(II) complexes was relatively straightforward using ligand exchange between dichloro-*bis*(acetonitrile)palladium and a triarylphosphine to afford the dichloro-*bis*(triarylphosphine)palladium complex (Scheme 2.18).[20] Five complexes of this type, **8-11** & **25**, were synthesised and fully characterised by ^{1}H, ^{19}F & ^{31}P NMR spectroscopy. The non-fluorous-derivative, [PdCl$_2$(PPh$_3$)$_2$] **25**, was also prepared for comparative purposes. Recrystallisation from DCM/petroleum ether afforded the *trans*-isomer as the major product in all cases. Analysis of ^{31}P NMR spectra for complexes **8, 9, 11** & **25** showed a minor peak approximately 10 ppm further downfield than the signal for the *trans*-isomer that was attributed to the *cis*-isomer.[21, 22] All of the complexes were synthesised in good yield (69 - 93 %) to give yellow or orange solids that are air- and moisture-stable. The EI and FAB mass spectrometry of complexes **8-11** & **25** were inconclusive, however large peaks corresponding to [M-2Cl]$^+$ were observed by positive ion mode MALDI mass spectrometry.

$$P \left(\text{—} \left(\bigcirc \right) \text{—} R_f \right)_3 \xrightarrow{\text{(i)}} Cl_2Pd \leftarrow \left[P \left(\text{—} \left(\bigcirc \right) \text{—} R_f \right)_3 \right]_2$$
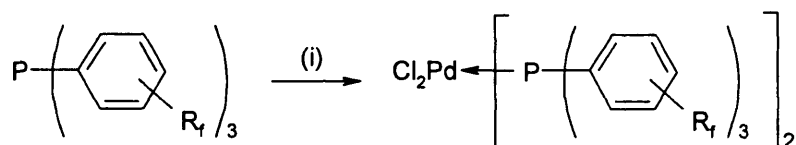
8 $R_f = p\text{-}C_8F_{17}$ **10** $R_f = p\text{-}C_2H_4C_8F_{17}$ **25** $R_f = H$
9 $R_f = m\text{-}C_8F_{17}$ **11** $R_f = m\text{-}C_2H_4C_8F_{17}$

(i) [PdCl$_2$(MeCN)$_2$], DCM, Reflux, 2 h.

Scheme 2.18. *Formation of triarylphosphine palladium complexes.*

Unlike the free ligands, the metal compounds were not soluble in deuterated chloroform. Attempts to dissolve the metal complexes in other deuterated solvents were also unsuccessful, so the complexes were dissolved in hexafluorobenzene and a deuterated chloroform insert tube was used in the NMR spectroscopy.

The difference between the ^{31}P NMR shifts for the metal complex and the free ligand for the non-fluorous parent complex **25** can be compared with these for the fluorous-derivatives **8-11** (Table 2.5). Compounds **8, 10, & 11** have similar Δ ^{31}P NMR values to that for compound **25**, within experimental error, whilst that for compound **9** is larger, suggesting the bulky perfluoroalkyl groups in the *meta*-positions of this phosphine may be significant.

Ligand	^{31}P NMR data (Free ligand)/ppm^a	^{31}P NMR data (Metal Complex)/ppm^b	Δ ^{31}P NMR data/ppm^c
8	s, -6.2	s, 23.2	29.4
9	s, -6.9	s, 24.5	31.4
10	s, -7.6	s, 21.9	29.5
11	s, -5.2	s, 23.5	28.7
25	s, -5.3	s, 23.3	28.6

^{a}NMR solvent was CDCl$_3$. ^{b}NMR solvent was C$_6$F$_6$ with a CDCl$_3$ insert tube. $^c\Delta$ ^{31}P NMR data = δ_P (Metal Complex)- δ_P (Free ligand).

Table 2.5. *^{31}P NMR spectroscopy data for triarylphosphine complexes.*

The Pt(II) complex was also prepared by ligand exchange of [PtCl$_2$(MeCN)$_2$] with triarylphosphine **15** to afford the platinum complex **26** (Scheme 2.19).[20] This time, the metal complex was almost completely insoluble in chloroform and, therefore, washing the crude reaction mixture with chloroform left the desired complex as a mixture of the *trans-* and *cis-* isomers. Washing the metal complex with copious amounts of chloroform isolated the *trans-* isomer only. However, with time in solution, the *trans*-isomer isomerised to form the *cis-* isomer as shown by the ^1H, ^{19}F & ^{31}P NMR spectra. The metal complex was not soluble in

any deuterated solvents and, therefore, the complex was dissolved in hexafluorobenzene and a deuterated benzene insert tube was used for NMR experiments. The data for **26** was compared with that for the parent complex as well as that for other fluorous phosphine complexes (Table 2.6).[23] Complex **26** showed the greatest difference in $^1J_{PtP}$ values from the parent complex, indicating aryl spacer is not sufficient to completely shield the phosphorus donor atom from the electron-withdrawing effects of the perfluoroalkyl chain.

15   **26**

(i) [PtCl$_2$(MeCN)$_2$], DCM/BTF, Reflux.
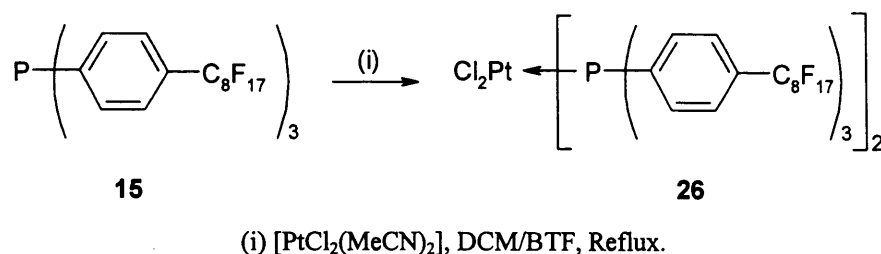
Scheme 2.19. *Formation of triarylphosphine platinum complex.*

Ligand	$^1J_{PtP}$ (cis)/Hz	$^1J_{PtP}$ (trans)/Hz
PPh$_3$	3675	2635
P(4-C$_6$H$_4$C$_6$F$_{13}$)$_3$	3615	2712
P(4-C$_6$H$_4$C$_8$F$_{17}$)$_3$ **15**	3570	2741
P(4-C$_6$H$_4$C$_2$H$_4$C$_6$F$_{13}$)$_3$	3679	-

Table 2.6. *Coupling constant data for cis-/trans-[PtCl$_2$L$_2$] complexes.*

2.4 Separation Studies of Pd(II) Complexes

The ability to isolate the catalyst and reuse it in further catalytic reactions is an important issue. It was envisaged that, after a catalytic reaction had taken place, the reaction mixture could be loaded onto a column of FRPSG. One solvent would be used to wash off the product while the catalyst was retained on the column. The catalyst would then be recovered from the column with another solvent and be reused in further reactions.

Catalyst **10** (100 mg) was dry-loaded onto a short column of FRPSG (~2 g). The column was eluted with acetonitrile, a fluorophobic solvent, and a yellow band of catalyst was retained at the top of the column. Thin layer chromatography was used to analyse the eluted acetonitrile fraction and showed that no UV-active compounds were eluted from the column, thus showing that the catalyst was retained on FRSPG. The column was then washed with benzotrifluoride to elute the catalyst. Thin layer chromatography was used to determine when all of the catalyst had been eluted. Only 86 % of the catalyst was recovered from the column. The FRPSG analysed by inductively coupled plasma – optical emission spectrometry (ICP-OES), showed palladium levels of 1.12 ppm, which corresponds to 7 % of the palladium demonstrating that a small amount of the catalyst was irreversibly bound to the silica. The ^{1}H,

^{31}P & ^{19}F NMR spectra of the recovered catalyst were found to be identical to the spectra of the catalyst before loading onto FRPSG indicating that there was no unwanted reaction between catalyst and silica whilst on the column.

The catalyst recovery could be increased to 95 % of the isolated catalyst, by pre-treating the column with acetonitrile before loading the catalyst. This minimised the exotherm caused when the catalyst, in solution, came into contact with the FRPSG causing less irreversible binding of the catalyst to the free OH groups on the FRPSG.

All this evidence shows that the fluorous pre-catalyst **10** can be successfully loaded, retained and eluted from the column of FRPSG successfully, indicating that it should be possible to separate the active catalyst from the reaction products, as long it survives the reaction conditions and has similar fluorous properties to the pre-catalyst.

2.5 Catalytic Testing

2.5.1 Initial Reaction Conditions

Fluorous triarylphosphine palladium complexes (**8-11**) have been used previously in Stille, Suzuki and Sonogashira reactions in FBC and using FRPSG as a solid support. The work of Bannwarth *et al.* was to be extended by investigating a Suzuki reaction in a conventional organic solvent as well as attempting to recover the catalyst using fluorous solid phase extraction with FRPSG. Parallel studies were carried out with the non-fluorous parent compound **25** for comparison.

It is thought that the catalytic cycle for the palladium catalysts (**8-11** & **25**) is likely to go through a traditional Pd(0)/Pd(II) mechanism rather than a Pd(II)/Pd(IV) and will be reduced *in situ* to form a palladium(0) complex (See Section 1.2). Catalysts that are speculated to go through a Pd(II)/Pd(IV) mechanism generally have a carbon sigma-bond to the palladium centre. This strong bond is thought to stay intact throughout the catalytic cycle and therefore force an alternative catalytic pathway to the traditional Pd(0)/Pd(II) cycle. As these catalysts contain monodentate phosphine ligands with no carbon sigma-bonds to the palladium centre, the Pd(II)/Pd(IV) mechanism seems extremely unlikely.

It was speculated that the palladium(II) catalyst precursor can form the active catalyst *in situ* by a number of proposed steps (Scheme 2.20). Firstly, a metathesis reaction occurs replacing one of the chloride ions with a hydroxyl group. Transmetallation with phenylboronic acid occurs to form phenylpalladium(II) chloride. This again will undergo metathesis and a further transmetallation step to form a diphenylpalladium(II) species. This can undergo a reductive elimination step, to form the palladium(0) active catalyst and biphenyl as a byproduct. This type of mechanism has been supported in the literature.[24]

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The active catalyst will then undergo the traditional catalytic cycle; oxidative addition of the aryl bromide, followed by a metathesis reaction, transmetallation with phenylboronic acid and reductive elimination to produce the desired product and regenerate the active catalyst.
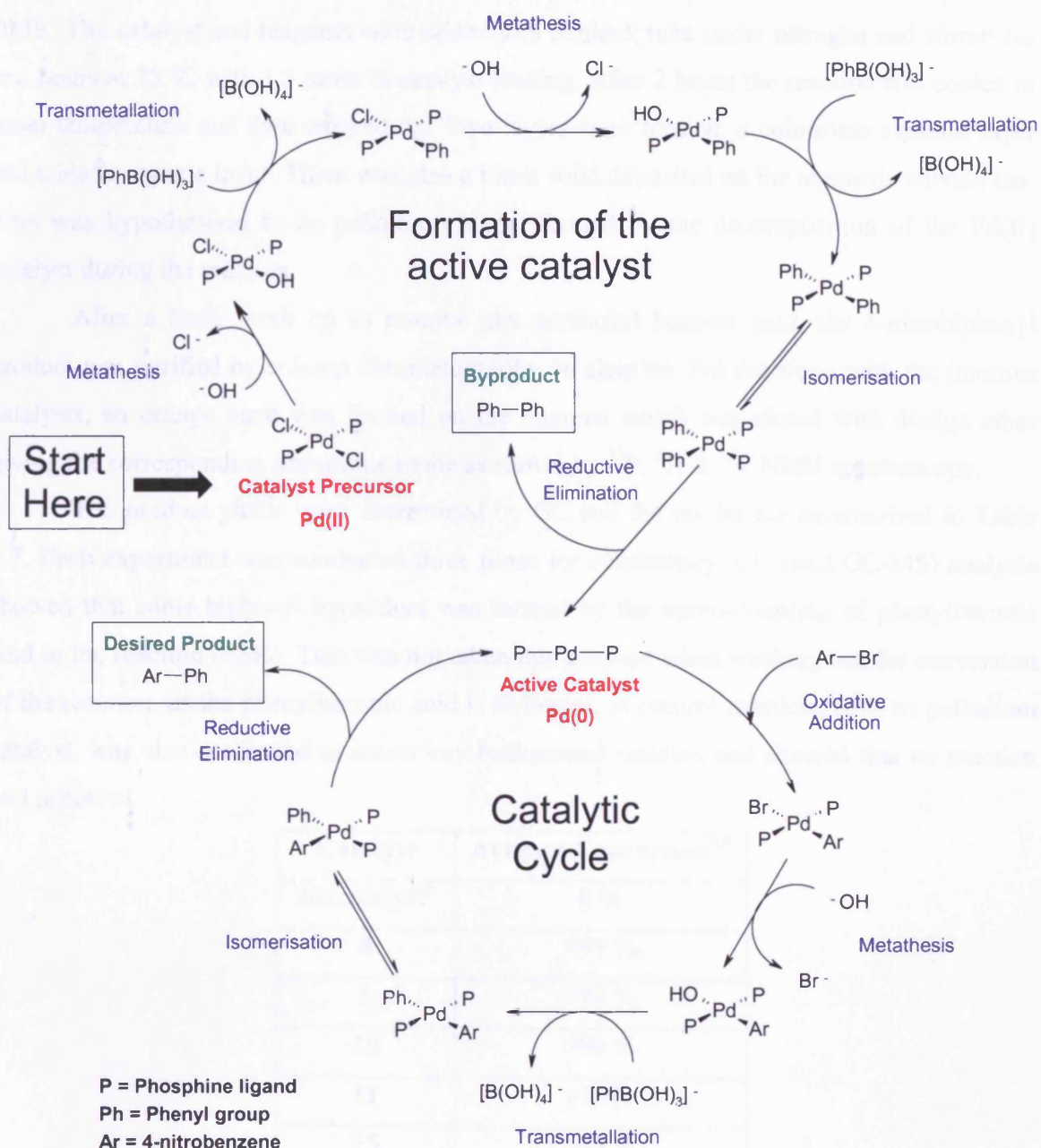
Scheme 2.20. *Proposed catalytic cycle for palladium(II) catalysts.*
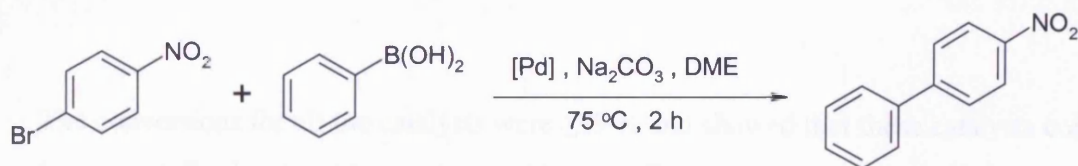
Scheme 2.21. *Suzuki coupling between 4-nitrobromobenzene and phenylboronic acid.*

4-Nitrobromobenzene and phenylboronic acid were chosen as the substrates for the model Suzuki reaction (Scheme 2.21) and the reaction conditions were modified from previous work.[16, 18] Initial studies were carried out without any attempts to recover the catalyst. Stock solutions of 4-nitrobromobenzene and phenylboronic acid were prepared in DME. The catalyst and reagents were added to a Schlenk tube under nitrogen and stirred for two hours at 75 °C with 1.5 mole % catalyst loading. After 2 hours the reaction was cooled to room temperature and then worked up. Two layers were formed; a colourless aqueous layer and a black organic layer. There was also a black solid deposited on the magnetic stirring bar. This was hypothesised to be palladium black, formed by the decomposition of the Pd(II) catalyst during the reaction.

After a basic work up to remove any unreacted boronic acid, the 4-nitrobiphenyl product was purified by column chromatography on alumina. For reactions with the fluorous catalysts, an orange band was formed on the alumina which was eluted with diethyl ether giving the corresponding phosphine oxide as shown by ^{31}P, ^{1}H & ^{19}F NMR spectroscopy.

The product yields were determined by GC and the results are summarised in Table 2.7. Each experiment was conducted three times for consistency. GC (and GC-MS) analysis showed that some biphenyl byproduct was formed by the homo-coupling of phenylboronic acid in the reaction (<3%). This was not taken into account when working out the conversion of the reaction, as the phenylboronic acid is in excess. A control reaction, with no palladium catalyst, was also conducted to detect any background reaction and showed that no reaction had occurred.

Catalyst	Average Conversion[a,b]
No catalyst[c]	0 %
8	>99 %
9	>99 %
10	>99 %
11	>99%
25	>99 %

[a]Determined by GC. [b]Average conversion taken over 3 runs .[c]Only 1 run carried out.

Table 2.7. *Results from the Suzuki reaction with 4-nitrobromobenzene and phenylboronic acid.*

The conversions for all the catalysts were ≥99 % and showed that these catalysts could be used successfully in Suzuki reactions without a fluorous support or perfluorocarbon solvent. Higher conversions were achieved here in comparison to previous work.[16] This is due

to a homogeneous system being obtained at elevated temperatures, which was not fully achieved in the biphase system.

The mechanism for the homo-coupling of arylboronic acids has been reported by Moreno-Manas and co-workers (Scheme 2.22)[24] This involves two consecutive oxidative additions of phenylboronic acid to the palladium(0) centre to create a palladium(IV) species. Reductive elimination of the organic groups gives the biphenyl byproduct, and a diboronpalladium(II) species. This undergoes β-hydride elimination to form a dihydridepalladium(II) species which undergoes reductive elimination, releasing dihydrogen, along with ligand association to reform the active catalyst.
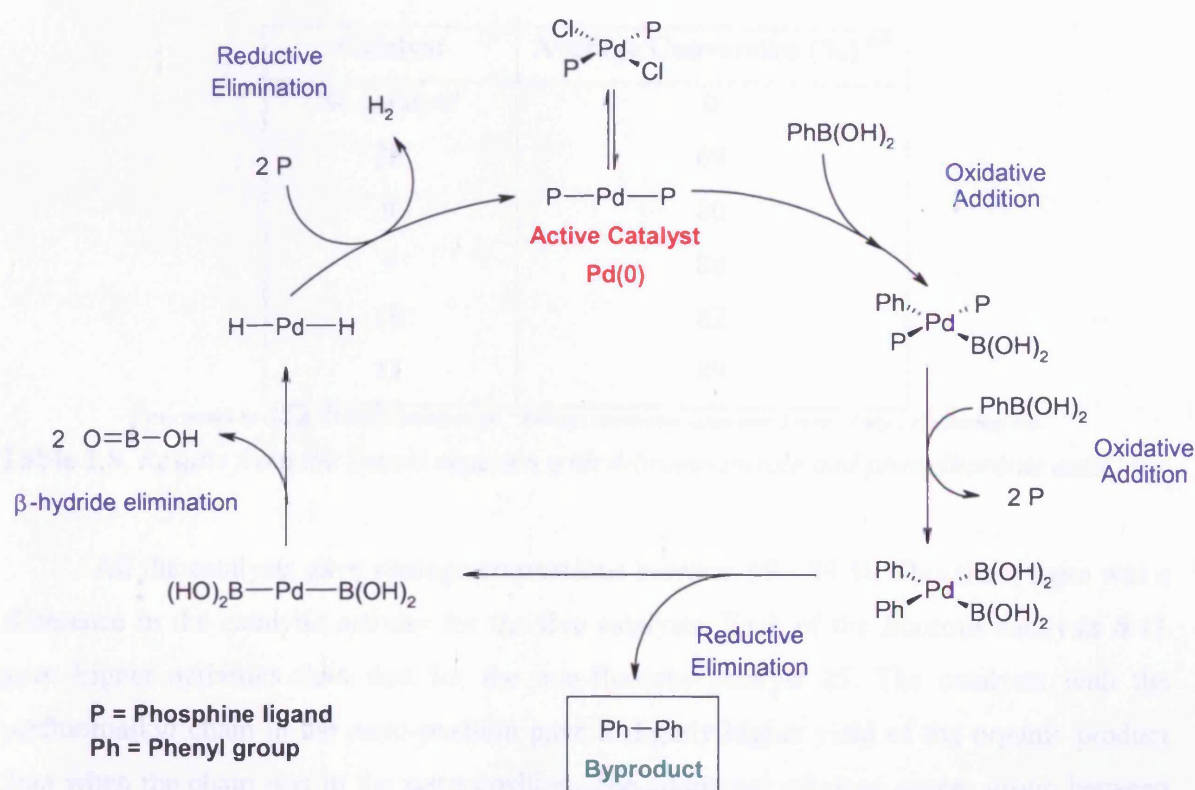
Scheme 2.22. *Catalytic cycle for the homo-coupling of phenylboronic acid.*

In order to differentiate the catalytic activity between the five catalysts a more demanding substrate was used, 4-bromoanisole. It is more difficult for 4-bromoanisole to undergo oxidative addition since the methoxy group donates electron density to the aromatic ring making the C-Br bond stronger.

The same reaction conditions were used, however, reaction times were increased from 2 to 4 h, as the product conversions for all five catalysts were lower. Tolyl ether was also added to the reaction mixture as an internal standard. After 4 hours, the reactions were allowed to cool to room temperature. Again, a considerable amount of insoluble palladium

black had formed during the reaction, which is evidence for the decomposition of the catalysts. Diethyl ether (10 mL) was added to the reaction mixture to help create a better separation between the organic and aqueous layers. It was noted that the insoluble colloidal palladium almost completely dissolved in the ether layer. Therefore, a sample was taken from each reaction vial, loaded onto a small plug of silica and eluted with diethyl ether (1.5 mL), to remove any palladium that may have been present.

The product conversions were determined by GC and ^{1}H NMR spectroscopy and the results are summarised in Table 2.8. Each experiment was conducted twice for consistency. Again, biphenyl was formed as a byproduct (<3 %).

Catalyst	Average Conversion (%)^{a,b}
No catalyst^c	0
25	69
8	80
9	88
10	82
11	89

^{a}Determined by GC &.^{1}H NMR spectroscopy. ^{b}Average conversion taken over 2 runs . ^{c}Only 1 run carried out.

Table 2.8. *Results from the Suzuki reaction with 4-bromoanisole and phenylboronic acid.*

All the catalysts gave average conversions between 69 - 89 %. This time, there was a difference in the catalytic activity for the five catalysts. Each of the fluorous catalysts 8-11 gave higher activities than that for the non-fluorous catalyst 25. The catalysts with the perfluoroalkyl chain in the *meta*-position gave a slightly higher yield of the organic product than when the chain was in the *para*-position. The additional ethylene spacer group between the perfluoroalkyl chain and the aromatic ring was shown not to have any effect on the activity of the fluorous catalysts.

These results were very surprising, as previously it had been reported that electron-rich metal centres are necessary for high activities of unactivated substrates. The results suggest that the electron withdrawing effects of the perfluoroalkyl chains had actually enhanced the activity of the catalysts instead of decreasing it.

The mechanism of the decomposition of the catalyst was still uncertain. It was necessary to prove that the phosphine oxide had been formed before the reaction mixture had been loaded onto the alumina column and not during the column chromatography. The fluorous material from the reaction was extracted using PP3 (3 x 10 mL) and the solvent was removed. The crude material was mainly determined to be the corresponding phosphine oxide 27-30 as

well as some of the organic product by ^1H, $^{31}P\{^1H\}$ and $^{19}F\{^1H\}$ NMR spectroscopy and FAB-MS. The fluorous phosphine oxide was purified by flash column chromatography to give the pure compound. This indicated that the phosphine ligand had dissociated from the palladium metal and had been oxidised during the reaction. Palladium metal was also deposited in the crude product that had dissolved in the PP3 from the reaction mixture during the fluorous extraction.

It was not clear whether the phosphine oxide had been formed in the reaction mixture *via* a decomposition pathway or whether it was the free phosphine ligand that had been oxidised in air. Attempts to analyse the reaction mixture *in situ* failed due to the low percentage of phosphine in the reaction mixture.

Alper has shown that there is an alkali-induced disproportionation reaction between a Pd(II) tertiary phosphine complex to a Pd(0) species and the corresponding phosphine oxide (Scheme 2.23).[25, 26] The proposed mechanism suggests a metathesis reaction between one of the chloride ions and hydroxide on the palladium(II) centre. The oxygen is then transferred from the palladium onto the phosphine and the phosphine oxide is eliminated forming a palladium(II) species which is then reduced to a palladium(0) complex.

Scheme 2.23. *Formation of phosphine oxide from $PdCl_2(PR_3)_2$.*

The formation of the active catalyst involves the loss of one of the phosphine ligands and the formation of phosphine oxide before any catalysis has taken place.[26, 27] The phosphine oxide can no longer stabilize the palladium centre to prevent the formation of colloidal palladium. If the remaining phosphine ligand dissociates, then the palladium centre would be ligandless and, therefore, there would be no fluorous domain to enable efficient recycling.

The recovery of phosphine oxide from all the catalytic reactions agrees with the mechanism in the literature. However, it can only account for the formation of 1 mole of phosphine oxide and so further investigation into analysis of the fluorous material under anaerobic conditions was needed. Attempts to analyse the catalyst *in situ* by HPLC, LC-MS and NMR spectroscopy failed mainly due to the low concentration of the catalyst in solution.

The explanation for the difference in the catalytic activities of **8-11** & **25** may now become clear. In order for the catalytic cycle to commence, the palladium(II) centre needs to

be reduced to a palladium(0) centre. As show above, for this to occur one of the phosphine ligands needs to be oxidized to the phosphine oxide. The more electron density that is removed from the phosphorus centre, the easier it should be to form the palladium(0) complex. Even though there are hydrocarbon spacers between the phosphorus atom and the perfluoroalkyl chains it is possible that the phosphorus centre is not completely shielded and, therefore, some electron density is still removed. This could explain why all of the fluorous catalysts were more active than the non-fluorous catalyst.

A further look at the position of the perfluoroalkyl chains showed that catalysts with the perfluoroalkyl chain in the *meta*-position **9** and **11** had a higher activity than the catalysts with the perfluoroalkyl chain in the *para*-position **8** and **10**. This can again be explained in terms of the increased inductive effect of the perfluoroalkyl chain in the *meta*-position in comparison to that in the *para*-position.

The observation that the fluorous solvent, PP3, dissolves colloidal palladium may explain why Bannwarth did not see any colloidal palladium and, therefore, detect any decomposition of the fluorous catalyst **8-11** in the Suzuki reaction under fluorous biphase conditions. It could also be tentatively suggested that, due to lack of solubility of free palladium metal in both DME and water, the palladium metal would reside in the fluorous solvent with very low amounts of leaching being observed and so the catalyst could be recycled with no, or very little, loss in activity being observed. The recycle of fluorous phase soluble palladium nanoparticles has also been reported.[28]

2.5.2 Catalyst Recovery and Reuse

From the initial work, it seemed unlikely that these catalysts could be recycled using Fluorous SPE, as there was strong evidence for decomposition of the catalysts in the reaction. However, the approach still needed to be carried out to confirm whether the catalysts could be recycled and, if so, reused. Identical reaction conditions were used as previously described using **10** as the catalyst along with 4-nitrobromobenzene and, once the work-up had been completed, the reaction mixture was loaded onto a column of FRPSG with a small amount of diethyl ether. Acetonitrile was used to elute the product from the column, the solvent removed and a conversion of >99 % to product was determined by GC. There no signs of catalyst/ligand leaching into the organic product ^{1}H, ^{19}F and ^{31}P NMR spectroscopy, however, ICP-OES determined 9.96 ppm of palladium had leached into the organic product, corresponding to 99 % of the total palladium. BTF was used to recover the fluorous compound, which was determined to be the corresponding phosphine oxide.

The recovered material was employed in an identical reaction and worked up under identical conditions. The residue was loaded onto a column of FRPSG using a small amount

of diethyl ether as solvent and the organic product eluted with acetonitrile. The conversion for the desired product was <1 % by GC, showing that the recycled compound was inactive. The column was washed with BTF to recover any fluorous material, however this was unsuccessful and no material was recovered. This is evidence for the hypothesis that the catalysts are decomposing and, therefore cannot be recycled.

However, Bannwarth was able to recycle 10 when using FRPSG as a catalyst solid support. This work was repeated to gauge the reproducibility of the results published and to confirm reaction conditions used in the catalyst testing were not the cause of the decomposition. The reaction conditions were identical to those described in Bannwarth's paper except nitrogen was used as the inert gas instead of argon (Scheme 2.24).

The solid support was synthesised by adding 1g of FRPSG to 10 mg of catalyst 10 in ether and hexafluorobenzene. The mixture was allowed to stir for 1 h before the solvent was removed to give the immobilised pre-catalyst as a yellow free-following solid. The supported catalyst was loaded into a Schlenk tube. Stock solutions of 4-nitrobromobenzene, phenylboronic acid and sodium carbonate were added to the Schlenk tube under nitrogen and stirred for 15 hours at 80 °C. After cooling, the reaction mixture was cooled to 0 °C and the liquid phase was removed under nitrogen using a syringe. The solid support was washed with DME and water to remove any free organic or inorganic products. The crude organic phase was purified by flash column chromatography on alumina to give the pure product with conversion >98 % by GC. There were no signs of catalyst leaching into the organic product by ^{1}H, ^{19}F and ^{31}P NMR spectroscopy, however, their analysis by ICP-OES to confirm palladium leaching had not occurred was not carried out. The support had changed in colour from bright yellow to brown, which may be due to formation of palladium black, spread over the FRPSG. The solid support was dried under vacuum and fresh reagents were added under the same reaction conditions. A conversion of >98 % was determined by GC for the 1st recycle and the solid support remained brown in colour.
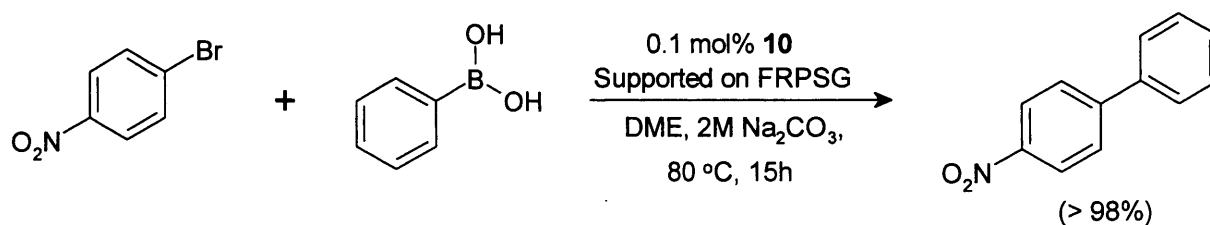
Scheme 2.24. *Suzuki coupling using 10 supported on FRPSG.*

These results do show that Bannwarth's results are reproducible, but it may be possible that the catalyst does decompose as in the previous system. This would lead to the formation of palladium metal supported on FRPSG. Therefore, if this were found to be true,

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the FRPSG would not be supporting a recyclable fluorous catalyst, but rather supporting catalytically active, recyclable palladium metal only.

After this work had been carried out, Bannwarth published an assessment of the reusability of palladium complexes supported on FRPSG as catalysts for Suzuki couplings.[29] A less active substrate, 4-bromobenzyl alcohol, was used instead of the highly active 4-nitrobromobenzene. Kinetic data was used to assess whether the catalyst could be recycled. When complex 10 was supported on FRPSG and used in a Suzuki reaction using DME as a solvent, the catalytic activity dramatically decreased upon reuse of the catalyst. The author attributed this drop in activity to catalyst decomposition and not catalyst leaching.

2.6 Triarylphosphines – Conclusions

The synthesis and coordination chemistry of fluorous-derivatised triarylphosphines has been investigated using novel chemistry and modified literature methods. In some cases, yields obtained were greater than those reported in the literature, showing an improvement in the synthesis. The fluorous-derivatised triarylphosphine complexes were shown to be more active in the Suzuki reaction, compared with the non-fluorous analogue. However, it is unlikely that the reaction proceeds as originally thought and, rather, the catalysts are decomposing to form palladium black such that it is not the fluorous catalysts that are recycled.

Separation studies using 10 have shown that the catalyst precursor can be recovered successfully using FRPSG. However, recycling experiments using Fluorous SPE have been unsuccessful due to the decomposition of the catalyst, confirmed by the formation of palladium black and the isolation of the corresponding phosphine oxide.

2.7 Reference for Chapter Two

1   E. G. Hope and A. M. Stuart, *J. Fluorine Chem.*, 1999, **100**, 75.

2   P. Bhattacharyya, D. Gudmunsen, E. G. Hope, R. D. W. Kemmitt, D. R. Paige, and A. M. Stuart, *J. Chem. Soc., Perkins Trans. 1*, 1997, 3609.

3   B. Betzemeier and P. Knochel, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2623.

4   B. Croxtall, J. Fawcett, E. G. Hope, and A. M. Stuart, *J. Chem. Soc., Dalton Trans.*, 2002, 491.

5   E. G. Hope, R. D. W. Kemmitt, D. R. Paige, A. M. Stuart, and D. R. W. Wood, *Polyhedron*, 1999, **18**, 2913.

6   D. J. Adams, E. G. Hope, and A. M. Stuart, 'Unpublished work.'

7   S. Schneider and W. Bannwarth, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 4142.

8   W. Chen and J. Xiao, *Tetrahedron Lett.*, 2000, **41**, 3697.

9   S. Kainz, D. Koch, W. Baumann, and W. Leitner, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 1628.

10   Q. Zhang, Z. Luo, and D. P. Curran, *J. Org. Chem.*, 2000, **65**, 8866.

11   S. Darses, M. Pucheault, and J.-P. Genêt, *Eur. J. Org. Chem.*, 2001, 1121.

12   W. Chen, L. Xu, Y. Hu, A. B. Banet Osuna, and J. Xiao, *Tetrahedron*, 2002, **58**, 3889.

13   D. Sinou, G. Pozzi, E. G. Hope, and A. M. Stuart, *Tetrahedron Lett.*, 1999, **40**, 849.

14   B. Richter, E. de Wolf, G. van Koten, and B. J. Deelman, *J. Org. Chem.*, 2000, **65**, 3885.

15   J. Moineau, G. Pozzi, S. Quici, and D. Sinou, *Tetrahedron Lett.*, 1999, **40**, 7683.

16   S. Schneider and W. Bannwarth, *Helv. Chim. Acta*, 2001, **84**, 735.

17   C. Markert and W. Bannwarth, *Helv. Chim. Acta*, 2002, **85**, 1877.

18   C. C. Tzschucke, C. Markert, H. Glatz, and W. Bannwarth, *Angew. Chem. Int. Ed. Engl.*, 2002, **41**, 4500.

19   V. C. R. McLoughlin and J. Thrower, *Tetrahedron*, 1969, **25**, 5921.

20   J. Fawcett, E. G. Hope, R. D. W. Kemmitt, D. R. Paige, D. R. Russel, and A. M. Stuart, *J. Chem. Soc., Dalton Trans.*, 1998, 3751.

21   J. J. MacDougall and J. H. Nelson, *Inorg. Nucl. Chem. Letters*, 1979, **15**, 315.

22   S. O. Grim and R. L. Keiter, *Inorg. Chim. Acta*, 1970, **4**, 56.

23   D. J. Adams, J. A. Bennett, D. Duncan, E. G. Hope, J. Hopewell, A. M. Stuart, and A. J. West, *Polyhedron*, 2007, **26**, 1505.

24   M. Moreno-Manas, M. Pérez, and R. Pleixats, *J. Org. Chem.*, 1996, **61**, 2346.

25   V. V. Grushin and H. Alper, *Organometallics*, 1993, **12**, 1890.

26   N. J. Whitcombe, K. K. Hii, and S. E. Gibson, *Tetrahedron*, 2001, **57**, 7449.

27   I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009.

28   M. Moreno-Manas, R. Pleixats, and S. Villarroya, *Organometallics*, 2001, **20**, 4524.

29   C. C. Tzschucke, V. Andrushko, and W. Bannwarth, *Eur. J. Org. Chem.*, 2005, 5248.

Chapter Three

University *of* Leicester

3. Investigation into PCP Pincers

3.1 Introduction

3.1.1 Non-fluorous Pincer Complexes

Pincer complexes were first reported in the 1970's and have been extensively studied due to their unique properties. The general structure for a pincer complex is a metal centre bound through a σ-bond to a carbon atom of the ligand backbone, which is generally a benzene ring (Figure 3.1). The metal centre is stabilised by two donor atoms, typically P, N, S or O, which are linked to the carbon-backbone by the bridging atoms, typically C but sometimes O. There are many different types of pincer complexes that have been reported but the most common types are the PCP, SCS, and NCN complexes.

M = Metal

X = Bridging Group

Y = Donor Atom
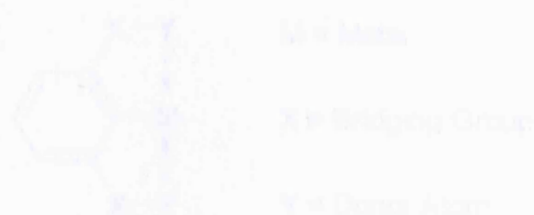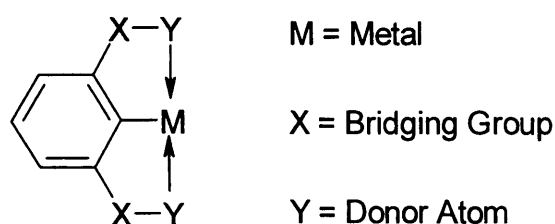
Figure 3.1. *General structure of pincer complexes.*

The carbon-metal σ-bond is responsible for the high stability of the pincer complexes. They have been shown to be thermally stable, allowing reactions to be carried out at high temperatures for long durations. This is advantageous as the metal cannot easily dissociate from the ligand. Reactions can also be carried out in air, demonstrating a resistance to reactions with oxygen and moisture.

The properties of the metal complex can be finely tuned by varying the reactivity for specific reactions. The steric hinderance around the metal centre can be varied depending on the substituents on the donor atoms, as well as changing the metal, which influences the geometry and coordination number. Electronic properties can also be extremely varied, with donor atoms, as well as the aryl backbone, bearing a range of electron-donating, -withdrawing or -neutral groups.

In 1976, Shaw and Moulton reported the first pincer complexes, based on a PCP ligand bearing *t*-butyl groups **31** (Figure 3.2).[1] A range of different transition metal complexes **32** were synthesised and characterised but there were no applications reported at this time. It was not until the late 1990's, that the first application of this type of metal complex was reported. Milstein *et al.* synthesised three new anionic palladium(II) PCP pincer complexes **36-38** and demonstrated their use in Heck reactions.[2] The complexes were prepared in high yield, by treatment of [Pd(TFA)$_2$] with the corresponding *bis*-phosphines **33-35** in THF at 80 °C (Scheme 3.1).

M = Pd, X = Cl
M = Pt, X = Cl
M = Ni, X = Cl
M = Rh, X = HCl
M = Ir, X = HCl

31   **32**
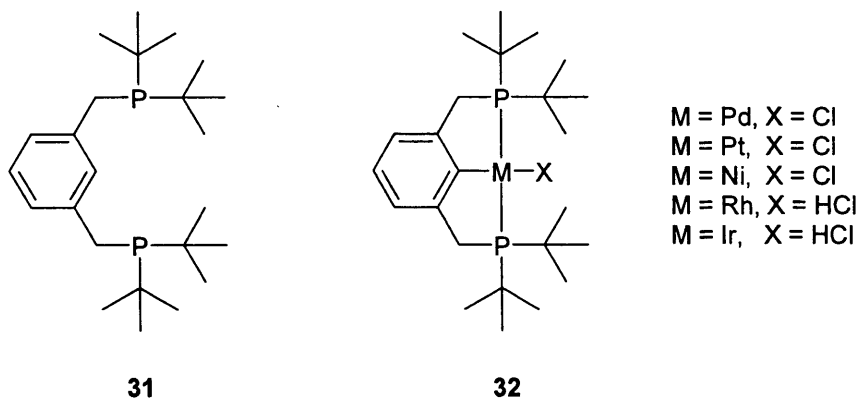
Figure 3.2. *First reported pincer ligand and transition metal complexes.*

34 R = *i*-Pr   **37** R = *i*-Pr
33   **36**   **35** R = *t*-Bu   **38** R = *t*-Bu

(i) [Pd(TFA)$_2$], THF, 80 °C.
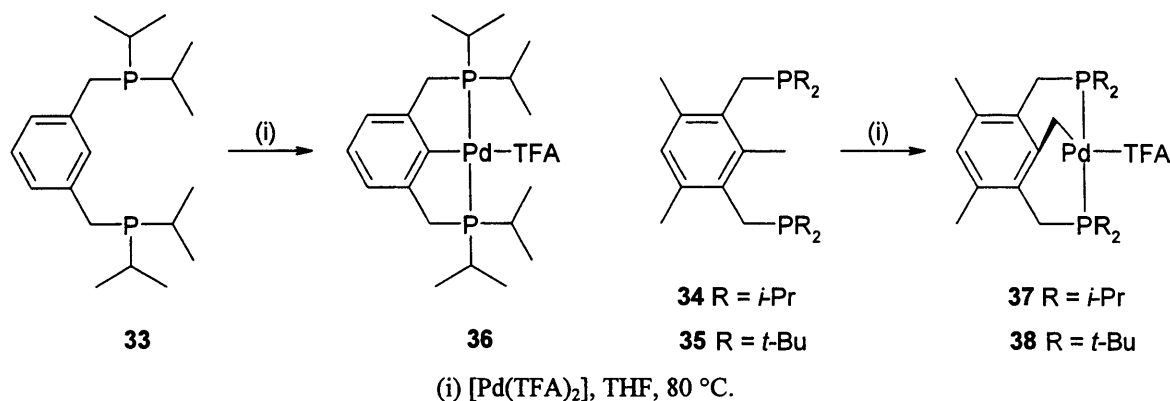
Scheme 3.1. *Synthesis of anionic palladium PCP pincer complexes 34, 37 and 38.*

Complexes **36-38** are extremely thermally stable and are not sensitive to oxygen and moisture; with no decomposition observed at temperatures up to 180 °C and reactions carried out in air with no change in rate or yield. Catalysts **36-38** were extremely active in Heck reactions coupling aryl iodides and bromides with alkenes in the presence of extremely low catalyst loadings of < 10^{-4} mol-% (Scheme 3.2 & Table 3.1). NMP was used as solvent and one equivalent of sodium carbonate was used as a base, along with lengthy reaction times gave high conversions. All reactions with iodobenzene and methyl acrylate went essentially to complete conversion, achieving turnover numbers (TONs) greater than 500,000. Lower conversions were achieved with aryl bromides, however, high TONs were still achieved. There was almost no catalytic activity observed with chlorobenzene. Catalyst **37** was found to be the most active catalyst achieving turnover numbers of 528,700 for the reaction with iodobenzene and 132,900 for the reaction with bromobenzene.
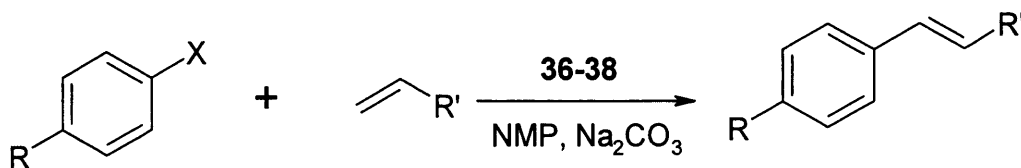
Scheme 3.2. *Heck reactions with catalysts 36-38.*

R	X	R'	Cat.	Cat. (mol-%)	Temp/°C	Time/h	TON	Yield/%
H	I	COOMe	36	7.0×10^{-5}	40	60	142,900	100
H	I	COOMe	36	1.8×10^{-5}	140	350	520,500	91
H	I	COOMe	37	1.8×10^{-5}	140	40	528,700	95
H	I	COOMe	38	7.0×10^{-5}	140	40	142,900	100
H	I	COOBu	36	7.0×10^{-5}	140	40	5,650	4
H	I	COOBu	36	7.0×10^{-5}	160	88	108,000	77
H	I	COOBu	37	7.0×10^{-5}	140	64	142,900	100
H	I	COOBu	37	7.0×10^{-5}	160	14	142,900	100
MeO	I	COOMe	37	7.0×10^{-5}	140	16	142,900	100
H	Br	COOMe	37	7.0×10^{-5}	140	63	132,900	93
CHO	Br	COOMe	37	7.0×10^{-5}	140	63	113,300	79

Table 3.1. *Selected results from Heck reactions with 36-38.*[2]

At the end of the reactions the catalyst remained highly active and upon the addition of more substrates the reaction continued at essentially the same rate. The authors report no evidence of catalyst decomposition by ^{31}P NMR spectroscopy, with the only noted change being the substitution of the TFA ion to the corresponding palladium halide complex. However, with the small amounts of catalyst present in the reaction mixture, along with the limited sensitivity of the NMR spectrometer, it may be possible that a small amount of decomposition could have occurred and not have been detected.

Since this time there has been an increased interest in pincer complexes as catalysts for organic reactions.[3-6] Jensen *et al.* have reported the synthesis and catalysis of a phosphinito palladium PCP pincer complex **39** that shows extremely high activity towards aryl chlorides in Heck reactions with styrene (Scheme 3.3 & Table 3.2).[7] Reactions were carried out in dioxane and caesium carbonate was generally used as the base. When the reaction temperature was 120 °C, reaction times were typically 5 days to achieve a high conversion to the product, however, due to the pincer complex's high thermal stability, reaction temperatures of up to 180 °C could be achieved, thereby allowing a dramatic reduction in the reaction time to 24 h.

39 R = *i*Pr
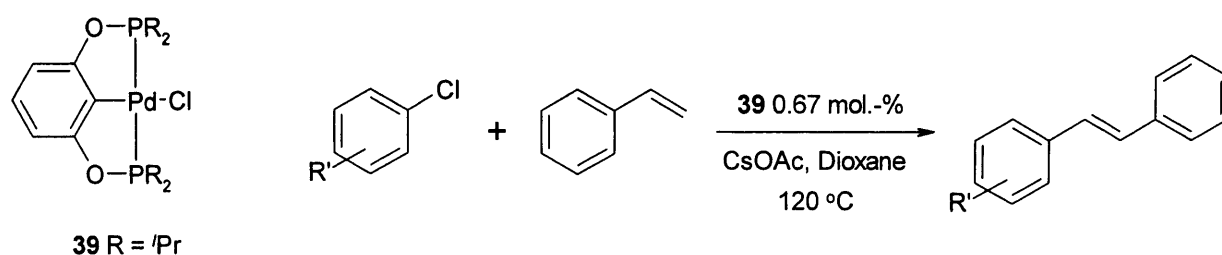
Scheme 3.3. *Heck reactions catalysed by phosphinito palladium PCP pincer complex 39.*

63

R'	Yield/%
H	> 99
4-MeCO	> 99
4-MeO	86
4-CHO	81
2-Me	83

Table 3.2. *Results from Heck reactions with catalyst 39.*[7]

Shibasaki *et al.* reported the synthesis of a phosphito palladium PCP pincer complex **40** and its application in catalysis that generated an isolated yield of 60 % of the organic product with a TON of 6,000,000 (Figure 3.3).[8] The reaction of iodobenzene and butyl acrylate was catalysed by 0.1 ppm of **40**, in NMP with sodium carbonate as the base at 180 °C. When hydroquinone was used as an additive a TON of 8,900,000 was achieved.
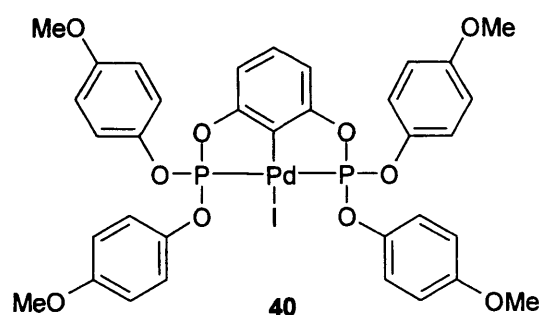
Figure 3.3. *Phosphito palladium PCP pincer complex 40.*

In 2000, Bedford *et al.* reported the first palladium PCP pincer complexes to successfully catalyse Suzuki reactions.[9] The *bis*-phosphinito complexes **41-42** catalysed a range of deactivated and sterically hindered aryl bromides and activated aryl chlorides with catalyst loadings between 0.1 - 0.0001 mol-% (Scheme 3.4 & Table 3.3).
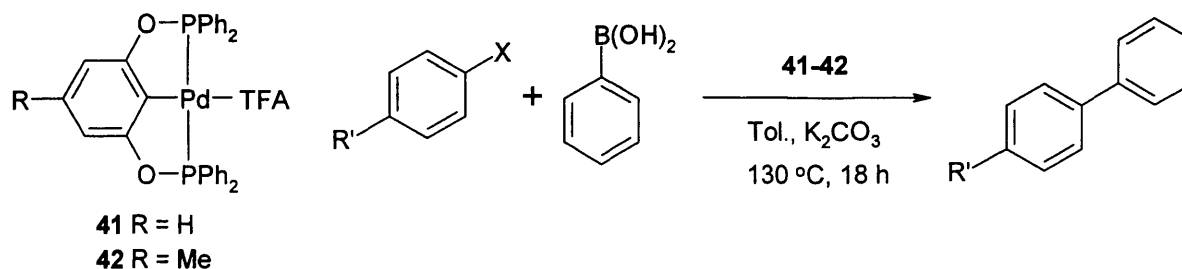
Scheme 3.4. *Catalysts 41 & 42 in Suzuki reactions.*

R'	X	Cat.	Cat. (mol-%)	Yield/%	TON
MeCO	Br	41	0.001	59	59,000
MeCO	Br	42	0.001	92	92,000
MeCO	Br	41	0.0001	19	190,000
MeCO	Br	42	0.0001	18	180,000
MeO	Br	41	0.0001	19	190,000
MeO	Br	42	0.0001	15	150,000
2-Me	Br	41	0.01	87	8,700
NO$_2$	Cl	41	0.01	43	4,300
NO$_2$	Cl	42	0.01	40	4,000

Table 3.3. *Selected results for the catalysis of 41-42 in Suzuki reactions.* [9]

3.1.2 Reusable Catalysts

Pincer complexes have been demonstrated to be highly active and robust catalysts, which in turn has made them highly attractive candidates for the synthesis of a variety of recyclable complexes. The 5-position of the aryl backbone gives an ideal site for the modification of complexes, to add an appendage to enable the recovery of these complexes from their organic products, for reuse in further catalytic reactions. Examples of some methods used include immobilisation on hyperbranched polyglycerol,[10] fullerenes[11, 12] and supports such as silica,[13, 14] dendrimers,[15, 16] polymers,[13] clays[17] and PEG.[18]

Bergbreiter *et al.* synthesised a soluble poly(ethylene glycol)-bound 5-amido SCS palladium pincer **43**.[18] The catalyst was active in Heck reactions with a range of aryl iodides and was successfully recycled three times in two different systems; iodobenzene with methyl acrylate and styrene. Reactions were carried out at 115 °C in air, using DMF as the solvent with triethylamine (Scheme 3.5). At the end of the reaction the catalyst was precipitated out of solution with diethyl ether, filtered and the catalyst was redissolved in DMF before fresh substrates were added. Both systems gave constant yields over the three runs with no signs of loss in activity, achieving accumulative TONs of 1815 and 2780 for the acrylate and styrene substrates respectively (Table 3.4).
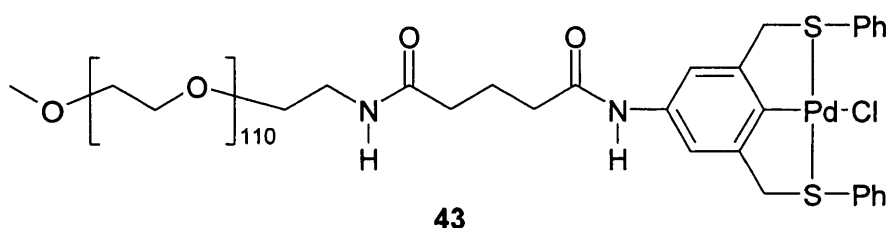
Figure 3.4. *Poly(ethylene glycol)-bound 5-amido SCS palladium pincer 43.*
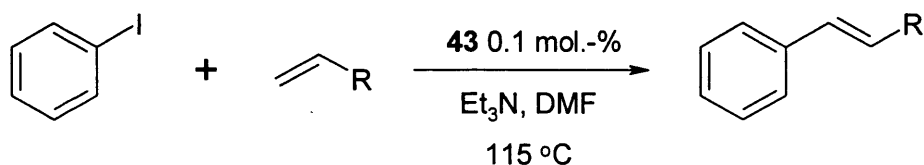
Scheme 3.5. *PEG-supported SCS pincer in Heck catalysis.*

R	Run	Time/h	Prod. Yield/%
CO₂Me	1	2.5	91
	2^a	2.5	95
	3^a	2.5	92
Ph	1	6.5	85
	2^a	6.5	87
	3^a	6.5	92

Data from Ref 18. ^{a}Catalysis carried out using 43 from the previous run.

Table 3.4. *Recycling results for 43 in Heck reactions.*

Despite the encouraging recycling results, there was no reported analysis of palladium leaching from the supported catalyst to the organic product for either of the systems or the amount of palladium/support recovered. This is an important consideration as moderate losses could be obtained without a noticeable drop in reaction yields.

There are also some disadvantages to this system. Under the reactions conditions the catalyst was limited to reactions with aryl iodides only as aryl bromides were shown to be significantly less reactive. Extensive ligand modification was necessary for the synthesis of **43**, which could be extremely time consuming and expensive.

Apler and Chanthateyanonth reported the first synthesis of a palladium(II) PCP catalyst supported on silica, **44**.[14] The supported catalyst was shown to be extremely thermally stable, withstanding temperatures up to 170 °C and was air stable. **44** successfully catalysed Heck reactions with iodobenzene and a range aryl bromides with styrene and acrylates. Reactions were carried out at 140 °C in NMP with sodium carbonate and catalyst loadings of 0.03 mol-% and 0.8 mol-% for iodobenzene and aryl bromides respectively.

44   **45**
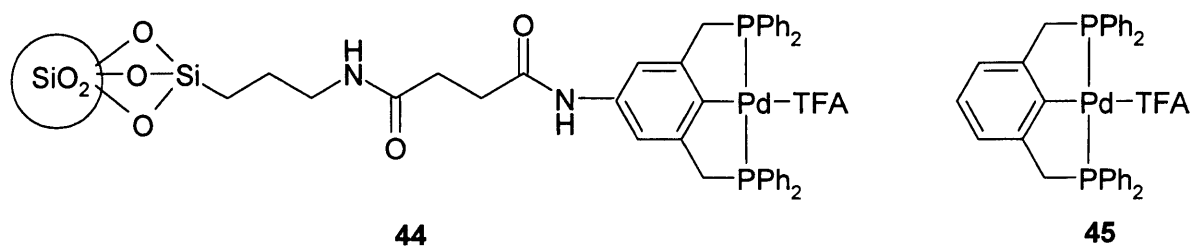
Figure 3.5. *Palladium(II) PCP catalyst supported on silica* **44** *& the unsupported analogue* **45**.

The supported catalyst **44** was successfully recovered by filtration and reused in a range of Heck reactions with aryl bromides (Scheme 3.6 & Table 3.5). Recycling results were generally good with yields for the organic product remaining fairly constant over three runs and yields for the reaction between bromobenzene and butyl acrylate remaining consistent over five runs. After the third run with 4-bromoanisole and methyl acrylate, the support was analysed for its palladium content by ICP. The results showed that the total palladium content was 1.45 mass %, which was 87 % of the original amount, indicating that there had been some leaching of the metal throughout the process.

When 4-bromotoluene and methyl acrylate were used, poor recycling results were obtained with significant drops in the product yield. ICP analysis showed that there was a large drop in palladium content to 0.7 mass % of palladium after the third run, indicating decomposition of the catalyst in this system. Again, extensive ligand modification was necessary and, due to the heterogeneous nature of the support, lower activity was achieved when **44** was compared with the homogeneous unsupported catalyst **45**.
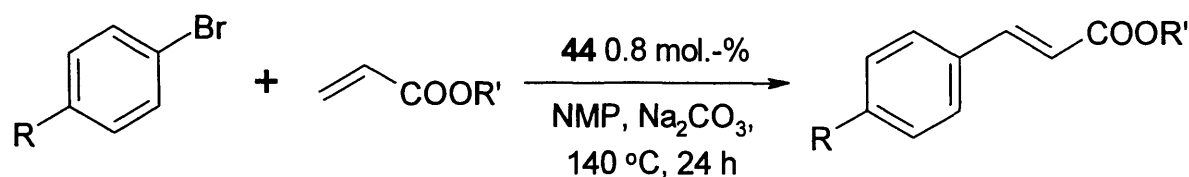
Scheme 3.6. *Recycling of* **44** *in Heck reactions.*

R	R'	Run	Yield/%
H	Bu	1	86
		2	86
		3	79
		4	70
		5	79
OMe	Me	1	95
		2	92
		3	94
Me	Bu	1	> 99
		2	85
		3	58

Table 3.5. *Selected results from recycling of* **44** *in Heck reactions.*[14]

3.1.3 Fluorous Pincer Complexes

There have been four variably successful reports on the synthesis and application of pincer complexes incorporating perfluoroalkyl groups. The first fluorous pincer complex was reported by van Koten *et al.* in 1998, using a modified protocol to synthesise fluorous NCN nickel and platinum complexes (Scheme 3.7).[19] The metal complexes were synthesised with the intention for use in FBC. The synthesis of the ligands was achieved starting with **46**, which was modified with a silyl group bearing a perfluoroalkyl chain. A second lithiation followed by the addition of either [NiCl₂(PEt₃)₂] or [PtCl₂(SEt₂)₂] gave the nickel and platinum NCN pincer complexes **49-52** in good yields.

(i) 2 eq. *t*-BuLi; (ii) ClSiMe₂(CH₂CH₂Rf); (iii) *t*-BuLi; (iv) [NiCl₂(PEt₃)₂] or [PtCl₂(SEt₂)₂].
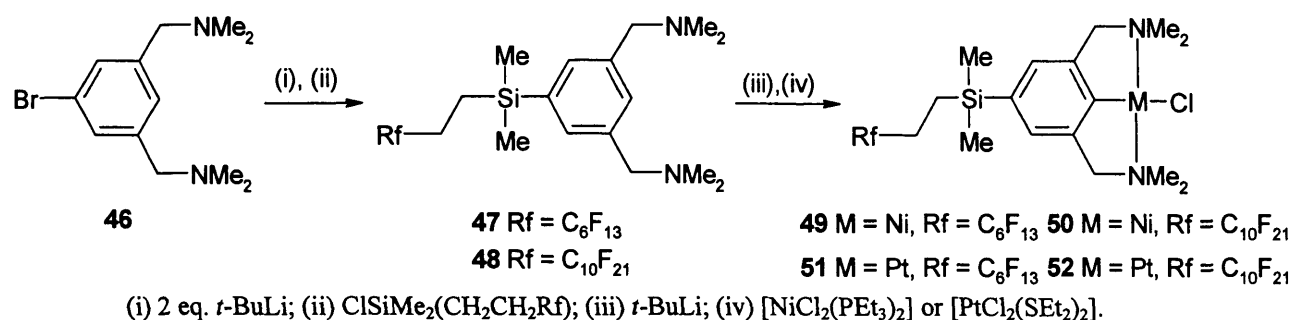
Scheme 3.7. *Synthesis of Nickel and Platinum NCN pincer complexes 49-52.*

Nickel complexes **49** & **50** were tested in the Kharasch addition of CCl₄ and methylmethacrylate (Scheme 3.8). When compared to the non-fluorous parent complex, almost identical catalytic activities were observed with similar rates of reaction and selectivity. Unfortunately, neither complex **49** nor **50** were sufficiently soluble for use in FBC, probably due to the low percentage of fluorine, by weight, present in each of the complexes.
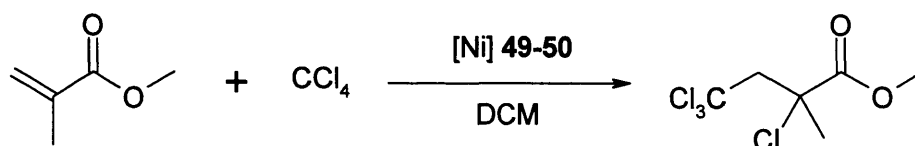
Scheme 3.8. *Catalysis of Nickel NCN 49-50 in Kharasch Addition Reaction.*

After this, van Koten reported the synthesis of a ruthenium PCP pincer catalyst, however, this ligand contained three perfluoroalkyl chains on the silicon atom, providing greater fluorine content by weight (Scheme 3.9).[20] Again the silyl group was attached to the aryl ring of the backbone of the pincer structure providing insulation to the metal centre from the electron withdrawing perfluoroalkyl chains.

68

Reaction of *bis*-phosphine **53** with two equivalents of *t*-BuLi before reacting with the silyl bromide bearing the perfluoroalkyl component gave **54** in excellent yield. Heating ligand **54** in the presence of [RuCl$_2$(PPh$_3$)$_3$] produced the pincer complex **55** in good yield.

53   **54**   **55**

(i) 2 eq *t*-BuLi, Et$_2$O, -80 °C; (ii) BrSi(C$_2$H$_4$C$_8$F$_{17}$)$_3$, -80 °C to rt; (iii) [RuCl$_2$(PPh$_3$)$_3$], DCE, reflux.
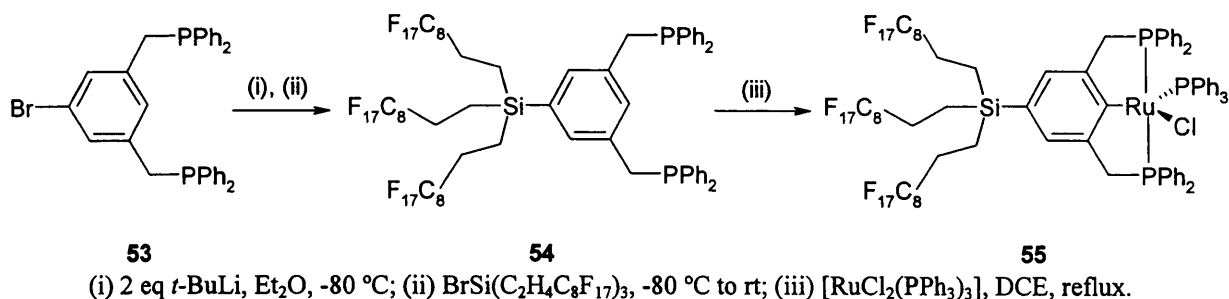
Scheme 3.9. *Synthesis of Ruthenium PCP pincer complex 55.*

The pincer complex **55** has reasonable fluorine content, 43 % by weight, and shows good solubility in FC-72, a mixture of perfluorohexanes, therefore showing promise for use in biphase catalysis. However, since this initial report there have been no further publications on this catalyst or its use in catalysis.

In 2004, Curran *et al.* reported the synthesis of a fluorous palladium SCS pincer catalyst (Scheme 3.10).[21] Perfluoroalkylated bromobenzene **56** was lithiated and thiolated before reacting with acetyl chloride to give **57** in moderate yield. Deacylation followed by direct treatment with 1,3-*bis*(bromomethyl)benzene provided the fluorous SCS ligand **58** and subsequent reaction with [PdCl$_2$(MeCN)$_2$] gave the pincer complex **59** in 71 % yield.

56   **57**

58   **59**

(i) *t*-BuLi; (ii) S$_8$; (iii) AcCl; (iv) MeLi; (v) 1,3-BrCH$_2$C$_6$H$_4$CH$_2$Br; (vi) [PdCl$_2$(MeCN)$_2$].
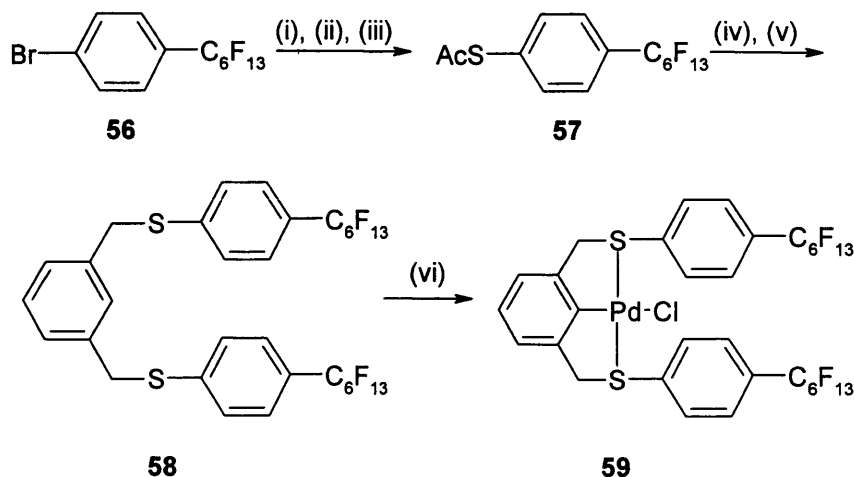
Scheme 3.10. *Synthesis of Palladium SCS pincer complex 59.*

The fluorous palladium SCS pincer catalyst **59** has successfully been used in the catalysis of a number of Heck reactions coupling either methyl acrylate or styrene. Using a catalyst loading of 3 mol-% with tributylamine as a base along with DMA as a solvent, good to excellent reaction yields were achieved under microwave conditions within 45 minutes or

less (Scheme 3.11 & Table 3.6). Several of the reactions were also successful under thermal conditions although longer reaction times were needed.
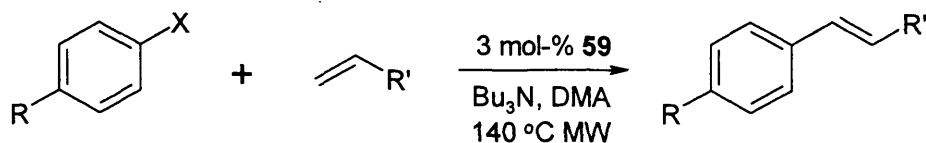
Scheme 3.11. *Complex 59 in Heck Reaction.*

R	X	R'	Time/min	Yield/%
MeO	I	CO₂Me	45	89
CN	Br	CO₂Me	45	84
COMe	I	CO₂Me	30	90
COMe	Br	CO₂Me	30	94
COMe	OTf	CO₂Me	30	87
NO₂	I	CO₂Me	30	79
H	I	Ph	30	82
MeO	I	Ph	45	76
CN	Br	Ph	45	78
COMe	I	Ph	45	89
COMe	Br	Ph	45	92

Table 3.6. *Selected results from fluorous SCS pincer 59 in Heck reactions.*[21]

The catalyst **59** was successfully recovered and reused in a number of reactions between 4-bromoacetophenone and methyl acrylate (Scheme 3.12 & Table 3.7). After 30 minutes the reaction was cooled before the mixture was loaded onto a column of FRPSG. The non-fluorous compounds were eluted with a MeOH/H₂O (90:10) mixture whilst the fluorous catalyst **59** remained on the column. Elution of the column with diethyl ether gave the recovered catalyst, which was recrystallised before being reused in the next reaction.
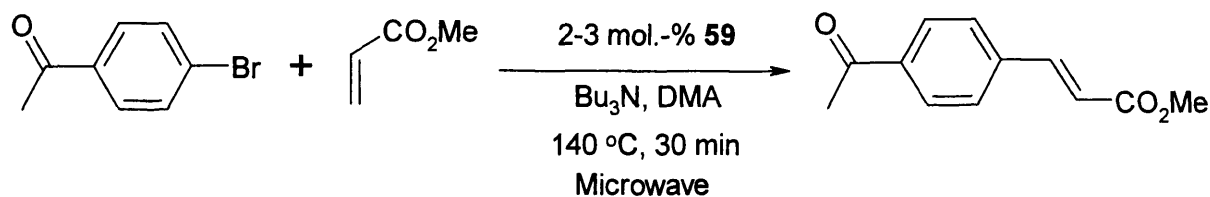
Scheme 3.12. *Complex 59 in Heck recycling reactions.*

Run	Amount [59] used/mg	Cat. Loading/ mol.-%	Prod. Yield./%	Amount [59] recovered
1	41.5	3.00	94	31.4 mg, 76 %
2[a]	31.4	2.28	97	26.0 mg, 83 %
3[a]	26.0	1.88	98	19.6 mg, 75 %

Data from Ref 21.[a]Catalysis carried out using [PdCl(Rf-PCP)] from the previous run.

Table 3.7. *Recycling results for fluorous SCS pincer 59.*

Interestingly, the yield of the reaction is not affected by the drastic change in catalyst loading, from 3 mol-% in the first run to less than 2 mol-% in the third run suggesting that that there is an excess of catalyst in the reaction.

On a larger scale reaction, the organic product was analysed for traces of palladium. 74 ppm was found, corresponding to 0.45% of the original palladium. However, although this is a low amount of palladium, it is important to note that the product was subjected to further purification after recovery from the FRPSG column that may have removed some residual palladium.

In 2005 Gladysz *et al.* reported the synthesis of fluorous palladium and iridium PCP complexes where the fluorous appendage was attached to the phosphorus donor atoms.[22] Several different syntheses were used to isolate the final PCP ligand **61**, however, the yields for these reactions were extremely poor. Radial reactions between *bis*-phosphine **60** and fluorous alkenes in the presence of AIBN produced poor yields of the desired pincer ligand **61** with large amounts of byproduct **62** (Scheme 3.13). Similar yields were achieved using thermal and photochemical methods.

60

61

Rf = C_8F_{17}, 4-17 %

Rf = C_6F_{13}, 11 %

62

Rf = C_8F_{17}, 35 %

Rf = C_6F_{13}, 30 %
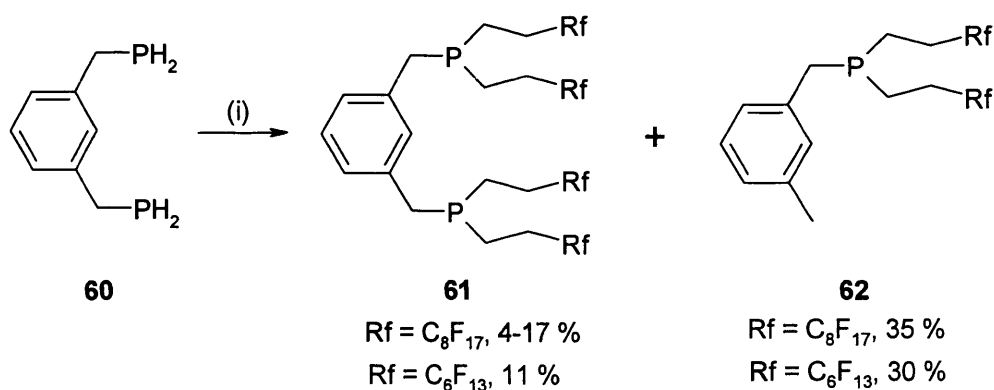
(i) 4 eq RfCH=CH$_2$, AIBN; 75 °C or UV.

Scheme 3.13. *Attempted synthesis of PCP pincer ligand 61.*

Reaction of 1,3-*bis*(bromomethyl)benzene with phosphine **63** formed diphosphonium salts **64**, which when treated with LiAlH$_4$ isolated **61** in a 20 % yield along with considerable

byproducts, including **62** (Scheme 3.14). Further attempts to optimise the reaction using this method were unsuccessful achieving similar results.
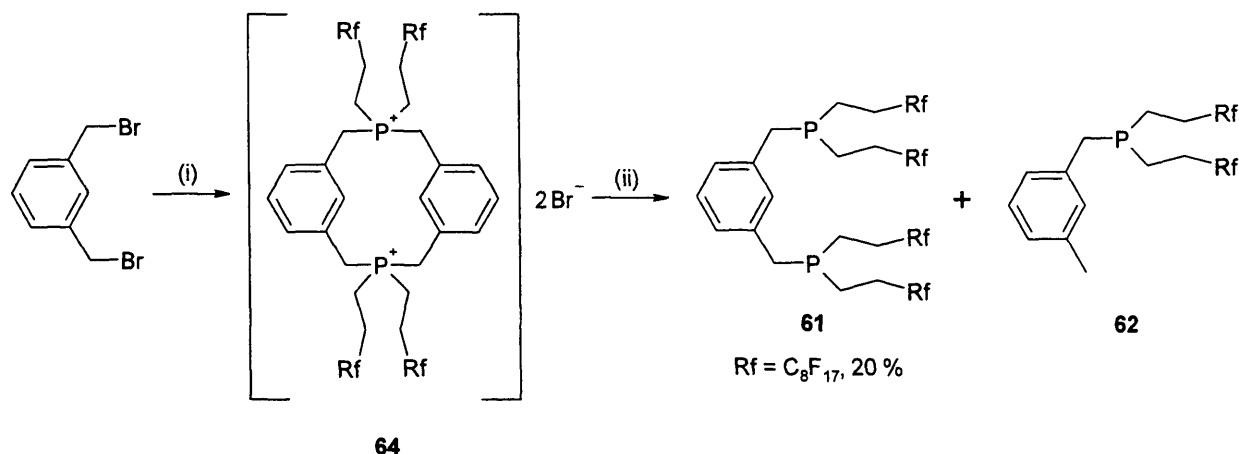
(i) 2 eq HP(C$_2$H$_4$C$_8$F$_{17}$)$_2$ **63**, 80 °C; (ii) LiAlH$_4$, THF, 0 °C.

Scheme 3.14. *Attempted synthesis of PCP pincer ligand 61.*

In an alternative method, a borane-protected phosphine **65** was used, which upon deprotonation could react with 1,3-*bis*(bromomethyl)benzene and then subsequent reaction with diethylamine would give the free pincer phosphine ligand **62** (Scheme 3.15). When KOH, *n*-BuLi or *t*BuOK were used as the base only trace amounts of the desired ligand **62** were detected.
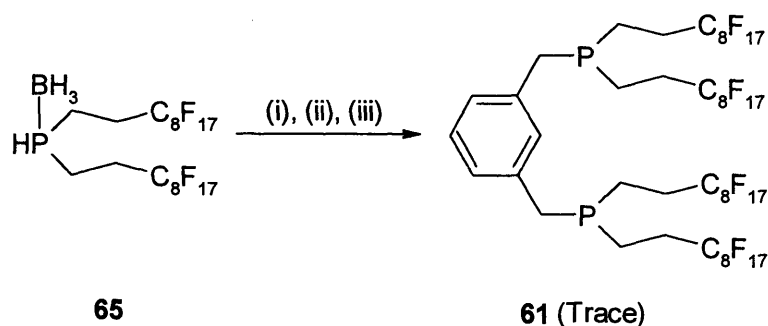
(i) KOH or *n*-BuLi or *t*BuOK; (ii) 1,3-(BrCH$_2$)$_2$C$_6$H$_4$; HNEt$_2$.

Scheme 3.15. *Failed synthesis of PCP pincer ligand 61.*

In spite of the poor yields achieved in the synthesis of **61**, the palladium and iridium complexes were synthesised using [Pd(TFA)$_2$] or [{IrCl(COE)$_2$}$_2$] respectively (Scheme 3.16). Both complexes containing perfluorooctyl chains obtained partition coefficients that were biased towards a fluorous solvent system; a CF$_3$C$_6$F$_{11}$/toluene system gave >96:<4 partition coefficient respectively.

The palladium complexes **66** were tested in catalytic Heck reactions between aryl halides and alkenes. Complexes that were isolated by extraction were found to be highly active, however, complexes isolated by column chromatography were nearly inactive. The authors speculate that the presence of impurities may have enhanced the activity of the catalyst.

Rf = C_8F_{17}, 80 %
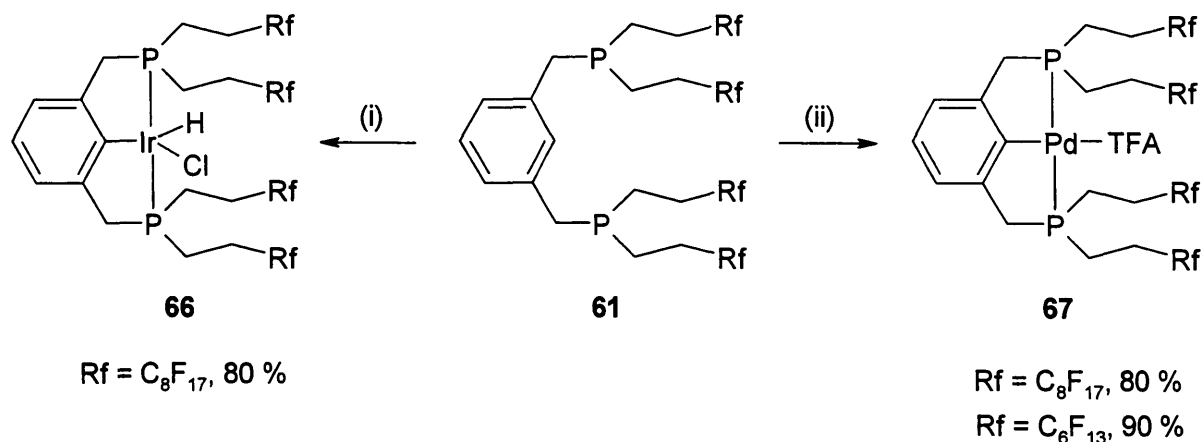
(i) [IrCl(COE)$_2$]$_2$, THF, 80 °C; (ii) [Pd(TFA)$_2$], THF, 80 °C or RT.

Rf = C_8F_{17}, 80 %
Rf = C_6F_{13}, 90 %

Scheme 3.16. *Synthesis of Iridium and Palladium PCP pincer complexes **66** & **67**.*

Pincer complexes have been demonstrated to be highly stable and robust catalysts, which make them ideal candidates for recycling. Over the past years several different approaches have been used in an attempt to recover and reuse the pincer complexes after catalysis. However, in most of the cases extensive ligand modification has been necessary in order to achieve this. When the catalyst was bound to a support, the catalyst becomes heterogenised losing the desired homogeneous activity and thus resulting in longer reaction times necessitating higher catalyst loadings. When the fluorous approach has been used, there has not been enough fluorine content to enable successful reactions using the intended fluorous biphase approach or the recycling results have not been published. Curran's fluorous SCS pincer shows promising recycling results, however, there is a large loss of catalyst in each cycle. This work proposes the synthesis of a fluorous PCP pincer complex with the intention to recover the complex by fluorous solid phase extraction, thus continuing homogeneous catalysis along with the ability to successfully recover and reuse the fluorous catalyst.

3.2 Results and Discussion

3.2.1 Synthesis of PCP ligand - Route 1

Pincer complexes have been shown to be robust catalysts and would therefore make ideal candidates for recyclable catalysts. Complex **68** was chosen as an appropriate catalyst to be investigated, especially since the phosphorus donor atoms bind strongly to the metal centre. There have been many reports of PCP pincer complexes that have successfully catalysed reactions.[3, 5, 8, 13, 23] The aryl spacer group was chosen in preference to an alkyl spacer since it offers greater insulation of the phosphorus donor atom from the electron withdrawing effects of the perfluoroalkyl chains and it provides the least air sensitive ligand to synthesise.

There are many possible routes for the synthesis of the PCP pincer ligands. Analysing the final product using retrosynthetic analysis provided a strategy for the synthesis (Scheme 3.17). The strategy was chosen as it predominately uses compounds which are not air-sensitive and compound **71** could be reacted with a range of different aryl lithiates/Grignard reagents to quickly access a number of different palladium pincer complexes, containing perfluoroalkyl chains with either different lengths or positions around the aryl ring.

The retrosynthetic analysis converts the palladium pincer complex **68** to the free pincer ligand **69**. A functional group interconversion to the phosphine oxide **70** provides compounds which are air stable and are much easier to handle than the corresponding phosphine compounds. Cleavage of the aromatic carbon-phosphorus bond provides **71**, which can be synthesised from commercially available 1,3-*bis*(bromomethyl)benzene and **73**, which can be prepared using known literature procedures.
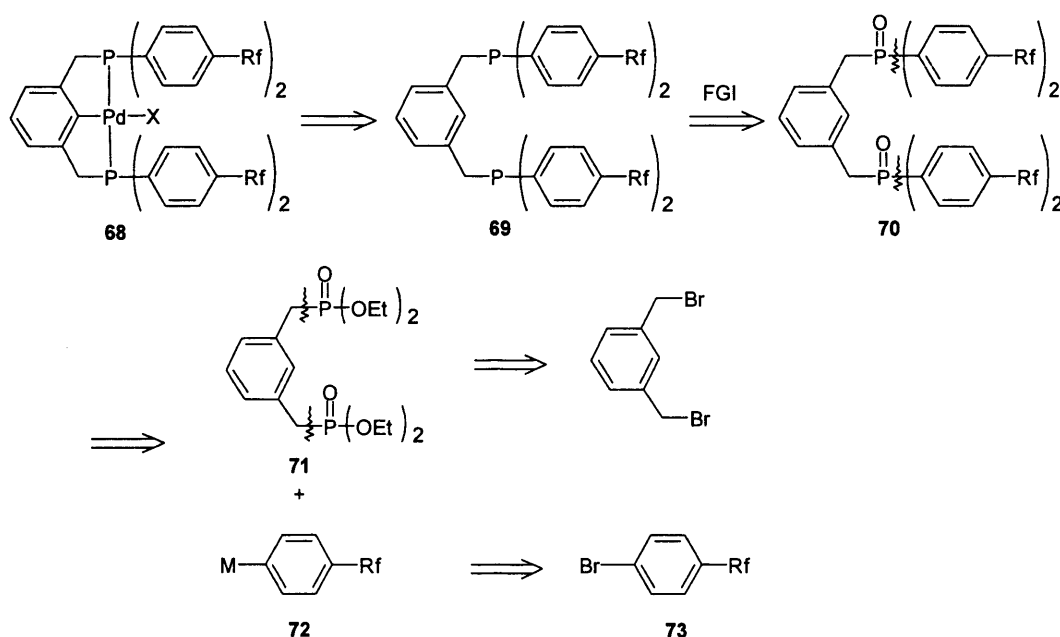
Scheme 3.17. *Retrosynthetic analysis of fluorous PCP pincer ligand.*

In order to simplify the system the initial scoping reactions were performed using benzyl bromide, instead of 1,3-*bis*(bromomethyl)benzene. After optimising the chemistry, the reaction would then be carried out using 1,3-*bis*(bromomethyl)benzene to give the desired PCP pincer ligand. The overall synthetic route starting from benzyl bromide is shown below (Scheme 3.18).

(i) P(OEt)$_3$, 120 °C, 2 h, then 2h, 150 °C; (ii) M-(ArRf); (iii) HSiCl$_3$, Et$_3$N, 110 °C.
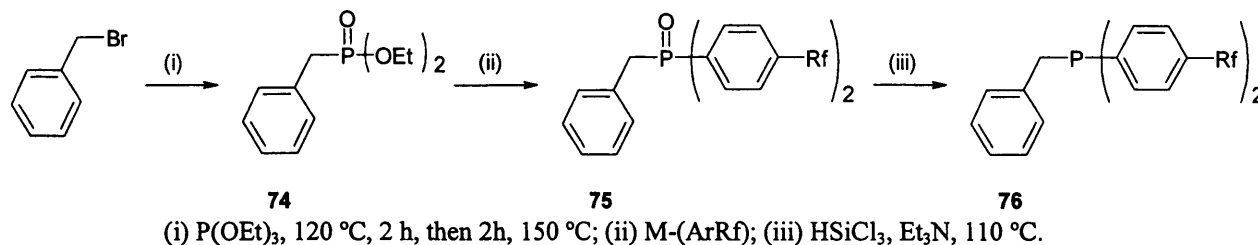
Scheme 3.18. *Proposed synthetic route for PC ligand 76.*

The first step was a Michaelis-Arbuzov Rearrangement. Following a literature method, benzyl bromide was heated with an excess of triethylphosphite for 2 hours at 120 °C and then for 2 hours at 150 °C.[24] Initially, an S_N2 reaction between triethylphosphite and benzyl bromide formed a phosphonium ion intermediate, which then reacts with bromide to form the desired product, diethyl benzylphosphonate **74**, and bromoethane as the byproduct.

The corresponding reaction was carried out, using 1,3-*bis*(bromomethyl)benzene with an excess of triethylphosphite.[25] The reaction mixture was gradually heated to 160 °C over 2 hours and then the temperature was maintained for 6 hours to give the corresponding 1,3-*bis*(diethoxyphosphinylmethyl)benzene **71**, in almost quantitative yields (Scheme 3.19).
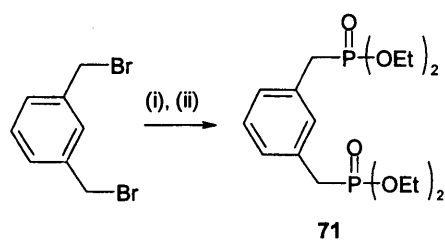
(i)P(OEt)$_3$, 2 h gradual heat to reflux; (ii) 6 h reflux.

Scheme 3.19. *The Michaelis-Arbuzov Rearrangement between 3-bis(bromomethyl)benzene and triethylphosphite.*

In an attempt to form *bis*aryl benzylphosphine oxide derivative **77**, an excess of aryl bromide **21** was treated with an equimolar amount of butyl lithium before the addition of diethyl benzylphosphonate **74** (Scheme 3.20). The ^{31}P NMR spectrum of the crude product was inconclusive with a major peak at δ_P 29.3 ppm but the ^{1}H NMR spectrum showed no sign of any doublet signals for the benzylic protons, which led to the belief that the desired product had not been formed. As the bromine-lithium exchange reaction had previously been

established, it was assumed that the reaction of the aryl lithiate with **74** was the problematic step.

(i) *n*-BuLi, Et₂O/THF, -30 °C; (ii) BnP(O)(OEt)₂, Et₂O, -30 °C to rt.
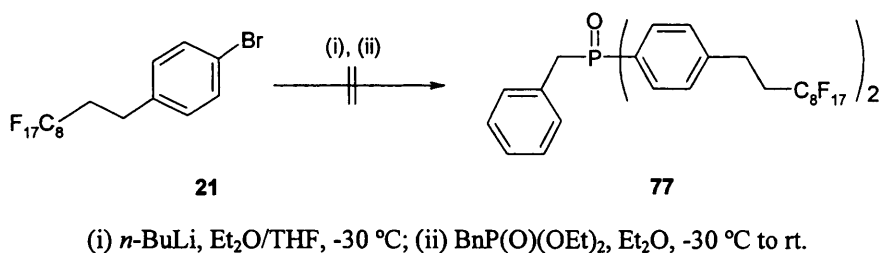
Scheme 3.20. *Failed route to* **77** *using fluorous aryl bromide.*

4-Bromomethoxybenzene was next used as a less expensive aryl bromide to optimise the reaction conditions (Scheme 3.21). The same reaction conditions were used as before, but there was a major peak in the crude ³¹P NMR spectrum at δ$_P$ 31.8 ppm as well as a less prominent signal at δ$_P$ 29.3 ppm. The ¹H NMR spectrum again showed no sign of any doublet signals for the benzylic protons, which led to the belief that the desired product had not been formed.

(i) *n*-BuLi, Et₂O/THF, -30 °C; (ii) BnP(O)(OEt)₂, Et₂O, -30 °C to rt.
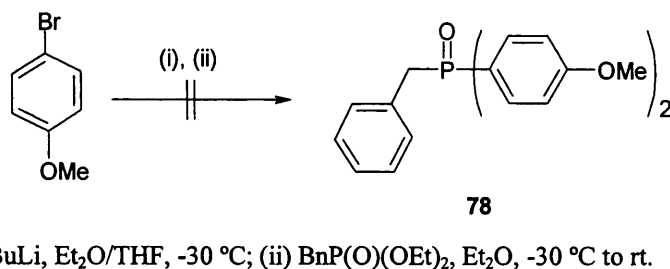
Scheme 3.21. *Failed route to* **78** *using 4-bromomethoxybenzene.*

It was thought that the lithiates may be too basic and consequently deprotonating one of the benzylic protons. This in turn, could then react with another diethyl benzylphosphonate molecule **74** to form a '*pseudo* dimer'**79** (Scheme 3.22).
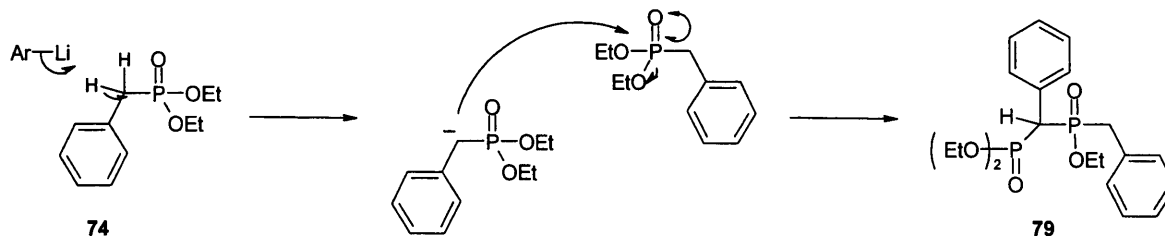
Scheme 3.22. *Proposed reaction with aryl lithiates and diethyl benzylphosphonate* **74.**

Aryl Grignard reagents were therefore investigated as less basic alternatives to aryl lithiates. It was hoped that substitution of the ethoxy groups would take precedence over deprotonation of the benzylic protons. Searching the literature produced an abundance of examples of Grignard substitution reactions[26, 27] with alkyl and aryl phosphonate methyl/ethyl esters. However, there were no records of a successful reaction with benzyl phosphonates. In spite of this, the substitution reaction was attempted with an aryl Grignard reagent.

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The ^{31}P NMR spectrum of the crude product showed a major peak at δ_P 31.4 ppm as well as a less prominent signal at δ_P 29.3 ppm. ^{1}H NMR spectroscopy showed two singlet signals, which were in the characteristic range for the methoxy protons. There were also only weak doublet signals for the benzylic protons, which led to the belief that the desired product had not been formed. The crude reaction mixture was purified by column chromatography using petroleum ether/diethyl ether (9:1) as the eluant. Two products were separated successfully from the column, however, they were determined to be non-phosphorus containing materials. ES-MS and ^{1}H NMR spectroscopy identified the two products as 4-bromomethoxybenzene and methoxybenzene; the first from an excess of reagent added and the second from protonation of the Grignard reagent.

A yellow band was retained at the top of the column and so the column was eluted with diethyl ether in order to recover the compound(s) using a more polar solvent. After a significant amount of solvent had been eluted, the diethyl ether fractions were concentrated to give a mixture of three products with the major peak at δ_P 29.1 ppm in the ^{31}P NMR spectrum. The ^{1}H NMR spectrum was cleaner in the aromatic region but gave no convincing evidence that the desired product had been formed.
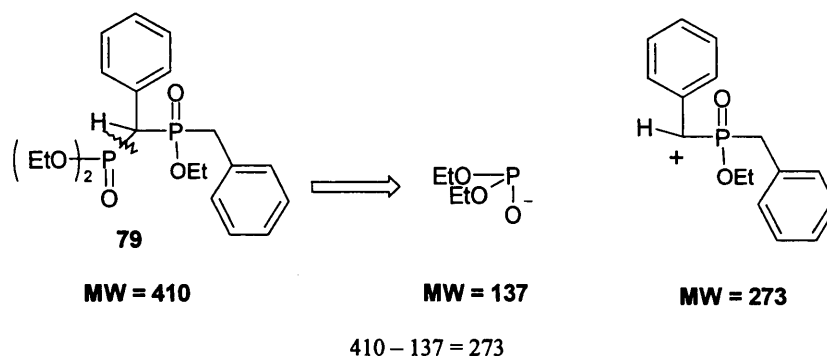
Figure 3.6. Possible structures from ES-MS analysis.

Since a compound was still retained at the top of the column the silica was stirred in diethyl ether, the resulting mixture filtered and concentrated to give one major product and one minor product. ^{31}P NMR spectroscopy showed the major product peak at δ_P 29.1 ppm and the minor product peak at δ_P 32.0 ppm. There were 2 x dd around the benzylic region, which collapsed to 2 x d in the ^{1}H$\{^{31}$P$\}$ NMR spectrum. This type of multiplicity would be possible if there were two inequivalent protons in the benzylic position, induced by two inequivalent groups on the phosphorus atom and is consistent with a product such as compound **10**, however, the ^{31}P NMR spectrum did not completely agree with this structure since the two phosphorus centres in **79** non-equivalent and would be expected be ^{31}P-^{31}P coupling. ES-MS did show a peak at m/z 411 and 274, in the positive spectrum, which could be characteristic of a '*pseudo* dimer' **10** or possibly an oligomeric species (Figure 3.6).

The silica was finally stirred in a mixture of DCM/acetone (1:1) and the resulting mixture was filtered and concentrated to give one product that yielded a peak at δ_P 29.3 ppm in the ^{31}P NMR spectrum. The ^1H NMR spectrum was cleaner in the aromatic region and again there were 2 x dd which collaspsed to 2 x d in the $^1H\{^{31}P\}$ NMR spectrum. There were additional multiplets in the alkyl region of the spectrum which could not be assigned.

All the evidence pointed towards a 'pseudo dimer' 79 or oligomeric species which meant that the Grignard reagent was too basic and deprotonation of the benzylphosphonate 74 was occurring. With this in mind, chloride was considered as an alternative leaving group to the ethoxy group as chloride was a better leaving group and may promote a substitution reaction over a deprotonation reaction. Benzylphosphonic dichloride 80 could easily be accessed from the benzylphosphonate ester 74 by acid hydrolysis to give benzylphosphonic acid 81, followed by chlorination to give benzylphosphonic dichloride 80 (Scheme 3.23).

Acid hydrolysis of benzylphosphonate 74 gave the corresponding acid 81 in excellent yield.[28] This method was also applied to 1,3-bis(diethoxyphosphinylmethyl)benzene 71 to give the desired product in excellent yields (Scheme 3.24).
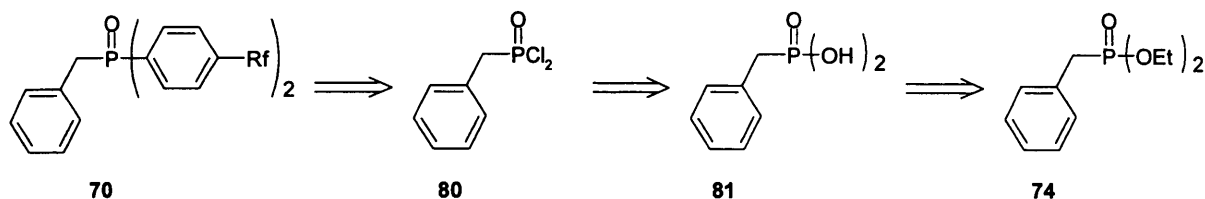
Scheme 3.23. *Possible synthetic route to 70 via benzylphosphonic dichloride 80.*

(i) Conc. HCl, reflux.
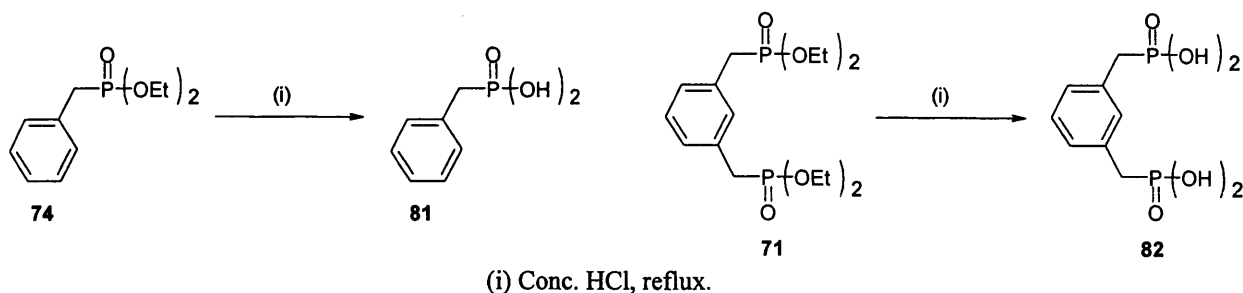
Scheme 3.24. *Conversion of phosphonate esters to the corresponding acids.*

The acid 81 was converted to the dichloride 80 using thionyl chloride and a catalytic amount of DMF.[29] The reaction mixture was heated until the ^{31}P NMR spectrum of the crude reaction mixture showed that there was no starting material present. Volatile material was removed by heating under vacuum. The crude product was further purified by heating in a Kugelröhr oven to distil off any impurities.

78
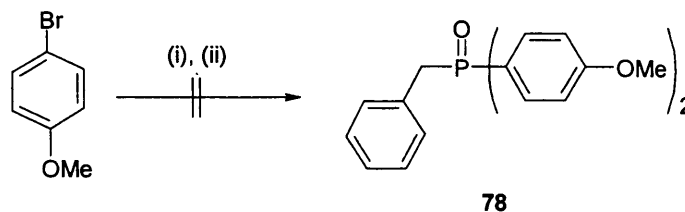
(i) *n*-BuLi, Et$_2$O, -30 °C.; (ii) BnP(O)Cl$_2$, -30 °C to rt.

Scheme 3.25. *Failed route to 78 using an aryl lithiate and benzylphosphonic dichloride 80.*

In Scheme 3.25 the dichloride **80** was reacted with the aryl lithiate formed from 4-bromoanisole. The crude ^{31}P NMR spectrum showed a set of signals for multiple products ranging from δ$_P$ 19-27 ppm. ^{1}H NMR spectroscopy showed two singlets, which were in the characteristic range for the methoxy protons, however, GC-MS confirmed the presence of 4-bromomethoxybenzene and methoxybenzene. The signals in the ^{1}H NMR spectrum were therefore, again, accounted for firstly from the excess of aryl bromide added and secondly from protonation of the lithiate and so could not be assigned to the desired product **78**.

The reaction was repeated, but this time an aryl Grignard reagent was employed (Scheme 3.26). There were again multiple product signals in the crude ^{31}P NMR spectrum ranging from δ$_P$ 20-42 ppm, with a major peak at δ$_P$ 39.6 ppm. The ^{1}H NMR spectrum showed a few doublets that may be attributed to benzylic protons but their integration was very small compared with the rest of resonances in the NMR spectrum.

78
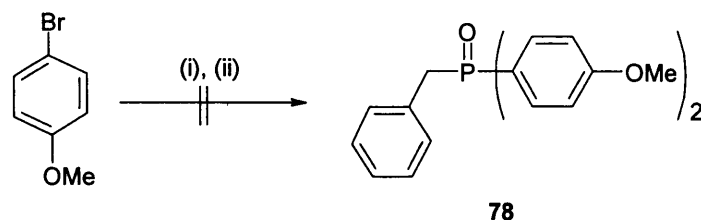
(i) Mg, Et$_2$O, 45 °C.; (ii) BnP(O)Cl$_2$, 0 °C to 45 °C.

Scheme 3.26. *Failed route to 78 using an aryl Grignard reagent and benzylphosphonic dichloride 80.*

This route was completely unsuccessful and it is doubtful that the desired products, **77** and **78**, were synthesised. The benzylic protons appeared to be too acidic and deprotonation occurred instead of the anticipated substitution. Similar phosphine oxide species have reacted in this manner in a Horner-Wadsworth-Emmons reaction. The oxygen on the phosphorus atom helps to stabilise the negative charge and, therefore, promotes deprotonation over substitution (Scheme 3.27). Therefore, an alternative synthesis was required.

74/80

X = OEt, Cl

Scheme 3.27. *Resonance stabilisation from deprotonation in the benzylic position.*

3.2.2 Synthesis of PCP ligand - Route 2

An alternative retrosynthetic analysis of the fluorous PCP pincer ligands gave a novel strategy for which the synthesis could be investigated (Scheme 3.28). After the same functional group interconversion from the free pincer ligand **69** to the phosphine oxide **3**, the benzylic carbon-phosphorus bond was cleaved this time to provide 1,3-*bis*(bromomethyl)benzene, which was commercially available, and **83** which could be prepared using known literature procedures.

69 **70** **83**

Scheme 3.28. *Retrosynthesis of fluorous PCP pincer ligand.*

In order to simplify the system, benzyl bromide was initially used instead of 1,3-*bis*(bromomethyl)benzene. Once the chemistry was optimised, then the reaction would be carried out using 1,3-*bis*(bromomethyl)benzene. The synthetic route, starting from benzyl bromide, is outlined in Scheme 3.29.

83 **75** **76**

(i) Base; (ii) BnBr; (iii) HSiCl$_3$, Et$_3$N, 110 °C.

Scheme 3.29. *Proposed synthesis of PC ligand.*

The *bis*-arylphosphine oxide **86** was synthesised using modified literature procedures (Scheme 3.30).[30] The corresponding fluorous bromobenzene **21** undergoes a lithiation

reaction followed by reaction with diethylphosphoramidous dichloride to give the protected *bis*-arylphosphine **84**. This was reacted *in situ* with concentrated HCl to form the phosphinous acid **85**, which tautomerises to the desired *bis*-arylphosphine oxide **86**. The equilibrium between the two tautomers lies completely on the side of *bis*-arylphosphine oxide **86** at room temperature, with the phosphinous acid **85** not detected by ^{31}P, ^{1}H and ^{19}F NMR spectroscopy.
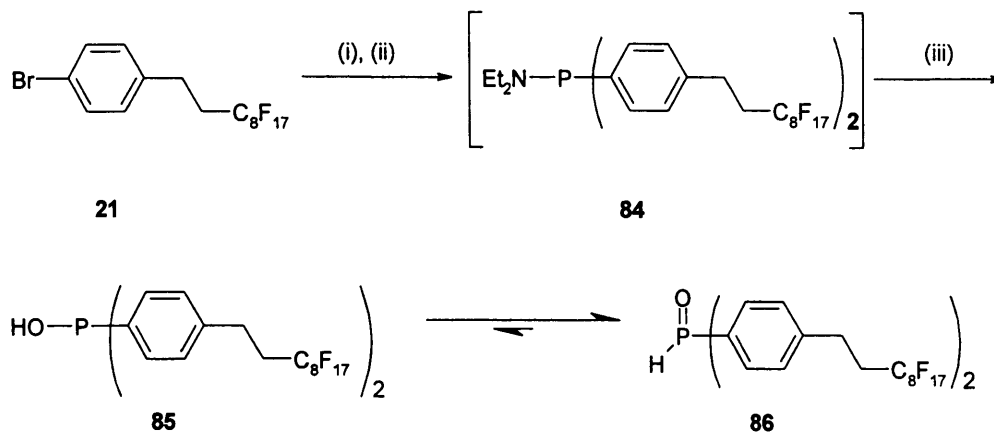
(i) *n*-BuLi, Et$_2$O/THF, -30 °C; (ii) (Et$_2$N)PCl$_2$, -30 °C to RT; (iii) Conc. HCl, 0 °C to RT.

Scheme 3.30. *Synthesis of bis(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine oxide 86.*

Initially, a Kugelröhr distillation was employed to isolate the desired product from any starting materials. Unfortunately, the *bis*-arylphosphine oxide **86** decomposed under vacuum at 125 °C undergoing a disproportionation to form the corresponding *bis*-arylphosphinic acid **87** and *bis*-arylphosphine **88** (Scheme 3.31). This observation is supported by reports in the literature[31] for the non-fluorous parent compound.[32, 33] It was later found that washing the crude product with cold diethyl ether resulted in **86** being isolated as an analytically pure sample, thereby, avoiding the distillation.

(i) 125 °C under vacuum.
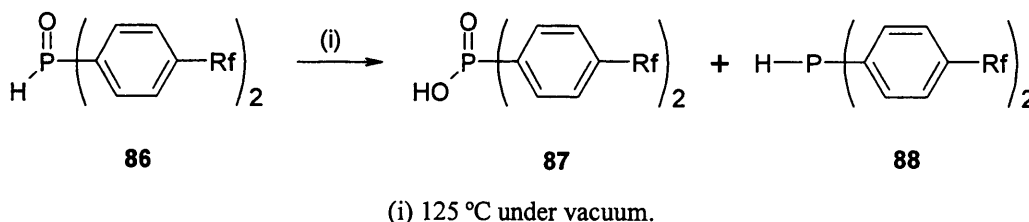
Scheme 3.31. *Disproportionation reaction of 86 to form 87 & 88.*

The next step was to react *bis*-arylphosphine oxide **86** with benzyl bromide. There are many numerous procedures for this type of reaction in the literature. The first method that was investigated used KOH in the presence of a phase transfer catalyst, to deprotonate the proton on the phosphorus atom which was then reacted with benzyl bromide (Scheme 3.32).[34] The crude ^{31}P NMR spectrum showed three different products at δ_P 29.0, 31.9 and 32.4 ppm.

Although the peak at δ_P 29.0 ppm was determined to be the desired product, it was only a minor product. Another minor peak at 32.4 ppm was determined to be *bis*-arylphosphinic acid **87**. The major peak at δ_P 31.9 ppm was determined to be the corresponding benzyl *bis*-arylphosphinic ester **89** by ^{31}P & ^{1}H NMR spectroscopy and FAB-MS.
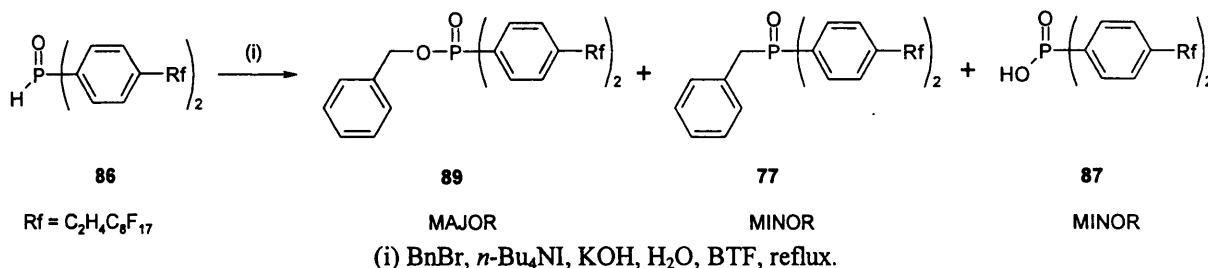
Scheme 3.32. *Synthesis of 89 using KOH and n-Bu₄NI.*

It was thought that the KOH was not only acting as a base but also as a nucleophile, producing the acid **87**. This observation has been reported in the literature.[34, 35] It was thought that **87** could then, in turn, be deprotonated and react with benzyl bromide to form the ester **89** (Scheme 3.33).

Another set of conditions employed the use of *n*-BuLi as the base (Scheme 3.34).[36] *n*-BuLi and **86** were reacted at -10 °C for 2 h before benzyl bromide was added. The reaction was then warmed to room temperature and stirred for a further 20 h, before heating under reflux for 2 h. The crude ^{31}P NMR spectrum showed many different products, none of which were the desired product or byproducts that had previously been synthesised. This reaction was not investigated further.
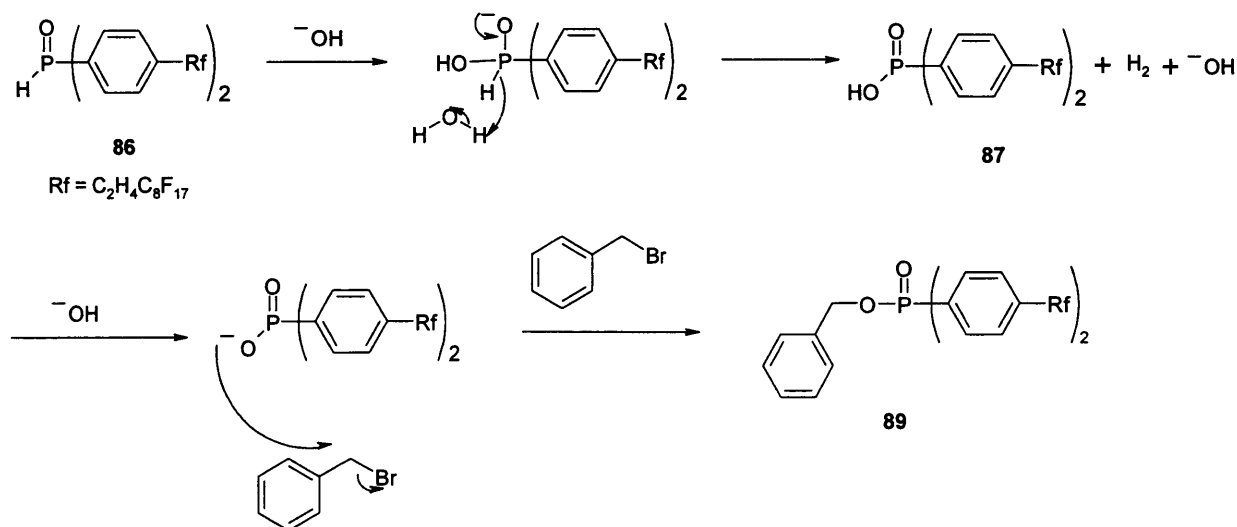
Scheme 3.33. *Mechanism for the formation of 87 and 89.*
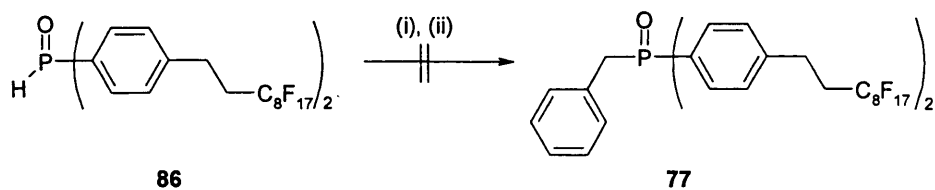
(i) *n*-BuLi, THF/Et$_2$O, -10 °C, 2 h; (ii) BnBr, THF, -10 °C to RT, 20 h, then reflux 2 h.

Scheme 3.34. *Attempted synthesis of 77 using n-BuLi as the base.*

The final approach employed NaH as the base (Scheme 3.35).[30] Sodium hydride and **86** were reacted at room temperature for 1 h before benzyl bromide was added. The reaction was stirred for a further 17 h. The crude ^{31}P NMR spectrum showed that only the desired product **77** was formed. The product was washed with hot petroleum ether (40-60 °C), to eliminate oil impurities from the sodium hydride, giving the pure product. As this method gave the cleanest reaction, it was used to synthesise the PCP pincer oxide **90**.

(i) NaH, THF, RT, 1h; (ii) BnBr, THF, RT.
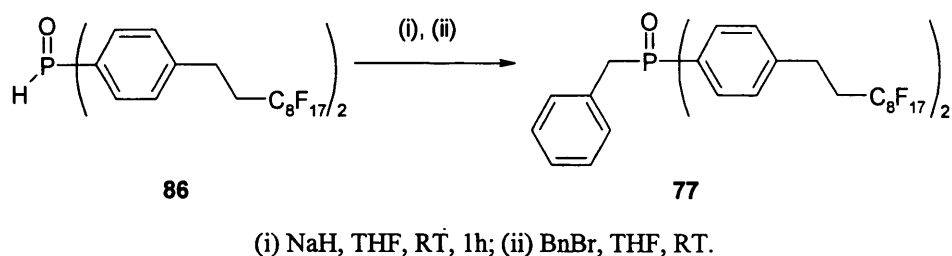
Scheme 3.35. *Synthesis of 77 using NaH as a base.*

Initially, *bis*-arylphosphine oxide **86**, NaH and 1,3-*bis*(bromomethyl)benzene **4** were stirred overnight at room temperature and worked up using the standard procedure (Scheme 3.36). The crude ^{31}P NMR spectrum showed mainly the *bis*-arylphosphine oxide **86** starting material and two products at δ_P 29.1 and 29.5 ppm. These were later determined to be the desired product **90** and the mono-substituted product **91**, by FAB-MS. The crude ^{1}H NMR spectrum showed mainly the *bis*-arylphosphine oxide **86** and 1,3-*bis*(bromomethyl)benzene starting materials as well as a doublet at δ_H 3.5 ppm, which collapsed to a singlet in the ^{1}H{^{31}P} NMR spectrum. This is in the correct region for the benzylic protons of the desired product **90**.

(i) NaH, THF, RT.
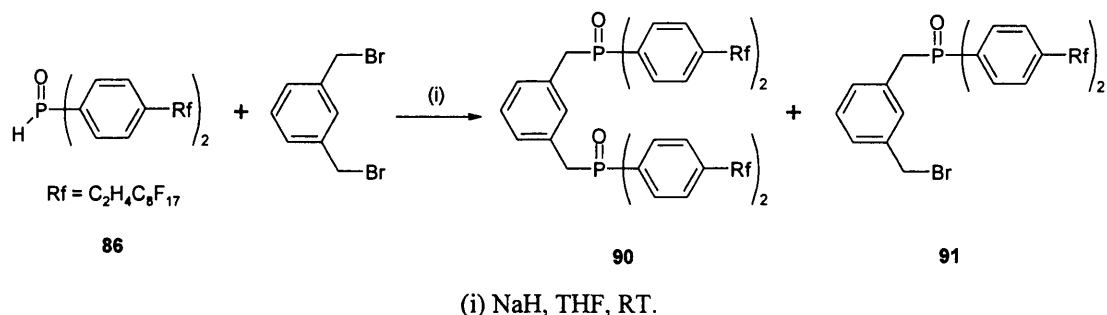
Scheme 3.36. *Attempted synthesis of 90.*

83

Even though the reaction did not go to completion, the outcome still looked promising and, therefore, the previous reaction conditions used to synthesise 77, were used. 86 and NaH were allowed to react at room temperature for 1 h before 1,3-bis(bromomethyl)benzene was added (Scheme 3.37). The reaction was stirred at room temperature overnight and then quenched with water. The reaction was worked up and the crude ^{31}P & ^{1}H NMR spectra showed only the presence of starting material.
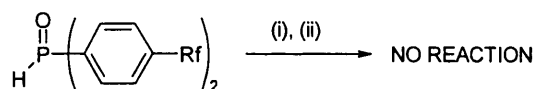
(i) NaH, THF, RT, 1 h; (ii) m-BrCH$_2$PhCH$_2$Br, THF, RT.

Scheme 3.37. *Attempted synthesis of 90 using reaction conditions used for 77.*

Several other attempts were pursued to synthesise the PCP pincer oxide 90, including:

- the addition of BTF as a co-solvent to help solubilise the fluorous compounds;

- heating the reaction overnight to improve solubility and reaction rates;

- using an excess of base.

However, all of the above attempts either gave unreacted starting materials or insoluble solids that were to be the desired product. It was thought that the reaction did not work due to the low solubility of the fluorous compounds in THF. With this in mind, the bis-arylphosphine oxide 92 was synthesised with a shorter perfluoroalkyl chain, C$_6$F$_{13}$, as fluorous compounds with shorter chains are normally more soluble in organic solvents.

The corresponding bromobenzene 94 was prepared similarly to 4-(1H,1H,2H,2H-perfluorodecyl)bromobenzene 22 (Scheme 3.38). Diazonium salt 17 was synthesised and reacted, *in situ*, in a Heck reaction with 1H,1H,2H-perfluorooct-1-ene. Hydrogenation of the alkene 93, using rhodium on carbon catalyst, led to the formation of the fluorous-derivatised bromobenzene 94 in high yield.
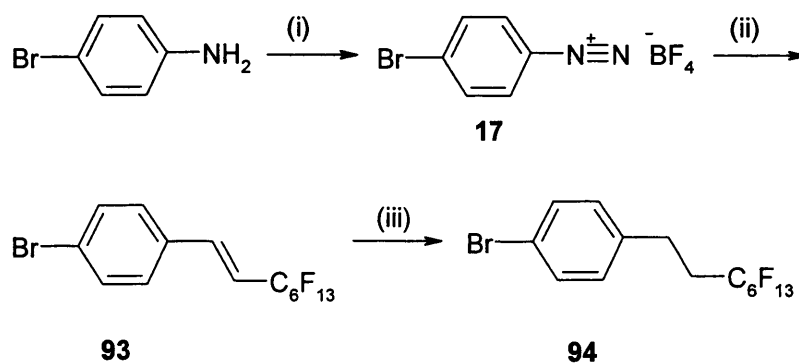
(i) HBF$_4$, NaNO$_2$, H$_2$O, 0 °C; (ii) CH$_2$=CHC$_6$F$_{13}$, Pd(OAc)$_2$, MeOH; (iii) H$_2$, 50 bar, Rh/C, MeOH, 20 °C.

Scheme 3.38. *Synthesis of 4-(1H,1H,2H,2H-perfluorooctyl)bromobenzene 94.*

$Rf = p\text{-}C_2H_4C_6F_{13}$

94   **95**   **96**
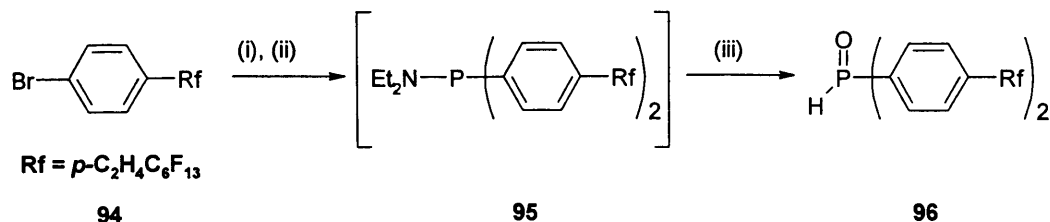
(i) n-BuLi, -30 °C, Et₂O/THF; (ii) (Et₂N)PCl₂, -30 °C to RT; (iii) Conc. HCl, 0 °C to RT.

**Scheme 3.39.** *Synthesis of bis(4-1H,1H,2H,2H-perfluorooctylphenyl)phosphine oxide* **96**.

The synthesis of **96** was carried out in a similar manner to **86**, and the pure product was obtained by recrystallisation with petroleum ether (Scheme 3.39). After reacting **96** with NaH for 1 h before 1,3-*bis*(bromomethyl)benzene was added to afford the corresponding PCP pincer oxide **97** (Scheme 3.40). The crude ^{31}P and ^{1}H NMR spectra showed mainly the desired product, with a small amount of mono-substituted product and starting material. To overcome this problem a slight excess of **96** was used. At the end of the reaction, if there was any of **96** left, treatment of the crude reaction mixture with concentrated NaOH transformed **96** to the corresponding *bis*-arylphosphinic acid **98**, which could easily be removed by aqueous extraction (Scheme 3.40). Washing with hot petroleum ether gave the desired product. Interesting, **97** had surfactant-type properties due to the different environments within the molecule; a highly polar P=O and non-polar perfluoroalkyl chains.

$Rf = p\text{-}C_2H_4C_6F_{13}$

92   **97**   **92**   **98**   **97**

(i) NaH, THF, RT, 1 h; (ii) m-BrCH₂C₆H₄CH₂Br, THF, RT; (iii) conc. NaOH, then aq. extraction.
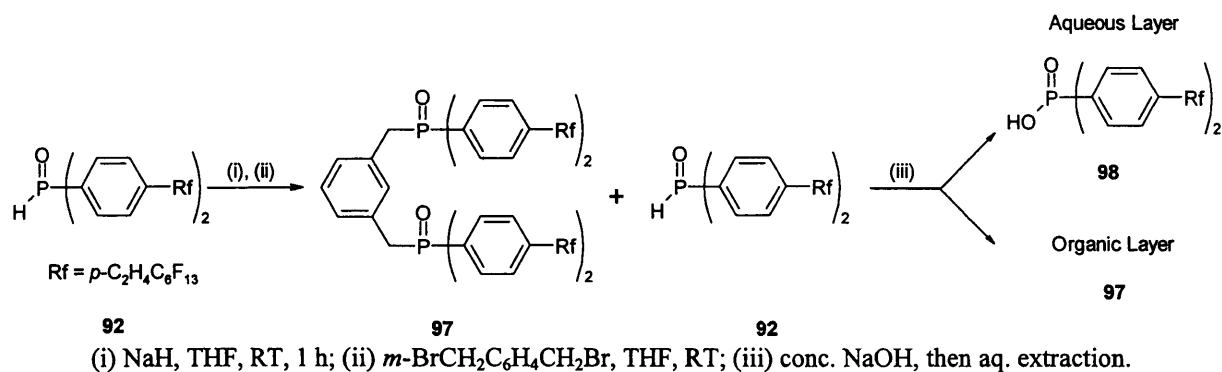
Scheme 3.40. *Synthesis and purification of 1,3-bis[bis(4-1H,1H,2H,2H-perfluorooctylphenyl) phosphinemethyl]benzene* **97** *using NaH as the base.*

The non-fluorous PCP pincer catalyst was prepared for direct comparison with the fluorous derivative. As for the fluorous derivatives, the synthesis started with diphenylphosphine oxide **99**, which is commercially available or can be readily accessed *via* the synthesis used for the fluorous derivatives. Sodium hydride and **99** were reacted at room temperature for 1 h before 1,3-*bis*(bromomethyl)benzene was added (Scheme 3.41). The reaction was stirred at room temperature overnight. The crude reaction mixture was quenched with water and worked up. The ^{31}P and ^{1}H NMR spectra of the crude product showed only the desired product **100**. In the ES-MS the parent ion was present as well as (M+17). This was

85

believed to be water that had hydrogen bonded to the P=O double bond and the coordinated water molecules were observed in the ^{1}H NMR spectrum at δ_H 2.50 ppm. It was, therefore, necessary to ensure that the phosphine oxide **100** was completely dry before attempting the next step. In an alternative synthesis of **100**, the authors find water hydrogen bonded to the P=O in the crystal structure.[37] Washing the crude product with hot petroleum ether eliminated oil impurities from the NaH to give the desired product in almost quantitative yield.

99   100

(i) NaH, THF, RT, 1h; (ii) m-BrCH$_2$PhCH$_2$Br, THF, RT.
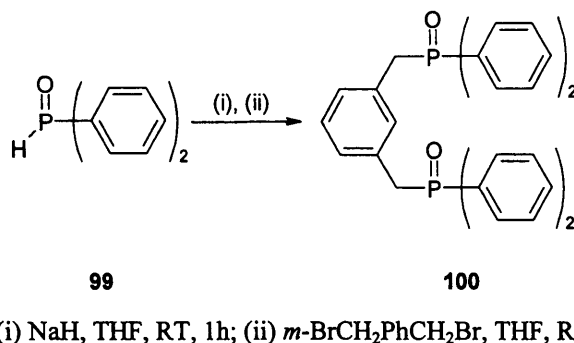
Scheme 3.41. *Synthesis of 1,3*-bis*[diphenylphosphinomethyl]benzene* **100** *using NaH as the base.*

The phosphine oxide **77** was reduced with trichlorosilane in the presence of triethylamine at 110 °C for 15.5 h. (Scheme 3.42).[38] The corresponding phosphine **101** was obtained; however, a small amount of the *bis*-arylphosphine **88** (~5%) was also observed by ^{31}P NMR specroscopy. It was thought that once the phosphine oxide was reduced the trichlorosilane reacted further with the phosphine to cleave the benzyl group. This could, therefore, be prevented by using shorter reaction times.

Rf = C$_2$H$_4$C$_8$F$_{17}$

77   101   88

(i) HSiCl$_3$, Et$_3$N, BTF, reflux.
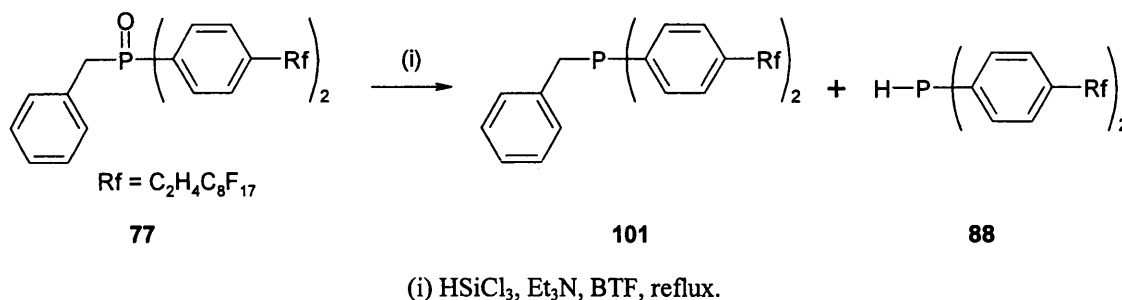
Scheme 3.42. *Reduction of 77 to the free phosphine 101.*

Initially, the phosphine oxide **100** was reduced using the same method but this time there was significant cleavage of the benzylic carbon-phosphorus bond, as seen in the synthesis of **101**. The decomposition of tertiary alkyl phosphines has previously been reported in this type of reaction.[39]

An alternative method was modified, where the phosphine oxide **100** was heated to 110 °C, in toluene, before treating with an excess of trichlorosilane in the absence of base.[15] After a basic aqueous work up, the product was analysed by ^{31}P and ^{1}H NMR spectroscopy to

give a mixture of phosphine **102** and byproducts. It was thought that the phosphine was decomposing for two reasons; the first, that the temperature of the reaction was too high and the second, that HCl formed in the work up was reacting with the phosphine to give a phosphonium salt that decomposed under basic aqueous conditions.

To overcome this problem, excess trichlorosilane was removed at the end of the reaction before the basic aqueous work up. An excess of base was also used in the work up. The reaction solvent was changed from toluene to BTF, as it had a lower boiling point and had previously been shown to minimise the decomposition (Scheme 3.43). The phosphine was isolated in a 90 % yield. The combined synthesis for the formation of the phosphine oxide and phosphine was significantly greater (overall yield = 88 %) than the yield recorded in the literature for the one step synthesis starting from diphenylphosphine (60 %).[40, 41]
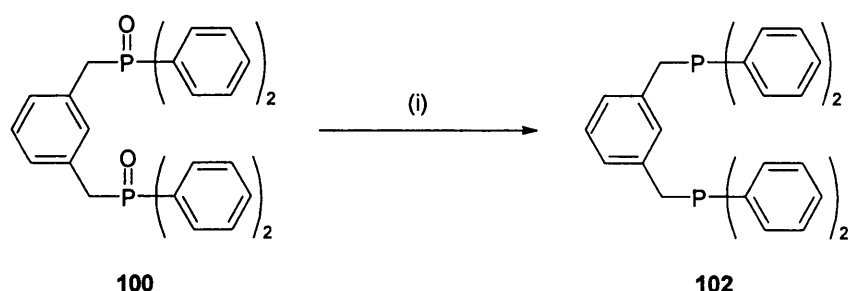
(i) HSiCl₃, BTF, 105 °C.

Scheme 3.43. *Reduction of phosphine oxide 100.*

Exactly the same reaction conditions were used for the synthesis of the fluorous PCP phosphine **103** and the desired product was isolated in a moderate yield (Scheme 3.44). Both phosphines were extremely air sensitive, in both solution and the solid state, so were kept under an inert atmosphere. The $^{31}P\{^1H\}$ NMR spectra showed one signal at δ_P -10.0 ppm for **102** and δ_P -11.5 ppm for **103**. However, when the compounds were exposed to air and the $^{31}P\{^1H\}$ NMR spectra were rerun, two additional peaks appeared at δ_P -9.9, 29.6 ppm and δ_P -11.4, 29.3 ppm. These were assigned as the mono-oxidised phosphine compound **104/105** for the non-fluorous and fluorous compounds respectively. Analysis after 14 h showed only one peak remained, the di-oxidised phosphine compounds **102-103** (Scheme 3.45).
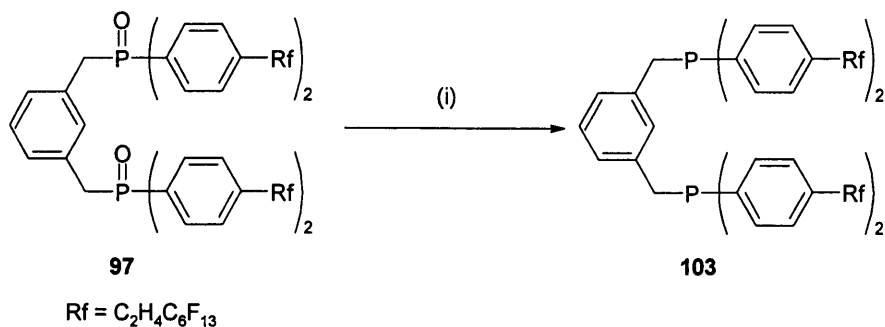
Rf = C₂H₄C₆F₁₃

(i) HSiCl₃, BTF, 105 °C.

Scheme 3.44. *Reduction of phosphine oxide 97.*

87
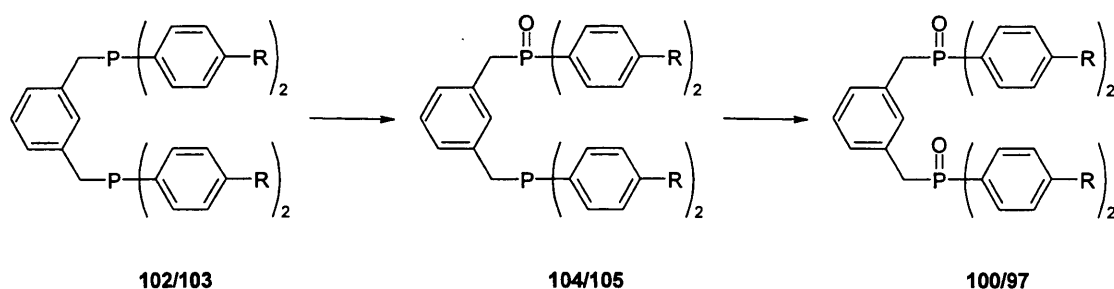
R = H, $C_2H_4C_6F_{13}$

Scheme 3.45. *Oxidation products of the PCP ligands in air.*

3.3 Coordination Chemistry

The PCP ligand is extremely versatile, therefore, many coordination complexes have been synthesised using a range of transition metals. These, in turn, have successfully catalysed a wide range of catalytic reactions. To determine the effects of the perfluoroalkyl chains on the ligand binding properties, a variety of coordination complexes were synthesised. Differences in electronic properties of the ligand and metal complexes can be gauged by variations in spectroscopic data, determining any effects of the perfluoroalkyl chains on the phosphorus donor atom and hence, used to evaluate the suitability of the fluorous ligand for catalysis.

All of the following complexes were fully characterised by ^{1}H, ^{31}P, and ^{19}F NMR spectroscopy, FAB-MS, elemental analysis, infrared and melting points.

3.3.1 Palladium(II) Complexes

There are a number of syntheses of PCP palladium complexes bearing PPh$_2$ groups reported in the literature, using different sources of palladium. Rimml and Venanzi reported the synthesis of complex **106**, using a neutral source of palladium.[40] This preparation was used with little modification. The PCP ligand **102** was treated with [PdCl$_2$(MeCN)$_2$] in DCM and heated to reflux under a nitrogen atmosphere for 1.75 h (Scheme 3.46). The reaction mixture changed from a yellow solution to an orange solution with yellow precipitate. The reaction was then cooled, washed with EtOH/H$_2$O (4 mL, 3:1) and the solvent removed. The crude ^{31}P NMR spectrum showed two resonances at δ_P 32.4 & 20.6 ppm as well as the signal corresponding to the desired complex **106** at δ_P 33.5 ppm. The conversion to **106** was extremely low, around 12 % (by ^{31}P NMR spectroscopy). This was extremely surprising as the authors had isolated complex **106** in a good yield (75 %). The reaction was repeated, but a similar outcome was reached.

88
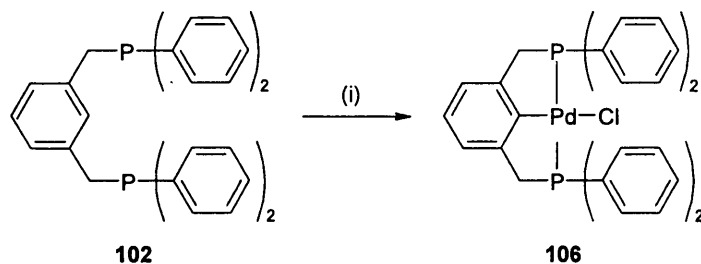
(i) [PdCl$_2$(MeCN)$_2$], DCM, reflux.

Scheme 3.46. *Synthesis of [PdCl(PCP)] 106.*

Cross and co-workers investigated the cyclometallation of sterically-demanding pincer ligands bearing cyclohexyl groups on the phosphorus atoms.[42] The ligand **107** was treated with [PdCl$_2$(PhCN)$_2$] in 2-methoxyethanol and stirred at 130 °C for 25 min (Scheme 3.47). The authors isolated mainly the non-cyclometallated oligomer product **109** (δ_P 25.0 ppm) and a small amount of the cyclometallated product **108**. Continued heating of **109** in 2-methoxyethanol yielded more of the cyclometallated product **108**.
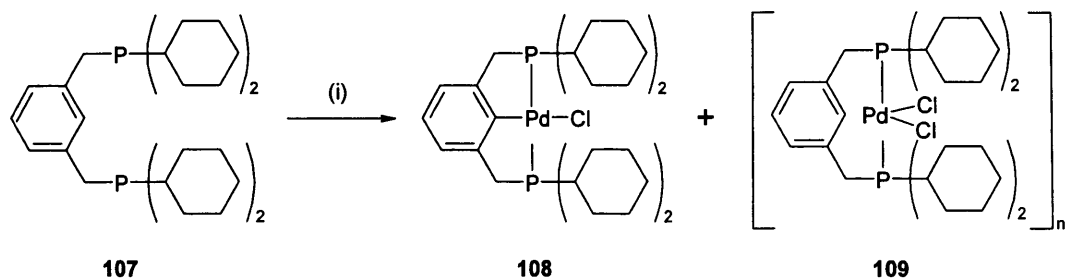
(i) [PdCl$_2$(PhCN)$_2$], 2-methoxyethanol, reflux.

Scheme 3.47. *Formation of cyclometalled pincer complex 108 and non-cyclometalled complex 109.*

It was quite possible that the same type of byproduct/intermediate was formed in the synthesis of [PdCl(PCP)] **106** and the resonances at δ_P 32.4 & 20.6 ppm were non-cyclometallated oligomer products, similar to **109**. It was proposed that the resonance at δ_P 20.6 ppm was the *trans*-oligomer **111** and the resonance at δ_P 32.4 ppm was the *cis*-oligomer **110**. These values are typical for *trans*- and *cis*-[PdCl$_2$(PPh$_3$)$_2$] complexes (see Chapter 2). The *cis*-isomer would not be able to cyclometallate as the C-H, which needs to be activated, is not close enough to the metal centre.[40] Only the *trans*-isomer **111** brings the C-H close enough to the metal centre and, therefore, the *cis*-isomer **110** needs to be isomerised to the *trans*-isomer before cyclometallation can occur. Heating these byproducts/intermediates at elevated temperature would isomerise the *cis*-isomer to the *trans*-isomer and then facilitate the cyclometallation.

Recrystallisation from DCM/hexane isolated the byproducts from the desired complex. It was important to ensure that the byproducts did not contain any of the

cyclometallated product to ensure that cyclometallation only occurred under the reaction conditions.

The isolated byproducts/intermediates were heated to reflux in 2-methoxyethanol for 24 h (Scheme 3.48). The reaction mixture changed from a yellow to a grey solution and a grey solid formed. A sample was taken and analysed by ^{31}P NMR spectroscopy, which showed that only one signal was present at δ_P 33.5 (s) ppm, characteristic of the cyclometallated product. A characteristic virtual triplet was also observed in the ^{1}H NMR spectrum at δ_H 3.89 ppm for the benzylic protons, which collapsed to a singlet in the $^{1}H\{^{31}P\}$ NMR spectrum. This is typical of two phosphorus atoms in *trans*-arrangement coupling with a proton, $\frac{1}{2} \mid ^{2}J_{HP} + ^{4}J_{HP} \mid$. The complex 106 was obtained as a yellow powder.
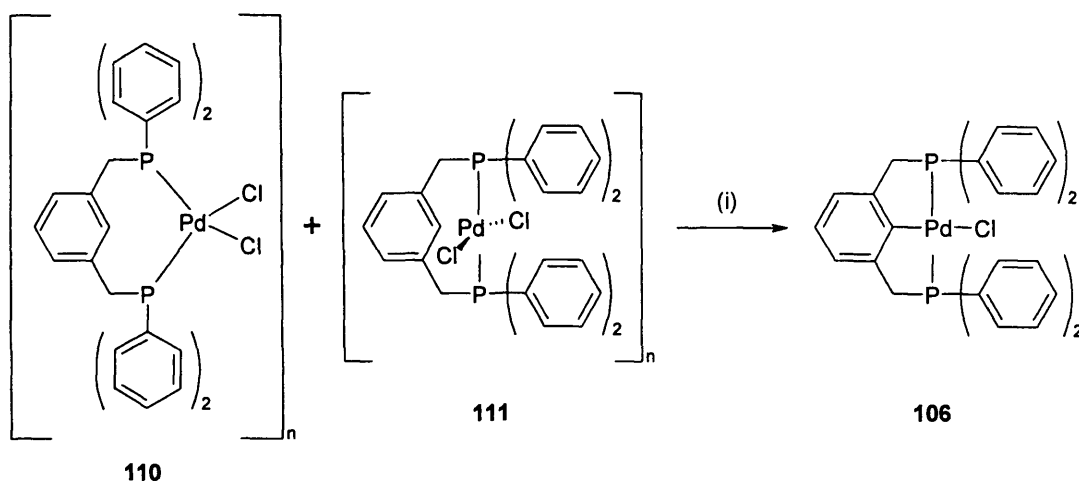
(i) 2-methoxyethanol, reflux, 24 h.

Scheme 3.48. *Cyclometallation at high temperature.*

It was surprising that such harsh reaction conditions were needed for the cyclometallation of complex 106 as Rimml and Venanzi had reported that this took place at room temperature in 10 min. However, the cyclometallated complex could be obtained directly from the phosphine ligand 102 by refluxing directly in 2-methoxyethanol with [PdCl$_2$(MeCN)$_2$] (Scheme 3.49). Crystals of 106 suitable for X-ray crystallography were grown by slow diffusion of hexane into a solution of DCM containing 106 (Figure 3.7). Selected bond distances and angles are summarised in Table 3.8.
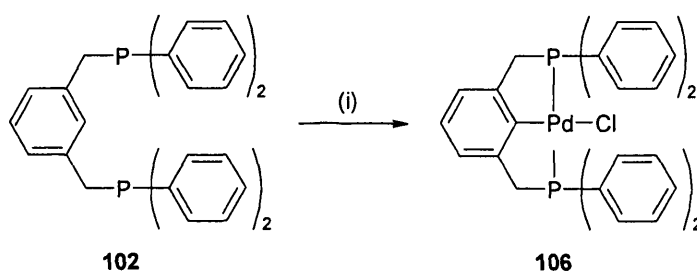
(i) [PdCl$_2$(MeCN)$_2$], 2-methoxyethanol, reflux, 14 h.

Scheme 3.49. *Direct formation of palladium pincer complex 106 from phosphine 102.*
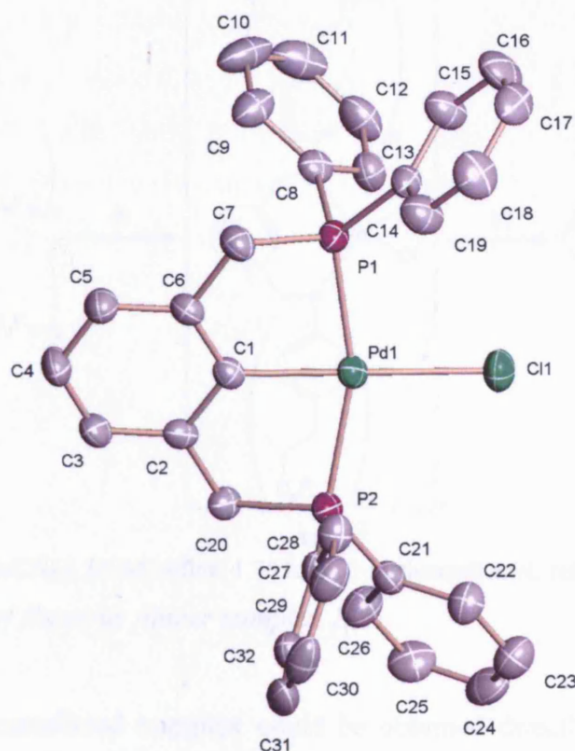
Figure 3.7. *Crystal structure of [PdCl(PCP)] 106. The figures show 50% displacement ellipsoids. The hydrogen atoms have been omitted for clarity.*

The fluorous complex **113** could also be obtained using both routes. The fluorous PCP ligand **113** was treated with $[PdCl_2(MeCN)_2]$ in DCM and heated at reflux under a nitrogen atmosphere for 1.75 h (Scheme 3.50.). The reaction mixture changed from a yellow solution to an orange solution with a yellow precipitate. After washing with $EtOH/H_2O$ (4 mL, 3:1) and removing the solvent, the crude ^{31}P NMR spectrum showed a resonance at δ_P 31.4 ppm, which was thought to the *cis*-oligmer **112**. After heating the byproduct/intermediate to reflux in 2-methoxyethanol for 24 h, ^{31}P NMR spectroscopy demonstrated that the resonance at δ_P 31.4 ppm was no longer present and there was only one signal present at δ_P 32.7 (s) ppm, determined to be the cyclometallated product. Again, this was determined by the virtual triplet at δ_H 3.88 ppm in the ^1H NMR spectrum for the benzylic protons, which collapsed to a singlet in the $^1H\{^{31}P\}$ NMR spectrum. Purification gave complex **113** as a yellow/orange powder.

(i) [PdCl$_2$(MeCN)$_2$], DCM, reflux, 1.75 h; (ii) 2-methoxyethanol, reflux, 24 h.
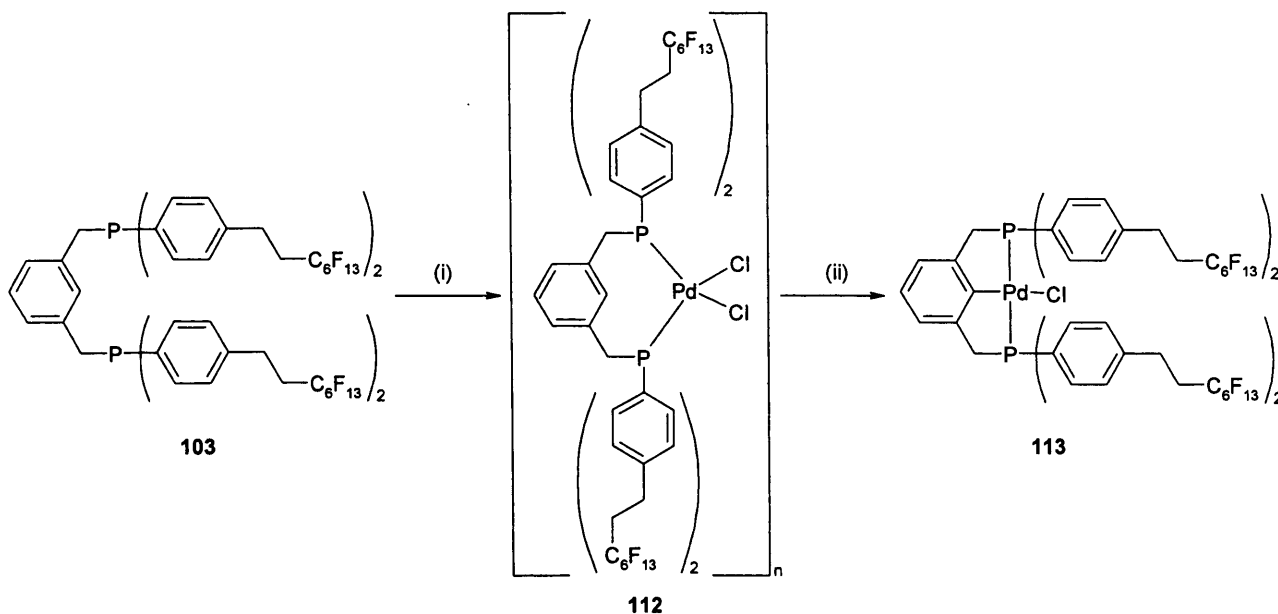
Scheme 3.50. *Synthesis of fluorous pincer complex 113.*

Again, the cyclometallated complex could be obtained directly from the phosphine ligand **113** by refluxing in 2-methoxyethanol and [PdCl$_2$(MeCN)$_2$] (Scheme 3.51). Crystals were grown by slow evaporation of a chloroform solution containing **113**, however, despite several attempts, the crystals were found to be too small for X-ray crystallography.

(i) [PdCl$_2$(MeCN)$_2$], 2-methoxyethanol, reflux, 14 h.
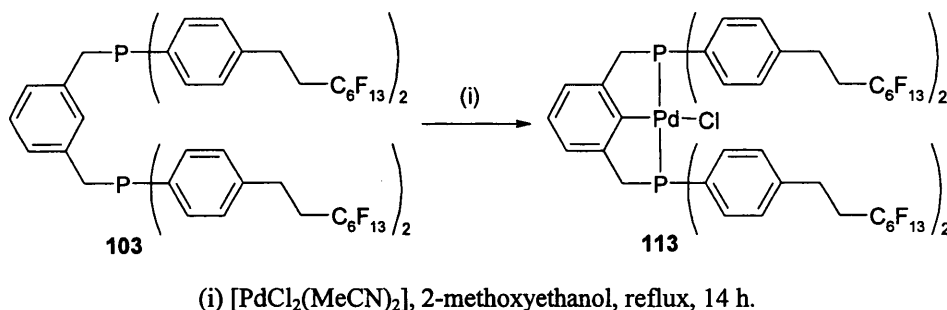
Scheme 3.51. *Synthesis of fluorous pincer complex 113.*

3.3.2 Nickel(II) Complexes

Nickel complexes can provide useful information about the binding properties of ligands and the complexes can also be used to catalyse a number of reactions, such as the Kharasch Addition reaction.[43]

Rimml and Venanzi have synthesised a nickel pincer complex **114** from phosphine **102**.[40] Using modified reaction conditions, the non-fluorous and fluorous derivatives were synthesised. The pincer phosphines **103** and **102** were treated with [NiCl$_2$.6H$_2$O] in 2-methoxyethanol, (Scheme 3.52). Instantly the colour changed from green to purple. The reaction was heated to 60 °C for 3 h before di*iso*propylethylamine was carefully added. The reaction was heated and maintained at reflux overnight within 5 min the colour had changed

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from purple to golden yellow. Work up of the reaction mixture gave the non-fluorous complex **114** as a dark yellow powder and the fluorous complex **115** as lime green crystals. Both structures showed a virtual triplet at ~δ_H 3.8 ppm in the ^{1}H NMR spectrum for the benzylic protons, which collapsed to a singlet in the ^{1}H{^{31}P} NMR spectrum. This is characteristic of two phosphorus atoms in a *trans*-arrangement coupling with a proton, ½ | $^2J_{HP}$ + $^4J_{HP}$ |. Crystals of **114** suitable for X-ray crystallography were grown by slow diffusion of hexane into a solution of DCM containing **114** (Figure 3.8). Selected bond distances and angles are summarised in Table 3.8.

R= H, C$_2$H$_4$C$_6$F$_{13}$
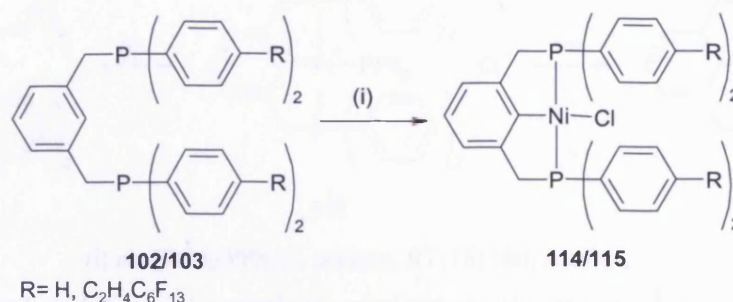
(i) [NiCl$_2$.6H$_2$O], 2-methoxyethanol, 60 °C, 3 h then ^{i}Pr$_2$EtN, reflux, 14 h.

Scheme 3.52. *Synthesis of nickel pincer complexes.*
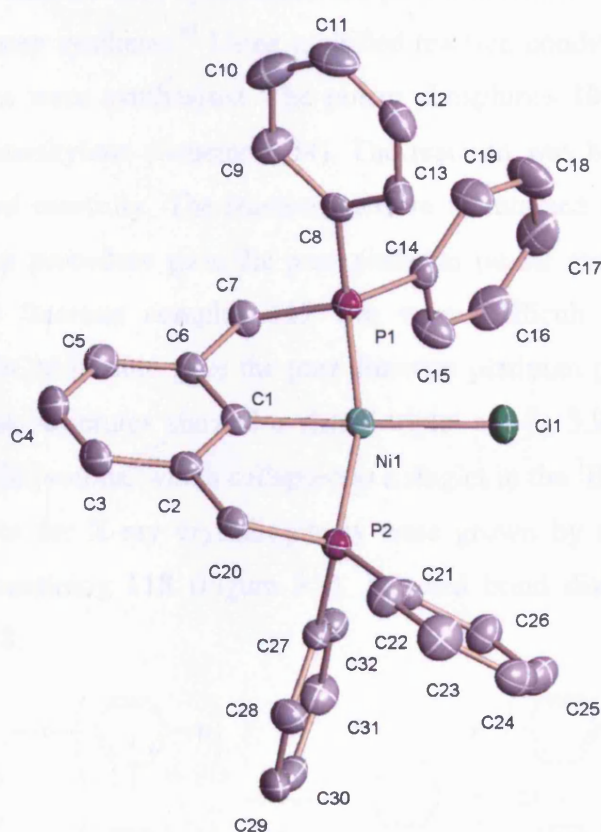
Figure 3.8. *Crystal structure of [NiCl(PCP)] 114. The figures show 50% displacement ellipsoids. The hydrogen atoms have been omitted for clarity.*

3.3.3 Platinum(II) Complexes

Platinum complexes can also provide useful information about the binding properties of ligands especially from their ^{195}Pt-^{31}P coupling constants. Rimml and Venanzi had previously synthesised a platinum iodide pincer complex from phosphine **102**, using a two step synthesis (Scheme 3.53).[40] Reaction of phosphine **102** with *cis*-[PtCl$_2$(PPh$_3$)$_2$] in acetone gave [(Pt(PCP)(PPh$_3$))Cl] **116**. Further reaction with NaI gave the platinum pincer complex, [PtI(PCP)] **117**.
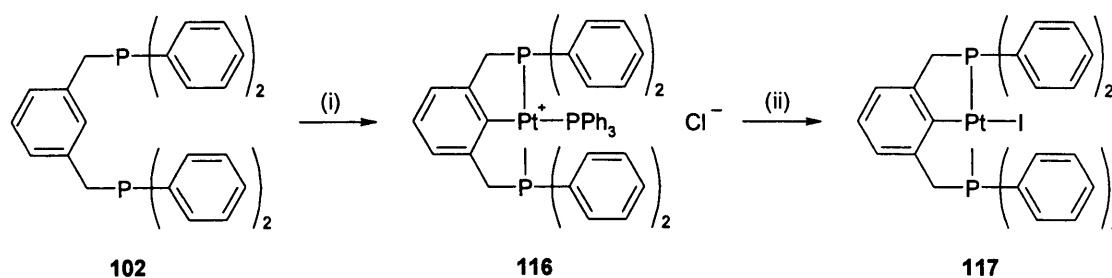
(i) *cis*-[PtCl$_2$(PPh$_3$)$_2$], acetone, RT; (ii) NaI, acetone.

Scheme 3.53. *Rimml and Venanzi's synthesis of platinum pincer complex.*

Bennett and co-workers later synthesised the platinum chloride pincer complex from phosphine **2c** in a one step synthesis.[41] Using modified reaction conditions, the non-fluorous and fluorous derivatives were synthesised. The pincer phosphines **102** & **103** were treated with [PtCl$_2$(COD)] in mesitylene (Scheme 3.54). The reaction was heated to reflux before triethylamine was added carefully. The reaction mixture maintained at reflux overnight. A straightforward work up procedure gave the pure platinum pincer complex **118** as a cream powder, however, the fluorous complex **119** was more difficult to purify. A reverse recrystallisation from DCM/hexane gave the pure fluorous platinum pincer complex **119** as colourless crystals. Both structures showed a virtual triplet at $\sim\delta_H$ 3.9 ppm in the ^1H NMR spectrum for the benzylic protons, which collapsed to a singlet in the $^1H\{^{31}P\}$ NMR spectrum. Crystals of **118** suitable for X-ray crystallography were grown by slow evaporation of a chloroform solution containing **118** (Figure 3.9). Selected bond distances and angles are summarised in Table 3.8.


R= H, C$_2$H$_4$C$_6$F$_{13}$
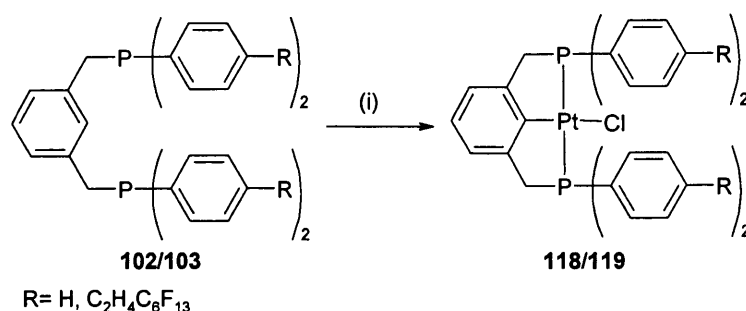
(i) [PtCl$_2$(COD)], mesitylene, reflux, then Et$_3$N, reflux, 14 h.

Scheme 3.54. *Synthesis of platinum pincer complexes 118-119.*
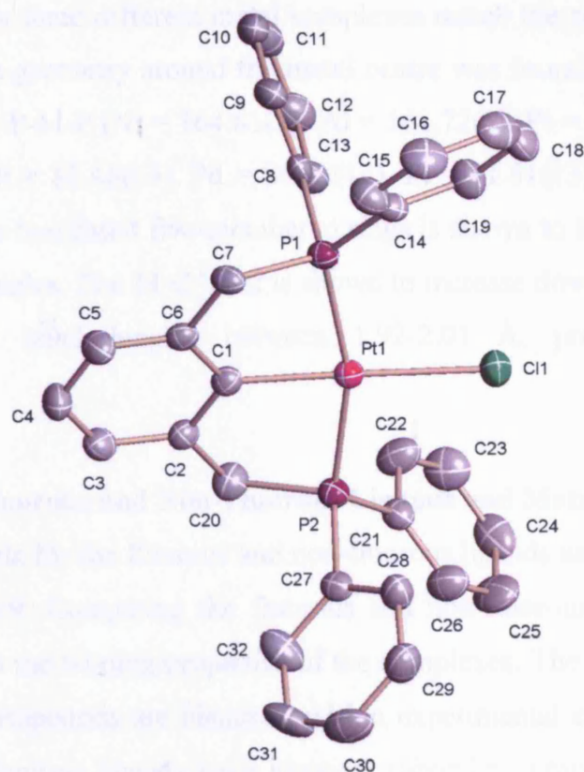
Figure 3.9. *Crystal structure of [PtCl(PCP)] 118. The figures show 50% displacement ellipsoids. The hydrogen atoms have been omitted for clarity.*

Bond lengths / Å	[NiX(PCP)] 114	Lit.[a,b]	[PdCl(PCP)] 106	Lit.[c]	[PtCl(PCP)] 118	Lit.[d]
M-X	2.1979(13)	2.3290(5)	2.3712(13)	2.384(2)	2.3784(17)	2.3831(10)
M-P(1)	2.1693(14)	2.177(1)	2.2953(12)	2.288(3)	2.2784(16)	2.2749(10)
M-P(2)	2.1732(13)	2.173(1)	2.2973(13)	2.294(3)	2.272(2)	2.2794(9)
M-C(1)	1.923(4)	1.920(3)	2.017(4)	1.998(8)	2.013(4)	2.002(3)
Bond Angles / °						
P(1)-M-P(2)	164.81(5)	165.14(3)	161.72(5)	162.0(1)	163.11(4)	163.11(3)
C(1)-M-X	178.39(12)	179.75(9)	179.22(13)	178.7(3)	178.46(12)	178.53(9)
P(1)-M-X	97.11(5)	97.81(3)	98.32(5)	98.1(1)	99.33(7)	99.51(3)
P(2)-M-X	98.01(5)	96.88(2)	99.84(5)	99.9(1)	97.49(7)	97.31(4)
C(1)-M-P(1)	82.50(13)	82.1(1)	81.63(13)	81.3(3)	81.14(13)	81.04(9)
C(1)-M-P(2)	82.43(13)	83.2(1)	80.23(13)	80.8(3)	82.08(13)	82.18(9)

[a] *Literature values for [NiBrPCP];* [b] *Ref [44];* [c] *Ref [45];* [d] *Ref [41].*

Table 3.8. *Selected Bond Distances and Angles of the Ni, Pd and Pt PCP pincer complexes.*

All of the data for three different metal complexes match the corresponding literature values. The coordination geometry around the metal centre was found to be distorted square planar, which affects the P-M-P (Ni = 164.81(5), Pd = 161.72(5), Pt = 163.11(4)) and P-M-C bond angles (Average Ni = 82.46(63), Pd = 80.93(13), Pt = 81.61(13)). For each individual complex the strain of the two fused five-membered rings is shown to be unequal by differing M-P lengths and bond angles. The M-C bond is shown to increase down the group 10 metals, from Ni to Pt, with bond lengths between 1.92-2.01 Å, providing evidence for cyclometallation.

3.3.4 Comparison of Fluorous and Non-Fluorous Ligands and Metal Complexes

The ^{31}P NMR data for the fluorous and non-fluorous ligands and metal complexes are summarised in Table 3.9. Comparing the fluorous and non-fluorous complexes, there are negligible differences in the binding properties of the complexes. The $^{1}J_{PPt}$ coupling constant for the two platinum compounds are identical, within experimental error, showing both the non-fluorous and the fluorous ligands have identical σ-bonding properties. All of this data shows that there is little difference in the binding properties of the fluorous and non-fluorous ligands and that the perfluoroalkyl chains do not affect the phosphorus donor atom. This, therefore, insinuates that the fluorous metal complexes should be acceptable for catalysis.

Compound	^{31}P NMR data/ ppm^a	Δ ^{31}P NMR data /ppm^b	Compound	^{31}P NMR data/ ppm^a	Δ ^{31}P NMR data /ppm^b
PCP	-9.9	-	Rf-PCP	-11.5	-
[PdCl(PCP)]	33.5	43.4	[PdCl(Rf-PCP)]	32.7	44.2
[NiCl(PCP)]	34.8	44.7	[NiCl(Rf-PCP)]	33.8	45.3
[PtCl(PCP)]	33.1	43.0 ($^{1}J_{PPt}$ = 2968 Hz)	[PtCl(Rf-PCP)]	32.3	43.8 ($^{1}J_{PPt}$ = 2969 Hz)

^{a}NMR solvent was CDCl$_3$. ^{b}Δ ^{31}P NMR data = (Metal Complex)- (Free ligand).

Table 3.9. ^{31}P NMR spectroscopy data for pincer ligands and complexes.

3.4 Separation Studies

In order to separate the fluorous catalyst from the organic product, it was necessary to find a fluorophobic solvent that would retain the catalyst on the column whilst the product was eluted. A fluorophilic solvent could then be used to elute the catalyst with a high recovery from the column. Chromatography tests were run with TLC plates coated in FRPSG to find suitable fluorophobic and fluorophilic solvents. The fluorous palladium complex was dissolved in a small amount of solvent and spotted onto a fluorous TLC plate. A range of

solvents were evaluated and their R_f value recorded (Table 3.10). The non-fluorous catalyst was tested for comparison.

Solvent	PdCl(Rf-PCP)	PdCl(PCP)
MeOH	0	0-0.95[a]
MeCN	0	1
DCM	0.16	0.06
Hexane	0	0
Ether	1	0.92
THF	0.66	0.83
BTF	0.76	0.04
EtOAc	1	1

[a]Some decomposition seen on the TLC plate.

Table 3.10. R_f values of Pd catalysts on FRPSG with different solvents.

Methanol, acetonitrile and hexane gave R_f values of 0 for the fluorous catalyst on FRPSG and so can be used as fluorophobic solvents to elute the organic product from the column whilst retaining the fluorous catalyst. Despite the fact that hexane gave a R_f value of 0, it would not be a good choice of fluorophilic solvent as it is non-polar and, therefore, it would be difficult to dissolve polar organic compounds.

DCM gave an R_f value of 0.16 for the fluorous catalyst on FRPSG, so would not be a good choice as either a fluorophobic or a fluorophilic solvent. However, DCM is a relatively polar solvent and will not only dissolve many polar organic compounds but, most importantly, the fluorous catalyst. Therefore, DCM could be used to load the reaction mixture onto the FRPSG column before washing the column with the chosen fluorophobic solvent. This will ensure that all of the fluorous catalyst is loaded onto the column.

Diethyl ether, THF, BTF and ethyl acetate gave R_f values of >0.66 for the fluorous catalyst and so could be used as fluorophilic solvents to elute the catalyst from the column.

The non-fluorous catalyst was also tested to compare the effects that the perfluoroalkyl chains had on the retention of the catalysts on FRPSG in different solvents. Hexane, DCM and BTF gave R_f values close to 0 for the non-fluorous catalyst on FRPSG and so could be used to elute the organic product from the column whilst retaining the non-fluorous catalyst.

Acetonitrile, diethyl ether, THF and ethyl acetate all gave R_f values close to 1 for the non-fluorous catalyst on FRPSG and so could be used to elute the catalyst from the column. Methanol gave a range of R_f values from 0-0.95 for the non-fluorous catalyst because of

decomposition of the catalyst on the TLC plate and, therefore, methanol was not considered as a solvent to elute the catalyst from the column.

From the data above, it is clear that the perfluoroalkyl chains on the catalyst definitely have an effect on the R_f values for the catalysts on FRPSG. It was possible to select solvents that will, individually, retain both the fluorous and non-fluorous catalysts on FRPSG and then select a different solvent in order to recover the catalyst.

Both the fluorous and non-fluorous catalysts were also evaluated on normal silica gel using the same method (Table 3.11). Again, selecting particular solvents carefully could lead to successful catalyst/product separation. However, methanol could not be used in this instance as it is known to dissolve silica gel, therefore, only leaving acetonitrile for [PdCl(Rf-PCP)] and BTF for [PdCl(PCP]) as possible solvents for eluting the product from the column whist retaining the catalyst. Even though it would be advantageous to use silica gel, associated with cost, there are some factors that would need to be considered. The first is that more silica gel would be needed for effective loading and separation of the reaction mixture, 25 – 50 times the mass of the reaction mixture is needed compared with only 10 times the mass of the reaction mixture needed with FRPSG. This is due to the different separating properties of the silicas; normal silica separates compounds based on their polarity and FRSPG separates compounds based on their fluorine content. The second, and the most important factor, is that silica has an abundance of free hydroxyl groups that can bind irreversibly to the catalyst leaving the catalyst retained on the column. FRPSG has most of the free hydroxyl groups capped, therefore, minimising this effect.

Solvent	PdCl(Rf-PCP)	PdCl(PCP)
MeOH	0	0.38
MeCN	0	0.88
DCM	0.91	0.38
Hexane	0	0
Ether	0.97	0.55
THF	0.81	0.70
BTF	0.58	0

Table 3.11. R_f values of Pd catalysts on silica gel with different solvents.

High catalyst recovery is an important issue when trying to recycle a catalyst. It was, therefore, necessary to evaluate the recovery of the fluorous catalyst from a column of FRPSG. PdCl(Rf-PCP) (25.6 mg) was dissolved in DCM and loaded onto a column of

FRPSG (500 mg) that had been pre-treated with acetonitrile. The column was washed with acetonitrile, a fluorophobic solvent. The catalyst was retained at the top of the column as a yellow band. The acetonitrile fractions were analysed by TLC and found to contain no UV-active compounds present, indicating that the catalyst was successfully retained on the column. The column was then eluted with ethyl acetate to recover the catalyst. Again, TLC was used to gauge when all of the catalyst had been eluted. 94 % of the catalyst was recovered after the column was eluted with only 6 mL of ethyl acetate. ^{1}H, ^{31}P & ^{19}F NMR analysis of the recovered catalyst gave spectra that were identical to those of the catalyst before loading onto FRPSG, indicating that there were no unwanted reactions between catalyst and silica.

3.5 Catalytic Testing

The mechanism for the catalysis for palladium pincer complexes is a subject of debate. Some authors speculate a Pd(II)/Pd(IV) mechanism, rather than the traditional Pd(0)/Pd(II) mechanism.[2-4, 6-8] Jensen *et al.* have proposed this catalytic cycle would be initiated by the oxidative addition of the alkene to the pincer complex, followed by the loss of the HX salt. Oxidative addition of the aryl halide onto the metal centre produces a palladium(IV) species before reductive elimination of the organic product regenerates the catalyst (Scheme 3.55). Although this postulated mechanism was not supported with any direct experimental evidence, it was based on key observations with other pincer catalysts.[2, 46] The transformation from Pd(IV) species to a Pd(II) species to give the reductive elimination product was thought to be the rate determining step and, therefore, the use of electron-withdrawing groups on the phosphine would reduce electron density around the metal and facilitate this step.

There have also been reports from authors who believe that the pincer catalysts are merely pre-catalysts decomposing to form small amounts of soluble palladium and, therefore, operate through the traditional Pd(0)/Pd(II) mechanism.[5, 13, 23, 47] It is still unclear which mechanism is actually taking place in the catalytic cycle, but the recovery of the fluorous catalyst may give a useful insight.

Although the synthesis of the non-fluorous catalyst had previously been reported in the literature, there are no reports of catalysis with **106** in a Suzuki or Heck reaction. Before testing the reaction with the fluorous pincer catalyst **113**, the reaction conditions were optimised with the non-fluorous catalyst first. The optimised conditions would then be applied to the fluorous catalyst **113**.
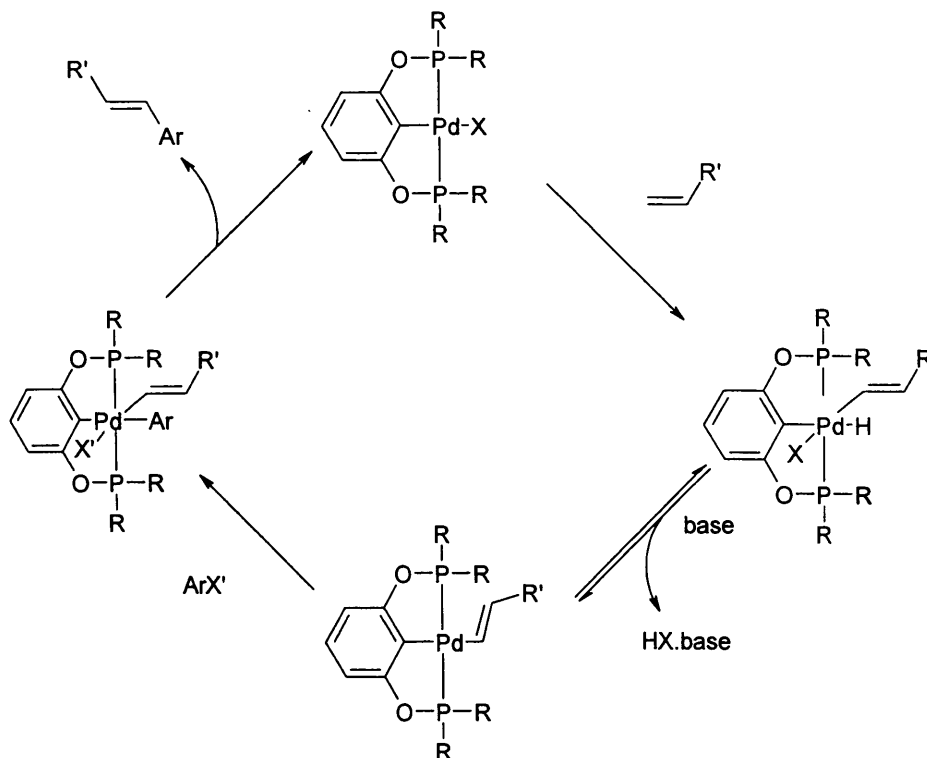
Scheme 3.55. *Proposed mechanism for Pd(II)/Pd(IV) catalytic cycle.*

3.5.1 Suzuki Reaction - Initial Reaction Conditions

Fluorous monodentate palladium complexes **8-11** have successfully been used to catalyse the Suzuki reaction between 4-bromoanisole and phenylboronic acid (Chapter 2). Therefore, the non-fluorous catalyst **106** was tested using the same reaction conditions. (Scheme 3.56). GC analysis was used to determine that no product was formed after 2 h and so another set of reaction conditions was required.
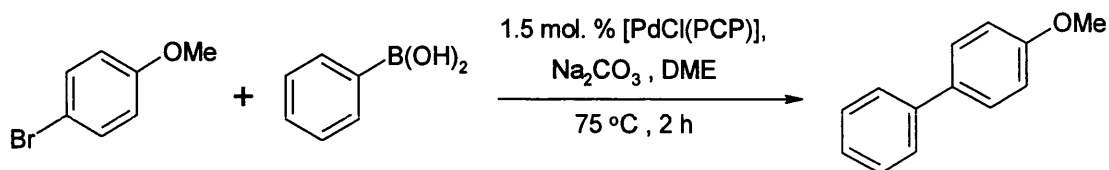
Scheme 3.56. *Suzuki coupling between 4-bromoanisole and phenylboronic acid.*

Bedford *et al.* successfully catalysed the Suzuki reaction between 4-chloroanisole and phenylboronic acid with a palladacycle in good yield, using caesium carbonate as the base in dioxane.[48] Following an adaptation of Bedford's method, 1 mole % of [PdCl(PCP)] **106**, phenylboronic acid, caesium carbonate and 4-bromoanisole were heated in dioxane at 100 °C under a nitrogen atmosphere (Scheme 3.57 and Table 3.12). The non-fluorous complex **116** successfully catalysed the Suzuki reaction with a 76 % conversion of starting materials, after 20.5 h.
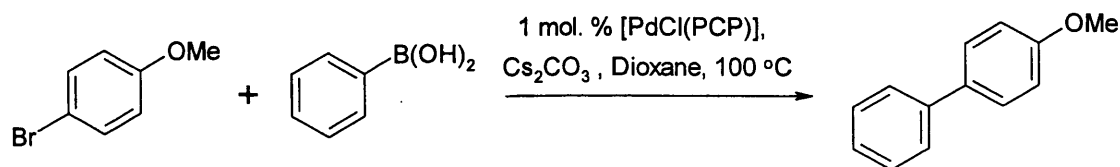
Scheme 3.57. *Suzuki coupling between 4-bromoanisole and phenylboronic acid using Bedford's method.*

Time/h	Conversion^a
0.5	12 %
20.5	76 %

^{a}*Determined by GC uning tolyl ether as an internal standard.*

Table 3.12. *Results from the Suzuki reaction with 4-bromoanisole and phenylboronic acid using Bedford's method.*

Now that appropriate reaction conditions had been determined the fluorous catalyst **113** and the limits of the reaction were tested. Reaction conditions were used without an internal standard and argon was used, instead of nitrogen, as the inert gas. Samples were taken over the course of the reaction and analysed by HPLC (Table 3.13). The non-fluorous catalyst was retested to show the reproducibility of the previous result.

PhX	Catalyst	Time/h	Yield/%^{a,b}
4-bromoanisole	PdCl(PCP)	20.5	81
4-bromoanisole	PdCl(Rf-PCP)	6	89
4-chloroanisole	PdCl(PCP)	73	0

^{a}*Determined by HPLC.* ^{b}*Assay Yield.*

Table 3.13. *Results from the Suzuki reaction with aryl halides and phenylboronic acid using Bedford's method.*

When [PdCl(Rf-PCP)] **113** was used to catalyse the Suzuki reaction between 4-bromoanisole and phenylboronic acid the reaction was complete after 6 h with an assay yield of 89 %. Analysis of the crude reaction product by ^{1}H NMR spectroscopy showed protons associated with the catalyst, indicating that there was still some pincer complex present and attempts to recover the catalyst should be possible.

When [PdCl(PCP)] **106** was used to catalyse the Suzuki reaction between 4-chloroanisole and phenylboronic acid the reaction yielded no product, with only starting materials and biphenyl observed by HPLC analysis after 73 h. This was disappointing and showed the limitation of the catalyst under these reaction conditions.

Phase transfer catalysts (PTCs) can be used to transfer inorganic anions into an organic solvent. In this reaction the carbonate base has very little solubility in dioxane. Under solid-liquid phase transfer conditions, the use of a PTC would increase the transfer rate of the base to the organic substrates, hence, increasing the reaction rate. More recently, PTC have also been used to stabilise palladium intermediates during the catalytic cycle.[49] In the case of Suzuki reactions, the PTC facilitates solvation of the inorganic substrates in the solvent medium. Secondly, they are thought to enhance the rate of the coupling reaction by activating the boronic acid *via* formation of a boronate complex, $[ArB(OH)_3]^-[R_4N]^+$.[50] Therefore, the introduction of a PTC could enhance the activity of the pincer catalysts.

The addition of TBAB was evaluated in the Suzuki reaction. Two identical reactions were carried out with the non-fluorous catalyst **106**, one reaction mixture containing TBAB and one without. HPLC analysis showed that the reaction mixture containing TBAB produced the product faster with 60 % conversion to product after 2 h, compared with the reaction without TBAB showing a conversion of 45 % after the same time.

The catalyst stability is crucial to the recovery and reuse of the pincer complexes. Heating the catalysts in their reaction solvents at the reaction temperature was used to evaluate the catalyst stability. [PdCl(PCP)] was heated in dioxane at 100 °C for 4 h under an argon atmosphere (Scheme 3.58). There were no visible signs of decomposition in the tube and removal of the solvent followed by analysis ^{31}P & ^{1}H NMR spectroscopy showed the product to be identical to the original complex **106**.

(i) Dioxane, 100 °C, 4 h.
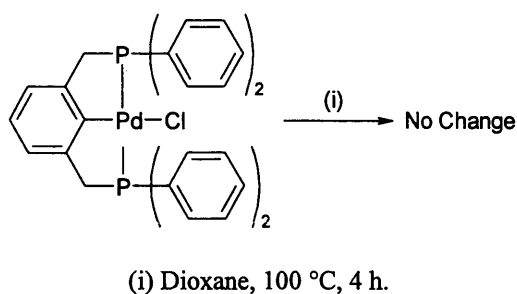
Scheme 3.58. *Decomposition test of [PdCl(PCP)] in reaction solvent.*

The complex stability was then tested in the presence of base. [PdCl(PCP)] and caesium carbonate were heated in dioxane at 100 °C for 4 h under an argon atmosphere (Scheme 3.59). The suspension darkened, with signs of palladium black present. The solvent was removed *in vacuo*, the residue was analysed by ^{31}P & ^{1}H NMR spectroscopy and the original complex **106** and the corresponding PCP-oxide **100** were observed, in approximately a 3:2 ratio. The PCP-oxide was identified by its characteristic NMR shifts, δ_P 29.4 (s) ppm and δ_H 3.45 (d) ppm which collapses to a singlet in the $^1H\{^{31}P\}$ NMR spectrum. The decomposition pathway is still unclear, however, there was no decomposition seen in the initial catalyst testing when the substrates were present. Therefore, it can be assumed that the

decomposition only occurs without the presence of substrate and reactions should be monitored closely to prevent decomposition from occurring.

(i) Dioxane, Cs₂CO₃, 100 °C, 4 h.
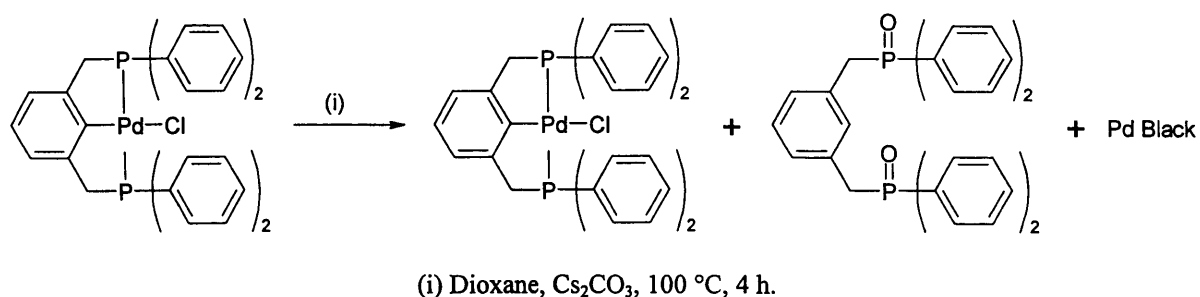
Scheme 3.59. *Decomposition test of [PdCl(PCP)] in reaction solvent and base.*

3.5.2 Heck Reaction - Initial Reaction Conditions

As neither of the pincer complexes had previously been tested in a Heck reaction, common reaction solvents and bases were evaluated from literature sources. Typical reaction conditions consisted of a tertiary alkyl amine base with a dipolar aprotic solvent at high temperature (>100 °C). [3, 5, 8, 13, 23] Initial reactions used triethylamine in DMF at 120 °C with a catalyst loading of 1.5 mole % with iodobenzene as the substrate due to its general high yields in Heck reactions. 1.5 mole % of [PdCl(PCP)] **106**, iodobenzene, methyl acrylate, triethylamine were heated in DMF at 120 °C under a nitrogen atmosphere (Scheme 3.60 and Table 3.14).
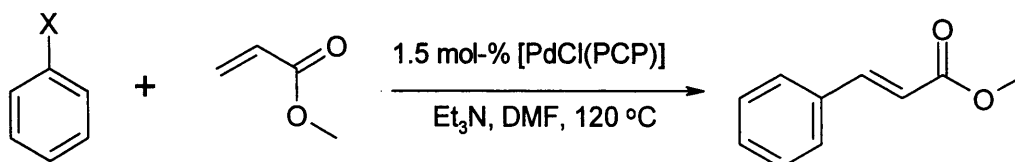
Scheme 3.60. *Initial conditions for Heck reaction.*

Substrate	Atmosphere	Time/h	Prod:SM Ratio[a]
PhI	N₂	1	75:25
PhI	N₂	25	97:3

[a]Determined by GC.

Table 3.14. *Results from Heck reaction using [PdCl(PCP)].*

The reaction proceeded well, with a high product ratio after only 1 h. The reaction was found to be complete after 25 h, with almost quantitative conversion to *trans*-methyl cinnamate product exclusively. There was no visible sign of catalyst decomposition after the reaction was complete. Removal of the solvent from the crude reaction mixture and analysis of the residue by ¹H NMR spectroscopy showed the catalyst to be intact after the reaction

from the characteristic virtual triplet at δ_H 3.95 ppm in the ^1H NMR spectrum for the benzylic protons with a coupling constant of J_{HP} = 4.7 Hz. The virtual triplet collapsed to a singlet in the $^1H\{^{31}P\}$ NMR spectrum.

This was a promising result and so the fluorous catalyst was tested with iodobenzene in the Heck reaction using the same method (Table 3.15). The reaction proceeded with a high product ratio after 1 h. There was no visible sign of catalyst decomposition after the reaction was complete. Removal of the solvent from the crude reaction mixture and analysis of the residue by ^1H NMR spectroscopy showed the catalyst to still be intact.

Substrate	Atmosphere	Time/h	Prod:SM Ratio[a]
PhI	N₂	1	85:15
PhI	N₂	25	93:7

[a]Determined by GC.

Table 3.15. *Results from Heck reaction using [PdCl(Rf-PCP)].*

Many pincer complexes have been reported to catalyse reactions without the requirement of an inert atmosphere. Therefore, the Heck reaction was repeated for iodobenzene with **106** under the same reaction conditions previously used, except, the reaction was carried out under air instead of nitrogen (Table 3.16). The reaction was successful with a high ratio of product formed after 25 h, however, it is not clear why the reaction rate was much slower than the previous reaction carried out under nitrogen. Therefore, in order to maximise the turnover frequency of the pincer catalysts, reactions should be carried out under an inert atmosphere. There was no visible sign of catalyst decomposition after the reaction was complete.

Substrate	Atmosphere	Time/h	Prod:SM Ratio[a]
PhI	AIR	1	20:80
PhI	AIR	25	67:33

[a]Determined by GC.

Table 3.16. *Results from Heck reaction using [PdCl(PCP)] in air.*

Other aryl halides were tested to evaluate the catalyst and the limitations in the reaction conditions. Bromobenzene and chlorobenzene were both independently tested in the Heck reaction using the same method under a nitrogen atmosphere (Scheme 3.61 and Table 3.17). Although good activity was previously observed with iodobenzene, no reaction was seen with either bromobenzene or chlorobenzene, even when longer reaction times were employed. This was a surprising result as **106** had previously been used to catalyse an

unactivated aryl bromide in a Suzuki reaction. Both the Heck and Suzuki reaction undergo a similar catalytic cycle, with one of the steps being an oxidative addition reaction. It was anticipated that if the catalyst could undergo an oxidative addition reaction with the more difficult 4-bromoanisole, then the same catalyst should be able to undergo an oxidative addition reaction with the more facile bromobenzene. This gave a strong indication that the reaction conditions were not suited to the catalyst and needed to be optimised to achieve better results.
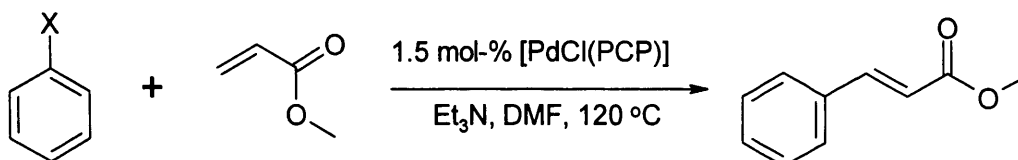
Scheme 3.61. *Initial conditions for Heck reactions with bromobenzene and chlorobenzene.*

Substrate	Time/h	Prod:SM Ratio[a]
PhBr	64	0:100
PhCl	64	0:100

[a]*Determined by GC.*

Table 3.17. *Results from Heck reaction using [PdCl(PCP)]with bromobenzene and chlorobenzene.*

In order to increase the reaction rate, the reaction temperature was increased from 120 to 150 °C. Reactions were carried out as previously reported, except that argon was used as the inert gas and the reaction tube was purged with argon before liquid reagents were added. The Heck reactions with iodobenzene and bromobenzene conducted at 120 °C were repeated to provide a point of reference (Table 3.18).

Substrate	Temp./ °C	Time/h	Yield/%[a,b]
PhI	120	5.5	85
PhBr	120	95	4
PhBr	150	24	11

[a]*Determined by HPLC.* [b]*Assay Yield.*

Table 3.18. *Results from Heck reaction using [PdCl(PCP)] with different reaction temperatures.*

When bromobenzene was allowed to react for 95 h at 120 °C, a small amount of product was formed, however, the yield was far from adequate. Increasing the reaction

temperature achieved a higher reaction rate, yielding 11 % of the product after 24 h. This was still far from satisfactory and optimum reaction conditions were sought.

As for the Suzuki reaction, the catalyst stability is crucial to the recovery and reuse of the pincer complexes. It was necessary to heat the catalysts in their reaction solvents at the reaction temperature to see if any degradation occurred. It was already noted that [PdCl(PCP)] could successfully undergo Heck reactions at 150 °C without any signs of degradation and therefore the stability of the fluorous catalyst was tested.

[PdCl(Rf-PCP)] was heated in DMF for 120 °C for 21.5 h (Scheme 3.62). However, a fine black solid formed in the reaction tube, which was attributed to palladium black formed due to decomposition of the catalyst. Removal of the solvent and analysis of the residue by ^{31}P & ^{1}H NMR spectroscopy, found mainly signals attributed to the original complex and some minor signals for a new compound that has been formed. The ^{31}P NMR spectrum showed a signal at δ_P 31.9 ppm for the decomposition product but the ^{1}H NMR spectrum was uninformative, due to the small amount of the decomposition product and the masking of any new signals by the signals for **113**. There was no further information given in the ^{1}H$\{^{31}$P$\}$ NMR spectrum.
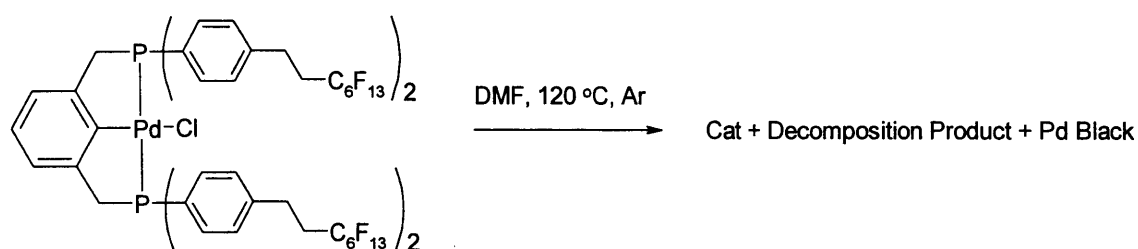
Scheme 3.62. *Decomposition test of [PdCl(Rf-PCP)] in reaction solvent.*

This was quite alarming. If the catalyst was slowly decomposing, its recovery and reuse would be limited. However, there was no visible catalyst decomposition when the catalyst was employed in a catalytic reaction. As with the Suzuki reaction, it is possible that catalyst decomposition only occurs when there is no longer any substrate in the reaction mixture. Therefore, in order to prevent catalyst decomposition, it is necessary to deduce when all the starting material has been consumed and to stop the reaction promptly to prevent any unwanted side reactions.

3.5.3 Heck Reaction – Optimisation

To maximise the efficiency of the pincer catalyst, new reaction conditions were investigated. There are a number of different reaction parameters that could be modified. It was not possible to investigate all of these and so a number of the parameters were fixed. A model Heck reaction was selected, with bromobenzene and methyl acrylate as the starting

materials. The aryl bromide was selected to maximise reaction efficiency and to exemplify conditions that could be further investigated. The reaction temperature was retained at 120 °C (or to reflux if the solvent b.p. was <120 °C) to prevent any possible catalyst decomposition and a reaction time of 24 h was employed (Scheme 3.63). The catalyst loading was lowered from 1.5 to 1 mole %, again to maximise efficiency. Different solvents and bases were evaluated using a solvent-base screen. Using SIMCA, a Design of Experiment (DoE) software package, a range of solvents and bases were characterised by a number factors, i.e. solvents by polarity and bases by basicity. The solvents and bases were then paired in such a way to cover all the possible combinations of the different factors, i.e. a polar solvent with a base with a low pK_a, a polar solvent with a base with a high pK_a, a non-polar solvent with a base with a low pK_a and a non-polar solvent with a base with a high pK_a.

There are number of different bases, organic and inorganic, that have been used successfully in Heck reactions. Therefore, a solvent-base screen was carried out, individually, with organic and inorganic bases. Organic bases were screened first and the different solvents and bases are shown in Table 3.19.

1 mol-% [PdCl(PCP)]

Solvent, Base
Temp = 120 °C or reflux if b.p. is lower
24 h
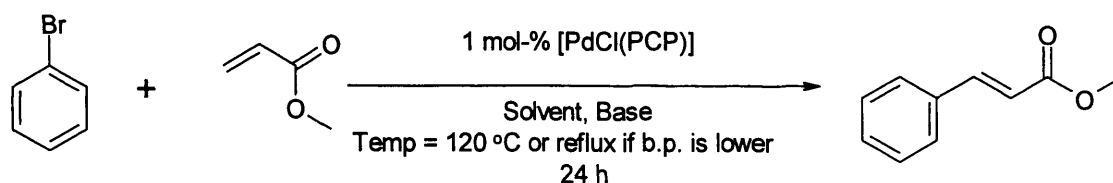
Scheme 3.63. *Solvent/base screen for model Heck reaction.*

Solvent		Organic Base	
Ethylene glycol	Cyclohexane	Diethylamine	4-Methylmorpholine
THF	DMF	Piperidine	Dicyclohexylamine
n-Butyl acetate	2-Propanol	*t*-Butylamine	4-Methylcyclohexylamine
t-Butanol	3-Methyl-1-butanol	DIPEA	2,6-Lutidine
Acetonitrile	Mesitylene	DBU	DABCO
Dioxane	Diisopropyl ether	*N*-Methylpiperidine	Diphenylamine
Di(ethylene glycol) dimethyl ether	NMP (1-Methyl-2-pyrrolidinone)	2,6-Di-*tert*-butylpyridine	Triisopropylamine
Formamide	Butanone	Isoquinoline	2,4,6-Collidine
Cyclohexane		DMAP	Pyridine
Toluene		DBN (1,5-Diazabicyclo[4.3.0]non-5-ene)	

Table 3.19. *Range of different solvents and bases for screening model Heck reaction.*

Reactions were carried out on a small scale in microvate reaction tubes using a microvate reactor. [PdCl(PCP)] and any solid bases were added to the microvate reaction

tubes. The microvate reactor was purged with argon for 30 min before bromobenzene, methyl acrylate, any liquid bases and solvents were added. The reactions were heated to 120 °C (or to reflux if the solvent b.p. was <120 °C) for 24 h under argon. The microvate tubes were cooled and the reaction mixtures were analysed by HPLC and LC-MS (Table 3.20). The conversion of the bromobenzene was recorded as well as the yield of the *trans*-methyl cinnamate product to determine if any unwanted side reactions had occurred.

Entry	Temp./ °C	Solvent	Organic Base	Yield/% [a,b]
1	120	Ethylene glycol	Diethylamine	6.2 [c]
2	67	THF	Piperidine	3.8
3	120	*n*-Butyl acetate	*t*-Butylamine	2.9
4	83	*t*-Butanol	DIPEA	2.2
5	82	Acetonitrile	DBU	1.9
6	102	Dioxane	DBN	1.8
7	120	Di(ethylene glycol) dimethyl ether	2,6-Di-*tert*-butylpyridine	1.0
8	120	Formamide	Isoquinoline	0.6 [c]
9	81	Cyclohexane	DMAP	0.6
10	102	Dioxane	2,6-Di-tert-butylpyridine	0.5
11	81	Cyclohexane	4-Methylmorpholine	0.5 [c]
12	120	DMF	Dicyclohexylamine	0.4
13	82	2-Propanol	4-Methylcyclohexylamine	0.4
14	120	3-Methyl-1-butanol	2,6-Lutidine	0.4
15	120	Mesitylene	DABCO	0.3
16	69	Diisopropyl ether	Diphenylamine	0.3
17	120	NMP	Triisopropylamine	0.3
18	120	3-Methyl-1-butanol	2,4,6-Collidine	0.2
19	80	Butanone	Pyridine	0.1
20	111	Toluene	*N*-Methylpiperidine	0.1

[a]*Determined by HPLC.* [b]*Assay Yield of Product.* [c]*Palladium Black present in reaction mixture.*

Table 3.20. *Results from solvent/base screen.*

The results from the solvent-organic base screen were disappointing. Although all of the reactions produced product, over half of the reactions yielded <1 % of the desired *trans*-methyl cinnamate product. The greatest reaction yield was achieved when diethylamine was used as the base and ethylene glycol was used as the solvent (Entry 1). However, the yield of

the product was still unacceptable, 6 %, and some palladium black was visible in the reaction mixture. Two other reactions (*Entries 8 & 11*) also formed palladium black in the reaction mixture. Therefore, it would not be prudent to further investigate these combinations of solvents and bases as the recovery of the catalyst would seem doubtful if the catalyst cannot survive the reaction conditions.

As *Entries 1-6* all gave reaction yields >1 %, their HPLC traces were analysed in more detail. All of the HPLC UV traces showed an unknown compound with a retention time (R_t) = 6.22 min. LC-MS was used to analyse the crude reaction mixtures and found no Buchwald-type (phenols, arylamines) products. However, analysis by mass spectrometry showed the unknown compound to have a molecular ion at m/z = 523. It was speculated that this was the corresponding PCP-oxide.H_2O, formed through decomposition of the catalyst, as this molecular ion had been seen previously (Scheme 3.64). The proposed route of decomposition would follow a Pd(II)/Pd(IV) mechanism, initiated by the coordination of the alkene to form **120**. Instead of elimination of HCl, one of the phosphines could dissociate from the metal centre **121** to set up a reductive elimination reaction, although phosphine dissociation may not be necessary. The reductive elimination of the hydride and aryl ring followed by ligand dissociation from the metal centre would lead to the free phosphine ligand **102**. Rapid oxidation would occur in air to form the phosphine oxide **100**, which could then pick up a water molecule to show a [M+17]$^+$ at *m/z* = 523.
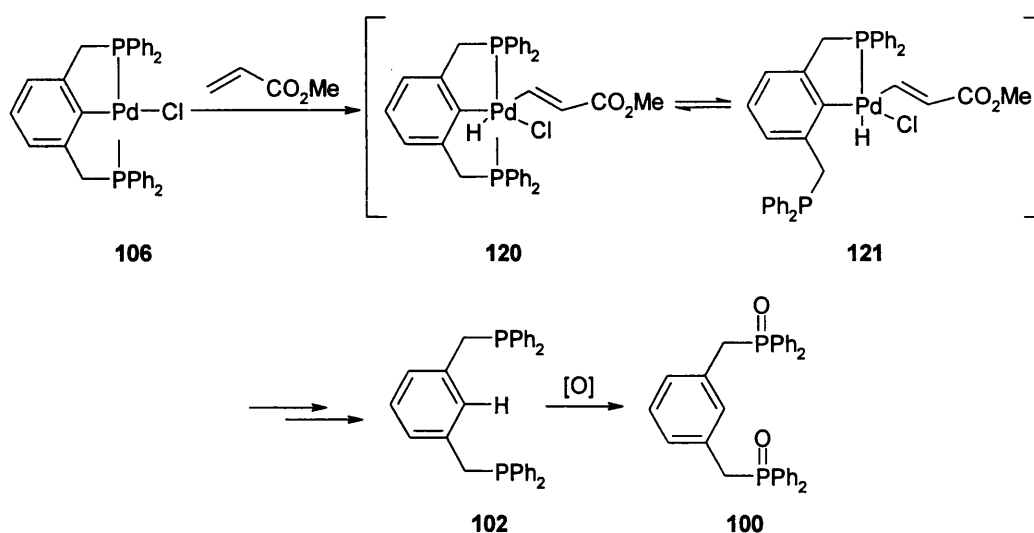
Scheme 3.64. *Proposed mechanism of decomposition of [PdCl(PCP)].*

It is uncertain whether this unknown compound is the corresponding PCP-oxide and ^{1}H NMR spectroscopy had shown that the pincer complex was intact after preliminary reactions. Therefore, optimisation was continued but further reactions would be analysed for this impurity.

DoE software is a new powerful tool in synthetic chemistry. The software can be used to interpret experimental data collected and, if results give a close to perfect model fit, predictions regarding untested solvents and bases can be reliably made. The experimental data from the solvent-organic base screen was analysed using DoE software.

Principal Component Analysis-Projection to Latent Spaces (PCA-PLS) analysis of product % yield only gave a model fit of $R^2 = 0.52$ and $Q^2 = 0.34$. R^2 is a measure of how much a variable is explained by the model and Q^2 is a measure of how well a variable can be predicted. For a good model both R^2 and Q^2 are required to be greater than 0.5. A perfect model would have R^2 and $Q^2 = 1$. The data for the solvent-organic base screen gave a reasonable fit, allowing good correlation of the response with the properties, but any predictions of untested solvent/base combination made from the data would need to be treated with caution.

PLS analysis indicated that the following variables were correlated with percentage yield of the product formed (Figure 3.10).

- Base pK_a has the biggest effect on yield.

- Reaction temperature has no effect on yield.

- Solvent density and base pK_a have a positive correlation with yield and, therefore, bases with the highest pK_a and solvents with the highest density give higher yields.

- Bases of low molecular mass, refractive index, density and boiling point correlate with high yield.
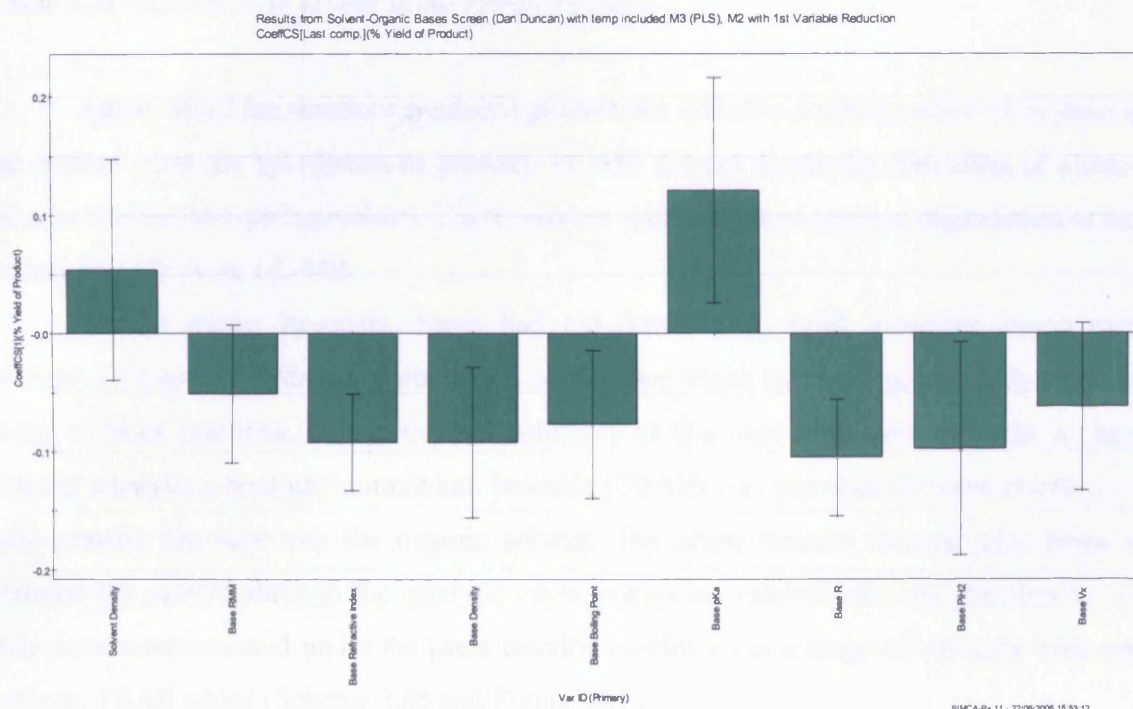
Figure 3.10. *PLS analysis from solvent/base screen.*

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The model fit may be <1 due to the decomposition of the catalyst in some reactions, that therefore, go through a different reaction pathway. The PLS analysis, indicating that temperature has no effect on the reaction yields, contradicts previous experiments where a reaction carried out at 150 °C gave higher reaction yield than the same reaction carried out at 120 °C.

Consequently, predictions of untested solvent/base combinations made from the data would need to be treated with caution. Therefore, when DoE software gave predictions for a solvent-inorganic base combination using the data from the solvent-base screen a small set of trial experiments were conducted. Bases with a high pK_a were selected, as PLS analysis had indicated that bases with high pK_a should give the greatest yield. There was some concern that strong bases could possibly form phenols, Buchwald-type (phenols, arylamines) products or, even worse, cause catalyst attrition. Reactions were carried out using the same method as for the solvent-organic base screen. The results are summarised in Table 3.21.

Solvent	Base	Yield[a,b]
NMP	Potassium t-butoxide	1.5
Dioxane	Cesium hydroxide	0.2
THF	Sodium methoxide	0.1
Toluene	Sodium amide	0.1

[a]Determined by HPLC. [b]Assay Yield of Product.

Table 3.21. Solvent/base screen using inorganic bases.

Again, all of the reactions produced product but all led to reactions with <2 % yield of the desired trans-methyl cinnamate product. LC-MS did not detect the formation of phenol, ether or Buchwald-type byproducts. There were no visible signs of catalyst degradation or any detected by HPLC or LC-MS.

As the strong inorganic bases had not faired well, mild inorganic bases were evaluated. Potassium hydrogen carbonate is a mild base which has been successfully used in a range of Heck reactions. Due to the low solubility of this base in organic solvents, a phase transfer catalyst, n-tetrabutylammonium bromide (TBAB) was screened in these reactions to help transfer the base into the organic solvent. The phase transfer catalyst also helps to stabilise the catalyst through the catalytic cycle, enhancing catalytic activity (Section 3.5.1). Reactions were screened under the same reaction conditions in a range of solvents with, and without, TBAB added (Scheme 3.65 and Figure 3.11).
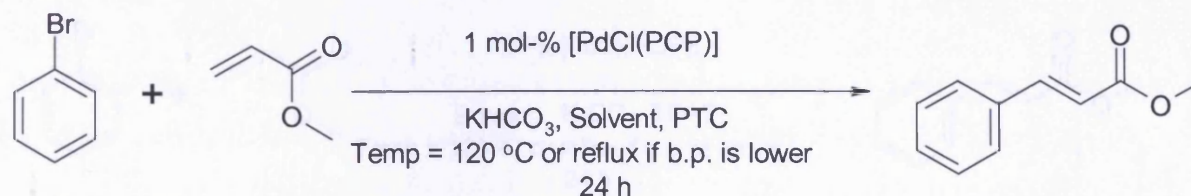
Scheme 3.65. *Solvent screen with and without PTC.*
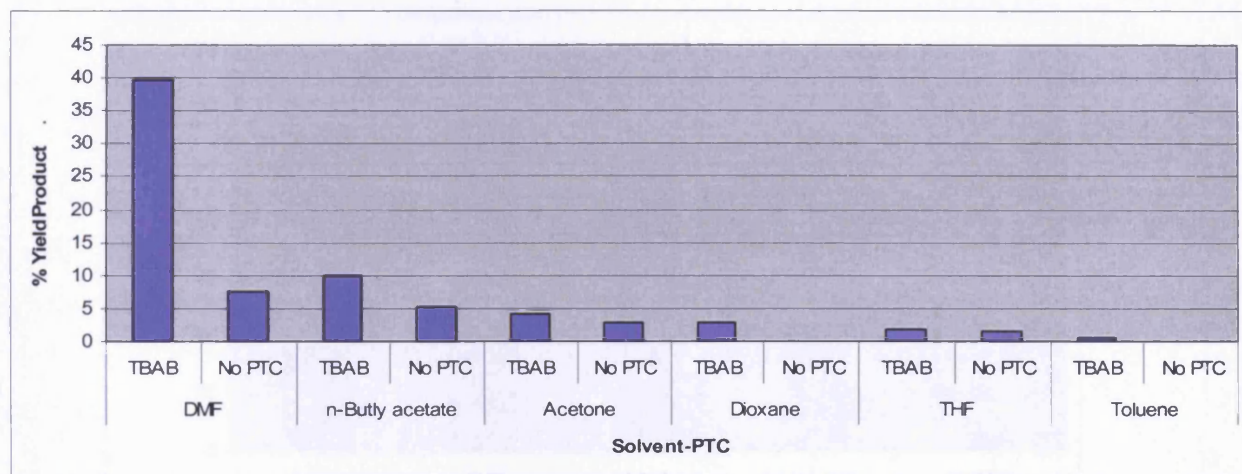
Figure 3.11. *Results from solvent screen with and without PTC.*

Not all of the reactions yielded product but there was a general increase in reaction yield. Reactions that contained TBAB gave higher yields of the product than the reactions that did not contain a phase transfer catalyst. When the reaction was carried out in DMF without a phase transfer catalyst an 8 % yield was achieved. The introduction of TBAB significantly increased the reaction rate achieving a 40 % yield. This was by far the best result achieved during the solvent-base screen.

Potassium carbonate is a stronger base then potassium hydrogen carbonate, and so it was then screened. The same reaction conditions were carried out using DMF as the solvent and TBAB. The reaction gave an increased reaction yield of 58 %. The reaction conditions were now starting to produce acceptable yields and since potassium carbonate was found to give the best yield, it was possible to home in on the optimum solvent and PTC.

Other dipolar aprotic solvents were screened with potassium carbonate as the base and TBAB as the PTC (Scheme 3.66 and Figure 3.12). NMP, DMF and DMA all gave good yields of the product, with NMP being the best (62 %). Having selected NMP as the solvent of choice all that remained was to screen the PTCs to see if there was any improvement in reaction yield. Phase transfer catalysts with different cations and anions were evaluated (Scheme 3.67 and Figure 3.13).
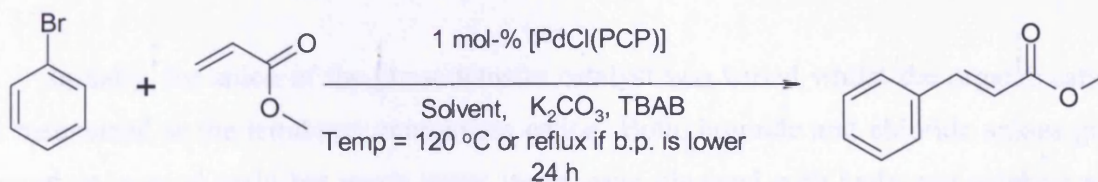
Scheme 3.66. *Solvent screen of dipolar aprotic solvents.*
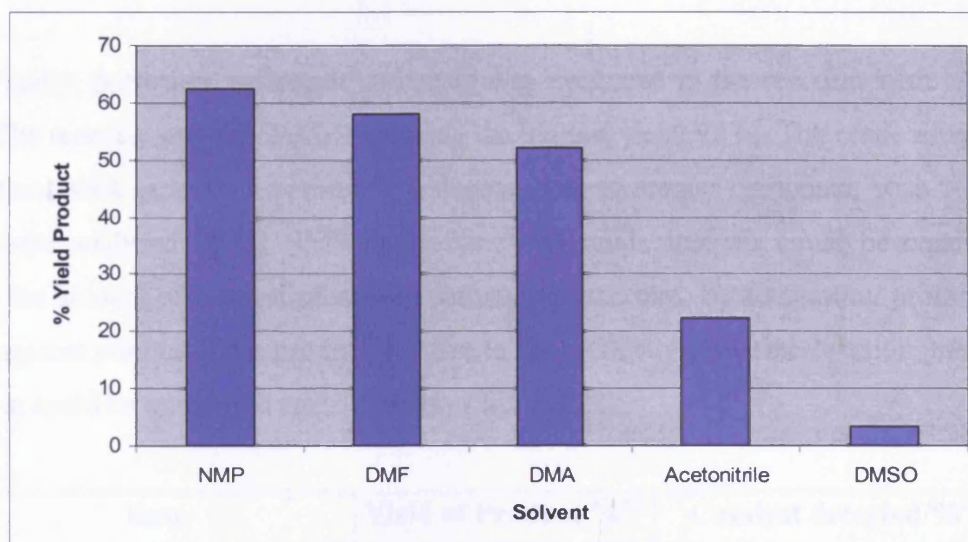
Figure 3.12. *Results from solvent screen of dipolar aprotic solvents.*
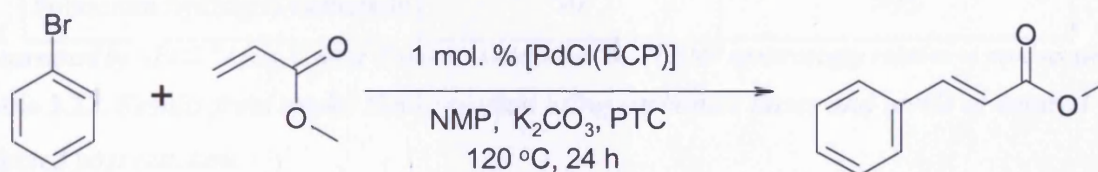
Scheme 3.67. *PTC screen for model Heck reaction.*
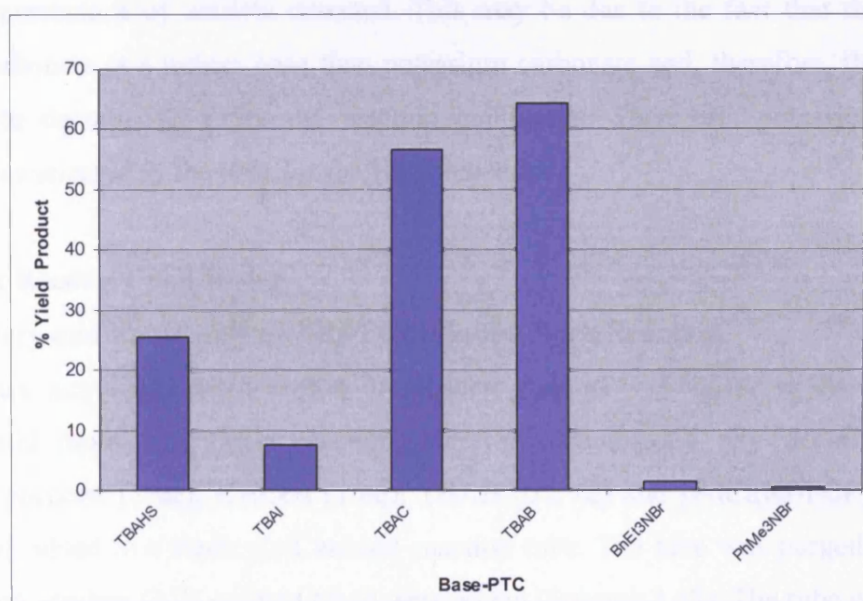
Figure 3.13. *Results from PTC screen for model Heck reaction.*

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Initially, the anion of the phase transfer catalyst was varied whilst the organic cation was maintained as the tetrabutyl ammonium cation. Both, bromide and chloride anions give the product in good yield but much lower yields were obtained with hydrogen sulphate and iodide. The cation component was also varied but the best results were obtained with the more organophilic tetrabutyl ammonium cation, which presumably has the highest solubility in NMP.

Finally, potassium hydrogen carbonate was evaluated in the reaction with NMP and TBAB. The reaction was successful achieving the highest yield, 70 %. The crude mixtures for the reactions with potassium carbonate and potassium hydrogen carbonate, with NMP and TBAB, were analysed by ^{1}H NMR spectroscopy. A crude analysis could be conducted to estimate the amount of catalyst present in the reaction mixture. By integrating protons of the catalyst against protons of the product, relative to the product yield in the reaction, the amount of catalyst could be quantified approximately (Table 3.22).

Base	Yield of Product/%^{a,b}	Catalyst detected/%^{c}
Potassium carbonate	64	77
Potassium hydrogen carbonate	70	>95

^{a}Determined by HPLC. ^{b}Assay Yield of Product. ^{c}Determined by ^{1}H NMR spectroscopy relative to product yield.

Table 3.22. *Results from model Heck reaction using carbonate bases and levels of catalyst detected post reaction.*

The crude reaction mixture from the reaction using potassium hydrogen carbonate had the highest percentage of catalyst detected. This may be due to the fact that the potassium hydrogen carbonate is a milder base than potassium carbonate and, therefore, the catalyst is less likely to decompose under the reaction conditions. Therefore, potassium hydrogen carbonate was selected as the base for the Heck reaction.

3.6 Catalyst Recovery and Reuse

3.6.1 Recovery and Reuse of [PdCl(Rf-PCP)] in the Heck Reaction

For the recycling experiments, 4-bromoacetophenone was chosen as the aryl bromide as this would produce a facile reaction, therefore, minimising any decomposition. 4-Bromoacetophenone (1 eq), KHCO$_3$ (1 eq), TBAB (0.2 eq) and [PdCl(Rf-PCP)] (50 mg, 1 mol-%) were added to a Radley's Carousel reaction tube. The tube was purged with argon, before methyl acrylate (1.25 eq) and NMP were added (Scheme 3.68). The tube was placed in a preheated oil bath (120 °C), samples were taken over the course of the reaction and analysed

by HPLC. After removing the solvent and the remaining volatiles by Kugelröhr distillation, the resulting solid was taken up in acetonitrile and DCM, then loaded onto a column of FRPSG (4 g), which had been pre-treated with acetonitrile. The column was eluted with acetonitrile to give the organic products and then ethyl acetate to give the fluorous catalyst (Figure 3.14). The recovered catalyst was reused in the next run using exactly the same reactions conditions (Figure 3.15 & Table 3.23).
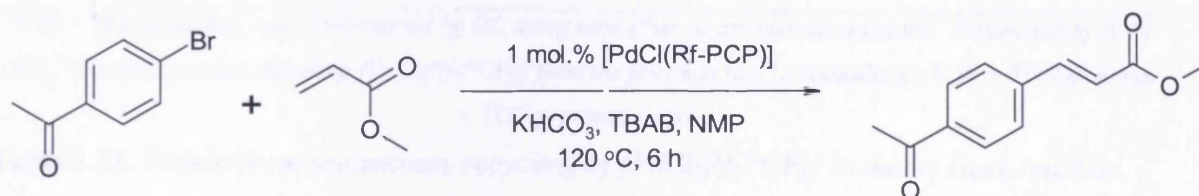
Scheme 3.68. *Model Heck reaction for recycling protocol.*
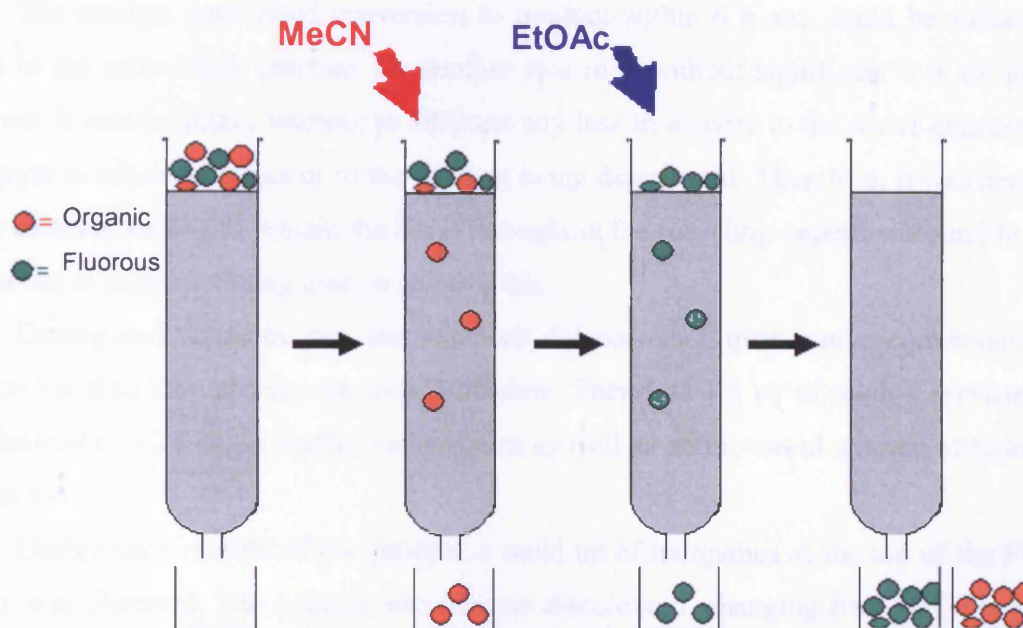
Figure 3.14. *Recycle of [PdCl(Rf-PCP)] using fluorous SPE.*
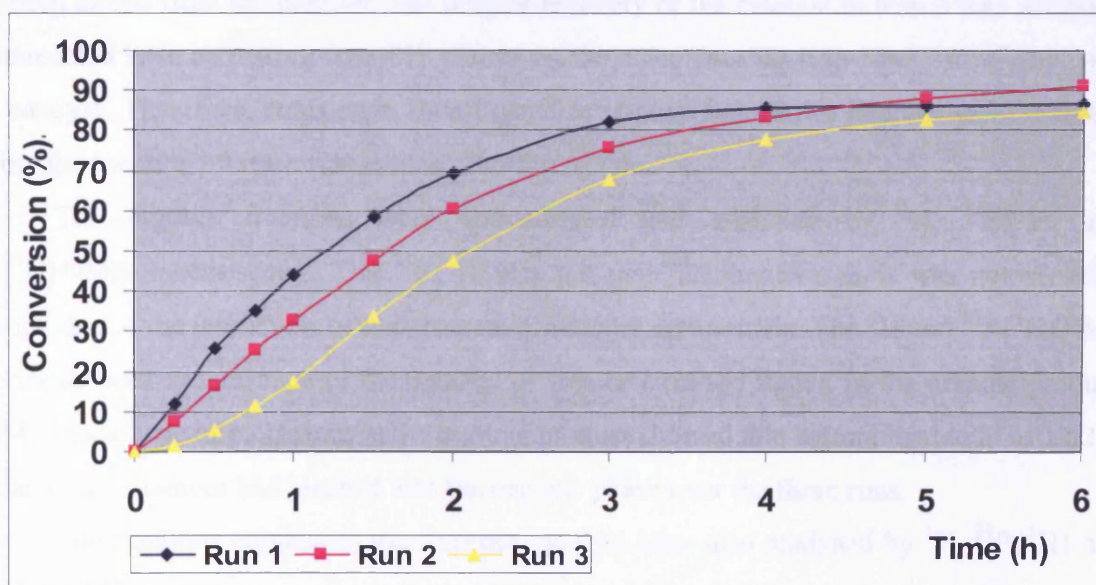
Figure 3.15. *Results from preliminary recycling of [PdCl(Rf-PCP)] in model Heck reaction.*

Run	Amount [Pd] used/mg	Cat. Loading/ mol-%	Accumulative TON^a	$Conv./\%^b$	Amount [Pd] recovered	% Pd in Prod per Run^c
1	50.0	1.00	86	86	44.3 mg, 89 %	0.81
2^d	44.3	0.93	184^e	91	38.0 mg, 86 %	0.62
3^d	38.0	0.82	288^e	85	18.0 mg, 48 %	0.19

^{a}TON = (mol prod/mol cat). ^{b}Determined by GC using tolyl ether as an internal standard. ^{c}Detemined by ICP-OES. ^{d}Catalysis carried out using [PdCl(Rf-PCP)] from the previous run. ^{e}Accumulative TON = TON from rxn + TON previous rxn(s).

Table 3.23. Results from preliminary recycling of [PdCl(Rf-PCP)] in model Heck reaction.

The catalyst gave good conversion to product within 6 h and could be successfully reused in the same Heck reaction for another two runs without significant loss of activity. However, it was uncertain whether to attribute any loss in activity to the lower concentration of catalyst in successive runs or to the catalyst being deactivated. Therefore, it was necessary for the catalyst loading to remain the same throughout the recycling experiments and to lower the amount of substrate being used to achieve this.

During each catalytic run, the reactions did not reach quantitative conversion. This was attributed to the volatility of methyl acrylate. Therefore 1.5 eq of methyl acrylate were used, instead of 1.25 eq, in further experiments as well as an increased amount of base, 1.05 eq from 1 eq.

During each recycle of the catalyst, a build up of inorganics at the top of the FRPSG column was observed. The column also became discoloured, changing from white to yellow in colour. The yellow intensity grew after each recycle and was attributed to TBAB that had not been eluted from the column. The drop in recovery of the catalyst in Run 3 was attributed to unreacted base activating free OH groups on the silica causing it to bind irreversibly with the catalyst. Therefore, steps were investigated to remove the TBAB and inorganic material before the reaction mixture was loaded onto the column.

The organic fractions were concentrated and analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H}NMR spectroscopy. The ^{31}P{^{1}H}was not very informative as it was not sensitive enough due to the low levels of phosphorus-containing compounds. The ^{1}H and ^{19}F{^{1}H}NMR spectra showed no presence of the catalyst or free or oxidised ligand in the organic product. ICP-OES analysis of palladium in the organic product showed that a combined total of 1.62 % of the total palladium had leached into the organic phase over the three runs.

The fractions containing the fluorous catalyst were also analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H}NMR spectroscopy and indicated that the catalyst was in the same state but was the bromide instead of the chloride. FAB-MS again showed no parent ion peaks, but a peak

corresponding to [M-Br]$^+$. It was also noted that TBAB was present with the fluorous catalyst in the fluorophilic fractions. The catalyst recovery was amended to take this into account for the previous runs, but it would be preferable to remove the TBAB before the reaction mixture was loaded onto the column.

In order to optimise the recycling results the reaction work up was modified. Before the reaction mixture was loaded onto the column of FRPSG an aqueous wash was employed to remove any inorganic material and TBAB from the reaction mixture. The recycling was conducted using the same method as before used and the recovered catalyst was reused in the same Heck reaction (Figure 3.16 and Table 3.24).
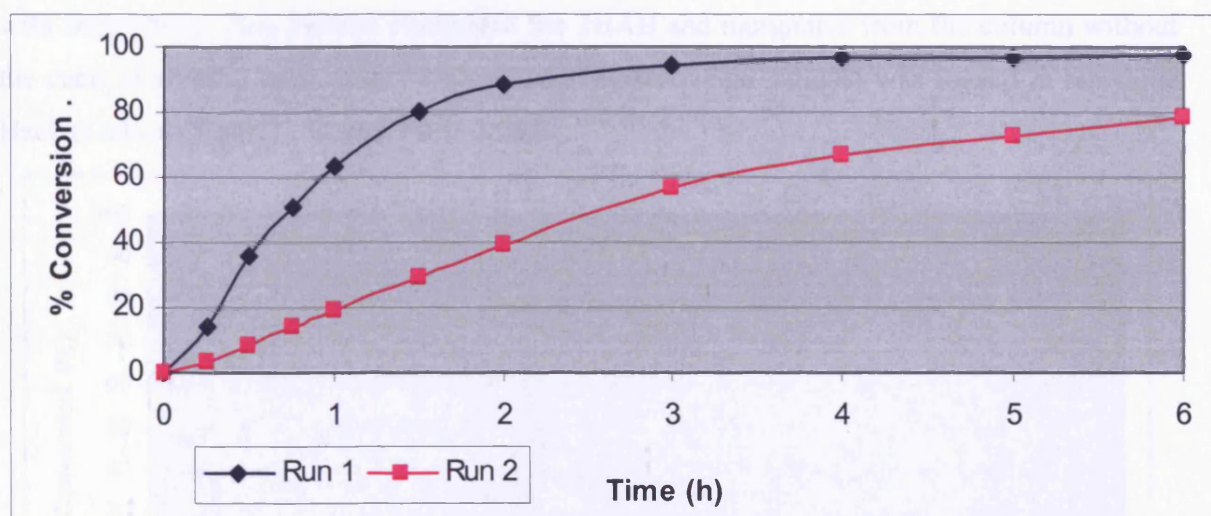
Figure 3.16. *Results from recycling experiments using an aqueous work up.*

Run	Amount [Pd] used/mg	Cat. Loading/ mol-%	Accumulative TON^a	Conv./%^{b}	Amount [Pd] recovered	% Pd in Prod per Run^c
1	50.0	1.00	98	98	45.4 mg, 91 %	0.86
2^d	45.4	1.00	176^e	78	41.0 mg, 90 %	0.26

^{a}TON = (mol prod/mol cat). ^{b}Determined by GC using tolyl ether as an internal standard. ^{c}Detemined by ICP-OES. ^{d}Catalysis carried out using [PdCl(Rf-PCP)] from the previous run. ^{e}Accumulative TON = TON from rxn + TON previous rxn(s).

Table 3.24. *Results from recycling experiments using an aqueous work up.*

This time the reaction went to quantitative conversion for the first run. However, there was a large drop in activity observed in the second run, indicating that the catalyst had been deactivated during the recycling process. Analysis of the fluorophilic fractions by ^{1}H, ^{31}P$\{^1$H$\}$ and ^{19}F$\{^1$H$\}$ NMR spectroscopy indicated that the catalyst was still intact and no TBAB was present, however, a small amount of water was shown to be present by ^{1}H NMR

spectroscopy. This suggests that the catalyst is deactivated by water in the catalytic system and, therefore, further recycling experiments should avoid the catalyst coming into contact with water.

The organic fractions were also analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H} NMR spectroscopy and no presence of the catalyst or free or oxidised ligand was observed. ICP-OES analysis of palladium leached into the organic product showed a combined total of 1.12 % of the total palladium for the two runs.

The recycling experiments were repeated again, taking into account the previous findings. The reaction was carried out using the same method, however, after the catalyst was recovered from the FRPSG column, the column was washed with water and then regenerated with acetonitrile. This method eliminated the TBAB and inorganics from the column without the catalyst coming into contact with water. The recovered catalyst was reused in the same Heck reaction (Figure 3.17 and Table 3.25).

Figure 3.17. *Results from recycling experiments of [PdCl(Rf-PCP)] in model Heck reaction.*

Run	Amount [Pd] used/mg	Cat. Loading/ mol-%	Accumulative TON[b]	Conv./%[b]	Amount [Pd] recovered	% Pd in Prod per Run[c]
1	50.0	1.00	100	>99	48.2 mg, 96 %	0.19
2[d]	48.2	1.00	200[e]	>99	45.0 mg, 93 %	0.06
3[d]	45.0	1.00	300[e]	>99	40.5 mg, 90 %	0.05
4[d]	40.5	1.00	400[e]	>99	36.4 mg, 90 %	0.05

[a]*TON = (mol prod/mol cat).* [b]*Determined by GC using tolyl ether as an internal standard.* [c]*Detemined by ICP-OES.* [d]*Catalysis carried out using [PdCl(Rf-PCP)] from the previous run.* [e]*Accumulative TON = TON from rxn + TON previous rxn(s).*
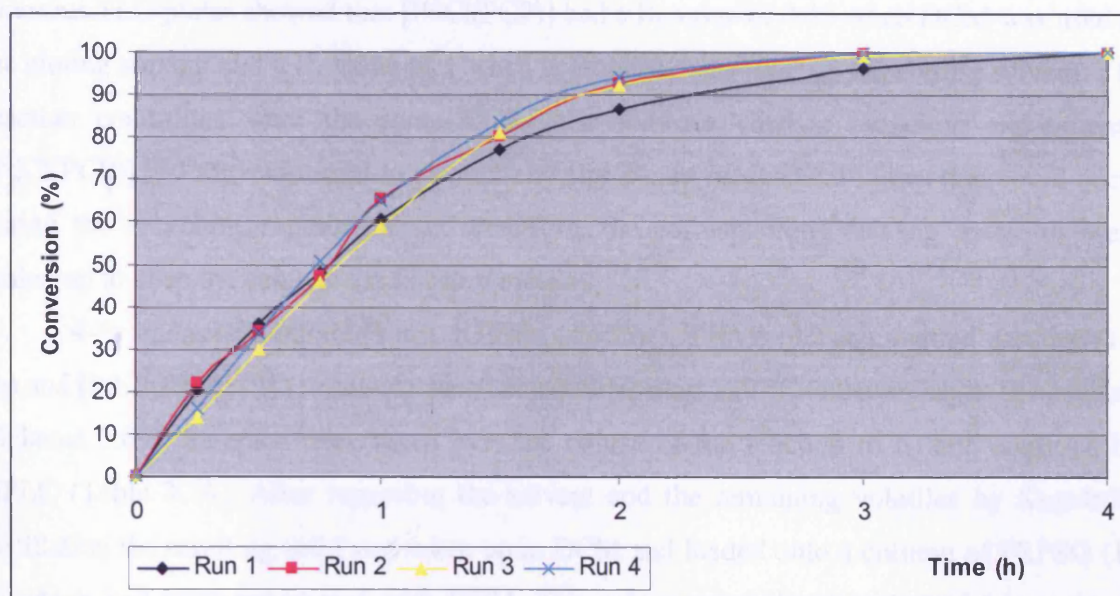
Table 3.25. *Results from recycling experiments of [PdCl(Rf-PCP)] in model Heck reaction.*

This time, the catalyst successfully catalysed the reaction with no loss in catalytic activity over the four runs. The catalytic conversion remained quantitative over the four runs, achieving an accumulative turnover number (TON) of 400. Recovery of the fluorous catalyst was extremely good, ranging from 90–96 % of the isolated catalyst. This time, the organic product was dissolved in methanol and filtered through a plug of cotton wool before ICP-OES analysis. The amount of palladium leached into the organic product was a combined total of 0.35 % of the total palladium for the four runs. This could be further reduced to 0.20 % of the total palladium by filtering the organic product through a pad of alumina.

3.6.2 Recovery and Reuse of [PdCl(PCP)] in the Heck Reaction

Even though the [PdCl(PCP)] does not contain a fluorous domain, it may be possible to recover the catalyst using FRPSG due to the differences in polarity (see Section 3.4). Fluorous TLC plates showed that [PdCl(PCP)] had a R_f value of 0.06 when DCM was used as the eluting solvent and a R_f value of 1 when acetonitrile was used as the eluting solvent. The reaction conditions were the same as for the fluorous catalyst recycling experiments. [PdCl(PCP)] (50 mg) was used to prevent any significant mechanical losses that could occur during the recycling experiment and therefore, the corresponding starting materials were scaled up to keep the catalyst loading at 1 mole %.

4-Bromoacetophenone (1 eq), KHCO$_3$ (1.05 eq), TBAB (0.2 eq), methyl acrylate (1.5 eq) and [PdCl(Rf-PCP)] (1 mol-%) were heated in NMP at 120 °C under an argon atmosphere (Scheme 3.69). Samples were taken over the course of the reaction (6 h) and analysed by HPLC (Table 3.26). After removing the solvent and the remaining volatiles by Kugelröhr distillation the resulting solid was taken up in DCM and loaded onto a column of FRPSG (10 g) which had been pre-treated with DCM. The column was eluted with DCM in order to obtain the organic products and then acetonitrile to give the catalyst. However, when the fractions were analysed by ^{1}H NMR spectroscopy, the DCM fractions contained both the organic product and the catalyst and the acetonitrile fractions contained TBAB only. The column had failed to separate the catalyst from the organic product providing evidence that the perfluoroalkyl chains are crucial for efficient separation.
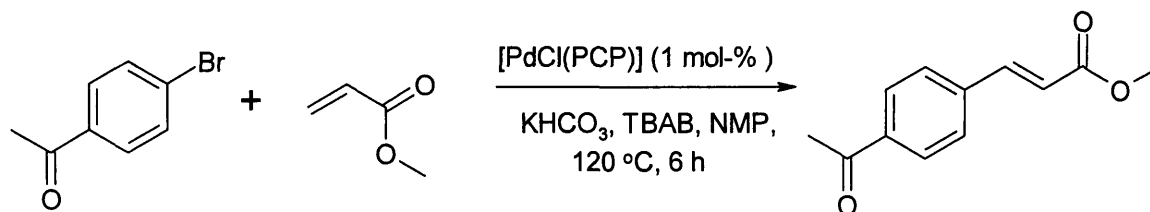
Scheme 3.69. *Recycling experiments of [PdCl(PCP)] in model Heck reaction.*

Run	Amount [Pd] used/mg	Cat. Loading/ mol-%	Conv./%[a]	Amount [Pd] recovered
1	50.0	1.00	96	0 mg, 0 %

[a]Determined by HPLC.

Table 3.26. *Results from recycling experiments of [PdCl(PCP)] in model Heck reaction.*

Looking at the difference in activities for the two catalysts, it is clear that under these reaction conditions, [PdCl(Rf-PCP)] is slightly more active than [PdCl(PCP)] (Figure 3.18). The reaction is complete after 4 h with the fluorous catalyst but is only complete after 6 h with the non-fluorous catalyst.
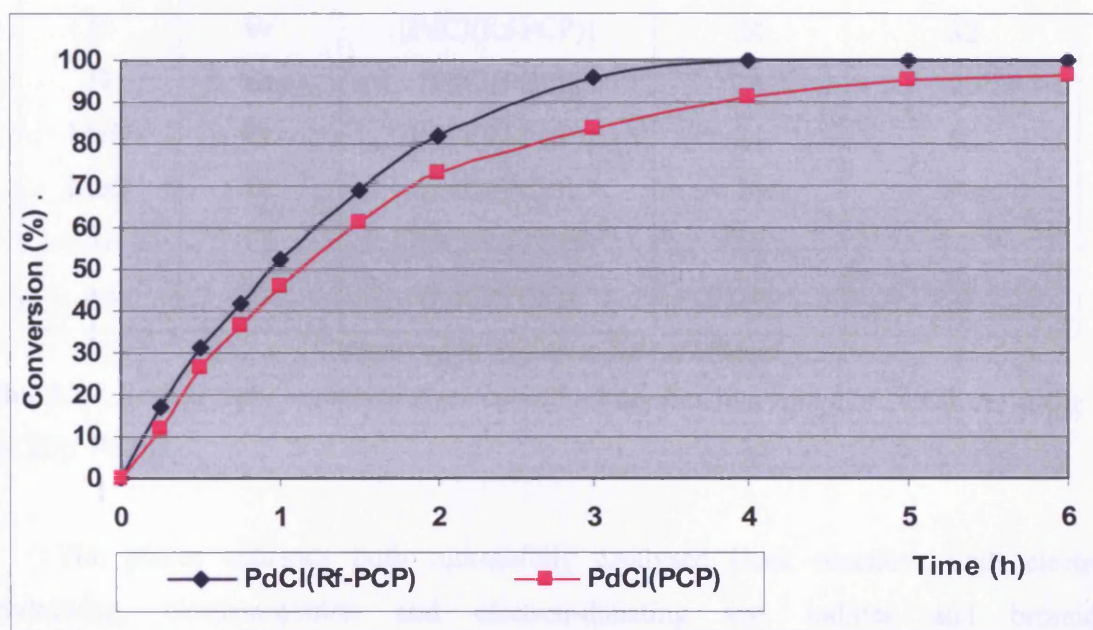
Figure 3.18. *Comparison of [PdCl(Rf-PCP)] vs [PdCl(PCP)] in model Heck reaction.*

3.6.3 Application of Pincer Catalysts to a Range Substrates

The pincer complexes were tested in a range of Heck reactions to evaluate their versatility towards different substrates. Aryl iodides, bromides and chlorides with different electronic properties were tested using the standard conditions previously used (Scheme 3.70). At the end of the reaction, the reaction mixtures were poured into volumetric flasks, diluted and samples were analysed by GC (Table 3.27).
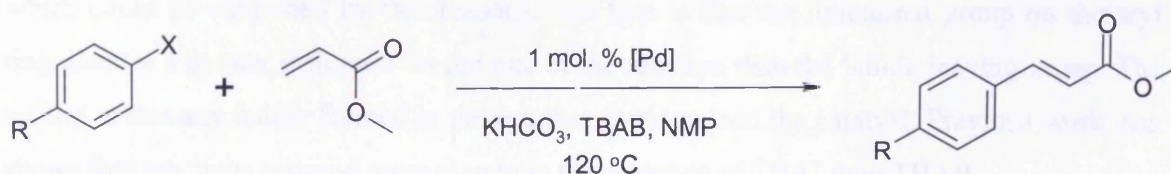
Scheme 3.70. *Optimised Heck conditions applied to a range of substrates using [PdCl(Rf-PCP)].*

Substrate		Catalyst	Time/h	Yield/%^{a,b}
R	X			
Ac	I	[PdCl(Rf-PCP)]	5	>98
Ac	I	[PdCl(PCP)]	5	87
H	I	[PdCl(Rf-PCP)]	5	91
H	I	[PdCl(PCP)]	5	81
MeO	I	[PdCl(Rf-PCP)]	5	66
MeO	I	[PdCl(PCP)]	5	>98
Ac	Br	[PdCl(Rf-PCP)]	5	>98
Ac	Br	[PdCl(PCP)]	5	95
H	Br	[PdCl(Rf-PCP)]	24	82
H	Br	[PdCl(PCP)]	24	79
MeO	Br	[PdCl(Rf-PCP)]	24	57
MeO	Br	[PdCl(PCP)]	24	>98
Ac	Cl	[PdCl(Rf-PCP)]	24	0
Ac	Cl	[PdCl(PCP)]	24	0

^{a}Determined by GC. ^{b}Assay Yield of Product.

Table 3.27. *Results from optimised Heck conditions applied to a range of substrates using [PdCl(Rf-PCP)].*

The pincer catalysts both successfully catalysed Heck reactions with electron-withdrawing, electron-neutral and electron-donating aryl iodides and bromides. Unfortunately, neither of the catalysts were able to catalyse the Heck reaction with 4-chloroacetophenone under the reaction conditions used.

The fluorous catalyst was more active than the non-fluorous catalyst for electron-withdrawing and electron-neutral aryl halides. However, the non-fluorous catalyst was more active than the fluorous catalyst for electron-donating aryl halides. This result was strange, but must be due to the slightly different electronic environments of the palladium metal centre.

The reaction with 4-bromoacetophenone was faster than for most of the aryl iodides, which could be explained by two reasons. The first is that the functional group on the aryl ring dictates a greater influence on the rate of the reaction than the halide leaving group. The second is that any iodide formed in the reaction could poison the catalyst. Previous work, has shown that reactions proceed more slowly in the presence of TBAI than TBAB.

3.6.4 Recovery and Reuse of [PdCl(Rf-PCP)] in the Suzuki Reaction

Due to the success of the recycling experiments for the Heck reaction and initial studies of the Suzuki reaction, it was hoped that similar recycling results could be achieved. For the recycling experiments, 4-bromoacetophenone was chosen as the aryl bromide as this would produce a facile reaction, therefore, minimising any decomposition. Also, the activity of catalyst could be compared between systems.

4-Bromoacetophenone (1 eq), phenylboronic acid (1.5 eq), caesium carbonate (2 eq), TBAB (0.2 eq), tolyl ether as an internal standard (1 eq) and [PdCl(Rf-PCP)] (50 mg, 1 mol-%) were heated at 100 °C under an atmosphere of argon in dioxane (Scheme 3.71). Samples were taken over 2 h and analysed by GC. After removing the solvent *in vacuo*, acetonitrile was used to load the reaction mixture onto the column and as the fluorophobic solvent, but the boronic acid was not soluble in acetonitrile and was not eluted efficiently from the column. Therefore, methanol was used to load the reaction mixture onto the column and as the fluorophilic solvent. The resulting solid was taken up in methanol and DCM, then loaded onto a column of FRPSG (5 g) that had been pre-treated with methanol. The column was eluted with methanol to give the organic products and then ethyl acetate to give the fluorous catalyst. The recovered catalyst was reused in the next run using the same reactions conditions (Figure 3.19 & Table 3.28).
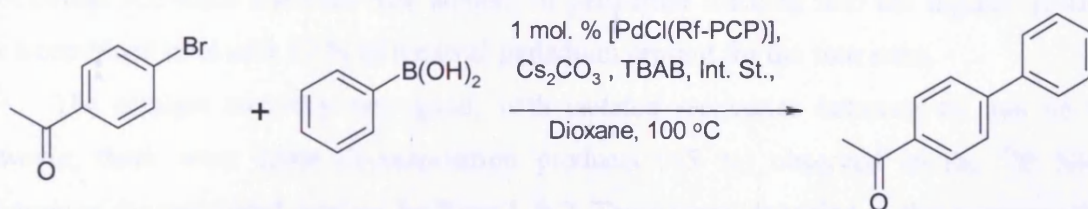
Scheme 3.71. *Recycling experiment for [PdCl(Rf-PCP)] in a Suzuki reaction.*
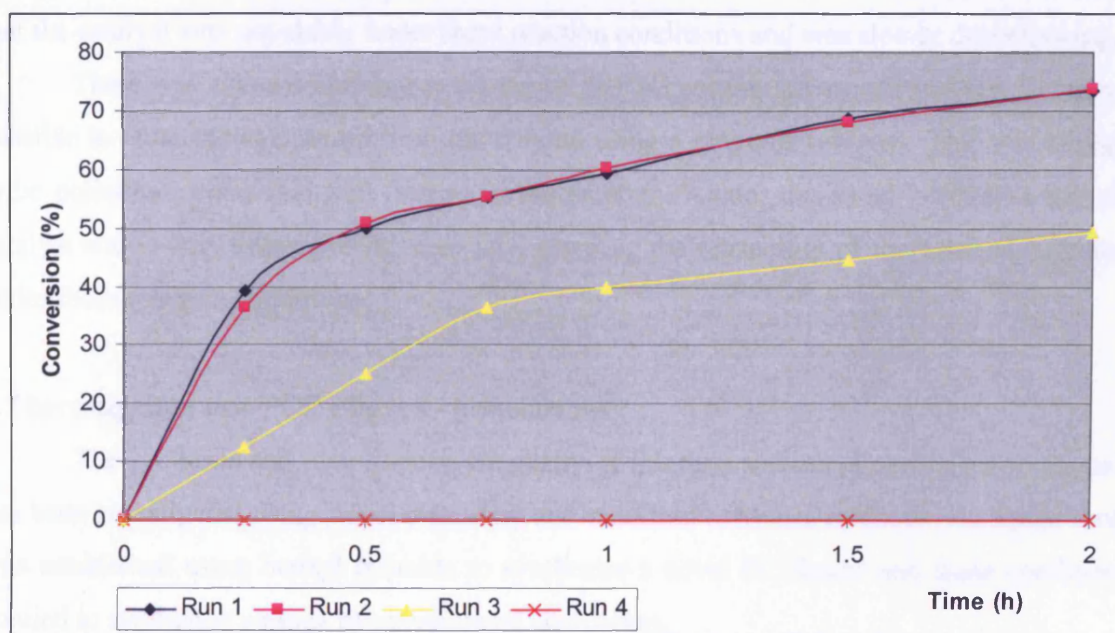
Figure 3.19. *Results from recycling experiment for [PdCl(Rf-PCP)] in a Suzuki reaction.*

Run	Amount [Pd] used/mg	Cat. Loading/ mol-%	Accumulative TON^a	Conv./%^{b}	Amount [Pd] recovered	% Pd in Prod per Run^c
1	50.0	1.00	74	74	43.6 mg, 87 %	0.05
2^d	43.6	1.00	148^e	74	30.3 mg, 69 %	0.02
3^d	30.3	1.00	197^e	49	29.2 mg, 96 %	0.03
4^d	29.2	1.00	197^e	0	27.5 mg, 94 %	0.02

^{a}TON = (mol prod/mol cat). ^{b}Determined by GC using tolyl ether as an internal standard. ^{c}Detemined by ICP-OES. ^{d}Catalysis carried out using [PdCl(Rf-PCP)] from the previous run. ^{e}Accumulative TON = TON from rxn + TON previous rxn(s).

Table 3.28. *Results from recycling experiment for [PdCl(Rf-PCP)] in a Suzuki reaction.*

The fluorous pincer catalyst successfully catalysed the Suzuki reaction over three runs. The activity remained the same for the first two runs, however, there was a significant drop in activity in the third run and no further reaction in the fourth run. An accumulative TON of 197 was achieved over the three runs. Analysis of the organic product by ^{1}H, ^{31}P$\{^1$H$\}$ and ^{19}F$\{^1$H$\}$NMR spectroscopy showed no presence of the catalyst or free or oxidised ligand. Again, the organic product was dissolved in methanol and filtered through a plug of cotton wool before ICP-OES analysis. The amount of palladium leaching into the organic product was a combined total of 0.12 % of the total palladium present for the four runs.

The catalyst recovery was good, with isolated recoveries between 69 and 96 %. However, there were some decomposition products (<5 %) observed in the ^{31}P NMR spectrum of the recovered catalyst for Runs 1 & 2. These were identified as the corresponding pincer phosphine and phosphine oxide due to their characteristic ^{31}P NMR shifts, indicating that the catalyst was not stable under these reaction conditions and was slowly decomposing.

There was also a darkening at the top of FRPSG column after each recycle. It was not possible to elute the compound from the column using a range of solvents. This was thought to be palladium black that had formed in the reaction. Again, this is an indication that the catalyst was slowly decomposing, therefore, showing the reusability of the catalyst is limited under these reaction conditions.

3.7 Investigation into PCP Pincers - Conclusions

The synthesis and coordination chemistry of fluorous and non-fluorous pincer ligands has been investigated using novel chemistry and modified literature methods. An initial route was established using benzyl bromide to synthesise a novel PC ligand and these conditions applied to synthesise a range of pincer metal complexes.

Both synthesised palladium pincer catalysts successfully catalyse a range of Heck and Suzuki reactions. However, recovery and reuse was only possible with the fluorous pincer catalyst, which could be successfully recovered and reused four times in the Heck reaction with no loss in activity.

In the Suzuki reaction, recovery and reuse of the fluorous pincer catalyst was possible, however, decomposition of the catalyst was detected under the reaction conditions leading to an inevitable loss in activity.

3.8 References for Chapter Three

1   C. J. Moulton and B. L. Shaw, *J. Chem. Soc., Dalton Trans.*, 1976, 1020.

2   M. Ohff, A. Ohff, M. E. van der Boom, and D. Milstein, *J. Am. Chem. Soc.*, 1997, **119**, 11687.

3   J. T. Singleton, *Tetrahedron*, 2003, **59**, 1837.

4   M. E. van der Boom and D. Milstein, *Chem. Rev.*, 2003, **103**, 1759.

5   I. P. Beletskaya and A. V. Cheprakov, *J. Organometal. Chem.*, 2004, **689**, 4055.

6   M. Albrecht and G. van Koten, *Angew. Chem. Int. Ed. Engl.*, 2001, **40**, 3750.

7   D. Morales-Morales, R. Redon, C. Yung, and C. M. Jensen, *Chem. Comm.*, 2000, 1619.

8   F. Miyazaki, K. Yamaguchi, and M. Shibasaki, *Tetrahedron Lett.*, 1999, **40**, 7379.

9   R. B. Bedford, S. M. Draper, P. N. Scully, and S. L. Welch, *New J. Chem.*, 2000, **24**, 745.

10   M. Q. Slagt, S. E. Stiriba, H. Kautz, R. Gebbink, H. Frey, and G. van Koten, *Organometallics*, 2004, **23**, 1525.

11   M. D. Meijer, N. Ronde, D. Vogt, G. P. M. van Klink, and G. van Koten, *Organometallics*, 2001, **20**, 3993.

12   M. D. Meijer, M. Rump, R. A. Gossage, J. Jastrzebski, and G. van Koten, *Tetrahedron Lett.*, 1998, **39**, 6773.

13   W. J. Sommer, K. Q. Yu, J. S. Sears, Y. Y. Ji, X. L. Zheng, R. J. Davis, C. D. Sherrill, C. W. Jones, and M. Weck, *Organometallics*, 2005, **24**, 4351.

14   R. Chanthateyanonth and H. Alper, *J. Mol. Cat. A: Chem.*, 2003, **201**, 23.

15   I. P. Beletskaya, A. V. Chuchuryukin, G. van Koten, H. P. Dijkstra, G. P. M. van Klink, A. N. Kashin, S. E. Nefedov, and I. L. Eremenko, *Russ. J. Org. Chem.*, 2003, **39**, 1268.

16   R. A. Gossage, E. Munoz-Martinez, and G. van Koten, *Tetrahedron Lett.*, 1998, **39**, 2397.

17   E. Mas-Marza, A. M. Segarra, C. Claver, E. Peris, and E. Fernandez, *Tetrahedron Lett.*, 2003, **44**, 6595.

18   D. E. Bergbreiter, P. L. Osburn, and Y. S. Liu, *J. Am. Chem. Soc.*, 1999, **121**, 9531.

19   H. Kleijn, J. Jastrzebski, R. A. Gossage, H. Kooijman, A. L. Spek, and G. van Koten, *Tetrahedron*, 1998, **54**, 1145.

20   P. Dani, B. Richter, G. P. M. van Klink, and G. van Koten, *Eur. J. Inorg. Chem.*, 2001, 125.

21   D. P. Curran, K. Fischer, and G. Moura-Letts, *Synlett*, 2004, 1379.

22   R. Tuba, V. Tesevic, L. V. Dinh, F. Hampel, and J. A. Gladysz, *J. Chem. Soc., Dalton Trans.*, 2005, 2275.

23   M. R. Eberhard, *Org. Lett.*, 2004, **6**, 2125.

24   S. Gronowitz, K. Stenhammar, and L. Svensson, *Heterocycles*, 1981, **15**, 947.

25   J. M. Plater and T. Jaskson, *Tetrahedron*, 2003, **59**, 4673.

26   J. Yin and S. L. Buchwald, *J. Am. Chem. Soc.*, 2001, **122**, 12051.

27   R. T. V. Babu, N. Nomura, J. Jin, M. Nandi, H. Park, and X. Sun, *J. Org. Chem.*, 2003, **68**, 8431.

28   C. Yuan and H. Feng, *Synthesis*, 1990, 140.

29   M. J. P. Harger, *J. Chem. Soc., Perkin Trans. 2*, 2001, 41.

30   K. S. Vallin, Q. Zhang, M. Larhed, D. P. Curran, and A. Hallberg, *J. Org. Chem.*, 2003, **68**, 6639.

31   G. M. Kosolapoff and L. Maier, 'Organic Phosphorus Compounds', John Wiley & Son, 1972.

32   P. Wyatt, H. Eley, J. Charmant, B. J. Daniel, and A. Kantacha, *Euro. J. Org. Chem.*, 2003, 4216.

33   M. Stankiewicz, J. Nycz, and J. Rachon, *Heteroatom Chem.*, 2002, **13**, 330.

34   E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Synthesis*, 1985, 198.

35   I. G. M. Campbell and I. D. R. Stevens, *Chem. Comm.*, 1966, **15**, 505.

36   P. V. Kapoor, LM, *Helv. Chim. Acta*, 1977, **60**, 2824.

37   Y.-C. Tan, X.-M. Gan, J. L. Stanchfield, E. N. Duesler, and R. T. Paine, *Inorg. Chem.*, 2001, **40**, 2910.

38   W. Chen, L. Xu, Y. Hu, A. M. Banet-Osuna, and J. Xiao, *Tetrahedron*, 2002, **58**, 3889.

39   L. J. Alvey, D. Rutherford, J. J. J. Juliette, and J. A. Gladysz, *J. Org. Chem.*, 1998, **63**, 6302.

40   H. Rimml and L. M. Venanzi, *J. Organometal. Chem.*, 1983, **259**, C6.

41   M. A. Bennett, H. Jin, and A. C. Willis, *J. Organometal. Chem.*, 1993, **451**, 249.

42   R. J. Cross, A. R. Kennedy, and K. W. Muir, *J. Organometal. Chem.*, 1995, **487**, 227.

43   L. A. van de Kuil, D. M. Grove, R. A. Gossage, J. W. Zwikker, L. W. Jenneskens, W. Drenth, and G. van Koten, *Organometallics*, 1997, **16**, 4985.

44   F. Bachechi, *Structual Chemistry*, 2003, **14**, 263.

45   F. Gorla, L. M. Venanzi, and A. Albinati, *Organometallics*, 1994, **13**, 41.

46   D. W. Lee, W. C. Kaska, and C. M. Jensen, *Organometallics*, 1998, **17**, 1.

47   D. Olsson, P. Nilsson, M. El Masnaouy, and O. F. Wendt, *J. Chem. Soc., Dalton Trans.*, 2005, 1924.

48   R. B. Bedford, C. S. J. Cazin, and S. L. Hazelwood, *Angew. Chem. Int. Ed. Engl.*, 2002, **41**, 4120.

49   R. B. Bedford, M. E. Blake, C. P. Butts, and D. Holder, *Chem. Comm.*, 2003, 466.

50   R. K. Arvela, N. E. Leadbeater, M. S. Sangi, V. A. Williams, P. Granados, and R. D. Singer, *J. Org. Chem.*, 2005, **70**, 161.

Chapter Four

University *of* Leicester

4. Investigation into N-Heterocyclic carbenes

4.1 Introduction

4.1.1 Non-fluorous NHC Complexes

N-Heterocyclic carbenes (NHC) were first reported independently by Wanzlick and Öfele in 1968.[1, 2] However, it was not until 1991, when Arduengo et al. reported the first crystalline NHC that they became utilised in synthetic chemistry[3] and Herrmann et al. first exploited their use in homogeneous catalysis.[4]

NHC metal complexes have since become widespread in catalysis due to their unique properties. As they are often synthesised from imidazolium salts they are relatively cheap and easy to prepare. The carbene ligands donate electrons through strong σ-bonds producing metal complexes that are often extremely thermally robust and not sensitive to air and moisture. NHCs are often thought to be alternatives to phosphines and in some instances have been demonstrated to be even more superior.

The first catalysis with NHC complexes was reported in 1995 by Herrmann and co-workers.[4] Catalysts **122** & **123** were demonstrated to be highly efficient catalysts in Heck reactions. The Pd(II) complexes were reduced in situ with sodium formate or hydrazine, generating the active Pd(0) complex. Low catalyst loadings of 10^{-3} mol-% were used to achieve yields > 99% for aryl bromides and 0.1-1 mol-% for aryl chlorides. There was no detection that the carbene ligand had dissociated from the metal centre or that formation colloidal palladium had formed.

122   **123**
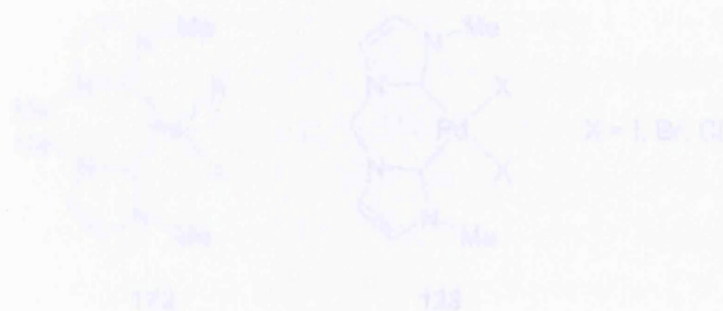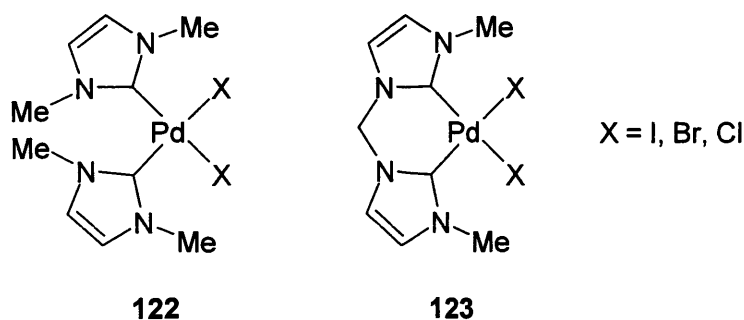
Figure 4.1. *First NHC complexes used in catalysis.*

Subsequently, a range of NHC palladium complexes have been synthesised and utilised in C-C bond forming reactions (Figure 4.2).[5-14] Complex **126** was shown to be highly active in Heck and Suzuki reactions using 4-bromoacetophenone with butyl acrylate and phenylboronic acid respectively.[8] TONs of 1,700,000 for the Heck reaction and 110,000 for the Suzuki reaction were achieved.

In a Heck reaction, complex **127** was highly active with low catalyst loadings of 1 x 10^{-4} mol-% achieving a TON of 970,000 with 4-bromoacetophenone.[7] Complex **128** was shown to be a highly active catalyst for Heck reactions with aryl iodides and bromides.[9]

128

TONs of 7,110,000 and 681,000 were achieved when coupling butyl acrylate at 140 °C with iodobenzene and 4-bromonitrobenzene respectively.
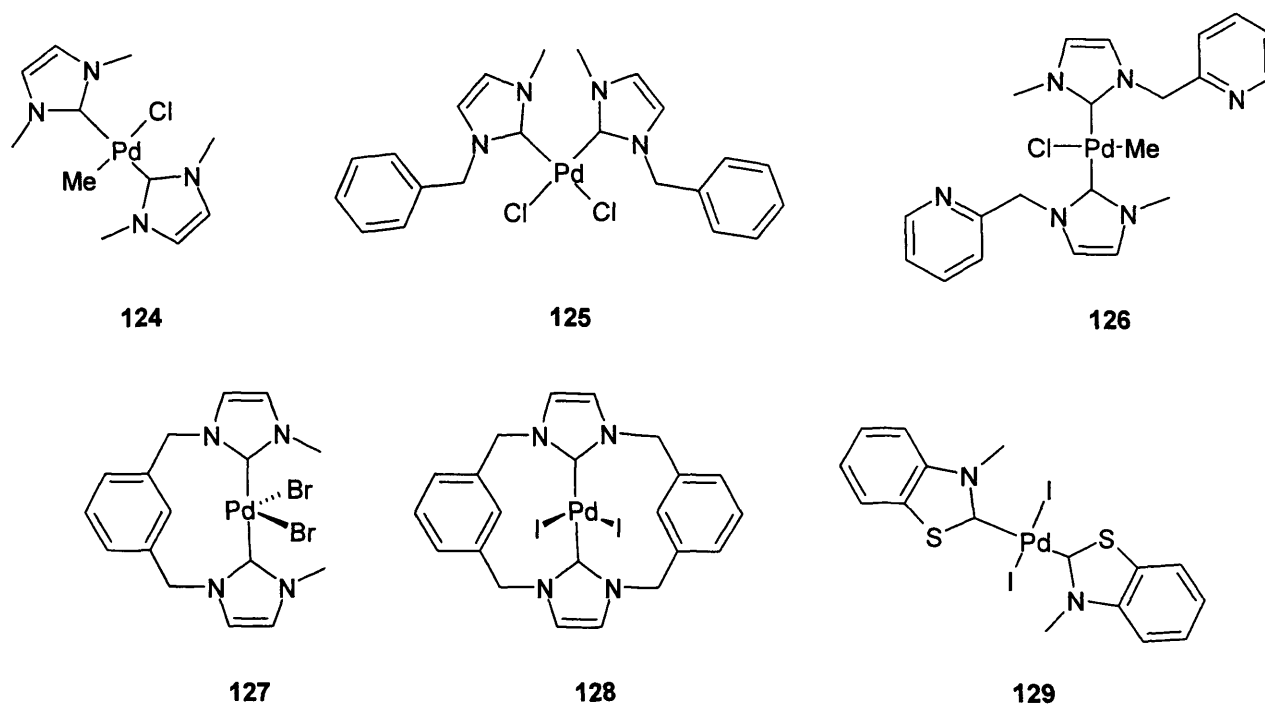
Figure 4.2. *A range of NHC palladium complexes used in catalysis.*

Pincer complexes have been demonstrated to be extremely stable and highly active catalysts. Crabtree *et al.* have reported the synthesis of NHC palladium pincer complexes, CNC **130** & CCC **131**.[15] Both complexes were successfully used to catalyse Heck reactions with aryl chlorides using catalyst loadings of 0.2 mol-%. Catalysis **130** was found to be more active than the CCC pincer complex **131**. Crabtree *et al.* later reported the synthesis and catalysis of the CNC pincer **132**. The complex **132** demonstrated excellent stability to heat up to 165 °C, moisture and oxygen. Good catalytic activities were obtained in Heck reactions with aryl chlorides achieving TONs 47,500 – 75,000 with catalyst loadings of 2 x 10^{-4} mol-%.[16] The complex was also active in Suzuki and Sonogashira reactions.[17]
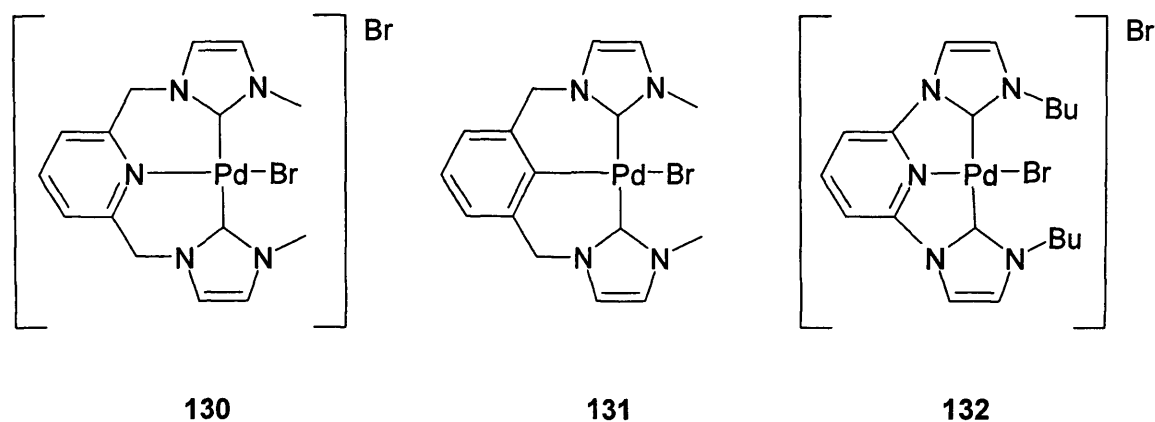
Figure 4.3. *CCC & CNC pincer complexes.*

4.1.2 Recyclable NHC complexes

Although NHC complexes have been demonstrated to be highly active and robust catalysts, in order for NHC catalysts to become more attractive to industry, several groups have modified the carbene ligand to enable recovery and reuse. Herrmann *et al.* reported the synthesis and catalysis of a *bis*-carbene palladium complex bound to Wang's resin, (4-bromomethyl)phenoxymethylpolystyrene, **133**.[18] Good activities were achieved with activated and non-activated aryl bromides, demonstrating excellent stability with no significant loss of catalytic activity over fifteen runs. However, large levels of palladium leaching were found after the first run, from 1.0 wt % to 0.4 wt %, but the level of catalyst level remained fairly constant over the remaining runs.

X = I, Br   n = 2, 3

133
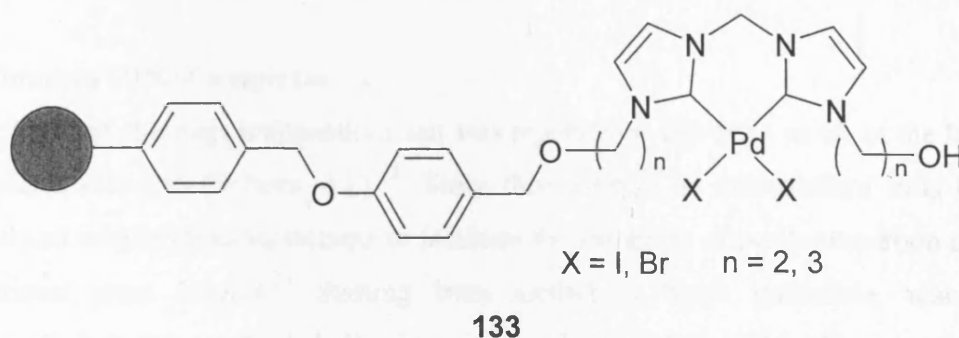
Figure 4.4. *Polystyrene supported NHC palladium catalyst.*

Peris *et al.* immobilised palladium CNC pincer catalysts on montmorillonite K-10 (MK-10), a clay support, **134**.[13] The catalyst was used in a Heck reaction with iodobenzene and styrene with a catalyst loading of 0.1 mol-%. When triethylamine was used as base the catalyst could be successfully used over ten runs without any significant loss of activity. When **134** was used in Heck reactions with aryl bromides, the catalyst was used for five consecutive runs. Analysis of the support before and after the consecutive experiments showed that the palladium content was essentially the same, indicating that there was no significant leaching of the catalyst. Other examples of recyclable carbene catalysts include supported ruthenium catalysts for ring-closing metathesis reactions using polymers and PEG supports.[19-21]

134
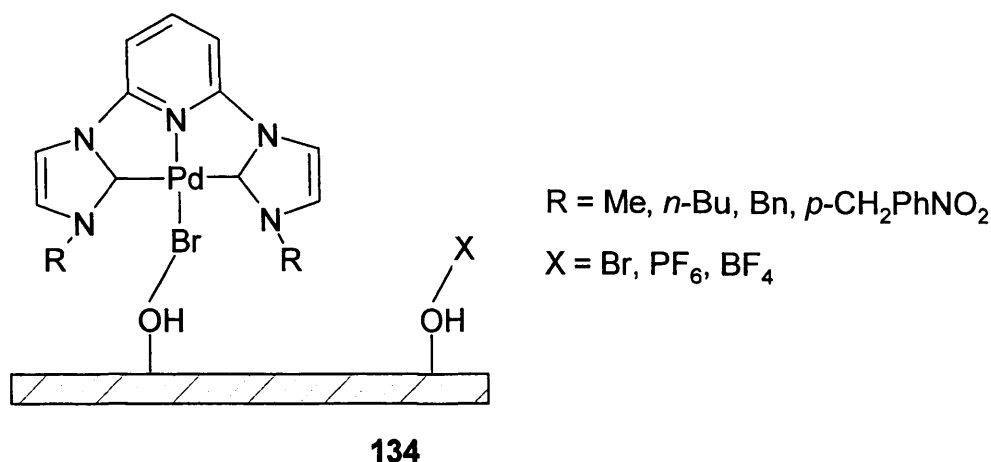
Figure 4.5. *MK-10 supported NHC palladium catalyst.*

4.1.3 Fluorous NHC Complexes

The first fluorous imidazolium salt was reported by Davis Jr. *et al.* in the late 1990's from miconazole **135** (Scheme 4.1).[22] Since then a range of imidazolium salts have been reported and employed as surfactants to facilitate the solubility of perfluorocarbon solvents in conventional ionic liquids.[23] Starting from methyl or butyl imidazole, reaction with perfluoroalkyl iodides afforded fluorous imidazolium iodides **136-139**. Metathesis with AgPF₆ then gave the ionic liquids in good yield (Scheme 4.2).

135

(i) C₆F₁₃CH₂CH₂I, THF, reflux.
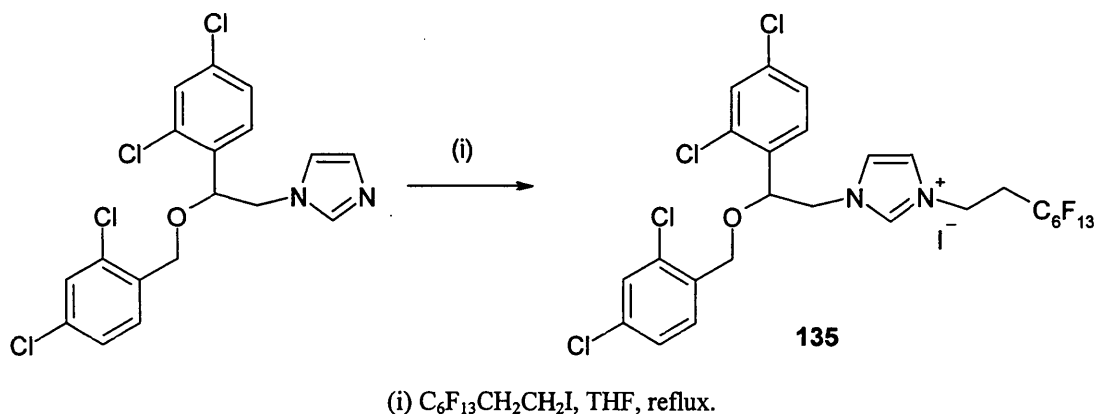
Scheme 4.1. *Synthesis of the first fluorous imidazolium salt.*

136 R = Me, Rf = C₆F₁₃ **137** R = Bu, Rf = C₆F₁₃

138 R = Me, Rf = C₈F₁₇ **139** R = Bu, Rf = C₈F₁₇

(i) RfCH₂CH₂I, Tol., reflux; (ii) AgPF₆, Acetone.
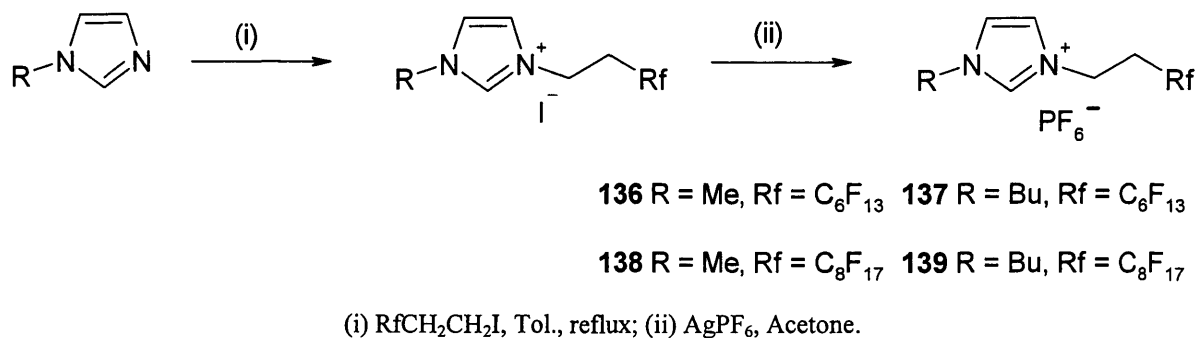
Scheme 4.2. *Synthesis of fluorous imidazolium salts for ionic liquids.*

131

There were no reports of fluorous NHC complexes until 2000 when Xiao *et al.* reported the synthesis of a range of monodentate fluorous carbene palladium complexes.[24] The ligands incorporated either 1*H*,1*H*,2*H*,2*H*-perfluorooctyl, alkyl or a mixture of fluorous and non-fluorous chains (Scheme 4.3). The imidazolium salts containing perfluoroalkyl chains were isolated in moderate yields due to the decomposition of the perfluoroalkyl iodide under the reaction conditions. The palladium complexes **140-143** were synthesised from the imidazolium iodide with palladium acetate to afford the *trans*-isomers exclusively in good yield.

140 R = R' = $CH_2CH_2C_6F_{13}$ **142** R = R' = C_8H_{17}

141 R = Me, R' = $CH_2CH_2C_6F_{13}$ **143** R = Me, R' = C_8H_{17}

(i) RBr, EtOAc, reflux; (ii) R'I, Tol., reflux; (iii) [Pd(OAc)₂], THF, reflux.
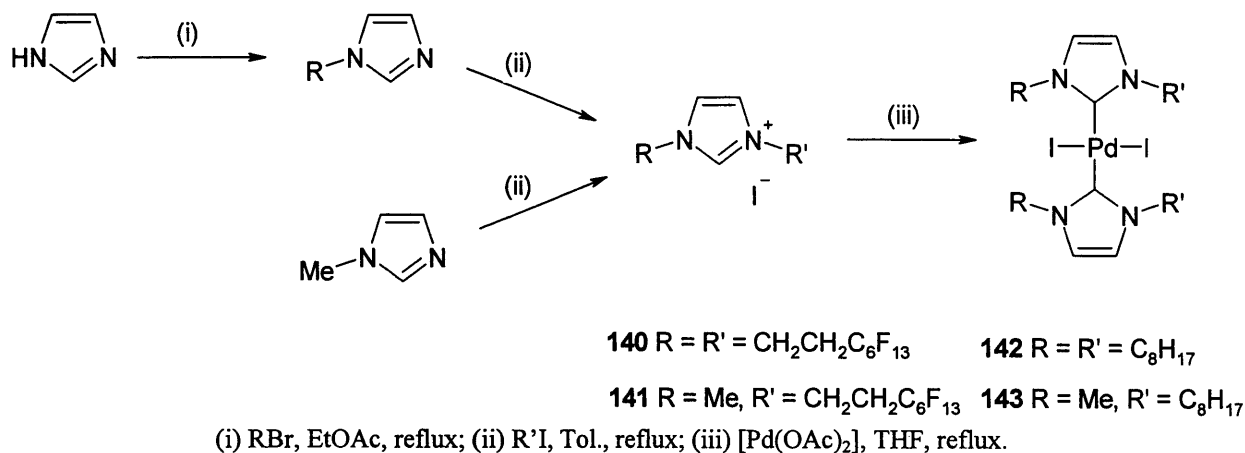
Scheme 4.3. *Synthesis of fluorous and non-fluorous NHC palladium complexes.*

The complexes were used to catalyse the Heck reaction between 4-bromobenzaldehyde and *n*-butyl acrylate to afford the *trans*-cinnamate in > 99% yield in DMF (Scheme 4.4). However, when the catalysts were used in supercritical carbon dioxide, with triethylamine as the base, poor yields (≤10 %) were achieved for all the catalysts **140-142**, except for **143** affording the product in a 90 % yield. The authors gave no clear indication for the difference in activity, however, it is thought that the change of base could have a significant effect on the activity. There is no obvious reason why catalyst **143** had such a dramatic increase in activity compared to the other catalysts and at this time it is not fully understood.

0.5 mol-% [Pd] **140-143**

NaOAc, DMF, 125 °C, 12 h
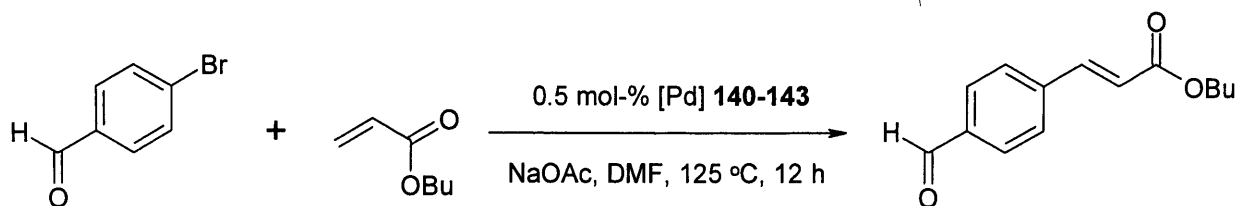
Scheme 4.4. *Heck reaction catalysed by 140-143.*

132

Since this report, Ryu *et al.* reported the synthesis and catalysis of fluorous carbene complex **145**, (Scheme 4.5).[25] The catalyst was tested in Heck reactions in a fluorous solvent to produce cinnamic acids (Scheme 4.6). At room temperature there were two phases, with the fluorous catalyst, aryl iodide and amine base in the fluorous solvent, F-626 ($1H,1H,2H,2H$-perfluorooctyl 1,3-dimethylbutyl ether), whilst the undissolved acrylic acid layered on top. After heating to 120 °C, the two phases became miscible and the reaction proceeded homogeneously. After the reaction, the cinnamic acid and amine salt precipitated out of solution allowing the product to be filtered off and the fluorous solvent and catalyst to be used in another reaction.

(i) [Pd(OAc)₂], PPh₃, Et₃N, LiCl, THF, 70 °C, 12 h.
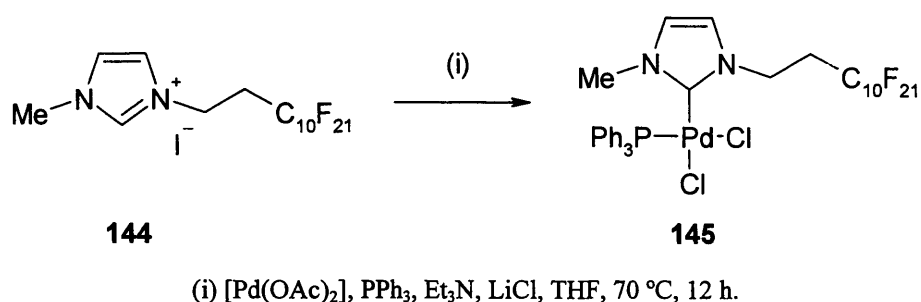
Scheme 4.5. *Synthesis of fluorous catalyst 145.*
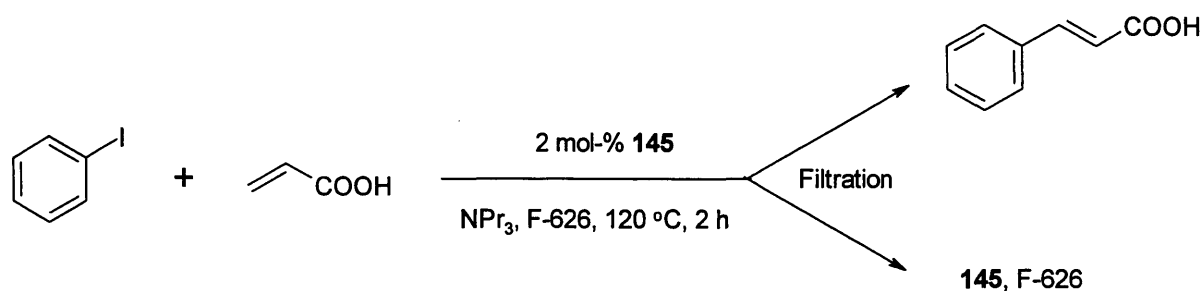
Scheme 4.6. *Catalysis and recovery of 145.*

In the reaction between iodobenzene and acrylic acid, the fluorous solvent and catalyst were reused successfully three times without any significant loss in activity and excellent recovery of the fluorous solvent (Table 4.1). Similar activity was observed when the catalyst was formed *in situ* or when the *bis*-carbene complex formed *in situ* was used instead. However, this approach was limited to polar organic products to achieve separation of the organic and fluorous phase.

Shreeve *et al.* have reported the synthesis of a range of fluorinated and non-fluorinated NHC ionic liquids (Scheme 4.7).[26] Starting from imidazole, the bidentate backbone was synthesised by reaction with dichloromethane or dibromomethane, providing a methylene bridge between the two imidazole units. The backbone was functionalised with a range of alkyl or polyfluoroalkyl halides followed by a metathesis reaction to give the ionic liquids **146-149** in good yield

Catalyst	Product Yield (%)		Fluorous Solvent Recovery (%)
145	Run 1	88	96
	Run 2	85	94
	Run 3	86	97
	Run 4	85	95
2 mol.-% [Pd(OAc)₂], 2 mol.-% **144** (ligand), 2 mol.-% PPh₃	Run 1	88	96
2 mol.-% [Pd(OAc)₂], 2 mol.-% **144** (ligand)	Run 1	88	98
	Run 2	85	97
	Run 3	83	93
	Run 4	84	96
	Run 5	78	95
	Run 6	83	94

Table 4.1. *Catalysis and recycling results for fluorous catalyst and F-626.*
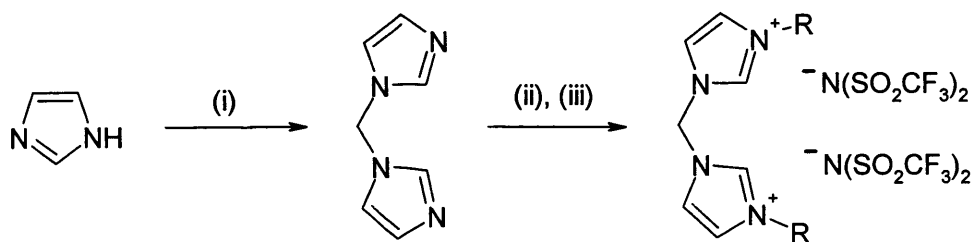
146 R = Bu **148** R = $CH_2CH_2CH_2CF_3$

147 R = Me **149** R = $CH_2CH_2C_4F_9$

(i) CH_2Br_2 or CH_2Cl_2, KOH, TBAB; (ii) RI or RBr, neat or DMF, 110 °C; $LiN(SO_2CF_3)_2$, MeOH/H₂O (10:1), RT.

Scheme 4.7. *Synthesis of a range of fluorinated and non-fluorinated NHC ionic liquids.*

The non-fluorinated palladium complex **150** was easily accessed by reaction of the ionic liquid **146** with palladium dichloride in the presence of sodium acetate (Scheme 4.8). There were no reported attempts to recycle or to form the palladium complexes using the fluorinated NHC ionic liquids **148** & **149**.

146 → **150**

(i) [PdCl$_2$], NaCl, NaOAc, DMSO, 90 °C.
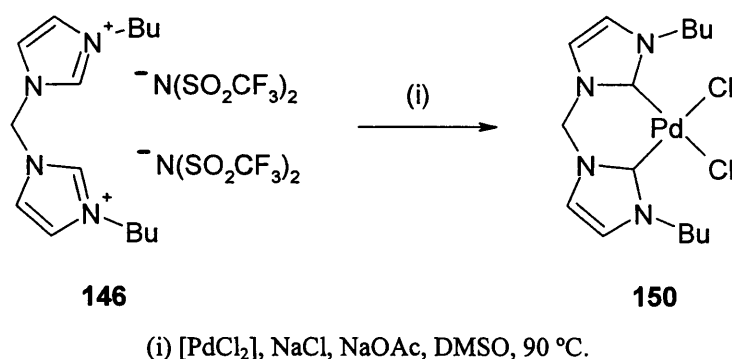
Scheme 4.8. *Synthesis of bidentate NHC palladium complex 150.*

Catalyst **150** successfully catalysed a range of Heck reactions between aryl halides and *n*-butyl acrylate to afford a range of butyl cinnamates. The catalyst was generally formed *in situ* by addition of [PdCl$_2$] (1 mol-%) to the ionic liquid **146** in the presence of sodium acetate, although the pre-formed catalyst **150** could also be used. Recovery and reuse of the ionic liquid containing the palladium catalyst led to two further catalytic runs achieving similar yields of the Heck product over the three runs.

NHC have proven to be active and robust catalysts enabling the catalyst to be recovered and reused. However, in most cases extensive ligand modification was necessary in order to achieve this. When the catalyst was bound to a support through covalent bonds, the catalyst becomes heterogenised losing the desired homogeneous catalytic activity and thus resulting in longer reaction times and higher catalyst loadings. This was not the case when a clay support was used. Fluorous NHCs are catalytically active, however, the recovery and reuse of the complexes has still to be developed further. Even though Ryu showed that their catalyst reused over a number of catalytic cycles, the amount of catalyst recovered from each run was not quantified. This is an important issue as a loss in catalyst may not necessarily result in a loss in catalytic activity.

Xaio *et al.* have proven that their fluorous carbenes are as active as the parent non-fluorous complexes, but the recovery of the catalysts using supercritical fluids was not successful. With the low amount of fluorine, by weight, it would not be possible to recover these catalysts in a fluorous biphase system, but using fluorous solid phase extraction it may be possible to recover and reuse the catalyst.

This work proposes the synthesis of a range of fluorous monodentate, bidentate and pincer NHC palladium complexes with the intention to recover the complexes by fluorous solid phase extraction, thus continuing homogeneous catalysis along with the ability to successfully recover and reuse the fluorous catalyst.

4.2 Results and Discussion

4.2.1 Monodentate NHC Complexes

Three new monodentate carbene complexes **159-161** were synthesised using an adaptation of Xiao's method, however, longer perfluoroalkyl chains were used to aid the catalyst recovery and a propylene spacer group was used to provide better insulation for the donor atom from the electron-withdrawing effects of the perfluoroalkyl chains (Scheme 4.10).[27]

The perfluoroalkyl chains were synthesised using a modification of Fish's method (Scheme 4.9).[27] Starting from allyl alcohol, addition of perfluorooctyl iodide *via* a radical reaction with AIBN gave the perfluoroiodoalcohol **151** exclusively. Reduction with $LiAlH_4$ followed by reaction with potassium iodide gave the corresponding perfluoroalkyl iodide **153** in an overall good yield.
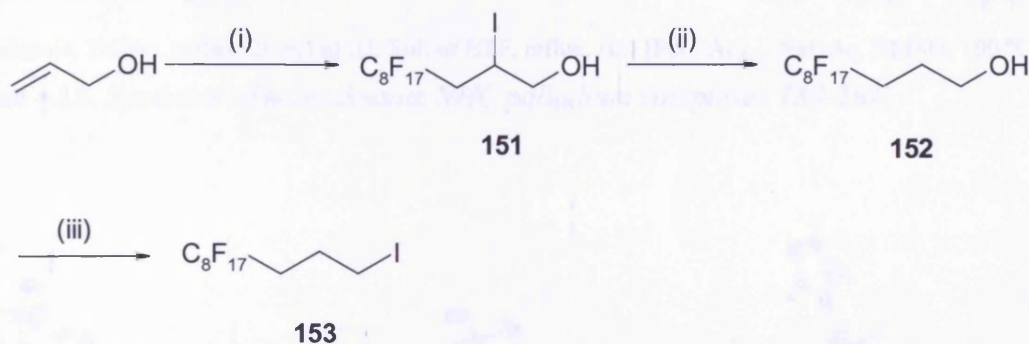
(i) $C_8F_{17}I$, AIBN, 85 °C, 24 h; (ii) $LiAlH_4$, Et_2O, reflux, 12 h; (iii) H_3PO_4, P_2O_5, KI, 130 °C, 18 h.

Scheme 4.9. *Synthesis of perfluoroalkyl iodide 153.*

The alkyl imidazoles were accessed in good yield *via* quaternisation of imidazole with the corresponding alkyl iodide (Scheme 4.10).[24] An excess of imidazole was used to act as a base, complexing with the hydrogen iodide to give the free alkyl imidazole.
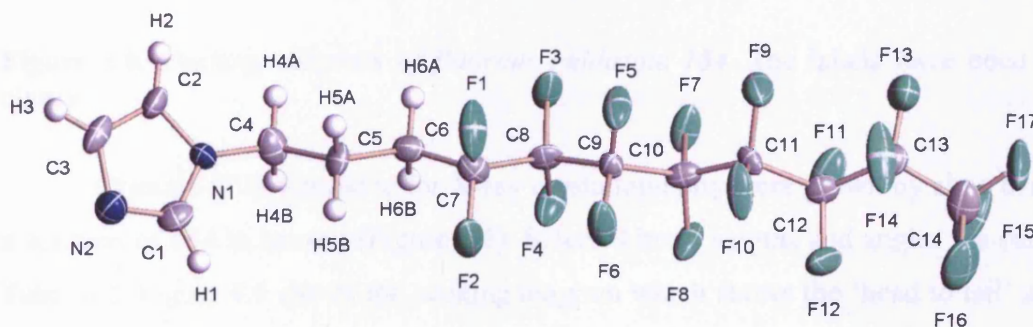
Figure 4.5. *Crystal structure of fluorous imidazole 154. Figures show 50% displacement ellipsoids.*

154 R = C$_8$F$_{17}$
155 R = CH$_3$

156 R = R' = C$_8$F$_{17}$
157 R = R' = CH$_3$
158 R = CH$_3$, R' = C$_8$F$_{17}$

159 R = R' = C$_8$F$_{17}$
160 R = R' = CH$_3$
161 R = CH$_3$, R' = C$_8$F$_{17}$
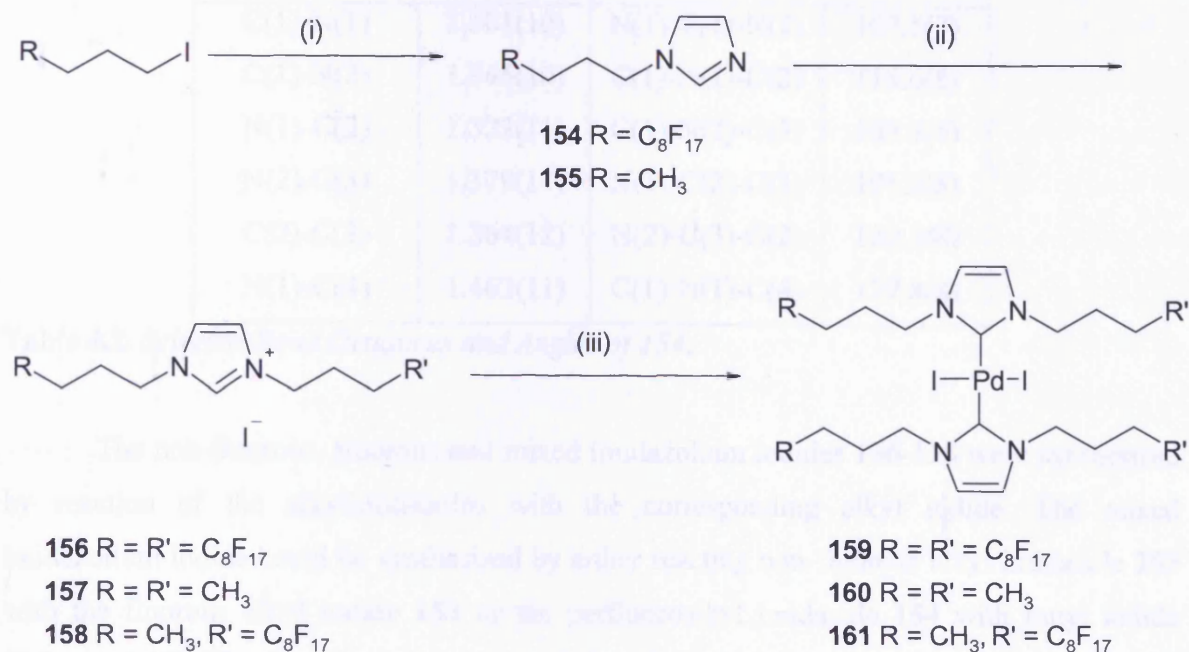
(i) Imidazole, EtOAc, reflux, 20 h; (ii) RI, Tol. or BTF, reflux; (iii) [Pd(OAc)$_2$], NaOAc, DMSO, 100 °C, 14 h.

Scheme 4.10. *Synthesis of monodentate NHC palladium complexes 159-161.*
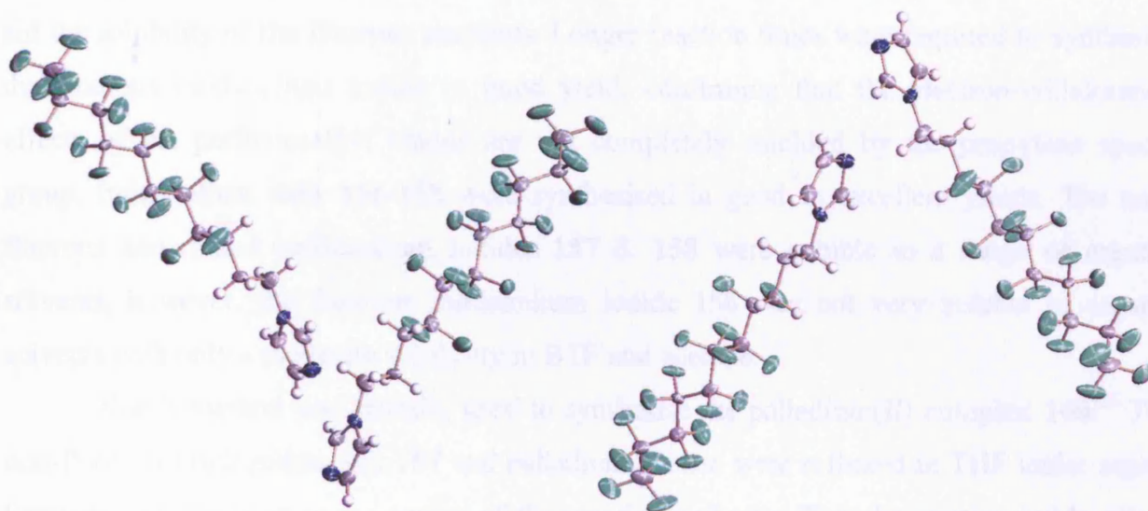
Figure 4.6. *Packing diagram of fluorous imidazole 154.* The labels have been omitted for clarity.

Crystals of **154** suitable for X-ray crystallography were grown by slow evaporation of a solution of **154** in hexane (Figure 4.5). Selected bond lengths and angles are summarised in Table 4.2. Figure 4.6 shows the packing diagram which shows the 'head to tail' alignment of the fluorous imidazole **154** in the solid state.

Bond lengths / Å		Bond Angles / °	
C(1)-N(1)	1.301(10)	N(1)-C(1)-N(2)	107.5(7)
C(1)-N(2)	1.346(10)	C(1)-N(1)-C(2)	113.6(8)
N(1)-C(2)	1.322(11)	C(1)-N(2)-C(3)	103.3(8)
N(2)-C(3)	1.379(11)	N(1)-C(2)-C(3)	106.2(8)
C(2)-C(3)	1.364(12)	N(2)-C(3)-C(2)	109.3(8)
N(1)-C(4)	1.463(11)	C(1)-N(1)-C(4)	127.8(8)

Table 4.2. *Selected Bond Distances and Angles of 154.*

The non-fluorous, fluorous and mixed imidazolium iodides **156-158** were synthesised by reaction of the alkylimidazoles with the corresponding alkyl iodide. The mixed imidazolium iodide could be synthesised by either reacting non-fluorous alkyl imidazole **155** with the fluorous alkyl iodide **153** or the perfluoroalkyl imidazole **154** with butyl iodide (Scheme 4.10). The former synthesis was preferred since there were some concerns that the electron-withdrawing effects of the perfluoroalkyl chains might inhibit the quarternisation of the perfluoroalkyl imidazole with alkyl iodide generating a slower reaction.

The fluorous and mixed imidazolium iodides **156** & **158** were synthesised in BTF to aid the solubility of the fluorous reactants. Longer reaction times were required to synthesise the fluorous imidazolium iodide in good yield, confirming that the electron-withdrawing effects of the perfluoroalkyl chains are not completely shielded by the propylene spacer group. Imidazolium salts **156-158** were synthesised in good to excellent yields. The non-fluorous and mixed imidazolium iodides **157** & **158** were soluble in a range of organic solvents, however, the fluorous imidazolium iodide **156** was not very soluble in organic solvents with only a moderate solubility in BTF and acetone.

Xiao's method was initially used to synthesise the palladium(II) complex **160**.[24] The non-fluorous imidazolium salt **157** and palladium acetate were refluxed in THF under argon. Samples were taken over the course of the reaction and after 72 h the starting imidazolium salt **157**, the palladium complex **160** and an unknown species were observed in the ^{1}H NMR spectrum. Further analysis by ^{13}C NMR spectroscopy showed a characteristic peak at δ_C 151 ppm identifying the unknown species as the corresponding palladium dimer **162**.[24] Xiao had speculated that the imidazolium salt was first deprotonated at the C1 position before the formation of the palladium dimer which reacted with another equivalent of carbene to form the desired palladium complex (Scheme 4.11). It was speculated that due to the hygroscopic nature of the imidazolium salts, complexed water could quench the reaction necessitating additional base. Therefore, additional imidazolium iodide and base were added to the reaction,

and with prolonged heating there was an increase in product conversion, but the reaction still did not go to completion.

Changing the solvent to DMSO and heating at 100 °C saw an increase in conversion to product. Previous work had indicated that some palladium catalysts become deactivated after contact with water (see Chapter 3), therefore, the reaction solvent was removed by Kugelröhr distillation rather than by extraction from water. The pure palladium complex was isolated by recrystallisation from DCM/hexane. The ^{13}C NMR spectra exhibited the carbenoid signal at δ_C 167 ppm clearly indicating the *trans*-geometry of the complex. Crystals of **160** suitable for X-ray crystallography were grown by slow cooling of a solution of **160** in DMSO (Figure 4.7).

157   **162**   **160**

(i) [Pd(OAc)$_2$], (ii) **157**, $^-$OAc.
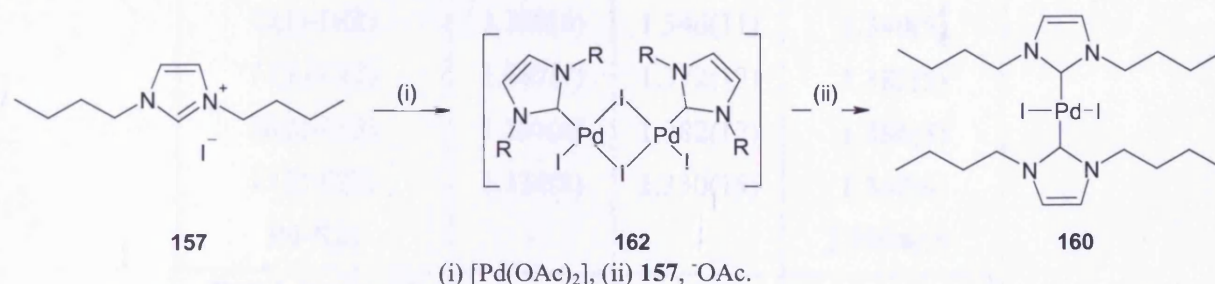
Scheme 4.11. *Proposed route of the synthesis of palladium complex 160.*
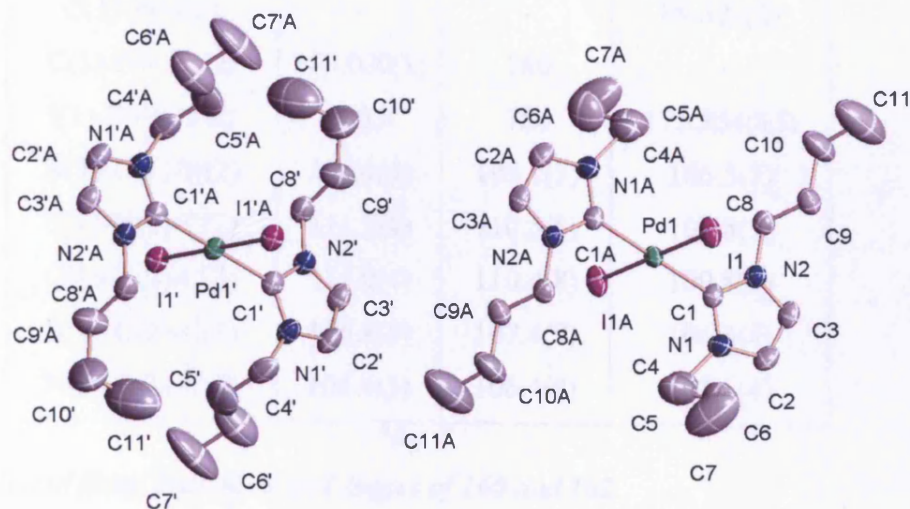
Figure 4.7. *Crystal structure of palladium complex 160. The figures show 50% displacement ellipsoids. The hydrogen atoms have been omitted for clarity.*

Separation of the dimer **162** was also achieved by slow diffusion of a solution of **160** and **162** in chloroform with hexane to give crystals suitable for X-ray crystallography and to the best of our knowledge, is the first reported crystal structure for this type of compound (Figure 4.8). Selected bond lengths and angles are summarised for **160** and **162** in Table 4.3, along with literature values of the fluorous NHC palladium **140** for comparison. Both

compounds have similar bond lengths and angles as for the literature compound and have the expected square-planar geometry around the palladium centre. In **160**, the carbene ligands are arrange in a *trans*-geometry. The Pd-C bond lengths are 2.037(5) Å and 1.971(4) Å for **160** and **162** respectively, which are typical for palladium complexes.[4, 24]

Bond lengths / Å	[PdI$_2$(NHC)$_2$]		[Pd$_2$I$_4$(NHC)$_2$]
	160	**Lit. (140)**[a]	**162**
Pd-I(1)	2.6029(6)	2.5982(8)	2.5954(19)
Pd-C(1)	2.037(5)	2.040(8)	1.971(4)
C(1)-N(1)	1.342(7)	1.339(11)	1.348(5)
C(1)-N(2)	1.348(6)	1.346(11)	1.340(5)
N(1)-C(2)	1.387(7)	1.372(12)	1.385(5)
N(2)-C(3)	1.391(6)	1.382(12)	1.386(5)
C(2)-C(3)	1.334(8)	1.330(15)	1.347(6)
Pd-I(2)	-	-	2.5994(19)
Bond Angles / °			
C(1)-Pd-I(1)	89.96(14)	91.4(2)	86.65(12)
C(1)-Pd-I(2)	-	-	89.32(12)
C(1)-Pd- C(1a)	180.000(1)	180	-
I(1)-Pd-I(1a/2)	180.0	180	175.854(15)
N(1)-C(1)-N(2)	104.6(4)	105.1(7)	106.5(3)
C(1)-N(1)-C(2)	111.2(4)	110.5(8)	109.8(3)
C(1)-N(2)-C(3)	111.0(4)	110.4(8)	109.8(3)
N(1)-C(2)-C(3)	106.8(5)	107.4(9)	106.8(4)
N(2)-C(3)-C(2)	106.4(5)	106.4(9)	107.1(4)

[a]*Ref.* [24]

Table 4.3. *Selected Bond Distances and Angles of 160 and 162.*

Complex **160** was also synthesised using DMSO and additional base. The mixed and the fluorous complexes **161** and **159** were synthesised using the same conditions, however, in neither cases were the corresponding palladium dimer complexes detected by ^{1}H NMR spectroscopy. Both complexes were determined to have the *trans*-geometry, exhibiting the carbenoid signal at δ_C 166 and 168 ppm for **161** and **159** respectively

Other less sterically-demanding *bis*-carbene palladium complexes have been isolated in both the *trans* and *cis* arrangement around the palladium centre.[28] The *trans* arrangement of

complexes **159-161** reflects the sterically demanding nature of the perfluoroalkyl and alkyl chains on the nitrogen atoms
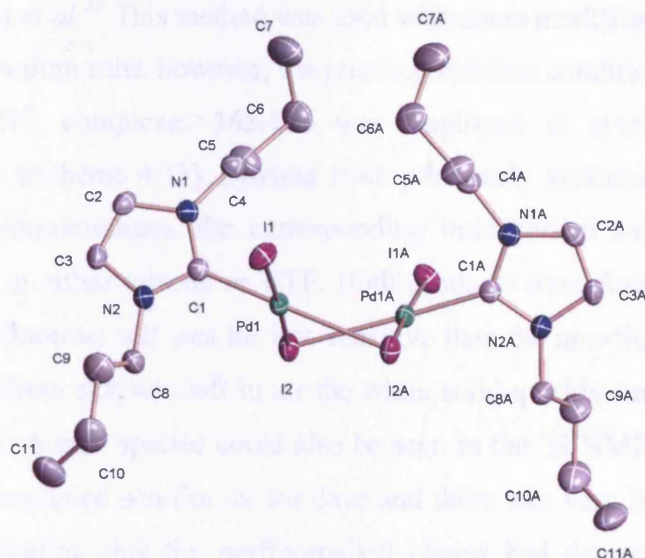
Figure 4.8. *Crystal structure of palladium dimer 162. The figures show 50% displacement ellipsoids. The hydrogen atoms have been omitted for clarity.*

Due to the asymmetry of the substitution on imidazole in the mixed fluorous complex **161**, the NMR data suggested the presence of equilibrating rotamers (Scheme 4.12). The ^{1}H, ^{19}F and ^{13}C NMR spectra show the presence of additional signals lower field, which were tentatively assigned as the *trans-syn* rotamer based on work reported by Xiao.[28] When **161** was initially dissolved in CDCl$_3$ there were two sets of signals, however, the signals attributed to the *trans-anti* rotamer showed greater intensity. Over time, whilst the complex was in solution, the intensity of the *trans-syn* rotamer signals grew and the signals for the *trans-anti* rotamer decreased until approximately an equal ratio of the rotamers was observed.
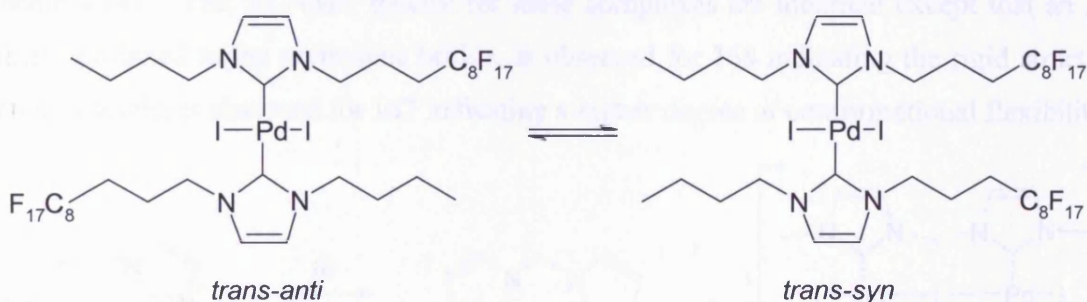
Scheme 4.12. *Equilibrium of rotamers of 161.*

All of the pure complexes were characterised by ^{1}H, ^{19}F and ^{13}C NMR spectroscopy, FAB-MS, elemental analysis, infrared and their melting points.

4.2.2 Bidentate NHC Complexes

The synthesis of the non-fluorous bidentate NHC complex **166** had previously been reported by Sugiyama *et al.*[29] This method was used with some modification to synthesise the corresponding imidazolium salts, however, the previous reaction conditions used to synthesise the monodentate NHC complexes **165-166** was employed to synthesise the bidentate palladium complexes (Scheme 4.13). Starting from previously synthesised alkyl imidazoles **154 & 155** and dibromomethane, the corresponding imidazolium salts **163 & 164** were formed by refluxing in either toluene or BTF. Both products were found to be hygroscopic solids, however, the fluorous salt was far less sensitive than the non-fluorous salt. When the non-fluorous imidazolium salt was left in air the white solid quickly turned into a brown oil within a few minutes. A new species could also be seen in the ^{1}H NMR spectrum whilst the fluorous compound remained solid in air for days and there was very little change in the ^{1}H NMR spectrum, indicating that the perfluoroalkyl chains had decreased the hygroscopic nature of the imidazolium salt.

154 R = C_8F_{17}
155 R = CH_3

163 R = C_8F_{17}
164 R = CH_3

165 R = C_8F_{17}
166 R = CH_3

(i) CH₂Br₂, Tol. or BTF, reflux; (ii) [Pd(OAc)₂], NaOAc, DMSO, 100 °C, 14 h.
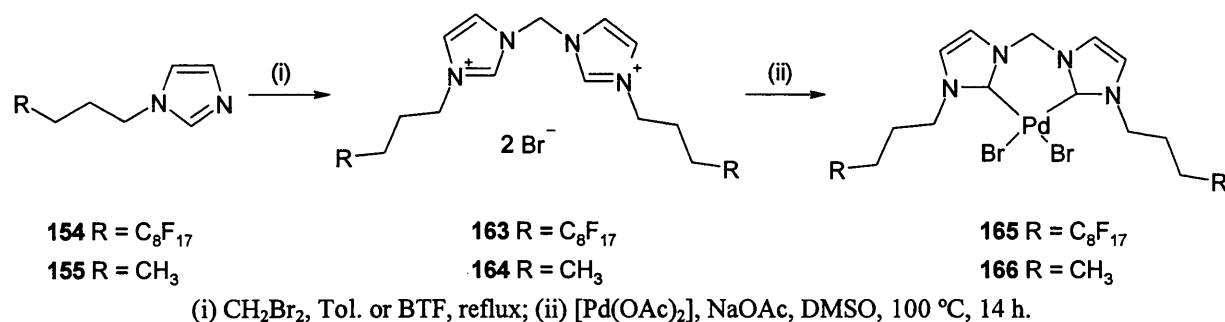
Scheme 4.13. *Synthesis of fluorous and non-fluorous palladium bidentate NHC complexes.*

Albrecht *et al.* have demonstrated that the coordination chemistry of palladium is not straightforward and bridged bimetallic complexes can also be synthesised as a byproduct (Scheme 4.14).[30] The ^{1}H NMR spectra for these complexes are identical except that an AB doublet, attributed to the methylene bridge, is observed for **168** indicating the rigid structure whereas a singlet is observed for **167** indicating a higher degree of conformational flexibility.

167

168

2 : 1

(i) [Pd(OAc)₂], DMSO, 50 °C, 3 h, 110 °C, 2 h.
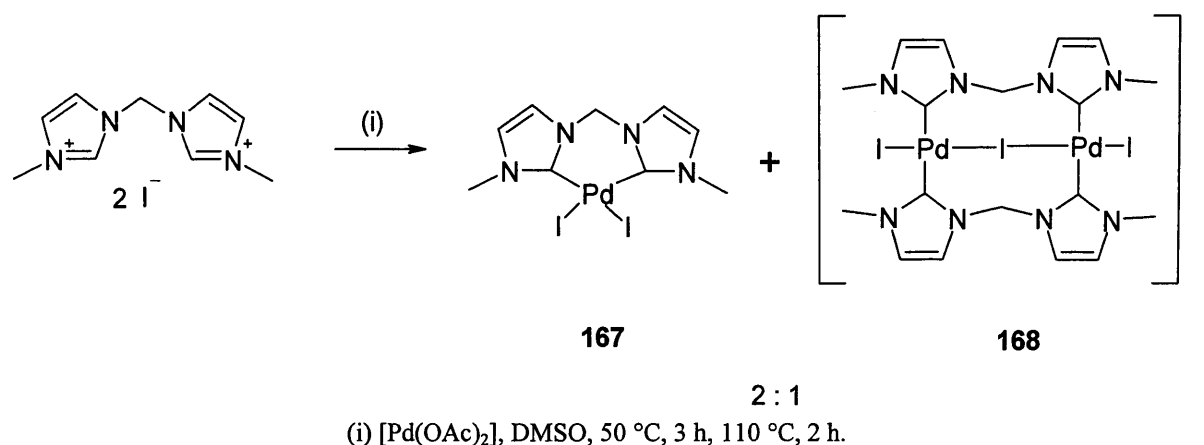
Scheme 4.14. *Formation of bridged bimetallic NHC complex 168.*

142

The choice of base is particularly important, as reaction with the imidazolium salt, palladium acetate and triethylamine affords ionic tetracarbene palladium complexes **170** in high yields (Scheme 4.15). Again, the ^{1}H NMR spectrum was different to the bidentate carbene **169**, with an AB doublet observed, attributed to the methylene bridge.

169 R = CH$_3$, ^{i}Pr   **170** R = CH$_3$, ^{i}Pr

(i) Et$_3$N, DMSO; (ii) 0.5 [Pd(OAc)$_2$].
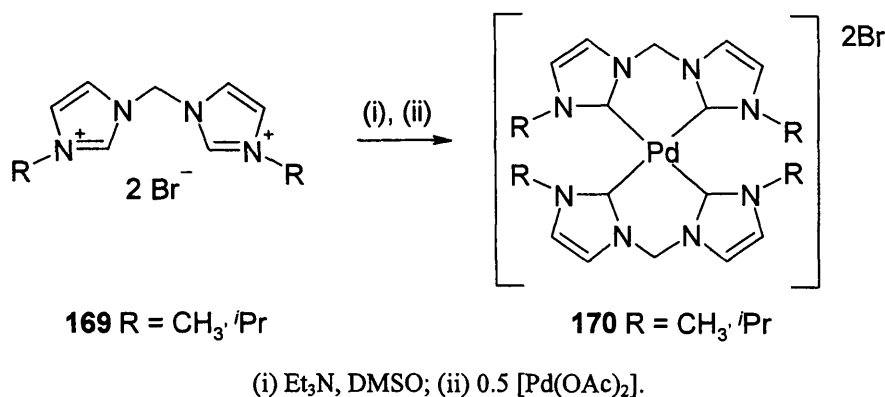
Scheme 4.15. *Formation of tetracarbene palladium complexes.*

The palladium complexes were synthesised using the method previously described to synthesise the monodentate carbene palladium complexes (Scheme 4.13). These conditions were chosen as they were milder than previous literature routes[4] and used additional base to aid the reaction to go to completion. The complexes were isolated in moderate yield and both complexes had a reduced solubility in organic solvents. Crystals suitable for X-ray crystallography were grown by slow evaporation of a DMSO solution containing **166** (Figure 4.9). Selected bond lengths and angles are summarised for **166** in Table 4.4, along with literature values of the corresponding palladium chloride compound **150** for comparison. Apart from the Pd-halide bond, both compounds have similar bond lengths and angles.

Bond lengths / Å	[PdX$_2$(NHC)]		Bond Angles / °	[PdX$_2$(NHC)]	
	166	Lit. (150)^{a,b}		**166**	Lit. (150)^{a,b}
Pd-X(1)	2.4850(8)	2.3623(10)	C(1)-M-X(1)	91.71(17)	92.36(12)
Pd-X(2)	2.4875(8)	2.3747(10)	C(1)-M- C(7)	83.4(2)	85.14(18)
Pd-C(1)	1.965(6)	1.959(4)	X(1)-M-X(2)	91.88(3)	89.37(3)
Pd-C(7)	1.975(5)	1.961(5)	N(1)-C(1)-N(2)	104.6(5)	104.1(3)
C(1)-N(1)	1.357(7)	1.363(5)	C(1)-N(1)-C(2)	110.2(5)	110.6(3)
C(1)-N(2)	1.373(8)	1.351(5)	C(1)-N(2)-C(3)	111.1(5)	111.2(3)
N(1)-C(2)	1.373(8)	1.387(5)	N(1)-C(2)-C(3)	107.5(6)	107.4(4)
N(2)-C(3)	1.381(7)	1.391(5)	N(2)-C(3)-C(2)	106.5(6)	106.7(4)
C(2)-C(3)	1.326(9)	1.326(6)	N(2)-C(4)-N(3)	108.2(5)	108.7(4)

^{a}*Literature values for [PdCl$_2$(NHC)]; ^{b}Ref^{26}.*

Table 4.4. *Selected Bond Distances and Angles of 166.*
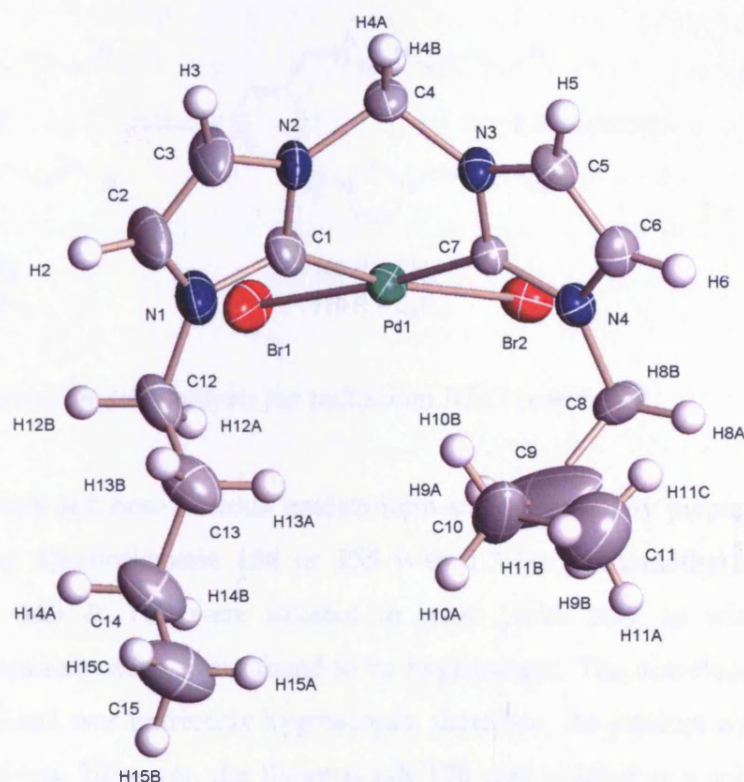
Figure 4.9. *Crystal structure of bidentate NHC palladium complex **166**. Figures show 50% displacement ellipsoids. Disordered DMSO was omitted for clarity.*

The non-fluorous complex only had a low solubility in common organic solvents, with an increased solubility in dipolar aprotic solvents such as DMF and DMSO. However, the fluorous complex was insoluble in most organic and perfluorocarbon solvents and was only soluble in trifluoroethanol making it impossible to obtain any NMR data for this compound. Both the compounds were characterised by FAB-MS, elemental analysis, infrared and their melting points.

4.2.3 NHC Pincer Complexes

There have been no reported syntheses of fluorous NHC pincer complexes and only two successful reports of non-fluorous analogues. It was envisaged that the palladium carbene complex could be accessed *via* the corresponding imidazolium salt, which could be synthesised using similar chemistry to the bidentate imidazolium salts (Scheme 4.16). However, there are no reports of the cyclometallation of imidazolium salts bearing alkyl chains, with successful syntheses only bearing aryl components on the carbene fragment.

144

167 R = CH₃ → **169** R = CH₃ → **155** R = CH₃
168 R = C₈F₁₇ → **170** R = C₈F₁₇ → **154** R = C₈F₁₇

167 $R = CH_3$

168 $R = C_8F_{17}$

169 $R = CH_3$

170 $R = C_8F_{17}$

155 $R = CH_3$

154 $R = C_8F_{17}$
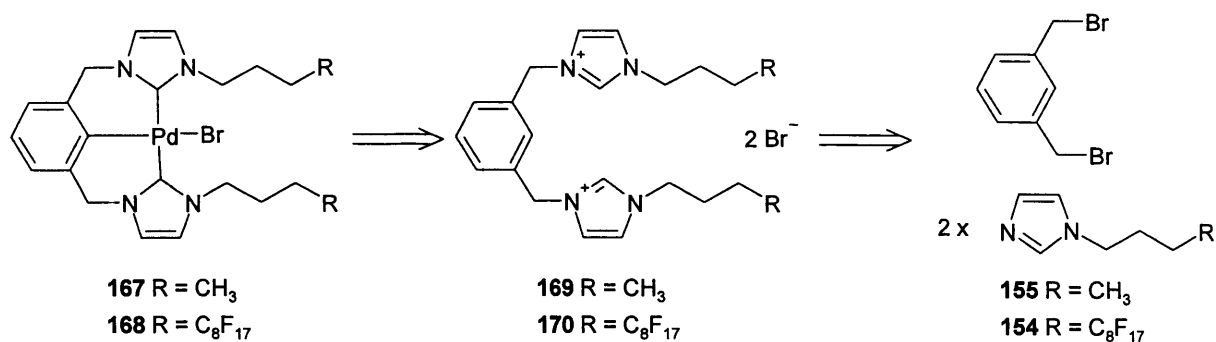
Scheme 4.16. *Retrosynthetic analysis for palladium NHC complexes.*

The fluorous and non-fluorous imidazolium salts were easily prepared by reaction of the corresponding alkylimidazole **154** or **155** with 1,3-*bis*(bromomethyl)benzene (Scheme 4.17). The salts **169** & **179** were isolated in good yields and, as with the previously synthesised imidazolium salts, were found to be hygroscopic. The non-fluorous salt **169** was isolated as an oil and was extremely hygroscopic, therefore, the product was worked up and stored under nitrogen. However, the fluorous salt **170** was isolated as a solid which was not very hygroscopic and so had no special storage requirements.

154 $R = C_8F_{17}$
155 $R = CH_3$

170 $R = C_8F_{17}$
169 $R = CH_3$
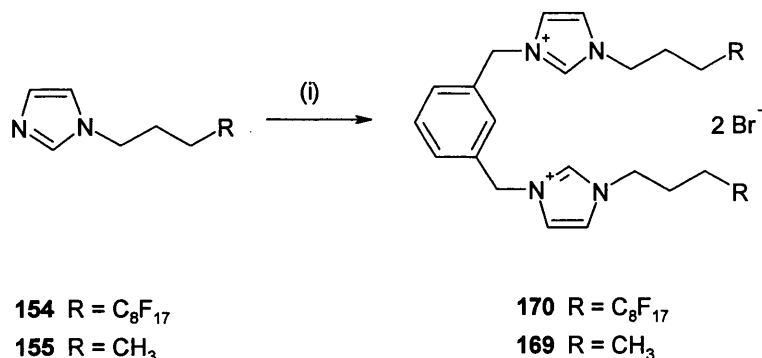
(i) m-BrCH₂PhCH₂Br, Tol. or BTF, reflux.

Scheme 4.17. *Synthesis of fluorous and non-fluorous imidazolium salts 170 & 169.*

Having synthesised the imidazolium salts, the coordination of palladium was attempted. As the previous coordination chemistry had been successful, it was envisaged that the carbene centres would coordinate with palladium, however, it was uncertain whether the conditions would aid the successful cyclometallation to produce the pincer complex. Due to this uncertainty, reaction conditions using the non-fluorous imidazolium salt were investigated.

Using an adaptation of Danopoulos's method, the imidazolium salt and palladium acetate were heated in DMA at 140 °C (Scheme 4.18).[31] Sodium acetate was again used as an additional base to prevent any water in the system quenching the reaction. After 24 h a sample was taken and analysed by ¹H NMR spectroscopy to find no desired product present. The

reaction was further reacted at 160 °C for 24 h. The reaction was then allowed to cool and it was clear that a large amount of palladium black had formed in the reaction. Analysis of the crude reaction by ^{1}H NMR spectroscopy was not very informative as the spectrum was extremely broad and complicated. However, there were no characteristic AB doublets accounting for the benzylic protons around δ_H 5 ppm, indicating that the cyclometallated complex had not formed. However, mass spectrometry showed the presence of an ion with the correct isotope pattern for the dipalladium non-cyclometallated dimer **171**. It was uncertain whether the dimer was formed before analysis by mass spectrometry or whether it had formed during ionisation, but it gave another strong indication that the cyclometallated pincer complex had not formed.

(i) [Pd(OAc)$_2$], NaOAc, DMA, 140 °C, 24 h, then 160 °C, 24 h.
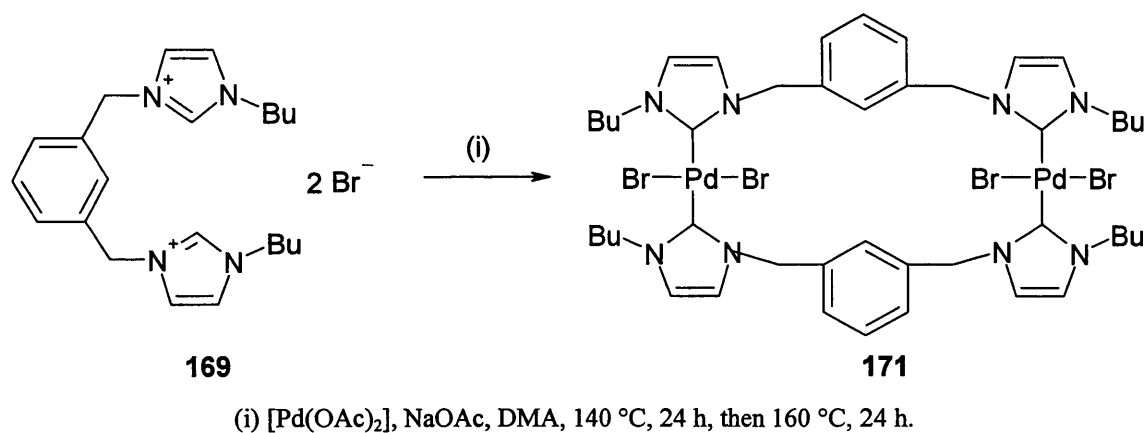
Scheme 4.18. *Formation of dipalladium dimer 171.*

Cavell *et al.* have previously attempted to cyclometallate alkyl imidazolium salts to form carbene pincer complexes without success.[7] Instead they isolated only bidentate complexes that had not cyclometallated. The reported ^{1}H NMR spectra was fairly uninformative and only showed very broad signals thought to be caused by either rapid *cis/trans* isomerisation or dynamic ring flipping of the xylene ring. Crabtree *et al.* also fail to cyclometallate their CCC pincer precursor.[15]

As it was thought that the palladium complex was not cyclometallating, similar conditions used to aid cyclometallation of the PCP pincer complexes were used (see Chapter 3). The imidazolium salt **169**, palladium acetate and sodium acetate were heated in 2-methoxyethanol at 130 °C for 14 h (Scheme 4.19). Upon cooling a sample was taken, the solvent removed and analysis by ^{1}H NMR spectroscopy showed that only starting material was present.

146
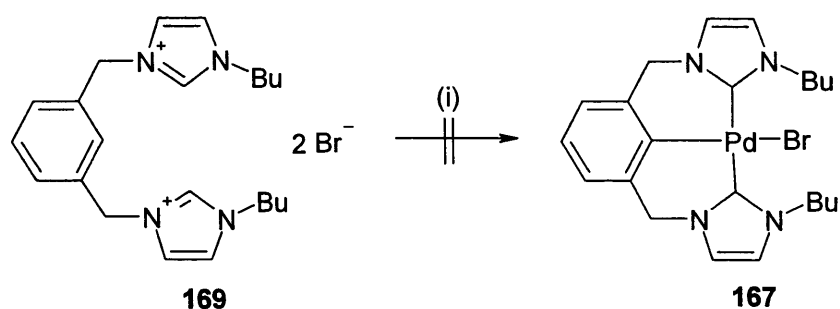
(i) [Pd(OAc)₂], NaOAc, 2-methoxyethanol, 130 °C, 14 h

Scheme 4.19. *Attempted synthesis of 167.*

In a final attempt, the imidazolium salt **169**, palladium acetate and sodium acetate were heated in DMSO at 100 °C for 14 h (Scheme 4.20). The solvent was removed and the crude residue was analysed by ^{1}H NMR spectroscopy to find a mixture of the desired pincer complex **167** and other unknown compounds. The residue was dissolved in chloroform and filtered through a short pad of silica gel to give a brown solid (Fraction 1). The silica was then eluted with DCM/Acetone (3:2) to give a yellow solid (Fraction 2). Both products were analysed by ^{1}H & ^{13}C NMR spectroscopy and MS. Fraction 1 contained mainly the desired pincer but it was still contaminated with an unknown compound, thought to be similar to Fraction 2. Further attempts to isolate the pure compound by column chromatography and recrystallisation failed. The ^{1}H NMR spectrum signals for the pincer complex **167** were not broad and the spectroscopic data could be extracted from the impure sample. Characteristic AB doublets were observed at δ_H 4.55 and 5.36 ppm. The (M-Br)$^+$ was confirmed by HRMS and also confirmed the loss of the proton, attributed to the position of cyclometallation.
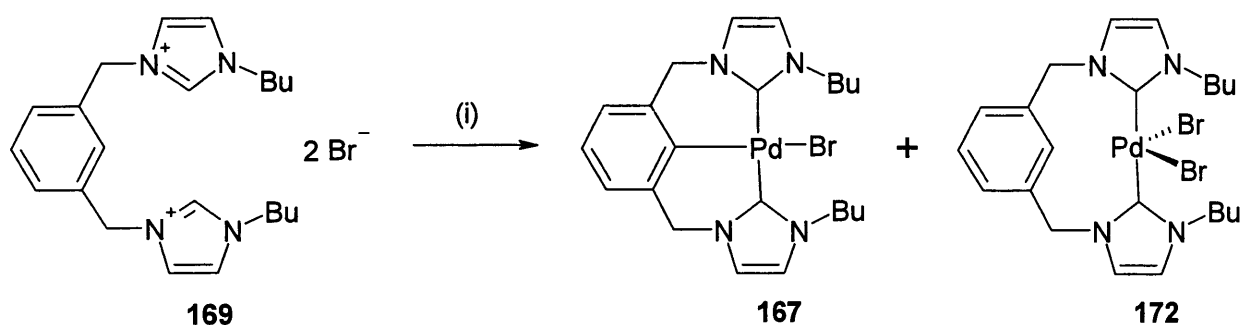
(i) [Pd(OAc)₂], NaOAc, DMSO, 100 °C, 14 h.

Scheme 4.20. *Synthesis of cyclometalled palladium NHC complex 167.*

Broad and complicated signals were observed in ^{1}H NMR spectrum of fraction 2. The ^{13}C NMR spectrum was more informative. It was not possible to obtain the ^{13}C NMR spectrum using CDCl₃ due to the compound's low solubility in this solvent at room temperature and elevated temperatures. For this reason the compound was dissolved in d^6-DMSO. It was possible to see that there were only two quaternary carbons present, one for the

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carbenoid of the carbene and the other for the benzylic backbone of the pincer, indicating that the ligand had bound to the palladium but not cyclometalled. HRMS observed an ion, similar to that found in Fraction 1, however, it was one mass unit heavier confirming the presence of an extra proton and was therefore attributed to $(M-2Br)^+$ for the uncyclometalled complex **172**.

Further attempts to facilitate the cyclometallation of this compound failed and no further attempts were carried to synthesise the pincer complex **167**.

4.3 Separation Studies

It was necessary to find a solvent system that gave good product/catalyst separation when using fluorous solid phase extraction. A range of solvents were evaluated using TLC plates coated with FRPSG and the Rf values are summarised in Table 4.5. In some systems it was possible to see the separation of the two rotamers of **161**.

Solvent	Catalyst 161		Catalyst 159
	Rotamer 1	Rotamer 2	
DCM	0.69	0.78	0.00
Toluene	0.29	0.39	0.00
MeCN	0.25	0.41	0.00
MeOH	0.03	0.33	0.00
MeCN:H$_2$O (80:20)	0.00	0.24	0.00
MeOH:H$_2$O (80:20)	0.00	0.00	0.00
Et$_2$O	0.97	0.97	0.00
BTF	0.56	0.62	0.00
EtOAc	0.91	0.91	0.00
CF$_3$CH$_2$OH	0.68	0.68	0.00

Table 4.5. R_f values of the fluorous Pd catalysts **159** & **161** on FRPSG with different solvents.

For catalyst **161**, MeOH:H$_2$O (80:20) gave no movement of the fluorous catalyst on the TLC plate and, therefore, could be used as the fluorophobic solvent. Diethyl ether gave the greatest Rf value and, therefore, could be used as the fluorophilic solvent.

For Catalyst **159**, all of the solvents gave no movement of catalyst on the TLC plate, which was good for product/catalyst separation, but there was no means of recovering the catalyst for further catalytic runs. With this in mind, a different approach would be required for recycling catalyst **159**. The catalyst could be supported on FRPSG and after the reaction the catalyst could be recycled by simple filtration.

Catalyst **161** (100 mg) was dissolved in a minimum amount of methanol and loaded onto a short column of FRPSG (4 g). The column was washed with methanol/water (80:20), a fluorophobic solvent. The catalyst was retained at the top of the column as a yellow band. The methanol/water fractions were analysed by TLC and no UV-active compounds were present, indicating that the catalyst was successfully retained on the column. The column was then eluted with diethyl ether to recover the catalyst. Again, TLC was used to gauge when all of the catalyst had been eluted and 95 % of the catalyst was recovered from the column.

4.4 Catalytic Testing

Catalytic testing was carried out by an undergraduate student.[32] Initial catalyst tests were carried out on the non-fluorous catalyst. Optimised conditions from Chapter 3 were used for the Heck reactions. A catalyst loading of 1 mol-% of **160** was added to 4-bromoacetophenone and methyl acrylate in NMP with potassium hydrogen carbonate as a base and TBAB as an additive. The reaction was heated at 120 °C for 18 h but after this time no product was detected by GC. Therefore, different combinations of solvents and bases were evaluated (Scheme 4.21 & Table 4.6). The greatest yield of the product was achieved when DMF was used as the reaction solvent and sodium acetate was used as base, in the presence of TBAB. All of the reactions gave greater yields in the presence of TBAB.
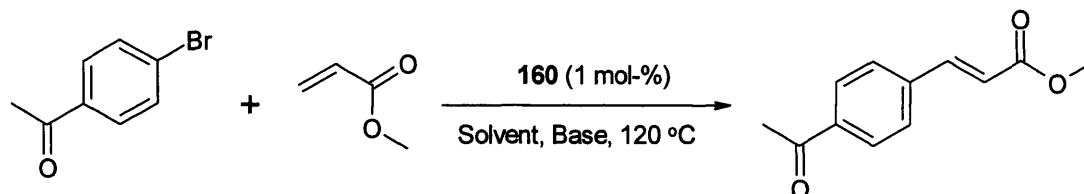
Scheme 4.21. *Heck reactions with catalyst 160 using different solvents and bases.*

Solvent	Base	Additive	Time/h	Conversion/%[a]
NMP	KHCO$_3$	TBAB	18	0
NMP	Et$_3$N	TBAB	22	48
DMF	NaOAc	TBAB	24	65
DMF	NaOAc	-	24	2
DMF	Et$_3$N	TBAB	24	19
DMF	Et$_3$N	-	24	3
NMP	NaOAc	TBAB	24	0
NMP	NaOAc	-	24	0

[a]Determined by GC using tolyl ether as an internal standard.

Table 4.6. *Results from Heck reactions using catalyst 160.*

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Even though the reaction conversions had increased dramatically, the reactions were not going to completion within 24 h. Herrmann *et al.* previously demonstrated that palladium (II) NHC catalysts undergo an induction period in catalysis where the palladium centre is reduced from Pd(II) to Pd(0).[4] Once this has occurred catalysis can take place, however, during this induction period reaction rates are slow when 4-bromoacetophenone is used. The addition of hydrazine hydrate showed a dramatic increase in the rate of reaction. However, when 4-bromobenzaldehyde was used as the substrate, a faster rate of reaction was observed without the use of hydrazine hydrate, therefore, further studies were conducted with this substrate.

All three catalysts **159-161** were now evaluated in the Heck reaction using 4-bromobenzaldehyde and butyl acrylate (Scheme 4.22). Identical reaction conditions were used and reactions were carried out with and without TBAB (Figures 4.10 and 4.11). For these systems, the activities of the catalysts were greater in the reactions without TBAB compared to the reaction with TBAB and, therefore, TBAB was not used in further reactions. In the reactions without TBAB, both fluorous catalysts were more active then the non-fluorous catalyst after 2.5 h. However, after 7 h both catalysts **160** and **161** achieved almost quantitative conversion of the product, whereas, the conversion for catalyst **159** remained <80 %.
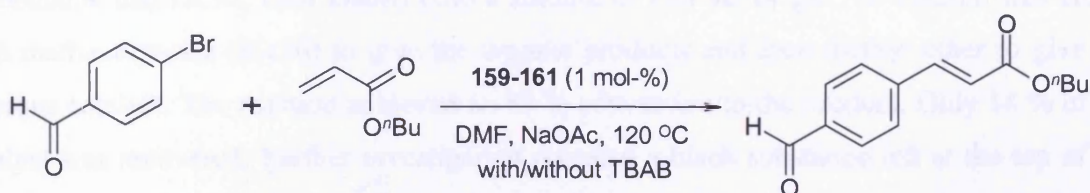
Scheme 4.22. *Comparison of catalysts 159-161 with and without TBAB.*
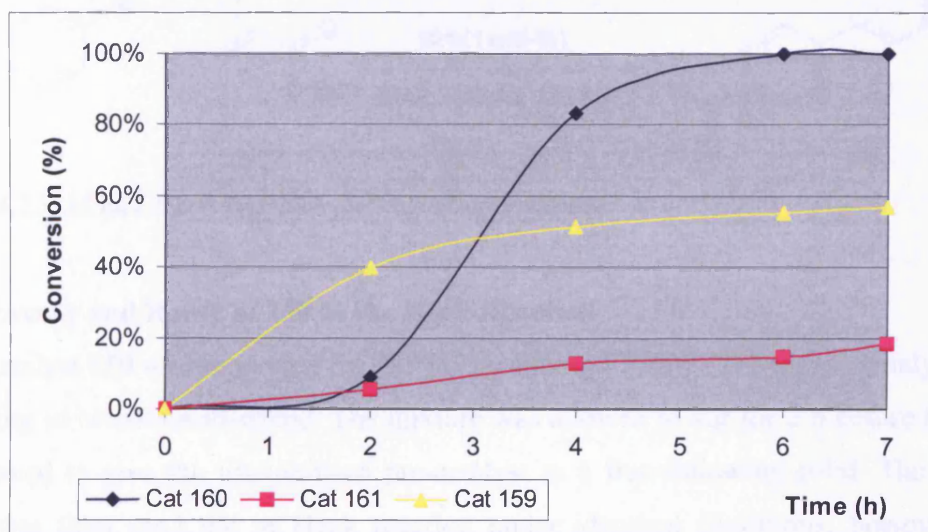
Figure 4.10. *Results from Heck reactions with TBAB.*

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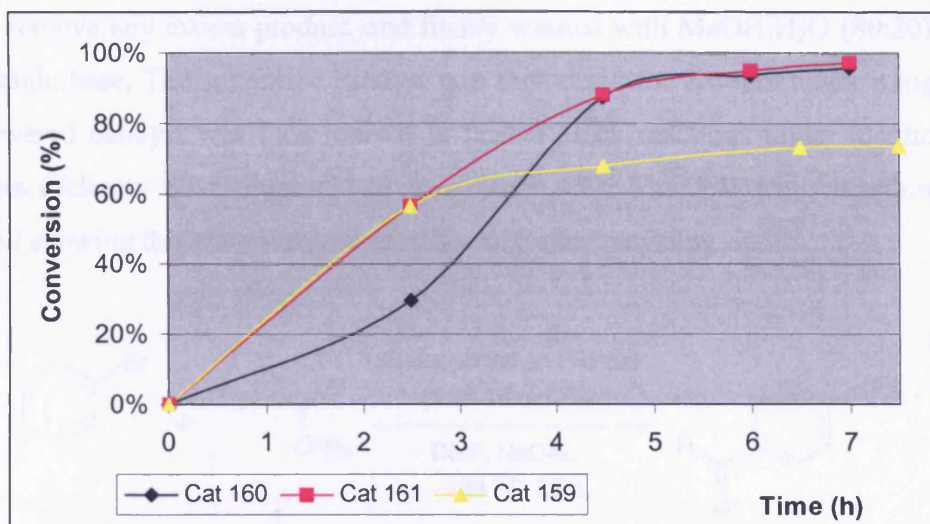
Figure 4.11. *Results from Heck reactions without TBAB.*

4.5 Catalyst Recovery and Reuse

4.5.1 Recovery and Reuse of 161 in the Heck Reaction

Recycling experiments were conducted with catalyst **161** (50 mg, 1 mol-%) under the optimised reaction conditions under an argon atmosphere (Scheme 4.23). After removing the solvent and the remaining volatiles by Kugelröhr distillation, the resulting solid was taken up in methanol and DCM, then loaded onto a column of FRPSG (4 g). The column was eluted with methanol:water (80:20) to give the organic products and then diethyl ether to give the fluorous catalyst. The reaction achieved an 85 % conversion to the product. Only 14 % of the catalyst was recovered. Further investigation revealed a black substance left at the top of the column, suggesting the formation of palladium black during the catalytic cycle. No further catalysis was carried out.
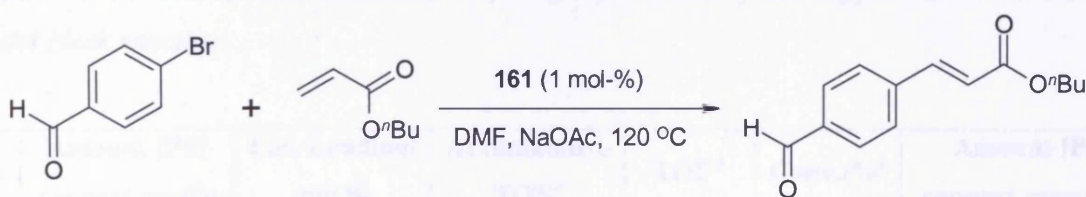
Scheme 4.23. *Model Heck reaction for recycling protocol.*

4.5.2 Recovery and Reuse of 159 in the Heck Reaction

Catalyst **159** was supported on FRPSG by adding FRPSG (213 mg) to catalyst **159** (11 mg) stirring in hexafluorobenzene. The mixture was allowed to stir for 2 h before the solvent was removed to give the immobilised pre-catalyst as a free-following solid. The supported catalyst was then used the in Heck reaction under identical conditions, however, longer reaction times were employed to compensate for loss of activity due to the heterogeneous nature of the support. After the reaction, the crude reaction mixture was filtered, washed with

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DCM to remove any excess product, and finally washed with MeOH:H$_2$O (80:20) to remove the inorganic base. The supported catalyst was then dried for 2 hours under a high vacuum. The recovered catalyst was then re-used in further Heck reactions under identical reaction conditions (Scheme 4.23, Figure 4.12 and Table 4.7). The following reactions were all successful showing that the catalyst was still active after recycling.
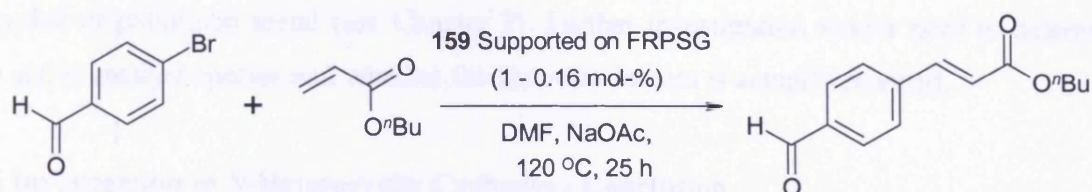
Scheme 4.24. *Recycling of 159 supported on FRPSG in model Heck reaction.*
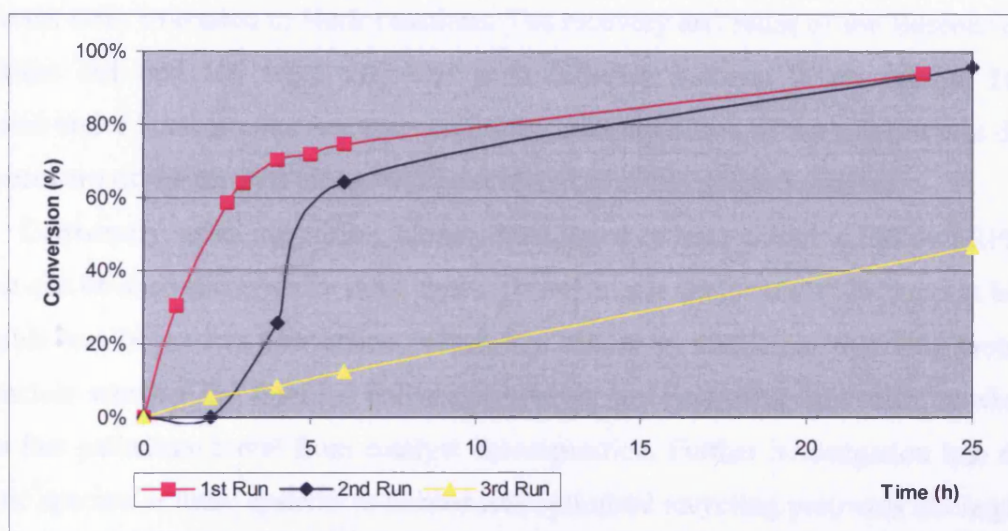
Figure 4.12. *Results from preliminary recycling experiments of 159 supported on FRPSG in model Heck reaction.*

Run	Amount [Pd] support used/g	Cat. Loading/ mol.%	Accumulative TON^a	TOF^b	Conv./%^{c}	Amount [Pd] support recovered
1	0.2243	1.00	94	3.9	94^d	0.1132 g, 50 %
2^e	0.1041	0.46	303^f	8.3	96	0.0355 g, 36 %
3^e	0.0348	0.16	597^f	11.8	47	-

^{a}TON = (mol prod/mol cat). ^{b}TOF = (mol prod/mol cat/Time). ^{c}Determined by GC using tolyl ether as an internal standard. ^{d}Conversion after 24 h. ^{e}Catalysis carried out using **159** supported on FRPSG from the previous run. ^{f}Accumulative TON = TON from rxn + TON previous rxn(s).

Table 4.7. *Results from preliminary recycling experiments of 159 supported on FRPSG in model Heck reaction.*

Certainly, the recovery of the supported catalyst was far from optimised with large losses of the support being observed between runs due to poor manipulation leading to an expected drop in conversion to product. Conversely, the turnover frequency increased from run 1 to 3, showing the catalyst to be more active than in the previous run. However, in light of the recycling results for **161** using fluorous SPE, where decomposition of the catalyst was observed, it was unclear whether it is truly the fluorous palladium catalyst which is being recycled or palladium metal (see Chapter 2). Further investigation would need to determine the active catalyst species and whether the fluorous domain is actually retained.

4.6 Investigation to *N*-Heterocyclic Carbenes - Conclusion

A range of fluorous and non-fluorous NHC ligands and palladium complexes were synthesised using novel chemistry and modified literature methods. The monodentate NHC complexes were evaluated in Heck reactions. The recovery and reuse of the fluorous carbene complexes **161** and **159** were evaluated with differing success. When catalyst **161** was evaluated under homogenous reaction conditions, decomposition of the catalyst was detected upon recovery of the catalyst along with poor recovery of the isolated catalyst.

Conversely, when supporting heavily fluorinated carbene complex **159** on FRPSG, the catalyst can be used successfully three times. However, poor recovery of the support led to an inevitable loss in product conversion, which was due to an inefficient recycling protocol. It was unclear whether the fluorous palladium catalyst was being truly recycled or whether it was in fact palladium metal from catalyst decomposition. Further investigation into the true catalytic species in these systems is needed and optimised recycling protocols are required in order to have a better understanding of these complexes.

4.7 References for Chapter Four

1   K. Ofele, *J. Organometal. Chem.*, 1968, **12**, 42.

2   H.-W. Wanzlick and H.-J. Schronherr, *Angew. Chem. Int. Ed. Engl.*, 1968, **7**, 141.

3   A. J. Arduengo III, R. L. Harlow, and M. Kline, *J. Am. Chem. Soc.*, 1991, **113**, 361.

4   W. A. Herrmann, M. Elison, J. Fischer, C. Kocher, and G. R. J. Artus, *Angew. Chem. Int. Ed. Engl.*, 1995, **34**, 2371.

5   W. A. Herrmann and C. Kocher, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2163.

6   W. A. Herrmann, *Angew. Chem. Int. Ed. Engl.*, 2002, **41**, 1291.

7   A. M. Magill, D. S. McGuinness, K. J. Cavell, G. J. P. Britovsek, V. C. Gibson, A. J. P. White, D. J. Williams, A. H. White, and B. W. Skelton, *J. Organometal. Chem.*, 2001, **617**, 546.

8   D. S. McGuinness and K. J. Cavell, *Organometallics*, 2000, **19**, 741.

9   M. V. Baker, B. W. Skelton, A. H. White, and C. C. Williams, *J. Chem. Soc., Dalton Trans.*, 2001, 111.

10   W. A. Herrmann, V. P. W. Bohm, and C. P. Reisinger, *J. Organometal. Chem.*, 1999, **576**, 23.

11   W. A. Herrmann, K. Ofele, D. Von Preysing, and S. K. Schneider, *J. Organometal. Chem.*, 2003, **687**, 229.

12   D. Bourissou, O. Guerret, F. P. Gabbai, and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39.

13   E. Peris and R. H. Crabtree, *Coord. Chem. Rev.*, 2004, **248**, 2239.

14   V. Calo, R. Del Sole, A. Nacci, E. Schingaro, and F. Scordari, *Eur. J. Org. Chem.*, 2000, 869.

15   S. Grundemann, M. Albrecht, J. A. Loch, J. W. Faller, and R. H. Crabtree, *Organometallics*, 2001, **20**, 5485.

16   J. A. Loch, M. Albrecht, E. Peris, J. Mata, J. W. Faller, and R. H. Crabtree, *Organometallics*, 2002, **21**, 700.

17   E. Mas-Marza, A. M. Segarra, C. Claver, E. Peris, and E. Fernandez, *Tetrahedron Lett.*, 2003, **44**, 6595.

18   J. Schwarz, V. P. W. Bohm, M. G. Gardiner, M. Grosche, W. A. Herrmann, W. Hieringer, and G. Raudaschl-Sieber, *Chem. Eur. J.*, 2000, **6**, 1773.

19   S. C. Schurer, S. Gessler, N. Buschmann, and S. Blechert, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 3898.

20   Q. W. Yao, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 3896.

21   M. Ahmed, T. Arnauld, A. G. M. Barrett, D. C. Braddock, and P. A. Procopiou, *Synlett*, 2000, 1007.

22   J. H. Davis, K. J. Forrester, and T. Merrigan, *Tetrahedron Lett.*, 1998, **39**, 8955.

23   T. L. Merrigan, E. D. Bates, S. C. Dorman, and J. H. Davis, *Chem. Comm.*, 2000, 2051.

24   L. J. Xu, W. P. Chen, J. F. Bickley, A. Steiner, and J. L. Xiao, *J. Organometal. Chem.*, 2000, **598**, 409.

25   T. Fukuyama, M. Arai, H. Matsubara, and L. Ryu, *J. Org. Chem.*, 2004, **69**, 8105.

26   C. M. Jin, B. Twamley, and J. M. Shreeve, *Organometallics*, 2005, **24**, 3020.

27   J. M. Vincent, A. Rabion, V. K. Yachandra, and R. H. Fish, *Can. J. Chem.*, 2001, **79**, 888.

28   L. J. Xu, W. P. Chen, and J. L. Xiao, *Organometallics*, 2000, **19**, 1123.

29   K. Okuyama, J. Sugiyama, R. Nagahata, M. Asai, M. Ueda, and K. Takeuchi, *J. Mol. Cat. A: Chem.*, 2003, **203**, 21.

30   M. Heckenroth, A. Neels, H. Stoeckli-Evans, and M. Albrecht, *Inorg. Chim. Acta*, 2006, **359**, 1929.

31   A. A. Danopoulos, A. A. D. Tulloch, S. Winston, G. Eastham, and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.*, 2003, 1009.

32   D. Robbins, *M. Chem. Report*, 2007.

Chapter Five

5. Overall Conclusions

Catalysis with palladium complexes is a fundamental tool for organic chemists in the synthesis of carbon-carbon bonds, providing a range of versatile reactions and solutions. Fluorous methodologies for separation have evolved over the last 10 years, but their application in palladium catalysed reactions has been limited. The aim of the research described in this thesis was to synthesise a range of perfluoroalkylated palladium catalysts and evaluate fluorous solid phase extraction as a 'separation technique' for recycling homogeneous palladium catalysts following catalysis in "conventional" organic solvents. These objectives have been substantially achieved and the work has demonstrated that fluorous solid phase extraction for the separation of perfluoroalkylated catalysts and organic products is compatible with palladium-based catalysis.

A series of new and established monodentate *tris*-perfluoroalkylated arylphosphines have been synthesised using a combination of novel synthetic routes and modified literature methods. The ligands synthesised contain either C_8F_{17} or $C_2H_4C_8F_{17}$ substituents in the 3- or 4-positions around the aryl ring and, in some cases, yields obtained were greater than those reported in the literature, showing an improvement in the synthetic route. The palladium dichloride complexes of these ligands have also been prepared and fully characterised. The palladium catalysts incorporating these ligands proved to be active in Suzuki reactions with both 4-bromonitrobenzene and 4-bromoanisole; with the latter substrate, a difference in activities between the catalysts was observed. Here, the fluorous-derivatised triarylphosphine complexes were shown to be more active than the non-fluorous analogue.

However, attempts to use fluorous solid phase extraction for the separation, recovery and reuse of these perfluoroalkylated palladium catalysts were unsuccessful. The observation of palladium black and the isolation of the perfluoroalkylated triarylphosphine oxides from the catalytic reaction mixture indicated that these catalysts were not stable under the reaction conditions. Therefore, the remaining work in the thesis focuses on attempts to improve catalyst stability by the incorporation of either chelating or alternative donor ligands. Two classes of metal complexes have been investigated; palladium catalysts incorporating PCP pincer ligands or N-heterocyclic carbene ligands.

Pincer ligands are typically highly stable with a metal-carbon bond and two chelating rings. Although some work on perfluoroalkylated pincer ligands had previously been reported, work here focussed on a novel PCP ligand with $4\text{-}C_2H_4C_8F_{17}$ substituents on the aryl rings at phosphorus. Having established an initial methodology using benzyl bromide in the synthesis of a benzyl *bis*-arylphosphine ligand, the approach was extended to reactions involving 1,3-*bis*(bromomethyl)benzene to yield the novel perfluoroalkylated PCP ligand.

This approach also gave a new, improved, synthesis of the parent, non-fluorous PCP ligand. Both ligands were used in coordination chemistry to form nickel, palladium and platinum [M(PCP)Cl] complexes. Spectroscopic data for these complexes showed that there was virtually no difference in the electronic properties of the two ligands.

After extensive reaction optimisation through solvent/base screening with a "Design of Experiment" software package, the palladium pincer catalysts were successfully evaluated as catalysts for a range of Heck and Suzuki reactions. In recycling studies of the fluorous pincer catalyst by fluorous solid phase extraction following a Suzuki reaction, decomposition of the catalyst was detected under the reaction conditions leading to an inevitable loss in activity in subsequent catalytic runs. However, excellent recovery and reuse was possible with a 1 mol-% loading of fluorous pincer catalyst in the Heck reaction of 4-bromoacetophenone with methyl acrylate, in which the catalyst could be successfully recovered using fluorous solid phase extraction and reused four times with no loss in activity. Crucially, monitoring the reaction profile by measuring conversions at regular intervals showed no change in reactivity throughout the four recycles. In a comparison of a range of substrates, greater reactivity was obtained for the fluorous catalyst with electron-withdrawing or electron-neutral substituents on the aryl substrate, whilst greater reactivity was obtained for the non-fluorous catalyst with electron-donating substituents. Neither catalysts gave reactivity with arylchloride substrates.

A series of perfluoroalkylated imidazolium and *bis*-imidazolium salts, incorporating $C_3H_6C_8F_{17}$ units and linked *via* either a methylene or 1,3-*bis*methylene-benzene unit, have been prepared and fully characterised. Reactions with palladium(II) salts have afforded a number of novel NHC palladium complexes incorporating either two monodentate, one bidentate or one pincer (CCC) ligands. After a short solvent/base screen, the *bis*-monodentate NHC palladium complexes were evaluated as catalysts for the Heck reaction using 4-bromobenzaldehyde as the substrate where, again, the incorporation of the perfluoroalkyl groups appeared to have little impact on the reaction profile. Under homogenous reaction conditions followed by fluorous solid phase extraction, poor recovery and decomposition of the catalyst was detected. Conversely, supporting of the heavily perfluoroalkylated palladium carbene complex on fluorous reverse phase silica gel and conducting the catalysis in solid supported mode, the catalyst could be used successfully three times but poor recovery of the support material led to an inevitable loss of catalyst and reduction in product conversion. It is likely that this was mainly due to an inefficient recycling protocol. However, it was unclear whether the fluorous palladium catalyst was being truly recycled or whether the recycled material contained palladium metal from catalyst decomposition. Further investigation into the true catalytic species in these systems is needed and optimised recycling protocols are

required in order to have a better understanding of the chemistry associated with these catalysts.

This work illustrates the basic fundamental science associated with catalyst recovery and reuse that in future may be extended to a range of different systems. In the PCP pincer area, alternative ligand systems could be prepared with 3- or 4-aryl-C_6F_{13} or 3-aryl-$C_2H_4C_8F_{17}$ substitutions, to evaluate the relative impact of these substitution patterns on the catalyst activity and recovery. Alternatively, other metal-pincer ligand combinations using, for example, ruthenium or iridium could be evaluated for other reactions, e.g. transfer hydrogenation. Ultimately, the possibility of making a chiral PCP ligand for asymmetric induction in these sorts of reaction would be very interesting. Metal-carbene complexes are continuing to find widespread application in organic synthesis and catalysis. In this regard, the incorporation of the perfluoroalkyl substituents does not appear to have a significant impact on the chemistry of these ligands, such that applications in areas such as metathesis, C-H activation or polymerisation, incorporating either early and late transitions metals may be interesting.

Overall, this work provides the key preliminary data to support the proposal that fluorous solid phase extraction could be a valuable methodological tool for the application of transition metal catalysis in pharmaceutical/speciality chemical industries.

Chapter Six

University *of* Leicester

6. Experimental Procedures

6.1 General Experimental Procedures

6.1.1 NMR Spectroscopy

^{1}H, ^{19}F, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR spectra were recorded on Bruker DRX 400 and Bruker DPX 300 spectrometers at ambient temperature of the probe unless otherwise stated. ^{1}H and ^{13}C{^{1}H} NMR spectra were referenced internally using the residual *protio* solvent resonance relative to SiMe$_4$ (δ = 0 ppm), whilst ^{19}F{^{1}H} NMR spectra were referenced externally to CFCl$_3$ (δ = 0 ppm) and ^{31}P{^{1}H} NMR spectra were referenced externally to 85 % H$_3$PO$_4$ (δ = 0 ppm). All chemical shifts are quoted in δ (ppm) and coupling constants in Hertz (Hz), using high-frequency positive convention. The following spectrometer frequencies were used:

Bruker DPX 300 Spectrometer:
^{1}H NMR spectra, 300.13 MHz,

^{19}F{^{1}H} NMR spectra, 283.57 MHz,

^{13}C{^{1}H} NMR spectra, 75.47 MHz,

^{31}P{^{1}H} NMR spectra, 121.99 MHz.

Bruker DRX 400 Spectrometer:
^{1}H NMR spectra, 400.13 MHz,

^{19}F{^{1}H} NMR spectra, 376.46 MHz,

^{13}C{^{1}H} NMR spectra, 100.62 MHz,

^{31}P{^{1}H} NMR spectra, 161.98 MHz.

The solvent most frequently used was deuterated chloroform (CDCl$_3$). However, if this was not possible due to solubility problems, a common laboratory solvent was used with a sealed, deuterated chloroform (CDCl$_3$), capillary insert tube.

6.1.2 Mass Spectrometry

Electron impact (EI) and Fast atom bombardment (FAB) mass spectra were recorded on a Kratos Concept 1 H, double focussing, forward geometry mass spectrometer. 3-Nitrobenzyl alcohol was used as the matrix for FAB spectra. Matrix-assisted laser desorption/ionization (MALDI) mass spectra were recorded on a Voyager.

6.1.3 Inductively Coupled Plasma Optical Emission Spectra

Inductively coupled plasma optical emission spectra (ICP-OES) was carried out by the Geology Department at the University of Leicester using a Uttima 2 ICP-OES spectrometer.

6.1.4 Gas Chromatography

Gas chromatography was conducted on a PerkinElmer Autosystem XL fitted with a PE-5 column 29.5 m.

6.1.5 Infrared Spectroscopy

Infrared spectra were recorded on a PerkinElmer FT-IR spectrometer at 4 cm^{-1} resolution (16 scans) with a Universal ATR Sampling Accessory.

6.1.6 High Performance Liquid Chromatography

High Performance Liquid Chromatography was conducted on a Agilent 1100 fitted with a Phenomenex Luna C18(2) column (3um, 50 mm x 2.0 mm) using 0.05% v/v TFA in Water and 0.05% v/v TFA in Acetonitrile as eluants with a 0% Acetonitrile to 95% Acetonitrile gradient over 8 min.

6.1.7 X-Ray Crystallography

X-Ray crystallography data were collected on a Bruker Apex SMART 2000 diffractometer. Crystal data and structure refinement can be found in the appendicies.

6.1.8 Starting Materials

Compounds were generally supplied from Sigma-Aldrich, Fluorochem, Lancaster or Apollo, whilst solvents were dried according to literature methods; dichloromethane was dried over calcium hydride, potassium metal was employed to dry THF, whilst diethyl ether was dried over sodium wire. Solvents were also obtained dried from a distillation machine model Puresolve™. All solvents were stored in sealed ampoules under an atmosphere of dry nitrogen over 4Å molecular sieves. Where necessary, solvents were freeze-pump-thawed degassed at least three times prior to use.

6.2 Synthetic Procedures
6.2.1 Compounds for Chapter Two
Preparation of 4-(heptadecafluorooctyl)bromobenzene (13)

The title compound was synthesised using a modification of Hope's method.[1] A 500 mL, three-necked round-bottomed flask, equipped with a magnetic stirring bar, pressure-

equalising dropping funnel, thermometer and condenser, was purged with nitrogen for 10 min. The flask was charged with 4-bromoiodobenzene (25.00 g, 88.3 mmol), copper powder (12.36 g, 193.1 mmol), 2,2'-bipyridine (0.98 g, 6.4 mmol), DMSO (200 mL) and fluorobenzene (150 mL). The flask was purged with nitrogen for a further 20 min whilst the suspension was vigorously stirred. The mixture was heated to exactly 70 °C and the perfluoro-n-octyl iodide was added over 7 h with the internal temperature being maintained at 70 °C. The mixture was stirred for a further 72-120 h at 70 °C. The reaction mixture was then cooled to room temperature and was added to a 1 L conical flask containing water (250 mL) and diethyl ether (500 mL). The solids that precipitated were removed by filtration through a Buchner funnel and are washed with diethyl ether (2 x 50 mL). The organic layer was separated, washed with water (5 x 300 mL), dried (magnesium sulphate) and the solvent removed using a reduced pressure rotary evaporator to give the crude products. The desired product was purified by recrystallisation from methanol to give a white powder (28.07 g, 55%). mp 39-40 °C (from methanol); ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.58 (2 H, d, $^3J_{HH}$ = 8.8 Hz, ArH), 7.38 (2 H, d, $^3J_{HH}$ = 8.6 Hz, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.80 (3 F, t, $^4J_{FF}$ = 9.6 Hz, CF$_3$), -110.86 (2 F, t, $^4J_{FF}$ = 14.2 Hz, α-CF$_2$), -121.20 (2 F, m, CF$_2$), -121.84 (6 F, m, 3 x CF$_2$), -122.70 (2 F, m, CF$_2$), -126.11 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 137.98 (C), 132.03 (CH), 128.43 (t, $^3J_{CF}$ = 13.0 Hz, CH), 127.94 (t, $^2J_{CF}$ = 25.1 Hz, C); m/z (EI) 574/6 (M$^+$) (20%); IR (Solid State, cm^{-1}) 1598.9 (w), 1243.6 (m), 1190.7 (s), 1142.1 (s), 1115.7 (s), 1107.7 (s), 1092.3 (m).

Preparation of 3-(heptadecafluorooctyl)bromobenzene (14)

The title compound was prepared similarly to (13), using 3-bromoiodobenzene (25.00 g, 88.3 mmol) to give a sparkling white solid (39.30 g, 77%); mp 37-38 °C (from methanol); ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.67 (1 H, s, ArH), 7.65 (1 H, d, $^3J_{HH}$ = 8.6 Hz, ArH), 7.46 (1 H, d, $^3J_{HH}$ = 7.8 Hz, ArH), 7.32 (1 H, t, $^3J_{HH}$ = 7.8 Hz, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.79 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -110.83 (2 F, t, $^4J_{FF}$ = 13.6 Hz, α-CF$_2$), -121.20 (2 F, m, CF$_2$), -121.64 (2 F, m, CF$_2$), -121.86 (4 F, m, 2 x CF$_2$), -122.69 (2 F, m, CF$_2$), -126.09 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 134.12 (CH), 130.98 (t, $^2J_{CF}$ = 25.1 Hz, C), 130.09 (CH), 129.95 (t, $^3J_{CF}$ = 7.2 Hz, CH), 125.45 (t, $^3J_{CF}$ = 6.0 Hz, CH), 122.69 (C); m/z (EI) 574/6 (M$^+$) (55%); IR (Solid State, cm^{-1}) 1573.9 (w), 1226.9 (m), 1196.3 (br), 1145.3 (s), 1133.1 (s), 1116.2 (s).

Preparation of *tris*(4-heptadecafluorooctylphenyl)phosphine (15)

The title compound was synthesised using a modification of Hope's method.[1] A 1 L, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-

equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-(heptadecafluorooctyl)bromobenzene **(13)** (5.00 g, 8.70 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding dry diethyl ether (400 mL) to the main flask. Dry diethyl ether (30 mL) and *n*-butyllithium (5.48 mL, 1.6 M, in hexane 8.77 mmol) are both added to the dropping funnel and the flask was cooled to -78 °C using a dry ice/acetone bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise over -70 °C. The reaction temperature was then allowed to rise to -55 °C and stirred at this temperature for 2 h. The flask was then cooled back down to −78 °C. After rinsing the dropping funnel with dry diethyl ether (10 mL), it was charged with dry diethyl ether (30 mL) and phosphorus trichloride (0.25 mL, 2.88 mmol). The phosphorus trichloride solution was added dropwise over 60 min with the internal temperature never being allowed to rise over -70 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight. Water (100 mL) was then added and the reaction mixture was stirred for 20 min before transferring the organic phase under nitrogen to a flame-dried, 500 mL flask containing magnesium sulphate. After stirring for 20 min, the solution was transferred to a flame-dried, 500 mL flask under nitrogen and the solvent was removed *in vacuo* to give the crude product. This was heated in a Kugelröhr oven to distill off any impurities to give a pale green solid (2.16 g, 49%). mp 92 °C (lit. 92-95 °C).[2] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.53 (6 H, d, $^3J_{HH}$ = 7.9 Hz, 3-C$_6$H$_4$), 7.35 (6 H, vt, $^3J_{HH}$ ≈ $^3J_{HP}$ = 7.7 Hz, 2-C$_6$H$_4$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.76 (9 F, t, $^4J_{FF}$ = 8.9 Hz, CF$_3$), -110.99 (6 F, t, $^4J_{FF}$ = 14.0 Hz, α-CF$_2$), -121.17 (6 F, m, CF$_2$), -121.72 (18 F, m, 3 x CF$_2$), -122.67 (6 F, m, CF$_2$), -126.08 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -6.2 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 140.39 (d, $^1J_{CP}$ = 14.4 Hz, C), 132.77 (d, $^2J_{CP}$ = 21.1 Hz, CH), 130.09 (t, $^2J_{CF}$ = 23.9 Hz, C), 126.25 (t, $^3J_{CF}$ = 6.0 Hz, CH); *m/z* (FAB) 1516 (M$^+$) (30%); IR (Solid State, cm^{-1}) 1602.9 (w), 1196.7 (m), 1196.3 (br), 1145.3 (s), 1116.2 (s).

Preparation of *tris*(3-heptadecafluorooctylphenyl)phosphine (16)

The title compound was synthesised using a modification of Genêt's method.[3] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 3-(heptadecafluorooctyl)bromobenzene **(14)** (6.11 g, 10.8 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding dry diethyl ether (30 mL) and dry THF (30 mL) to the main flask. Dry

diethyl ether (30 mL) and *n*-butyllithium (6.19 mL, 1.6 M solution in hexane, 9.9 mmol) are both added to the dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -25 °C. The reaction stirred at this temperature for 1 h. After rinsing the dropping funnel with dry THF (20 mL) it was then charged with dry THF (10 mL) and phosphorus trichloride (0.26 mL, 3.0 mmol). The phosphorus trichloride solution was added dropwise above 30 min with the internal temperature never being allowed to rise above -25 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight. A 10% solution of ammonium chloride (50 mL) was added and the reaction mixture was stirred for 20 min before transferring the organic layer under nitrogen to a flame-dried, 500 mL flask containing magnesium sulphate. After stirring for 20 min, the solution was transferred to flame-dried, 500 mL flask under nitrogen and the solvent was removed *in vacuo* to give the crude product. This was heated in a Kugelröhr oven to distill off any impurities to give a pale brown solid (3.08 g, 68%). mp 77-78 °C (lit. 84-86 °C);[2] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.59-7.46 (9 H, m, ArH), 7.35 (3 H, d, $^3J_{HP}$ = 6.3 Hz, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.92 (9 F, t, $^4J_{FF}$ = 9.4 Hz, CF$_3$), -111.47 (6 F, t, $^4J_{FF}$ = 14.0 Hz, α-CF$_2$), -121.45 (6 F, m, CF$_2$), -122.10 (18 F, m, 3 x CF$_2$), -122.90 (6 F, m, CF$_2$), -126.29 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -6.9 (s); ^{13}C NMR (100 MHz, CDCl$_3$) δ_C 137.15 (d, $^2J_{CP}$ = 24.5 Hz, CH), 137.01 (d, $^1J_{CP}$ = 14.6 Hz, C), 131.38 (dt, $^2J_{CP}$ = 16.2 Hz, $^3J_{CF}$ = 7.2 Hz, CH), 130.03 (t, $^2J_{CF}$ = 24.5 Hz, C), 129.12 (d, $^3J_{CP}$ = 8.1 Hz, CH), 127.84 (t, $^3J_{CF}$ = 6.2 Hz, CH); (EI) 1516 (M$^+$) (32%); IR (Solid State, cm^{-1}) 1602.8 (w), 1196.3 (br), 1144.1 (s), 1114.9 (m).

Preparation of 4-bromobenzene diazonium tetrafluoroborate (17)

A 100 mL, round-bottomed flask equipped with a magnetic stirring bar was charged with 4-bromoaniline (3.44 g, 20.00 mmol) and tetrafluoroboric acid (7.00 mL, 20.00 mmol). The mixture was cooled using an ice bath and stirred for 20 min. Sodium nitrite (1.38 g, 20.00 mmol) was dissolved in water (5 mL) and was added dropwise to the reaction mixture over 15 min. After stirring for a further 15 min, the mixture was filtered, washed with diethyl ether and used in the next reaction step without any further purification or analysis. Pale brown solid (5.29 g, 98 %).

Preparation of 3-bromobenzene diazonium tetrafluoroborate (18)

The title compound was prepared similarly to (17), using 3-bromoaniline (3.44 g, 20.00 mmol). The product was used in the next reaction step without any further purification or analysis. Brown solid (6.03 g, Quant.).

Preparation of 4-(1H,2H-perfluorodec-1-ene)bromobenzene (19)

The title compound was synthesised using Genêt's method without any modification.[3] A 250 mL, round-bottomed flask equipped with a magnetic stirring bar was charged with 4-bromobenzene diazonium tetrafluoroborate (17) (5.29 g, 19.50 mmol), methanol (50 mL) and palladium acetate (200 mg, 0.89 mmol). The mixture was stirred as 1H,1H,2H-perfluorodec-1-ene (8.70 g, 19.50 mmol) was added dropwise over 15 min. The mixture was stirred for a further hour until the colour changes from orange to black. The solvent was removed using a rotary evaporator, the residue was re-dissolved in petroleum ether (40-60 °C) and filtered through silica to remove the Pd catalyst. The solvent was finally removed using a rotary evaporator to give a white crystalline solid (10.09 g, 86%). mp 42-43 °C (from pet. ether) (lit 45 °C).[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.47 (2 H, d, $^3J_{HH}$ = 8.5 Hz, ArH), 7.28 (2 H, d, $^3J_{HH}$ = 8.5 Hz, ArH), 7.05 (1 H, dt, $^3J_{HH}$ = 16.1 Hz, $^4J_{HF}$ = 2.2 Hz, CH), 6.13 (1 H, dt, $^3J_{HH}$ = 16.1 Hz, $^3J_{HF}$ = 11.9 Hz, CH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.71 (3 F, t, $^4J_{FF}$ = 9.4 Hz, CF$_3$), -111.18 (2 F, t, $^4J_{FF}$ = 12.1 Hz, α-CF$_2$), -121.30 (2 F, m, CF$_2$), -121.83 (4 F, m, 2 x CF$_2$), -122.63 (2 F, m, CF$_2$), -123.06 (2 F, m, CF$_2$), -126.03 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.54 (t, $^3J_{CF}$ = 8.2 Hz, CH), 132.42 (C), 132.22 (CH), 129.06 (CH), 124.48 (C), 115.10 (t, $^2J_{CF}$ = 22.6 Hz, CH); m/z (EI) 600/2 (M$^+$) (63%); IR (Solid State, cm^{-1}) 1660.2 (w), 1242.2 (m), 1193.9 (br), 1142.3 (s), 1112.0 (m), 970.1 (m).

Preparation of 3-(1H,2H-perfluorodec-1-ene)bromobenzene (20)

The title compound was prepared similarly to (19), using 3-bromobenzene diazonium tetrafluoroborate (18) (6.03 g, 20.00 mmol). Colourless oil (9.09 g, 76 %). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.52 (1 H, s, ArH), 7.42 (1 H, d, $^3J_{HH}$ = 7.9 Hz, ArH), 7.28 (1 H, d, $^3J_{HH}$ = 7.8 Hz, ArH), 7.16 (1 H, t, $^3J_{HH}$ = 7.8 Hz, ArH), 7.00 (1 H, dt, $^3J_{HH}$ = 16.2 Hz, $^4J_{HF}$ = 2.2 Hz, CH), 6.11 (1 H, dt, $^3J_{HH}$ = 16.1 Hz, $^3J_{HF}$ = 12.0 Hz, CH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.09 (3 F, t, $^4J_{FF}$ = 8.6 Hz, CF$_3$), -111.54 (2 F, t, $^4J_{FF}$ = 11.2 Hz, α-CF$_2$), -121.50 (2 F, m, CF$_2$), -122.04 (4 F, m, 2 x CF$_2$), -122.87 (2 F, m, CF$_2$), -123.23 (2 F, m, CF$_2$), -126.32 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.21 (t, $^3J_{CF}$ = 9.6 Hz, CH), 135.56 (C), 133.01 (CH), 130.39 (CH), 130.36 (CH), 126.19 (CH), 123.09 (C), 118.23 (t, $^2J_{CF}$ = 22.7 Hz, CH); m/z (EI) 600/2 (M$^+$) (47%); IR (Solid State, cm^{-1}) 1660.4 (w), 1242.9 (m), 1194.3 (br), 1142.4 (s).

Preparation of 4-(1H,1H,2H,2H-perfluorodecyl)bromobenzene (21)

The title compound was synthesised using Genêt's method without any modification.[3] A suspension of the 4-(1H,2H-perfluorodec-1-ene)bromobenzene (19) (10.00 g, 16.64 mmol)

and rhodium on carbon (200 mg) in DCM (50 mL) was placed under hydrogen (50 bar) at 20 °C for 24 h. At the end of the reaction the solvent was removed using a rotary evaporator, the residues were re-dissolved in petroleum ether (40-60 °C) and filtered through silica. The solvent was finally removed to give a white solid (9.77 g, 97%). mp 53-53.5 °C (from pet. ether) (lit 54 °C).[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.38 (2 H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.02 (2 H, d, $^3J_{HH}$ = 8.3 Hz, ArH), 2.86-2.76 (2 H, m, CH$_2$), 2.42-2.18 (2 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.73 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.49 (2 F, t, $^4J_{FF}$ = 12.1 Hz, α-CF$_2$), -121.63 (2 F, m, CF$_2$), -121.82 (4 F, m, 2 x CF$_2$), -122.64 (2 F, m, CF$_2$), -123.39 (2 F, m, CF$_2$), -126.04 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.04 (C), 131.88 (CH), 130.01 (CH), 120.58 (C), 32.76 (t, $^2J_{CF}$ = 21.5 Hz, CH$_2$), 25.96 (CH$_2$); m/z (EI) 602/4 (M$^+$) (51%); IR (Solid State, cm^{-1}) 1489.6 (w), 1198.2 (br s), 1144.3 (s), 1114.1 (m).

Preparation of 3-(1H,1H,2H,2H-perfluorodecyl)bromobenzene (22)

The title compound was prepared similarly to (21), using 3-(1H,2H-perfluorodec-1-ene)bromobenzene (20) (14.08 g, 23.42 mmol) to give a white solid (13.09 g, 93%). mp 37-38 °C (from pet. ether) (lit 45 °C).[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.34-7.26 (2 H, m, ArH), 7.16-7.04 (2 H, m, ArH), 2.87-2.77 (2 H, m, CH$_2$), 2.39-2.18 (2 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.80 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.52 (2 F, t, $^4J_{FF}$ = 13.2 Hz, α-CF$_2$), -121.49 (6 F, m, 3 x CF$_2$), -122.69 (2 F, m, CF$_2$), -123.43 (2 F, m, CF$_2$), -126.11 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 141.35 (C), 131.38 (CH), 130.30 (CH), 129.92 (CH), 126.92 (CH), 122.77 (C), 32.73 (t, $^2J_{CF}$ = 24.0 Hz CH$_2$), 26.12 (CH$_2$); m/z (EI) 602/4 (M$^+$) (72%). IR (Solid State, cm^{-1}) 1604.3 (w), 1180.2 (br s), 1143.2 (s), 1113.6 (m).

Preparation of *tris*(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine (23a)

The title compound was synthesised using a modification of Hope's method.[1] A 1 L, three-necked round-bottomed flask, equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock, was attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-(1H,1H,2H,2H-perfluorodecyl)bromobenzene (21) (5.00 g, 8.29 mmol) and was degassed under high vacuum. The flask was refilled with nitrogen before adding dry diethyl ether (400 mL) to the main flask. Dry diethyl ether (30 mL) and n-butyllithium (4.44 mL, 1.6 M solution in hexane, 7.11 mmol) were both added to the dropping funnel and the flask was cooled to -40 °C using a dry ice/acetonitrile bath. The n-butyllithium solution was added dropwise over 60 min with the internal temperature never allowed to rise over -40 °C. The reaction temperature was then raised to 0 °C, using an ice bath, and was stirred for 2 h. The flask was then cooled back down

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to -40 °C. After rinsing the dropping funnel with dry diethyl ether (10 mL), it was charged with dry diethyl ether (30 mL) and phosphorus trichloride (0.81 g, 5.92 mmol). The phosphorus trichloride solution was added dropwise over 60 min with the internal temperature never allowed to rise over -40 °C. The reaction mixture was then allowed to warm to room temperature overnight. Water (100 mL) was then added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude desired product. This was washed with hexane (3 x 5 mL) and then heated in a Kugelröhr oven to distill off any impurities to give a yellow/orange solid (1.73 g, 55%). mp 89-90 °C (Lit. 89-91 °C).[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.22-7.08 (12 H, m, ArH), 2.95-2.87 (6 H, m, CH$_2$), 2.41-2.18 (6 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.76 (9 F, t, $^4J_{FF}$ = 9.4 Hz, CF$_3$), -114.54 (6 F, t, $^4J_{FF}$ = 11.8 Hz, α-CF$_2$), -121.64 (6 F, m, CF$_2$), -121.87 (12 F, m, 2 x CF$_2$), -122.67 (6 F, m, CF$_2$), -123.45 (6 F, m, CF$_2$), -126.07 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -7.6 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 139.92 (C), 135.34 (d, $^1J_{CP}$ = 10.8 Hz, C), 134.09 (d, $^2J_{CP}$ = 21.5 Hz, CH), 128.53 (d, $^3J_{CP}$ = 6.8 Hz, CH), 32.71 (t, $^2J_{CF}$ = 18.0 Hz, CH$_2$), 26.23 (CH$_2$); m/z (FAB) 1600 (M$^+$, 100 %); IR (Solid State, cm^{-1}) 1602.8 (w), 1196.7 (br s), 1143.3 (s), 1113.8 (m).

Preparation of *tris*(4-1*H*,1*H*,2*H*,2*H* -perfluorodecylphenyl)phosphine (23b)

The title compound was synthesised using a modification of Genêt's method.[3] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-(1*H*,1*H*,2*H*,2*H*-perfluorodecyl)bromobenzene (21) (5.00 g, 8.29 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding dry diethyl ether (30 mL) and dry THF (30 mL) to the main flask. Dry diethyl ether (30 mL) and *n*-butyllithium (4.44 ml, 1.6 M solution in hexane, 7.11 mmol) are both added to the dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -25 °C. The reaction mixture was stirred at this temperature for 1 h. After rinsing the dropping funnel with dry THF (20 mL), it was charged with dry THF (10 mL) and phosphorus trichloride (0.17 mL, 1.97 mmol). The phosphorus trichloride solution was added dropwise over 30 min with the internal temperature never being allowed to rise above -25 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight. Water (50 mL) was then added and the reaction mixture was stirred for 20 min before separating the organic layer,

then drying ($MgSO_4$) and removing the solvent *in vacuo* to give the crude product. This was heated in a Kugelröhr oven to distill off any impurities to give a cream solid (1.04 g, 22%). Characterisation data was the same as above.

Preparation of *tris*(3-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine (24)

The title compound was prepared similarly to (16), using 3-(1*H*,1*H*,2*H*,2*H*-perfluorodecyl)bromobenzene (22) (3.80 g, 6.30 mmol) to give a yellow solid (0.94 g, 34%). mp 81-84 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.35-6.87 (12 H, m, ArH), 2.91-2.70 (6 H, m, ArH), 2.40-2.14 (6 H, m, ArH); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F -80.93 (9 F, t, $^4J_{FF}$ = 9.4 Hz, CF_3), -114.59 (6 F, t, $^4J_{FF}$ = 14.0 Hz, α-CF_2), -121.87 (18 F, m, 3 x CF_2), -122.80 (6 F, m, CF_2), -123.54 (6 F, m, CF_2), -126.13 (6 F, m, CF_2); ^{31}P{^{1}H} NMR (121 Hz, $CDCl_3$) δ_P -5.2 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 138.45 (d, J_{CP} = 7.2 Hz, C), 136.55 (d, J_{CP} = 12.0 Hz, C), 132.45 (d, J_{CP} = 20.3 Hz, CH), 131.03 (d, J_{CP} = 18.0 Hz, CH), 128.01 (CH), 127.88 (CH), 31.63 (t, $^2J_{CF}$ = 21.9 Hz, CH_2), 25.33 (CH_2); m/z (FAB) 1600 (M^+) (8%); IR (Solid State, cm^{-1}) 1602.6 (w), 1196.7 (br s), 1143.4 (s), 1113.8 (m).

Preparation of *trans*-dichloro*bis*(triphenylphosphine)palladium (25)

The title compound was synthesised using a modification of Hope's method.[4] A 100 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, condenser and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with triphenylphosphine (0.75 g, 2.85 mmol) and *cis*-[$PdCl_2(MeCN)_2$] (0.37 g, 1.42 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding dry dichloromethane (60 mL) to the flask. The flask was heated to reflux for 2 h then allowed to cool to room temperature. The solvent was removed and the crude product was recrystallised from dichloromethane/light petroleum ether to give a bright yellow powder (0.69 g, 69%). mp 294-299 °C (from pet. ether) (lit 280-285 °C).[5] ^{1}H NMR (300 MHz, $CDCl_3/C_6F_6$) δ_H 7.69-7.59 (5 H, m, ArH), 7.41-7.25 (10 H, m, ArH); ^{31}P{^{1}H} NMR (121 Hz, $CDCl_3/C_6F_6$) δ_P 23.3 (s); m/z (FAB) *Not conclusive*. IR (Solid State, cm^{-1}) 1481.7 (w), 1435.1 (m), 1099.2 (m), 744.6 (m), 707.9 (m), 691.6 (s).

Preparation of *trans*-dichloro*bis*[*tris*(4-heptadecafluorooctylphenyl)phosphine] palladium (8)

The title compound was prepared similarly to (25) using *tris*(4-heptadecafluorooctylphenyl)phosphine (15) to give a yellow/orange powder (1.55 g, 87%). mp 181-184 °C (from pet. ether) (lit. 186-187 °C).[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.95-7.89

(6 H, m, ArH), 7.70 (3 H, d, $^3J_{HH}$ = 7.9 Hz, ArH), 7.64 (3 H, d, $^3J_{HH}$ = 8.0 Hz, ArH) ; ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -82.03 (18 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -115.62 (12 F, t, $^4J_{FF}$ = 14.8 Hz, α-CF$_2$), -122.44 (12 F, m, CF$_2$), -122.69 (24 F, m, 2 x CF$_2$), -123.50 (12 F, m, CF$_2$), -124.21 (12 F, m, CF$_2$), -127.03 (12 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$/C$_6$F$_6$) δ_P 23.2 (s); m/z (MALDI) 3138 [M-2Cl]$^+$; IR (Solid State, cm^{-1}) 1366.0 (s), 1192.7 (br s), 1142.3 (s), 1115.9 (s).

Preparation of *trans*-dichloro*bis*[*tris*(3-heptadecafluorooctylphenyl)phosphine] palladium (9)

The title compound was prepared similarly to **(25)** using *tris*(3-heptadecafluorooctylphenyl)phosphine **(16)** to give a pale yellow powder (2.41 g, 93%). mp 122-124 °C (from pet. ether) (lit. 134-136 °C).^{2} ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 8.04 (6 H, dd, J = 6.5, J = 5.9, ArH) 7.87 (6 H, t, J = 5.3, ArH), 7.80-7.63 (12 H, m, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -83.49 (18 F, t, $^4J_{FF}$ = 10.2 Hz, CF$_3$), -113.42 (12 F, t, $^4J_{FF}$ = 15.1 Hz, α-CF$_2$), -122.92 (12 F, m, CF$_2$), -123.53 (36 F, m, 3 x CF$_2$), -124.39 (12 F, m, CF$_2$), -128.14 (12 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$/C$_6$F$_6$) δ_P 24.5 (s); m/z (MALDI) 3137 [M-2Cl-H]$^+$; IR (Solid State, cm^{-1}) 1365.7 (m), 1193.8 (br s), 1144.7 (s), 1116.0 (s).

Preparation of *trans*-dichloro*bis*[*tris*(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine]palladium (10)

The title compound was prepared similarly to **(25)** using *tris*(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine **(23)** to give a bright yellow powder (0.67 g, 69%). mp 177-180 °C (from pet. ether) (lit. 182-184 °C).^{6} ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.62-7.51 (12 H, m, ArH), 7.23-7.15 (12 H, m, ArH), 2.93-2.79 (12 H, m, CH$_2$), 2.42-2.19 (12 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -82.22 (18 F, t, $^4J_{FF}$ = 10.5 Hz, CF$_3$), -112.34 (12 F, t, $^4J_{FF}$ = 12.5 Hz, α-CF$_2$), -122.00 (12 F, m, CF$_2$), -122.29 (12 F, m, CF$_2$), -122.68 (24 F, m, 2 x CF$_2$), -123.60 (12 F, m, CF$_2$), -127.05 (12 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$/C$_6$F$_6$) δ_P 21.9 (s); m/z (MALDI) 3307 [M-2Cl]$^+$; IR (Solid State, cm^{-1}) 1363.7 (s), 1194.5 (br s), 1145.8 (s), 1115.4 (s).

Preparation of *trans*-dichloro*bis*[*tris*(3-1H,1H,2H,2H-perfluorodecylphenyl)phosphine]palladium (11)

The title compound was prepared similarly to **(25)** using *tris*(3-1H,1H,2H,2H-perfluorodecylphenyl)phosphine **(24)** to give a yellow powder (0.64 g, 72%). mp 121-123 °C (from pet. ether) (lit. 139-141 °C).^{6} ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.64 (6 H, t, J = 5.3, ArH), 7.46 (6 H, d, J = 6.4, ArH), 7.36-7.27 (12 H, m, ArH), 2.93-2.79 (12 H, m, CH$_2$), 2.42-

2.19 (12 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.83 (18 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -115.20 (12 F, t, $^4J_{FF}$ = 14.8 Hz, α-CF$_2$), -122.49 (36 F, m, 3 x CF$_2$), -123.44 (12 F, m, CF$_2$), -124.04 (12 F, m, CF$_2$), -126.83 (12 F, m, CF$_2$); ^{31}P$\{^1$H$\}$ NMR (121 Hz, CDCl$_3$/C$_6$F$_6$) δ_P 23.3 (s); m/z (MALDI) 3306 [M-2Cl]$^+$; IR (Solid State, cm^{-1}) 1367.0 (s), 1192.7 (br s), 1142.8 (s), 1114.8 (s).

Preparation of *trans*-dichloro*bis*[*tris*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine]palladium (10) supported on FRPSG

The title compound was prepared using Bannwarth's method.[7] A 25 mL round-bottomed flask equipped with a magnetic stirring bar was charged with *trans*-dichloro*bis*[*tris*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine] palladium (10) (10 mg, 2.96 μmol), FRPSG (1 g), diethyl ether (3.5 mL) and hexafluorobenzene (3.5 mL) and stirred for 2 h. The solvent was removed by oil pump vacuum to produce the supported catalyst as a yellow free-flowing powder.

Preparation of *trans/cis*-dichloro*bis*[*tris(4-heptadecafluorooctylphenyl)phosphine*] platinum (26)

The title compound was prepared similarly to (25) using *tris*(4-heptadecafluorooctylphenyl)phosphine (15) (0.202 g, 0.133 mmol), [PtCl$_2$(MeCN)$_2$] (0.022 g, 0.067 mmol), DCM (30 mL) and BTF (30 mL). The reaction was heated at 50 °C overnight. The reaction was cooled, filtered and the residues washed with chloroform (3 x 50 mL) to give the complex as white powder (0.159 g, 72 %). The isolated compound was determined to be a mixture of trans/cis-isomers. Anal. Calcd for C$_{84}$H$_{24}$F$_{102}$P$_2$Cl$_2$Pt: C, 30.58; H, 0.73. Found C, 30.50; H, 0.64; *trans*-isomer: ^{1}H NMR (300 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_H 7.98 (6 H, dd, $^3J_{HH}$ = 8.2 Hz, $^3J_{HP}$ = 5.5 Hz, ArH), 7.72 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH); ^{1}H$\{^{31}$P$\}$ NMR (300 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_H 7.98 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.72 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH); ^{19}F NMR (282 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_F -83.48 (18 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -113.30 (12 F, t, $^4J_{FF}$ = 14.6 Hz, α-CF$_2$), -122.92 (12 F, m, CF$_2$), -123.33 (24 F, m, 2 x CF$_2$), -123.49 (12 F, m, CF$_2$), -124.34 (12 F, m, CF$_2$), -128.04 (12 F, m, CF$_2$); ^{31}P$\{^1$H$\}$ NMR (162 Hz, C$_6$D$_6$/C$_6$F$_6$) δ_P 20.5 (s, $^1J_{PPt}$ = 2751 Hz); m/z (MALDI-TOF) 3227 [M-HCl$_2$]$^+$. *cis*-isomer: ^{1}H NMR (300 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_H 7.79 (6 H, dd, $^3J_{HP}$ = 8.5 Hz, $^3J_{HH}$ = 8.2 Hz, ArH), 7.72 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH); ^{1}H$\{^{31}$P$\}$ NMR (300 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_H 7.79 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.72 (6 H, d, $^3J_{HH}$ = 8.2 Hz, ArH); ^{19}F NMR (282 MHz, C$_6$D$_6$/C$_6$F$_6$) δ_F -83.48 (18 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -113.43 (12 F, t, $^4J_{FF}$ = 15.5 Hz, α-CF$_2$), -122.92 (12 F, m, CF$_2$), -123.33 (24 F, m, 2 x CF$_2$), -123.49 (12 F, m, CF$_2$), -124.34 (12 F, m, CF$_2$), -128.04 (12 F, m, CF$_2$); ^{31}P$\{^1$H$\}$ NMR

(162 Hz, C_6D_6/C_6F_6) δ_P 15.2 (s, $^1J_{PPt}$ = 3570 Hz); IR (Solid State, cm^{-1}) 1370.2 (s), 1198.1 (br s), 1148.9 (s), 1115.0 (s).

6.2.2 Catalytic Testing for Chapter Two

General procedure for the Suzuki coupling reaction between 4-nitrobromo-benzene and phenylboronic acid (C2.1-C2.6)

The following catalysis method was conducted using a modification of Bannwarth's method.[7] A 50 mL Schlenk tube, equipped with a magnetic stirring bar, was charged with sodium carbonate (1.33 g, 12.55 mmol) and palladium catalyst **(8-11 & 25)** (18.8 μmol), evacuated and refilled with nitrogen. Stock solutions of 4-nitrobromobenzene (0.30 M in 1,2-dimethoxyethane, 4.18 mL, 1.25 mmol), phenylboronic acid (0.33 M in 1,2-dimethoxyethane, 4.18 mL, 1.38 mmol) and water (6.27 mL) were added to the tube, before it was sealed and stirred at 75 °C for 2 h. The reaction mixture was cooled to room temperature and then poured into a separating funnel. The Schlenk tube was washed with diethyl ether (2 x 10 mL) and water (2 x 10 mL). The combined phases were diluted with brine (20 mL) and sodium hydroxide (1 M, 20 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic phases were concentrated, redissolved in diethyl ether (5 mL) and washed through a plug of neutral alumina (9 mL, activity 1) with diethyl ether (~30 mL). The solvent was removed to give product. Conversions were determined by GC using PE-5 column (200 °C for 6 min, injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. R_t 5.6 min (4-nitrobophenyl)).

Suzuki Reaction using recycled catalyst from C2.5 (C2.7)

The reaction mixture from **C2.5** was loaded onto a column of FRPSG (9 mL) with a small amount of diethyl ether. The product was washed off with acetonitrile and the catalyst was washed off using benzotrifluoride. The solvents were removed and the solid catalyst was added to a Schlenk tube. The general procedure for the Suzuki reaction between 4-nitrobromobenzene and phenylboronic acid was then followed. GC determined a conversion of <1 % of the starting material to the product. R_t 2.23 min (4-nitrobromobenzene).

General procedure for the Suzuki coupling reaction between 4-bromoanisole and phenylboronic acid (C2.8-C2.13)

A 50 mL Radley's Carousel reaction tube, equipped with a magnetic stirring bar, was charged with sodium carbonate (1.33 g, 12.55 mmol), tolyl ether (0.238g, 1.25 mmol) and palladium catalyst **(8-11 & 25)** (18.8 μmol), evacuated and refilled with nitrogen. Solutions of phenylboronic acid (0.33 M in 1,2-dimethoxyethane, 4.18 mL, 1.38 mmol) and water (6.27 mL) were added to the tube. The reaction tube was heated at 75 °C and at this temperature, 4-

bromoanisole (0.30 M in 1,2-dimethoxyethane, 4.18 mL, 1.25 mmol) was added. The reaction mixture was stirred at 75 °C for 4 h before cooling to room temperature. Diethyl ether (10 mL) was added to the reaction mixture to produce a homogeneous organic phase before a sample was taken and analysed by GC. Conversions were determined by GC using tolyl ether as the internal standard, (100 °C for 3 min, followed by 45 °C min^{-1} to 200 °C, held for 3 min. Injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. R_t 2.2 min (4-bromoanisole), 3.9 min (tolyl ether), 4.1 min (4-methoxybiphenyl).

Phosphine oxide isolation (27-30)

The reaction mixtures from **C2.10-C2.13** were extracted with PP3 (3 x 10 mL). The fluorous fractions were combined and the solvent was removed. The crude material was analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H} NMR spectroscopy and was determined to be the corresponding phosphine oxide and some organic product. The fluorous phosphine oxide was purified by flash column chromatography.

tris(4-heptadecafluorooctylphenyl)phosphine oxide (27)

^{1}H{^{31}P } NMR (300 MHz, CDCl$_3$) δ_H 7.77 (6 H, d, $^3J_{HH}$ = 8.2 Hz, 3-C$_6$H$_4$), 7.70 (6 H, d, $^3J_{HH}$ = 8.2 Hz, 2-C$_6$H$_4$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.71 (9 F, t, $^4J_{FF}$ = 9.5 Hz, CF$_3$), -111.27 (6 F, t, $^4J_{FF}$ = 14.8 Hz, α-CF$_2$), -121.55 (6 F, m, CF$_2$), -121.84 (12 F, m, 2 x CF$_2$), -122.69 (6 F, m, CF$_2$), -123.41 (6 F, m, CF$_2$), -126.06 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 25.8 (s); m/z (FAB) 1532 (M$^+$) (12%).

tris(3-heptadecafluorooctylphenyl)phosphine oxide (28)

^{1}H{^{31}P } NMR (300 MHz, CDCl$_3$) δ_H 8.00 (3 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.66 (3 H, t, $^3J_{HH}$ = 7.7 Hz, ArH), 7.59 (3 H, s, ArH), 7.55 (3 H, d, $^3J_{HH}$ = 7.7 Hz, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.82 (9 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -111.65 (6 F, t, $^4J_{FF}$ = 14.6 Hz, α-CF$_2$), -121.69 (6 F, m, CF$_2$), -121.93 (12 F, m, 2 x CF$_2$), -123.45 (6 F, m, CF$_2$), -126.13 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 25.6 (s); m/z (FAB) 1532 (M$^+$) (100%).

tris(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (29)

^{1}H{^{31}P } NMR (300 MHz, CDCl$_3$) δ_H 7.55 (6 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.26 (6 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 2.95-2.87 (6 H, m, CH$_2$), 2.42-2.20 (6 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.71 (9 F, t, $^4J_{FF}$ = 9.8 Hz, CF$_3$), -114.46 (6 F, t, $^4J_{FF}$ = 13.1 Hz, α-CF$_2$), -121.62 (6 F, m, CF$_2$), -121.85 (12 F, m, 2 x CF$_2$), -122.66 (6 F, m, CF$_2$), -123.39 (6 F, m, CF$_2$), -126.05 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 28.4 (s); m/z (FAB) 1616 (M$^+$) (80%).

tris(3-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (30)

^{1}H{^{31}P } NMR (300 MHz, CDCl$_3$) δ_H 7.54 (3 H, s, ArH), 7.40-7.32 (9 H, m, ArH), 2.91-2.85 (6 H, m, ArH), 2.38-2.20 (6 H, m, ArH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.78 (9 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.50 (6 F, t, $^4J_{FF}$ = 12.7 Hz, α-CF$_2$), -121.71 (6 F, m, CF$_2$), -121.94 (12 F, m, 2 x CF$_2$), -122.73 (6 F, m, CF$_2$), -123.48 (6 F, m, CF$_2$), -126.11 (6 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 28.8 (s); *m/z* (FAB) 1616 (M$^+$) (14%).

General procedure for the Suzuki coupling reaction between 4-nitrobromo-benzene and phenylboronic acid using a solid support (C2.14)

A 50 mL Schlenk tube, equipped with a magnetic stirring bar, was charged with palladium catalyst (10) on FRPSG (100 mg, 0.1 mol.%), evacuated and refilled with nitrogen. Stock solutions of 4-nitrobromobenzene (0.30 M in 1,2-dimethoxyethane, 1.00 mL, 0.30 mmol), phenylboronic acid (0.33 M in 1,2-dimethoxyethane, 1.00 mL, 0.33 mmol) and sodium carbonate (2 M in water, 1.0 mL) were added to the tube, before it was sealed and stirred at 80 °C for 15 h. The reaction mixture was cooled to 0 °C and the liquid phase was removed under nitrogen with a syringe. The solid support was washed with diethyl ether (2 x 10 mL), water (2 x 10 mL) and diethyl ether (2 x 10 mL). The combined phases were diluted with brine (20 mL) and sodium hydroxide (1 M, 20 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic phases were concentrated, redissolved in diethyl ether (5 mL) and washed through a plug of neutral alumina (3 mL, activity 1) with diethyl ether (~14 mL). The solvent was removed to give product. GC determined a conversion >98 % of the starting material to the product.

Suzuki reaction using recycled solid support catalyst from C2.14 (C2.15)

The solid support was dried under vacuum to remove any residual solvents. Fresh reagents were added and the general procedure (C2.14) was then followed. GC determined a conversion >98 % of the starting material to the product.

6.2.3 Compounds for Chapter Three
Preparation of Diethyl benzylphosphonate (74)

The title compound was prepared using Gronowitz's method.[8] A flame-dried 100 mL, three-necked round-bottomed flask, equipped with a thermometer, magnetic stirring bar and condenser was purged with nitrogen for 10 min. The flask was charged with benzyl bromide (11.96 g, 8.32 mL, 69.93 mmol) and triethylphosphite (15.12 g, 15.60 mL, 91.00 mmol). The mixture was heated to 120 °C for 2 h and then the temperature was raised to 160 °C for 2 h. After cooling the crude reaction mixture to room temperature, it was distilled using a Kugelröhr oven (80 °C, 0.05 mbar), to distill off any starting materials or by-products to give a clear colourless oil (14.92 g, 93 %). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.24-7.14 (5 H, m, ArH), 4.00-3.87 (4 H, m, CH$_2$), 3.07 (2 H, d, $^2J_{HP}$ = 21.6 Hz, PhCH$_2$), 1.16 (6 H, td, $^3J_{HH}$ = 7.0 Hz, $^4J_{HP}$ = 0.6 Hz, CH$_3$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.24-7.14 (5 H, m, ArH), 4.00-3.87 (2 H, m, CH$_2$), 3.07 (2 H, s, PhCH$_2$), 1.16 (6 H, t, $^3J_{HH}$ = 7.0 Hz, CH$_3$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 26.6 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 131.54 (d, $^2J_{CP}$ = 8.4 Hz, C), 129.74 (d, J_{CP} = 7.2 Hz, CH), 128.49 (d, J_{CP} = 2.4 Hz, CH), 126.83 (d, J_{CP} = 3.6 Hz, CH), 62.12 (d, $^2J_{CP}$ = 6.0 Hz, CH$_2$), 33.73 (d, $^1J_{CP}$ = 137.6 Hz, CH$_2$), 16.32 (d, $^3J_{CP}$ = 6.0 Hz, CH$_3$); m/z (ES) 229 (M+1) (100%); IR (KBr, cm^{-1}) 3525.2 (m), 2930.6 (s), 1608.2 (s), 1488.8 (m), 1391.4 (m), 1207.9 (s), 1056.3 (s), 1037.1 (m), 937.6 (m), 843.8 (m), 778.1 (m), 626.0 (m).

Preparation of 1,3-*bis*(diethoxyphosphinylmethyl)benzene (71)

The title compound was prepared using Plater's method.[9] A flame-dried 100 mL, three-necked round-bottomed flask, equipped with a thermometer, magnetic stirring bar and condenser was purged with nitrogen for 10 min. The flask was charged with 1,3-*bis*(bromomethyl)benzene (5.00 g, 18.94 mmol) and triethylphosphite (9.44 g, 9.74 mL, 56.83 mmol). The mixture was gradually heated to 160 °C over 2 h and maintained for a further 6 h. After cooling the crude reaction mixture to room temperature, it was then distilled using a Kugelröhr oven (100 °C, 0.05 mbar) to distill off any starting materials or by-products to give a clear colourless oil (7.02 g, 98 %). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.21-7.10 (4 H, m, ArH), 3.94 (8 H, m, CH$_2$), 3.06 (4 H, d, $^2J_{HP}$ = 21.9 Hz, PhCH$_2$), 1.16 (12 H, t, $^3J_{HH}$ = 7.3 Hz, CH$_3$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.21-7.10 (4 H, m, ArH), 3.95 (8 H, m, CH$_2$), 3.06 (4 H, s, PhCH$_2$), 1.16 (12 H, t, $^3J_{HH}$ = 7.0 Hz, CH$_3$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 26.4 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 131.90 (d, $^2J_{CP}$ = 12.0 Hz, C), 131.16 (t, J_{CP} = 7.2 Hz, CH), 128.67 (t, J_{CP} = 3.6 Hz, CH), 128.33 (t, J_{CP} = 4.8 Hz, CH), 62.08 (d, $^2J_{CP}$ = 7.1 Hz, CH$_2$), 33.61 (d, $^1J_{CP}$ = 138.8 Hz, CH$_2$), 16.35 (d, $^3J_{CP}$ = 6.0 Hz, CH$_3$); m/z (ES) 379 (M+1) (100 %); IR (KBr, cm^{-1}) 3524.0 (m), 2929.9 (s), 1606.7 (s), 1489.1 (m), 1390.7 (m), 1207.4 (s), 1057.0 (s), 1035.8 (s), 937.4 (s), 844.8 (s), 779.2 (s), 624.9 (m).

Preparation of Benzylphosphonic acid (81)

The title compound was prepared by an adaptation of Yuan's method.[10] A 100 mL, round-bottomed flask, equipped with a magnetic stirring bar and condenser, was charged with diethyl benzylphosphonate (74) (2.00 g, 8.76 mmol) and conc. HCl (12 M, 20 mL). The mixture was refluxed for 27 h and the water was removed *in vacuo* to give the crude product. Traces of HCl and water were removed on a Schlenk line to give the desired product as white fluffy solid (1.42 g, 94 %). mp 159-162 °C (from H_2O) (lit.173-175 °C).[11] ^1H NMR (300 MHz, D_2O) δ_H 7.26-7.10 (5 H, m, ArH), 3.04 (2 H, d, $^2J_{HP}$ = 21.2 Hz, $PhCH_2$); $^{31}P\{^1H\}$ NMR (121 Hz, D_2O) δ_P 25.9; ^{13}C NMR (75 MHz, D_2O) δ_C 132.91 (d, $^2J_{CP}$ = 9.6 Hz, C), 129.58 (d, J_{CP} = 7.2 Hz, CH), 128.67 (d, J_{CP} = 3.6 Hz, CH), 126.74 (s, CH), 34.42 (d, $^1J_{CP}$ = 130.4 Hz, CH_2); m/z (ES^+) 173 (M+1) (100%), (ES^-) 171 (M-1) (100%); IR (Solid State, cm^{-1}) 2756.4 (br w), 2286.1 (br w), 1496.6 (w), 1457.8 (w), 1258.7 (m), 1201.9 (m), 1072.9 (m), 979.7 (s), 939.2 (s), 777.8 (s) 691.4 (s).

Preparation of 1,3-*bis*(phosphonomethyl)benzene (82)

The title compound was prepared by an adaptation of Yuan's method.[10] A 100 mL, round-bottomed flask, equipped with a magnetic stirring bar and condenser, was charged with 1,3-*bis*(diethoxyphosphinylmethyl)benzene (71) (2.11 g, 5.58 mmol) and conc. HCl (12 M, 20 mL). The mixture was refluxed for 27 h and the water was removed *in vacuo* to give the crude product. Traces of HCl and water were removed on a Schlenk line to give the desired product as white fluffy solid (1.57 g, 100 %). mp 200-203 °C (from H_2O). ^1H NMR (300 MHz, D_2O) δ_H 7.21-7.10 (4 H, m, ArH), 3.04 (4 H, d, $^2J_{HP}$ = 21.5 Hz, $PhCH_2$); $^{31}P\{^1H\}$ NMR (121 Hz, D_2O) δ_P 25.5 (s); ^{13}C NMR (75 MHz, D_2O) δ_C 132.85 (t, $^2J_{CP}$ = 4.8 Hz, C), 130.67 (t, J_{CP} = 6.0 Hz, CH), 128.89 (t, J_{CP} = 3.6 Hz, CH), 128.00 (t, J_{CP} = 4.8 Hz, CH), 34.07 (d, $^1J_{CP}$ = 131.6 Hz, CH_2); m/z (ES) 267 (M+1) (100%), (ES^-) 265 (M-1) (10%); IR (Solid State, cm^{-1}) 2748.6 (br w), 2278.4 (br w), 1486.0 (w), 1163.2 (m), 1105.2 (m), 937.3 (s), 760.7 (s), 700.3 (s).

Preparation of Benzylphosphonic dichloride (80)

The title compound was prepared by an adaptation of Harger's method.[12] A 100 mL, three-necked round-bottomed flask, was equipped with a magnetic stirring bar, thermometer, condenser and drying tube. The flask was charged with benzylphosphonic acid (81) (2.50 g, 14.52 mmol), thionyl chloride (20.74 g, 12.72 mL, 174.3 mmol) and a catalytic amount of DMF (1 drop). The reaction was heated at 100 °C for 3 h and ^{31}P NMR spectroscopy showed no presence of starting material. The reaction mixture was allowed to cool to room temperature and the excess thionyl chloride was removed *in vacuo* to give the crude product. This was distilled in a Kugelröhr oven (130 °C, 0.01 mbar) to give a white crystalline product

(3.14 g, 100%). mp 65-67 °C (lit 57.5 °C)[13]. ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.35-7.27 (5 H, m, ArH), 3.87 (2 H, d, $^2J_{HP}$ = 17.5 Hz, PhCH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 45.6 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 130.46 (d, J_{CP} = 8.4 Hz, CH), 129.13 (d, J_{CP} = 4.8 Hz, CH), 128.69 (d, J_{CP} = 6.0 Hz, CH), 127.90 (d, $^2J_{CP}$ = 12.0 Hz, C), 49.84 (d, $^1J_{CP}$ = 94.5 Hz, CH$_2$); m/z (EI) 208/210/212 (M$^+$) (5%); IR (Solid State, cm^{-1}) 2959.6 (m), 1736.5 (br m), 1493.1 (m), 1456.5 (m), 1395.6 (m), 1260.0 (s), 1070.6 (m), 1028.5 (m), 923.9 (s), 838.5 (s), 778.1 (m), 722.4 (m).

Attempted preparations of diphenyl benzylphosphine oxide derivatives (77 & 78)

Reaction Part A - Reaction of aryl fluorous lithiate (21) with diethyl benzylphosphonate (74).

A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-(1H,1H,2H,2H-perfluorodecyl)bromobenzene (21) (2.50 g, 4.15 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding diethyl ether (30 mL) and THF (30 mL) to the main flask. Diethyl ether (30 mL) and n-butyllithium (2.56 mL, 1.6 M solution in hexane, 4.10 mmol) were both added to the dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The n-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -30 °C. The reaction was stirred at this temperature for 1 h, maintaining it at -30 °C. The dropping funnel was charged with diethyl ether (30 mL) and diethyl benzylphosphonate (74) (0.378 g, 1.66 mmol). The solution was added dropwise over 60 min with the internal temperature never allowed to rise over -30 °C. The reaction mixture was then allowed to warm to room temperature overnight. Water (40 mL) was added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude product.

Reaction Part B - Reaction of aryl lithiate with diethyl benzylphosphonate (74).

A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-bromoanisole (0.94 g, 5.00 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding diethyl ether (30 mL) and THF (30 mL) to the main flask. Diethyl ether (30 mL) and n-butyllithium (4.76 ml, 0.98 M solution in hexane, 4.67 mmol) were both added to the

dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -30 °C. The reaction was stirred at this temperature for 1 h, maintaining it at -30 °C. The dropping funnel was charged with diethyl ether (30 mL) and diethyl benzylphosphonate (74) (0.380 g, 1.67 mmol). The solution was added dropwise over 60 min with the internal temperature never allowed to rise over -30 °C. The reaction mixture was then allowed to warm to room temperature overnight. Water (40 mL) was added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude product.

Reaction Part C - Reaction of aryl Grignard reagent with diethyl benzylphosphonate (74).

A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with magnesium turnings (0.30 g, 12.48 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding diethyl ether (30 mL) to the main flask. Diethyl ether (20 mL) and 4-bromoanisole (0.94 g, 5.00 mmol) were both added to the dropping funnel and were added dropwise to the main flask. If there was no exotherm observed, iodine was added to the main flask to initiate the reaction. The reaction mixture was refluxed for 2 h. After cooling to room temperature the mixture was filtered under nitrogen to give the Grignard reagent. This was then cooled to 0 °C. The dropping funnel was charged with diethyl ether (30 mL) and diethyl benzylphosphonate (74) (1.02 g, 4.46 mmol). The solution was added dropwise over 60 min with the internal temperature never allowed to rise over 0 °C. The reaction mixture was finally heated to 45 °C overnight. 6M HCl (20 mL) was then added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude product.

Reaction Part D - Reaction of aryl lithiate with benzylphosphonic dichloride (80).

A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-bromoanisole (0.805 g, 4.31 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding diethyl ether (30 mL) and THF (30 mL) to the main flask. Diethyl ether (30 mL) and *n*-

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butyllithium (2.51 mL, 0.98 M solution in hexane, 4.02 mmol) were both added to the dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -30 °C. The reaction was stirred at this temperature for 1 h. The dropping funnel was charged with diethyl ether (30 mL) and benzylphosphonic dichloride (80) (0.30 g, 1.44 mmol). The solution was added dropwise over 60 min with the internal temperature never allowed to rise over -30 °C. The reaction mixture was then allowed to warm to room temperature overnight. Water (40 mL) was added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude product.
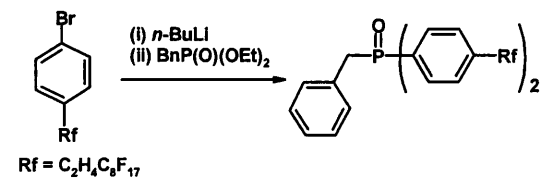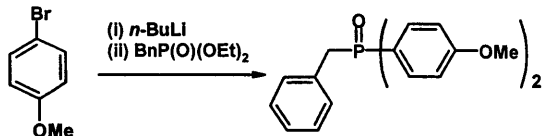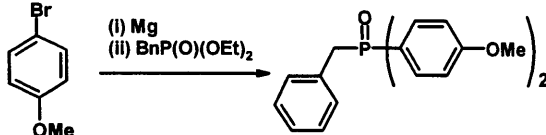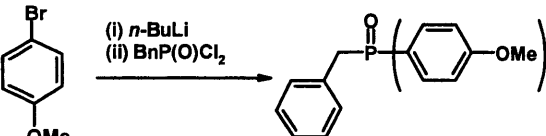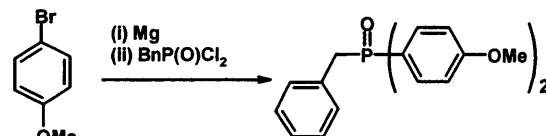
Reaction Part E - Reaction of aryl Grignard reagent with benzylphosphonic dichloride (80).
A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with magnesium turnings (0.097 g, 4.02 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding diethyl ether (30 mL) to the main flask. Diethyl ether (20 mL) and 4-bromoanisole (0.805 g, 4.31 mmol) were both added to the dropping funnel and were added dropwise to the main flask. If there was no exotherm observed, iodine was added to the main flask to initiate the reaction. The reaction mixture was refluxed for 2 h. After cooling to room temperature, the mixture was filtered under nitrogen to give the Grignard reagent. This was then cooled to 0 °C. The dropping funnel was charged with diethyl ether (30 mL) and diethyl benzylphosphonic dichloride (80) (0.30 g, 1.44 mmol). The solution was added dropwise over 60 min with the internal temperature never allowed to rise over 0 °C. The reaction mixture was heated to 45 °C overnight. 6 M HCl (20 mL) was then added and the reaction mixture was stirred for 20 min. The organic layer was separated, dried with magnesium sulphate and the solvent was removed using a reduced pressure rotary evaporator to give the crude product.

Rxn	Scheme	^{31}P NMR Shifts in Crude Product	%^{a}
A	Rf = $C_2H_4C_6F_{17}$	29.1	3
		29.3	82
		31.8	13
		31.9	2

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	Reaction	δ (ppm)[a]	Integration
B	4-bromoanisole → (i) n-BuLi (ii) BnP(O)(OEt)₂ → BnP(O)(4-C₆H₄OMe)₂	29.1	4
		29.3	14
		31.7	65
		31.8	14
		36.8	3
C	4-bromoanisole → (i) Mg (ii) BnP(O)(OEt)₂ → BnP(O)(4-C₆H₄OMe)₂	18.7	3
		29.1	17
		29.3	18
		31.4	54
		32.1	4
		34.3	2
		44.2	2
D	4-bromoanisole → (i) n-BuLi (ii) BnP(O)Cl₂ → BnP(O)(4-C₆H₄OMe)₂	18.9	3
		19.0	3
		20.4	23
		20.9	3
		23.7	28
		23.7	13
		24.3	3
		26.5	15
		26.6	9
E	4-bromoanisole → (i) Mg (ii) BnP(O)Cl₂ → BnP(O)(4-C₆H₄OMe)₂	20.3	10
		23.7	2
		24.0	3
		27.7	7
		29.8	2
		31.8	27
		39.6	34
		40.6	7
		41.6	8

[a] by ^{31}P NMR Spectroscopy integration determined.

Table 6.1. *Summary of results for the attempted synthesis of (77 & 78).*

Preparation of *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (86)

The title compound was prepared by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-

equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with 4-(1H,1H,2H,2H-perfluorodecyl)bromobenzene (21) (5.00 g, 8.29 mmol) and was degassed under high vacuum. The flask was again filled with nitrogen before adding dry diethyl ether (20 mL) and dry THF (30 mL) to the main flask. Dry diethyl ether (30 mL) and n-butyllithium (5.77 mL, 1.42 M solution in hexane, 5.77 mL, 8.20 mmol) were both added to the dropping funnel and the flask was cooled to -30 °C using a dry ice/acetonitrile bath. The n-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -30 °C. The reaction mixture was stirred at this temperature for 2 h. After rinsing the dropping funnel with dry THF (10 mL), it was charged with dry THF (10 mL) and diethylphosphoramidous dichloride (0.679 g, 0.57 mL, 3.90 mmol). The diethylphosphoramidous dichloride solution was added dropwise over 15 min with the internal temperature never being allowed to rise above -30 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight. After cooling the reaction to 0 °C, conc. HCl (2 mL, 24.0 mmol) was added dropwise maintaining the internal temperature below 5 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 4 h. The reaction was quenched with water (50 mL), the organic layer was separated and the aqueous layer was extracted with BTF (3 x 50 mL). The combined organic layers were dried (MgSO$_4$) and the solvent was removed to give the crude product, which was washed with cold ether to give a white solid (5.53 g, 63%). mp 107-108 °C (from diethyl ether). Anal. Calcd for C$_{32}$H$_{17}$F$_{34}$OP: C, 35.12; H, 1.57. Found C, 35.13; H, 1.51; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 8.00 (1 H, d, $^1J_{HP}$ = 481.9 Hz, PH), 7.59 (4 H, dd, $^3J_{HP}$ = 13.8 Hz, $^3J_{HH}$ = 8.0 Hz, ArH), 7.30 (4 H, dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{PH}$ = 2.2 Hz, ArH), 2.94-2.88 (4 H, m, CH$_2$), 2.40-2.23 (4 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 8.00 (1 H, s, PH), 7.59 (4 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.30 (4 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 2.94-2.88 (4 H, m, CH$_2$), 2.40-2.23 (4 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.92 (6 F, t, $^4J_{FF}$ = 9.1 Hz, CF$_3$), -114.57 (4 F, t, $^4J_{FF}$ = 10.2 Hz, α-CF$_2$), -121.74 (4 F, m, CF$_2$), -121.98 (8 F, m, 2 x CF$_2$), -122.80 (4 F, m, CF$_2$), -123.49 (4 F, m, CF$_2$), -126.22 (4 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 20.6 (s); ^{31}P NMR (121 Hz, CDCl$_3$) δ_P 20.6 (dquint., $^1J_{PH}$ = 481.9 Hz, $^3J_{PH}$ = 13.8 Hz, PH); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 144.17 (d, $^4J_{CP}$ = 2.4 Hz, C), 131.25 (d, J_{CP} = 12.0 Hz, CH), 129.87 (d, $^1J_{CP}$ = 102.9 Hz, C), 128.96 (d, J_{CP} = 13.2 Hz, CH), 32.47 (t, $^2J_{CF}$ = 22.7 Hz, CH$_2$), 26.60 (CH$_2$); m/z (FAB) 1095 (MH$^+$, 100%); IR (Solid State, cm^{-1}) 1604.9 (w), 1198.1 (br,s), 1145.1 (s), 1114.2 (s).

Preparation of benzyl *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (77)

The title compound was prepared by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (86) (0.500 g, 0.457 mmol) and sodium hydride (60 % in oil, 0.018 g, 0.457 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (50 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. Dry THF (10 mL) and benzyl bromide (0.117 g, 0.08 ml, 0.686 mmol) were both added to the dropping funnel. The benzyl bromide solution was added dropwise to the main flask over 15 min. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (10 mL) and stirred for 30 min. The reaction mixture was extracted with BTF (3 x 50 mL), dried (Na_2SO_4) and concentrated to give the crude product as a white powder. This was washed with hot petroleum ether (40-60 °C) to give the desired product as a white solid (0.48 g, 89 %). mp 164-166 °C (from petroleum ether). Anal. Calcd for $C_{39}H_{23}F_{34}OP$: C, 39.55; H, 1.96. Found C, 39.68; H, 2.00; ^1H NMR (400 MHz, $CDCl_3$) δ_H 7.67 (4 H, dd, $^3J_{PH}$ = 10.4 Hz, $^3J_{HH}$ = 7.7 Hz, ArH), 7.31 (4 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.22-7.18 (3 H, m, ArH), 7.16-7.11 (2 H, m, ArH), 3.67 (2 H, d, $^2J_{PH}$ = 13.6 Hz, $PhCH_2$), 3.00-2.96 (4 H, m, CH_2), 2.47-2.33 (4 H, m, CH_2); $^1H\{^{31}P\}$ NMR (300 MHz, $CDCl_3$) δ_H 7.67 (4 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.31 (4 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.22-7.18 (3 H, m, ArH), 7.16-7.11 (2 H, m, ArH), 3.67 (2 H, s, $PhCH_2$), 3.00-2.96 (4 H, m, CH_2), 2.47-2.33 (4 H, m, CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ_F -80.77 (6 F, t, $^4J_{FF}$ = 8.6 Hz, CF_3), -114.47 (4 F, t, $^4J_{FF}$ = 10.4 Hz, α-CF_2), -121.65 (4 F, m, CF_2), -121.85 (8 F, m, 2 x CF_2), -122.67 (4 F, m, CF_2), -123.37 (4 F, m, CF_2), -126.08 (4 F, m, CF_2); $^{31}P\{^1H\}$ NMR (121 Hz, $CDCl_3$) δ_P 29.1 (s); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 143.26 (C), 131.70 (d, J_{CP} = 9.2 Hz, CH), 131.07 (d, $^2J_{CP}$ = 7.0 Hz, C), 130.90 (d, $^1J_{CP}$ = 102.0 Hz, C), 130.14 (d, J_{CP} = 4.5 Hz, CH), 128.47 (d, J_{CP} = 13.0 Hz, CH), 128.37 (CH), 126.86 (CH), 38.20 (d, $^1J_{CP}$ = 66.1 Hz, $PhCH_2$), 32.50 (t, $^2J_{CF}$ = 22.5 Hz, CH_2), 26.48 (CH_2); m/z (FAB) 1184 (M^+, 100%); IR (Solid State, cm^{-1}) 1605.4 (w), 1197.0 (br s), 1144.8 (s), 1115.2 (m).

Attempted preparation of benzyl *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (77) using KOH

The title compound was attempted by an adaptation of Tsvetkov's method.[15] A 50 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and condenser

and attached to a Schlenk line. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide **(86)** (0.500 g, 0.457 mmol), benzyl bromide (0.086 g, 0.06 mL, 0.503 mmol), potassium hydroxide (0.250 g, 4.46 mmol), tetra-*n*-butylammonium iodide (0.017 g, 0.046 mmol) and BTF (25 mL). The reaction mixture was heated to 110 °C and allowed to stir for 15 h. The solvent was removed to give a pale brown solid. Crude ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 29.0 (s), 31.9 (s) & 32.9 (s) ppm. Major peak at 31.9 ppm determined to be benzyl *bis*-arylphosphinic ester **(89)**. *m/z* (FAB) 1200 (M$^+$, 62%).

Attempted preparation of benzyl *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (77) using *n*-BuLi

A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, pressure-equalising dropping funnel, low temperature thermometer and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide **(86)** (0.500 g, 0.457 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (70 mL) and diethyl ether (35 mL) to the main flask. Dry diethyl ether (15 mL) and *n*-butyllithium (5.77 mL, 1.42 M solution in hexane, 8.20 mmol) were both added to the dropping funnel and the flask was cooled to -10 °C using a dry ice/acetonitrile bath. The *n*-butyllithium solution was added dropwise over 60 min with the internal temperature never being allowed to rise above -10 °C. The reaction mixture was stirred at this temperature for 2 h. After rinsing the dropping funnel with dry THF (10 mL), it was charged with dry THF (10 mL) and benzyl bromide (0.117 g, 0.08 mL, 0.686 mmol). The benzyl bromide solution was added dropwise over 30 min with the internal temperature never being allowed to rise above -10 °C. The reaction mixture was then allowed to warm to room temperature and stirred overnight (20 h). The reaction was cooled to 0 °C and slowly quenched with HCl (1.5 M, 10 mL) and stirred for 30 min. The reaction mixture was extracted with BTF (3 x 50 mL), dried (MgSO$_4$) and concentrated to give the crude product as a yellow oil. Both the crude ^{31}P{^{1}H} and ^{1}H NMR spectra showed no signs of the desired product.

Attempted preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine oxide]benzene (90) (all in together)

The preparation of the title compound was attempted by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under

high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide **(86)** (0.468 g, 0.428 mmol), 1,3-*bis*(bromomethyl)benzene (0.056 g, 0.214 mmol) and sodium hydride (60 % in oil, 0.022 g, 0.428 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (100 mL) to the main flask. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (1 mL) and stirred for 10 min. The organic layer was extracted with BTF (3 x 50 mL), dried (MgSO$_4$) and concentrated to give the crude product as a white powder. Crude ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 29.3, 29.0 & 20.5 ppm. Peak at δ_P 29.3 ppm determined to be 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl) phosphine oxide]benzene. *m\z* (FAB) 2292 (MH$^+$, 12%). Peak at δ_P 29.3 ppm determined to be 1-[methylbromide]-3-[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecyl-phenyl)phosphine oxide]benzene. *m\z* (FAB) 1279/1277 (MH$^+$, 9%).

Attempted preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine oxide]benzene (90) using standard conditions

The preparation of the title compound was attempted by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide **(86)** (1.000 g, 0.911 mmol) and sodium hydride (60 % in oil, 0.0364 g, 0.911 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (80 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. 1,3-*Bis*(bromomethyl)benzene (0.191 M solution in THF, 2.38 ml, 0.455 mmol) was added slowly to the main flask. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (1 mL) and stirred for 10 min. The organic layer was extracted with BTF (3 x 50 mL), dried (MgSO$_4$) and concentrated to give the crude product as a white solid. This was determined to be starting material by ^{31}P{^{1}H} and ^{1}H NMR spectroscopy.

Attempted preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine oxide]benzene (90) using standard conditions with BTF as a co-solvent

The preparation of the title compound was attempted by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under

high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (86) (1.212 g, 1.107 mmol) and sodium hydride (60 % in oil, 0.044 g, 1.107 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (100 mL) and BTF (10 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. Dry THF (15 mL) and 1,3-*bis*(bromomethyl)benzene (0.146 g, 0.554 mmol) were added slowly to the main flask. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (1 mL) and stirred for 10 min. The organic layer was extracted with BTF (3 x 50 mL), dried (MgSO$_4$) and concentrated to give the crude product as a white solid. This was determined to be starting material by ^{31}P$\{^1$H$\}$ and ^{1}H NMR spectroscopy.

Attempted preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)-phosphine oxide]benzene (90) using standard conditions and heat

The preparation of the title compound was attempted by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (86) (1.212 g, 1.107 mmol) and sodium hydride (60 % on oil, 0.044 g, 1.107 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (100 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. Dry THF (15 mL) and 1,3-*bis*(bromomethyl)benzene (0.146 g, 0.554 mmol) were added slowly to the main flask. The reaction mixture was heated to reflux and then stirred overnight at this temperature. The reaction was cooled and slowly quenched with water (1 mL) and stirred for 10 min. The THF layer was decanted and the solid left was washed with fresh THF (3 x 20 mL). The solid was dried under vacuum and the THF layer was concentrated to give a second crude product. This was determined to be starting material by ^{31}P$\{^1$H$\}$ and ^{1}H NMR spectroscopy.

Preparation of 4-(1*H*,2*H*-perfluorooct-1-ene)bromobenzene (93)

The title compound was prepared by Genêt's method.[3] A 250 mL, round-bottomed flask equipped with a magnetic stirring bar was charged with 4-bromobenzene diazonium tetrafluoroborate (17) (10.62 g, 39.21 mmol), methanol (80 mL) and palladium acetate (200 mg, 0.89 mmol). The mixture was stirred as 1*H*,1*H*,2*H*-perfluorooct-1-ene (13.57 g, 39.21 mmol) was added dropwise over 15 min. The mixture was stirred for a further 15 min until

the colour changes from orange to black. The solvent was removed using a rotary evaporator, the residue was redissolved in petroleum ether (40-60 °C) and filtered through silica to remove the Pd catalyst. The solvent was finally removed using a rotary evaporator to give a white crystalline solid (17.32 g, 89%). mp <30 °C (from petroleum ether) (lit., <30 °C)[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.34 (2 H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 6.99 (2 H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 7.05 (1 H, dt, $^3J_{HH}$ = 16.1 Hz, $^4J_{HF}$ = 2.2 Hz, ArCH), 6.13 (1 H, dt, $^3J_{HH}$ = 16.1 Hz, $^3J_{HF}$ = 11.9 Hz, CHC$_6$F$_{13}$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.87 (3 F, t, $^4J_{FF}$ = 8.3 Hz, CF$_3$), -111.35 (2 F, t, $^4J_{FF}$ = 11.2 Hz, α-CF$_2$), -121.67 (2 F, m, CF$_2$), -122.94 (2 F, m, CF$_2$), -123.21 (2 F, m, CF$_2$), -126.23 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.54 (t, $^3J_{CF}$ = 8.7 Hz, CH), 132.38 (C), 132.19 (CH), 129.06 (CH), 124.47 (C), 115.02 (t, $^2J_{CF}$ = 23.1 Hz, CH); m/z (EI) 500/2 (M$^+$, 56%); IR (Solid State, cm^{-1}) 1658.6 (w), 1245.3 (m), 1194.0 (br), 1143.2 (s), 1111.7 (m).

Preparation of 4-(1H,1H,2H,2H-perfluorooctyl)bromobenzene (94)

The title compound was prepared by Genêt's method.[3] A suspension of the 4-(1H,2H-perfluorooct-1-ene)bromobenzene (93) (33.90 g, 67.38 mmol) and rhodium on carbon (200 mg) in DCM (50 mL) was placed under hydrogen (50 bar) at 20 °C for 24 h. At the end of the reaction the solvent was removed using a rotary evaporator, the residues were redissolved in petroleum ether (40-60 °C) and filtered through silica. The solvent was finally removed to give a white solid (32.87 g, 97%). mp 29-31 °C (from petroleum ether) (lit., 30 °C).[3] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.34 (2 H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 6.99 (2 H, d, $^3J_{HH}$ = 8.4 Hz, ArH), 2.80-2.75 (2 H, m, CH$_2$), 2.34-2.15 (2 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.07 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.72 (2 F, t, $^4J_{FF}$ = 13.8 Hz, α-CF$_2$), -122.01 (2 F, m, CF$_2$), -123.00 (2 F, m, CF$_2$), -123.57 (2 F, m, CF$_2$), -126.28 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.03 (C), 131.02 (CH), 130.02 (CH), 120.56 (C), 32.73 (t, $^2J_{CF}$ = 21.9 Hz, CH$_2$), 25.97 (CH$_2$); m/z (EI) 502/4 (M$^+$, 79%); IR (Solid State, cm^{-1}) 1489.3 (w), 1198.0 (br), 1144.0 (s), 1113.8 (m).

Preparation of bis(4-1H,1H,2H,2H-perfluorooctylphenyl)phosphine oxide (96)

The title compound was prepared similarly to bis(4-1H,1H,2H,2H-perfluorodecylphenyl)phosphine oxide (86), using 4-(1H,1H,2H,2H-perfluorooctyl)bromobenzene (94) (15.10 g, 30.01 mmol). The crude product was dissolved in hot hexane. Upon cooling an orange solid precipitated and the filtrate was decanted off. The solvent was removed and the solid was recrystallised from hexane to give a cream solid (7.61 g, 57%). mp 72-73 °C (from hexane). Anal. Calcd for C$_{28}$H$_{17}$F$_{26}$OP: C, 37.60; H, 1.92. Found C, 37.75; H, 2.01; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 8.00 (1 H, d, 482.4 Hz, PH), 7.59 (4

H, dd, $^3J_{PH}$ = 13.5 Hz, $^3J_{HH}$ = 8.1 Hz, ArH), 7.29 (4 H, dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{PH}$ = 2.4 Hz, ArH), 2.94-2.88 (4 H, m, CH$_2$), 2.40-2.23 (4 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 8.00 (1 H, s, PH), 7.59 (4 H, d, $^3J_{HH}$ = 8.1 Hz, ArH), 7.29 (4 H, d, $^3J_{HH}$ = 8.1 Hz, ArH), 2.94-2.88 (4 H, m, CH$_2$), 2.40-2.23 (4 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.89 (3 F, t, $^4J_{FF}$ = 9.6 Hz, CF$_3$), -114.58 (2 F, t, $^4J_{FF}$ = 14.1 Hz, α-CF$_2$), -121.94 (2 F, m, CF$_2$), -122.92 (2 F, m, CF$_2$), -123.52 (2 F, m, CF$_2$), -126.22 (2 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 20.6 (s); ^{31}P NMR (121 Hz, CDCl$_3$) δ_P 20.6 (dquint., $^1J_{PH}$ = 482.4 Hz, $^3J_{PH}$ = 14.6 Hz, PH); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 144.20 (d, $^4J_{CP}$ = 1.6 Hz, C), 131.23 (d, J_{CP} = 11.8 Hz, CH), 129.80 (d, $^1J_{CP}$ = 103.2 Hz, C), 128.94 (d, J_{CP} = 13.1 Hz, CH), 32.45 (t, $^2J_{CF}$ = 22.3 Hz, CH$_2$), 26.54 (CH$_2$); m/z (FAB) 895 (M+1, 100%); IR (Solid State, cm^{-1}) 1604.8 (w), 1180.8 (br s), 1140.1 (s), 1073.8 (s).

Preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)phosphine oxide]benzene (97)

The title compound was prepared by an adaptation of Curran's method.[14] A 250 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)phosphine oxide (96) (3.856 g, 4.311 mmol) and sodium hydride (60 % on oil, 0.172 g, 4.311 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (40 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. Dry THF (15 mL) and 1,3-*bis*(bromomethyl)benzene (0.554 g, 2.100 mmol) were added slowly to the main flask. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (1 mL) and stirred for 10 min. The organic layer was extracted with CHCl$_3$ (3 x 50 mL), dried (MgSO$_4$) and concentrated to give the crude product as a brown oil. This was washed with hot petroleum ether (40-60 °C) to the desired product as a white powder (3.267 g, 82 %). mp 162-164 °C (from petroleum ether). Anal. Calcd for C$_{64}$H$_{40}$F$_{52}$O$_2$P$_2$: C, 40.65; H, 2.13. Found C, 40.64; H, 2.11; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.50 (8 H, dd, $^3J_{HP}$ = 11.0 Hz, $^3J_{HH}$ = 8.0 Hz, ArH), 7.14 (8 H, dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HP}$ = 1.6 Hz, ArH), 7.11 (1 H, br s, ArH^2), 6.86 (1 H, m, ArH^5), 6.82 (2 H, d, $^3J_{HH}$ = 7.3 Hz, ArH^4), 3.46 (4 H, d, $^2J_{HP}$ = 13.5 Hz, PhCH$_2$), 2.86-2.81 (8 H, m, CH$_2$), 2.34-2.17 (8 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.50 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.14 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.11 (1 H, s, ArH^2), 6.86 (1 H, m, ArH^5), 6.82 (2 H, d, $^3J_{HH}$ = 7.3 Hz, ArH^4), 3.46 (4 H, s, PhCH$_2$), 2.86-2.81 (8 H, m, CH$_2$), 2.34-2.17 (8 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.13 (12 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.82 (8 F, t, $^4J_{FF}$ = 13.8 Hz, α-CF$_2$), -122.12

(8 F, m, CF_2), -123.12 (8 F, m, CF_2), -123.78 (8 F, m, CF_2), -126.43 (8 F, m, CF_2); $^{31}P\{^1H\}$ NMR (121 Hz, $CDCl_3$) δ_P 29.4 (s); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 143.24 (C), 132.27 (t, J_{CP} = $J_{CP'}$ = 4.4 Hz, CH), 131.96 (d, J_{CP} = 9.5 Hz, CH), 131.57 (d, J_{CP} = 9.5 Hz, CH), 130.60 (d, $^1J_{CP}$ = 100.7 Hz, C), 128.55 (d, J_{CP} = 12.1 Hz, CH), 37.88 (d, $^1J_{CP}$ = 66.5 Hz, $PhCH_2$), 32.38 (t, $^2J_{CF}$ = 22.4 Hz, CH_2), 26.38 (CH_2); Despite several attempts using different deuterated solvents and high field NMR spectroscopy, two peaks are missing in the ^{13}C NMR spectrum maybe due to overlapping of the aryl peaks. m/z (FAB) 1891 (M+1, 100%); IR (Solid State, cm^{-1}) 1604.3 (w), 1180.8 (br s), 1139.5 (s), 1073.2 (s).

Preparation of 1,3-*bis*[methyldiphenylphosphine oxide]benzene (100)

The title compound was prepared by an adaptation of Curran's method.[14] A 100 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with diphenylphosphine oxide (99) (1.186 g, 5.866 mmol) and sodium hydride (60 % in oil, 0.235 g, 5.866 mmol). The flask was degassed under high vacuum and was again filled with nitrogen. This was repeated a further two times before adding dry THF (60 mL) to the main flask. The reaction mixture was allowed to stir for 1 h. 1,3-*bis*(bromomethyl)benzene (0.191 M solution in THF, 15.36 mL, 2.933 mmol) was added slowly to the main flask. The reaction mixture was then allowed to stir overnight at room temperature. The reaction was slowly quenched with water (1 mL) and stirred for 10 min. The THF was removed and the residue was extracted with $CHCl_3$ (3 x 50 mL), dried ($MgSO_4$) and concentrated to give the crude product as a white solid. This was washed with hot petroleum ether (40-60 °C) to give the desired product as a white solid (1.51 g, 98 %). mp 91-93 °C (from petroleum ether) (lit., 77-79 °C).[16] Anal. Calcd for $C_{32}H_{28}O_2P_2 \cdot H_2O$: C, 73.27; H, 5.78. Found C, 73.26; H, 5.25; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.56 (8 H, dd, $^3J_{HP}$ = 8.1 Hz, $^3J_{HH}$ = 7.3 Hz, ArH), 7.40-7.36 (4 H, m, ArH), 7.31 (8 H, td, $^3J_{HH}$ = 7.3 Hz, $^4J_{HP}$ = 2.4 Hz, ArH), 6.98 (1 H, s, ArH^2), 6.88-6.83 (1 H, m, ArH^5), 6.79 (2 H, d, $^3J_{HH}$ = 6.8 Hz, $ArH^{4,6}$), 3.46 (4 H, d, $^2J_{HP}$ = 13.7 Hz, $PhCH_2$); $^1H\{^{31}P\}$ NMR (300 MHz, $CDCl_3$) δ_H 7.56 (8 H, d, $^3J_{HH}$ = 7.3 Hz, ArH), 7.40-7.36 (4 H, m, ArH), 7.31 (8 H, t, $^3J_{HH}$ = 7.3 Hz, ArH), 6.98 (1 H, s, ArH^2), 6.88-6.83 (1 H, m, ArH^5), 6.79 (2 H, d, $^3J_{HH}$ = 6.8 Hz, $ArH^{4,6}$), 3.46 (4 H, s, $PhCH_2$); $^{31}P\{^1H\}$ NMR (121 Hz, $CDCl_3$) δ_P 30.0 (s); ^{13}C NMR (75 MHz, d^6-DMSO) δ_C 133.42 (d, $^1J_{CP}$ = 96.9 Hz, C), 132.26 (t, J_{CP} = $J_{CP'}$ = 4.8 Hz, CH), 131.94 (d, $^2J_{CP}$ = 9.8 Hz, C), 131.51 (CH), 130.69 (d, J_{CP} = 9.4 Hz, CH), 128.48 (d, J_{CP} = 11.6 Hz, CH), 128.11 (CH), 127.54 (CH), 36.04 (d, $^1J_{CP}$ = 66.2 Hz, $PhCH_2$); m/z (FAB) 507 (M+1, 30%); HRMS(FAB) 507.16425 (M+1. $C_{32}H_{29}O_2P_2$ requires 507.16428); IR (Solid State, cm^{-1}) 3436.1 (br, w), 1679.6 (m), 1486.7 (s), 1160.4 (s), 1117.7 (s), 694.9 (s).

Preparation of benzyl *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine (101)

The title compound was prepared by an adaptation of Chen's method.[17] A 50 mL, three-necked round-bottomed flask was equipped with a magnetic stirring bar, condenser and Rotaflow stopcock and attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with benzyl *bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorodecylphenyl)phosphine oxide (77) (0.105 g, 88.6 µmol). The flask was evacuated and refilled with nitrogen (x 3). The flask was then charged with dry BTF (20 mL), trichlorosilane (0.600 g, 0.45 mL, 4.43 mmol) and triethylamine (0.493 g, 0.68 mL, 4.88 mmol) and was then heated at 110 °C for 15.5 h. The reaction was quenched with a saturated solution of sodium hydrogen carbonate (0.5 mL) and was allowed to stir for 30 min. The solution was filtered through a pad of alumina and the alumina was washed with BTF (3 x 20 mL). The solvent was removed to give the desired product as a white solid (0.072 g, 70 %). mp 143-146 °C (from BTF). ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.26 (4 H, vt, $^3J_{PH}$ = $^3J_{HH}$ = 8.2 Hz, ArH), 7.09 (4 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.00-6.98 (3 H, m, ArH), 6.98-6.94 (2 H, m, ArH), 3.31 (2 H, s, PhCH$_2$), 2.86-2.80 (4 H, m, CH$_2$), 2.38-2.20 (4 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.26 (4 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.09 (4 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.00-6.98 (3 H, m, ArH), 6.98-6.94 (2 H, m, ArH), 3.31 (2 H, s, PhCH$_2$), 2.86-2.80 (4 H, m, CH$_2$), 2.38-2.20 (4 H, m, CH$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.86 (6 F, t, $^4J_{FF}$ = 8.9 Hz, CF$_3$), -114.60 (4 F, t, $^4J_{FF}$ = 7.1 Hz, α-CF$_2$), -121.70 (4 F, m, CF$_2$), -121.91 (8 F, m, 2 x CF$_2$), -122.72 (4 F, m, CF$_2$), -123.45 (4 F, m, CF$_2$), -126.15 (4 F, m, CF$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -11.5 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 139.82 (C), 137.26 (d, J_{CP} = 7.9 Hz, C), 136.28 (d, J_{CP} = 14.8 Hz, C), 133.32 (d, J_{CP} = 18.4 Hz, CH), 129.32 (d, J_{CP} = 6.5 Hz, CH), 128.40 (d, J_{CP} = 6.7 Hz, CH), 128.29 (CH), 125.97 (d, J_{CP} = 1.7 Hz, CH), 36.00 (d, $^1J_{CP}$ = 15.2 Hz, PhCH$_2$), 32.72 (t, $^2J_{CF}$ = 21.9 Hz, CH$_2$), 26.22 (CH$_2$); m/z (FAB) 1169 (MH$^+$, 13%). IR (Solid State, cm^{-1}) 1604.3 (w), 1180.4 (br s), 1141.8 (s), 1073.5 (s).

Preparation of 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)phosphine] benzene (103)

The title compound was prepared by an adaptation of van Koten's method.[18] A flame-dried 200 mL Schlenk flask was charged with phosphine oxide (97) (4.35 g, 2.30 mmol) and BTF (20 mL). The reaction mixture was heated to reflux before HSiCl$_3$ (2.18 g, 1.63 mL, 16.10 mmol) was added. The reaction was refluxed for 3 h, cooled and the excess HSiCl$_3$ was removed under vacuum. NaOH (3.22 g, 80.50 mmol) and degassed water (20 mL) were added to the flask and the reaction mixture was stirred for 15 min. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 x 30 mL). The combined organic

layers were dried (MgSO$_4$) and concentrated to give the desired product as an orange solid (1.77 g, 41 %). mp 80-82 °C (from hexane). Anal. Calcd for C$_{64}$H$_{40}$F$_{52}$P$_2$: C, 41.35; H, 2.17. Found C, 41.25; H, 2.17; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.19 (8 H, vt, $^3J_{HH}$ = $^3J_{HP}$ = 7.7 Hz, ArH), 7.04 (8 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 6.87 (1 H, m, ArH), 6.78 (1 H, s, ArH), 6.68 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 3.18 (4 H, s, PhCH$_2$), 2.82-2.76 (8 H, m, CH$_2$), 2.33-2.16 (8 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.19 (8 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.04 (8 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 6.87 (1 H, m, ArH), 6.78 (1 H, s, ArH), 6.68 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 3.18 (4 H, s, PhCH$_2$), 2.82-2.76 (8 H, m, CH$_2$), 2.33-2.16 (8 H, m, CH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -11.5 (s); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.13 (12 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -114.76 (8 F, t, $^4J_{FF}$ = 13.9 Hz, α-CF$_2$), -122.04 (8 F, m, CF$_2$), -123.03 (8 F, m, CF$_2$), -123.62 (8 F, m, CF$_2$), -126.35 (8 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 139.79 (C), 137.27 (d, $^2J_{CP}$ = 7.5 Hz, C), 136.56 (d, $^1J_{CP}$ = 15.4 Hz, C), 133.28 (d, J_{CP} = 18.5 Hz, CH), 131.65 (t, J_{CP} = $J_{CP'}$ = 8.5 Hz, CH), 130.48 (t, J_{CP} = $J_{CP'}$ = 6.8 Hz, CH), 128.34 (d, J_{CP} = 6.5 Hz, CH), 127.06 (d, J_{CP} = 4.0 Hz, CH), 35.98 (d, $^1J_{CP}$ = 15.7 Hz, PhCH$_2$), 32.72 (t, $^2J_{CF}$ = 22.0 Hz, CH$_2$), 26.21 (CH$_2$); m/z (FAB) 1858 (M$^+$, 72%); IR (Solid State, cm^{-1}) 1605.2 (w), 1193.9 (br s), 1145.8 (s), 1119.6 (m).

Preparation of 1,3-*bis*[methyldiphenylphosphine]benzene (102)

The title compound was prepared by an adaptation of van Koten's method.[18] A flame-dried 200 mL Schlenk flask was charged with phosphine oxide (100) (1.48 g, 2.82 mmol) and BTF (20 mL). The reaction mixture was heated to reflux before HSiCl$_3$ (2.68 g, 2.00 mL, 19.67mmol) was added. The reaction was refluxed for 3 h, cooled and the excess HSiCl$_3$ was removed under vacuum. NaOH (3.96 g, 99.45 mmol) and degassed water (20 mL) were added to flask and the reaction mixture was stirred for 15 min. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 x 30 mL). The combined organic layers were dried and concentrated to give the desired product as a white oil (1.21 g, 90 %). Anal. Calcd for C$_{32}$H$_{28}$P$_2$: C, 81.00; H, 5.95. Found C, 77.83; H, 5.63; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.65-7.58 (8 H, m, ArH), 7.50-7.48 (12 H, m, ArH), 7.22 (1 H, s, ArH), 7.19 (1 H, m, ArH), 7.06 (2 H, d, $^3J_{HH}$ = 7.8 Hz, ArH), 3.56 (4 H, s, PhCH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.65-7.58 (8 H, m, ArH), 7.50-7.48 (12 H, m, ArH), 7.22 (1 H, s, ArH), 7.19 (1 H, m, ArH), 7.06 (2 H, d, $^3J_{HH}$ = 7.8 Hz, ArH), 3.56 (4 H, s, PhCH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P -9.9 (s); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 138.47 (d, $^1J_{CP}$ = 15.4 Hz, C), 137.47 (d, $^2J_{CP}$ = 7.7 Hz, C), 133.02 (d, J_{CP} = 18.4 Hz, CH), 131.90 (CH), 131.32 (d, J_{CP} = 9.0 Hz, CH), 130.61 (t, J_{CP} = $J_{CP'}$ = 6.8 Hz, CH), 128.78 (CH), 128.48 (d, J_{CP} = 6.5 Hz, CH), 36.03 (d, $^1J_{CP}$ = 15.8 Hz, PhCH$_2$); m/z (FAB) 475 (MH$^+$, 100%); HRMS(FAB) 475.17441

[(M+1).$C_{32}H_{29}P_2$ requires 475.17445]; IR (Solid State, cm^{-1}) 1672.5 (m), 1488.8 (s), 1162.7 (s), 1100.7 (s), 892.2 (m).

Preparation of {2,6-*bis*[methyl(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenylphosphino)]phenyl} palladium chloride (113)

Method A

The title compound was prepared by an adaptation of Rimml and Venanzi's method.[19] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)phosphine]benzene (103) (0.387 g, 0.208 mmol), [PdCl$_2$(MeCN)$_2$] (0.054 g, 0.208 mmol) and DCM (10 mL). The reaction mixture was heated to reflux for 1.75 h. The reaction mixture was then cooled, washed with EtOH/H$_2$O (4 mL, 3:1) and the solvent was removed. The crude ^{31}P NMR spectrum showed a resonance at δ_P 31.4 ppm only. The reaction mixture was dissolved in 2-methoxyethanol (20 mL) and heated at 130 °C for 24 h. The reaction mixture was allowed to cool to room temperature before the solvent was removed. The crude material was dissolved in CHCl$_3$, filtered to remove any palladium metal and the solvent was removed to give an orange solid. This was then washed with hexane (3 x 10 mL) to give the desired product as a yellow/orange powder (0.197 g, 47 %). mp 140-142 °C (from CHCl$_3$). Anal. Calcd for $C_{64}H_{39}F_{52}ClP_2Pd$: C, 38.44; H, 1.97. Found C, 38.39; H, 1.96; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.74 (8 H, ddd, $^3J_{HH}$ = 8.0 Hz, $^3J_{HP}$ = 5.7 Hz, $^5J_{HP}$ = 2.7 Hz, ArH), 7.18 (8 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.05 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 6.98-6.93 (1 H, m, ArH), 6.68 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 3.88 (4 H, vt, J_{HP} = 4.7 Hz, PhCH$_2$), 2.87-2.80 (8 H, m, CH$_2$), 2.36-2.18 (8 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.74 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.18 (8 H, d, $^3J_{HH}$ = 7.7 Hz, ArH), 7.05 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 6.98-6.93 (1 H, m, ArH), 6.68 (1 H, d, $^3J_{HH}$ = 7.5 Hz, ArH), 3.88 (4 H, s, PhCH$_2$), 2.87-2.80 (8 H, m, CH$_2$), 2.36-2.18 (8 H, m, CH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 32.7 (s); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.00 (12 F, t, $^4J_{FF}$ = 11.3 Hz, CF$_3$), -114.67 (8 F, t, $^4J_{FF}$ = 14.1 Hz, α-CF$_2$), -121.94 (8 F, m, CF$_2$), -122.95 (8 F, m, CF$_2$), -123.57 (8 F, m, CF$_2$), -126.29 (8 F, m, CF$_2$); m/z (FAB) 1963 (M-Cl)$^+$; IR (Solid State, cm^{-1}) 1191.0 (br s), 1141.8 (s), 1085.8 (m), 1072.9 (m)

Method B

The title compound was prepared by an adaptation of Cross's method.[20] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)-phosphine]benzene (103) (1.770 g, 0.952 mmol), [PdCl$_2$(MeCN)$_2$] (0.247 g, 0.952 mmol) and 2-methoxyethanol (20 mL). The reaction mixture was heated to 130 °C for 62 h. The reaction mixture was allowed to cool to room temperature before the solvent was removed. The crude

material was dissolved in $CHCl_3$, filtered to remove any palladium metal and the solvent was removed to give an orange solid. This was then washed with hexane (3 x 10 mL) to give the desired product as a yellow/orange powder (1.014 g, 53 %). Characterisation data was the same as above.

Preparation of {2,6-*bis*[methyl(diphenylphosphino)]phenyl}palladium chloride (106)

Method A

The title compound was prepared by an adaptation of Rimml and Venanzi's method.[19] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyldiphenylphosphine]benzene (102) (0.584 g, 1.23 mmol), [$PdCl_2(MeCN)_2$] (0.319 g, 0.123 mmol) and DCM (10 mL). The reaction mixture was heated to reflux for 1.75 h. The reaction mixture was then cooled, washed with $EtOH/H_2O$ (4 mL, 3:1) and the solvent was removed. The crude ^{31}P NMR spectrum showed a number resonances at δ_P 32.4 & 20.6 ppm as well as the signal corresponding to the desired product at δ_P 33.5 ppm. The crude mixture was recrystallised from DCM/Hexane to give the byproducts as an orange solid (0.500 g). These were dissolved in 2-methoxyethanol (20 mL) and heated at 130 °C for 24 h. The reaction mixture was allowed to cool to room temperature before the solvent was removed. The crude material was dissolved in $CHCl_3$, filtered to remove any palladium metal and the solvent was removed to give an orange solid. This was then washed with hexane (3 x 10 mL) to give the desired product as a yellow solid (0.347 g, 69 % {from 0.500 g}). Crystals suitable for X-ray crystallography were grown by slow diffusion of hexane into a solution of DCM containing the title compound. mp 250 °C (dec.) (from hexane). Anal. Calcd for $C_{32}H_{27}ClP_2Pd$: C, 62.46; H, 4.42. Found C, 62.33; H, 4.49; ^1H NMR (300 MHz, $CDCl_3$) δ_H 7.83-7.70 (8 H, m, ArH), 7.35-7.29 (12 H, m, ArH), 7.04 (2 H, d, $^3J_{HH}$ = 7.3 Hz, ArH), 6.95 (1 H, m, ArH), 3.89 (4 H, vt, J_{HP} = 4.7 Hz, $PhCH_2$); $^1H\{^{31}P\}$ NMR (300 MHz, $CDCl_3$) δ_H 7.83-7.70 (8 H, m, ArH), 7.35-7.29 (12 H, m, ArH), 7.04 (2 H, d, $^3J_{HH}$ = 7.3 Hz, ArH), 6.95 (1 H, m, ArH), 3.89 (4 H, s, $PhCH_2$); $^{31}P\{^1H\}$ NMR (121 Hz, $CDCl_3$) δ_P 33.5 (s); m/z (FAB) 579 (M-Cl)$^+$; HRMS(FAB) found 577.06248 [(M-Cl)$^+$. $C_{32}H_{27}P_2Pd$ requires 577.06240]; IR (Solid State, cm^{-1}) 1483.5 (s), 1434.9 (m), 1102.2 (m), 1025.4 (m), 958.3 (m), 845.6 (m), 741.3 (m), 690.8 (s).

Method B

The title compound was prepared by an adaptation of Cross's method.[20] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyldiphenylphosphine]benzene (102) (0.620 g, 1.307 mmol), [$PdCl_2(MeCN)_2$] (0.300 g, 1.157 mmol) and 2-methoxyethanol (20 mL). The reaction mixture was heated to 130 °C for 62 h. The reaction mixture was allowed to cool to room temperature before the solvent was removed. The crude material was dissolved in

CHCl$_3$, filtered to remove any palladium metal and the solvent was removed to give a yellow powder. This was then washed with hexane (3 x 10 mL) to give the desired product as a yellow powder (0.651 g, 91 %). Characterisation data was the same as above.

Attempted preparation of {2,6-*bis*[methyl(diphenylphosphino)]phenyl}palladium chloride (106)

The title compound was prepared by an adaptation of van Koten's method.[18] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyldiphenylphosphine]benzene (102) (0.110 g, 0.229 mmol), [Pd(MeCN)$_4$(BF$_4$)$_2$] (0.102 g, 0.229 mmol) and MeCN (40 mL). The reaction mixture was heated to reflux for 2 h before cooling to room temperature. The reaction mixture changed from a yellow solution to a dark green solution containing solid palladium precipitate. The solvent was removed before the residue was dissolved in DCM (40 mL) and stirred with a saturated solution of sodium chloride for 12 h. The organic layer was separated and the solvent was removed *in vacuo*. The crude product was analysed by ^{31}P{^{1}H}, ^{1}H & ^{19}F{^{1}H} NMR spectroscopy. There were three different signals, all with roughly the same integration, in the ^{31}P{^{1}H} NMR spectrum at δ_P 56.6, 37.6 & 33.6 (product) ppm.

Preparation of {2,6-*bis*[methyl(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenylphosphino)]phenyl} nickel chloride (115)

The title compound was prepared by an adaptation of Rimml and Venanzi's method.[19] A 50 mL Schlenk flask was charged with 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl)phosphine]benzene (103) (0.753 g, 0.405 mmol), NiCl$_2$.6H$_2$O (0.0520 g, 0.405 mmol), and 2-methoxyethanol (20 mL). The colour instantly changed from green to purple. The reaction was heated to 60 °C for 3 h before di*iso*propylethylamine (0.291 g, 2.25 mmol) was carefully added. The reaction was heated to reflux and within 5 min the colour had changed from purple to golden yellow. The reaction was maintained at reflux overnight. Removal of the solvent and recrystallisation from ethanol isolated the complex as lime green crystals (0.546 g, 69 %). mp 113-115 °C (from EtOH). Anal. Calcd for C$_{64}$H$_{39}$F$_{52}$ClP$_2$Ni: C, 39.38; H, 2.01. Found C, 39.42; H, 2.15. ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.73 (8 H, vt, $^3J_{HH}$ = 8.2 Hz, $^3J_{HP}$ = 8.2 Hz, ArH), 7.16 (8 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.07 (2 H, d, $^3J_{HH}$ = 6.7 Hz, ArH), 6.89-6.80 (1 H, m, ArH), 3.77 (4 H, vt, J_{HP} = 4.7 Hz, PhCH$_2$), 2.90-2.81 (8 H, m, CH$_2$), 2.40-2.19 (8 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.73 (8 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.16 (8 H, d, $^3J_{HH}$ = 8.2 Hz, ArH), 7.07 (2 H, d, $^3J_{HH}$ = 6.7 Hz, ArH), 6.89-6.80 (1 H, m, ArH), 3.77 (4 H, s, PhCH$_2$), 2.90-2.81 (8 H, m, CH$_2$), 2.40-2.19 (8 H, m, CH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 33.8 (s); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.81 (12 F, t, $^4J_{FF}$ = 9.4 Hz,

CF$_3$), -114.60 (8 F, t, $^4J_{FF}$ = 14.1 Hz, α-CF$_2$), -121.88 (8 F, m, CF$_2$), -122.87 (8 F, m, CF$_2$), -123.46 (8 F, m, CF$_2$), -126.15 (8 F, m, CF$_2$); m/z (FAB) 1915 (M-Cl)$^+$; IR (Solid State, cm^{-1}) 1203.8 (br s), 1186.5 (s), 1141.4 (s), 1118.8 (s), 697.4 (m).

Preparation of {2,6-*bis*[methyl(diphenylphosphino)]phenyl}nickel chloride (114)

The title compound was prepared similarly to **(115)**, using 1,3-*bis*[methyldiphenylphosphine]benzene **(102)** (0.890 g, 1.88 mmol) (0.753 g, 0.405 mmol), NiCl$_2$.6H$_2$O (0.428 g, 0.180 mmol), di*iso*propylethylamine (0.0630 g, 0.486 mmol) and 2-methoxyethanol (20 mL). Recrystallisation from ethanol isolated the complex as a dark yellow powder (0.762 g, 75 %). Crystals suitable for X-ray crystallography were grown by slow diffusion of hexane into a solution of DCM containing the title compound. mp 280-282 °C (from ethanol). Anal. Calcd for C$_{32}$H$_{27}$ClP$_2$Ni: C, 67.71; H, 4.79. Found C, 67.60; H, 4.72; ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$ 7.87-7.73 (8 H, m, ArH), 7.42-7.25 (12 H, m, ArH), 6.89 (3 H, s, ArH), 3.78 (4 H, vt, J_{HP} = 3.8 Hz, PhCH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ$_H$ 7.78 (8 H, d, $^3J_{HH}$ = 6.6 Hz, ArH), 7.40-7.25 (12 H, m, ArH), 6.89 (3 H, s, ArH), 3.78 (4 H, s, PhCH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ$_P$ 34.8 (s); m/z (FAB) 566 (M)$^+$, 531 (M-Cl)$^+$; HRMS (FAB) calculated for C$_{32}$H$_{27}$ClP$_2$Ni: 566.06296, found: 566.06296; IR (Solid State, cm^{-1}) 2929.0 (w), 1462.6 (m), 1171.0 (m), 740.9 (m).

Preparation of {2,6-*bis*[methyl(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenylphosphino)] phenyl}platinum chloride (119)

The title compound was prepared by an adaptation of Bennets's method.[21] A 500 mL Schlenk flask was charged with 1,3-*bis*[methyl*bis*(4-1*H*,1*H*,2*H*,2*H*-perfluorooctylphenyl) phosphine]benzene **(103)** (0.700 g, 0.377 mmol), [PtCl$_2$(COD)] (0.141 g, 0.377 mmol) and mesitylene (250 mL). The reaction was heated to reflux before triethylamine (0.0460 g, 0.452 mmol) was carefully added. The reaction was then heated to reflux overnight and after cooling to room temperature,it was filtered through Celite. The solvent was removed and the residue was purified by a reverse recrystallisation from DCM/hexane to give the pure complex as colourless crystals (0.312 g, 40 %). mp 128-130 °C (from hexane). Anal. Calcd for C$_{64}$H$_{39}$F$_{52}$ClP$_2$Pt: C, 36.81; H, 1.88. Found C, 36.71; H, 1.96. ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$ 7.77 (8 H, vt, $^3J_{HP}$ = 8.0 Hz, $^3J_{HH}$ = 8.0 Hz, ArH), 7.20 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.03 (2 H, d, $^3J_{HH}$ = 7.0 Hz, ArH), 6.98-6.92 (1 H, m, ArH), 3.81 (4 H, vt, J_{HP} = 4.7 Hz, PhCH$_2$), 2.90-2.79 (8 H, m, CH$_2$), 2.37-2.18 (8 H, m, CH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ$_H$ 7.77 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.20 (8 H, d, $^3J_{HH}$ = 8.0 Hz, ArH), 7.03 (2 H, d, $^3J_{HH}$ = 7.0 Hz, ArH), 6.98-6.92 (1 H, m, ArH), 3.81 (4 H, br s, PhCH$_2$), 2.90-2.79 (8 H, m, CH$_2$), 2.37-2.18 (8 H, m, CH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ$_P$ 32.3 (s, $^1J_{PPt}$ = 2969 Hz); ^{19}F NMR (282

MHz, CDCl$_3$) δ_F -81.00 (12 F, t, $^4J_{FF}$ = 9.8 Hz, CF$_3$), -114.67 (8 F, t, $^4J_{FF}$ = 13.6 Hz, α-CF$_2$), -121.95 (8 F, m, CF$_2$), -122.96 (8 F, m, CF$_2$), -123.59 (8 F, m, CF$_2$), -126.26 (8 F, m, CF$_2$); m/z (FAB) 2087 (M)$^+$, 2068 (M-F)$^+$, 2052 (M-Cl)$^+$; IR (Solid State, cm^{-1}) 1186.7 (br s), 1186.5 (s), 1141.4 (s), 1119.1 (s), 8111 (m), 697.9 (m).

Preparation of {2,6-*bis*[methyl(diphenylphosphino)]phenyl}platinum chloride (118)

The title compound was prepared similarly to (119), using 1,3-*bis*[methyldiphenylphosphine]benzene (102) (0.880 g, 0.185 mmol), [PtCl$_2$(COD)] (0.674 g, 1.80 mmol), triethylamine (0.225 g, 2.22 mmol) and mesitylene (250 mL). The residue was purified by washing with ethanol (3 x 20 mL) to give the pure complex as a white powder (0.863 g, 62 %). Crystals suitable for X-ray crystallography were grown by slow evaporation of a chloroform solution containing the title compound. mp 281-283 °C (from ethanol). Anal. Calcd for C$_{32}$H$_{27}$ClP$_2$Pt: C, 54.59; H, 3.87. Found C, 54.52; H, 3.82; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 7.89-7.79 (8 H, m, ArH), 7.43-7.30 (12 H, m, ArH), 6.89 (3 H, s, ArH), 3.89 (4 H, t, $^3J_{HPt}$ = 50.0 Hz, J_{HP} = 4.7 Hz, PhCH$_2$); ^{1}H{^{31}P} NMR (300 MHz, CDCl$_3$) δ_H 7.89-7.79 (8 H, m, ArH), 7.43-7.30 (12 H, m, ArH), 7.03 (2 H, d, $^3J_{HH}$ = 7.0 Hz, ArH), 6.96-6.92 (1 H, m, ArH), 3.89 (4 H, s, J_{HPt} = 50.0 Hz, PhCH$_2$); ^{31}P{^{1}H} NMR (121 Hz, CDCl$_3$) δ_P 33.1 (s, $^1J_{PPt}$ = 2968 Hz); m/z (FAB) 702 ([M$^+$], 26%), 667 ([M-Cl]$^+$, 42%); HRMS (FAB) calculated for C$_{32}$H$_{27}$ClP$_2$Pt: 702.09046, found: 702.09054; IR (Solid State, cm^{-1}) 3017.1 (br, w), 1434.9 (s), 1217.0 (s), 1103.1 (m), 689.9 (s).

6.2.4 Catalysis and Recycling Procedures for Chapter Three

General procedure for Heck reaction using triethylamine as base (C3.1-C.3.8)

[PdCl(Rf-PCP)] (113) or [PdCl(PCP)] (106) (1.5 mol-%, 0.0180 mmol) was added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with nitrogen (x3) (or purged with argon for 20 min), before aryl halide (1.20 mmol), methyl acrylate (0.14 mL, 1.50 mmol), triethylamine (0.17 mL, 1.20 mmol) and DMF (5.00 mL) were added. The tube was placed into a preheated oil bath (120 °C), samples (0.01 mL) were taken over 25 hours and analysed by GC or HPLC. GC: using PE-5 column, injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. 200 °C for 8 min: R_t 4.4 min (iodobenzene), 7.0 min (*trans*-methyl cinnamate). 60 °C for 6 min, followed by 45 °C min^{-1} to 200 °C, held for 2 min: R_t 3.2 min (bromobenzene), 5.1 min (chlorobenzene). HPLC: using Phenomenex Luna C18(2), Detector: UV, 220 nm, Temp.: 40 °C, Flow rate: 1.0 mL min^{-1} for 10 min. R_t 5.3 min (iodobenzene), 5.1 min (bromobenzene), 4.4 min (4-bromoacetophenone), 4.8 min (*trans*-methyl cinnamate), 4.3 min (*trans*-methyl 4-acetylcinnamate). Yields of product were assay determined.

General procedure for solvent/base/PTC for Heck reaction using Microvate reactor (C3.9-C3.56)

[PdCl(PCP)] (**106**) (3.0 mg, 1 mol-%, 0.0048 mmol), solid bases (0.48 mmol) and PTC (0.096 mmol) were added to microvate reaction tubes. The microvates were purged with argon for 30 min before bromobenzene (0.754 g, 0.48 mmol), methyl acrylate (0.0517 g, 0.60 mmol), any liquid bases (0.48 mmol) and solvent (1.00 mL) were added. The were heated to 120 °C (or reflux if the solvent b.p. was <120 °C) for 24 h. The tubes were cooled and the reaction mixtures poured into volumetric flask (25 mL) before methanol was added. Samples were taken and analysed by HPLC and yields of product were determined by assay.

General procedure for the Heck reaction between aryl halides and methyl acrylate (C3.57-C3.71)

Solid aryl halides (0.48 mmol), KHCO₃ (0.0505 g, 0.504 mmol), TBAB (0.0309 g, 0.096 mmol) and [PdCl(Rf-PCP)] (**113**) or [PdCl(PCP)] (**106**) (1 mol-%, 0.0048 mmol) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with argon (x3), before liquid aryl halides (0.48 mmol), methyl acrylate (0.0620 g, 0.0650 mL, 0.72 mmol) and NMP (2.00 mL) were added. The tube was placed into a preheated oil bath (120 °C) for the reaction time. The reactions were cooled poured into volumetric flask (25 mL) before methanol was added. Samples were taken and analysed by GC using PE-5 column, injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. 200 °C for 5 min: R_t 2.5 min (4-iodoacetophenone), 2.2 min (4-bromoacetophenone), 2.0 min (4-chloroacetophenone), 4.5 min (*trans*-methyl 4-acetylcinnamate) Conditions 200 °C for 5 min: R_t 2.1 min (4-iodoanisole), 2.0 min (4-bromoanisole), 3.5 min (*trans*-methyl 4-methoxycinnamate). Yields of product were determined by assay.

General recycling procedure for the Heck reaction between 4-bromoacetophenone and methyl acrylate (C3.72-C3.76)

4-Bromoacetophenone (0.4976 g, 2.500 mmol), KHCO₃ (0.2628 g, 2.630 mmol), TBAB (0.1612 g, 0.5000 mmol), tolyl ether (0.4957 g, 2.500 mmol) and [PdCl(Rf-PCP)] (**113**) (50 mg, 1 mol-%, 0.025 mmol) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with argon (x3), before methyl acrylate (0.3228 g, 0.338 mL, 3.750 mmol) and NMP (5.00 mL) were added. The tube was placed into a preheated oil bath (120 °C), samples (0.01 mL) were taken over 4 hours and analysed by GC. The reaction mixture was allowed to cool to room temperature under argon before the solvent and the remaining volatiles were removed by Kugelröhr distillation (0.1 mbar, 40 °C). The resulting solid was taken up in MeCN (8 mL) and loaded onto a column of FRPSG (4 g) which had

been pre-treated with MeCN. The flask was washed with DCM (0.5 mL x 2) and finally with MeCN (2 mL). The column was eluted with MeCN (28 mL) to give the organic products and then EtOAc (90 mL) to give the fluorous catalyst. Both fractions were concentrated and analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H}NMR spectroscopy. The organic compound was also analysed by ICP-OES for any palladium leaching. The FRPSG column was washed with H_2O (20 mL) to remove any inorganic salts and was finally regenerated with MeCN. GC: using PE-5 column, injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. 200 °C for 5 min: R_t 2.2 min (4-bromoacetophenone), 3.2 min (tolyl ether), 4.5 min (*trans*-methyl 4-acetylcinnamate).

General procedure for Suzuki reaction (C3.77-C3.83)

[PdCl(Rf-PCP)] (113) or [PdCl(PCP)] (106) (1 mol-%, 0.0120 mmol), 4-bromoanisole (0.224 g, 1.20 mmol), phenyl boronic acid (0.220 g, 1.80 mmol) and Cs_2CO_3 (0.782 g, 2.40 mmol) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with nitrogen (x3) (or purged with argon for 20 min), before dioxane (4.00 mL) was added. The tube was placed into a preheated oil bath (100 °C), samples (0.01 mL) were taken over 20.5 hours and analysed by GC, using tolyl ether as an internal standard, or HPLC. GC: using PE-5 column, 100 °C for 3 min, followed by 45 °C min^{-1} to 200 °C, held for 3 min, injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. R_t 2.2 min (4-bromoanisole), 3.9 min (tolyl ether), 4.1 min (4-methoxybiphenyl). HPLC: using Phenomenex Luna C18(2), Detector: UV, 220 nm, Temp.: 40 °C, Flow rate: 1.0 mL min^{-1} for 10 min. R_t 5.8 min (4-bromoanisole), 5.1 min (4-methoxybiphenyl).

General recycling procedure for the Suzuki coupling reaction between 4-bromoacetophenone and phenyl boronic acid (C3.87-C3.91)

4-Bromoacetophenone (0.4976 g, 2.500 mmol), phenyl boronic acid (0.4573 g, 3.75 mmol), Cs_2CO_3 (1.629 g, 5.000 mmol), TBAB (0.1612 g, 0.5000 mmol), tolyl ether (0.4957 g, 2.500 mmol) and [PdCl(Rf-PCP)] (113) (50 mg, 1 mol-%, 0.025 mmol) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with argon (x3), before dioxane (10.00 mL) was added. The tube was placed into a preheated oil bath (110 °C), samples (0.01 mL) were taken over 2 hours and analysed by GC. The reaction mixture was allowed to cool to room temperature under argon before the solvent was removed. The resulting solid was taken up in MeOH (8 mL) and loaded onto a column of FRPSG (5 g) which had been pre-treated with MeOH. The flask was washed with DCM (0.5 mL x 2) and finally with MeOH (2 mL). The column was eluted with MeOH (40 mL) to give the organic products and then EtOAc (100 mL) to give the fluorous catalyst. Both fractions were

concentrated and analysed by ^{1}H, ^{31}P{^{1}H} and ^{19}F{^{1}H}NMR spectroscopy. The organic compound was also analysed by ICP-OES for any palladium leaching. The FRPSG column was washed with H_2O (20 mL) to remove any inorganic salts and was finally regenerated with MeOH. Yields were determined by GC using tolyl ether as an internal standard, using PE-5 column, 200 °C for 5.50 min, Injector: 250 °C, detector: 240 °C. Flow rate 1 mL/min. R_t 2.2 min (4-bromoacetophenone), 3.2 min (tolyl ether), 4.9 min (4-methoxybiphenyl).

6.2.5 Compounds for Chapter Four

Preparation of $1H,1H,2H,3H,3H$-perfluoro-2-iodo-n-undecanol (151)

The title compound was prepared by modification of Fish's method.[22] A 50 mL Schlenk tube was charged with perfluoro-n-octyl iodide (33.8 g, 60.0 mmol), allyl alcohol (4.5 mL, 60.0 mmol) and AIBN (985 mg, 6 mmol). The tube was purged with nitrogen before heating the reaction mixture at 85 °C for 24 h. After cooling to 50 °C, the reaction mixture was dissolved in diethyl ether (120 mL) and then washed with sodium thiosulphate (5 x 120 mL, 0.1 M) and brine. The organic layer was dried (MgSO$_4$) and the solvent was removed to give an off white solid. This was dried under reduced pressure (40 °C, 2 h) to give the pure compound as a white solid (24.98 g, 69 %). mp 92-94 °C (from diethyl ether) (lit mp 93-94 °C).[22] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 4.42-4.34 (1 H, m, CHI), 3.81-3.68 (2 H, m, CH$_2$CF$_2$), 3.05-2.85 (1 H, m, CHHOH), 2.80-2.57 (1 H, m, CHHOH), 1.83 (1 H, br s, OH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.76 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -112.53 (1 F, dt, $^2J_{FF}$ = 269.5 Hz, $^4J_{FF}$ = 13.8 Hz, α-CFF), -114.21 (1 F, dt, $^2J_{FF}$ = 269.5 Hz, $^4J_{FF}$ = 13.8 Hz, α-CFF), -121.53 (2 F, m, CF$_2$), -121.85 (4 F, m, 2 x CF$_2$), -122.69 (2 F, m, CF$_2$), -123.09 (2 F, m, CF$_2$), -126.10 (2 F, m, CF$_2$); δ_C 67.88 (CH$_2$), 37.47 (t, $^2J_{CF}$ = 21.1 Hz, CH$_2$), 21.65 (CH); m/z (EI) 604 (M$^+$, 10 %), 477 ([M-I]$^+$, 100 %); HRMS (EI) calculated for C$_{11}$H$_6$OF$_{17}$I: 603.91920, found: 603.91929; IR (Solid State, cm^{-1}) 3408.4 (br, w) (OH), 1197.7 (br s), 1145.1 (s), 1116.0 (s).

Preparation of $1H,1H,2H,2H,3H,3H$-perfluoro-n-undecanol (152)

The title compound was prepared by modification of Fish's method.[22] A 250 mL, three-necked round-bottomed flask, equipped with a magnetic stirring bar, pressure-equalising dropping funnel, condenser and Rotaflow adaptor, was attached to a Schlenk line. After flame-drying under high vacuum, the flask was cooled and filled with nitrogen. The flask was charged with lithium aluminium hydride (1.50 g, 38.2 mmol) and dry diethyl ether (40 mL). The dropping funnel was charged with $1H,1H$, $2H,3H,3H$-perfluoro-2-iodo-n-undecanol (151) (23.1 g, 38.2 mmol) in dry diethyl ether (80 mL), which was added dropwise to the main reaction flask over 1 h. The reaction mixture was refluxed for 12 h before cooling to 0 °C. Water (1.2 mL) was added slowly to the reaction mixture, followed by aqueous sodium hydroxide (1.2 mL, 15 %) and additional water (3.6 mL). The reaction mixture was filtered through Celite and the inorganic salts were washed with THF (2 x 80 mL). The solvent was removed and the residue was taken up in diethyl ether before washing with brine, drying (MgSO$_4$) and concentrating to give the pure compound as a white solid (14.18 g, 78 %). mp 162-164 °C (from diethyl ether) (lit 166-168 °C)[23] ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 4.00 (2 H, t, $^3J_{HH}$ = 6.0 Hz, CH$_2$OH), 2.25-2.05 (2 H, m, CF$_2$CH$_2$), 1.85-1.75 (2 H, m, CH$_2$), 1.33 (1 H, br s, OH); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -80.78 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -

114.25 (2 F, t, $^4J_{FF}$ = 12.0 Hz, α-CF$_2$), -121.72 (2 F, m, CF$_2$), -121.91 (4 F, m, 2 x CF$_2$), -122.71 (2 F, m, CF$_2$), -123.50 (2 F, m, CF$_2$), -126.10 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ$_C$ 60.39 (CH$_2$), 26.59 (t, $^2J_{CF}$ = 22.3 Hz, CH$_2$), 22.37 (CH$_2$); m/z (FAB) 477 ([M-H]$^+$, 23 %); HRMS (FAB) calculated for C$_{11}$H$_7$OF$_{17}$: 478.02255, found: 478.02253; IR (Solid State, cm^{-1}) 3345.0 (w br), 1197.7 (br s), 1145.1 (s), 1115.7 (s).

Preparation of 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl iodide (153)

The title compound was prepared by Fish's method.[22] A 500 mL, round-bottomed flask, equipped with a condenser, was cooled to 0 °C and charged with aqueous phosphoric acid (129 ml, 85 % solution, 1.88 mol) and then, phosphorus pentoxide (53.5 g, 377 mmol). Potassium iodide (31.3 g, 188 mmol) and 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecanol (152) (18.0 g, 37.7 mmol) were successively added to the reaction mixture before stirring vigorously at 130 °C for 18 h. After cooling to room temperature, water (240 mL) and diethyl ether (120 mL) were added carefully to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with diethyl ether (2 x 120 mL). The combined organic layers were washed with sodium thiosulphate (120 mL, 0.1 M), brine, dried (MgSO$_4$) and concentrated to give an off white solid (20.6 g, 93 %). mp 36-38 °C (from diethyl ether) (lit 37-39 °C).[23] ^{1}H NMR (300 MHz, CDCl$_3$) δ$_H$ 3.16 (2 H, t, $^3J_{HH}$ = 6.3 Hz, ICH$_2$), 2.23-1.88 (4 H, m, C*H*$_2$C*H*$_2$CF$_2$); ^{19}F NMR (282 MHz, CDCl$_3$) δ$_F$ -80.46 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.16 (2 F, t, $^4J_{FF}$ = 12.8 Hz, α-CF$_2$), -122.08 (2 F, m, CF$_2$), -122.29 (4 F, m, 2 x CF$_2$), -123.15 (2 F, m, CF$_2$), -123.78 (2 F, m, CF$_2$), -126.63 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ$_C$ 31.06 (t, $^2J_{CF}$ = 22.3 Hz, CH$_2$), 23.43 (CH$_2$), 2.25 (CH$_2$); m/z (FAB) 588 (M$^+$, 100 %); HRMS (FAB) calculated for C$_{11}$H$_6$IF$_{17}$: 587.92428, found: 587.92450; IR (Solid State, cm^{-1}) 1197.5 (br s), 1144.3 (s), 1115.2 (s).

Preparation of *N*-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazole (154)

The title compound was prepared by an adaptation of Xiao's method.[24] A 50 mL Schlenk tube was charged with 1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl iodide (153) (0.500 g, 0.850 mmol), imidazole (0.145 g, 2.22 mmol) and ethyl acetate (5 mL). The flask was evacuated and refilled with argon (x 3), before the tube was sealed and refluxed for 20 h. After cooling to room temperature, the reaction mixture was washed with sodium thiosulphate (10 mL, 0.1 M) and water (2 x 5 mL). The organic layer was dried (MgSO$_4$) and the solvent was removed. Recrystallisation from hexane gave the pure compound as a white solid (0.383 g, 80 %). Crystals suitable for X-ray crystallography were grown by slow evaporation of a hexane solution containing the title compound. mp 58-60 °C (from hexane). Anal. Calcd for C$_{14}$H$_9$N$_2$F$_{17}$: C, 31.83; H, 1.72; N, 5.30. Found C, 31.76; H, 1.73; N, 5.30; ^{1}H NMR (300

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MHz, CDCl₃) δ_H 7.42 (1 H, s, NCHN), 7.04 (1 H, s, NCHCHN), 6.86 (1 H, s, NCHCHN), 4.00 (2 H, t, $^3J_{HH}$ = 6.5 Hz, NCH₂), 2.13-1.86 (4 H, m, CH_2CH_2CF₂); ^{19}F NMR (282 MHz, CDCl₃) δ_F -80.72 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF₃), -113.88 (2 F, t, $^4J_{FF}$ = 12.7 Hz, α-CF₂), -121.67 (2 F, m, CF₂), -121.89 (4 F, m, 2 x CF₂), -122.67 (2 F, m, CF₂), -123.31 (2 F, m, CF₂), -126.06 (2 F, m, CF₂); ^{13}C NMR (75 MHz, CDCl₃) δ_C 137.04 (CH), 130.19 (CH), 118.45 (CH), 45.78 (CH₂), 27.85 (t, $^2J_{CF}$ = 22.6 Hz, CH₂), 22.32 (CH₂); m/z (FAB) 529 ([M+H], 100 %); HRMS (FAB) calculated for C₁₄H₁₀N₂F₁₇: 529.05725, found: 529.05716; IR (Solid State, cm⁻¹) 1513.3 (w), 1196.8 (br s), 1148.0 (s), 1116.8 (s).

Preparation of *N*-butylimidazole (155)

The title compound was prepared similarly to (154), using butyl iodide (6.48 g, 35.2 mmol), imidazole (6.00 g, 88.1 mmol) and ethyl acetate (25 mL). The pure compound was obtained as a pale yellow oil (2.40 g, 56 %). ^{1}H NMR (300 MHz, CDCl₃) δ_H 7.39 (1 H, s, NCHN), 6.98 (1 H, s, NCHCHN), 6.83 (1 H, s, NCHCHN), 3.86 (2 H, t, $^3J_{HH}$ = 7.4 Hz, NCH₂), 1.69 (2 H, quint., $^3J_{HH}$ = 7.4 Hz, NCH₂CH_2), 1.26 (2 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH₂)₂CH_2CH₃), 0.87 (3 H, t, $^3J_{HH}$ = 7.4 Hz, CH₃); ^{13}C NMR (75 MHz, CDCl₃) δ_C 136.93 (CH), 129.10 (CH), 118.72 (CH), 46.62 (CH₂), 32.96 (CH₂), 19.60 (CH₂), 13.39 (CH₃); m/z (FAB) 125 ([MH]⁺, 100 %); HRMS (FAB) calculated for C₇H₁₃N₂: 125.10787, found: 125.10793; IR (KBr, neat, cm⁻¹) 3105.4 (s), 2958.8 (s), 2872.0 (s), 1506.4 (s), 1460.1 (s), 1226.73 (s), 734.8 (m).

Preparation of 1,3-dibutylimidazolium iodide (157)

A 50 mL Schlenk tube was charged with *N*-butylimidazole (155) (0.750 g, 6.00 mmol), butyl iodide (1.47 g, 8.00 mmol) and toluene (10 mL). The flask was purged with argon, before the tube was sealed and heated to reflux for 24 h. After cooling to room temperature, the solvent was removed and the crude reaction mixture was washed with diethyl ether (3 x 10 mL) to remove excess butyl iodide. The compound was heated under high vacuum (40 °C) to give the desired compound as a thick dark orange oil (1.84 g, 83 %). Anal. Calcd for C₁₁H₂₁N₂I: C, 42.87; H, 6.87; N, 9.09. Found C, 42.97; H, 6.82; N, 8.92; ^{1}H NMR (400 MHz, CDCl₃) δ_H 10.02 (1 H, t, $^4J_{HH}$ = 1.5 Hz, NCHN), 7.54 (2 H, $^4J_{HH}$ = 1.5 Hz, NCH), 4.36 (4 H, t, $^3J_{HH}$ = 7.5 Hz, NCH₂), 1.89 (4 H, quint., $^3J_{HH}$ = 7.5 Hz, NCH₂CH_2), 1.35 (4 H, sext., $^3J_{HH}$ = 7.5 Hz, N(CH₂)₂CH_2CH₃), 0.93 (6 H, t, $^3J_{HH}$ = 7.5 Hz, CH₃); ^{13}C NMR (75 MHz, CDCl₃) δ_C 135.85 (CH), 122.50 (CH), 49.73 (CH₂), 32.08 (CH₂), 19.31 (CH₂), 13.40 (CH₃); m/z (FAB) 181 ([M-I]⁺, 100 %); HRMS (FAB) calculated for C₁₁H₂₁N₂: 181.17047, found: 181.17042; IR (KBr, neat, cm⁻¹) 3073.1 (s), 2959.0 (s), 2871.2 (s), 1561.4 (s), 1462.1 (s), 1164.5 (s), 752.8 (m).

Preparation of 1-butyl-3-(1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl)imidazolium iodide (158)

The title compound was prepared similarly to **(157)**. A 50 mL Schlenk tube was charged with N-butylimidazole **(155)** (0.250 g, 2.00 mmol), 1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl iodide **(153)** (1.18 g, 2.00 mmol) and BTF (10 mL). The flask was purged with argon, before the tube was sealed and refluxed for 72 h. After cooling to room temperature, the solvent was removed and the crude reaction mixture was taken up in a minimum amount of DCM before being washed with hexane (2 x 10 mL) to remove excess starting material. The solvent was removed to give the desired compound as a fluffy yellow solid (1.43 g, 100 %). mp 60-62 °C (from hexane). Anal. Calcd for $C_{18}H_{18}N_2F_{17}I$: C, 30.36; H, 2.55; N, 3.93. Found C, 30.37; H, 2.51; N, 3.82; ^{1}H NMR (400 MHz, CDCl$_3$) δ_H 10.21 (1 H, t, $^4J_{HH}$ = 1.8 Hz, NCHN), 7.67 (1 H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.8 Hz, NCHCHN), 7.47 (1 H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.8 Hz, NCHCHN), 4.64 (2 H, t, $^3J_{HH}$ = 7.4 Hz, NCH_2(CH$_2$)$_2$CF$_2$), 4.34 (2 H, t, $^3J_{HH}$ = 7.4 Hz, NCH_2(CH$_2$)$_2$CH$_3$), 2.40-2.21 (4 H, m, CH_2CH_2CF$_2$), 1.95 (2 H, quint., $^3J_{HH}$ = 7.4 Hz, NCH$_2$CH_2), 1.41 (2 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH$_2$)$_2$CH_2CH$_3$), 0.98 (3 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$); ^{19}F NMR (282 MHz, CDCl$_3$) δ_F -81.17 (3 F, t, $^4J_{FF}$ = 9.9 Hz, CF$_3$), -114.00 (2 F, t, $^4J_{FF}$ = 14.1 Hz, α-CF$_2$), -121.94 (2 F, m, CF$_2$), -122.96 (4 F, m, 2 x CF$_2$), -123.03 (2 F, m, CF$_2$), -123.34 (2 F, m, CF$_2$), -126.46 (2 F, m, CF$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 136.22 (CH), 122.72 (CH), 122.46 (CH), 50.05 (CH$_2$), 48.55 (CH$_2$), 31.92 (CH$_2$), 27.53 (t, $^2J_{CF}$ = 22.6 Hz, CH$_2$), 22.03 (CH$_2$), 19.36 (CH$_2$), 13.22 (CH$_3$); m/z (FAB) 585 ([M-I]$^+$, 100 %); HRMS (FAB) calculated for $C_{18}H_{18}N_2F_{17}$: 585.11985, found: 585.11970; IR (Solid State, cm^{-1}) 1513.3 (w), 1198.9 (br s), 1145.3 (s), 1115.8 (s).

Preparation of 1,3-bis(1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl)imidazolium iodide (156)

The title compound was prepared similarly to **(157)**, using N-(1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl)imidazole **(154)** (0.247 g, 0.468 mmol), 1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl iodide **(153)** (0.275 g, 0.468 mmol) and BTF (5 mL). The crude compound was washed with chloroform and the residue was taken up in acetone, filtered and concentrated to give the desired product as an orange solid (0.302 g, 58 %). mp 198-200 °C (from acetone). Anal. Calcd for $C_{25}H_{15}N_2F_{34}I$: C, 26.90; H, 1.35; N, 2.51. Found C, 26.79; H, 1.42; N, 2.44; ^{1}H NMR (400 MHz, d^6-Acetone) δ_H 9.77 (1 H, t, $^4J_{HH}$ = 1.6 Hz, NCHN), 8.02 (2 H, d, $^4J_{HH}$ = 1.6 Hz, NCH), 4.69 (4 H, t, $^3J_{HH}$ = 6.9 Hz, NCH$_2$), 2.58-2.35 (8 H, m, CH_2CH_2CF$_2$); ^{19}F NMR (282 MHz, d^6-Acetone) δ_F -81.65 (6 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -114.62 (4 F, t, $^4J_{FF}$ = 13.3 Hz, α-CF$_2$), -122.33 (4 F, m, CF$_2$), -122.49 (8 F, m, 2 x CF$_2$), -123.31 (4 F, m, CF$_2$), -123.89 (4 F, m, CF$_2$), -126.77 (4 F, m, CF$_2$); ^{13}C NMR (100 MHz, 323 K, d^6-Acetone) δ_C 137.05 (CH),

122.83 (CH), 48.51 (CH$_2$), 27.64 (t, $^2J_{CF}$ = 22.1 Hz, CH$_2$), 21.48 (CH$_2$); m/z (FAB) 989 ([M-I]$^+$, 100 %); IR (Solid State, cm^{-1}) 1566.3 (w), 1198.0 (br s), 1144.6 (s), 1115.5 (s).

Preparation of *trans-bis*[1,3-dibutylimidazol-2-ylidene]palladium diiodide (160)

The title compound was prepared by an adaptation of Xiao's method.[24] A 50 mL Schlenk tube was charged with 1,3-dibutylimidazolium iodide (157) (0.770 g, 2.49 mmol), palladium acetate (0.280 g, 1.25 mmol), sodium acetate (0.204 g, 2.49 mmol) and DMSO (20 mL). The flask was evacuated and refilled with argon (x 3), before the tube was sealed and heated to 90 °C for 14 h. After cooling to room temperature, the solvent was removed by heating under high vacuum (0.1 mbar, 75 °C). The residue was dissolved in THF and filtered through a short pad of silica gel. The solvent was removed and the crude material was recrystallised from DCM/hexane to give the desired product as an orange solid (0.766 g 85 %). Crystals suitable for X-ray crystallography were grown by slow evaporation of a DMSO solution containing the title compound. mp 220-222 °C (from hexane); Anal. Calcd for C$_{22}$H$_{40}$N$_4$I$_2$Pd: C, 36.66; H, 5.59; N, 7.77. Found C, 36.50; H, 5.71; N, 7.65; ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 6.72 (4 H, s, NCH), 4.20 (8 H, t, $^3J_{HH}$ = 7.7 Hz, NCH$_2$), 1.87 (4 H, m, NCH$_2$CH_2), 1.28 (4 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH$_2$)$_2$CH_2CH$_3$), 0.84 (6 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 166.71 (C), 120.90 (CH), 51.15 (CH$_2$), 32.09 (CH$_2$), 20.12 (CH$_2$), 13.79 (CH$_3$); m/z (FAB) 720 (M$^+$, 12 %), 593 ([M-I]$^+$, 100 %); HRMS (FAB) calculated for C$_{22}$H$_{40}$N$_4$I$_2$Pd: 720.03745, found 720.03734; IR (Solid State, cm^{-1}) 2925.1 (m), 1421.6 (m), 1234.24 (s) (C-N), 693.68 (s). **1,3-dibutylimidazol-2-ylidene]diiodo-μμ'-palladium diiodide (162)** was isolated by recrystallisation from CHCl$_3$/hexane and crystals suitable for X-ray crystallography were obtained.

Preparation of *trans-bis*[1-butyl-3-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)-imidazol-2-ylidene]palladium diiodide (161)

The title compound was prepared similarly to (160), using 1-butyl-3-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazolium iodide (158) (1.16 g, 1.63 mmol), palladium acetate (0.180 g, 0.802 mmol), sodium acetate (0.134 g, 1.63 mmol) and DMSO (15 mL). The compound was obtained as a yellow solid, which was found to be a mixture of *trans*-rotamers (1.14 g, 93 %). mp 174-176 °C (from hexane). Anal. Calcd for C$_{36}$H$_{34}$N$_4$F$_{34}$I$_2$Pd: C, 28.28; H, 2.24; N, 3.66. Found C, 28.22; H, 2.37; N, 3.44; ^{1}H NMR (*trans-anti*, 300 MHz, CDCl$_3$) δ_H 6.87 (2 H, d, $^3J_{HH}$ = 1.8 Hz, NC*H*CHN), 6.85 (2 H, d, $^3J_{HH}$ = 1.8 Hz, NC*H*CHN), 4.43 (4 H, t, $^3J_{HH}$ = 7.4 Hz, NC*H*$_2$(CH$_2$)$_2$CF$_2$), 4.31 (4 H, t, $^3J_{HH}$ = 7.4 Hz, NC*H*$_2$(CH$_2$)$_2$CH$_3$), 2.43-2.27 (4 H, m, C*H*$_2$CF$_2$), 2.25-2.04 (4 H, m, C*H*$_2$CH$_2$CF$_2$), 2.02-1.90 (4 H, m, NCH$_2$C*H*$_2$), 1.43-1.29 (4 H, m, N(CH$_2$)$_2$C*H*$_2$CH$_3$), 0.93 (6 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$);

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^{19}F NMR (*trans-anti*, 282 MHz, CDCl$_3$) δ_F -81.03 (6 F, t, $^4J_{FF}$ = 9.6 Hz, CF$_3$), -113.97 (4 F, t, $^4J_{FF}$ = 13.5 Hz, α-CF$_2$), -121.92 (8 F, m, 2 x CF$_2$), -122.09 (4 F, m, CF$_2$), -122.92 (4 F, m, CF$_2$), -123.31 (4 F, m, CF$_2$), -126.34 (4 F, m, CF$_2$); ^{13}C NMR (*trans-anti*, 75 MHz, CDCl$_3$) δ_C 166.42 (C), 120.66 (CH), 119.72 (CH), 50.33 (CH$_2$), 49.16 (CH$_2$), 31.03 (CH$_2$), 27.24 (t, $^2J_{CF}$ = 22.3 Hz, CH$_2$), 20.15 (CH$_2$), 19.11 (CH$_2$), 12.73 (CH$_3$). The ^{1}H NMR spectrum for the *trans-syn* rotamer overlaps that of the *trans-anti* rotamer except at δ_H 4.40 (4 H, t, $^3J_{HH}$ = 7.4 Hz, NCH_2(CH$_2$)$_2$CF$_2$), 4.29 (4 H, t, $^3J_{HH}$ = 7.4 Hz, NCH_2(CH$_2$)$_2$CH$_3$), 0.92 (6 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$). ^{19}F NMR (*trans-syn*, 282 MHz, CDCl$_3$) δ_F -80.87 (6 F, t, $^4J_{FF}$ = 9.6 Hz, CF$_3$), -113.84 (4 F, t, $^4J_{FF}$ = 13.5 Hz, α-CF$_2$), -121.92 (8 F, m, 2 x CF$_2$), -122.09 (4 F, m, CF$_2$), -122.78 (4 F, m, CF$_2$), -123.31 (4 F, m, CF$_2$), -126.17 (4 F, m, CF$_2$); ^{13}C NMR (*trans-syn*, 75 MHz, CDCl$_3$) δ_C 166.47 (C), 120.66 (CH), 119.78 (CH), 50.33 (CH$_2$), 49.16 (CH$_2$), 31.93 (CH$_2$), 27.31 (t, $^2J_{CF}$ = 22.3 Hz, CH$_2$), 20.15 (CH$_2$), 19.11 (CH$_2$), 12.55 (CH$_3$). The *trans-anti/trans-syn* ratio was 1:1, but it varied with time in solution with the *trans-anti* rotamer gaining intensity as shown by the ^{1}H, ^{19}F & ^{13}C NMR spectra. The *anti* and *syn* assignment was only tentative.[25] *m/z* (FAB) 1527 ([M-H]$^+$, 12 %), 1401 ([M-I]$^+$, 100 %); 1274 ([M-2I]$^+$, 35 %); IR (Solid State, cm^{-1}) 1465.6 (w), 1197.6 (br s), 1144.9 (s), 1114.5 (s), 693.32 (s).

Preparation of *trans-bis*[1,3-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)-imidazol-2-ylidene]palladium diiodide (159)

The title compound was prepared similarly to (160), using 1,3-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazolium iodide (156) (0.0910 g, 0.0815 mmol), palladium acetate (0.0092 g, 0.0408 mmol), sodium acetate (0.0074 g, 0.0900 mmol) and DMSO (5 mL). After 14 h the reaction was allowed to cool to room temperature and the solvent was decanted off to leave a black precipitate. The crude reaction mixture was washed with acetone (2 x 10 mL) before being dissolved in hexafluorobenzene. The solution was filtered through a short pad of silica and the solvent was removed to give the pure product as a yellow/orange solid (0.0730 g, 77 %). mp 220-222 °C (from C$_6$F$_6$). Anal. Calcd for C$_{50}$H$_{28}$N$_4$F$_{68}$I$_2$Pd: C, 25.70; H, 1.21; N, 2.40. Found C, 25.67; H, 1.32; N, 2.35; ^{1}H NMR (300 MHz, d^8-THF/C$_6$F$_6$) δ_H 5.56 (4 H, s, NCH), 2.84 (8 H, t, $^3J_{HH}$ = 6.9 Hz, NCH$_2$), 0.87-0.48 (16 H, m, CH_2CH_2CF$_2$); ^{19}F NMR (282 MHz, d^8-THF/C$_6$F$_6$) δ_F -84.17 (12 F, t, $^4J_{FF}$ = 10.0 Hz, CF$_3$), -116.76 (8 F, t, $^4J_{FF}$ = 12.1 Hz, α-CF$_2$), -124.33 (8 F, m, CF$_2$), -124.59 (16 F, m, 2 x CF$_2$), -125.45 (8 F, m, CF$_2$), -125.81 (8 F, m, CF$_2$), -129.03 (8 F, m, CF$_2$); ^{13}C NMR (101 MHz, d^8-THF/C$_6$F$_6$) δ_C 168.34 (C), 121.42 (CH), 49.87 (CH$_2$), 26.18 (t, $^2J_{CF}$ = 22.1 Hz, CH$_2$), 20.80 (CH$_2$); *m/z* (FAB) 2208 ([M-HI]$^+$, 50 %); IR (Solid State, cm^{-1}) 1197.7 (br s), 1145.0 (s), 1115.0 (s).

Preparation of *trans-bis*[1,3-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazol-2-ylidene]palladium diiodide (159) supported on FRPSG

The title compound was prepared using Bannwarth's method.[7] A 50 mL carousel tube equipped with a magnetic stirring bar was charged with *trans-bis*[1,3-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazol-2-ylidene]palladium diiodide (159) (11.2 mg, 0.0048 mmol), FRPSG (0.213 g), a minimum amount of hexafluorobenzene and stirred for 2 h at room temperature. The solvent was removed to produce the supported catalyst as a free-flowing powder.

Preparation of 1,1'-dibutyl -3,3'-methyleneimidazolium dibromide (164)

The title compound was prepared by Sugiyama's method with some modification.[26] A 50 mL Schlenk tube was charged with *N*-butylimidazole (155) (1.00 g, 8.00 mmol), dibromomethane (0.0684 g, 3.93 mmol) and toluene (10 mL). The flask was purged with argon, before the tube was sealed and refluxed for 24 h. After cooling to room temperature, the solvent was removed and the crude reaction mixture was washed with diethyl ether (3 x 10 mL). The compound was dried under high vacuum (40 °C) to give the desired compound as a hygroscopic white solid (0.90 g, 58 %). mp 180-182 °C (from Et$_2$O); ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 10.92 (2 H, s, NCHN), 9.07 (2 H, s, NC*H*CHN), 7.47 (2 H, s, NC*H*CHN), 7.46 (2 H, s, NCH$_2$N), 4.22 (4 H, t, $^3J_{HH}$ = 7.7 Hz, NCH$_2$), 1.93-1.83 (4 H, m, NCH$_2$C*H*$_2$), 1.36 (4 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH$_2$)$_2$C*H*$_2$CH$_3$), 0.91 (6 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 137.81 (CH), 124.00 (CH), 122.45 (CH), 56.95 (CH$_2$), 50.61 (CH$_2$), 31.64 (CH$_2$), 19.54 (CH$_2$), 13.41 (CH$_3$); *m/z* (FAB) 343/341 ([M-Br]$^+$, 67 %), 261 ([M-2Br-H]$^+$, 100 %); HRMS (FAB) calculated for C$_{15}$H$_{26}$N$_4$Br: 341.13421, found 341.13421; IR (Solid State, cm^{-1}) 3049.9 (m), 2961.7 (m), 2872.3 (w), 1547.5 (m), 1170.6 (s), 761.0 (m).

Preparation of 1,1'-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)-3,3'-methylene-imidazolium dibromide (163)

The title compound was prepared similarly to (164). A 50 mL Schlenk tube was charged with *N*-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazole (154) (3.07 g, 5.81 mmol), dibromomethane (0.493 g, 2.84 mmol) and BTF (20 mL). The flask was purged with argon before the tube was sealed and refluxed for 72 h. After cooling to room temperature, the solvent was removed and the crude reaction mixture washed with THF (20 mL) and acetone (2 x 20 mL). The crude product was recrystallised from DMSO, washed with MeCN (2 x 20 mL) and dried under high vacuum to give a pale brown solid (1.62 g, 40 %). mp 302-304°C (from MeCN); Anal. Calcd for C$_{29}$H$_{20}$N$_4$F$_{34}$Br$_2$: C, 28.31; H, 1.64; N, 4.55. Found C, 28.22; H, 1.67; N, 4.51; ^{1}H NMR (400 MHz, d^6-DMSO, 353 K) δ_H 9.59 (2 H, br s, NCHN), 8.06 (2

H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.8 Hz, NCHCHN), 7.93 (2 H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.8 Hz, NCHCHN), 7.46 (2 H, s, NCH$_2$N), 4.39 (4 H, t, $^3J_{HH}$ = 7.3 Hz, NCH$_2$), 2.38 (4 H, tt, $^3J_{HF}$ = 19.2 Hz, $^3J_{HH}$ = 7.6 Hz, CH_2CF$_2$), 1.36 (4 H, quint., $^3J_{HH}$ = 7.6 Hz, NCH$_2$CH_2); ^{19}F NMR (376 MHz, d^6-DMSO, 353 K) δ_F -80.09 (6 F, t, $^4J_{FF}$ = 9.6 Hz, CF$_3$), -112.40 (4 F, t, $^4J_{FF}$ = 11.9 Hz, α-CF$_2$), -120.92 (4 F, m, CF$_2$), -121.00 (8 F, m, 2 x CF$_2$), -121.91 (4 F, m, CF$_2$), -122.34 (4 F, m, CF$_2$), -125.17 (4 F, m, CF$_2$); The compound was not soluble enough for ^{13}C NMR spectroscopy. m/z (FAB) 1069 ([M-H-2Br]$^+$, 100 %); IR (Solid State, cm^{-1}) 1555.7 (w), 1198.5 (br s), 1145.8 (s), 1117.6 (s).

Preparation of [1,1'-dibutyl-3,3'-methyleneimidazolin-2,2'-diylidene]palladium dibromide (166)

The title compound was prepared similarly to (160). A 50 mL Schlenk tube was charged with 1,1'-dibutyl-3,3'-methyleneimidazolium dibromide (164) (0.450 g, 1.15 mmol), palladium acetate (0.258g, 1.15 mmol), sodium acetate (0.189 g, 2.30 mmol) and DMSO (20 mL). The flask was evacuated and refilled with argon (x 3) before the tube was sealed and heated at 100 °C for 14 h. After cooling to room temperature, the solvent was removed by heating under high vacuum (0.1 mbar, 75 °C). The residue was taken up in CHCl$_3$ and filtered through a short pad of silica. The solvent was removed and the crude material was recrystallised from MeCN and washed with hexane to give the desired product as cream solid (0.173 g, 31 %). Crystals suitable for X-ray crystallography were grown by slow evaporation of a DMSO solution containing the title compound. mp 226-228 °C (from hexane); Anal. Calcd for C$_{15}$H$_{24}$N$_4$Br$_2$Pd: C, 34.21; H, 4.59; N, 10.64. Found C, 34.34; H, 4.63; N, 10.60. ^{1}H NMR (400 MHz, d^6-DMSO) δ_H 7.59 (2 H, s, NCHCHN), 7.40 (2 H, s, NCHCHN), 6.29 (2 H, s, NCH$_2$N), 4.95-4.75 (2 H, m, NCH$_2$), 4.20-4.02 (2 H, m, NCH$_2$), 1.87 (4 H, quint., $^3J_{HH}$ = 7.2 Hz, NCH$_2$CH_2), 1.21 (2 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH$_2$)$_2$CH_2CH$_3$), 1.19 (2 H, sext., $^3J_{HH}$ = 7.4 Hz, N(CH$_2$)$_2$CH_2CH$_3$), 0.89 (6 H, t, $^3J_{HH}$ = 7.4 Hz, CH$_3$); ^{13}C NMR (75 MHz, d^6-DMSO) δ_C 158.35 (C), 121.98 (CH), 121.34 (CH), 62.52 (CH$_2$), 49.96 (CH$_2$), 32.55 (CH$_2$), 19.06 (CH$_2$), 13.44 (CH$_3$); m/z (FAB) 447 ([M-Br]$^+$); HRMS (FAB) calculated for C$_{15}$H$_{24}$N$_4$BrPd: 445.02163, found 445.02159; IR (Solid State, cm^{-1}) 3094.7 (w), 2928.02 (w), 1426.7 (w), 1170.7 (w), 735.46 (m).

Preparation of [1,1'-bis(1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl)-3,3'-methylene-imidazolin-2,2'-diylidene] palladium dibromide (165)

The title compound was prepared similarly to (166), using 1,1'-bis-(1H,1H,2H,2H,3H,3H-perfluoro-n-undecyl)-3,3'-methyleneimidazolium dibromide (163) (1.00 g, 0.813 mmol), palladium acetate (0.183 g, 0.813 mmol), sodium acetate (0.133 g, 1.62

mmol) and DMSO (20 mL). The reaction solvent was decanted off and the crude material was washed with chloroform (2 x 10 mL), BTF (2 x 10 mL), acetone (2 x 10 mL) and hexane (2 x 10 mL). The residue was taken up in trifluoroethanol and filtered through a short pad of silica gel. The solvent was removed to give the pure compound as a dark yellow solid. This compound was not soluble in any deuterated solvents or perfluorocarbon solvents and hence, no NMR data could be obtained (0.445 g, 40 %). mp 226-228 °C (from CF_3CH_2OH); Anal. Calcd for $C_{29}H_{18}N_4F_{34}Br_2Pd$: C, 34.21; H, 4.59; N, 10.64. Found C, 34.34; H, 4.63; N, 10.60; m/z (FAB) *Not conclusive*; IR (Solid State, cm^{-1}) 1197.6 (br s), 1147.9 (s), 1116.5 (s).

Preparation of 1,1'-dibutyl -3,3'-[1,3-(methyl)benzene]imidazolium dibromide (169)

The title compound was prepared similarly to (164), using *N*-butylimidazole (155) (1.30 g, 10.48 mmol), 1,3-*bis*(bromomethyl)benzene (1.35 g, 5.11 mmol) and toluene (10 mL) to give a hygroscopic brown oil (1.63 g, 62 %). Anal. Calcd for $C_{22}H_{32}N_4Br_2.1.4H_2O$: C, 49.14; H, 6.48; N, 10.42. Found C, 48.79; H, 6.45; N, 9.92; ^1H NMR (300 MHz, $CDCl_3$) δ_H 10.38 (2 H, s, NC*H*N), 8.12 (2 H, s, NC*H*CHN), 8.11 (1 H, s, ArH-2), 7.58 (2 H, d, $^3J_{HH}$ = 7.8 Hz, ArH-4,6), 7.37 (2 H, s, NC*H*CHN), 7.17 (1 H, d, $^3J_{HH}$ = 7.8 Hz, ArH-5), 5.59 (4 H, s, ArCH$_2$N), 4.24 (4 H, t, $^3J_{HH}$ = 7.7 Hz, NCH$_2$), 1.87-1.76 (4 H, m, NCH$_2$C*H$_2$*), 1.34-1.22 (4 H, m, N(CH$_2$)$_2$C*H$_2$*CH$_3$), 0.87 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH$_3$), 0.86 (3 H, t, $^3J_{HH}$ = 7.2 Hz, CH$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 136.50 (CH), 134.77 (C), 130.39 (CH), 129.99 (CH), 129.92 (CH), 123.34 (CH), 121.98 (CH), 52.34 (CH$_2$), 49.88 (CH$_2$), 31.98 (CH$_2$), 19.43 (CH$_2$), 13.42 (CH$_3$); m/z (FAB) 433/431 ([M-Br]$^+$, 100 %), 351 ([M-2Br]$^+$, 49 %); HRMS (FAB) calculated for $C_{22}H_{32}N_4Br$: 431.18103, found 431.18100; IR (Solid State, cm^{-1}) 3058.2 (m), 2958.9 (m), 1558.3 (m), 1154.9 (m), 747.22 (m).

Preparation of 1,1'-*bis*(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)-3,3'-[1,3-(methyl)benzene]imidazolium dibromide (170)

The title compound was prepared similarly to (164), using *N*-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazole (154) (1.00 g, 1.89 mmol), 1,3-*bis*(bromomethyl)benzene (0.250 g, 0.947 mmol) and BTF (15 mL). The reaction was allowed to cool to room temperature and the solvent was removed. The crude reaction mixture was washed with hot diethyl ether (4 x 50 mL) and CHCl$_3$ (2 x 50 mL) to give the pure product as a white solid (0.400 g, 32 %). mp 262-264 °C (from CHCl$_3$); Anal. Calcd for $C_{36}H_{26}N_4F_{34}Br_2$: C, 32.75; H, 1.98; N, 4.24. Found C, 32.82; H, 2.03; N, 4.17; ^1H NMR (400 MHz, d^6-DMSO, 347 K) δ_H 9.51 (2 H, br s, NC*H*N), 7.86 (2 H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.6 Hz, NC*H*CHN), 7.84 (2 H, vt, $^3J_{HH}$ = $^4J_{HH}$ = 1.6 Hz, NC*H*CHN), 7.66 (1 H, br s, ArH-2), 7.49-7.45 (3 H, m, ArH-4,5,6), 5.50 (4 H, s, ArCH$_2$N), 4.37 (4 H, t, $^3J_{HH}$ = 7.3 Hz, NCH$_2$), 2.36 (4 H, tt, $^3J_{HF}$ = 19.2 Hz, $^3J_{HH}$ = 7.6

Hz, CH_2CF$_2$), 2.17 (4 H, quint., $^3J_{HH}$ = 7.6 Hz, NCH$_2$CH_2); ^{19}F NMR (376 MHz, d^6-DMSO, 347 K) δ_F -81.03 (6 F, m, CF$_3$), -113.11 (4 F, m, α-CF$_2$), -121.80 (4 F, m, CF$_2$), -122.06 (8 F, m, 2 x CF$_2$), -122.82 (4 F, m, CF$_2$), -123.27 (4 F, m, CF$_2$), -126.10 (4 F, m, CF$_2$); ^{13}C NMR (101 MHz, d^6-DMSO, 347 K) δ_C 137.15 (CH), 135.79 (C), 130.08 (CH), 129.26 (CH), 129.22 (CH), 123.20 (CH), 123.19 (CH), 52.37 (CH$_2$), 49.47 (CH$_2$), 27.74 (t, $^2J_{CF}$ = 21.6 Hz, CH$_2$), 21.42 (CH$_2$); m/z (FAB) 1241/1239 ([M-Br]$^+$, 60 %); IR (Solid State, cm^{-1}) 1513.3 (w), 1196.8 (br s), 1148.0 (s), 1116.8 (s).

Attempted preparation of 1,3-{[1,1'-dibutyl-3,3'imidazol-2-ylidene-](methyl)benzene]} palladium bromide (167a)

The title compound was prepared by an adaptation of Danopoulos's method.[27] A 50 mL Schlenk tube was charged with 1,1'-dibutyl-3,3'-[1,3-(methyl)benzene]imidazolium dibromide (169) (1.10 g, 2.15 mmol), palladium acetate (0.483 g, 2.15 mmol), sodium acetate (0.194 g, 2.37 mmol) and DMA (20 mL). The flask was evacuated and refilled with argon (x 3), before the tube was sealed and heated at 145 °C for 24 h and then 160 °C for 24 h. The reaction was cooled to room temperature, a sample taken and the solvent was removed. The residue was washed with MeOH (2 x 5 mL) and dried under high vacuum. The compound was analysed by ^{1}H NMR spectroscopy and MS. There was none of the imidazolium salt present but there were no signs of product. The ^{1}H NMR spectrum was very broad and complicated. m/z (FAB) 1233 ([C$_{44}$H$_{60}$N$_8$Br$_4$Pd$_2$]$^+$, 8 %), 1153 ([C$_{44}$H$_{60}$N$_8$Br$_3$Pd$_2$]$^+$, 20 %).

Attempted preparation of 1,3-{[1,1'-dibutyl-3,3'imidazol-2-ylidene-](methyl)benzene}-palladium bromide (167b)

A 50 mL Schlenk tube was charged with 1,1'-dibutyl-3,3'-[1,3-(methyl)benzene]imidazolium dibromide (169) (1.90 g, 3.71 mmol), palladium acetate (0.833 g, 3.71 mmol), sodium acetate (0.344 g, 4.08 mmol) and 2-methoxyethanol (20 mL). The flask was evacuated and refilled with argon (x 3) before the tube was sealed and heated at 130 °C for 14 h. A sample was taken and only starting material was detected by ^{1}H NMR spectrscopy.

Attempted preparation of 1,3-{[1,1'-dibutyl-3,3'imidazol-2-ylidene-](methyl)benzene}-palladium bromide (167c)

The title compound was prepared similarly to (160). A 50 mL Schlenk tube was charged with 1,1'-dibutyl-3,3'-[1,3-(methyl)benzene]imidazolium dibromide (169) (0.187 g, 0.365 mmol), palladium acetate (0.0820 g, 0.365 mmol), sodium acetate (0.0660 g, 0.803 mmol) and DMSO (20 mL). The flask was evacuated and refilled with argon (x 3) before the

tube was sealed and heated at 100 °C for 14 h. After cooling to room temperature, the solvent was removed by heating under high vacuum (0.1 mbar, 75 °C). The residue was taken up in CHCl$_3$ and filtered through a short pad of silica gel to give Fraction 1, which gave a brown solid. The silica was then eluted with DCM/Acetone (3:2) to give Fraction 2, which gave a yellow solid. Both products were analysed by ^{1}H & ^{13}C NMR spectroscopy and MS. **Fraction 1** (Crude **167**-Selected peaks): ^{1}H NMR (300 MHz, CDCl$_3$) δ_H 6.92 (2 H, d, $^3J_{HH}$ = 7.4 Hz, ArH-*3,5*), 6.89 (2 H, d, $^3J_{HH}$ = 1.8 Hz, NC*H*CHN), 6.83-6.77 (1 H, m, ArH-*4*), 6.67 (2 H, d, $^3J_{HH}$ = 1.8 Hz, NC*H*CHN), 5.36 (2 H, d, J_{HH} = 13.5 Hz, ArCH$_2$N), 4.77 (1 H, dd, J_{HH} = 13.5 Hz, J_{HH} = 6.7 Hz, NCH$_2$), 4.74 (1 H, dd, J_{HH} = 13.5 Hz, J_{HH} = 6.7 Hz, NCH$_2$), 4.55 (2 H, d, J_{HH} = 13.5 Hz, ArCH$_2$N), 4.24 (1 H, dd, J_{HH} = 9.0 Hz, J_{HH} = 5.6 Hz, NCH$_2$); ^{13}C NMR (75 MHz, CDCl$_3$) δ_C 176.42 (C), 140.06 (C), 127.84 (C), 127.08 (CH), 123.57 (CH), 118.90 (CH), 118.57 (CH), 64.99 (CH$_2$), 49.61 (CH$_2$), 32.60 (CH$_2$), 18.70 (CH$_2$), 12.87 (CH$_3$); HRMS (FAB) calculated for C$_{22}$H$_{29}$N$_4$Pd: 453.14282, found 453.14272; **Fraction 2 (172):** HRMS (FAB) calculated for C$_{22}$H$_{30}$N$_4$Pd: 454.15065, found 454.15068; Further attempts to form the cyclometallated product **(167)** failed.

6.2.6 Catalysis and Recycling for Chapter Four

General procedure for solvent/base/PTC optimisation for Heck reaction (C4.1-C4.14)

NHC palladium catalysts (1 mol-%, 0.0048 mmol), aryl bromide (0.480 mmol), solid bases (0.528 mmol), TBAB (0.0309 g, 0.0960 mmol) and tolyl ether (0.0952 g, 0.480 mmol) were added to Radley's Carousel reaction tubes. The tube was evacuated and refilled with nitrogen (x3) before alkyl acrylate (0.720 mmol), any liquid bases (0.528 mmol) and solvent (2 mL) were added. The tube was placed into a preheated oil bath (120 °C), samples (0.01 mL) were taken over 24 hours and analysed by GC using PE-5 column, injector: 250 °C, detector 240 °C. Flow rate 1 mL/min. 200 °C for 5 min, R_t 2.2 min (4-bromoacetophenone), 3.2 min (tolyl ether), 4.5 min (*trans*-methyl 4-acetylcinnamate). 150 °C, 20 °C min^{-1} to 240 °C over 4.5 min and held for 5 min; R_t 2.4 min (4-bromobenzaldehyde), 3.8 min (tolyl ether), 5.5 min (*trans-n*-butyl 4-formylcinnamate). Conversions of product were determined using tolyl ether as internal standard.

Recycling procedure for the Heck reaction between 4-bromobenzaldehyde and butyl acrylate (C4.15)

4-Bromobenzaldehyde (0.529 g, 2.86 mmol), NaOAc (0.258 g, 0.315 mmol), tolyl ether (0.571 g, 2.86 mmol) and **(161)** (45.0 mg, 1 mol-%) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with nitrogen (x3), before butyl acrylate (0.0923 g, 0.103 mL, 0.720 mmol) and DMF (2.00 mL) were added. The tube was placed into

a preheated oil bath (120 °C), samples (0.01 mL) were taken over 24 h and analysed by GC. The reaction mixture was allowed to cool to room temperature under argon before the solvent and the remaining volatiles were removed by Kugelröhr distillation (0.1 mbar, 40 °C). The resulting solid was taken up in MeOH (2 mL) before loading onto a column of FRPSG (4 g) which had been pre-treated with MeOH:H$_2$O (80:20). The flask was washed with DCM (0.5 mL x 2) and finally with MeOH (2 mL).The column was eluted with MeOH:H$_2$O (80:20, 90 mL) to give the organic products and then Et$_2$O (90 mL) to give fluorous catalyst. Conversion was determined by GC using tolyl ether as an internal standard.

Recycle procedure for the Heck coupling reaction between 4-bromobenzaldehyde and butyl acrylate using (159) supported on FRPSG (C4.16-C4.19)

4-Bromobenzaldehyde (0.0888 g, 0.480 mmol), NaOAc (0.0433 g, 0.528 mmol), tolyl ether (0.0952 g, 0.480 mmol) and palladium catalyst (159) on FRPSG (0.2243 g, 1 mol-%) were added to a Radley's Carousel reaction tube. The tube was evacuated and refilled with nitrogen (x3), before butyl acrylate (0.0923 g, 0.103 mL, 0.720 mmol) and DMF (2.00 mL) were added. The tube was placed into a preheated oil bath (120 °C), samples (0.01 mL) were taken over 24 hours and analysed by GC. After the reaction, the crude reaction mixture was then filtered, washed with DCM to remove any excess product, and finally washed with MeOH:H$_2$O (80:20) to remove the inorganic base. The solid support was dried under vacuum to remove any residual solvents. Fresh reagents were added and the general procedure was then followed reusing the supported catalyst for a further 2 runs.

6.3 References for Chapter Six .

1   P. Bhattacharyya, D. Gudmunsen, E. G. Hope, R. D. W. Kemmitt, D. R. Paige, and A. M. Stuart, *J. Chem. Soc., Perkin Trans. 1*, 1997, 3609.

2   S. Schneider and W. Bannwarth, *Angew. Chem. Int. Ed. Engl.*, 2000, **39**, 4142.

3   S. Darses, M. Pucheault, and J. P. Genet, *Euro. J. Org. Chem.*, 2001, 1121.

4   J. Fawcett, E. G. Hope, R. D. W. Kemmitt, D. R. Paige, D. R. Russell, and A. M. Stuart, *J. Chem. Soc.; Dalton Trans.*, 1998, 3751.

5   L. V. Rybin, E. A. Petrovskaya, M. I. Rubinskaya, L. G. Kuzmina, Y. T. Struchkov, V. V. Kaverin, and N. Y. Koneva, *J. Organometal. Chem.*, 1985, **288**, 119.

6   S. Schneider and W. Bannwarth, *Helv. Chim. Acta*, 2001, **84**, 735.

7   C. C. Tzschucke, C. Markert, H. Glatz, and W. Bannwarth, *Angew. Chem. Int. Ed. Engl.*, 2002, **41**, 4500.

8   S. Gronowitz, K. Stenhammar, and L. Svensson, *Heterocycles*, 1981, **15**, 947.

9   J. M. Plater and T. Jackson, *Tetrahedron*, 2003, **59**, 4673.

10 C. Yuan and H. Feng, *Synthesis*, 1990, 140.

11 F. Kagan, R. D. Birkenmeyer, and R. E. Strube, *J. Am. Chem. Soc.*, 1959, **81**, 3026.

12 M. J. P. Harger, *J. Chem. Soc., Perkin Trans 2*, 2001, 41.

13 A. M. Kinnear and E. A. Perren, *J. Chem. Soc.*, 1952, 3437.

14 K. S. Vallin, Q. Zhang, M. Larhed, D. P. Curran, and A. Hallberg, *J. Org. Chem.*, 2003, **68**, 6639.

15 E. N. Tsvetkov, N. A. Bondarenko, I. G. Malakhova, and M. I. Kabachnik, *Synthesis*, 1985, 198.

16 Y.-C. Tan, X.-M. Gan, J. L. Stanchfield, E. N. Duesler, and R. T. Paine, *Inorg. Chem.*, 2001, **40**, 2910.

17 W. P. Chen, L. J. Xu, Y. L. Hu, A. M. B. Osuna, and J. L. Xiao, *Tetrahedron*, 2002, **58**, 3889.

18 I. P. Beletskaya, A. V. Chuchuryukin, G. van Koten, H. P. Dijkstra, G. P. M. van Klink, A. N. Kashin, S. E. Nefedov, and I. L. Eremenko, *Russ. J. Org. Chem.*, 2003, **39**, 1268.

19 H. Rimml and L. M. Venanzi, *J. Organometal. Chem.*, 1983, **259**, C6.

20 R. J. Cross, A. R. Kennedy, and K. W. Muir, *J. Organometal Chem.*, 1995, **487**, 227.

21 M. A. Bennett, H. Jin, and A. C. Willis, *J. Organometal. Chem.*, 1993, **451**, 249.

22 J. M. Vincent, A. Rabion, V. K. Yachandra, and R. H. Fish, *Can. J. Chem.*, 2001, **79**, 888.

23 J. M. Vincent, A. Rabion, V. K. Yachandra, and R. H. Fish, *Angew. Chem. Int. Ed. Engl.*, 1997, **36**, 2346.

24 L. J. Xu, W. P. Chen, J. F. Bickley, A. Steiner, and J. L. Xiao, *J. Organometal. Chem.*, 2000, **598**, 409.

25 L. J. Xu, W. P. Chen, and J. L. Xiao, *Organometallics*, 2000, **19**, 1123.

26 K. Okuyama, J. Sugiyama, R. Nagahata, M. Asai, M. Ueda, and K. Takeuchi, *J. Mol. Cat. A: Chem.*, 2003, **203**, 21.

27 A. A. Danopoulos, A. A. D. Tulloch, S. Winston, G. Eastham, and M. B. Hursthouse, *J. Chem. Soc., Dalton Trans.*, 2003, 1009.

Appendix

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Appendix

A 1

Crystal Data and Structure Refinement for {2,6-*bis*[methyl(diphenylphosphino)]-phenyl}palladium chloride

Empirical formula	C32 H27 Cl P2 Pd
Formula weight	615.33
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/c
Unit cell dimensions	$a = 10.2316(17)$ Å $\quad \alpha = 90°$.
	$b = 15.959(3)$ Å $\quad \beta = 106.954(3)°$.
	$c = 17.300(3)$ Å $\quad \gamma = 90°$.
Volume	2702.1(8) Å^3
Z	4
Density (calculated)	1.513 Mg/m^3
Absorption coefficient	0.924 mm^{-1}
F(000)	1248
Crystal size	0.18 x 0.12 x 0.08 mm^3
Theta range for data collection	1.77 to 26.00°.
Index ranges	-12<=h<=12, -19<=k<=19, -21<=l<=21
Reflections collected	20831
Independent reflections	5308 [R(int) = 0.0520]
Completeness to theta = 26.00°	100.0 %
Absorption correction	Empirical
Max. and min. transmission	0.894 and 0.702
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5308 / 0 / 325
Goodness-of-fit on F^2	1.084
Final R indices [I>2sigma(I)]	R1 = 0.0561, wR2 = 0.1188
R indices (all data)	R1 = 0.0749, wR2 = 0.1267
Largest diff. peak and hole	2.266 and -0.466 e.Å^{-3}

I

A 2

Crystal Data and Structure Refinement for {2,6-*bis*[methyl(diphenylphosphino)]-phenyl}nickel chloride

Empirical formula	C32 H27 Cl Ni P2
Formula weight	567.64
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 10.146(4) Å α= 90°.
	b = 15.988(7) Å β= 105.768(8)°.
	c = 16.899(7) Å γ = 90°.
Volume	2638.0(18) Å^3
Z	4
Density (calculated)	1.429 Mg/m^3
Absorption coefficient	0.978 mm^{-1}
F(000)	1176
Crystal size	0.20 x 0.16 x 0.08 mm^3
Theta range for data collection	1.79 to 26.00°.
Index ranges	-12<=h<=12, -19<=k<=19, -20<=l<=20
Reflections collected	20425
Independent reflections	5182 [R(int) = 0.0789]
Completeness to theta = 26.00°	99.7 %
Absorption correction	Empirical
Max. and min. transmission	0.928 and 0.604
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5182 / 0 / 325
Goodness-of-fit on F^2	1.048
Final R indices [I>2sigma(I)]	R1 = 0.0591, wR2 = 0.1210
R indices (all data)	R1 = 0.0865, wR2 = 0.1308
Largest diff. peak and hole	0.881 and -0.548 e.Å^{-3}

A 3

Crystal Data and Structure Refinement for {2,6-*bis*[methyl(diphenylphosphino)]-phenyl}platinum chloride

Empirical formula	C32 H27 Cl P2 Pt
Formula weight	704.02
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	a = 10.234(9) Å, α= 90°.
	b = 15.960(14) Å, β= 105.502(14)°.
	c = 17.046(15) Å, γ = 90°.
Volume	2683(4) Å^3
Z	4
Density (calculated)	1.743 Mg/m^3
Absorption coefficient	5.469 mm^{-1}
F(000)	1376
Crystal size	0.40 x 0.31 x 0.21 mm^3
Theta range for data collection	1.78 to 26.00°.
Index ranges	-12<=h<=12, -19<=k<=19, -21<=l<=20
Reflections collected	20412
Independent reflections	5269 [R(int) = 0.0578]
Completeness to theta = 26.00°	99.9 %
Absorption correction	Empirical
Max. and min. transmission	0.563 and 0.295
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5269 / 0 / 325
Goodness-of-fit on F^2	1.032
Final R indices [I>2sigma(I)]	R1 = 0.0319, wR2 = 0.0768
R indices (all data)	R1 = 0.0375, wR2 = 0.0790
Largest diff. peak and hole	2.459 and -0.799 e.Å^{-3}

A 4

Crystal Data and Structure Refinement for *N*-(1*H*,1*H*,2*H*,2*H*,3*H*,3*H*-perfluoro-*n*-undecyl)imidazole

Empirical formula	C14 H9 F17 N2
Formula weight	528.23
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 6.1845(17) Å $\quad$ α= 90°.
	b = 7.371(2) Å $\quad$ β= 90°.
	c = 40.770(11) Å $\quad$ γ = 90°.
Volume	1858.6(9) Å^3
Z	4
Density (calculated)	1.888 Mg/m^3
Absorption coefficient	0.233 mm^{-1}
F(000)	1040
Crystal size	0.19 x 0.17 x 0.09 mm^3
Theta range for data collection	2.00 to 26.00°.
Index ranges	-7<=h<=7, -9<=k<=9, -48<=l<=50
Reflections collected	14410
Independent reflections	2167 [R(int) = 0.1184]
Completeness to theta = 26.00°	100.0 %
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2167 / 0 / 298
Goodness-of-fit on F^2	1.134
Final R indices [I>2sigma(I)]	R1 = 0.0849, wR2 = 0.1507
R indices (all data)	R1 = 0.1273, wR2 = 0.1647
Absolute structure parameter	-10(10)
Largest diff. peak and hole	0.278 and -0.306 e.Å^{-3}

A 5

Crystal Data and Structure Refinement for *trans-bis*[1,3-dibutylimidazol-2-ylidene]-palladium diiodide

Empirical formula	C48 H92 I4 N8 O2 Pd2 S2
Formula weight	1597.82
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions	a = 29.577(6) Å $\quad$ α= 90°.
	b = 13.056(3) Å $\quad$ β= 122.644(3)°.
	c = 18.488(4) Å $\quad$ γ = 90°.
Volume	6011(2) Å^3
Z	4
Density (calculated)	1.765 Mg/m^3
Absorption coefficient	2.764 mm^{-1}
F(000)	3152
Crystal size	0.37 x 0.32 x 0.26 mm^3
Theta range for data collection	1.76 to 25.00°.
Index ranges	-35<=h<=35, -15<=k<=15, -21<=l<=21
Reflections collected	21050
Independent reflections	5295 [R(int) = 0.0393]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Empirical
Max. and min. transmission	0.746 and 0.576
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5295 / 0 / 269
Goodness-of-fit on F^2	1.069
Final R indices [I>2sigma(I)]	R1 = 0.0401, wR2 = 0.1034
R indices (all data)	R1 = 0.0461, wR2 = 0.1068
Largest diff. peak and hole	1.172 and -0.803 e.Å^{-3}

A 6

Crystal Data and Structure Refinement for 1,3-dibutylimidazol-2-ylidene]diiodo-µµ'-palladium diiodide

Empirical formula	C22 H40 I4 N4 Pd2
Formula weight	1080.98
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions	a = 15.529(13) Å α= 90°.
	b = 15.137(12) Å β= 117.036(12)°.
	c = 15.364(13) Å γ = 90°.
Volume	3217(5) Å^3
Z	4
Density (calculated)	2.232 Mg/m^3
Absorption coefficient	4.974 mm^{-1}
F(000)	2016
Crystal size	0.29 x 0.21 x 0.18 mm^3
Theta range for data collection	1.99 to 27.00°.
Index ranges	-19<=h<=19, -19<=k<=19, -19<=l<=19
Reflections collected	13223
Independent reflections	3508 [R(int) = 0.0382]
Completeness to theta = 27.00°	99.9 %
Absorption correction	Empirical
Max. and min. transmission	0.694 and 0.467
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3508 / 0 / 147
Goodness-of-fit on F^2	1.169
Final R indices [I>2sigma(I)]	R1 = 0.0318, wR2 = 0.0759
R indices (all data)	R1 = 0.0349, wR2 = 0.0775
Largest diff. peak and hole	1.373 and -0.924 e.Å^{-3}

A 7

Crystal Data and Structure Refinement for [1,1'-dibutyl-3,3'-methyleneimidazolin-2,2'-diylidene]palladium dibromide

Empirical formula	C15.50 H25.50 Br2 N4 O0.25 Pd S0.25
Formula weight	546.13
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)/n
Unit cell dimensions	$a = 10.4849(18)$ Å $\quad \alpha = 90°$.
	$b = 15.282(3)$ Å $\quad \beta = 103.934(3)°$.
	$c = 13.612(2)$ Å $\quad \gamma = 90°$.
Volume	2116.9(6) Å^3
Z	4
Density (calculated)	1.714 Mg/m^3
Absorption coefficient	4.681 mm^{-1}
F(000)	1074
Crystal size	0.35 x 0.28 x 0.12 mm^3
Theta range for data collection	2.21 to 26.00°.
Index ranges	-12<=h<=12, -18<=k<=18, -16<=l<=16
Reflections collected	16237
Independent reflections	4151 [R(int) = 0.0540]
Completeness to theta = 26.00°	99.9 %
Absorption correction	Empirical
Max. and min. transmission	0.694 and 0.455
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4151 / 0 / 201
Goodness-of-fit on F^2	0.897
Final R indices [I>2sigma(I)]	R1 = 0.0440, wR2 = 0.0990
R indices (all data)	R1 = 0.0665, wR2 = 0.1036
Largest diff. peak and hole	1.229 and -0.811 e.Å^{-3}

A 8 Lecture Courses Attended

Title

Retrosynthetic Analysis   Dr. P. Jenkins

Organic Strategies   Dr. P. Jenkins / Dr. S. Handa

A 9 Organic/Inorganic Seminar Programme

2003

6th October , Dr. Chris Richards (Queen Mary, University of London), *Palladium and Platinum Metallacycles for Organic Synthesis*

8th October, Prof. Iain Campbell, FRS (University of Oxford), 2nd Tim Norwood Memorial Lecture, *NMR and Proteins*

20th October, Dr. Sandie Dann (University of Loughborough), *Unusual Complex Oxides and Sulfides*

27th October, Dr. Chris Hayes (University of Nottingham), *Natural and Non-natural Products: Total Synthesis and Biological Applications*

3rd November, Prof. Helen Fielding (U.C.L.), *Controlling Electrons and Molecules using Light*

14th November, Prof. Walter Leitner (Max Planck Institute, Mülheim), Greiss Lecture (RSC), *Green Solvents for Catalysis – From Molecular Understanding to Process Design*

24th November, Prof. Thomas Wirth (Cardiff University), *Scope and Potential of Chiral Electrophiles in Stereoselective Synthesis*

8th December, Professor Peter Hore (University of Oxford), *Bird Navigation: a Photochemical Magnetic Compass?*

2004

12th January, Dr. Liam Cox (University of Birmingham), *Exploiting Silicon Reagents in Asymmetric Reactions*

19th January, Prof. Bill Levason (University of Southampton), *Recent Developments in the Chemistry of Antimony Ligands*

2nd February, Dr. Adam Nelson (University of Leeds), *Synthesis of Biologically Active Compounds*

9th February, Dr. Michael Whitlesey (University of Bath), *Stoichiometric and Catalytic Ruthenium Carbene Systems*

23rd February, 3rd Leicester Half-Day Catalysis Symposium; Prof. P. Braunstein (University of Strasbourg), Prof. Sue Gibson (Imperial College, London), Dr. P. Kamer (University of Amsterdam), Dr. Gregory Solan (University of Leicester)

1st March, Dr. Iain Coldham (University of Sheffield), *Stereoselective Synthesis of Cyclic Amines using Chiral Organolithium Species and Cycloaddition Reactions*

15th March, Professor David Schiffrin (University of Liverpool), *Connectivity of Functionalised Nanoparticles and their Arrays*

29th March, Dr. Polly Arnold (University of Nottingham), *Synthesis and Reactivity of Organometallic Complexes*

26th April, Dr. Graham Sandford (University of Durham), *Polyfunctional Heterocycles and Macrocycles*

10th May, Dr. Dominic Wright (University of Cambridge), *Torocyclic Ligands*

31st May, Dr. Steve Allin (Loughborough University), *New Asymmetric Routes to Chiral Heterocycles*

7th June, Dr. Peter Scott (University of Warwick), *Catalysis with Chiral Metal Complexes*

15th October, Prof. Eric Herbst (Ohio State University), *Chemistry and Star Formation*

25th October, Prof. Alan Armstrong (Imperial College, London), *New Methods and Synthetic Applications of Asymmetric Heteroatom Transfer*

11th November, Dr Helen Aspinall (University of Liverpool), *Chiral Lanthanides Complexes for Organic Synthesis*

15th November, Dr Gareth J. Pritchard (University of Loughborough), *New Routes to Heterocyclic Systems From Vinylcyclopropanes*

2005

17th January, Dr Stuart McGregor (Heriot-Watt University, Edinburgh), *Non-innocent N-Heterocyclic Carbene and Phosphine Ligands*

7th February, Dr Mike Hill (Imperial College, London), *Molecular Catalysis with Group 2 Metals*

14th June, Dr Simon Jones (University of Sheffield), *Fiddling With Phosphorus*
13th June Dr. Robert (Stockmann, University of East Anglia),*Combining Two-Directional Synthesis and Tandem Reactions: Developing Efficient Strategies For Chemistry*

31th August Prof. Norio Shibata (Nagoya Institute of Technology, Japan), *Development of Enantioselective Fluorination Reaction and its Application to the Synthesis of Biologically Compounds*

10th October, Dr. Christopher Frost (University of Bath), *Exploring New Strategies in Organic Synthesis via Catalytic Conjugate Addition*

17th October, Prof Gary Attard (University of Cardiff), *Aspects of Chiral Surface Chemistry: an Electrochemical Perspective*

26th October, Prof. R.H. Holm (Harvard University), *Structural and Functional Analogues of Molybdenum and Tungsten Oxotransferases/Hydroxylases: What can be Learned?*

31st October, Prof. Matthew Davidson (University of Bath), *Metal and Metal-free Phenolates: Catalysts, Sensors and Surprises*

7th November, Prof. Richard Templar (Imperial College London), *How Cells Survive-from Lipids to Liquid Crystals*

9th November, Prof.. Peter H. Seeberger (ETH, Zurich), *Chemical Glycomics: Automated Synthesis of Carbohydrates as a Platform for Biological and Medical Research*

14th November, Dr. Richard S. Grainger (University of Birmingham), *Harnessing Reactive Intermediates for Organic Synthesis*

29th November, Prof. Tim Softley (University of Oxford), *From Highly Excited to Ultracold Molecules: Chemical Dynamics in the Extreme*

5th December, Prof. Tom Simpson (University of Bristol), *Chemical and Biochemical Studies on Polyketide Natural Products*

A 10 Conferences Attended

Organic Synthesis Symposium. University of Loughborough, October 2003

Sheffield Stereochemistry Meeting. University of Sheffield, December 2003

Leicester Catalysis Symposium. University of Leicester, February 2004

Bristol Synthesis Meeting. University of Bristol, April 2004

Coordination Chemistry Discussion Group. University of Leicester, June 2004

RSC Fluorine Subject Group Meeting. University of Durham, September 2004

Organic Synthesis Symposium. University of Loughborough, October 2004

RSC Industry Tour. November 2004

Sheffield Stereochemistry Meeting. University of Sheffield, December 2004

Bristol Synthesis Meeting. University of Bristol, April 2005

Fluorination Technologies-Applications and Challenges. Syngenta, April 2005

RSC Organic Division. University of Loughborough, April 2005

Catalysis Summer School, Liverpool University, September 2005

Organic Synthesis Symposium. University of Loughborough, October 2005

RSC Organic Division. University of Warwick, April 2006

Fluorine Symposium. University of Bremen, Germany, June 2006

Postgrad. Fluorine Subject Group Meeting. University of Manchester, September 2006

GSK Case Symposium. GSK Tonbridge, September 2006

A 11 Presentations

Presentation –'Fluorous Pincer Ligands for Palladium.' - University of Leicester.

Presentation –'Fluorous Pincer Ligands for Palladium.'(Updated) – GSK Tonbridge.

Poster – 'Synthesis of Fluorous Phosphine-derivatised Palladium(II) catalysts and their use in Suzuki Reactions.' D. Duncan, A. M. Stuart, E. G. Hope & M. Urquhart. Presented at Coordination Chemistry Discussion Group, RSC Industry Tour, RSC Fluorine Subject Group Meeting.

Poster – 'A Recyclable Fluorous Palladium Pincer Catalyst.' D. Duncan, A. M. Stuart, E. G. Hope & M. Urquhart. Presented at Organic Synthesis Symposium, Fluorine Symposium, Postgrad. Fluorine Subject Group Meeting.

A 12 Publications and Awards

D. J. Adams, J. A. Bennett, D. Duncan, E. G. Hope, J. Hopewell, A. M. Stuart A. J. West, *Polyhedron*, **2007**, *26*, 1505.