Complexes and Applications of

Substituted Bidentate P, S Ligands

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'Τα αγαθα κοποις κτωνται.'
'Good things in life are obtained through effort.'
'No pain, No gain.'
- Ancient Greek proverb

'We cannot teach people anything; we can only help them discover it within themselves.'
- Galileo Galilei, Italian scientist, 1564-1642

For my family

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Acknowledgements

Abstract

In recent years there has been great interest in developing bidentate systems where only one of the atoms is phosphorus. Mixed P, O– and P, N– donor ligands have been extensively applied in catalysis and there is growing interest with respect to potential applications of P, S-ligands. This thesis reports on the synthesis and application of a range of substituted P, S-ligands and the catalytic results obtained are discussed.

Chapter 2 describes the synthesis of several bidentate phosphinothiolate and -thioether (P, S) ligands. The P, S ligand 1-(diphenylphosphino)butane-2-thiol (L^1) was derived from a thiirane which was synthesised by the ring-opening reaction of an epoxide. The thioether tertiary-butyl derivative (L^2) was also synthesised along with the thioether methyl (L^3), thioether benzyl (L^4), thioether xylene (L^5), thioether naphthalene (L^6) and thioether anthracene (L^7). The ligands were subsequently coordinated to palladium and the resulting complexes (1-12) exhibit a monomeric or dimeric geometry.

Chapters 3 and 4 detail the application of the palladium complexes in catalytic reactions. The palladium phosphinothiolate and –thioether complexes have been tested as pre-catalysts in the Heck and Suzuki cross-coupling reactions which were performed under aerobic conditions. The Heck couplings with styrene and butyl acrylate were investigated along with a variety of haloarenes, and the Suzuki reactions have explored the cross-couplings of various haloarenes with benzene boronic acid. The complexes tested were highly efficient catalysts in the coupling reactions. Turnover numbers (TONs) of up to 1 million have been achieved for Heck couplings and 1.98×10^{10} for the Suzuki coupling reactions.

List of Abbreviations

Å	Angstroms
Anth	Anthracene
aq	Aqueous
Ar	Aromatic
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BINAPHOS	(R)-2-diphenylphosphino-1,1'-binaphthalen-2'-yl (S)-1,1'-binaphthalen-2,2'-diylphosphite
Bipy	2,2'-bipyridyl
Br	Broad
Bu	Butyl
Bn	Benzyl
^{13}C	Carbon thirteen isotope
cm	Centimetre
CN^-	Cyanide anion
Conc	Concentration
Coord-insert	Coordination-Insertion
Cy	Cyclohexyl
δ NMR	Chemical shift
d^6-benzene	Deuterated benzene
d	Doublet
damp	2-(N, N-dimethylaminomethyl)phenyl
dba	trans, trans-dibenzylideneacetone
dd	Double doublet
deg	Degree ($^\circ$)
DCM	Dichloromethane
DIPAMP	1,2-ethanediylbis(o-methoxyphenyl)phenylphosphine
DIPEA	Diisopropylethylamine
DIPHOS	1,2-ethanediylbis(diphosphine)
DIOP	{[2,2-dimethyl-1,3-dioxolan-4,5-diyl)bis(methylene)]-bis(diphenylphosphine)}
DMA	dimethylacetamide

DMF	N, N'-dimethylformamide, HCONMe$_2$
dppe	1,2-bis(diphenylphosphino)ethane
D$_{RF}$	Detector Response Factor
Elimin	Elimination
ES	Electrospray
Et	Ethyl
g	Grams
GC	Gas Chromatography
GC/MS	Gas Chromatography/Mass Spectrometry
GLC	Gas-Liquid Chromatography
GOF	Goodness-of-Fit
h	Hour
^{1}H	Proton
High Res	High Resolution
HPLC	High Performance Liquid Chromatography
IS	Internal Standard
J	Coupling Constant
K	Kelvin
L	Ligand
LDA	Lithium di-isopropylamide
λ	wavelength
Low Res	Low Resolution
m	Multiplet
M	Metal
Me	Methyl
MeCN	Acetonitrile
mg	Milligram
MHz	Mega Hertz
min	Minute
mL	Millilitre
mmol	Millimole
mol	Mole
Mol wt	Molecular Weight

m/z	Mass/charge ratio
MS	Mass Spectrometry
μ	Absorption Coefficient
Naphth	Naphthalene
NMR	Nuclear Magnetic Resonance
No.	Number
OA	Oxidative Addition
OAc	acetate anion
ppm	Parts per Million
Ph	Phenyl, C_6H_5
i-Pr	iso-propyl
Py	Pyridine
rt	Room Temperature
ρ	Density
R	Alkyl (preferably) or aryl group
rds	Rate Determining Step
RE	Reductive Elimination
rt	Room temperature, 25 °C
s	Singlet
sept	Septet
sext	Sextet
t	Triplet
T	Temperature
TBAB	tetrabutylammonium bromide
tert	Tertiary
THF	Tetrahydrofuran
THT	Tetrahydrothiophene
TLC	Thin Layer Chromatography
TMEDA	N, N, N', N'-tetramethyl-1,2-ethylenediamine
TMS	Tetramethylsilane
TOF	Turnover Frequency
TON	Turnover Number
X	Halogen

Xyl   Xylene

Chapter One

—— *Introduction* ——

1. Introduction

1.1 Group 10 metals

Group 10 consists of nickel, palladium and platinum. The general oxidation state for Ni is +II and for Pd and Pt are +II and +IV. When Pd and Pt are in the +II state (d^8 configuration) six electrons occupy the t_{2g} orbitals and two electrons lie in the e_g orbital (Figure 1). Pd^{2+} is a paramagnetic ion but the resulting complexes are square planar, bound to strong field ligands such as phosphines and are diamagnetic e.g. $[Pd(H_2O)_4]^{2+}$, along with other oxides, nitrates and sulphates. The simplest square planar complexes are $[PdCl_4]^{2-}$ and $[PtCl_4]^{2-}$. Octahedral complexes can also occur for Ni. As compounds in their II state, Pd and Pt tend to have an affinity for softer π-bonding ligands such as alkenes, alkynes, R_3P, R_2P, CN^- and NO_2^-. Pd and Pt can also occur as compounds with in the +IV state (d^6 configuration) with an octahedral geometry, such as the reactive complex $[PdX_6]^{2-}$ where X = F, Cl or Br and $[Pt(NH_3)_4Cl_2]^{2+}$. Pt(VI) is rare and is seen with an octahedral geometry also, for example PtF_6.

Octahedral	Square planar	Square planar
High spin d^8,	High spin d^8	Low spin d^8,
weak field		strong field
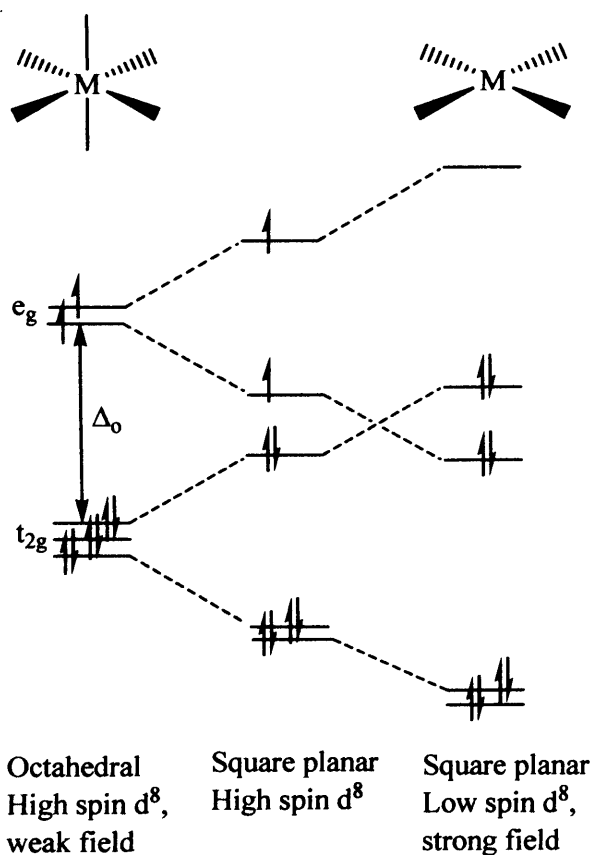
Figure 1. Energy level diagram for square planar complexes

1.2 Palladium

Palladium is one of the most important transition metals with wide use in industry and academia. Palladium is one of the most versatile catalysts used in organic chemistry due to its use in C-C coupling reactions (Heck, Suzuki etc) as well as catalysing C-H, C-O, C-P, C-N, C-S and C-CO-C bond forming reactions.

Palladium (0) can activate C-X bonds (where X = I, Br, Cl, O) by oxidative addition forming palladium (II) complexes which can then react with nucleophiles, and hence form the final complex after a number of steps. There exists a variety of Pd(0) complexes. These include Pd(0)L$_4$ where L = phosphine, which can catalyse any kind of reaction possessing a nucleophile. The second type of Pd(0) complex is generated in situ from a mixture of Pd$_2$(dba)$_3$ and phosphine, and is used in allylic substitution reactions, such as the Tsuji-Trost reaction.[1-5] The final Pd(0) complex is a mixture of divalent Pd(OAc)$_2$ and phosphine, which has shown catalytic efficiency in the Heck reaction. The efficiency of the palladium catalyst depends on the ligand attached and also on the Pd(0) precursor. The precursors of Pd(0) complexes have been determined to be Pd(II) complexes such as PdX$_2$L$_2$ (where X = Cl, Br, I). These complexes can catalyse cross-coupling and Stille reactions.[6]

1.2.1 History

The first Pd(IV) organic complex was reported in 1986 by Byers and co-workers.[7] The complex PdIMe$_3$(bpy) was synthesised by the oxidative addition of methyl iodide to the Pd(II) complex PdMe$_2$(bpy), as shown in Scheme 1.
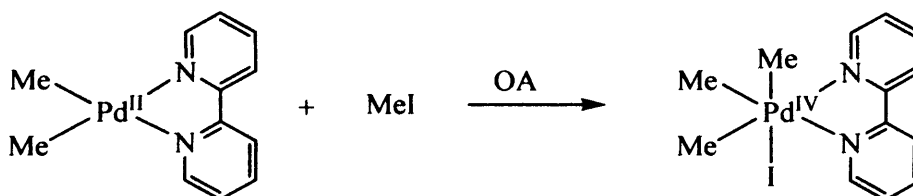
Scheme 1. Synthesis of the first Pd(IV) complex in 1986

This reaction has generated a great interest in Pd(IV) chemistry and allowed mechanisms to be studied that include oxidation and reductive elimination steps. The reactivity of the Pd(II) complex PdMe$_2$(bpy) has been studied by ^{1}H NMR investigations and results

showed that when reacted with MeI in $(CD_3)_2CO$ a cation of $[PdMe_3(bpy)((CD_3)_2CO)]^+I^-$ is formed. Following this the Pd(IV) complex is formed which reductively eliminates ethane to give the Pd(II) complex PdIMe(bpy).[8]

1.2.2 Reactivity

Organopalladium intermediates are often generated in situ from the inorganic palladium compounds or salts. Palladium is easily recoverable and reusable in subsequent reactions hence the use of stoichiometric amounts in organic synthesis is both economical and desirable.[9] Palladium(0) is usually an unreactive metal for use in organic chemistry but the finely divided metal supported on carbon has proven to be a useful catalyst for hydrogenations. Examples of this type of catalyst include tetrakis(triphenylphosphine)palladium(0) (the synthesis of which is shown in Scheme 2) and bis(dibenzylideneacetone)palladium(0).

$$2(Ph_3P)_2PdCl_2 + 4Ph_3P + 5N_2H_4 \longrightarrow 2(Ph_3P)_4Pd + 4N_2H_5^+Cl^- + N_2$$
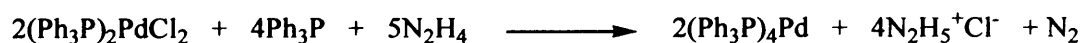
Scheme 2. Preparation of tetrakis(triphenylphosphine)palladium(0)

Palladium(II) σ-bonded complexes are stabilised by complexation with certain ligands such as phosphines, in particular triphenylphosphine due to its low cost and ease of accessibility. The first route to synthesising Pd(II) complexes (Scheme 3) is the oxidative addition of organic halides to the Pd(0) precursor, which produces monoalkyl, vinyl, heterocyclic or arylpalladium derivatives. The second general method of synthesis (Scheme 3) is the metathesis reaction with Main Group organometallics and palladium salts. The Pd(II) complexes produced are dependent on the reactants and the alkylating agent and can be mono- or dialkyl, or arylpalladium derivatives. Pd(II) complexes are generally seen as the in situ intermediates generated from palladium salts in palladium-catalysed reactions and from the oxidation reaction of an organic halide to a Pd(0) complex.

$$(C_2H_5)_3P \diagdown \diagup Br \\ Pd \\ Br \diagup \diagdown P(C_2H_5)_3 \quad + \quad 2CH_3Li \quad \longrightarrow \quad (C_2H_5)_3P \diagdown \diagup CH_3 \\ Pd \\ H_3C \diagup \diagdown P(C_2H_5)_3 \quad + \quad LiBr$$

$$C_6H_5Br \quad + \quad Pd(PPh_3)_4 \quad \longrightarrow \quad Ph_3P \diagdown \diagup Br \\ Pd \\ C_6H_5 \diagup \diagdown PPh_3 \quad + \quad 2PPh_3$$
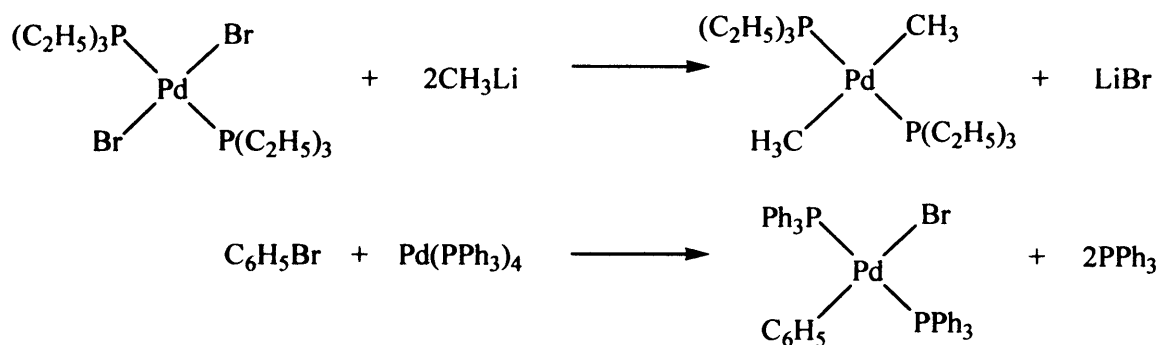
Scheme 3. Synthesis of Pd(II) complexes

More stable than the σ-allylic palladium derivatives are the π-allylic systems. Their stability is due to the delocalised system of π-electrons and the palladium atom being directly joined by two coordination positions to the allylic substrate. The five main methods of preparation for the π-allylic palladium complexes include the reaction of Pd(0) compounds with allylic halides by oxidative addition, the metathesis Pd(II) salts with main group allylic compounds, the reaction of Pd(II) salts with alkenes, the addition reaction of a Pd(II) compound to a conjugated diene and alkenes reacting with vinylic Pd compounds.[9]

The main chemistry that palladium is involved in includes palladium catalysed rearrangements (Pd(II) and Pd(0)), oxidation (Pd(II)) and coupling reactions. Palladium also plays a role in substitution reactions involving π alkenes. The palladium compounds formed can subsequently be utilised in elimination reactions which result in the formation of organic compounds.

Palladium has recently found widespread use as a catalyst, most notably in C-C coupling reactions, such as Heck[6,10-13] and Suzuki.[6,13-17] The parameters that must be fulfilled for the metal complex to display good catalytic activity are stability in the resting state but activation in solution allowing catalytic interaction with substrates.[18]

1.3 Phosphines

Phosphine ligands (PR₃) have found great importance in homogeneous catalysis and are considered one of the most important groups of ligands. Since their discovery in the late 19th century, including triphenylphosphine in 1885,[19] transition metal phosphine

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chemistry has been studied extensively and the phosphine ligands can be 'tuned' to possess the properties needed to synthesise a wide range of complexes which can be used in a variety of applications.

1.3.1 Diphosphines

Diphosphines have shown wide use in catalysis and other synthetic applications. In particular, chiral bidentate phosphines have been used broadly in asymmetric transformations. Symmetrical ligands of this type possess two donor atoms bearing similar steric and electronic parameters, examples include (+) or (-) DIOP and axially chiral BINAP. Phosphines bearing two donor atoms with different substituents show less symmetry. Ligands of this type include DIPAMP and BINAPHOS, as shown in Figure 2.[20]

DIOP

BINAP

DIPAMP

BINAPHOS
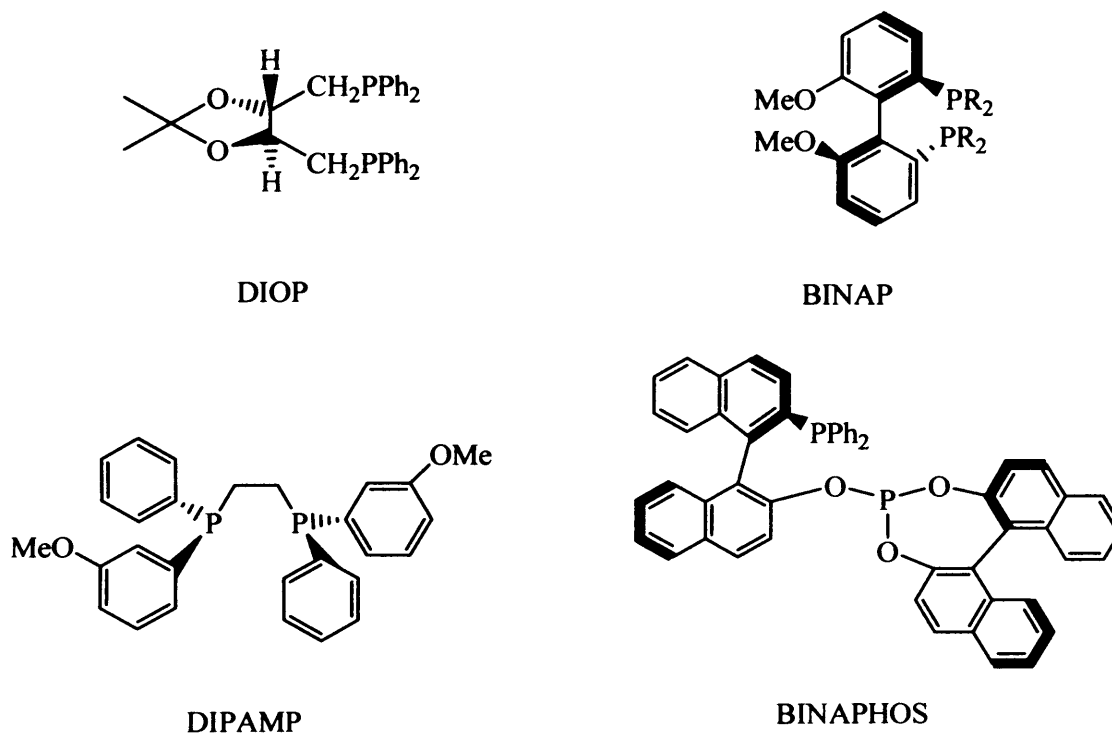
Figure 2. Symmetrical and unsymmetrical diphosphines

Symmetrical diphosphines which coordinate to transition metals form five membered rings in one of two conformations, δ- or λ-skew. For chiral diphosphines often one conformer is more favourable due to stereochemical differences of the ligand backbone i.e. equatorial vs. axial groups. Brunkan and co-workers showed the preferred

conformations to be δ for (S,S)-Chiraphos and both equally favourable for dppe (Figure 3).[21]

dppe - δ conformation   dppe - λ conformation   (S,S)-Chiraphos - δ conformation
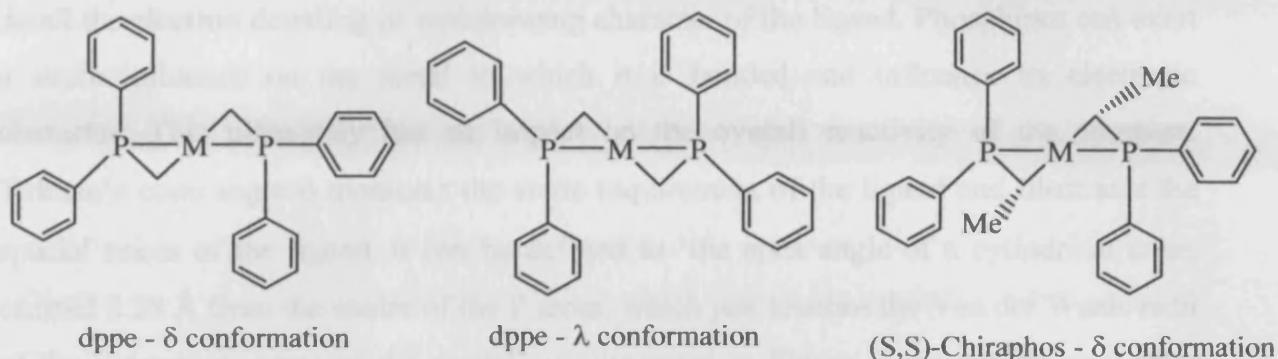
Figure 3. The preferred conformers for dppe and (S,S)-Chiraphos

(where M = Pt)

1.3.2 Steric and electronic effects

The stereochemistry and reactivity of phosphines are controlled by both the electronic and steric features they possess. The electronic properties in a phosphine-metal complex govern whether the bonding is σ- or π-type. A σ bond (Figure 4) is formed when a lone pair of electrons is donated from the phosphine to an empty p orbital on the metal. A π-type bond (Figure 4) is formed from 'back-donation' of electrons from the metal d orbitals. The orbitals involved in this 'back-donation' were thought to be empty 3d orbitals on the phosphine.[22] However experimental evidence has now shown that the σ^* anti-bonding orbitals are used, with some d-character.[23-26] The extent of π character is dependent on the nature of the substituents attached to the phosphine. Stronger π-bonds are formed from more electronegative substituents.

σ-bond

π*-bond
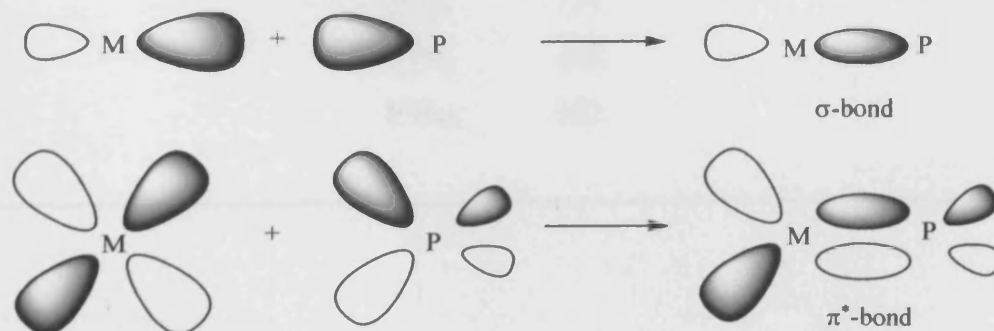
Figure 4. Definition of σ and π bonding

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It has been noted that steric effects dominate over electronic parameters. In 1977 Tolman[27] stated that the steric bulk of a phosphine ligand could be measured and hence detail the electron donating or withdrawing character of the ligand. Phosphines can exert a steric influence on the metal to which it is bonded and influence its electronic character. This ultimately has an impact on the overall reactivity of the complex. Tolman's cone angle θ measures the steric requirement of the ligand and illustrates the spacial needs of the ligand. θ can be defined as 'the apex angle of a cylindrical cone, centred 2.28 Å from the centre of the P atom, which just touches the Van der Waals radii of the outermost atoms of the model' as illustrated in Figure 5. As can be seen from Table 1.1 the larger θ the greater the steric influence of the ligand, for example for PH_3, $\theta = 87$ deg, for the bulky tertiary phosphine $P^tBu_3 = 182$ deg.
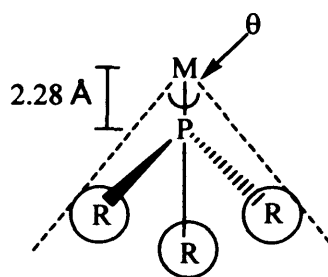
Figure 5. Tolman's cone angle

Table 1.1. Tolman cone angles for phosphine ligands

Phosphine	Cone angle (°)
PH_3	87
PMe_3	118
PEt_3	132
PPh_3	145
P^tBu_3	182

1.4 Chelates

Chelates are ligands that have two or more points of attachment on to the metal cation to which they are bound. They are more stable than the analogous unidentate ligands due to the greater number of bonds that need to be broken in the polydentate ligand for dissociation to occur. A ring structure is formed and the stability of chelates can be increased by the presence of delocalised bonding in the system, and the more rings that are formed the greater the stability of the resulting complex. Examples of bidentate ligands include 2,2-bipyridine (bipy) and 1,2-ethanediylbis(diphenylphosphine) (diphos) as shown in Figure 6.

bipy   diphos
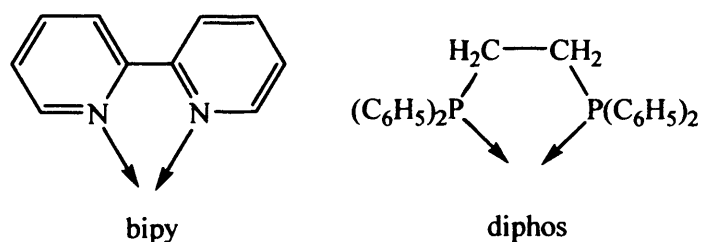
Figure 6. Five membered bidentate ligands

The chelate effect describes the higher stability constants that chelating ligands possess in comparison to the non-chelating analogs. The chelate ligands are more stable as when one end of the ligand falls off the metal to which it is attached and dissociates the ligand still has at least one point of attachment to the metal centre. It is more likely that the ligand would reattach back onto the metal than another dissociation to occur. A unidentate (non-chelating) ligand would fall off completely resulting in total loss of the ligand.

1.5 Mixed donor ligands

In recent years there has been great interest in the development of chiral bidentate systems for use in catalysis where only one of the donor atoms is phosphorus. In these mixed donor ligand systems (P, S;[28-36] P, O[37,38] and P, N[39,40]) differences are seen between the two coordinating groups i.e. varying electronic and steric properties. Here the symmetry which was previously seen for the classical diphosphine is broken, but these new ligands may be effective in a multitude of reactions where an unsymmetrical structure is advantageous. Mixed donor ligands have produced promising results as the precursors of catalysts in allylic alkylations[41,42] and Heck reactions.[29] Catalytic work using P,S ligands has been reported, however due to the possible danger of metal poisoning by sulfur, the scope of reactions is believed to be limited.[43]

1.5.1 Synthesis

Phosphinothiolate ligands possess a phosphine centre and thiol functionality. The combination of good donor atom properties from both phosphorus and sulfur and the low ionisation energy held by sulfur make these ligands excellent asymmetric multidentate ligands.[44] Well known examples include $R_2P(CH_2CH_2SH)$,[45] $R_2P(C_6H_4SH)$,[46-49] $R_2P(CH_2SH)$, $RP(C_6H_4SH)_2$[31,48,50-52] and $P(C_6H_4SH)_3$.[46]

In recent years a vast amount of work has been undertaken on the synthesis of P,S ligands. Early work on polydentate P,S ligands was reported in 1967 when Meek and co-workers[53] investigated three ligands of this class with aromatic backbones (diphenyl(o-methylthiophenyl)phosphine **1**, bis(o-methylthiophenyl)phenylphosphine **2** and tris(o-methylthiophenyl)phosphine **3**), which were complexed onto palladium. The synthesis of these ligands is shown in Scheme 4.

1
where n = 2

2
where n = 1

3
where n = 0

(1) Na, C₂H₅OH
(2) CH_3I

(1) $NaNO_2$, H_2SO_4
(2) CuBr, KBr

(1) C_4H_9Li
(2) $(C_6H_5)_nPCl_{3-n}$

$n(C_6H_5)P$

3-n

n = 0, 1, 2
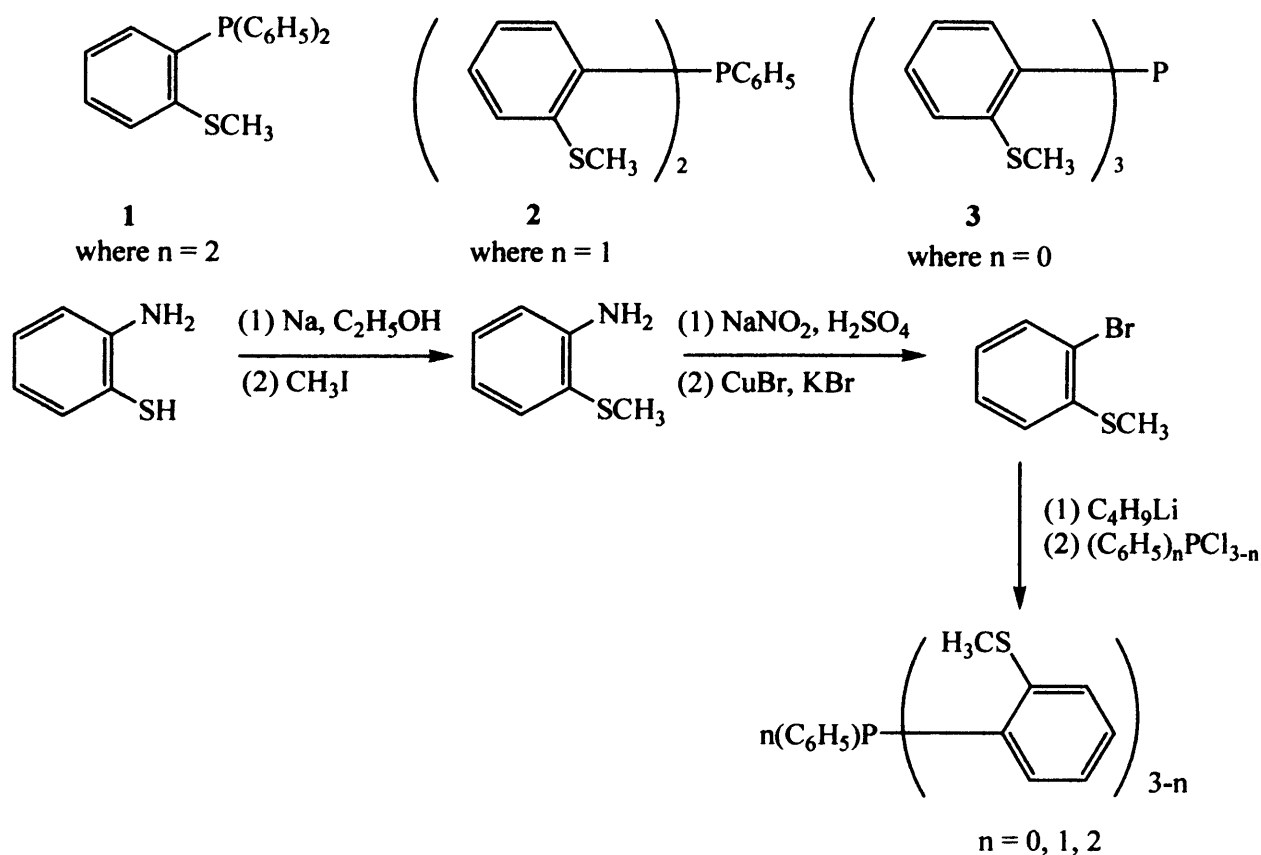
Scheme 4. The synthesis of polydentate P,S ligands by Meek and co-workers

The synthesis of $PPh(2-C_6H_4SH)_2$[31] and other 2-phosphino- and 2-phosphinylbenzenethiols[54] (Scheme 6) have been described, along with a range of ligands of the type $Ph_2(2-(RSCH_2)C_6H_4)P$,[42] the synthesis of which is shown in Scheme 5. Bidentate P,S ligands have also been reported by Romeo and co-workers,[34] shown in Figure 7 and by Evans and co-workers[41] (Scheme 7).

1 : R = CH_2CH_3
2 : R = cyclo-C_6H_{11}

3 : R =
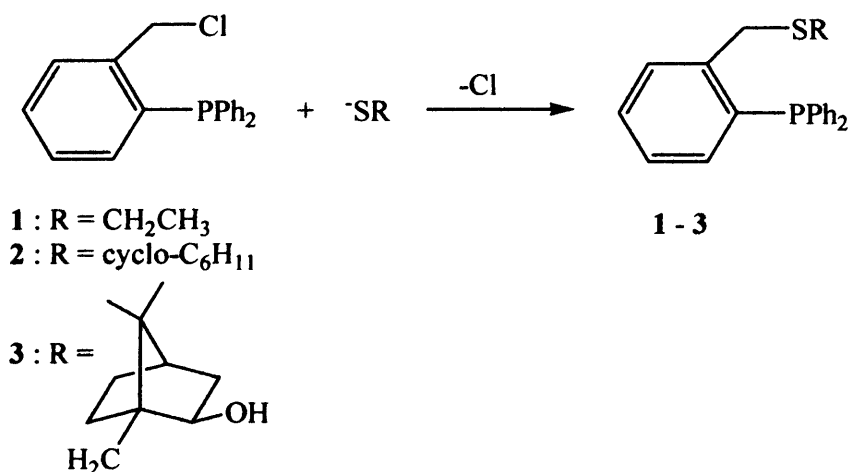
Scheme 5. Synthesis of $Ph_2(2-(RSCH_2)C_6H_4)P$ ligands
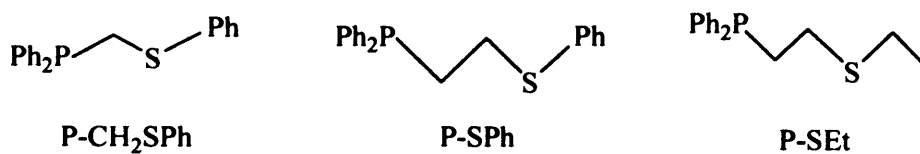
Figure 7. P,S ligands used by Romeo and co-workers
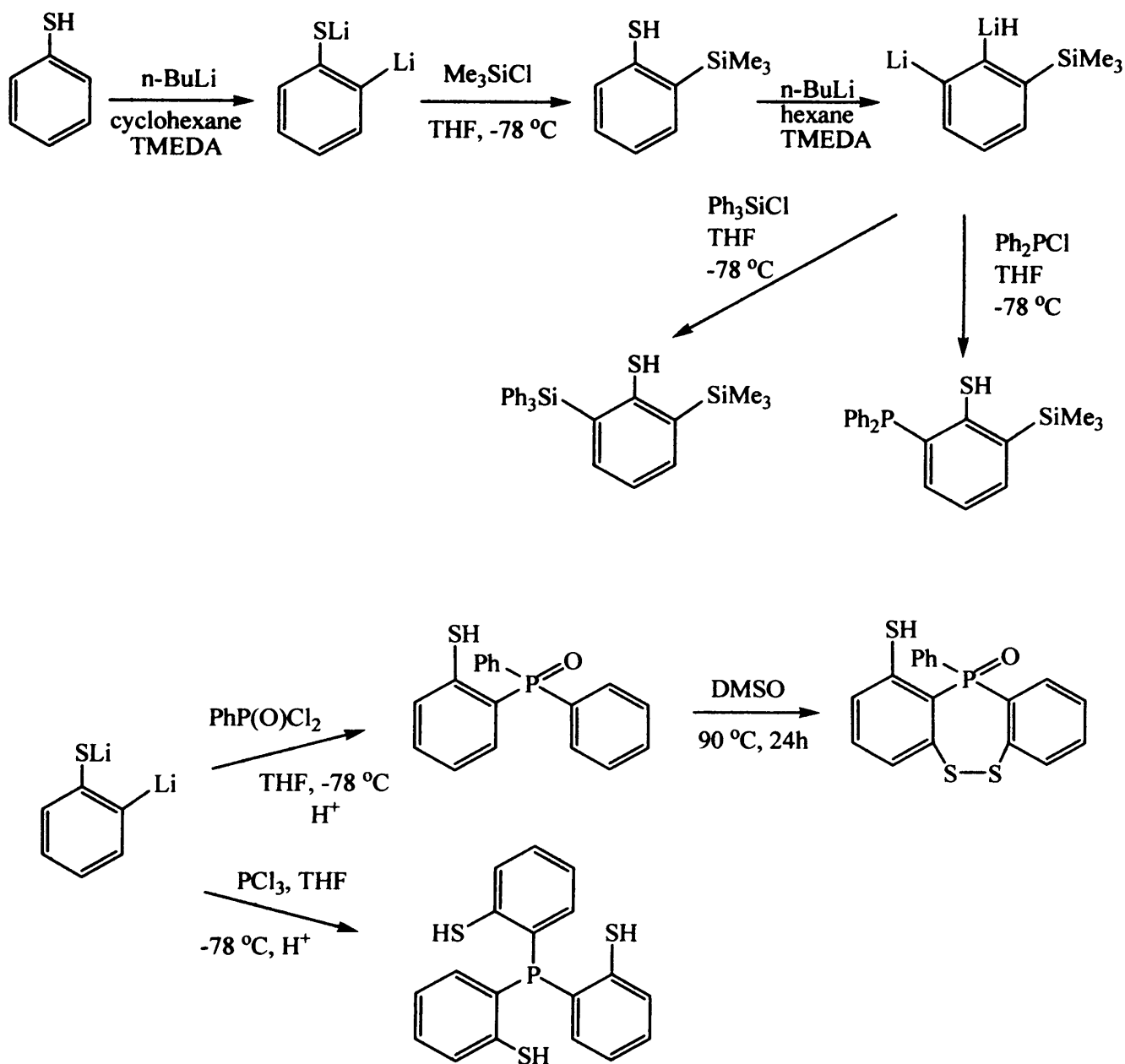
Scheme 6. Synthesis of 2-phoshino- and 2-phosphinylbenzenethiols and related compounds

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R' = Me, Ph, i-Pr
Reaction conditions :
a. (i) LDA, THF, -78 °C
   (ii) R'CHO
b. BH$_3$-THF, rt
c. n-BuLi, Ph$_2$PCl, 0 °C
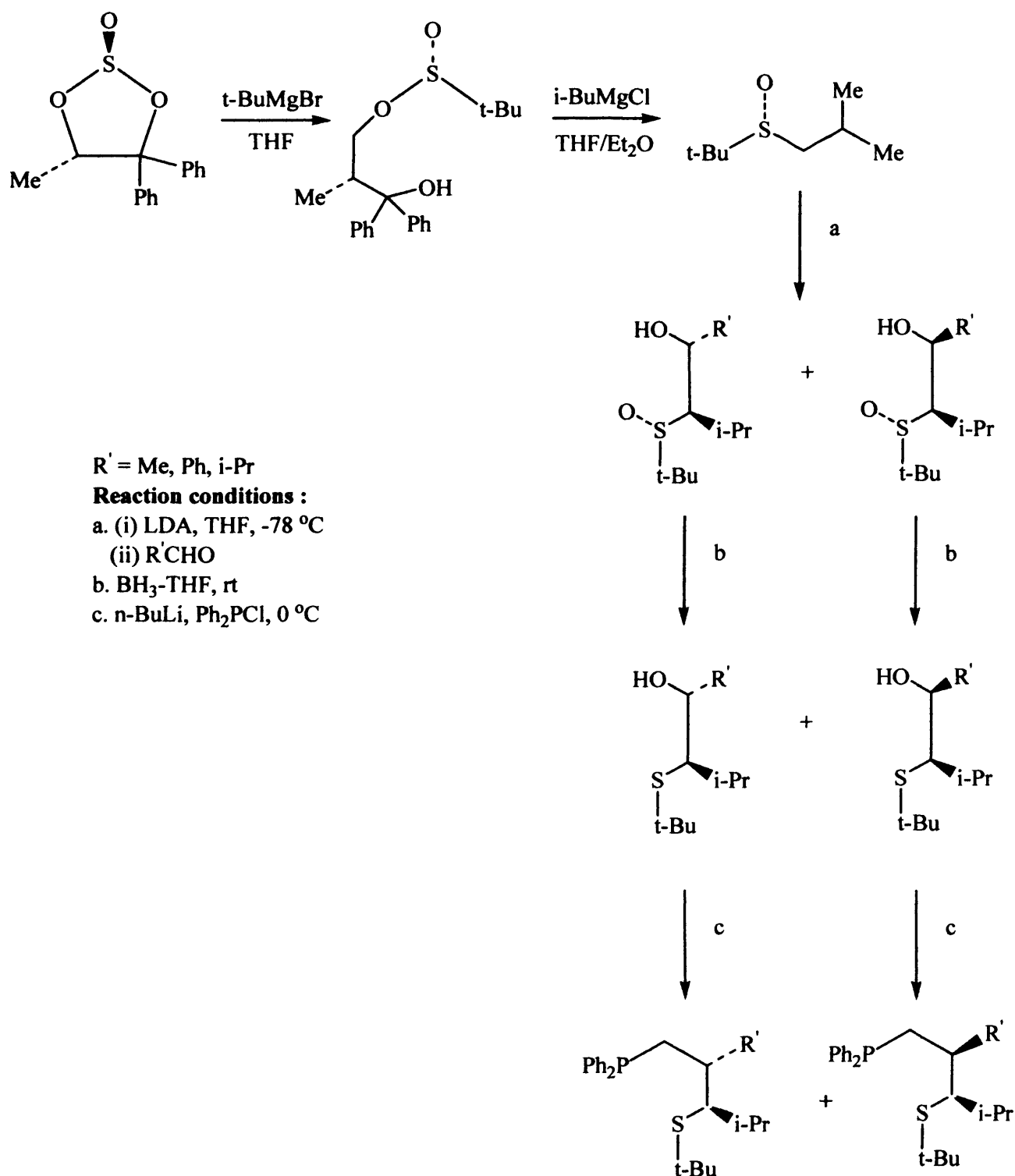
Scheme 7. Chiral mixed P,S ligands

Jalil and Hui have shown a method where by a cyclic sulfate has been attached to a S-containing heterocycle, thiophene,[55] as shown in Scheme 8. This method has enabled the specific requirements for the steric and electronic properties of the ligand to be selected

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by choosing different substituents on the phosphorus or heterocyclic rings and cyclic sulfates.
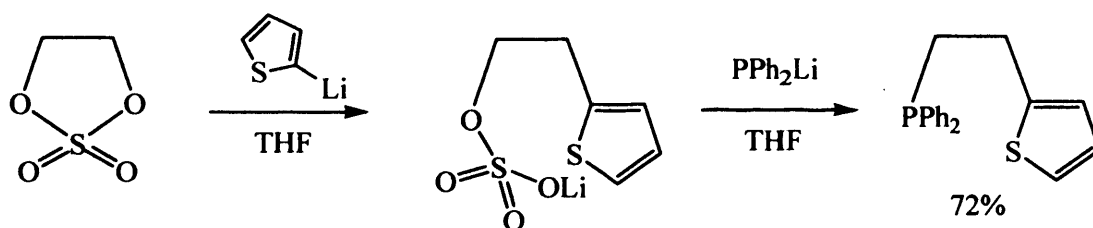
Scheme 8. Synthesis of P,S ligands by attachment of thiophene to a cyclic sulfate

The precursors used for the preparation of P,S ligands are pungent and toxic. There are seven main methods for the synthesis of phosphinothiolate ligands :[46]

i)   ring opening reactions of thiiranes and thietanes

ii)   nucleophilic substitution at the sp^3 carbon

iii)   free radical addition across C-C double bonds

iv)   addition of thioketones

v)   ortho-lithiation of phosphinothiols

vi)   preparation from thioethers

vii)   Arbuzov type rearrangement of aryl dithiophosphonates

The ring opening reaction of thiiranes and thietanes is the standard method for the formation of P,S ligands (Schemes 9 and 10).[43] The S-containing reactant is treated with a nucleophile (e.g. diphenylphosphide anion). The formation of poly(thioethers) could occur but this is avoided by using an attacking species that is a better nucleophile than the new thiol formed. A second problem that could be encountered is attack occurring at the sulfur instead of the expected carbon atom. This is unusual for thiiranes but desulfurisation can be caused by alkyl- and aryllithium compounds.[56]
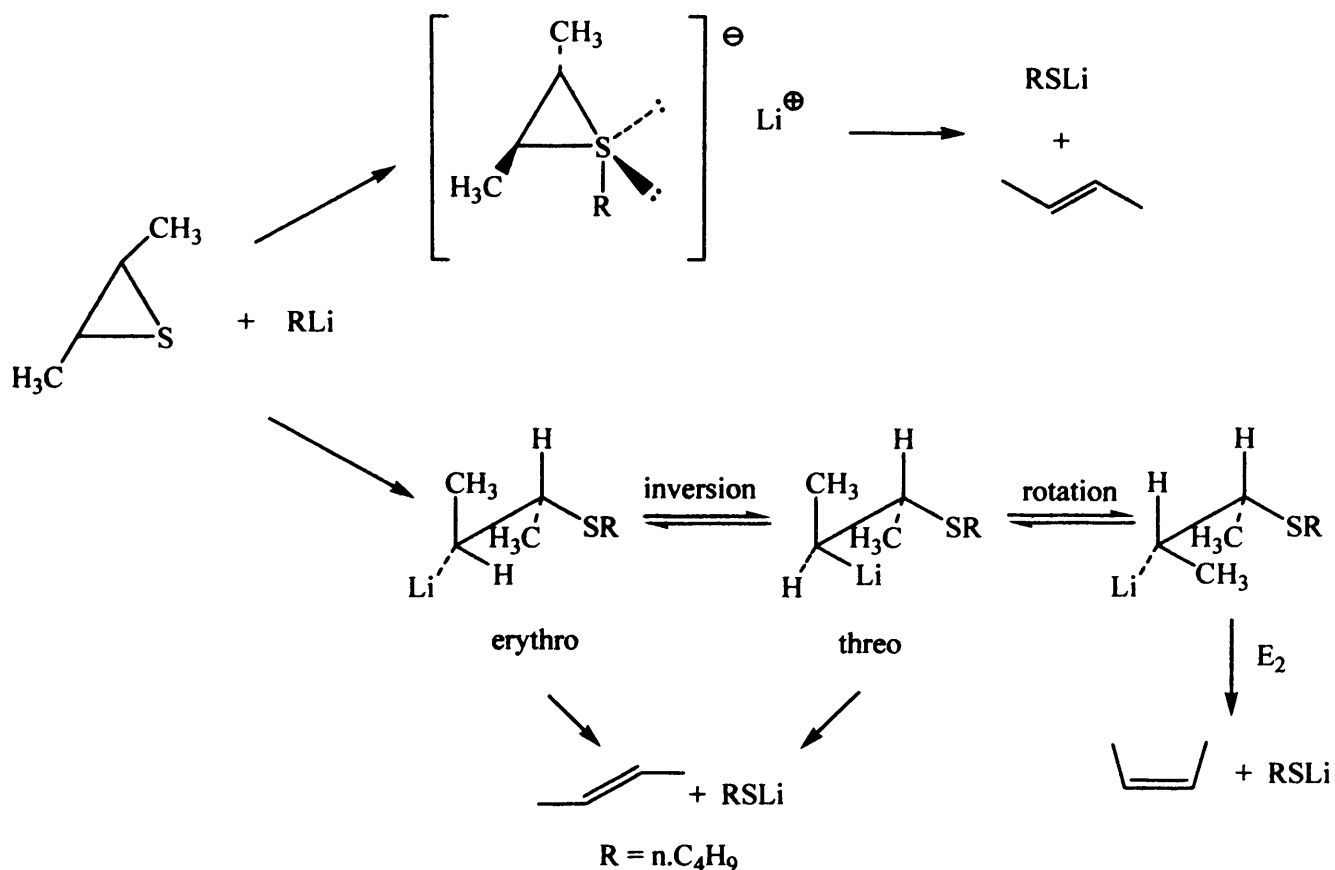
Scheme 9. Reaction of episulfide with n-BuLi
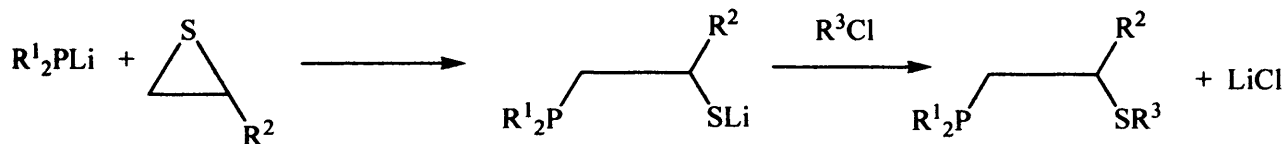
Scheme 10. The ring opening of a thiirane using lithium salts of phosphines

The nucleophilic substitution at the sp^3 carbon method is not often used as a mixture of products can be formed due to competition between the phosphorus nucleophile and the thiolate centre. The method has been used for a number of syntheses including 3-(diphenylphosphino)propanethiol.[57]

The third method involving the free-radical addition across carbon-carbon double bonds has been used for the formation of thioacetic S-esters of trimethylene- and tetramethylene- bridged phosphinothiols. The synthesis does not involve the formation of the by-product phosphine sulfide.

The addition of a phosphorus nucleophile to a thioketone is not as a simple a route as first anticipated due to the irregular reactivity of thioketones when compared to ketones[58-60] (Scheme 11). Examples of reactions of thiocarbonyl compounds with nucleophiles include the reaction of (dimethyloxosulfonio)methanide with thioketones to yield thiiranes. Reports have shown the phosphorus attacking the carbon rather than the sulfur and a tendency to form polymeric products.

$$\underset{R}{\overset{R}{>}} C=S \quad \xrightarrow{\text{reduction}} \quad \underset{R}{\overset{R}{>}} H-C-SH$$
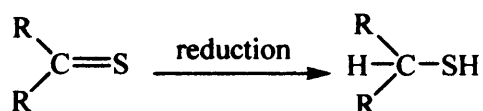
Scheme 11. Reaction of thioketone

The ortho-lithiation of benzenethiol (Scheme 12) has been used to study the chemistry of phenylene-bridged phosphinothiols.[61-63] This has allowed the development of a method for the preparation of substituted phosphinothiols but hindrance in the lithiation step has restricted this method.
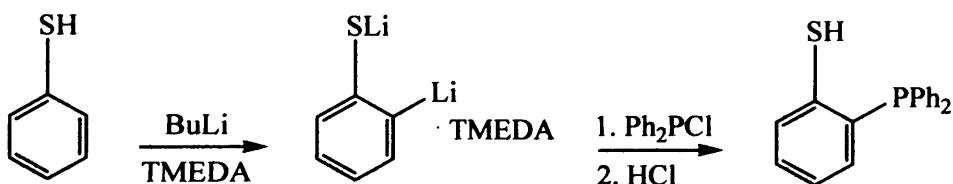
Scheme 12. Preparation of 2-(diphenylphosphino)benzenethiol by the ortho-lithiation of benzenethiol

The preparation from phosphinothioethers method accounted for the first complexes of phenylene-bridged phosphinothiols. The route involves the dealkylation of phosphinothioethers.

The final method for the preparation of phosphinothiolates is the Arbuzov-type rearrangement of aryl dithiophosphonates (Scheme 13).
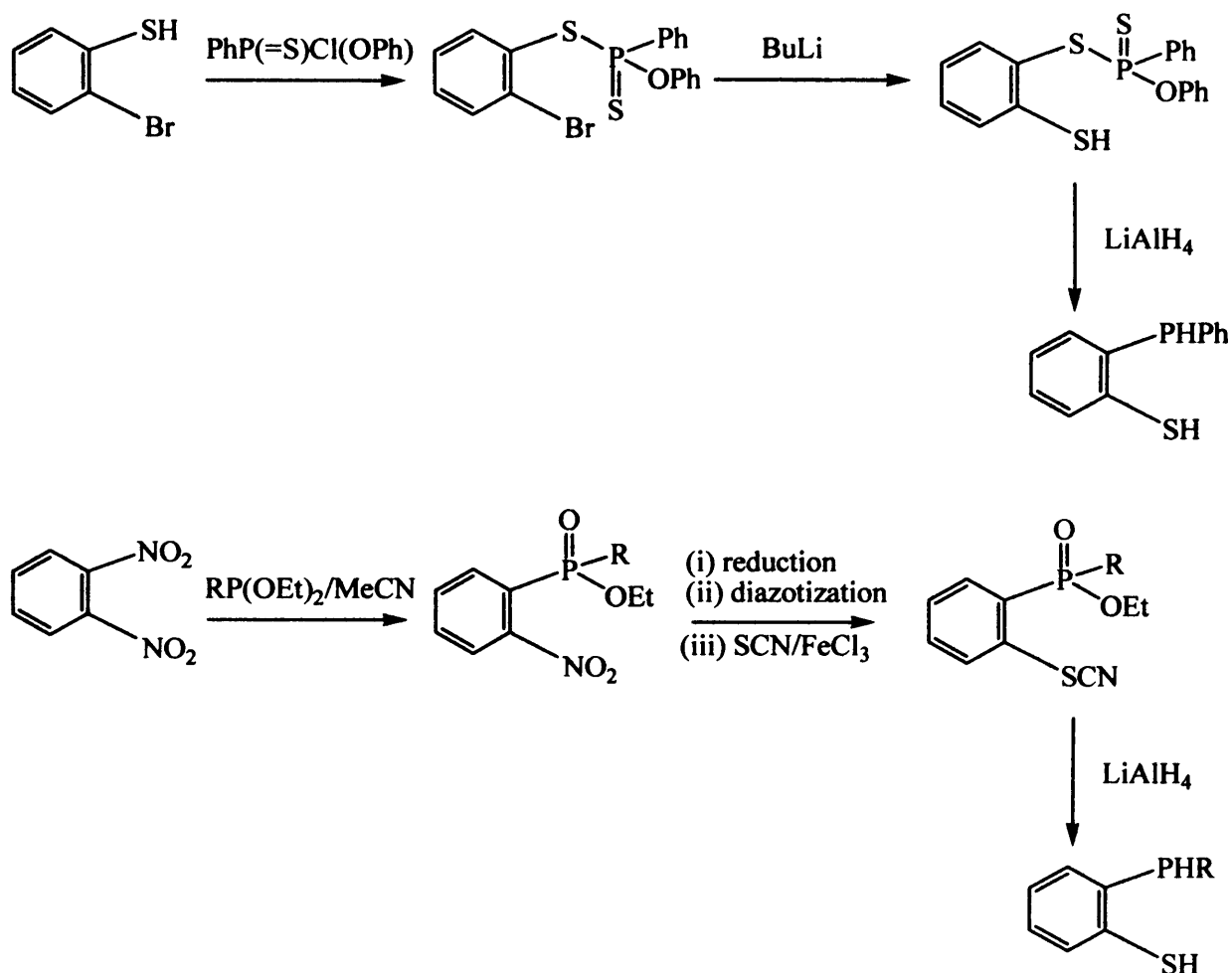
Scheme 13. Preparation of phosphinothiols by Arbuzov-type rearrangements

Phosphinothioethers can be prepared by the disconnection methods.[64] The bond broken can either be the phosphorus-carbon bond (forming a carbanion or carbocation) or the sulfur-carbon bond (forming an electrophilic carbon and also a thiolate anion).

Chiral thioether-phosphite ligands have been synthesised from 1,2-O-isopropylidene-α-D-xylofuranose **1** (Scheme 14)[65]. The first step involves the conversion of **1** into the monotriflate **2** by addition of triflic anhydride and pyridine. The next step afforded the thioethers **3 – 5**, which were subsequently reacted with (3, 3', 5, 5'-tetra-tert-butyl-1, 1'-biphenyl-2, 2'-diyl)phosphorochloridite **6** in the presence of base, to give the final thioether phosphite ligands **7 – 9** in a moderate yield of 50%.
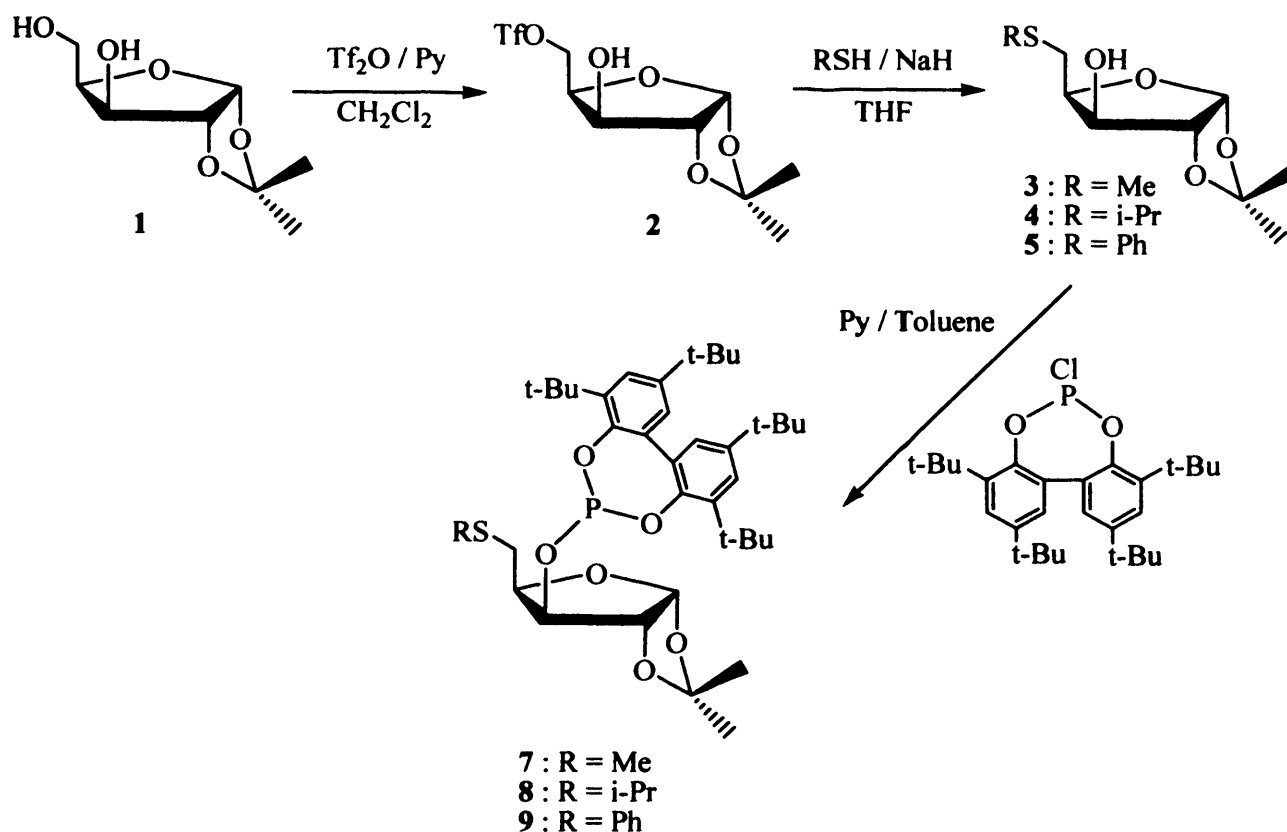
Scheme 14. Synthesis of thioether-phosphite ligands

1.5.2 Geometry

Investigations carried out on our P,S complexes have shown that for the dimeric forms a hinged structure is seen (Figure 8).[28] Examples of dimeric complexes that have shown this geometry include $[Pd(Ph_2PCH_2CHEtS)Cl]_2$ and $[Ni(Ph_2PCH_2CHEtS)Cl]_2$.
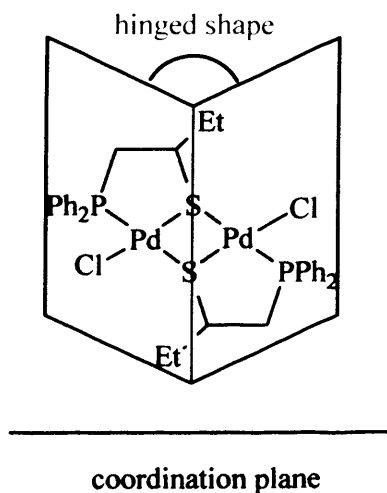
Figure 8. A schematic diagram (top view) showing the hinged shape of a P,S dimeric complex.

1.6 Catalytic Work

The application of palladium-mediated processes in synthetic chemistry has grown in the past 30 years. Highly active palladium catalysts are involved in a wide range of reactions including those discovered by Sonogashira; Migita and Stille; Heck; Suzuki and Miyaura and others. The discovery and growing interest in these reactions has encouraged the study of the processes and mechanisms involved.[66]

The Sonogashira reaction (Scheme 15) uses mild conditions (often room temperature) and a palladium (0) catalyst to encourage the coupling of terminal alkynes with aryl or vinyl halides. This coupling has found use in ene-diyne antibiotics. The reaction also requires the use of a base and the presence of a copper salt, which acts as a co-catalyst. The steps included in the mechanism involve oxidative addition of the starting material giving a palladium (II) intermediate. Transmetallation and reductive elimination affords the product and recycled palladium (0) catalyst.

Ar—X   +   H————R $\xrightarrow[\text{base, rt}]{\text{Pd(0), CuI}}$ Ar————R   +   Et₂NH.HX

aryl halide   terminal alkyne   coupled product
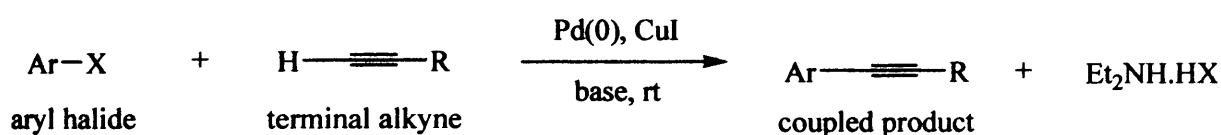
Scheme 15. Sonogashira reaction

Stille coupling (Scheme 16) follows similar mechanistic steps as the Sonogashira reaction. The coupling of aromatic and vinylic triflates or halides undergoes oxidative addition, giving a palladium intermediate, which subsequently undergoes transmetallation. The resulting organopalladium intermediate has σ-bonds. The final step is the reductive eliminative step and regeneration of the catalyst. The Stille coupling reaction accounts for over half of cross-coupling reactions today.
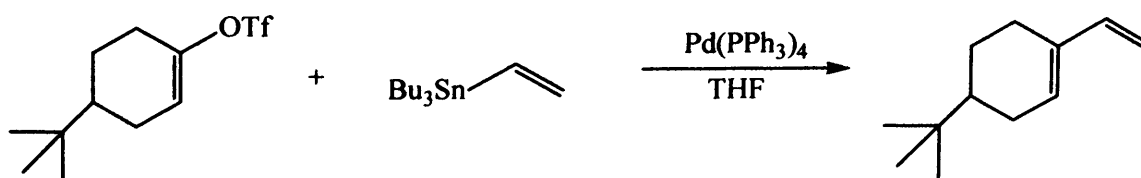
Scheme 16. Stille reaction

Heck coupling reactions (Scheme 17) are extremely efficient and have been labelled as one of the most synthetically useful palladium catalysed reactions. The halide or triflate undergoes nucleophilic addition to an alkene, resulting in the formation of a new alkene product. The reaction can occur with both electron donating and electron withdrawing groups and the base need not be strong. The R group can be aryl, vinyl or alkyl, but must not have β hydrogens on the sp^3 carbon atom. The X group can be a halide or a triflate.

R'—X   +   H $\diagdown\diagup$ R² $\xrightarrow[\text{base}]{\text{Pd(0) catalyst}}$ R' $\diagdown\diagup$ R²   +   H-X
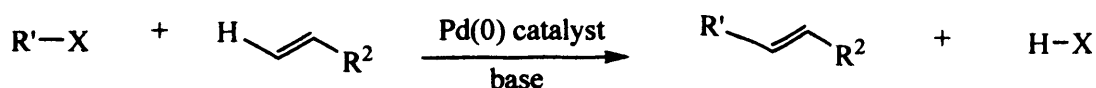
Scheme 17. Heck reaction

The Heck reaction was discovered in 1971. Previously, Heck and Tsuji had shown that organopalladium (II) compounds could be used to catalyse the conversion of olefins into coupled vinylic products. However, the active species was derived from mercury compounds, and hence an undesirable precursor. When it was found that oxidative addition of RX yields the coupled product, the palladium promoted C-C coupling was found to be a much safer and desirable route to synthesising the vinylic species. Together with the revelations that only a catalytic amount of the palladium complex is to be present (typically 1-5 mol%) and that base was needed for the reaction to go to completion, the Heck reaction opened a new door to the possibilities for organic synthesis.[67]

The Suzuki reaction (Scheme 18) has proven to be an important tool in organic synthesis. The reaction is defined as 'the palladium catalysed the cross-coupling reaction between organoboron compounds and organic halides or triflates as a general method for the formation of carbon-carbon bonds.'[17]

R—⟨benzene⟩—X   +   ⟨benzene⟩—B(OH)₂ $\xrightarrow[\text{base}]{\text{Pd catalyst}}$ R—⟨benzene⟩—⟨benzene⟩R'
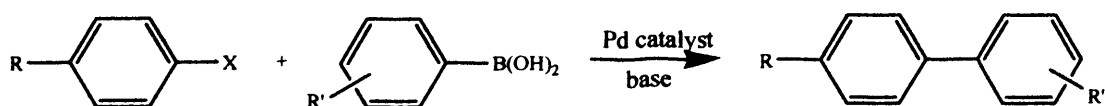
Scheme 18. Suzuki reaction

1.7 Aim and scope of this thesis

This project involves the development of novel P,S-ligands (Figure 9) and their corresponding palladium(II) complexes and their application in catalysis. Our investigations have concentrated specifically on the C-C coupling involved in the Heck and Suzuki reactions.
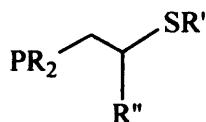
Figure 9. General structure of P,S ligands used in this work

P,S ligands have recently shown potential in catalytic applications due to their interesting steric and electronic properties. This has arisen from the differences between the two donor heteroatoms, with other similar examples including P,O and P,N ligands. A range of phosphinothiolate and –thioether ligands and their corresponding complexes have been prepared (Chapter 2).

To investigate the catalytic reactivity of phosphinothiolate and –thioether complexes the aim was to test a range of novel and previously reported complexes prepared by our group. Therefore catalytic testing was undertaken with our complexes in Heck (Chapter 3) and Suzuki couplings (Chapter 4). The differences in catalytic activity for various substrates with these complexes are discussed and compared to previous work.

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Chapter Two

— Phosphinothiolates —

and

— -thioethers —

2. Phosphinothiolates and -thioethers

2.1 Introduction

Phosphinothiolates are of particular interest due to the electronic effects exhibited by the phosphorus and sulphur atoms, which are known to influence the trans effect. The trans effect is defined as the ability that certain ligands hold to influence the rate of substitution of a leaving group trans to itself in square planar complexes. The rate of substitution of the ligand is accelerated if that ligand is either a strong σ-donor or π-acceptor. The correlation followed for σ-donor ligands is $OH^- < NH_3 < Cl^- < Br^- < CN^- < CO, CH_3 < I^- < SCN^- < PR_3 < H^-$. For π-acceptors, the order of effectiveness is $Br^- < I^- < NCS^- < NO_2^- < CN^- < CO, C_2H_4$. The greater the overlap of the orbitals of the ligand and metal, the stronger the trans effect.[1] Hence, the trans effect in turn plays a role in the reaction selectivities of the ligands. Mixed donor ligands have attracted a lot of attention due to the excellent potential they show in a number of reactions including carbonylations, hydrogenations, allylic alkylations, hydroformylations and aminations. In recent years P,S ligands have attracted particular interest with research into this area expanding.[2-11]

Metal ions can be classified as hard or soft, dependent on the strength of the bonds formed with ligands. For these acid-base interactions hard acids (metal ions that are small, from Groups 1 and 2 and the left hand side of the transition metals, which form high oxidation states) have an affinity for hard bases (ligands such as Cl^- and F^-), and soft acids (low oxidation state metals such as those from the right hand side of the transition metals) are attracted to soft bases (ligands such as I^-, SCN^- and CN^-). Pearson summarised this theory stating, 'hard acids prefer to react with hard bases, and soft acids react with soft bases.'[12] Phosphorus and sulphur are both soft donor atoms, and with the presence of two different coordinating groups this allows for varying electronic and steric properties. Hence, thiophosphines are stronger chelate complexes than diphosphines. The presence of lone electrons in the form of a non-bonding pair allows the S atom to act as a π-donor. The neutral P atom is assigned the role of the π-acceptor (or π-acid), due to it having no non-bonding electron pairs following the formation of a M-P bond.[13]

The combination of all of these factors presents a desirable class of new ligands to explore, both synthetically and catalytically. Phosphinothiolate ligands are coordinated onto Group 10 metals, in particular palladium. The resulting complexes typically possess a square planar geometry, and can have a bis-chelate, monomer or dimer structure. We report herein our attempts to synthesise novel phosphinothiolate ligands and their palladium complexes.

2.2 Results and Discussion

The path undertaken for the synthesis of new P, S ligands and the resulting complexes is reported. Characterisations are discussed along with unsuccessful syntheses.

2.2.1 Epoxides

In the complexation studies of these P,S ligands their racemates were used, although the enantiomerically pure ligands may be prepared by the method involving the hydrolytic kinetic resolution (HKR) of epoxides, as previously reported by Jacobsen.[14] HKR was used in the synthesis of terminal epoxides and 1,2-diols from racemic mixtures by Jacobsen and researchers (Scheme 1). This method yielded chiral thiiranes.
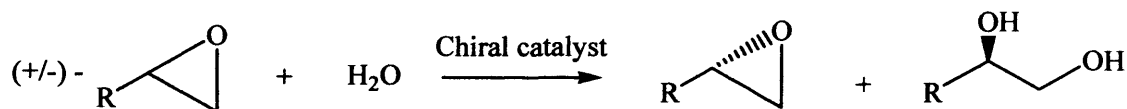
Scheme 1. Hydrolytic kinetic resolution of terminal epoxides with water

2.2.2 Thiiranes

The first step in the P, S ligand synthesis involves formation of a thiirane. Thiiranes (also known as alkene sulfides, episulfides, ethylene sulfides, thioalkyene oxides and thiacyclopropanes) are three-membered ring systems with one sulfur atom i.e. the simplest of the sulfur heterocycles.
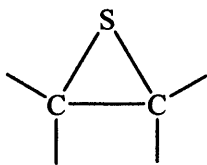
Figure 1. General structure of a thiirane

There are a number of possible methods of synthesis. The most important and widely used involves the conversion of an epoxide (alkene oxide) to the thiirane, with the use of thiourea or inorganic thiocyanates, as shown in Scheme 2.[15,16]
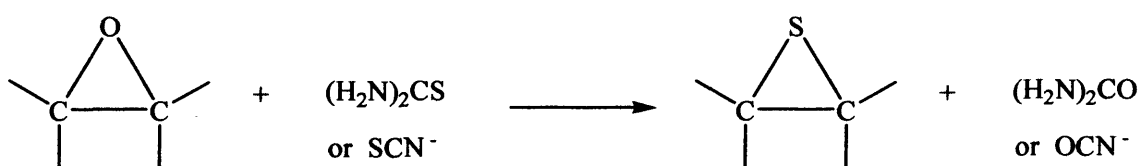
Scheme 2. Synthesis of a thiirane via the thiourea / thiocyanate route

The reaction proceeds at 0-20 °C in an aqueous or alcoholic solution. If temperatures above 60 °C are used then an undesirable side reaction of polymerisation occurs. The thiirane formed and any remaining epoxide can easily be separated by performing an aqueous work-up, as the thiirane is water insoluble while the epoxide is soluble in water. Cheap epoxides can give yields of thiirane, via the thiocyanate or thiourea routes, of up to 98%. The final step in the thiirane synthesis is purification which can be performed via a fractional distillation.[16] Previous attempts have shown that thiiranes cannot be made via the thiourea / thiocyanate method with certain epoxides which include stilbene oxide, styrene oxide and cycloalkene oxide.[15,17]

The thiirane is derived from the ring-opening reaction of an epoxide. The mechanism is S_N2, which is a one-step reaction and an inversion of stereochemistry occurs at the stereogenic carbon centre. The nucleophile enters at the opposite direction to the departing group, forming a new bond onto the carbon. The departing group leaves from the opposite side which inverts the stereochemistry of the molecule.[18]

During the thiirane formation the epoxide reacts with potassium thiocyanate in its nucleophilic form, NCS⁻, attacking the carbon atom adjacent to the oxygen atom. A five membered ring transition state is generated with a C=N double bond and finally the thiirane product is formed (Scheme 3).
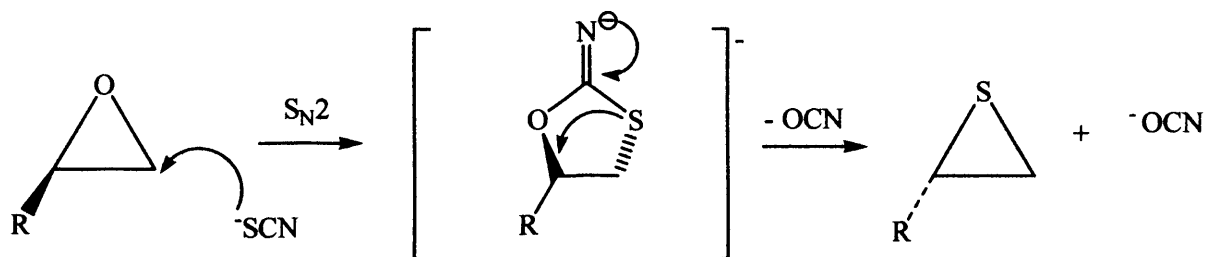
Scheme 3. Mechanism of thiirane formation

The mechanism for the reaction of epoxides with thiocyanates also undergoes a Walden inversion.[19] A Walden inversion involves an inversion of stereochemistry, for example, the conversion of a pure enantiomeric (+)-malic acid to the (-)- form, via nucleophilic substitution reactions. For this conversion to take place there must be an inversion or change of configuration at the stereogenic centre.[20]

The oxygen is activated as a leaving group during the intermediate step which involves intramolecular sulfur to oxygen cyanide migration, as shown in Scheme 4. The first two steps of the mechanism have been noted to proceed very quickly, while the last two steps are slower. Walden inversion occurs at the two carbon atoms of the three-membered ring (i.e. D-(+)-2-butene oxide forms L-(-)-2-butene oxide).[16] Inversions occur only in the trans orientation of respective rings. During the entire mechanism two Walden inversions take place – one for the opening of the epoxide ring, and one for the closing of the final thiirane ring made. Evidence for this mechanism includes the monitoring of pH during the reaction and the optical rotation.[21]
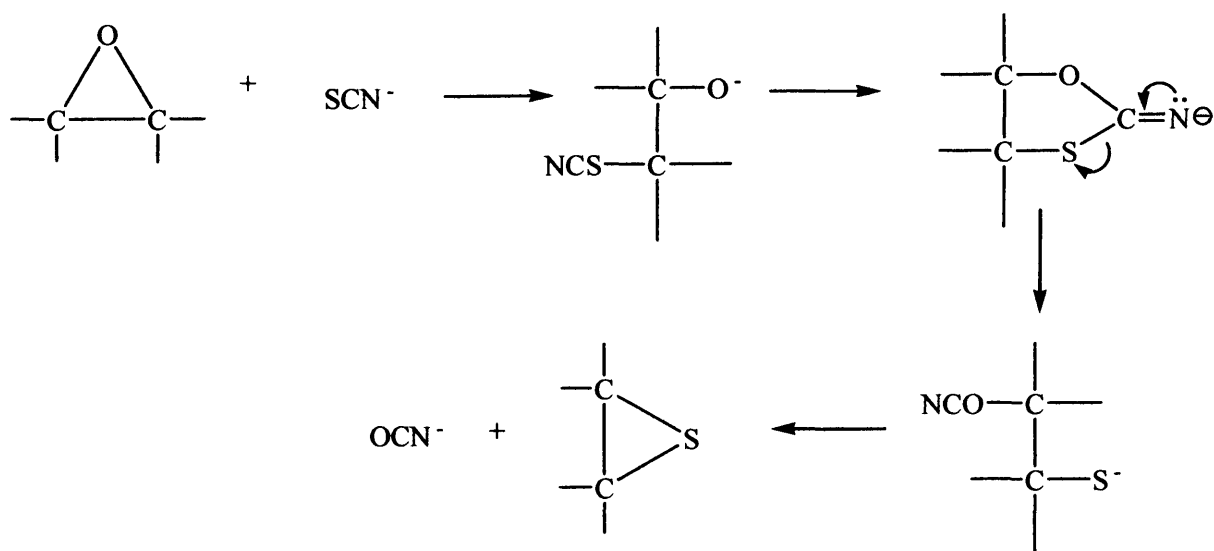
Scheme 4. Mechanism for the reaction of epoxides with thiocyanate

Other methods of thiirane formation include the reaction of epoxides with carbon disulfide, as shown in Scheme 5. The formation of the thiirane is dependent on the catalyst and reaction conditions employed. (5) and (6) can be made selectively at high temperature, while the synthesis of (2) – (4) is more difficult.[22]
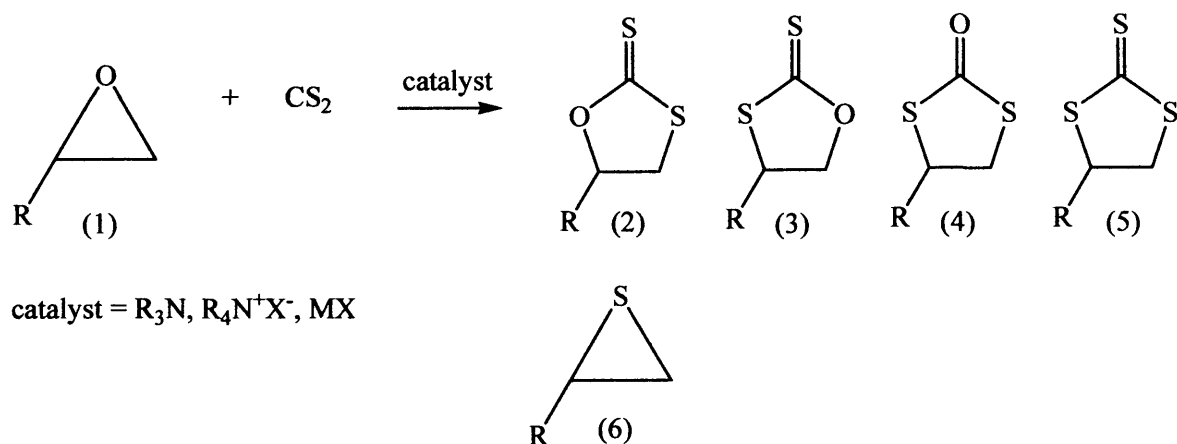
Scheme 5. Reaction of epoxides with carbon disulfide

The new method of thiirane formation via an epoxide route has also been reported whereby phosphorus pentasulfide in ethanol on alumina supported ammonium acetate was heated at reflux temperature in ethanol (or solvent free), and treated with microwave irradiation. Using this procedure a yield of 55% was obtained in 2 minutes, whilst without the microwave irradiation or alumina the yield was 46% in 24 hours.[17]

Another route for thiirane synthesis involves the addition of a sulfur-protected sulfenyl chloride to an alkene followed by closure of the ring (Scheme 6).[19]
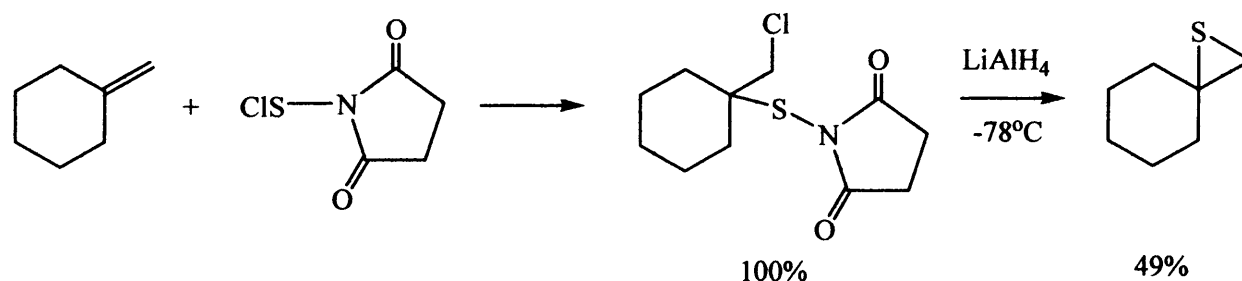
Scheme 6. Addition of a sulfenyl chloride to an alkene

The condensation of carbonyl compounds with sulfur-stabilised carbanions has also been reported (Scheme 7).[19]
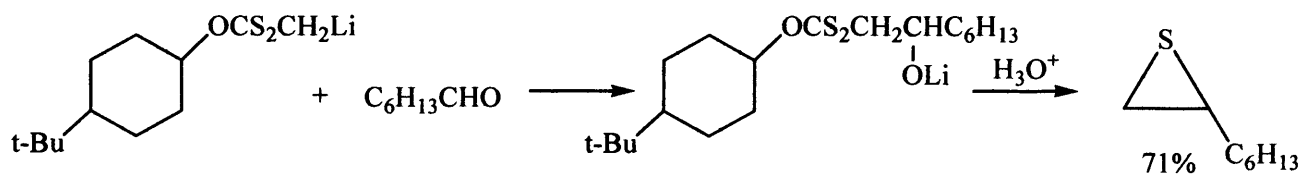
Scheme 7. Condensation of carbonyl compounds

The first reports on the synthesis of a thiirane came in 1916 by Staudinger and Pfenninger.[23] The classic route for the formation of thiiranes involved reactions which had poor yields, long reaction times and high temperatures and the use of reagents that had bad smells.[17]

2.2.3 Phosphinothioether and –thiolate ligands

The preferred route for the formation of the requisite thiiranes was by reaction of the corresponding epoxide with SCN⁻. Subsequent steps yield novel phosphinothiol and – thioether ligands via reaction with a phosphine source.

L³ : R = Et, R´ = Me
L⁴ : R = Et, R´ = Bn
L⁵ : R = Et, R' = CH₂Xyl
L⁶ : R = Et, R´ = CH₂Naphth
L⁷ : R = Et, R' = CH₂Anth
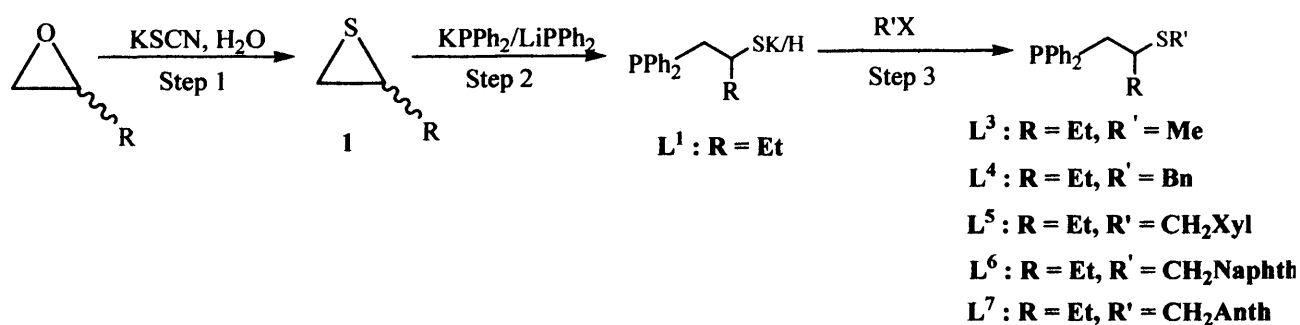
Scheme 8. General scheme for the synthesis of P, S ligands

The ligands were synthesised using standard Schlenk techniques throughout and generally once made were used in subsequent complexation reactions. The pure ligands were white or colourless oils or solids. Decomposition to the ligand-oxide was noted on exposure to air.

2.2.3.1 Synthesis of 2-butylene sulfide, 1
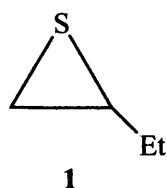
The synthesis of thiirane 1 is shown in Scheme 8, step 1 where R = Et. Reaction of 1 equivalent of potassium thiocyanate in water along with 1 equivalent of 1, 2-epoxybutane was the first stage of the thiirane synthesis. After stirring for a day, another ½ equivalent of potassium thiocyanate was added to the cloudy mixture and stirred. The reaction proceeded smoothly over another day at room temperature. A standard work-up was undertaken and the pure thiirane 1 was isolated by distillation of the crude product. Thiirane 1 distilled at 103-104 °C at atmospheric pressure. ¹H NMR spectrum proved the thiirane contained no proton-containing impurities and the yield of 1 was 54%.

2.2.3.2 Synthesis of phosphinothioether ligand L¹
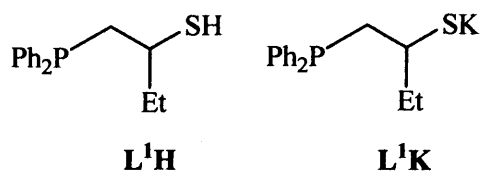
The phosphinothiolate ligand L¹ could be synthesised via two methods, as shown in step 2 of Scheme 8 where R = Et. The first path involved reaction of Ph₂PH with BuLi and

thiirane 1, followed by a hydrolysis reaction to give the P,S ligand, L^1H. The second route involved reaction of potassium diphenylphosphide and the thiirane 1 giving L^1K. Both paths gave L^1 in good yields (approx. 90%), which could then be used for subsequent steps without further purification. The preferred route was the second, yielding L^1K, as it was found to produce the ligand in greater purity.

L^1K was used for the synthesis of the naphthalene and anthracene ligands L^6 and L^7. The benzyl and xylene phosphinothioethers L^4 and L^5 could be prepared from either method, although they were made the first time via the lithium salt method.

Analysis of the $^{31}P\{^1H\}$ and ^1H NMR spectra confirmed formation of L^1. The ^1H NMR spectrum confirms the formation of L^1K by the appearance of characteristic peaks at 0.7 ppm (3H, triplet) for the methyl of the ethyl group and sets of multiplet peaks at 0.95 (1H, multiplet), 1.45 (2H, multiplet), 2.1 (1H, multiplet) and 2.4 ppm (1H, multiplet) assigned to the remaining five aliphatic protons. For L^1H the ^1H NMR spectrum was very similar, with only a slight shift in positioning of the peaks : 0.85 (3H, triplet), 1.55 (1H, multiplet), 1.8 (2H, multiplet) and 2.3 ppm (2H, multiplet). The signal due to the proton attached directly to the S was noted at 2.75 ppm (1H, multiplet). The main features of the ^{13}C NMR of L^1 are the four carbon atoms in the range 10.3-38.9 ppm, found in the 'backbone' of the ligand. In the $^{31}P\{^1H\}$ NMR spectrum a singlet appeared at -18 ppm. Further evidence supporting the expected structure of L^1 was the high resolution mass spectrum which determined the mass of the parent ion, L^1H^+, to be 275.1014, as expected for this ligand.

2.2.3.3 Synthesis of tertiary-butyl phosphinothioether ligand L^2
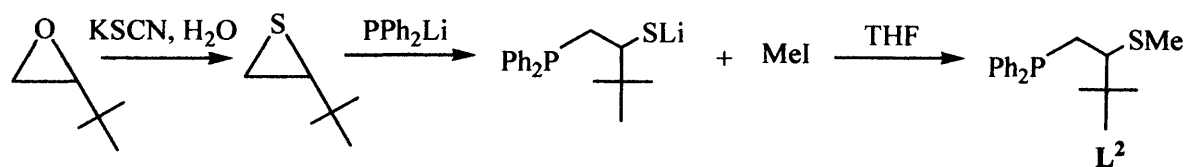
Scheme 9. Synthesis of ligand L^2

The methylated t-butyl phosphinothioether ligand L^2 was prepared in a one pot synthesis from the thiirane SC_6H_{12}, as shown in Scheme 9. The crude mixture was extracted with hexane and then toluene, finally being acquired in 83% yield. The $^{31}P\{^1H\}$ NMR in d^6-benzene revealed the ligand peak to be a singlet at -16.5 ppm, with a small amount of ligand at +65.7 ppm indicative of $MeP^+Ph_2(R)$ formation. The ^1H NMR clearly showed the methyl t-butyl protons as a doublet at 0.85 ppm, indicating the presence of a ^tBu group.

2.2.3.4 Synthesis of methyl phosphinothioether ligand L^3

Ph₂P⌒⌒—SMe
      |
      Et

L^3
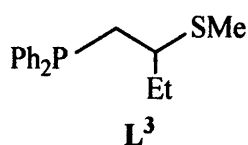
Addition of 1 equivalent of methyl iodide to a diethyl ether solution of L^1K afforded cleanly the methylated P,S ligand L^3. The structure of L^3 was supported by $^{31}P\{^1H\}$ NMR spectroscopy which revealed a peak at -20 ppm and the ^1H NMR spectrum showed a peak for the methyl group on sulfur at 2.0 ppm.

2.2.3.5 Synthesis of benzyl phosphinothioether ligand L^4

Ph₂P⌒⌒—S⌒⌒⟨phenyl⟩
      |
      Et

L^4
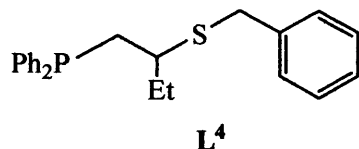
Addition of one equivalent of benzyl bromide to L^1K yielded ligand L^4 as a colourless liquid. Analysis of its $^{31}P\{^1H\}$ NMR did not reveal an appreciable chemical shift from the parent ligand L^1 (-18 ppm) to -20 ppm. Inspection of the ^1H NMR data, however, clearly showed 2 doublets corresponding to the two benzylic protons at 3.53 and 3.58 ppm. High resolution mass spectral analysis (365.1499 m/z) also supported the synthesis of a new benzylic-phosphinothioether ligand.

2.2.3.6 Synthesis of xylene phosphinothioether ligand L⁵

L⁵
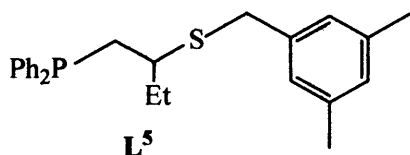
Reaction of **L¹K** with 3,5-dimethylbenzyl bromide in diethyl ether afforded **L⁵** as a colourless liquid, with a yield of 72%. The most notable features in the ^{1}H NMR spectrum were the 2 doublets at 3.47 and 3.52 ppm due to the 2 benzylic protons. The ^{31}P{^{1}H} NMR spectrum revealed a singlet peak at -20.8 ppm, as is typically observed for this class of ligand. The accurate mass spectrum was reported as 393.1793 m/z (for the calculated mass of 393.1806), favouring the proposed structure for **L⁵**.

2.2.3.7 Synthesis of naphthalene phosphinothioether ligand L⁶

L⁶
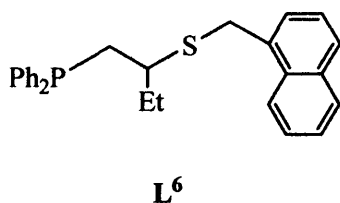
Ligand **L⁶** was prepared by reaction of **L¹K** with 1-chloromethylnaphthalene in a THF/diethyl ether solution. A yield of 65% was achieved for **L⁶**. **L⁶** gave satisfactory ^{31}P{^{1}H} NMR (-20.5 ppm) and ^{1}H NMR data (a set of double doublets at 4.0 ppm corresponding to the 2 benzylic protons). Elemental analysis by high resolution MS determined **LH⁺** as 415.1647.

2.2.3.8 Synthesis of anthracene phosphinothioether ligand L⁷

L⁷
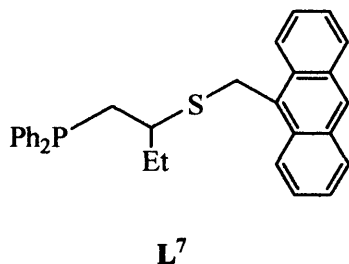
The new anthracene ligand was made by reaction of **L¹K** with 9-chloromethylanthracene. As for its naphthalene counterpart, **L⁷** produced good ^{31}P{^{1}H} and ^{1}H NMR data, which supported the proposed structure. The ^{31}P{^{1}H} NMR spectrum showed a singlet peak at -20.01 ppm and the two benzylic protons were noted in the ^{1}H NMR spectrum at 4.55 ppm, as two doublet. ^{13}C NMR spectroscopy also verified the

addition of the anthracene group onto L^1K. Low resolution MS found a peak at 481 m/z, corresponding to L^7 in its oxidised form.

2.2.4 Phosphinothioether and –thiolate complexes

The palladium P,S complexes are made by reaction of the various ligands with $Pd(PhCN)_2Cl_2$. The P,S complexes synthesised in our laboratory are brightly coloured solids ranging from deep red to, more typically, yellow or orange. Once synthesised, in general by reaction of the ligand with $Pd(PhCN)_2Cl_2$, the solids are stable in air and all manipulations there after can be performed aerobically. The phosphinothiolate and – thioether complexes are soluble in chlorinated solvents, THF and acetonitrile.

2.2.4.1 Synthesis of palladium phosphinothiolate dimers, 2 and 3
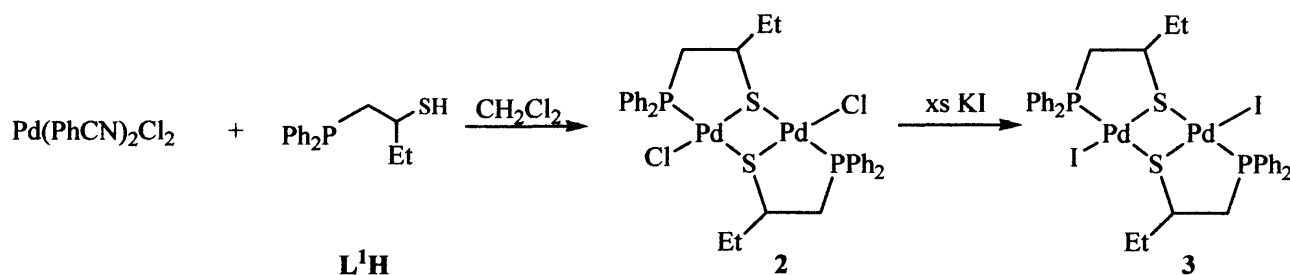
Scheme 10. Synthesis of complexes **2** and **3**

Table 2.1 compares NMR data for phosphinothiolates **2** and **3**. It can be noted that both complexes are produced in excellent yields and have similar $^{31}P\{^1H\}$ shifts : 41.4 ppm for **2** and 41.2 ppm for **3**. Inspection of the ^1H NMR data revealed the complexes to possess similar shifts in the spectra.

Table 2.1. Comparison of data for phosphinothiolate complexes **2, 3**

Complex	% yield	$^{31}P\{^1H\}$[a]	$^1H^{a,\,b}$	MS[c]
2	90	41.4	1.05 (3H, t),	
			1.84 (1H, m),	
			2.10 (1H, m),	
			2.62 (1H, td),	
			2.91 (1H, ddd),	
			3.71 (1H, br m)	
3	82	41.2	0.9 (3H, t),	1012.8
			1.65 (1H, m),	
			1.95 (1H, m),	
			2.65 (1H, td),	
			2.95 (1H, m),	
			3.85 (1H, br m).	

[a] NMR data reported in ppm; [b] ^1H NMR data for the aliphatic protons only; [c] MS data reported as $M\text{-}H^+$.

Reaction of ligand L^1H with $Pd(PhCN)_2Cl_2$ in equimolar amounts in a CH_2Cl_2 solution yielded the chloride dimer **2**. The crude orange solid was recovered which was purified by slow diffusion of diethyl ether into an acetonitrile solution of **2**. A respectable yield of 90% was confirmed for **2**, and the structure of the dimer complex was determined by NMR methods. The $^{31}P\{^1H\}$ NMR spectrum revealed a peak at 41.4 ppm, and the ^1H NMR spectrum showed features consistent with the dimeric structure of **2**.

The crystal structure of **2** has previously been reported by our group.[2] The main features were the Pd-P bond length which was measured as 2.2469(11) Å and Pd-S which measured 2.2732(10) Å. The P-Pd-S angle was reported as 87.10(4)° for the dimeric compound.
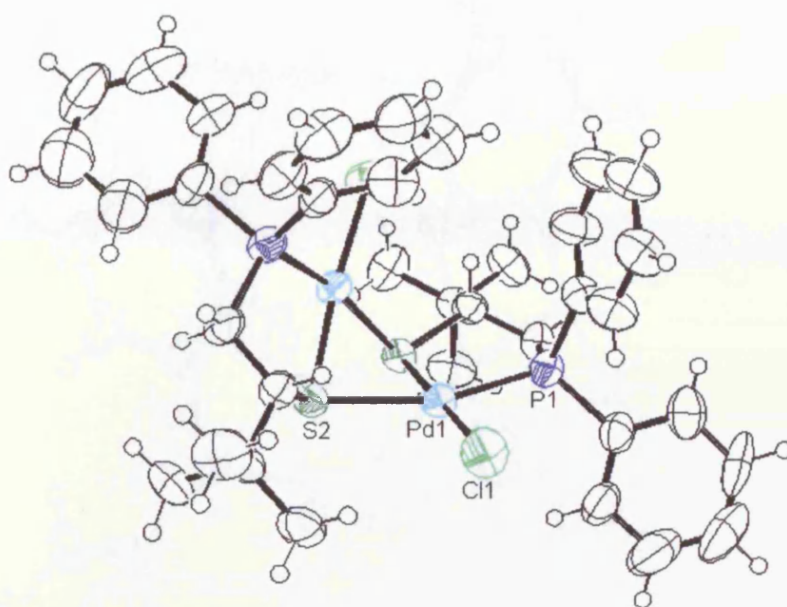
Figure 3. ORTEP diagram of $[Pd(Ph_2PCH_2CHSEtCl]_2$, **2**[2]

The iodide phosphinothiolate complex **3** was prepared by the reaction of the chloride dimer **2** with an excess of approximately 10 equivalents of potassium iodide, as shown in Scheme 10. An orange precipitate resulted which after washing in CH_2Cl_2 and filtering produced an oil. The oil was redissolved in CH_2Cl_2 and dried in vacuo to give **3** as a red solid. Formation of the iodide dimer was justified by NMR analysis, $^{31}P\{^1H\}$ NMR shift at 41.2 ppm and a high resolution mass spectrum, which positioned the parent ion at 1012.8002 m/z. Good quality crystals were obtained from CH_2Cl_2-petroleum ether. Selected geometric data for **3** are presented in Table 2.3. The crystal structure of **3** depicts a symmetrical dimeric system. Hence it can be seen that each Pd is bonded to a P and an I atom, and each Pd atom is attached to both S atoms. The Pd-P bond lengths are 2.2436(9) and 2.2570(10) Å. The Pd-S bond lengths range from 2.2947(9) to 2.3016(10) Å. When examining the P-Pd-S bond angles for the dimer **3** a large difference can be noted for P-Pd-S(1) and P-Pd-S(2) i.e. 166.71(3) and 86.76(3)° for Pd(1) and 86.76(3) and 165.31(4)° for Pd(2). Comparison to dimeric complex **2** reveals similar bond lengths and angles.
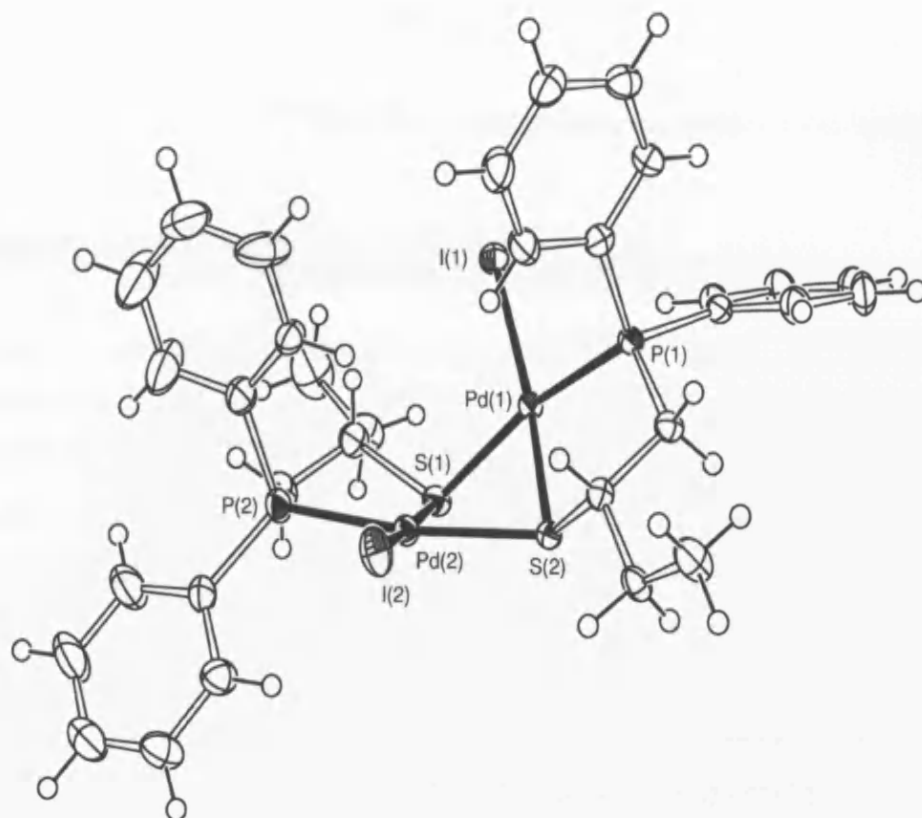
Figure 4. ORTEP diagram of $[PdPh_2PCH_2CHEtSI]_2$, **3**.

Table 2.2. Crystallographic data for the palladium phosphinothiolate **3**

Formula	$C_{32}H_{36}I_2P_2Pd_2S_2$
Mol wt	1013.27
Data collection T, K	150(2)
Diffractometer	Bruker-Nonius KappaCCD
Crystal system	Orthorhombic
Space group	P bca
a, Å	14.50820(10)
b, Å	16.0768(2)
c, Å	29.9895(2)
V, Å^3	6994.91(11)
Z	8
ρ, Mgm^{-3}	1.924
μ, mm^{-1}	3.026
θ range, deg	$2.98 < \theta < 30.06$
no. of indep data	10173[R(int) = 0.1120]

no. of obsd rflns (n_o)	76617
Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0776
R indices (all data)	R1 = 0.0595, wR2 = 0.0860
GOF	1.032
Largest diff. peak and hole	0.991 and -1.256 e.Å^{-3}

Table 2.3. Selected bond lengths (Å) and angles (deg) for the palladium phosphinothiolate **3**

C(1)-P(1)	1.823(4)	C(2)-C(1)-P(1)	120.2(3)
C(23)-P(2)	1.817(4)	C(13)-C(14)-S(2)	107.3(2)
C(14)-S(2)	1.859(4)	P(1)-Pd(1)-S(2)	86.76(3)
C(30)-S(1)	1.847(4)	P(2)-Pd(2)-I(2)	96.05(3)
I(1)-Pd(1)	2.6349(4)	S(2)-Pd(1)-I(1)	170.96(3)
I(2)-Pd(2)	2.6179(4)	C(23)-P(2)-C(17)	109.6(2)
P(1)-Pd(1)	2.2436(9)	C(23)-P(2)-Pd(2)	120.44(13)
P(2)-Pd(2)	2.2570(10)	C(14)-S(2)-Pd(1)	104.84(11)
Pd(2)-S(1)	2.3016(10)	Pd(1)-S(2)-Pd(2)	80.96(3)

2.2.4.2 Synthesis of palladium tertiary-butyl phosphinothiolate complex, 4
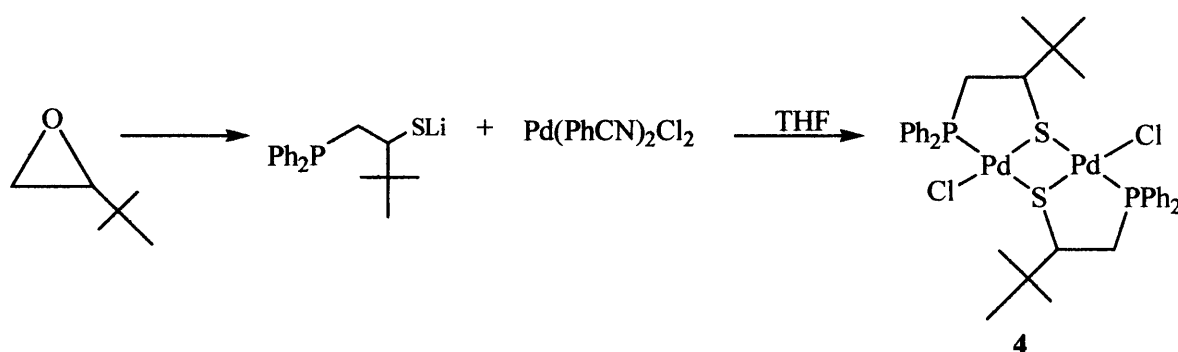
Scheme 11. Synthesis of complex **4**

The phosphinothiolate complex **4** was synthesied from the racemic ligand $Ph_2PCH_2CH(^tBu)SLi$, as shown in Scheme 11. The palladium source, $Pd(PhCN)_2Cl_2$, was added to a THF solution of the ligand and stirred overnight. Slow recrystallisations from acetonitrile-diethyl ether afforded the pure compound **4** in 49% yield. The $^{31}P\{^1H\}$

39

NMR showed a single peak at +39 ppm and both ^{1}H and ^{13}C NMR data were consistent with the proposed structure. It is worth noting that the tertiary butyl group was shown in the ^{1}H NMR as a singlet peak with a shift observed at 1.1 ppm, which intergrated to 9 protons (for each Pd). The main feature in the ^{13}C NMR was the tertiary butyl resonance which appeared at 28.4 ppm. High resolution mass spectrometry revealed a structure consistent with the palladium t-butyl dimer [M-Cl]$^+$ parent ion-Cl for ($C_{36}H_{44}P_2S_2Cl$), at 849.0114 (calculated mass = 849.0118).

2.2.4.3 Synthesis of palladium bis-chelate complex, 5
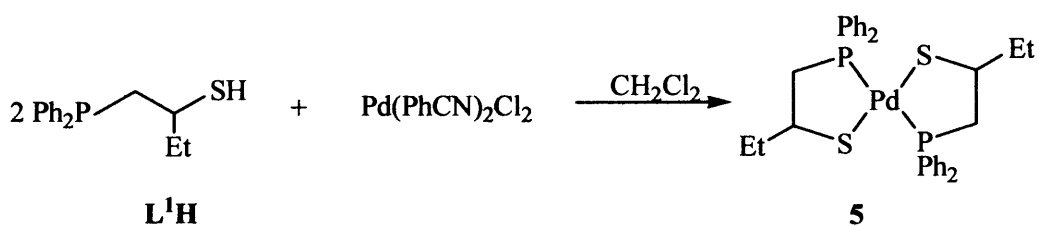
Scheme 12. Synthesis of complex **5**

Bis-chelate complexes (M(P-S)$_2$) have been reported to be the most common type of coordination compounds that can be formed from the complexation of phosphinothiolate ligands with Group 10 metals.[2] The favoured geometry has been found to be trans, although examples of cis have also been confirmed. The bis-chelate **5** was synthesised by reaction of 1 equivalent of Pd(PhCN)$_2$Cl$_2$ with 2 equivalents of the **L^{1}H** (Scheme 12).

Slow diffusion of petroleum ether into a CH$_2$Cl$_2$ solution of **5** yielded the bis-chelate complex, as indicated by two singlets in the ^{31}P{^{1}H} NMR spectrum, one at 48.1 ppm for the trans-rac isomer and one peak at 51.1 ppm for the trans-meso isomer. The same bis-chelate complex was synthesised from the S isomer of **L^{1}H** and the ^{31}P{^{1}H} NMR spectrum was identical to that of the rac isomer, supporting the assignment of the signals.[2] NMR spectroscopy also indicated the two isomers were obtained in approximately equal quantities. The accurate mass spectrum confirmed the molecular formula to be $C_{32}H_{37}PdP_2S_2$ with a measured mass of 653.0849, as anticipated.

Table 2.4 compares the main characteristic features for **L¹H** and the resulting complex **5**. A clear shift is noted in the $^{31}P\{^1H\}$ NMR spectrum from -18.0 ppm to 2 peaks at 48.1 and 51.1 ppm.

Table 2.4. Comparison of data for ligand **L¹H** and complex **5**

	% yield	$^{31}P\{^1H\}^a$	$^1H^a$
L¹H	90	-18.0	0.85 (3H, t), 1.55 (1H, m), 1.8 (2H, m), 2.3 (2H, 2 x m).
5	90	48.1 Trans-rac	0.89 (3H, t), 1.64 (1H, m), 1.72 (1H, m), 2.32 (1H, td), 2.73 (1H, br m), 2.89 (1H, m).
		51.1 Trans-meso	0.89 (3H, t), 1.64 (1H, m), 1.72 (1H, m), 2.32 (1H, td), 2.46 (1H, m), 2.73 (1H, br m).

^{a} NMR data reported in ppm;

2.2.4.4 Synthesis of palladium methyl tertiary-butyl phosphinothioether complex, 6
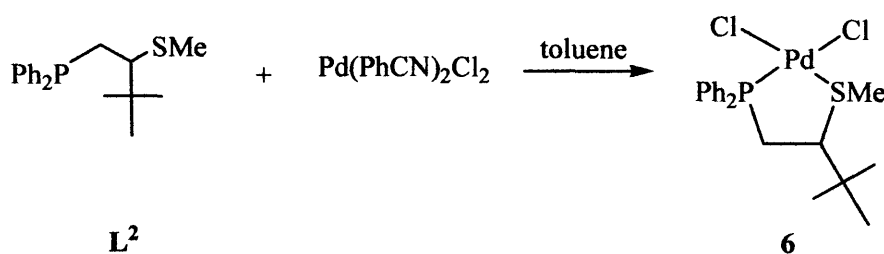
Scheme 13. Synthesis of complex **6**

Reaction of ligand **L²** with Pd(PhCN)₂Cl₂ in toluene afforded complex **6**. The crude product was isolated as a yellow/orange solid following precipitation with petroleum ether. The resulting solid was noted to be light sensitive. Recrystallisation of **6** was attempted using a diffusion of petroleum ether into a CH₂Cl₂ solution of **6**. However this method did not yield crystals suitable for x-ray crystallography. A notable feature in the $^{31}P\{^1H\}$ NMR spectrum was the characteristic peak for phosphinothioether complexes which for **6** was found at +46 ppm.

2.2.4.5 Synthesis of palladium methyl-phosphinothioether complex, 7
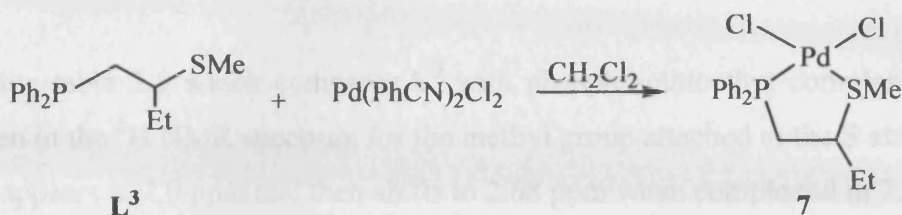
Scheme 14. Synthesis of complex **7**

The palladium complex **7** was prepared by complexation of ligand **L³** onto Pd(PhCN)₂Cl₂ in a 1:1 ratio in CH₂Cl₂. Upon complexation of **L³** a noticeable shift in the ³¹P{¹H} NMR spectrum was noted from δ -20 to δ +50 ppm. Mass spectral measurements (low resolution) established the expected parent ion peak at 467 m/z. Complex **7** was obtained with a yield of 88%. Recrystallisation from CH₂Cl₂-diethyl ether afforded yellow crystals. The crystal structure of **7** has been reported by our group.[2]
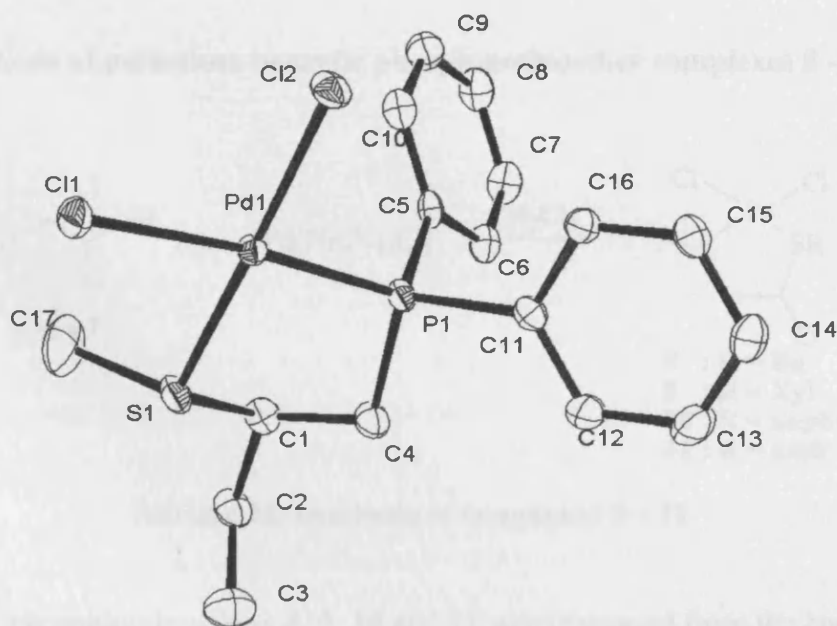
Figure 5. ORTEP diagram of Pd(Ph₂PCH₂CHEtSMe)Cl₂, **7**. The hydrogen atoms have been omitted.[2]

Notable bond lengths are Pd-P which measures 2.2441(7) Å and Pd-S which measures 2.2688(7) Å. The P-Pd-S angle corresponds to 86.98(3)° and can be marked as a

characteristic angle for the bidentate P,S complexes, as all such complexes have this angle. The structure is monomeric.

On studying table 2.5 which compares L^3 with phosphinothioether complex 7, a shift can be seen in the ^1H NMR spectrum for the methyl group attached to the S atom. For L^3 this peak appears at 2.0 ppm and then shifts to 2.68 ppm when complexed in 7.

Table 2.5. Comparison of data for ligand L^3 and complex 7

	% yield	$^{31}P\{^1H\}^a$	$^1H^a$
L^3	70	-20.4	1.03 (3H, t), 1.72 (1H, m),
			1.89 (1H, m), 2.0 (3H, s),
			2.3-2.65 (3H, m).
7	88	50.0	0.94 (3H, br), 1.70 (1H, br),
			2.59 (1H, br), 2.68 (3H, br s),
			2.84 (1H, br), 2.96 (1H, br).

^{a} NMR data reported in ppm;

2.2.4.6 Synthesis of palladium benzylic phosphinothioether complexes 8 - 11

8 : R = Bn
9 : R = Xyl
10 : R = naphth
11 : R = anth
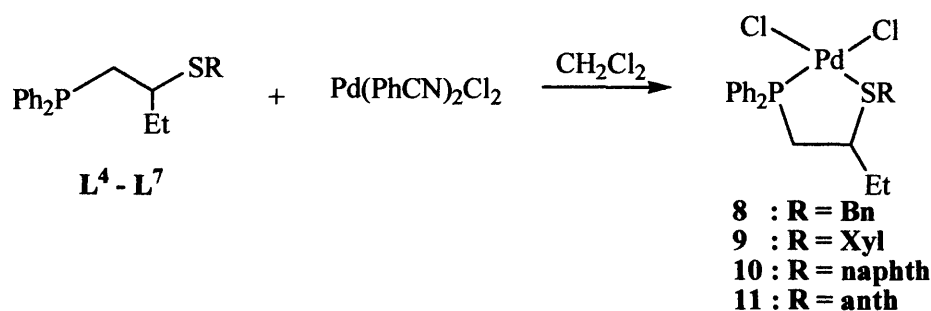
Scheme 15. Synthesis of complexes 8 – 11

The benzylic phosphinothioethers 8, 9, 10 and 11 were prepared from the corresponding ligands L^4-L^7 by reaction with Pd(PhCN)$_2$Cl$_2$ in a 1:1 ratio in CH$_2$Cl$_2$. The resulting complexes were characterised by $^{31}P\{^1H\}$ and ^1H NMR spectroscopy. $^{31}P\{^1H\}$ NMR spectroscopy indicates a single peak around 50 ppm which is consistent with previously determined bidentate structures. Mass spectral data also gave supporting evidence for the expected composition for complexes 8 and 9. Table 2.6 summarises the data obtained for

complexes **8 – 11**. Complexes **8 – 10** display the characteristic benzylic protons which are typically seen at around 4 – 5 ppm (Figure 6 and Table 2.6). Each proton is exhibited as an apparent doublet. Complex **11** shows only one benzylic proton in this region, suggesting that a dimer complex may have been formed.

Table 2.6. Comparison of selected data for phosphinothioether complexes **8, 9, 10** and phosphinothiolate complex **11**

Complex	% yield	$^{31}P\{^1H\}^a$	$^1H^{a,\,b}$	MS^c
8	83	50.4	3.95 (1H, d)	505
			4.95 (1H, d)	
9	88	52.4	3.8 (1H, d)	533
			4.7 (1H, d)	
10	69	54.2	4.75 (1H, d)	
			5.15 (1H, d)	
11	76	52.5	4.65 (1H, d)	

^{a} NMR data reported in ppm; ^{b} ^1H NMR data for the benzylic protons only; ^{c} MS data reported as $M-Cl^+$ for **8** and $M-Cl^-$ for **9**, no MS data collected for **10** and **11**.
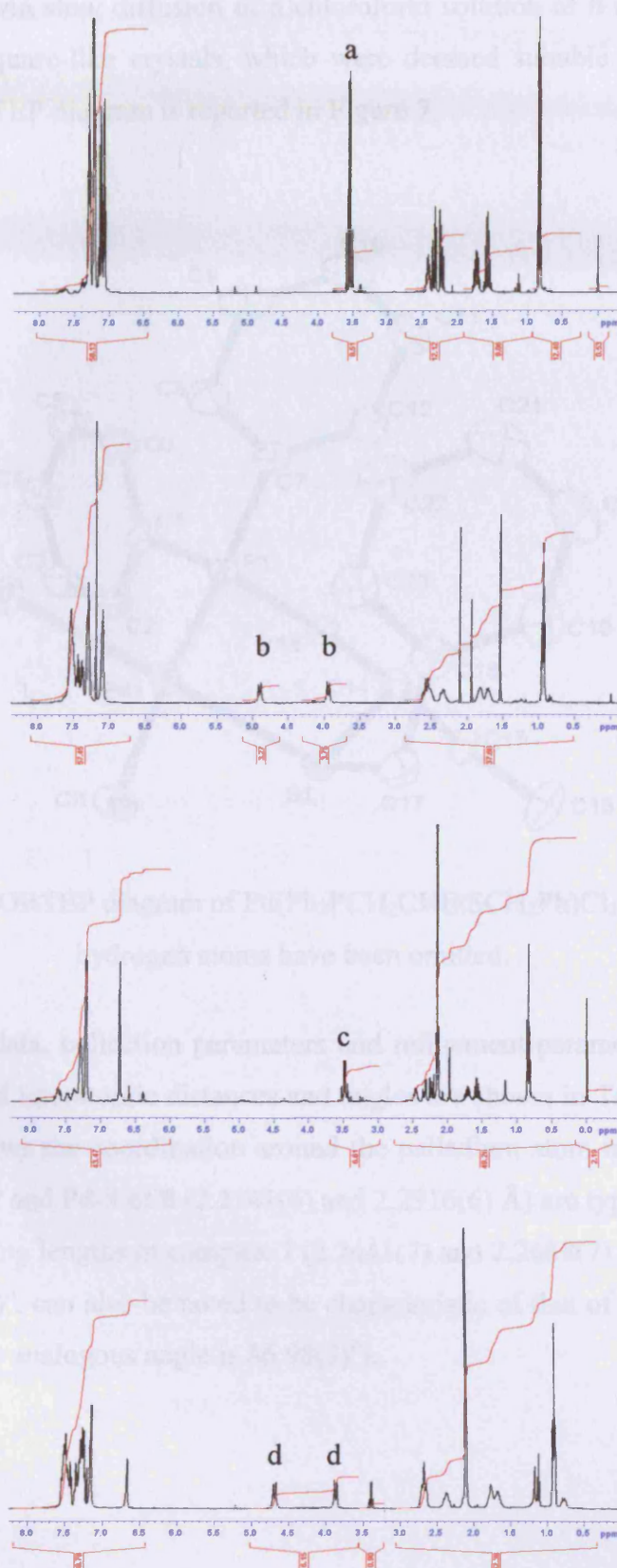
Figure 6. ^{1}H NMR spectra indicating the positions of benzylic protons for ligands $\mathbf{L^4}$ and $\mathbf{L^5}$ (labelled a and c) and their respective complexes **8** and **9** (labelled b and d).

Recrystallisation via slow diffusion of a chloroform solution of **8** into petroleum ether yielded orange square-like crystals, which were deemed suitable for crystallographic analysis. The ORTEP diagram is reported in Figure 7.
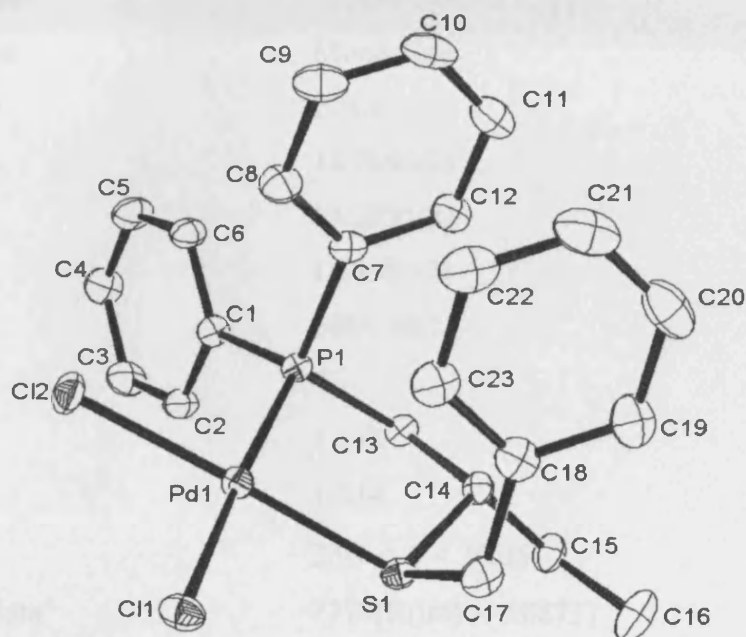
Figure 7. ORTEP diagram of Pd(Ph$_2$PCH$_2$CHEtSCH$_2$Ph)Cl$_2$, **8**. The hydrogen atoms have been omitted.

Crystallographic data, collection parameters and refinement parameters are reported in Table 2.7; selected interatomic distances and angles are shown in Table 2.8. The crystal structure of **8** shows the coordination around the palladium atom is square planar. The bond lengths Pd-P and Pd-S of **8** (2.2141(6) and 2.2916(6) Å) are typical, and are similar to the corresponding lengths in complex **7** (2.2441(7) and 2.2688(7) Å). The angle P-Pd-S of **8**, at 87.36(2)°, can also be noted to be characteristic of that of a bidentate complex (for complex **7** the analogous angle is 86.98(3)°).

Table 2.7. Crystallographic data for the palladium phosphinothioether **8**

Formula	$C_{24}H_{26}Cl_5PPdS$
Mol wt	661.13
Data collection T, K	150(2)
Diffractometer	Bruker-Nonius KappaCCD
Crystal system	Monoclinic
Space group	P21/c
a, Å	14.7145(2)
b, Å	13.2355(2)
c, Å	14.8381(3)
V, Å^3	2664.56(7)
Z	4
ρ, Mgm^{-3}	1.648
μ, mm^{-1}	1.349
θ range, deg	$2.93 < \theta < 30.05$
no. of indep data	7770[R(int) = 0.0873]
no. of obsd rflns (n_o)	39701
Final R indices [I>2sigma(I)]	R1 = 0.0350, wR2 = 0.0761
R indices (all data)	R1 = 0.0497, wR2 = 0.0817
GOF	1.020
Largest diff. peak and hole	0.851 and -1.046 e.Å^{-3}

Table 2.8. Selected bond lengths (Å) and angles (deg) for the palladium phosphinothioether **8**

C(1)-P(1)	1.809(2)	C(6)-C(1)-P(1)	122.13(17)
C(14)-S(1)	1.854(2)	C(13)-C(14)-S(1)	107.34(15)
C(17)-S(1)	1.846(2)	P(1)-Pd(1)-S(1)	87.36(2)
C(7)-P(1)	1.817(2)	P(1)-Pd(1)-Cl(2)	89.86(2)
C(13)-P(1)	1.820(2)	S(1)-Pd(1)-Cl(2)	174.01(2)
Cl(1)-Pd(1)	2.4082(6)	Cl(2)-Pd(1)-Cl(1)	93.00(2)
Cl(2)-Pd(1)	2.3163(6)	C(7)-P(1)-C(13)	108.24(11)
P(1)-Pd(1)	2.2141(6)	C(1)-P(1)-Pd(1)	119.45(8)
Pd(1)-S(1)	2.2916(6)	C(17)-S(1)-Pd(1)	106.76(8)

The structure of the xylene complex **9** was verified by ^{1}H and ^{13}C NMR data and by X-ray structural analysis from yellow crystals grown by slow diffusion of petroleum ether into a DCM solution of **9**. The ORTEP diagram is reported in Figure 8.
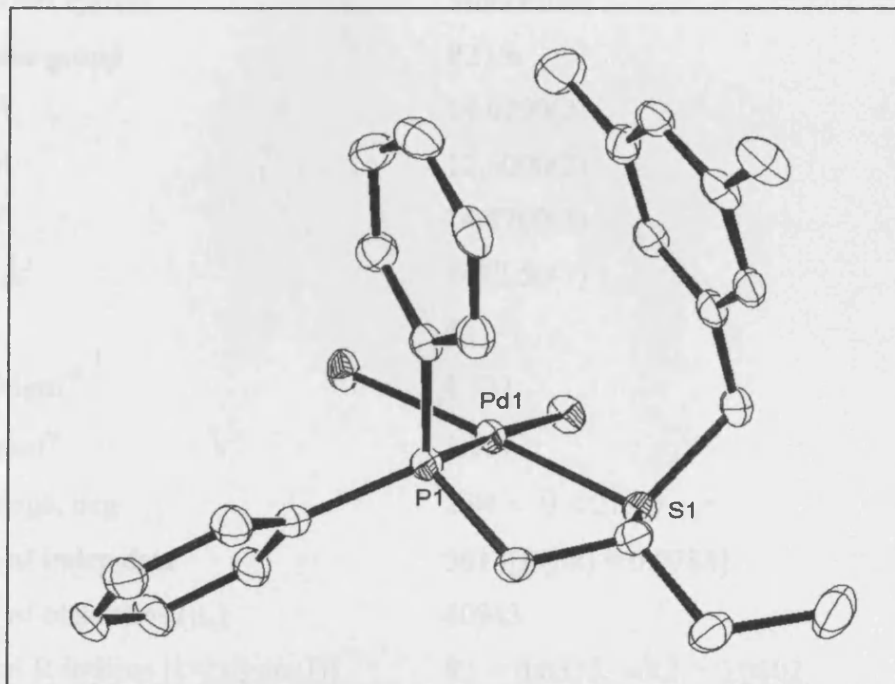
Figure 8. ORTEP diagram of Pd(Ph$_2$PCH$_2$CHEtSCH$_2$C$_8$H$_9$)Cl$_2$, **9.**
Hydrogen atoms have been omitted.

Selected geometric data are presented in Table 2.10. Comparison of the data for **9** to the previously reported compound **7** was undertaken. The crystal structure of **9** was noted to posses a similar structure to the benzyl compound **8**. The geometry about the metal for **9** is square planar. The Pd-S and Pd-P distances, 2.2825(8) and 2.2185(8) Å, respectively, are in a similar range to those of complex **7**, suggesting a Pd (II) complex. The P-Pd-S angle is reported as 86.95(3)°, falling within the range for bidentate complexes. The analogous angle in the benzyl complex was reported as 87.36(2)°.

Table 2.9. Crystallographic data for the palladium phosphinothioether **9**

Formula	$C_{25}H_{29}Cl_2PPdS$
Mol wt	569.81
Data collection T, K	150(2)
Diffractometer	Bruker-Nonius KappaCCD
Crystal system	Monoclinic
Space group	P21/n
a, Å	14.0290(2)
b, Å	12.6000(2)
c, Å	14.8700(3)
V, Å^3	2472.56(7)
Z	4
ρ, Mgm^{-3}	1.531
μ, mm^{-1}	1.127
θ range, deg	$2.91 < \theta < 27.40$
no. of indep data	5613[R(int) = 0.0784]
no. of obsd rflns (n_o)	40943
Final R indices [I>2sigma(I)]	R1 = 0.0355, wR2 = 0.0802
R indices (all data)	R1 = 0.0490, wR2 = 0.0856
GOF	1.034
Largest diff. peak and hole	0.724 and -0.939 e.Å^{-3}

Table 2.10. Selected bond lengths (Å) and angles (deg) for the palladium phosphinothiolate **9**

C(1)-P(1)	1.827(3)	C(2)-C(1)-P(1)	111.4(2)
C(2)-S(1)	1.847(3)	C(1)-C(2)-S(1)	107.1(2)
C(5)-S(1)	1.848(3)	P(1)-Pd(1)-S(1)	86.95(3)
C(14)-P(1)	1.812(3)	P(1)-Pd(1)-Cl(1)	90.99(3)
C(20)-P(1)	1.811(3)	S(1)-Pd(1)-Cl(1)	177.47(3)
Pd(1)-P(1)	2.2185(8)	Cl(1)-Pd(1)-Cl(2)	94.08(3)
Pd(1)-S(1)	2.2825(8)	C(20)-P(1)-C(14)	106.32(13)
Pd(1)-Cl(1)	2.3304(7)	C(1)-P(1)-Pd(1)	105.81(10)
Pd(1)-Cl(2)	2.3991(7)	C(2)-S(1)-C(5)	103.38(15)

Analysis of the naphthalene complex **10** by mass spectrum was attempted, using the electrospray method. However, the expected peak at 591.9 was not seen, instead a peak was noted at 546.2 m/z (45.7 less than anticipated). This could indicate that the detection method used was not entirely suitable for this complex. Orange crystals of **10** were grown from THF-diethyl ether, and the structure of the complex was established to be as shown in Figure 9.
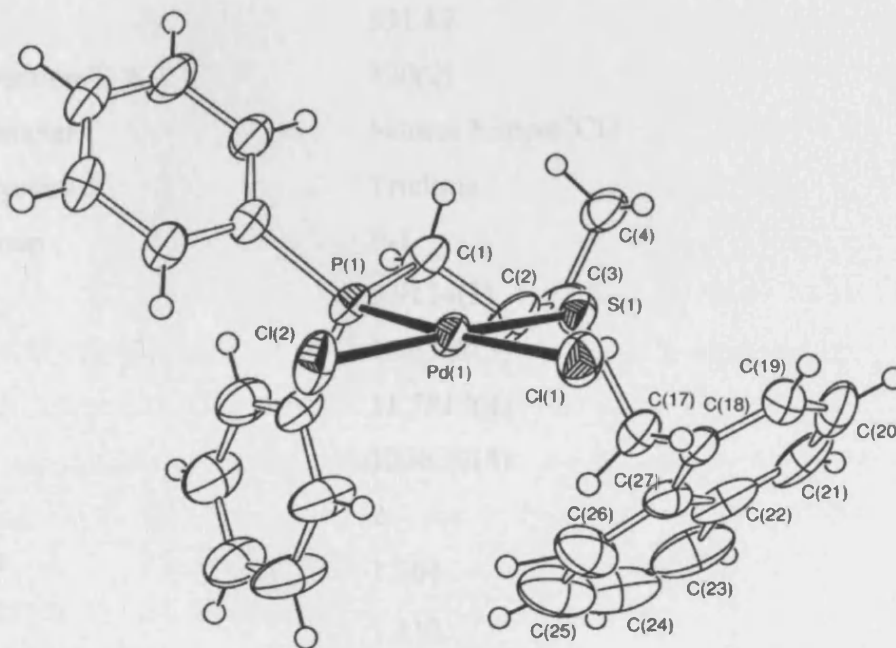
Figure 9. ORTEP diagram of $Pd(Ph_2PCH_2CHEtSCH_2C_{10}H_7)Cl_2$, **10**. Hydrogen atoms have been omitted.

Crystallographic data, collection parameters and refinement parameters are reported in Table 2.11; selected interatomic distances and angles are shown in Table 2.12. The structure revealed slight disorder in the naphthalene and ethyl groups; however the geometry showed a bidentate structure, as anticipated, with the ligand attaching onto the palladium, both being in a 1:1 ratio. The metal adopted a distorted square planar orientation which is consistent with the structures for our previous P,S monomer complexes. The P-Pd-S angle was shown to be 90.14(6)°. This angle is slightly smaller both in the benzyl complex **8** (87.36(2)°) and the xylene complex **9** (86.95(3)°), which suggests a larger ligand is present in **10**. The Pd-S and Pd-P distances in **10**, which correspond to 2.265(2) and 2.2187(7) Å respectively, are comparable to the distances in **8** and **9**. The Pd-S distance is slightly shorter in **10** (although longer than that of the

50

monomer which was used previously for comparative purposes, **7**, which had a Pd-S angle that measured 2.2441(7) Å). Hence, the data obtained by crystal structure determination supports the expected monomeric structure for the naphthalene complex **10**.

Table 2.11. Crystallographic data for the palladium phosphinothioether **10**

Formula	$C_{27}H_{27}Cl_2PPdS$
Mol wt	591.82
Data collection T, K	120(2)
Diffractometer	Nonius KappaCCD
Crystal system	Triclinic
Space group	P-1
a, Å	9.9134(3)
b, Å	11.6302(5)
c, Å	11.7817(4)
V, Å^3	1256.57(8)
Z	2
ρ, Mgm^{-3}	1.564
μ, mm^{-1}	1.112
θ range, deg	$2.03 < \theta < 27.48$
no. of indep data	5748[R(int) = 0.0408]
no. of obsd rflns (n_o)	24762
Final R indices [I>2sigma(I)]	R1 = 0.0341, wR2 = 0.0745
R indices (all data)	R1 = 0.0437, wR2 = 0.0785
GOF	1.056
Largest diff. peak and hole	0.515 and -0.633 e.Å^{-3}

Table 2.12. Selected bond lengths (Å) and angles (deg) for the palladium phosphinothioether **10**

C(1)-P(1)	1.823(3)	C(2)-C(1)-P(1)	109.33(19)
C(2)-S(1)	1.963(4)	C(1)-C(2)-S(1)	104.2(2)
C(17)-S(1)	1.859(5)	P(1)-Pd(1)-S(1)	90.14(6)
C(5)-P(1)	1.808(3)	P(1)-Pd(1)-Cl(2)	91.45(2)
C(11)-P(1)	1.813(2)	S(1)-Pd(1)-Cl(2)	177.85(6)
P(1)-Pd(1)	2.2187(7)	Cl(1)-Pd(1)-Cl(2)	93.16(3)
S(1)-Pd(1)	2.265(2)	C(5)-P(1)-C(11)	105.03(12)
Cl(1)-Pd(1)	2.3660(7)	C(5)-P(1)-Pd(1)	113.32(9)
Cl(2)-Pd(1)	2.2986(7)	C(17)-S(1)-C(2)	102.1(2)

A mass spectrum of the anthracene complex **11** displayed the parent ion at 771 m/z, not the expected 642. Recrystallisation was attempted using a toluene-diethyl ether system, producing yellow plate-like crystals. To assist the characterisation process the crystals of **11** were run on the x-ray diffractometer however the structure of the resulting complex was of the ethyl-dimer **2**. Inspection of the ^{1}H NMR data of **11** also showed a dimer complex.

2.2.5 Further investigation of palladium complexes

In previous years organopalladium chemistry has concentrated on the 0, +I and +II oxidation states. The first venture into Pd(IV) chemistry came in 1986 when Byers and co-workers isolated the first example of an alkylpalladium (IV) complex, PdIMe$_3$(bpy), where bpy = 2,2'-bipyridyl.
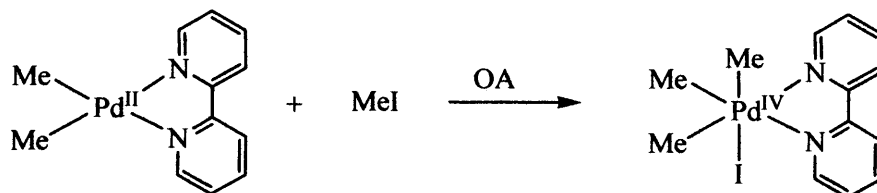
Scheme 16. Synthesis of the first Pd(IV) complex in 1986

The x-ray structure of the new Pd(IV) complex formed, fac-[PdMe$_3$(bpy)I], revealed an octahedral geometry.[24] Octahedral intermediates are thought to generally be formed by trans oxidative addition. However, Pd (IV) complexes bearing cis halide groups have

also been reported. Five coordinate or solvated octahedral cationic intermediates are reported in Pd(IV) chemistry.[25] Platinum has been noted to form many Pt(IV) complexes, with this metal holding a greater preference for the +IV oxidation state than Pd. Comparison of Pd(IV) and Pt(IV) bond lengths (M-C and M-I) showed similar distances.[24]

Early Pd(IV) chemistry used organohalides that could undergo S_N2 reactions at low temperatures.[25] Pd(II) precursors would often be used and to them halogens, alkyl halides or other electrophilic agents would be oxidatively added.[26] Exchange reactions involving the bromo ligand in $PdBrMe_2(CH_2Ph)(bpy)$ reacting with silver salts in CH_3CN, form various Pd(IV) complexes (Scheme 17). For this class of reaction low temperature and a coordinating solvent, for example acetonitrile, is needed, which assists with the stabilisation of the intermediate cation $[PdMe_2(CH_2Ph)(bpy)(NCMe)]^+$. The resulting Pd(IV) complexes are collected in 47-90% yields.[27]

$$PdBrMe_2(CH_2Ph)(bpy) \xrightarrow[\text{filtration}]{AgNO_3, \ X^- \ / \ AgX} Pd^{IV}XMe_2(CH_2Ph)(bpy)$$
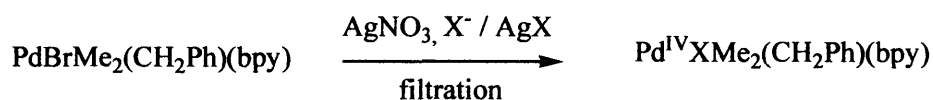
Scheme 17. Synthesis of Pd(IV) complexes

Recent developments have included the isolation of cationic complexes via oxidative addition of $Pd^{II}Me_2$ complexes with tripod ligands such as tris(pyrazol-1-yl)methane and 1,4,7-trithiacyclonane.[25] Anionic Pd(II) palladacycle precursors, in particular those with rigid tripodal ligands have been used as starting materials for the formation of Pd(IV) alkyl or aryl complexes.[26]

In 2005 Campora and co-workers detail a new method for the synthesis of Pd(IV) complexes whereby anionic Pd(II) is reacted with 2 equivalents of a one electron oxidant $[FeCp_2][PF_6]$.[26]
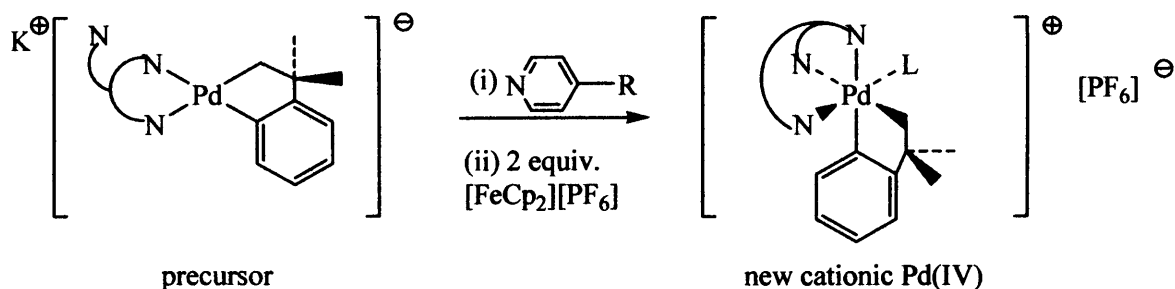
Scheme 18. New method for the synthesis of Pd(IV) complexes
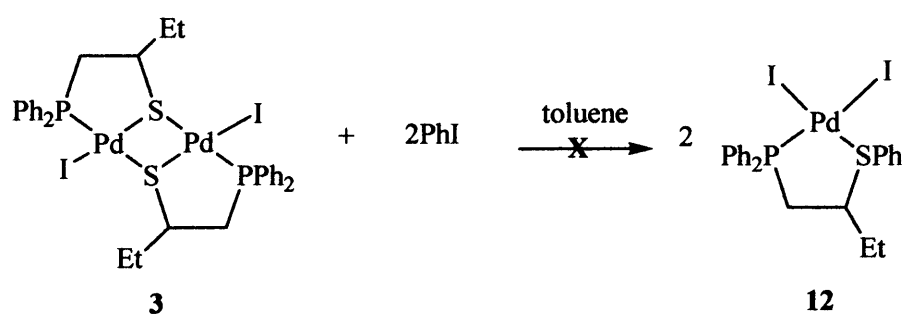
Scheme 19. First attempt of the conversion of phosphinothiolate **3** to -thioether **12**

Reaction of **3** with two equivalents of iodobenzene (Scheme 19) yielded an orange solution of 2 equivalents of **12**. The $^{31}P\{^1H\}$ NMR spectrum of the solution revealed a peak at 42.8 ppm, which was identical to the shift for **3** of 43 ppm. Following a work-up the ^1H NMR spectrum recorded revealed the expected peaks in the aliphatic region, 0-4 ppm. The aromatic region did not show the expected ten additional protons. Our second attempt involved the reaction of **3** with two equivalents of 4-iodoacetophenone heated too 80 °C, as shown in Scheme 20.
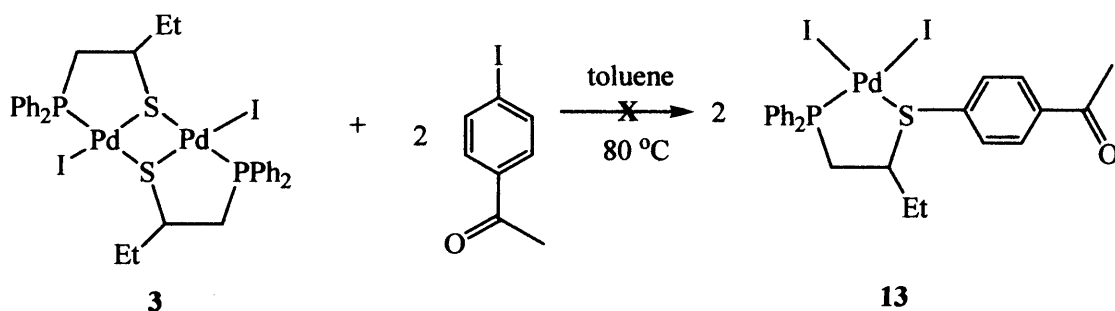
Scheme 20. Second attempt of the conversion of phosphinothiolate to -thioether

Spectral analysis of the orange solution showed a peak at 42.7 ppm and the ^1H spectrum showed the presence of unreacted ligand and 4-iodoacetophenone, with no apparent addition of the 4-iodoacetophenone on to **3**. The mass spectrum of **13** did not reveal the anticipated parent ion which expected at 996 m/z. Instead clusters of peaks were observed at 1031 m/z and 1539 m/z. Therefore our attempts at converting a phosphinothiolate to a phosphinothioether via addition of an aryl halide have proved inconclusive.

2.2.6 Investigation of gold complexes

The use of gold in homogeneous catalysis lies in two reactions: C-X bond formation (the addition of nucleophiles to alkenes or alkynes, where X = heteroatom) and C-C bond formation (the asymmetric aldol reaction). Recently it has been reported by Hashmi that both C-O and C-C bond formation can be produced via a gold catalysed reaction. This involved gold (III) catalysts which were shown to be very active and operated under mild conditions. Hashmi investigated a dimerisation reaction using Au(III) catalysts, which can be likened to a Pd(II)-d^8 system. The resulting system was very active and allowed mild conditions to be used. The reaction was noted to proceed extremely quickly and there was a possibility that the gold catalysts may allow cross-dimerisation with olefins, which was not possible with previously used palladium catalysts.[28]

Gold (I) catalysts have also been reported to be very efficient, in particular for the addition of alcohols to terminal alkynes, which was previously attempted with a mercury (II) catalyst. These reactions can operate under mild conditions (temperatures of 20-50 °C) and yield high TONs of 10^5 and TOFs of 5400 h^{-1}. The cationic gold (I) catalysts, [L-Au$^+$] (where L = phosphane, phosphite or arsine) can be used under desirable conditions, with the system being able to operate without the use of solvent, and the catalyst proved to be neither air or water sensitive.[29]

Steps that can be taken to synthesise gold precursors have been studied since the 1960's. A known route involves benzyl tertiary amines which are reacted with butyl lithium in diethyl ether, forming the metallated intermediates (Scheme 21).[30]
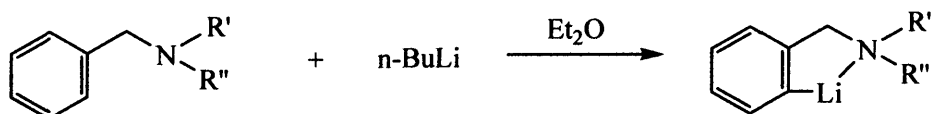
Scheme 21. Synthesis of a gold precursor using benzyl tertiary amines

The use of organomercury and organotin complexes as intermediates in the preparation of other organometallic complexes has been known for years. Recent work has focused on making aryl gold (III) compounds via transmetallation reactions between organomercury/organotin complexes and gold (III) salts (Scheme 22).[31]
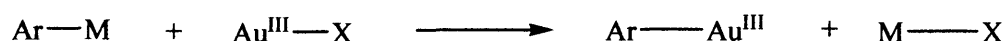
where M = Hg, Sn
   X = halogen

Scheme 22. Transmetallation reaction to synthesise aryl-gold (III) complexes

2-(dimethylamino)methylphenyl gold complexes have previously been made by trans metallations using lithium derivatives. They can also be made using mercury derivatives which act as arylating agents.[32] The use of (Bu$_4$N)[AuCl$_4$] and the gold complex [Au(damp-C^1,N)Cl$_2$], where damp = 2-(N,N-dimethylaminomethyl)phenyl, has been investigated with tri- and tetradentate phosphinothiolate ligands. The damp group is known to stabilise gold (III) when used along with thiolate and phosphine ligands. When [Au(damp-C^1,N)Cl$_2$] is used as a precursor to gold (III) reactions, the route followed does not typically involve the complete substitution of the damp$^-$ ligand, but sees the Au-C σ bond remain intact and chloro groups exchanged for the thiolates or phosphines. The use of the [Au(damp)] complex as a precursor can be supported by the fact that having an organometallic ligand does seem essential in the formation of mononuclear gold (III) complexes as the reduction of gold is inhibited and the reactions go to completion (forming [AuCl(L)]) with reasonable yields.[33]

Our investigations have focused on gold chemistry and its impact and use in homogeneous catalysis.
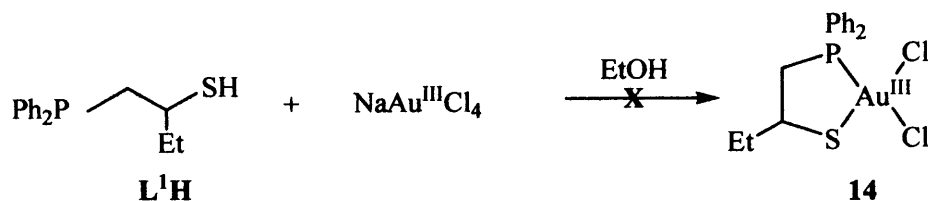
Scheme 23. Synthesis of Au(III) monomer **14**

Reaction of ligand L^1H with 1 equivalent of $NaAu^{II}Cl_4$ in ethanol produced an Au(III) monomer, complex **14**, in 46% yield (Scheme 23). The $^{31}P\{^1H\}$ and ^1H NMR data was inconclusive and recrystallisation attempts proved unsuccessful.
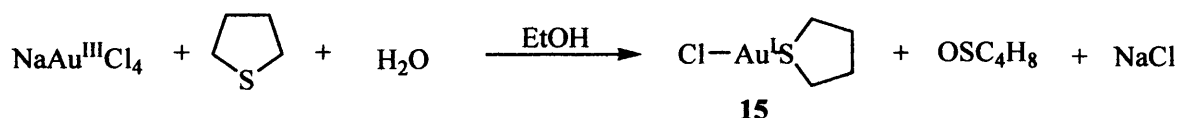
Scheme 24. Synthesis of Au(I)THT **15**

Reaction of tetrahydrothiophene (THT) with $NaAuCl_4$ in water yielded the Au(I)THT complex **15** (Scheme 24), as a precursor for the synthesis of P,S-Au(I) complexes. **15** was obtained as a white solid in 84% yield and was characterised by ^1H NMR spectroscopy. The literature stated a yield of 95% for this synthesis using $H[AuCl_4]$. **15** was subsequently used in C-C coupling reactions.[34]

For the synthesis of dimeric Au(I)-P,S complexes two routes were followed. The first involved reaction of the phosphinothiolate L^1 with the Au(I)THT complex **15** in CH_2Cl_2 (Scheme 25). The $^{31}P\{^1H\}$ NMR spectrum showed a peak at 26.6 ppm, but due to the insolubility of **16** in solvents (suggesting a possible polymer structure) a ^1H NMR spectrum was not recorded. Recrystallisation attempts were unsuccessful.
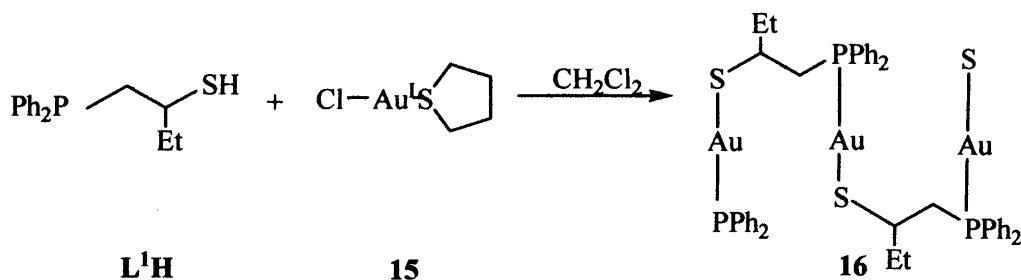
Scheme 25. First method for Au polymer **16** synthesis

The second method for the formation of dimeric Au(I)-P,S complexes involved reaction of L^1H with the Au(I)THT complex 16 and aqueous NaOH in CH_2Cl_2. The method followed by Weinstock[35] for the formation of an Au(I)-P,S dimer complex was followed and adapted for L^1H. Weinstock noted that the anion of the phosphinothiolate successfully reacted with the Au(I) complex yielding a symmetrical Au(III) dimer. Our attempts (Scheme 26) produced a black mixture, the $^{31}P\{^1H\}$ NMR spectrum of which showed a noisy cluster of peaks in the range 23-32 ppm. An orange solid was finally obtained.
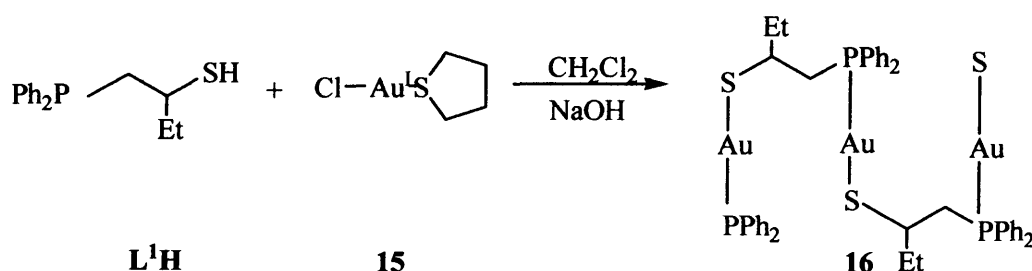
Scheme 26. Second method for Au polymer 16 synthesis

C-C bond formation with the aid of gold catalysts has received interest from Ito et al,[36] Togni et al,[37] Hayashi et al[38] and also Hashmi et al.[28] The cross-dimerisation reaction believed to be involved in the C-C bond formation was previously unsuccessful with Pd compounds (Scheme 27).[28]
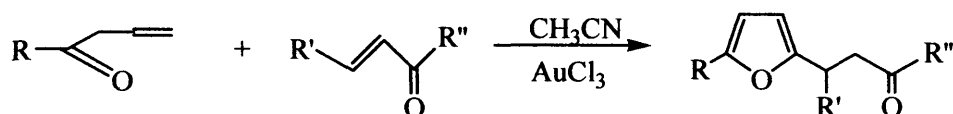
Scheme 27. General scheme for C-C bond formation

A Michael acceptor can be any compound that is able to undergo Michael addition, a conjugate addition. This type of addition (also known as 1, 4-addition) allows a nucleophile to add on to the C=C double bond of an α,β-unsaturated ketone or aldehyde. The enolate ion intermediate is formed following the conjugate addition of a nucleophile to the β carbon of the carbonyl. This is then protonated on the α carbon to give the final saturated product, as shown in Scheme 28.
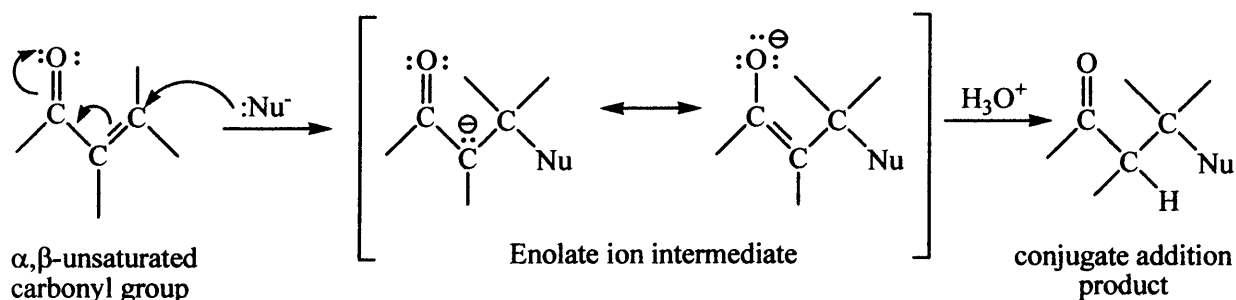
Scheme 28. 1,4-conjugate addition

The next investigation of gold chemistry included addition reactions using gold catalysts. The first which involved the reaction of 1-methylfuran with methylvinylketone was a cross-dimerisation reaction, as shown in Scheme 29. **17** was isolated through column chromatography (using a solvent mixture of petroleum ether:ethyl acetate in a ratio of 8:2). The ^{1}H NMR spectra showed the desired product, with the 2 vinylic protons being displayed as a double doublet at δ 5.73 ppm. Both Au(I) and Au(III) complexes catalysed the reaction, but the Au(I) catalyst, complex **15**, gave a higher yield of 63%, compared to 46% obtained with NaAu^{III}Cl$_4$. Literature methods by Hashmi and co-workers[28] have produced yields of 74% for the cross-dimerisation of an allenyl ketone with a Michael acceptor, with the aid of a Au(III) catalyst. The ^{1}H NMR data reported the characteristic vinylic protons appearing at δ 5.83 and 5.87 both as doublets.
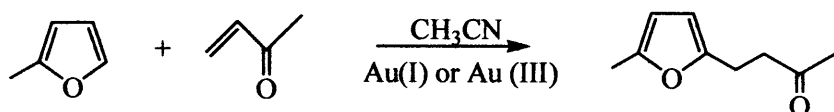
17

Scheme 29. Cross-dimerisation attempted

Reaction of 2,3-dihydrofuran and methylvinylketone with an acetonitrile solution of Au(III) was attempted but as expected for this cross-dimerisation the reaction did not proceed, as shown by TLC investigations (Scheme 30).
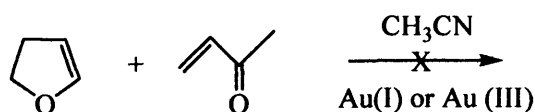
Scheme 30. Unsuccessful C-C bond formation

The addition of an alcohol to an alkyne has been previously reported using a mercury catalyst to promote the reaction.[29] The reaction yields an acetal and enol ether (Scheme 31) and the catalyst that successfully catalyses this reaction is of the type [L-Au$^+$] where L = a phosphane, phosphite or arsine. The reactions proceeds under mild conditions (T = 20 – 50 °C, H$^+$ acting as a co-catalyst), and TONs of up to 10^3 have been reported. Symmetrical alkynes yield only one product, whereas for unsymmetrical alkynes an acetal and enol ether is formed. For terminal alkynes the addition generally takes place at the more substituted carbon.
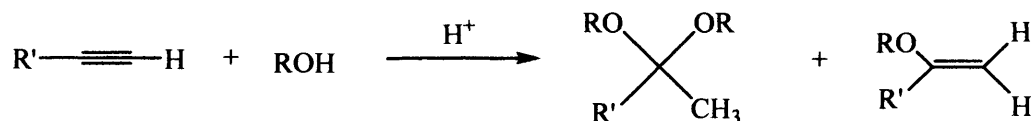
Scheme 31. Addition of alcohol to an unsubstituted alkyne

Teles and co-workers also reported the reaction of phenylactylene with an alcohol yielding an acetal and enol ether in a ratio of 2 : 1. In our attempt, reaction of phenylacetylene and methanol with NaAuCl$_4$ yielded the alkene **18** as shown in Scheme 32. The source of H$^+$ during the reaction was methanesulfonic acid and the mixture was stirred for 2 days. The alkene was isolated and purified by column chromatography with a yield of 41%. The ^{1}H NMR spectrum showed the vinylic protons as 2 doublets at 5.20 and 5.45 ppm.
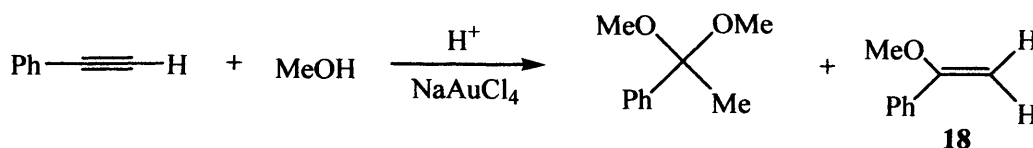
Scheme 32. Synthesis of alkene **18**

The reaction of **L^4** with NaAuCl$_4$ in CH$_2$Cl$_2$ was attempted to synthesise a possible tridentate monomer or dimer complex (Scheme 33). The oily white solid produced was

insoluble in a number of solvents including chloroform, toluene, THF, CH_2Cl_2, diethyl ether, hexane and ethanol. The spectroscopic data for **19** from both the $^{31}P\{^1H\}$ and ^1H NMR spectra were inconclusive.
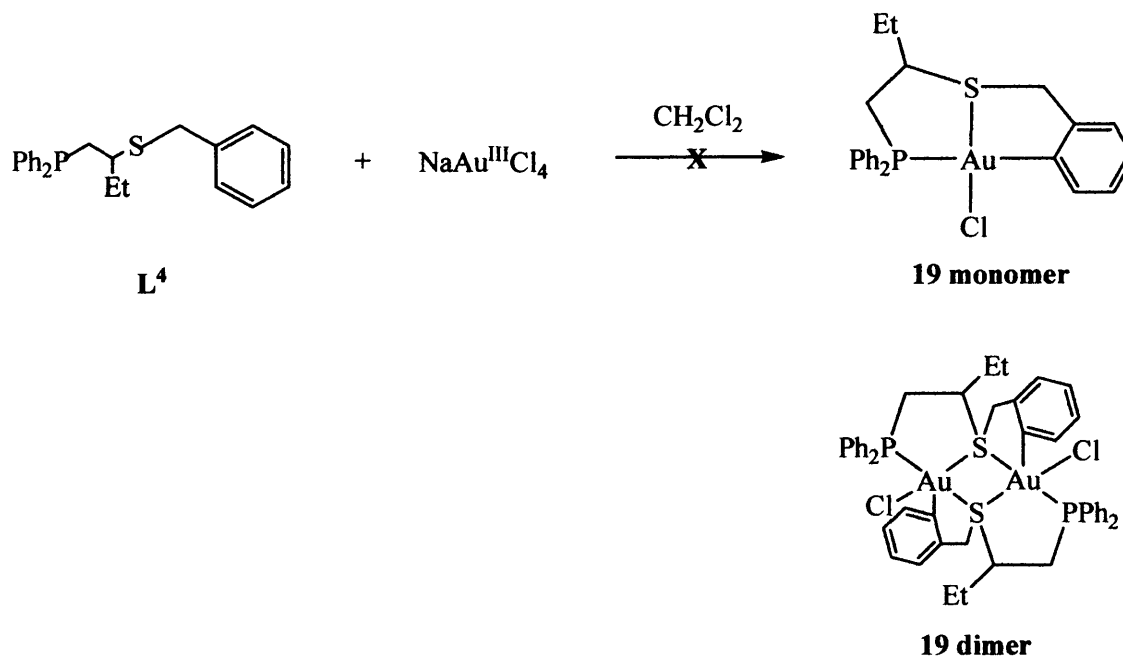
Scheme 33. Au tridentate complex **19** attempt

Hence, a new route was planned for the synthesis of a tridentate gold complex. The first step involved the synthesis of a mercury precursor **20**. The next step involved reaction of **20** with [$AuCl_3(tht)$] where tht = tetrahydrothiophene, and Me_4NCl, enabling the gold precursor complex to be made (Scheme 34).
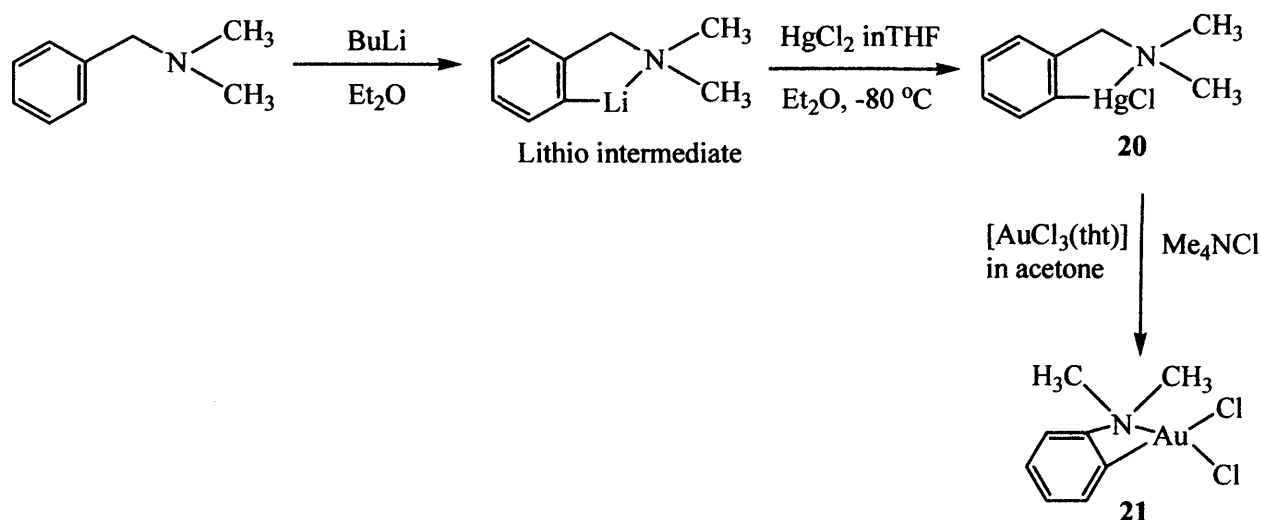
Scheme 34. Synthesis of gold complex **21**

The formation of the mercury complex **20** (Scheme 34) was attempted. The white solid obtained was sparingly soluble in hexane, chloroform, petroleum ether. The ^{1}H NMR spectrum (recorded in d^6-benzene in which the solid did not fully dissolve) revealed a doublet and triplet in the aromatic region which can be assigned to 4 protons on the aromatic ring - 2 in the 3,6 position (doublet signal) and 2 protons in the 4,5 position (triplet signal). The aliphatic protons were also noted in the spectrum. $Bu_4N[AuCl_4]$ has been reported as a useful precursor in gold chemistry, its synthesis is shown in Scheme 35.

$$[BuN]_4Cl \text{ in excess} \quad + \quad HAuCl_4 \text{ (aq)} \quad \longrightarrow \quad Bu_4N(AuCl_4)$$

22
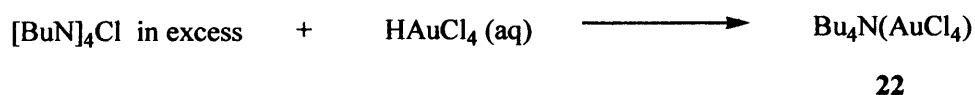
Scheme 35. Synthesis of $Bu_4N[AuCl_4]$ **22**

Reaction of $NaAuCl_4$ with $[BuN]_4Cl$ was attempted. However the product was noted to still have some reactant present after the reaction had been carried out.

2.2.7 Investigation of other Group 10 and 11 metal complexes

Work has been undertaken on the complexation of a selection of our ligands onto other Group 10 metals including nickel, platinum and copper. Mononuclear complexes with phosphinothiolate ligands have been synthesised for Group V to VIII transition metals and also tin, samarium and nickel. The nickel complexes were noted to be in a mixed-valence state i.e. a Ni (II)/Ni (III) complex. The structure of the nickel complexes was also noted to be unusual with a bridging arrangement around the metal centres.[33]
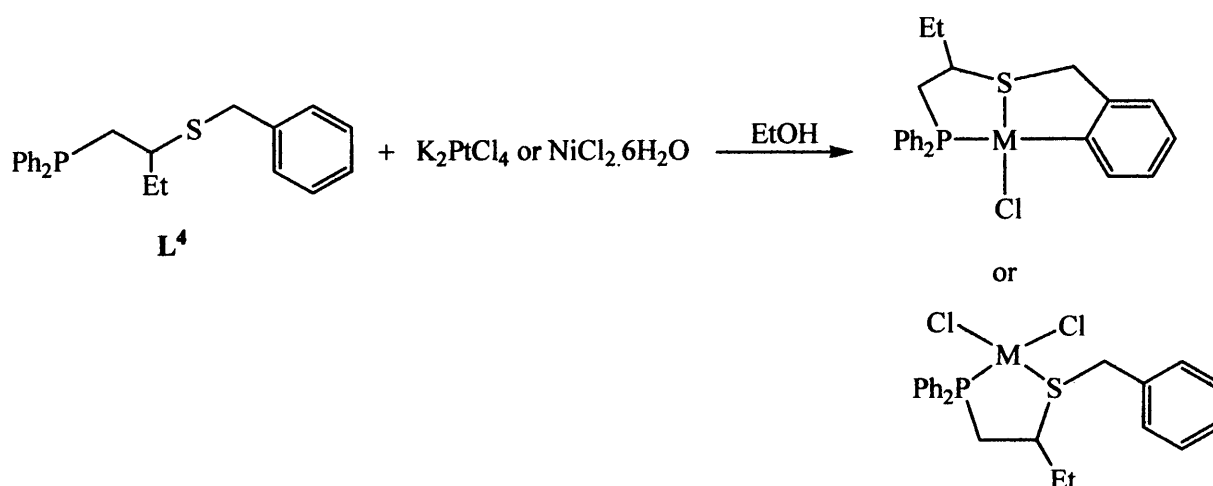
Scheme 36. Attempts at synthesising Pt and Ni complexes, where M = Pt **23** or Ni **24**

Reaction of platinum and nickel with ligand L^4 yielded complexes, the structure of which was anticipated to be bidentate or tridentate, as shown in Scheme 36. The platinum complex **23** revealed a single shift in its $^{31}P\{^1H\}$ NMR spectrum at 27.6 ppm, but recrystallisation attempts yielded no crystals. The nickel complex **24** was recrystallised, using an acetonitrile-petroleum ether diffusion, but the NMR spectra were noisy and inconclusive.
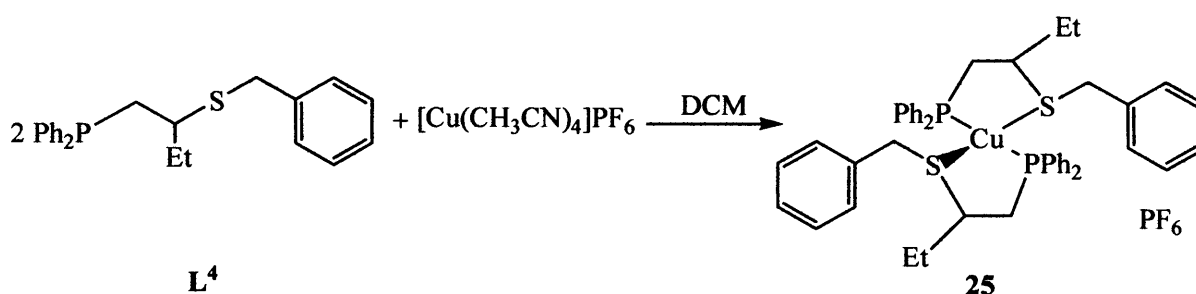
Scheme 37. Copper reaction attempted

Reaction of a copper precursor with 2 equivalents of ligand L^4 (Scheme 37) produced a pale yellow solution, which was recrystallised using a CH_2Cl_2-petroleum ether diffusion. The $^{31}P\{^1H\}$ NMR spectrum of the needle-like crystals did not show the presence of the expected copper complex.

2.3 Conclusions

New P,S ligands and their palladium complexes have been synthesised and for three new palladium complexes their crystal structures shown. High resolution mass spectra for a number of our ligands and complexes have shown further evidence in support of their chemical composition. High yields were obtained for the palladium complexes, in general between 80 and 90%.

Complexes **8** and **9** both revealed square planar geometries, as seen in their crystallographic characterisation. When compared to a complex of the same type, **7**, many key similarities were seen in their structures. The evidence supported the assumption that complexes **8** and **9** adopt a bidentate structure. The structure of complex **10**, the naphthalene complex, was also determined by X-ray diffraction methods, revealing a distorted square planar structure which was also bidentate. The synthesis of the anthracene complex **11** was undertaken and ^{1}H NMR analysis suggested a possible dimer structure.

The novel complexes are potentially useful catalysts in C-C coupling reactions, and future work will investigate their application in this area. Complexes **2, 3, 7** and **9** have been used in Heck and Suzuki couplings (Chapters 3 and 4) and have shown excellent catalytic activities.

Our gold work has successfully produced a gold complex and reactions involving gold catalysts have been investigated. The Au(I)-THT complex **15** was synthesised and characterised by ^{1}H NMR spectroscopy. **15** was subsequently used in the C-C coupling of 2-methylfuran with methylvinyl ketone. An Au(III) complex, $NaAuCl_4$, also successfully catalysed the reaction. The alkene **18** was synthesised by reaction of an alkyne with an alcohol, using $NaAuCl_4$ as the catalyst for the reaction.

A number of reactions proved unsuccessful during our gold investigations. This included synthesis of an Au(III)-P,S monomer **14** and Au(I)-P,S dimer **16**. The formations of possible tridentate complexes using ligand L^4 proved inconclusive.

Complexes of platinum, nickel and copper were also briefly investigated with ligand L^4. The results obtained for the platinum and nickel complexes were inconclusive and the copper investigation did not yield the desired bis-chelate type complex.

2.4 Experimental

General comments : All manipulations were performed using standard Schlenk techniques under nitrogen, except where otherwise noted. The palladium complexes were prepared under an inert atmosphere and once formed were stable in air. All other chemicals were purchased from Aldrich and Avocado and used as received, except where stated. Solvents for NMR measurements were distilled and dried under nitrogen following literature methods.[39] ^{1}H-NMR spectra and ^{13}C-NMR spectra were recorded using a Bruker Avance AMX 400 spectrometer and ^{31}P NMR spectra were recorded using a JEOL Eclipse 300 spectrometer, referenced to external TMS; δ values are reported in ppm; *J* values are reported in Hz. Mass spectra were obtained in ES (Electrospray) mode from EPRSC Mass Spectrometry Service (Swansea University), or from the Mass Spectrometry Service (Cardiff University). High-resolution mass spectra (ES) were recorded on a Waters Q-Tof micromass spectrometer, Cardiff University.

Synthesis of bis(benzonitrile)dichloropalladium, $Pd(PhCN)_2Cl_2$[40,41] : Palladium (II) chloride hydrate (2.937 g, 0.0166 mol) was added to a 250 ml round bottomed flask, equipped with a stirring bar. Benzonitrile (60 ml, 0.5877 mol) was added to the flask and attached to a reflux condenser. The dark red mixture was heated to 100 °C whilst stirring. After an hour, the majority of the solid had dissolved; leaving a reddish brown solution that was filtered hot (to prevent crystallisation). The clear orange filtrate was transferred to a round bottomed flask containing petroleum ether (350 ml). Immediately a bright yellow solid precipitated out and the solution was filtered under suction. The bright yellow powder was washed with petroleum ether (3 x 15 mL). A bright yellow powder resulted. Yield (5.845 g, 92 %).

2-butylenesulfide, C_4H_8S, 1 : Potassium thiocyanate (19.436 g, 0.2 mol) was dissolved in water (50 mL) in a round bottomed flask. An ice bath was placed under the round bottomed flask and 1, 2-epoxybutane (17.2 mL, 0.2 mol) was added to the reaction mixture, leaving a colourless solution which was allowed to stir for 1 day. After 1 day, more potassium thiocyanate (9.718 g, 0.1 mol) was added to the cloudy reaction

mixture. The mixture was left to stir for another day. The crude thiirane was obtained after extraction with diethyl ether (3 x 20 mL). The ethereal fractions were combined and extracted with aqueous saturated sodium chloride solution (50 mL), and dried over magnesium sulfate. The product was obtained after distillation under atmospheric pressure (distilled at 103/4 °C). Yield (9.477 g, 54%); ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 1.05 (3H, t, J = 7.4, CH$_3$), 1.42 (1H, sept, J = 7.2, CH$_2$), 1.9 (1H, sept, J = 7.2, CH$_2$), 2.13 (1H, d, J = 5.5, CH$_2$), 2.45 (1H, d, J = 6.6, CH$_2$), 2.9 (1H, pent, J = 4.2, CH). ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 13.76 (1C, s, CH$_3$), 26.11 (1C, s, CH$_2$), 30.08 (1C, s, CH$_2$), 38.11 (1C, s, CH).

L^1 (where L^1 = Ph$_2$PCH$_2$CHEtS) : Method 1, L^{1}H^2 : Diphenylphosphine (2.5 mL 14.4 mmol) was syringed into a Schlenk, along with dry diethyl ether (20 mL). The Schlenk was placed in an ice bath (-40 °C) and n-BuLi (7.4mL of 1.96M, 14.4 mmol) was syringed into the colourless reaction mixture, causing it to turn bright yellow. The solution was left to stir for 2 hours. In a separate Schlenk CH$_2$CHC$_2$H$_5$S 1 (1.3 mL, 14.4 mmol) was diluted in dry diethyl ether (10 mL) and transferred drop wise into the reaction Schlenk. An immediate colour change was seen from yellow to colourless. The solution was left to stir overnight. After stirring overnight, a water work-up was performed whereby degassed water (10 mL) was added and the diethyl ether layer collected. The aqueous layer was washed with dry diethyl ether (2 x 10mL) and the etheral extracts were combined and dried over MgSO$_4$. The ethereal extracts were filtered over celite and the solvents were removed *in vacuo* affording a pale yellow oil. The ligand was used without further purification. Yield (2.875 g, 90%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.85 (3H, t, $^3J_{HH}$ = 7.3, CH$_3$), 1.55 (1H, m, $^2J_{HH}$ = 6.9, p to Et), 1.8 (2H, m, J = 6.9, CH$_2$ o to Et), 2.3 (2H, dd, J_{HH} = 6.3, J_{HP} = 13.8, CH$_2$ o to SH), 2.75 (1H, m, SH), 7.1-7.5 (10H, m, ArH); ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 10.27 (1C, s, C^1), 31.42 (1C, d, $^3J_{CP}$ = 8.2, C^2), 38.11 (1C, d, $^1J_{CP}$ = 13.3, C^4), 38.91 (1C, d, $^2J_{CP}$ = 16.6, C^3), 127.47 (2C, d, $^3J_{CP}$ = 4.8, C^7), 127.53 (2C, d, $^3J_{CP}$ = 4.9, C^{11}), 127.60 (1C, s), 127.85 (1C, s), 131.57 (2C, d, $^2J_{CP}$ = 18.6, C^6), 131.94 (2C, d, $^2J_{CP}$ = 12.8, C^5); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : -18.01. MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 275.1023, measured : 275.1014.

Method 2, L^{1}K : Potassium diphenylphosphide (10 mL of 0.5 M in THF, 5 mmol) was syringed into a Schlenk, along with dry diethyl ether (10 mL) and dry THF (5 mL). The Schlenk was placed in a cold water bath and $CH_2CHC_2H_5S$ **1** (0.44 g, 5 mmol) was added dropwise to the orange reaction mixture, causing it to turn paler orange. The solution was left to stir for a couple of hours. After this time, a water work-up was performed whereby degassed water (10 mL) was added and the diethyl ether layer collected. The aqueous layer was washed with diethyl ether (2 x 10mL) and the etheral extracts were combined and dried over $MgSO_4$. The ethereal extracts were filtered over celite and the solvents were removed *in vacuo* affording a pale yellow oil. The ligand was used without further purification. ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.7 (3H, m, J = 7.3, CH$_3$), 0.95 (1H, m), 1.45 (2H, m), 2.1 (1H, m), 2.4 (1H, m), 7.1-7.7 (10H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : -17.71.

NB : Ph$_2$PCH$_2$CHEtSLi **L^{1}Li** or Ph$_2$PCH$_2$CHEtSK **L^{1}K** could be synthesised in the same manner as above, with the exception of not performing the water work-up at the end.

L^2 (where L^2 = Ph$_2$PCH$_2$CH(^{t}Bu)SCH$_3$) : A Schlenk was charged with **L^{1}Li** (0.633 g, 2.05 mmol) and dissolved in dry THF (10 mL). Methyl iodide (0.2 cm^3, 2.92 mmol) was then added dropwise. The solution was stirred for 1½ hours, after which the solvent was removed *in vacuo*. The colourless product was extracted with dry hexane (20 mL) followed by dry toluene (15 mL), and filtered. Solvents were removed *in vacuo*, from the filtrate, leaving a cloudy yellow solution. The ligand was used without further purification. Yield (0.54 g, 83%). ^{1}H NMR (d-benzene, 300 MHz), δ_H : 0.85 (9H, d, t-Bu), 1.95 (3H, m, CH$_3$), 2.1 (1H, t of d, CH$_2$), 2.2 (1H, t of d, CH$_2$), 2.55 (1H, ddd, CH p to t-Bu), 7.0-8.0 (10H, m, ArH); ^{31}P NMR (d-benzene, 121 MHz), δ_P : -16.51.

L^3 (where L^3 = Ph$_2$PCH$_2$CHEtSMe)^2 : **L^{1}H** (1.38 g, 5.03 mmol) was dissolved in dry diethyl ether (40 mL) and subsequently BuLi (2.6 mL, 5.03 mmol) was syringed into the Schlenk. After 30 minutes MeI (0.7139 g, 5.03 mmol) was introduced into the Schlenk and the yellow reaction mixture was left to stir overnight. A water work-up was performed whereby degassed water (30 mL) was added to the reaction mixture and the organic layer was collected. The aqueous layer was washed with dry diethyl ether (2 x

10 mL) and the organic extracts combined and dried over $MgSO_4$. The organic layers were filtered over celite and the solvents were removed *in vacuo*, leaving a thick pale oil. The ligand was used without further purification. Yield (1.0 g, 70%). ^1H NMR (CDCl$_3$, 300 MHz), δ_H : 1.03 (3H, t, $^3J_{HH}$ = 7.3, H^1), 1.72 (1H, m, $^3J_{HH}$ = 7.3, H^2), 1.89 (1H, m, $^3J_{HH}$ = 7.3, H^2), 2.00 (3H, s, SMe), 2.30-2.65 (3H, overlapping m, H^3 and H^4), 7.34 (6H, m, ArH), 7.50 (4H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : -20.35.

L^4 (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph) : **L^{1}Li** (5 mmol), benzyl bromide (0.996 g, 5 mmol), and dry diethyl ether (20 mL) were charged into a schlenk. The resulting cloudy solution was stirred overnight. The white solid (LiBr) was filtered away from the solution and rinsed with dry diethyl ether (2 x 10 mL). The yellow filtrate was concentrated down, leaving a yellow oil. The ligand was used without further purification. Yield (1.56 g, 73%). ^1H NMR (CDCl$_3$, 300 MHz), δ_H : 0.8 (3H, t, J = 7.3, CH$_3$), 1.55 (1H, m), 1.75 (1H, m), 2.3 (3H, m), 3.53 (1H, d, J = 10.0, benzylic H), 3.58 (1H, d, J = 10.8, benzylic H), 6.9-7.35 (15H, m); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : -20.8. ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 9.60 (1C, s, CH$_3$), 26.87 (s, 1C, CH$_2$), 34.48 (1C, s, CH), 42.72 (1C, d, J = 15.1, CH$_2$). MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 365.1493, measured : 365.1499.

L^5 (where L^5 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_8$H$_9$) : **L^{1}Li** (5.0 mmol), 3,5-dimethylbenzylbromide (0.996 g, 5.0 mmol) and dry diethyl ether (20 mL) were charged into a schlenk. The resulting cloudy solution was left to stir overnight. The solution was filtered through celite. A water work-up was performed whereby the solution was extracted with dry diethyl ether (2 x 10 ml) and dried over $MgSO_4$. The solvents were removed *in vacuo*, affording a colourless liquid. The ligand L^5 was used without further purification. Yield (1.41 g, 72%). ^1H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, t, J = 7.3, CH$_3$), 1.5 (1H, m, H), 1.7 (1H, m, H), 2.1 (6H, s, 2 x CH$_3$), 2.3 (1H, m, CH), 2.5 (1H, m, CH$_2$), 3.47 (1H, d, J = 7.0, benzylic H), 3.52 (1H, d, J = 7.0, benzylic H), 7.2 - 7.7 (13H, m, ArH). ^{31}P NMR (D$_2$O, 121 MHz), δ_P : -20.8. MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 393.1806, measured : 393.1793.

L^6 (where L^6 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_{10}$H$_7$) : **L^{1}K** (2.5 mmol in diethyl ether solution), 1-chloromethylnaphthalene (0.375 ml, 2.5 mmol) and dry diethyl ether (10 mL) were charged into a schlenk. The mixture was stirred, upon which a gradual colour change was seen from bright yellow to white. The mixture was left stirring overnight. The off-white solid (LiCl formed) was filtered away from the pale almost colourless solution. The solution was condensed down and made into a solution of known concentration. The ligand was used without further purification. Yield (0.65g, 65%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, m, CH$_3$), 1.65 (1H, m, CH$_2$), 1.8 (1H, m, CH$_2$), 2.3 (1H, m, CH$_2$), 2.45 (1H, m, CH$_2$), 2.55 (1H, m, CH), 4.0 (2H, dd, benz), 7.15-7.6 (19H, m, ArH); ^{31}P NMR (D$_2$O, 121 MHz), δ_P : -20.53. ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 9.69 (1C, s, CH$_3$), 27.04 (s, 1C, CH$_2$), 34.19 (1C, d, J = 10.1, CH), 43.75 (1C, d, J = 15.1, CH$_2$ benzylic). MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 415.1649, measured : 415.1647.

L^7 (where L^7 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_{14}$H$_9$) : 9-chloromethylanthracene (0.567 g, 2.5 mmol) was dissolved in a mixture of dry diethyl ether (10 ml) and dry THF (10 mL). **L^{1}K** (2.5 mmol in dry diethyl ether solution) was added to the solution and the resulting orange solution was left to stir overnight. The clear yellow solution was condensed down until almost all of the solvent had been removed, then redissolved in dichloromethane (15mL). The ligand was used without further purification. Yield (0.8 g, 69%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.95 (3H, t, J = 7.3, CH$_3$), 1.75 (1H, m, CH$_2$), 1.95 (1H, m, CH$_2$), 2.4 (2H, m, CH$_2$), 2.75 (1H, m, CH), 4.55 (2H, 2 x d, J = 11.8, J = 6.1, benz), 7.3-8.4 (21H, m, ArH); ^{31}P NMR (D$_2$O, 121 MHz), δ_P : -20.01. ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 10.14 (1C, s, CH$_3$), 27.22 (s, 1C, CH$_2$), 34.49 (1C, d, J = 14.1, CH), 45.53 (1C, d, J = 16.1, CH$_2$ benzylic).

[Pd(L^1)Cl]$_2$ (where L^1 = Ph$_2$PCH$_2$CHEtS), 2^2 : To a solution of Pd(PhCN)$_2$Cl$_2$ (0.192 g, 0.5 mmol) in dry dichloromethane (20 mL) **L^1** (0.138 g, 0.5 mmol) was added. The resulting bright orange solution was stirred overnight. Solvents were removed *in vacuo* leaving a bright orange solid. The orange solid was washed with diethyl ether (2 x 20 mL) and dried. The pure compound was obtained after slow diffusion of diethyl ether into an acetonitrile solution of 2. Yield (0.187 g, 90%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 1.05 (3H, t, $^3J_{HH}$ = 7.3, H^1), 1.84 (1H, m, $^2J_{HH}$ ≅ $^3J_{HH}$ = 13.8, $^2J_{HP}$ = 6.6, H$^4_{ax}$), 2.10

(1H, m, $^2J_{HH} \approx {}^3J_{HH}$ = 7.3, H^2), 2.62 (1H, td, $^2J_{HH} \approx {}^3J_{HH}$ = 13.8, $^2J_{HP}$ = 6.6, H^4 $_{ax}$), 2.91 (1H, ddd, $^2J_{HH}$ = 13.8, $^2J_{HP}$ = 11.4, $^3J_{HH}$ = 3.8, H$^4_{eq}$), 3.71 (1H, br m, H^3), 7.20-7.75 (6H, m, ArH), 7.93 (4H, m, ArH); ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C :12.76 (1C, s, C^1), 30.35 (1C, m, C^2), 43.65 (1C, m), 46.29 (1C, s), 129.41 (4C, m, C^{11}, C^7), 130.0 (1C, m), 130.5 (1C, m), 131.90 (1C, s), 132.00 (1C, s), 133.63 (2C, t, J$_{CP}$ = 5.1, C^6), 133.80 (2C, t, J$_{CP}$ = 5.7, C^{10}); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 41.39.

[Pd(L^1)I]$_2$ (where L^1 = Ph$_2$PCH$_2$CHEtS), 3 : 2 (0.49 g, 0.48 mmol) was dissolved in ethanol (20mL). In a separate round bottomed flask potassium iodide (0.8 g, 4.8 mmol) was dissolved in the minimum amount of methanol (5mL). The potassium iodide solution was added to the solution of 3 and left to stir for 48 hours. An orange precipitate was seen. Solvents were evaporated leaving an orange solid, which was washed with dichloromethane (10 mL) and filtered. The orange filtrate was concentrated leaving orange oil, which when dissolved in dichloromethane (10 mL) and dried *in vacuo*, leaving a red solid. The red solid was washed twice with diethyl ether (2 x 20 mL) and dried, resulting in a red crystalline solid. Yield (0.42 g, 82%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, t, J = 7.4, CH$_3$), 1.65 (1H, m), 1.95 (1H, m), 2.65 (1H,td), 2.95 (1H, m), 3.85 (1H, br m), 7.25-7.9 (10H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 41.19. ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 11.48 (1C, s, C^1), 28.58 (1C, m, C^2), 46.15 (1C, m), 46.39 (1C, s), 127.84 (1C, m), 127.97 (1C, m), 130.51 (1C, s), 132.63 (1C, m); ES-MS : m/z 1014.79 (MH$^+$, 100%). MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 1012.7971, measured : 1012.8002.

[Pd(μ-L^8)Cl]$_2$ (where L^8 = Ph$_2$PCH$_2$CH(^{t}Bu)S), 4 : To a solution of Pd(PhCN)$_2$Cl$_2$ (0.791 g, 2 mmol) in dry THF (10 mL) racemic Ph$_2$PCH$_2$CH(^{t}Bu)SLi (0.635 g, 2 mmol) was added. The resulting dark orange solution was left to stir overnight. The volatiles were evaporated *in vacuo*. The dark orange solid obtained was washed with diethyl ether (2 x 20 mL) and dried. A muddy orange compound resulted. The pure compound was obtained after slow diffusion of diethyl ether into an acetonitrile solution of 4. Yield (0.887 g, 49%). ^{1}H NMR (CDCl$_3$, 300 MHz), δ_H : 1.2 (9H, s, t-Bu), 2.87, (2H, m, CH$_2$), 3.81 (1H, m, CH), 7.24-7.9 (10H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 39.18; ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 28.38 (3C, s, t-Bu), 35.45 (1C, s), 42.89 (1C, s). MS (accurate mass, ES+) calculated mass for [M$_2$+Cl]$^+$: 849.0118, measured : 849.0114.

Pd(L^1)$_2$ (where L^1 = Ph$_2$PCH$_2$CHEtS), 5 : Pd(PhCN)$_2$Cl$_2$ (0.778 g, 2.034 mmol) and dry dichloromethane (10 mL) were charged into a schlenk. To the solution L^{1}Li (4 mL in dry toluene, 4.068 mmol) was added. The resulting orange solution was stirred overnight; subsequently the solvents were removed *in vacuo*. The yellow solid was washed with diethyl ether (20 mL) and dried. The pure compound was obtained after slow diffusion, in air, of petroleum ether into a dichloromethane solution of **5**. Yield (1.20 g, 90%). *trans-rac*-isomer: ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H : 0.89 (3H, t, $^3J_{HH}$ 7.4, H^1), 1.64 (1H, m, $^3J_{HH}$ = 7.4, H^2), 1.72 (1H, m, $^3J_{HH}$ = 7.4, H^2), 2.32 (1H, td, $^3J_{HH} \approx {}^3J_{HP}$ = 12.4, $^3J_{HH}$ = 3.0, H^4), 2.73 (1H, br m, H^3), 2.89 (1H, m, H^4), 7.35 (6H, m, ArH), 7.56 (2H, m, ArH), 7.87 (2H, m, ArH); ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 14.61 (1C, s), 32.70 (1C, t, J_{CP} = 10.3), 43.28 (1C, t, J_{CP} = 9.8), 43.68 (1C, t, J_{CP} = 17.5), 128.90 (2C, t, J_{CP} = 4.9), 129.06 (2C, t, J_{CP} = 5.1), 130.78 (1C, s), 131.23 (1C, s), 132.73 (2C, t, J_{CP} = 6.2), 134.64 (2C, t, J_{CP} =7.1); ^{31}P NMR (CDCl$_3$, 121 MHz) δ_P : 48.6; *trans-meso*-isomer : ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H : 2.46 (1H, m, H^4), 7.64 (2H, m, ArH), 7.81 (2H, m, ArH); all other ^{1}H resonances coincide with those of the *trans-rac*-isomer; ^{31}P NMR (CDCl$_3$, 121 MHz) δ_P : 51.1, *cis-rac*-isomer : ^{1}H NMR (CDCl$_3$, 400 MHz) δ_H : 2.46 (1H, m, H^4), 6.84 (2H, m, ArH), 6.96 (2H, m ArH), 7.11 (1H, m, ArH), 7.19 (2H, m, ArH), 7.46 (2H, m, ArH); all other resonances coincide with those of the *trans-rac*-isomer; ^{31}P NMR (CDCl$_3$, 121 MHz) δ_P : 44.5. MS (accurate mass, ES+) calculated mass for [M+H]$^+$: 653.0847, measured : 653.0879.

Pd(L^2)Cl$_2$ (where L^2 = Ph$_2$PCH$_2$CH(^{t}Bu)SCH$_3$), 6 : To a solution of Pd(PhCN)$_2$Cl$_2$ (0.19 g, 0.5 mmol) in dry dichloromethane (5 mL) was added a solution of L^2 (1 mL, 0.5 mmol) toluene. The resulting dark brown mixture was stirred for 2 hours. To complete precipitation of the yellow-brown solid petroleum ether (20 mL) was added. The solid was filtered and dried *in vacuo*. The resulting yellow/orange solid complex was light sensitive. Recrystallisation of the product was attempted, in air, by slow recrystallisations of petroleum ether into a dichloromethane solution of **6**. Yield (46%). ^{1}H NMR (CDCl$_3$, 300 MHz), δ_H : 1.15 (9H, s, t-Bu), 1.25 (3H, m, CH$_3$), 1.5 (2H, m, CH$_2$), 1.7 (1H, m, CH), 7.2-7.7 (12H, m, ArH) ; ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 46.03.

Pd(L^3) Cl$_2$ (where L^3 = Ph$_2$PCH$_2$CHEtSMe), 7^2 : To a solution of Pd(PhCN)$_2$Cl$_2$ (1.0 g, 2.6 mmol) in dichloromethane (40 mL) L^3 (5.8mL, 2.6 mmol) was added. The resulting dark orange solution was stirred overnight. Solvents were removed *in vacuo* leaving an orange solid. The crude solid was dissolved in hot acetonitrile. The pure compound was obtained after slow recrystallisation of diethyl ether into an acetonitrile solution of **7**, affording yellow crystals. Yield (1.07g, 88%). ^{1}H NMR (CD$_3$CN, 400 MHz), δ_H : 0.94 (3H, br, H^1), 1.70 (1H, br, H^2), 2.59 (1H, br, H^4), 2.68 (3H, br s, SMe), 2.84 (1H, br, H^3), 2.96 (1H, br, H^4), 7.3-7.7 (8H, m, ArH), 8.02 (2H, m, ArH); ^{31}P NMR (D$_2$O, 121 MHz), δ_P : 50.02. ES-MS : m/z 467 (MH$^+$, 100%).

Pd(L^4)Cl$_2$ (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph), 8 : To a solution of L^4 (0.8 mmol) in dry dichloromethane (10 mL) was added Pd(PhCN)$_2$Cl$_2$ (0.306 g, 0.8 mmol). The resulting orange solution was left stirring overnight. The solvents were evaporated, leaving an orange oil, which was washed with diethyl ether (2 x 10 mL) and dried. The crude product was a yellow solid. The pure compound was obtained after slow recrystallisation of petroleum ether into a chloroform solution of **8**. Yield (0.36 g, 83%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, t, J = 7.3, CH$_3$), 1.7 (1H, m, CH$_2$), 1.85 (1H, m, CH$_2$), 2.35 (1H, m, CH$_3$), 2.6 (2H, m, CH$_3$), 3.95 (1H, d, J = 14.1, benzylic H), 4.95 (1H, d, J = 13.6, benzylic H), 7.1-7.7 (10H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 50.35. ES-MS : m/z 505.0132 (M-Cl$^+$, 100%).

Pd(L^5)Cl$_2$ (where L^5 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_8$H$_9$) 9 : Pd(PhCN)$_2$Cl$_2$ (1.148 g, 3.0 mmol) and dry dichloromethane (10 mL) were charged into a schlenk. To the solution L^5 (3.0 mmol) was added. The resulting orange solution was stirred overnight; subsequently the solvents were removed *in vacuo*. The yellow solid was washed with diethyl ether (20 mL) and dried. The pure compound was obtained after slow diffusion, in air, of petroleum ether into a dichloromethane solution of **9**. Yield (1.50 g, 88%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, t, J = 7.3, CH$_3$), 1.6 (1H, m, H), 1.7 (1H, m, H), 2.1 (6H, s, CH$_3$), 2.3 (1H, m, CH), 2.6 (1H, t, CH$_2$), 3.8 (1H, d, J = 13.5, benzylic H), 4.7 (1H, d, J = 13.5, benzylic H), 7.3-7.65 (15H, m, ArH); ^{13}C NMR (CDCl$_3$, 100 MHz), δ_C : 12.31 (1C, s, CH$_3$), 21.30 (2C, s, CH$_3$), 26.05 (1C, d, CH$_2$), 37.10 (1C, d, CH), 41.28 (2C, s, benzylic CH$_2$); ^{31}P NMR (CDCl$_3$, 121 MHz) δ_P : 52.40. MS (ES$^+$) m/z (%), [M-H]$^+$: 533.0445. ES-MS : m/z 533.0445 (M-Cl$^-$, 100%);

Pd(L^6)Cl$_2$ (where L^6 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_{10}$H$_7$), 10 : To a solution of Pd(PhCN)$_2$Cl$_2$ (0.319g, 0.833 mmol) in dry dichloromethane (20 mL) was added L^6 (0.833 mmol). The orange solution was allowed to stir overnight. The dichloromethane solution was condensed (ca. 10 mL) and the solid product was precipitated with diethyl ether. The orange solid was washed twice with diethyl ether (2 x 20 mL) and dried. Yield (0.34 g, 69%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.55 (3H, t, J = 7.3, CH$_3$), 1.25 (2H, m, CH$_2$), 2.3 (1H, m, CH), 2.6 (2H, m, CH$_2$), 4.75 (1H, d, J = 13.5, benzylic), 5.15 (1H, d, J = 14.0, benzylic), 7.15-8.4 (19H, m, ArH); ^{31}P NMR (D$_2$O, 121 MHz), δ_P : 54.18.

Pd(L^7)Cl$_2$ (where L^7 = Ph$_2$PCH$_2$CHEtSCH$_2$C$_{14}$H$_9$), 11 : To a solution of Pd(PhCN)$_2$Cl$_2$ (0.319g, 0.833 mmol) in dry dichloromethane (20 mL) was added L^7 (0.833 mmol). The orange solution was allowed to stir overnight. The dichloromethane solution was condensed down slightly (ca. 10 mL) and the solid product was precipitated with diethyl ether. The orange solid was washed twice with diethyl ether (2 x 20 mL) and dried. Yield (0.406 g, 76%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.95 (3H, t, CH$_3$), 1.75 (2H, m, CH$_2$), 2.05 (1H, m, CH), 2.6 (1H, m, CH$_2$), 3.85 (1H, m, CH$_2$), 4.65 (1H, d, benzylic H), 7.15-8.0 (19H, m, ArH); ^{31}P NMR (D$_2$O, 121 MHz), δ_P : 52.50.

Pd(PPh$_2$CH$_2$CHEtSPh)I$_2$, 12 : To a Schlenk was added **3** (50 mg, 0.05 mmol), iodobenzene (0.02 g, 0.1 mmol) and toluene (10 mL). The orange/red solution was stirred overnight. The solvents were evaporated *in vacuo* and the resulting orange solid was washed with petroleum ether. ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 42.8.

Pd(PPh$_2$CH$_2$CHEtSC$_6$H$_4$COMe)I$_2$, 13 : To a Schlenk was added **3** (50 mg, 0.05 mmol), 4-iodoacetophenone (0.02 g, 0.1 mmol) and toluene (10 mL). The orange/red solution was stirred and heated at 80 °C overnight. The solvents were evaporated *in vacuo* and the resulting orange solid was washed with petroleum ether. ^{31}P NMR (CDCl$_3$, 121 MHz), δ_P : 42.7.

AuL^{1}Cl$_2$ (where L^1 = Ph$_2$PCH$_2$CHEtS), 14 : To a solution of NaAuCl$_4$ (0.181 g, 0.5 mmol) in dry ethanol (10 mL) was added L^{1}H (0.5 mmol). Immediately a precipitate

formed. The yellow mixture was stirred overnight. The supernatant yellow solution was decanted and dried *in vacuo*. A pale orange solid was obtained. Yield (0.124 g, 46%).

AuSC₄H₈Cl, 15[34] : A 100 mL round bottomed flask equipped with a stirring bar was charged with an aqueous solution of sodium tetrachloroaurate (III) (1.0 g, 2.24 mmol) in a mixture of distilled water (2 mL) and ethanol (10 mL). Tetrahydrothiophene (0.46 mL, 5.14 mmol) was added dropwise, causing the clear yellow solution to give rise to a brick red precipitate initially, then transforming into a white solid of $AuCl(SC_4H_8)$ whilst addition continued. The reaction mixture was stirred for 15 minutes at room temperature. The white precipitate of **15** was filtered, washed with ethanol (2 x 5 mL) and vacuum dried. Yield (0.74 g, 84%). ^1H NMR (CDCl₃, 400 MHz), δ_H : 2.15 (4H, br d, C_2H_4), 3.4 (4H, br d, C_2H_4).

AuL¹ polymer (where L¹ = Ph₂PCH₂CHEtS), 16 : To a solution of **15** (0.160 g, 0.5 mmol) in dry dichloromethane (10 mL) was added **L¹H** (0.5 mmol). The resulting yellow solution was stirred for 2 hours. The solvents were evaporated *in vacuo*. A white solid was precipitated with dichloromethane. Yield (0.241g).

C₉H₁₂O₂, 17[28] : (i) To a solution of sodium tetrachloroaurate (III) hydrate (0.011 g, 0.03 mmol) in acetonitrile (1 mL) was added 2-methylfuran (0.246 g, 3 mmol) and methylvinylketone (0.210 g, 3 mmol) in acetonitrile (3 mL). The resulting pale yellow solution was stirred for 2 days. Solvents were evaporated from the dark red/purple mixture leaving a dark red/brown oil. A column on silica was performed using a 9:1 petroleum ether:ethyl acetate solvent system. The collected product was concentrated leaving a yellow oil of **17**. Yield (0.207 g, 46%). ^1H NMR (CDCl₃, 400 MHz), δ_H : 2.05 (3H, s, CH₃), 2.15 (3H, s, OCH₃), 2.65 (2H, t, CH₂), 2.75 (2H, t, CH₂ o to OCH₃), 5.73 (2H, dd, vinylic).

(ii) To a solution of **15** (0.010 g, 0.03 mmol) in acetonitrile (1 mL) was added 2-methylfuran (0.246 g, 3 mmol) and methylvinylketone (0.210 g, 3 mmol) in acetonitrile (3 mL). A colourless solution resulted which was stirred overnight. Solvents were evaporated from the dark purple mixture leaving a dark red oil. A column on silica was performed using a 8:2 petroleum ether:ethyl acetate solvent system. The collected

product was concentrated leaving a yellow oil of **17**. Yield (0.286 g, 63%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 2.05 (3H, s, CH$_3$), 2.15 (3H, s, OCH$_3$), 2.65 (2H, t, CH$_2$), 2.75 (2H, t, CH$_2$ o to OCH$_3$), 5.73 (2H, dd, vinylic).

C$_6$H$_5$CH$_3$OC$_2$H$_2$, 18^{29} : Sodium tetrachloroaurate (III) hydrate (0.09 g, 0.25 mmol) was charged into a schlenk and dissolved in dry methanol (30 mL). **L^1** (0.25 mL, 0.25 mmol) was added and the resulting cloudy yellow solution was stirred. Into another schlenk was added phenylacetylene (2.74 mL, 25 mmol), dry methanol (20 mL) and methanesulfonic acid (0.16 mL, 2.5 mmol). The resulting dark green solution was decanted into the first schlenk, and the green solution was stirred. After two days the reaction mixture was neutralised with sodium hydroxide solution. The solvents were removed and a pale green solution remained which was washed with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The resulting clear yellow solution was dried over magnesium sulphate, filtered and solvents evaporated, leaving an orange solution of **18**. A column on silica was performed using a 9:1 petroleum ether:ethyl acetate solvent system and **18** isolated. Yield (1.380 g, 35%). ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 3.0 (3H, s, CH$_3$), 5.2 (1H, d, *J* = 3.0, cis to Ph), 5.45 (1H, d, *J* = 3.1, cis to MeO), 7.35-7.7.5 (6H, m, ArH).

AuL^{4}Cl or [AuL^{4}Cl]$_2$ (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph), 19 : To a Schlenk was added NaAuCl$_4$ (0.087 g, 0.24 mmol) dissolved in a mixture of ethanol (5 mL) and dichloromethane (5 mL). In a separate Schlenk was added **L^4** (0.121 g, 0.33 mmol) in dichloromethane (5 mL). The mixture from the second Schlenk was transferred to the first Schlenk resulting in a brown mixture. This Schlenk was covered in foil and stirred for 2 days. A white solid formed was insoluble in chloroform, toluene, THF, dichloromethane, diethyl ether, hexane and ethanol.

C$_6$H$_4$CH$_2$N(CH$_3$)$_2$HgCl, 20^{30,32} : To a Schlenk was added benzyldimethylamine (0.75 mL, 5 mmol) and Et$_2$O (5 mL). The Schlenk was placed in ice and n-BuLi (2.92 mL of 1.71M sol, 5 mmol) was added dropwise to the colourless reaction mixture. The yellow solution was stirred. In a separate Schlenk HgCl$_2$ (0.679 g, 5 mmol) was added to THF (15 mL). The first Schlenk was placed in a cold ice bath (at -60 °C) and to it was decanted the HgCl$_2$ solution. The resulting solution was stirred for 2 hours.

The mixture was filtered using a filter stick and celite, leaving a pale yellow solution. The filtrate was concentrated *in vacuo* resulting in a white solid. ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 2.2 (6H, s, 2 x CH$_3$), 3.35 (2H, s, benzylic CH$_2$), 7.3 (2H, t, J = 5.7, 2 x CH), 7.45 (2H, d, 2 x CH).

Bu$_4$N(AuCl$_4$), 22^{33} : Tetrabutylammonium chloride (1.390 g, 5 mmol) was dissolved in water (10 mL). To a separate flask sodium tetrachloroaurate (III) hydrate (0.362 g, 1 mmol) was added and dissolved in water (10 mL). Both solutions were stirred for ½ hour. The colourless tetrabutylammonium chloride solution was added to the orange sodium tetrachloroaurate (III) hydrate solution, causing a slight precipitation to form, and stirred for 1 ½ hours. The organic layer was extracted with DCM (3 x 10 mL), dissolving any remaining precipitate. The organic extractions were combined and dried over magnesium sulphate, filtered and solvents evaporated. The crude product was a bright orange solid. The pure compound was obtained after slow recrystallisation of petroleum ether into a DCM solution of **22**. ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.95 (12H, t, J = 7.3, Bu), 1.45 (8H, sext, J = 7.4, Bu), 1.6 (8H, m, Bu), 3.15 (8H, m, Bu).

PtL^{4}Cl$_2$ or Pt(Ph$_2$PCH$_2$CHEtSCH$_2$C$_6$H$_4$)Cl (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph), 23 : To a Schlenk was added PtCl$_2$ (0.213 g, 0.8 mmol) and acetonitrile (15 mL). The mixture was stirred for 1 ½ hours, after which time the brown solid had not dissolved. The Schlenk was heated at 70 °C and after 2 hours the solid had dissolved. L^4 (0.8 mmol) was added to the Schlenk and the resulting orange solution was stirred overnight. ^{31}P{^{1}H} NMR (121 MHz) , δ_P : 27.6.

NiL^{4}Cl$_2$ or Ni(Ph$_2$PCH$_2$CHEtSCH$_2$C$_6$H$_4$)Cl (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph), 24 : To a Schlenk was added NiCl$_2$.6H$_2$O (2.852 g, 12 mmol) dissolved in ethanol (15 mL). L^4 (12 mmol) was added to the Schlenk and the resulting brown solution was stirred overnight. The solvents were evaporated *in vacuo* leaving a red solid which was washed diethyl ether.

Cu(L^4)$_2$ (where L^4 = Ph$_2$PCH$_2$CHEtSCH$_2$Ph), 25 : To a Schlenk were added [Cu(CH$_3$CN)$_4$]PF$_6$ (1.28 g, 3.4 mmol), L^4 (6.8 mmol) and dichloromethane (15 mL). The

colourless solution was stirred overnight. The mixture had turned pale yellow and a white precipitate had formed.

Recovery of 3 : 3 was taken from an unsuccessful recrystallisation (0.748 g, 0.9 mmol) and was dissolved in 1,4-dioxane (10mL) and used in the following Heck reaction,
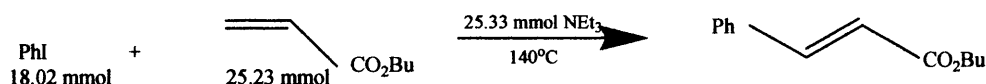
The solution was left to heat (140 °C) and stir for 1 hour. After this time palladium black was seen to form and the dark orange/brown mixture was filtered twice and washed with diethyl ether (2 x 10mL). A dark orange/red crystalline solid was recovered. A column on silica was performed (petroleum ether : ethyl acetate 9 : 1 to collect the yellow band, then methanol to collect the final orange band). The red crystals were extracted with diethyl ether (3 x 20mL), in which they were sparingly soluble, and washed with water (20ml). The organic extractions were concentrated, dried over magnesium sulfate, filtered and dried. A brick red solid remained. ^{1}H NMR (CDCl$_3$, 400 MHz), δ_H : 0.9 (3H, t, CH$_3$), 1.65 (1H, m), 1.95 (1H, m), 2.65 (1H,td), 2.95 (1H, m), 3.85 (1H, br m), 7.25-7.9 (10H, m, ArH); ^{31}P NMR (CDCl$_3$, 121 MHz), δ_p : 43.48.

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Chapter Three

— Heck Coupling —

— Reactions —

3. Heck Coupling Reactions

3.1 Introduction

In this chapter the Heck coupling reaction with palladium complexes of the phosphinothiolate and –thioether ligands presented in Chapter 2 is discussed. The palladium phosphinothiolate complexes 1-3 and phosphinothioether complex 4 (Figure 1) are highly efficient catalysts for the Heck arylation of styrene. High turnover numbers (TON) of up to a million, for reactions with bromo and iodobenzenes have been obtained. Various reagents have been explored along with a range of conditions.

1 : R = Et, X = I
2 : R = Et, X = Cl
3 : R = ^{t}Bu, X = Cl

4 : R = Me
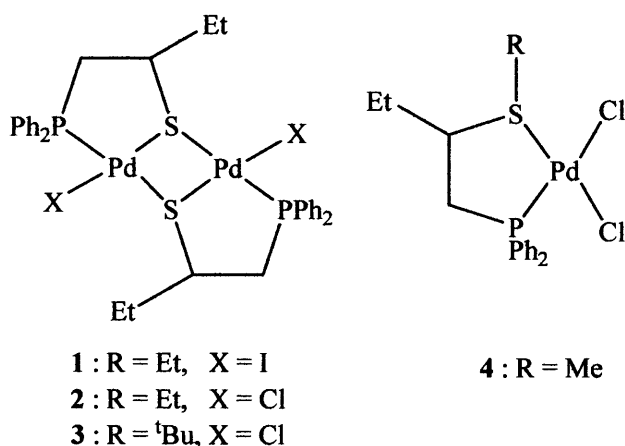
Fig 1. Palladium P, S-complexes used in Heck coupling reactions

3.1.1 Background

Much work has been carried out on palladium catalysed C-C coupling reactions, due to the fact that palladium is a very versatile and efficient catalyst, used in its Pd(0) and Pd(II) forms. The 'palladium catalysed arylation and vinylation of olefins' (the Heck reaction) has recently attracted attention (Scheme 1).[1-5]
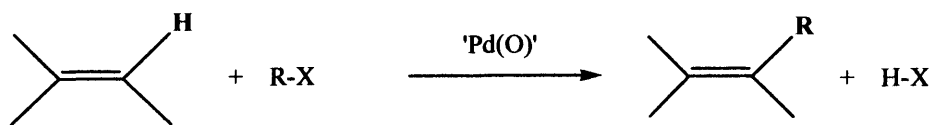
where R = aryl, vinyl
X = I, Br, COCl, OTf

Scheme 1. The Heck reaction

Investigations on the arylation of olefins using transition metal catalysts began in the late 1960s by Heck.[6] The Heck reaction was discovered in 1971 and since has been used as a powerful tool in standard organic synthesis. Mizoroki[7] had published his findings on the palladium-catalysed arylation reaction of olefins with aryl iodides along with the base potassium acetate in methanol at 120 °C. Shortly following this Heck independently reported his findings on the same coupling reaction with more favourable reaction conditions.[8]

Heck commented on the oxidative addition of organic halides onto a palladium complex resulting in a reactive organopalladium (II) halide, which subsequently undergoes an addition reaction with an olefin, abstracts hydridopalladium halide and finally results in the formation of a substituted olefin (Scheme 2).[8]
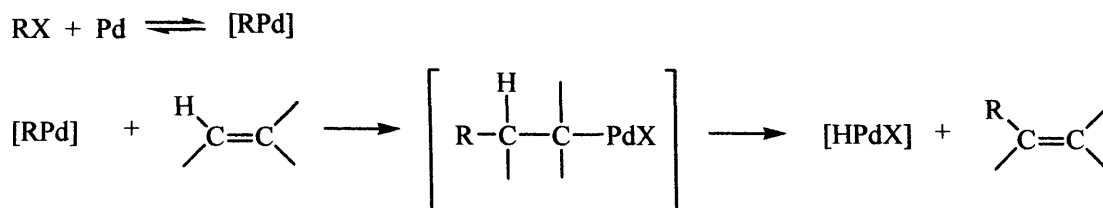
Scheme 2. Formation of substituted olefins

Today the Heck reaction is a versatile and important entity in organic synthesis. Palladium catalysts including phosphines[9-12] and N-hererocyclic carbenes[13-18] have shown excellent catalytic potential in a range of cross-coupling reactions. With the continual development of

catalysts for cross-coupling reactions sterically hindered, less reactive aryl halide substrates are now being employed.[3,19-21]

The mechanistic pathway for the Heck reaction consists of the oxidative addition of an aryl or vinylic halide, insertion of an olefin, β-hydride elimination of the product and finally regeneration of the Pd catalyst with aid from the base. The classical 'textbook' mechanism follows a $Pd(0)/Pd(II)$[22] cycle and experimental evidence has mostly disproved that a $Pd(II)/Pd(IV)$ cycle[23-31] could be functional.

$$Pd^0L_4 \quad or \quad Pd^{II}Y_2L_2$$
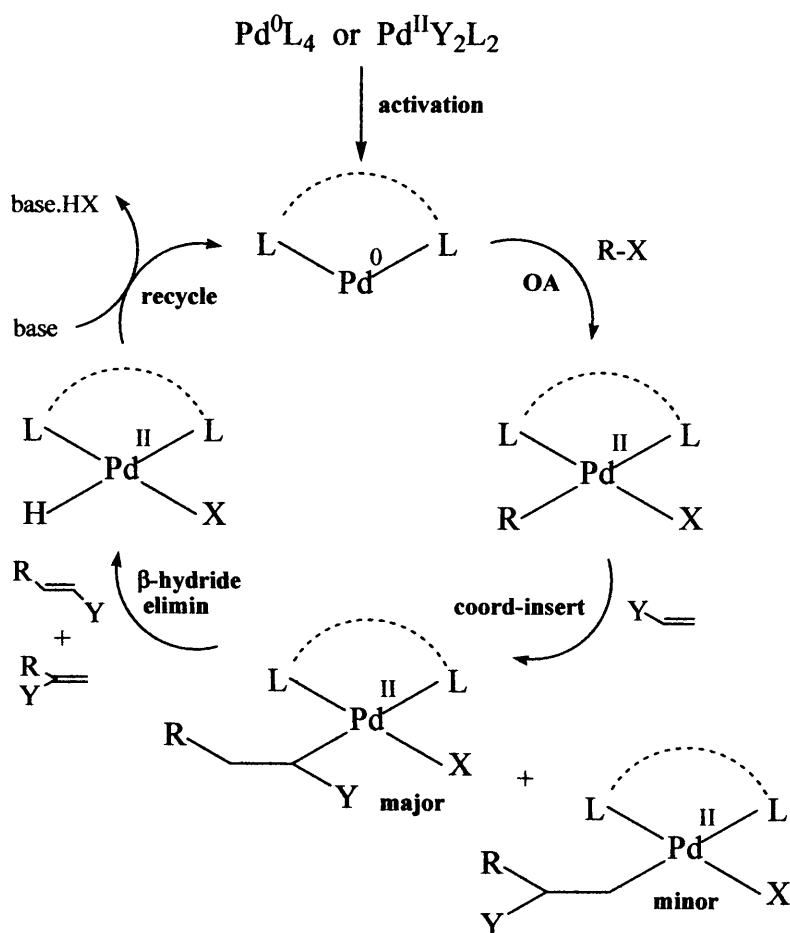
Scheme 3. The Heck reaction cycle

The classical mechanism, as shown in Scheme 3, begins with the catalytically active 14 electron Pd(0) species (such as Pd(PPh$_3$)$_2$)[32,33] coordinated with donor ligands, such as bidentate phosphines,[34,35] oxidatively adding to the aryl halide RX and yielding a σ-aryl Pd(II) intermediate complex. The presence of ligand is essential to promote this first step, except for the case of aryl iodides. The second step involves the addition of the olefin in a syn manner, as noted by Heck,[36] known as the coordination-insertion step, which is stereoselective. Experimental evidence supports the assumption that the coordination-insertion step could follow one of two paths,[37-39] via a tetracoordinated species, as shown in Scheme 4. In the first path the olefin is coordinated via dissociation of one neutral ligand, and the second path allows dissociation of an anionic ligand. These observations are supported by several catalytic studies.[40-43]
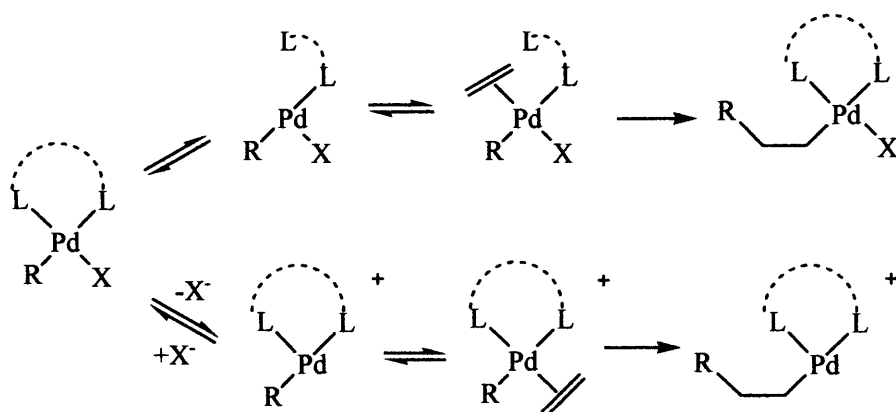
Scheme 4. The coordination-insertion process[44]

In order for the hydride to be in the correct position near to the metal centre for the next step's elimination an internal rotation around the C-C bond occurs. The stereoselective β-hydride elimination step then follows with the hydride being abstracted from the syn position. The olefin product thus formed usually possesses a trans geometry. The β-hydride elimination step is reversible and a number of different products can be formed dependent on the isomerisation of the double bond. The final step which closes the cycle is the recycling of the palladium catalyst to its original Pd(0) form by reductive elimination. Base is required for this final step to occur e.g. Et$_3$N or K$_2$CO$_3$.[44]

The reaction retains the double bond throughout, with the last step involving the base which acts to bind the acid from the hydrogen halide which was formed during the reaction. Electron-poor olefins have shown a greater affinity for coupling than the electron-rich variety,[45] although reactive systems with electron-rich and sterically hindered aryl halides have been reported.[46] Monosubstitued olefins have also shown more reactive tendencies than disubstituted and cyclic olefins. The reaction has high chemoselectivity and mild reaction conditions with catalysts being air and thermally stable and the use of undistilled solvents and reagents. The reaction has been applied to heterocycle and product chemistry.[47,48] The low toxicity and cost of reagents also make it desirable in industrial applications.[49]

Work has been carried out by various groups concerning the Heck reaction mechanism and rate. Palladacycles with phosphines and phosphine-free systems were compared and after inspection of their kinetic profiles were deduced to follow the same mechanism. Brown and co-workers[50,51] investigated the intermediate species in aryl triflate reactions. Beller and Hermann[24] revealed the dependence of the rate of reaction on the olefin type, and Van Leeuwen and co-workers[52] showed the rate of reaction to be 1st order for the olefin and zero order for the aryl halide. Kinetic investigations by Rosner and co-workers revealed the active monomeric and a dimeric species to be in equilibrium.[53]

Kinetic studies carried out by Hermann and co-workers in 1995[31] revealed the deactivation of catalysts containing 1 mol% $Pd(OAc)_2$ and 2-6 mol% triaryl phosphane at temperatures above 120 °C. This was attributed to the P-C bond cleavage at the elevated temperatures, leaving Pd deposits which starve the system of phosphane which is essential in stabilising the catalyst. Reduction of these Pd deposits is favourable for efficient catalysts.

Examples of catalysts used in the Heck reaction include in situ catalysts such as $[(Pd(OAc)_2)P/n(C_6H_5)_3]$ where n = 2 – 4, and Pd(0) phosphine complexes such as $[PdP(C_6H_5)_3]_4$. A common catalyst combination that has been reported is $Pd(OAc)_2$ and $P(C_6H_5)_3$.

Common reaction conditions describe the use of base, typically amines such as triethylamine $N(C_2H_5)_3$, and also inorganic bases such as K_2CO_3, NaOAc and $NaHCO_3$. Solvents used can be polar such as DMF, DMA or acetonitrile. The reaction temperature varies depending on the substrate used – iodo derivates are more reactive therefore can be coupled at lower temperatures (<100 °C) whereas bromo and chloro derivatives would require higher temperatures for activation. Aryl and vinyl iodides are the most reactive halides in Heck arylations and fluorides are not reactive at all due to the C-X bond dissociation energies, where Cl < Br < I.[54]

3.1.2. Catalyst preparation and testing

In our laboratory we have prepared a range of phosphinothiolate and –thioether ligands, L^1 (where $L^1 = Ph_2PCH_2CHEtS$), as shown in Scheme 5. The resulting ligands were complexed onto palladium (Figure 1) and are described in Chapter 2.
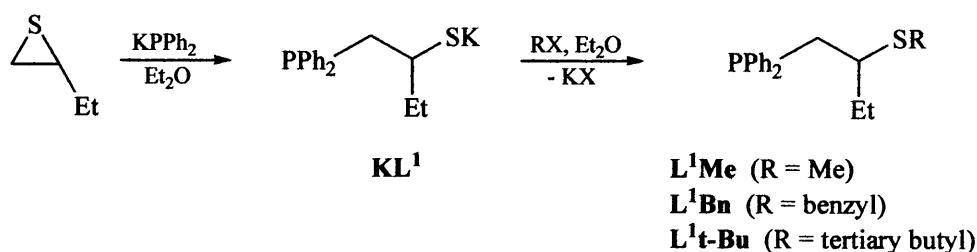
Scheme 5. Ligands synthesis.

Our work has concentrated on the use of our four P, S complexes **1 – 4** in arylations. As catalysts these complexes have been noted to be very efficient. They are air and thermally stable which has allowed runs to be carried out in air and up to high temperatures (reaching 160 °C) using undistilled solvents and reagents. We have also observed no catalyst decomposition at the end of the reaction, allowing the catalyst to be used for further reactions.

3.2. Results and Discussion

As a standard reaction to study the efficiency of catalyst precursors **1 - 4** in Heck arylations we have chosen the reaction of iodobenzene or bromobenzene with styrene, with a variety of solvents and bases. Investigations have been carried out concerning their efficiency in Heck reactions, the path followed during a reaction and the effect of different bases and solvents.

3.2.1 Temperature Effect

Investigations were carried out at temperatures of 120 and 140 °C. Reactions carried out at 120 °C were analysed by GC and HPLC, and those at 140 °C analysed by HPLC. 140 °C was found to be the more desirable temperature, and hence the majority of reactions were carried out at this temperature.

3.2.2 C-C coupling of iodobenzene with styrene

The cross-coupling reactions of iodobenzene with styrene were found to proceed best in dimethylacetamide (DMA) with triethylamine (NEt₃) as the base at a temperature of 140°C Table 1 shows the results for reactions performed at 120 and 140 °C. TONs of up to 85000 were obtained and in some cases reactions were complete in less than 6 hours.

Table 1. Heck couplings[a] of iodobenzene with styrene.
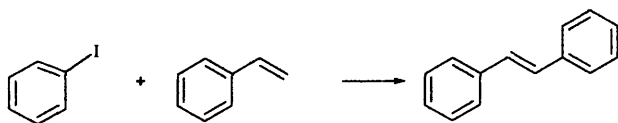
Run	Catalyst[b] (mol %)	Solvent	Base	T (°C)	Yield[c]	TON[d]	TOF[e]
1	1 (0.1)	1,4-dioxane	NEt₃	140	4	42	9
2	1 (0.001)	1,4-dioxane	NEt₃	140	65	64920	2679
3	1 (0.01)	DMA	NEt₃	140	82	8244	344
4	1 (0.001)	DMA	NEt₃	140	85	84700	3529
5	1 (0.001)	DMA/H₂O	NaOH[f]	140	77	77000	3208[g]
6	1 (0.0005)	DMA/H₂O	NaOH[f]	140	18	36000	1500[g]
7	2 (0.2)	1,4-dioxane	NEt₃	140	53	266	40
8	2 (0.12)	1,4-dioxane	NEt₃	140	80	698	279
9	2 (0.1)	1,4-dioxane	NEt₃	140	75	750	125
10	2 (0.01)	1,4-dioxane	NEt₃	140	74	7436	310
11	2 (0.03)	DMA	NEt₃	140	79	2591	1296
12	2 (0.0033)	DMA	NEt₃	140	70	21	3
13	3 (0.1)	DMF	Na₂CO₃	120	>99	113	5
14	3 (0.0001)	DMF	Na₂CO₃	120	48	1585	66
15	4 (0.02)	DMA	NEt₃	140	85	3	0.1
16	4 (0.04)	DMA	NEt₃	140	53	555	23

[a]Determined by HPLC (using naphthalene as standard), except 13-14, 16 (using GC (di(ethylene glycol)diethyl ether as the standard); Reaction conditions: Runs 1-4, 9-10, 16 : ArI (5mmol), styrene (7mmol), base (7mmol), solvent (5 mL); Runs 13-14 : ArI (12mmol), styrene (14mmol), base (14mmol), solvent (6 mL); Runs 8, 11-12, 15 : ArI (15mmol), styrene (75mmol), base (18mmol), solvent (15 mL); 7.5 mmol naphthalene; [b][Pd(Ph₂PCH₂CH(Et)S)I]₂ (1), [Pd(Ph₂PCH₂CH(Et)S)Cl]₂ (2), [Pd(Ph₂PCH₂CH(ᵗBu)S)Cl]₂ (3), Pd(Ph₂PCH₂CH(Et)SMe)Cl₂ (4); [c]Yield at 24 hours (except run1 = 5 h, run 7 = 7 h, run 8 = 2.5, run 9 = 6 h, run 11 = 2 h, run 12 = 3 h, run 15 = 21 h); [d]TON at 24 hours (except run1 = 5 h, run 7 = 7 h, run 8 = 2.5, run 9 = 6 h, run 11 = 2 h, run 12 = 3 h, run 15 = 21 h) = turnover number (mol product. mol⁻¹ catalyst); [e]TOF when reaction stopped = turnover frequency (mol product. mol⁻¹ catalyst. h⁻¹), for run1 = 5 h, run 7 = 7 h, run 8 = 2.5, run 9 = 6 h, run 11 = 2 h, run 12 = 3 h, run 15 = 21 h; [f]co-catalyst 2% NEt₃; [g]TOF at 24 h.

3.2.2.1 Catalyst Investigation

Pre-catalysts **1-4** have been used for the coupling of iodobenzene to styrene. On comparison of the four the deduction was made that the most active was **3** (due to the bulky t-butyl groups). The kinetic profiles of **1**, **2** and **4** are shown in Figure 2. The alteration of the phosphinothiolate species from a chloride to an iodide drastically improved the catalytic ability (by about 25%). The combination of DMA and NEt$_3$ has been noted to be the most beneficial.[55]
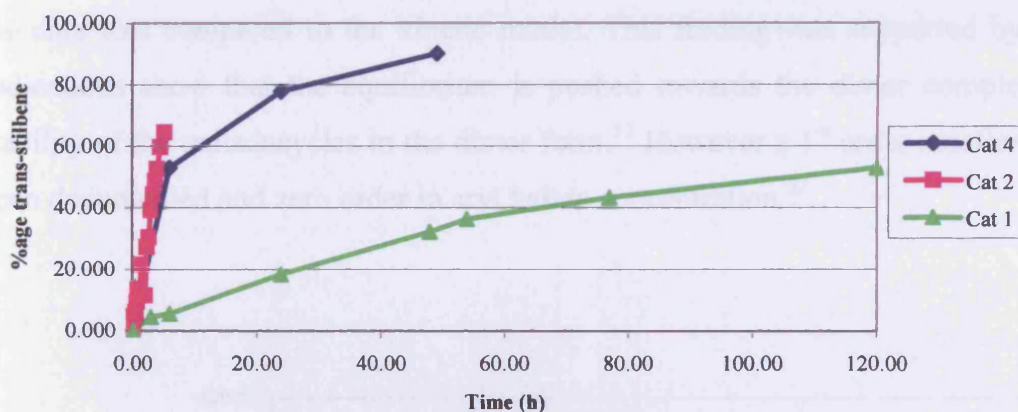
Fig 2. Comparison of catalysts **1**, **2** and **4** (0.001%). Determined by GC. Reaction conditions: styrene (7mmol), PhI (5mmol), NEt$_3$ (7mmol), DMA (5 mL), T = 120 °C.

Investigations were undertaken on the effect of catalyst concentration for the couplings of both iodobenzene and bromobenzene with styrene. It was noted for pre-catalyst **2** an increase in the catalyst concentration resulted in a decrease in catalytic activity, as shown in Tables 1 and 2. Hence an inverse dependence on catalyst concentration can be deduced. Rosner and co-workers commented on the catalytic efficiency of the palladacycle increasing with lower catalytic concentration.[53] Our findings are further supported by Vries and co-workers' results for their ligand-free Pd(OAc)$_2$ system. When runs were carried out using the catalyst within the range 0.001-0.1 mol % good conversions were obtained. Above this concentration palladium black was seen to form and the reaction stopped.[56]

The same trend of an improvement of catalytic efficiency with decreasing catalytic loading was determined for carbene complexes by Loch and co-workers. The TOF increases from 1250 h^{-1} at 2 x 10^{-1} mol % to 6250 h^{-1} at 2 x 10^{-3} mol %. TONs were also high, reaching values of 75000 at 2 x 10^{-4} mol % catalyst for aryl chlorides. The researchers also showed evidence for a monomer/dimer equilibrium. The monomer complex was noted to be more dominating at low catalyst loadings.[57] At low catalyst concentrations high TONs and TOFs are generally achieved, as has been displayed for palladacycles.[24,56] Our investigations on the pre-catalyst dimer **2** have supported reports that an equilibrium is formed between the monomer and dimer species. A plot of TOF (at 50% conversion) against varying concentrations of Pd, as shown in Figure 3, revealed the reaction rate was not 1st order when the data was compared to the kinetic model. This finding was supported by Rosner also. Indications show that the equilibrium is pushed towards the dimer complex, due to the stability of the palladacycles in the dimer form.[53] However a 1st order reaction in olefin has been documented and zero order in aryl halide concentration.[52]
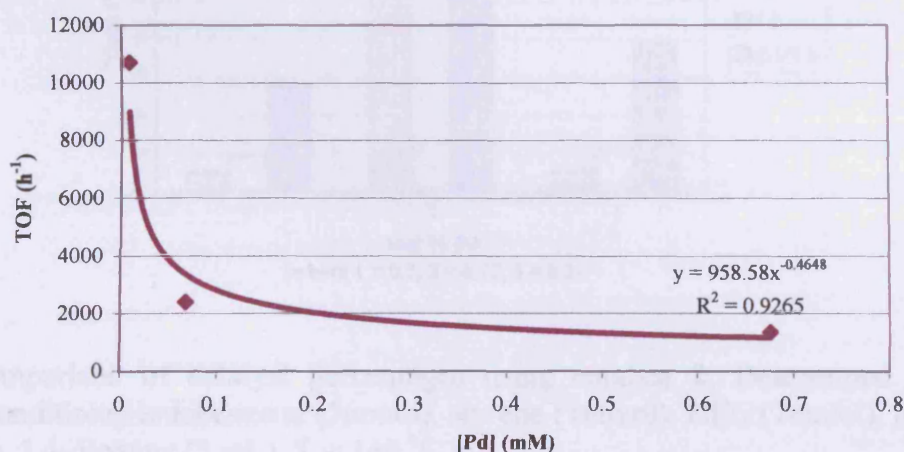
Fig 3. Reaction profile as a function of Pd concentration for the Heck coupling of iodobenzene with styrene using catalyst **2**. Determined by HPLC. Reaction conditions: iodobenzene (5mmol), styrene (7mmol), NEt$_3$ (7mmol), naphthalene (2.5 mmol), DMA (5 mL), T = 140 °C.

When testing pre-catalyst **2** for the arylation of iodobenzene with styrene, the reaction proceeded well with 0.1, 0.12 and 0.2 mol % Pd, as illustrated in Figure 4. Comparison at various time intervals during the reaction i.e. ½, 1 and 2 ½ hours, revealed the reaction rate to steadily increase indicating catalysis is proceeding well. The highest yield was obtained using 0.12 mol % catalyst (Table 1, Run 6) with results showing that after ½ hour the reaction is already 68% complete. When the catalyst percentage is increased to 0.2 mol % (Table 1, Run 5) the conversion appears to slow down slightly, suggesting the optimum percentage has been reached. However, further investigations should be taken to support these results as the trend is extreme, given the small increase in mol % Pd. The turnover frequency was greatest for 0.12 mol %, possibly due to a shift in the equilibrium between the Pd in the complex and the Pd in the catalytic cycle. If the cycle is favoured, as is anticipated at lower mol % Pd, the percentage of active catalyst in fact increases.[56]
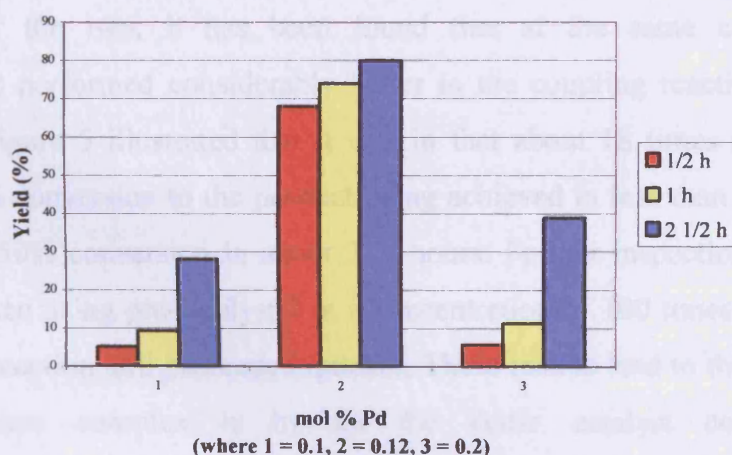
Fig 4. Comparison of catalyst percentages using catalyst **2**. Determined by HPLC. Reaction conditions: iodobenzene (5mmol), styrene (7mmol), NEt$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL), T = 140 °C.

3.2.2.2 Phosphinothiolate vs phosphinothioether

Work was carried out on two catalytic systems based on the phosphinothiolate and – thioether ligands, using pre-catalysts **2** and **4**. Investigations concerning their efficiency in Heck reactions and the path followed during a reaction have been undertaken.

90
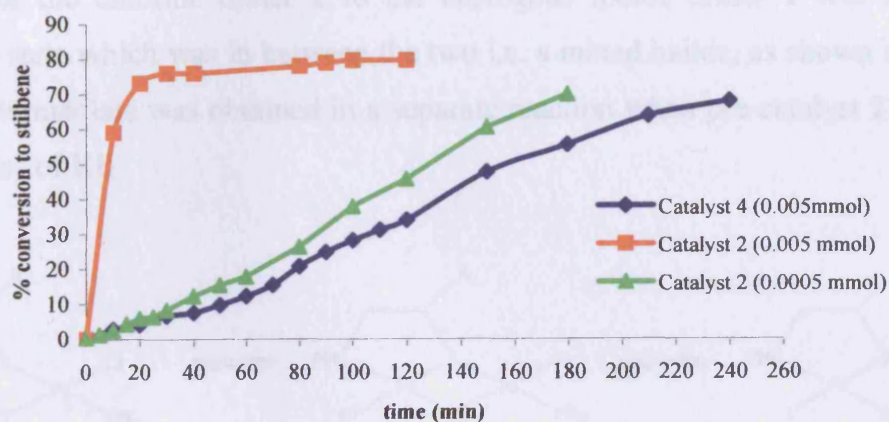
Fig 5. Heck reaction profile showing phosphinothiolate **2** vs phosphinothioether **4**. Determined by HPLC. Reaction conditions: styrene (75mmol), PhI (15mmol), NEt₃ (18mmol), 1,4-dioxane (15 mL), 7.5mmol naphthalene, T = 140 °C.

On comparison of the two, it has been found that at the same concentration the phosphinothiolate **2** performed considerably better in the coupling reaction. The reaction profile shown in Figure 5 illustrated that it was in fact about 18 times faster than the – thioether, with 50% conversion to the product being achieved in less than 10 minutes. Pre-catalyst **4** reached 50% conversion in about 2 ½ hours. Further inspection of the reaction profile revealed when using pre-catalyst **2** at a concentration of 100 times less than that of pre-catalyst **4**, the reaction still proceeded quicker. These results lead to the conclusion that the phosphinothiolate complex is by far the better catalyst compared to the phosphinothioether.

3.2.2.3 Recovery of complexes

Investigations were carried out to deduce whether the catalyst could be recovered and reused after a catalytic reaction of the coupling of iodobenzene with butyl acrylate in DMF at 140 °C. At the end of catalytic runs with pre-catalysts **2** and **4** a Pd complex was recovered and characterised. X-ray crystallography of the brick-red solid obtained revealed the structure of this complex to be [Pd(Ph₂PCH₂CHEtSI]₂. This indicates that cleavage of the S-Me bond may occur for the chloride monomer (catalyst **4**). On following the Heck

arylation of iodobenzene with butyl acrylate in DMF by $^{31}P\{^1H\}$ NMR spectroscopy results indicated that the catalyst was inactive below 100 °C. Above this temperature a slow conversion of the chloride dimer **2** to the analogous iodide dimer **1** was seen, via an intermediate state which was in between the two i.e. a mixed halide, as shown in Scheme 6. The same intermediate was obtained in a separate reaction when pre-catalyst **2** was reacted with an excess of KI.
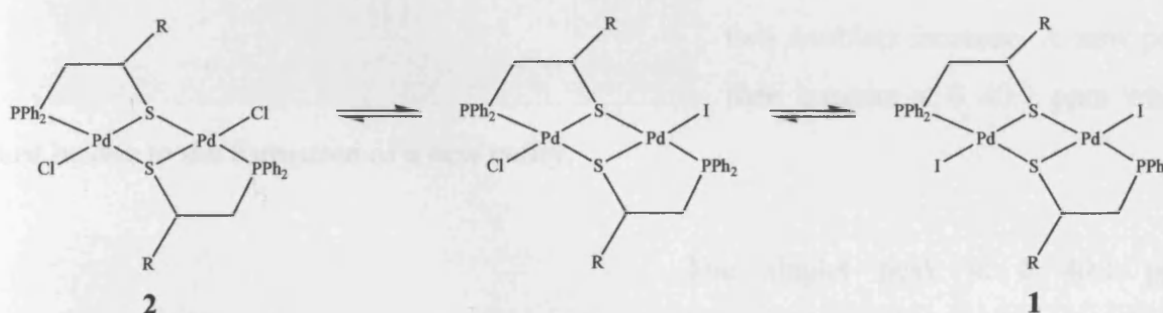
Scheme 6. The conversion of pre-catalysts **2** to **1** via a mixed halide state

3.2.2.4 Monitoring the conversion of pre-catalyst 2 to 1 using NMR

The reaction of iodobenzene with styrene using pre-catalyst **2** was followed by $^{31}P\{^1H\}$ NMR spectroscopy. Samples were taken from the reaction mixture at set time intervals and used to monitor the progression of the reaction by NMR.
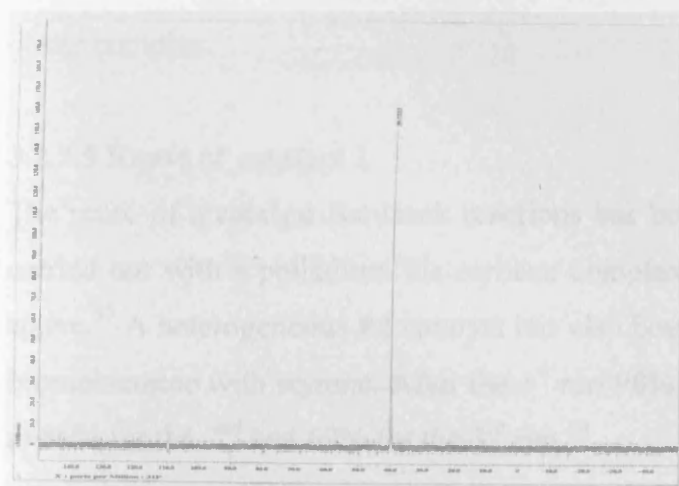
A symmetrical dimer was seen at the start and at the end of the reaction, as a singlet at δ 39.7 ppm and a singlet at δ 40.1 ppm. The singlet peaks could be attributed to all of the phosphorus atoms lying in the same environment.
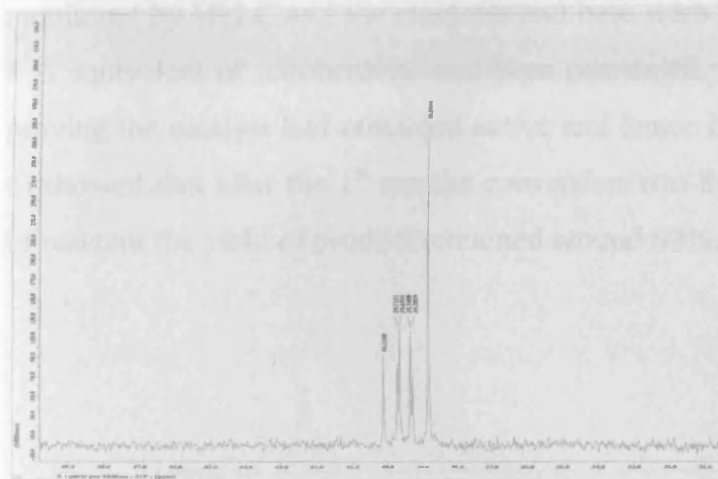
The intermediate could be seen as two doublets at δ 39.7 and 39.3 ppm due to the unsymmetrical mixed halide molecule. These two clusters were noted to change in intensity. As the singlet peak at δ 39.7 ppm decreases in intensity the two doublets increase. A new peak then appears at δ 40.1 ppm which must be due to the formation of a new entity.
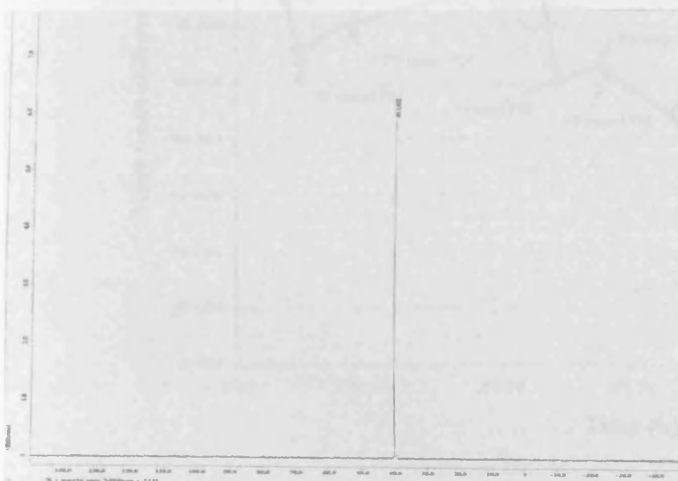
The singlet peak at δ 40.1 ppm eventually becomes the only peak at the end of the reaction and therefore it can be deduced that it is due to the formation of the iodide dimer, pre-catalyst **1**. It is thought that both the monomer and dimer systems follow the same catalytic cycles as **4** (monomer) is slowly transformed to a dimer complex.

3.2.2.5 Reuse of catalyst 1

The reuse of a catalyst for Heck reactions has been reported. A recycling experiment was carried out with a palladium bis-carbene complex, and after 6 cycles the catalyst was still active.[57] A heterogeneous Pd catalyst has also been recycled three times for the arylation of bromobenzene with styrene. After the 1st run 98% conversion was observed. This decreased to 86% for the 2nd and 69% for the 3rd run.[58]

The coupling of iodobenzene with styrene using pre-catalyst **1** was the experiment used to investigate the reuse of a catalyst in a Heck reaction. The disappearance of the reactants was

monitored by HPLC and the reactants and base were re-added to the reaction mixture when a ½ equivalent of iodobenzene had been consumed. In total another 10 loads were added, proving the catalyst had remained active and hence had been recycled. Our results (Figure 6) showed that after the 1st run the conversion was 84%. Following several more additions of reactant the yield of product remained around 60%.
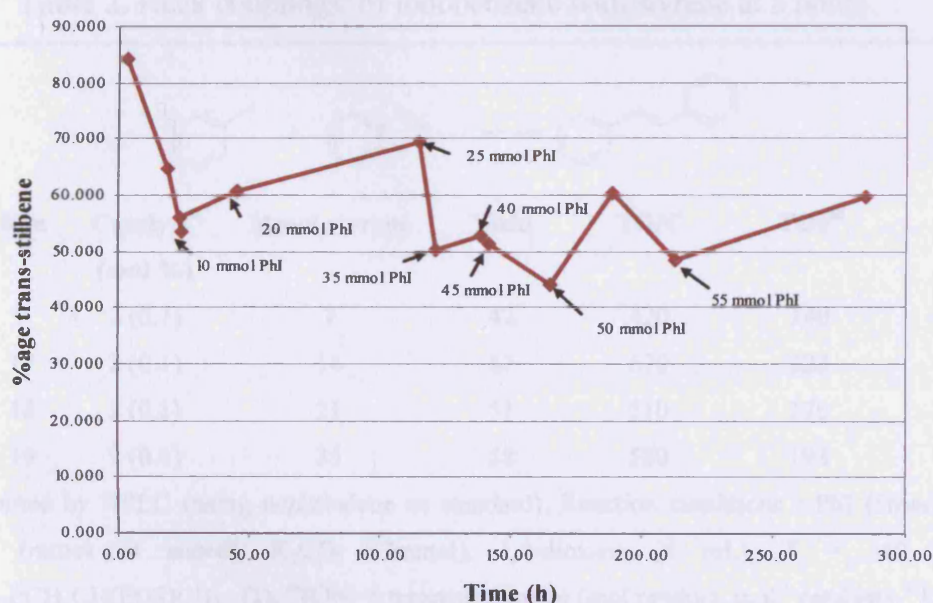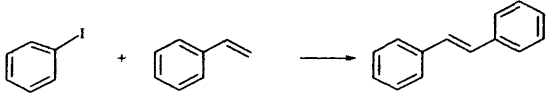
Fig 6. Reuse of catalyst using catalyst **1** (0.001 mol %). Determined by HPLC. Reaction conditions: PhI, styrene (7mmol), NEt$_3$ (7mmol), naphthalene (2.5 mmol), DMA (5 mL), T = 140 °C.

3.2.2.6 Olefin concentration

Research has been carried out by Hermann and co-workers[24] concerning the effect of olefin type on Heck arylations. The reaction studied was the coupling of a variety of aryl bromides with styrene, 1-methylstyrene and butyl vinyl ether catalysed by a palladacycle. The results revealed good TONs of up to 500 000 for the styrene arylations, using 0.0001 mol % Pd. The TONs for the 4-fluorostyrene, 4-methoxystyrene, 1-methylstyrene and butyl vinyl ether were >1000, indicating the catalytic activity was significantly lower for these olefins with extra substituents. Hermann concluded that the electronic character and steric effect of the

olefin play a role in the catalytic strength of the palladacycles. This evidence also pointed to the olefin insertion step of the Heck mechanism being rate-determining, not the previously assumed oxidative addition. Comparison of different concentrations of styrene for the coupling of iodobenzene with styrene using our P,S catalyst **2** was undertaken. Experiments with 7, 14, 21 and 35 mmol styrene were performed under the standard conditions and followed by HPLC. Results (Table 2) indicate that the optimum concentration was 14 mmol, with 50% conversion being achieved in less than 2 hours, as illustrated in Figure 7.

Table 2. Heck couplings[a] of iodobenzene with styrene at 3 hours

Run	Catalyst[b] (mol %)	Mmol styrene	Yield	TON[c]	TOF[d]
9	2 (0.1)	7	42	420	140
17	2 (0.1)	14	67	670	223
18	2 (0.1)	21	51	510	170
19	2 (0.1)	35	58	580	193

[a]Determined by HPLC (using naphthalene as standard). Reaction conditions : PhI (5mmol), styrene (mmol as stated), K_2CO_3 (7mmol), 1,4-dioxane (5 mL), T = 140 °C; [b][Pd(Ph$_2$PCH$_2$CH(Et)S)Cl]$_2$ (**2**); [c]TON = turnover number (mol product. mol^{-1} catalyst); [d]TOF at 24 hours = turnover frequency (mol product. mol^{-1} catalyst. h^{-1}).
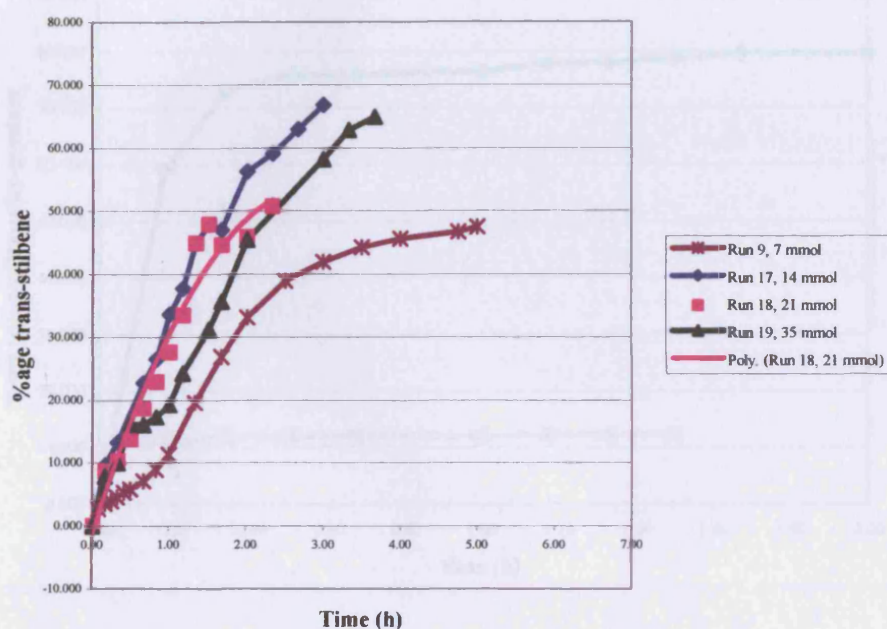
Fig 7. Comparison of styrene concentration using catalyst **2** (0.1 mol %). Determined by HPLC. Reaction conditions: PhI (5mmol), styrene (mmol as stated), NEt₃ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL), T = 140 °C.

3.2.2.7 By-product production

The conversion of the aryl halides to the trans-stilbene product and 1,1-diphenylethylene by-product was monitored (Table 1, Run 11). The two were distinguishable by their differing positions in the HPLC spectrum. Figure 8 illustrates the correlation between the product and by-product during a Heck reaction. The product increases in percentage, as expected, throughout the course of the reaction. The conversion to by-product can be seen to remain fairly constant as the reaction proceeds.
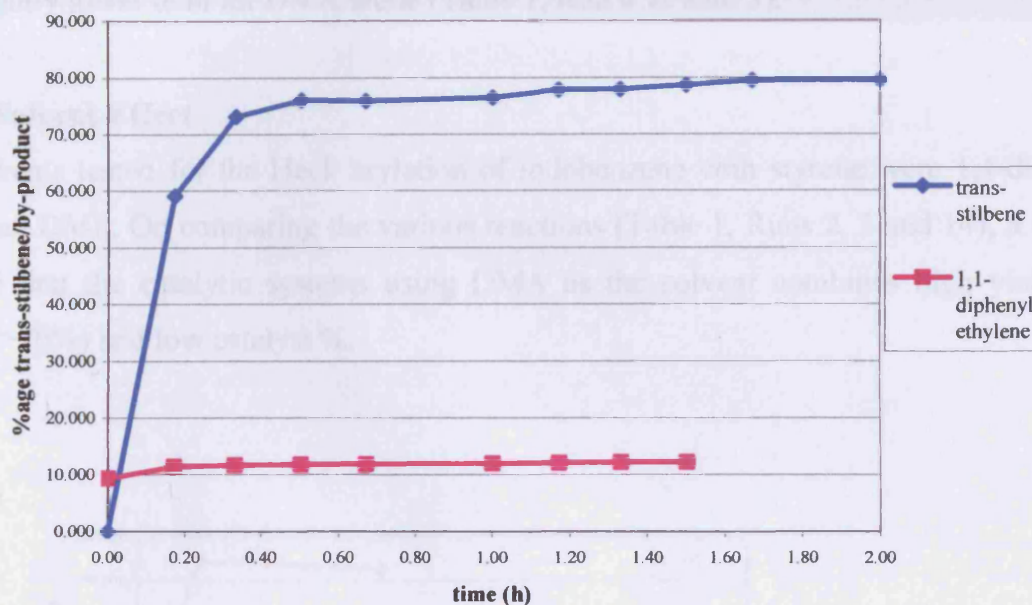
Fig 8. Trans-stilbene and 1,1-diphenylethylene formation, catalyst **2** (0.03 mol %). Determined by HPLC. Reaction conditions: PhI (15mmol), styrene (75mmol), NEt$_3$ (18mmol), naphthalene (7.5 mmol), DMA (15 mL), T = 140 $^\circ$C.

3.2.2.8 Water concentration

The use of water in Heck arylations on its own or in combination with another solvent, for example acetonitrile or DMA,[59] or sodium hydroxide,[60] has been documented. The rate accelerating effects of quaternary ammonium salts were found to be noticeable only when water was present in the reaction, as either the salt in its hydrated form or a solvent mixture with acetonitrile. This was corroborated by the evidence that when the arylation of iodobenzene with butyl acrylate was carried out in the presence of a dehydrating agent, n-Bu$_4$NCl.xH$_2$O did not improve the efficiency of the reaction (1% conversion with the dehydrating agent and 99% conversion without). Excellent yields of >90% have been achieved when using neat water in combination with quaternary ammonium salts.[61]

The iodobenzene/styrene system was tested under biphasic conditions. Water was added along with the solvent (in our case DMA) in a 1:1 ratio and a water soluble inorganic base,

NaOH. The resulting couplings were noted to proceed well with a yield and TON that was only slightly lower than for DMA alone (Table 1, Run 4 vs Run 5).

3.2.2.9 Solvent Effect

The solvents tested for the Heck arylation of iodobenzene with styrene were 1,4-dioxane, DMA and DMF. On comparing the various reactions (Table 1, Runs 2, 3 and 14), it can be deduced that the catalytic systems using DMA as the solvent combines high yields (in general >70%) and low catalyst %.
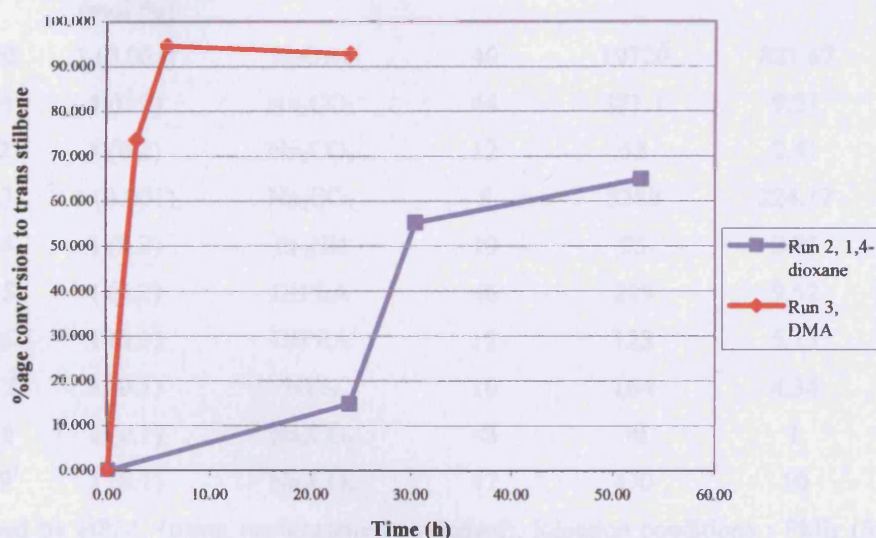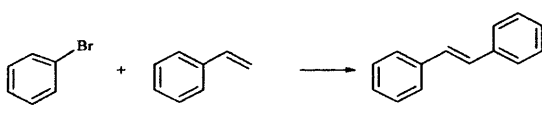
Fig 8. Comparison of solvents using catalyst **1** (0.001 mol %). Determined by HPLC. Reaction conditions: iodobenzene (5mmol), styrene (7mmol), NEt$_3$ (7mmol), naphthalene (2.5 mmol), solvent (5 mL), T = 140 °C.

3.2.3 C-C coupling of bromobenzene with styrene

The next aryl halide to be investigated was bromobenzene, which as anticipated proved to be a less active substrate than iodobenzene. TONs of up to 19000 were achieved with pre-catalyst **1** as shown in Table 3.

Table 3. Heck couplings[a] of bromobenzene with styrene.

Run	Catalyst[b] (mol %)	Base	Yield	TON[c]	TOF[d]
20	1 (0.001)	NaOAc	40	19720	821.67
21	1 (0.2)	Na_2CO_3	44	221.1	9.21
22[e]	1 (0.2)	Na_2CO_3	12	58	2.41
23	1 (0.001)	Na_2CO_3	5	5380	224.17
24	1 (0.2)	Et_2NH	19	95	3.95
25	1 (0.2)	DIPEA	46	229	9.52
26	1 (0.1)	DIPEA	12	123	5.13
27	1 (0.1)	NEt_3	10	104	4.34
28	1 (0.1)	Na_2CO_3	<3	30	1
29[f]	1 (0.1)	Na_2CO_3	47	470	10
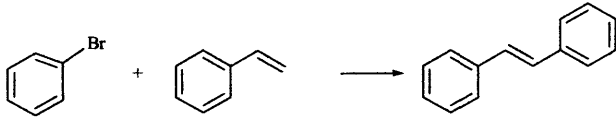
[a]Determined by HPLC (using naphthalene as standard). Reaction conditions : PhBr (5mmol), styrene (7mmol), base (7mmol), DMA (5 mL), T = 140 °C; [b]$[Pd(Ph_2PCH_2CH(Et)S)I]_2$ (1); [c]TON = turnover number (mol product. mol^{-1} catalyst); [d]TOF at 24 hours (except Run 28 at 30 hours and Run 29 at 48 hours)= turnover frequency (mol product. mol^{-1} catalyst. h^{-1}); [e]Reaction carried out under argon; [f]NBu_4I (7 mmol).

The percentage yields were low (<50%), and a variety of bases were tested. The calculated TOFs were also moderate reflecting the challenge of the conversion of aryl bromides like bromobenzene.

3.2.3.1 Base Effect

Previous papers have reported the nature of the base dramatically affecting the product distribution in coupling reactions. This is attributed to the double bond selectivity being influenced by the β-hydride elimination part of the Heck mechanism.[45] Previous work concerning Heck arylations using a palladium phosphinothioether complex detailed the affect of the base on the coupling reactions. Catalytic activity was dramatically improved with the use of inorganic bases, for example Na_2CO_3 or NaOAc. The use of P, S complexes yielded trans-stilbenes exclusively with excellent yields (in many cases > 99%) and TONs (> 1 million) for bromobenzenes.[46] Hence, we have investigated the possible effect that bases have on the rate of formation of product for the coupling of bromobenzene with styrene. The results obtained are shown in Table 4.

Table 4. Heck couplings[a] of bromobenzene with styrene using various bases.

Run	Base	Catalyst[b] (mol %)	Yield[c] (%)	TON[d]
30	DIPEA	1 (0.2)	46	228
31	Na_2CO_3	1 (0.2)	44	221
32[e]	Na_2CO_3	1 (0.2)	12	58
33	Et_2NH	1 (0.2)	19	95

[a]Reaction conditions : PhBr (5mmol), styrene (7mmol), base (7mmol), naphthalene (2.5 mmol), DMA (5 mL), T = 140 °C; [b][Pd(Ph$_2$PCH$_2$CH(Et)S)Cl]$_2$ (1); [c]Determined by HPLC; [d]TON = turnover number (mol product. mol^{-1} catalyst); [e]Reaction carried out under argon.

Beller et al[45] noted the difference between less coordinating bases, for example NaOAc and Na_2CO_3, and amines for example diisopropylethylamine (DIPEA). It was reported that the less coordinating bases yield terminal olefins as the main product while the amines yielded internal olefins as the dominant product. It was also demonstrated that the base influenced the reaction profile, in particular NaOAc vs DIPEA. Evans and co-workers[62] also

100
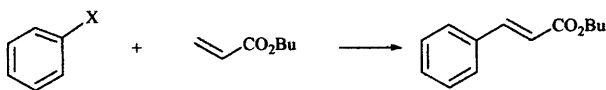
investigated the effects of base in Heck arylations, paying particular attention to inorganic acetates. The most effective were determined as KOAc and CsOAc. It was concluded that the nature of base does affect the Heck arylation reaction and mechanism, in the formation of the Pd(0) complex in the last step of the catalytic cycle.[23] Our investigations compared the three bases Et_2NH, DIPEA and Na_2CO_3 for the coupling of bromobenzene with styrene (Table 4, Runs 30-33). Results showed DIPEA to give the highest yield (Run 30, 46%) closely followed by Na_2CO_3 (Run 31, 44%). An interesting result was obtained using Na_2CO_3 under argon (Table 4, Run 32), where the yield was only 12% (the same reaction in air, Run 31, yielded 44%), indicating that the absence of air may slow or hinder the C-C coupling in some way. Tests on air stability have been performed by others and revealed that without air and water the catalyst was still as active and product still formed. This indicated that the catalyst is not decomposed by oxygen.[57] Our investigations have shown that for the coupling of bromobenzene and styrene the most effective bases are DIPEA and Na_2CO_3. These reactions have the highest yields but relatively low TONs.

3.2.4 C-C coupling of haloarenes with butyl acrylate

Our next investigation of substrates involved the Heck arylation of butyl acrylate with bromo- and iodobenzene. Table 5 shows the results obtained.

Table 5. Heck couplings[a] of haloarenes with butyl acrylate.

Run	X (mmol)	Catalyst[d] (mol %)	Base	t (h)	Yield (%)	TON[e]	TOF[f]
34[b]	I (100)	2 (0.01)	NEt₃	24	75	750000	31250
35[b]	I (5)	2 (0.1)	NEt₃	24	>99	5000	208
36[b]	I (5)	2 (0.05)	NEt₃	24	84	8400	350
37[b]	Br (5)	4 (0.01)	NEt₃	24	3	1500	63
38[c]	I (150)	2 (0.00007)	NEt₃	72	75	1346429	18700
39[c]	I (100)	2 (0.0001)	NEt₃	72	81	613636	8523
40[c]	I (1)	2 (1)	Na₂CO₃	72	82	82	1
41[c]	I (6)	2 (0.002)	Na₂CO₃	72	81	769230	10684

[a]Reaction conditions : ArX (mmol as stated), butyl acrylate (7mmol), base (7mmol), 1,4-dioxane (5 mL), T = 120 °C; [b]Determined by HPLC (using naphthalene as standard); [c]Determined by GC (using naphthalene as standard); [d][Pd(Ph₂PCH₂CH(Et)S)Cl]₂ (2), Pd(Ph₂PCH₂CH(Et)SMe)Cl₂ (4); [e]TON = turnover number (mol product. mol⁻¹ catalyst); [f]TOF at time stated= turnover frequency (mol product. mol⁻¹ catalyst. h⁻¹).

Excellent yields were obtained using pre-catalyst **2** for the arylation of iodobenzene (Table 5, Runs 34-36, 38-41). The attempted reaction with bromobenzene obtained a yield of only 3% after 24 hours (Table 5, Run 37).

3.2.5 Use of alkylammonium bromides

The Heck olefination of aryl chlorides can be aided with the use of alkali metal salts and alkylammonium bromides, such as NBu₄Br. Reports have shown that for reactions at low

catalyst loadings (2 x 10⁻¹ mol %) the reaction time is substantially lower when using NBu₄Br.[57] Others have also reported on alkyl ammonium halides noticeably improving Heck coupling reactions.[24,58,63] The use of NBu₄Br eliminated any by-products, hence increasing the percentage conversion to the desirable product.[31] Our investigations concentrated on the coupling of bromobenzene with styrene. Using pre-catalyst 1 at 0.1 mol % (Table 3, Run 28) the yield after 24 hours was less than 3%. A run was then carried out under the same conditions and also using the additive NBu₄I (Table 3, Run 29). The resulting yield was 47% after 24 hours, indicating the NBu₄I additive aided the coupling reaction substantially.

3.2.6 Effect of different substrates

Our catalysts have shown high catalytic activity for the Heck arylation of iodobenzene with styrene but have proven to be considerably slower for bromobenzene. Experiments concerning the effect of aryl bromides on Heck arylations have concluded that although the electronic nature of the substituent does effect the formation of terminal or internal olefin the base has a more dominating role.[45] Noticeable differences between aryl iodides and aryl bromides were shown for ligand-free palladium catalysts in Heck arylations. The ligand-free system successfully catalysed the aryl iodides but had no effect on the aryl bromides. This was attributed to differing rate determining steps (rds) for the two substrates – for aryl iodides the rds was the olefin insertion, and the resting state was a stable Pd(II), whereas for aryl bromides the rds is believed to be the oxidative addition step and the resting state a Pd(0) species.[56]

3.3 Conclusions

The Heck arylations performed with our P, S catalysts have been monitored by GC and HPLC. Our catalytic systems combine high activity and high TONs. For the coupling of styrene with iodobenzene the highest yields and TONs were achieved with a combination of DMA and NEt₃ at 140 °C. In general yields were above 60% for this substrate and TONs reached 85000. The formation of the cis by-product, 1,1-diphenylethylene, was also monitored. The percentage of the cis by-product during the reaction was around 10%.

Catalyst recovery and reuse were investigated with results confirming the possible reuse of the catalyst after the catalytic runs. The iodide dimer, pre-catalyst **1**, was recovered, as shown by $^{31}P\{^1H\}$ NMR spectroscopy. The catalyst was recycled and remained active after 10 additional loads of substrates were added to the reaction mixture. Investigations on the catalysts concluded that the best was pre-catalyst **3**.

Iodobenzene and bromobenzene were coupled to styrene and butyl acrylate. The arylation of bromobenzene with styrene was noted to speed up when 1 equivalent of NBu_4I was added to the reaction mixture. This can be attributed to halide exchange occurring.

3.4 Experimental

3.4.1 General procedure of coupling experiments

Reactions were performed in sealed pressure tubes. Reagents and solvents were used as received unless otherwise stated. A stock solution of Pd catalyst in DCM was prepared and the appropriate volume was calculated and added to the pressure tube. A solvent solution containing aryl halide, alkene or butyl acrylate, base and standard were charged into the pressure tube (quantities as stated for particular experiments). The pressure tube was sealed, heated and stirred at the stated temperature for the stated time. Samples (approximately 0.1 mL) were taken at set intervals during the reaction, filtered and extracted with water/DCM. Reagents and products were identified by GC or HPLC, as stated. Conversions and yields were quantified by GLC using naphthalene or di(ethylene glycol)diethyl ether as internal standard.

3.4.2 Typical reaction conditions for Heck reactions with iodobenzene

Iodobenzene (1.020 g, 5 mmol), styrene (0.729 g, 7 mmol), base (7 mmol), naphthalene (0.320 g, 2.5 mmol), solvent (5 mL), Pd catalyst (0.00008 – 0.1 mol% Pd), T = 120/140 °C, 2 - 24 h.

3.4.3 Typical reaction conditions for Heck reactions with bromobenzene

Bromobenzene (0.7601 g, 5 mmol), styrene (0.729 g, 7 mmol), base (7 mmol), naphthalene (0.320 g, 2.5 mmol), DMA (5 mL), Pd catalyst (0.001 – 0.1 mol% Pd), T = 140 °C, 24 h.

3.4.4 Typical reaction conditions for Heck reactions with butyl acrylate

Aryl halide (mmol as stated), butyl acrylate (0.897 g, 7 mmol), base (7 mmol), naphthalene (0.320 g, 2.5 mmol), 1,4-dioxane (5 mL), Pd catalyst (0.00007 – 1 mol% Pd), T = 120 °C, 24-72 h.

3.4.5 Reuse of catalyst experiments

Iodobenzene, styrene (0.729 g, 7 mmol), triethylamine (0.708 g, 7 mmol), naphthalene (0.320 g, 2.5 mmol), DMA (5 mL), catalyst 1 (0.001%), T = 140 °C, t = 285 h. The reaction was monitored by HPLC and addition amounts of reactants were added when ½ equivalent of iodobenzene had been consumed.

3.4.6 Description of GC and HPLC analysis used for Heck reactions

GC conditions : Yields and substrate identities were determined by GC analysis of reaction mixtures using a Hewlett Packard 5890 Series II GC system. Column : BPI 30 m x 0.5 mm, 0.5 μm coating. Initial temperature at 100 °C, held for 10 minutes, ramp 5 °C/minute next 100 °C.

Retention times for analytes (in minutes) : iodobenzene (12.3), bromobenzene (14.3), 4-bromotoluene (8.75), styrene (1.9), butyl acrylate (18.2), naphthalene (16.1), biphenyl (22.9), 4-phenyltoluene (20.0), di(ethylene glycol)diethyl ether (10.4).

GC Quantification : The instrument was used to monitor the formation of product / consumption of reactant during the course of the reaction. To determine the detector response factor (D_{RF}) equal amounts of reactant and internal standard (IS) were weighed out and made up to a known volume in solution.

D_{RF} = <u>Area of product peak</u>
    Area of IS

When analysing the reaction mixture a known amount / concentration of IS was added and the concentration of the product / reactant was calculated using the equation,

Product concentration = <u>Area product</u> x <u>Conc IS</u>
        Area IS   Rf product

HPLC conditions : Yields and substrate identities were determined by HPLC analysis of reaction mixtures using an Agilent 1100 Series HPLC. Synergi 4u column : 80A, 250 x 4.60 mm, 4u micron, 80:20 $CH_3CN:H_2O$, 2 mL/min, λ = 256 nm, 1mL/min. Luna 5u C18 column : 150 x 4.60 mm, 5u micron, 65:35 $CH_3CN:H_2O$, 2 mL/min.

The retention times for analytes (in minutes), iodobenzene (2.7), bromobenzene, styrene (2.7), naphthalene (3.0), trans-stilbene (4.25), cis-stilbene (4.8).

A number of samples of reactant and standard (naphthalene) in dichloromethane were run. The samples were made-up to recreate the conditions seen during the reaction i.e. the mass of the standard was kept constant throughout (0.320 g, 2.5 mmol) and the mass of reactant was varied (from 5 mmol to 2.5 mmol).

A calibration curve was plotted for the reactant (area of reactant / area of naphthalene vs moles of reactant) in order to determine the detector response factor (D_{RF}). D_{RF} = gradient of the graph.

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Chapter Four

Suzuki

Cross-Coupling—

Reactions

4. Suzuki Cross-Coupling Reactions

4.1 Introduction

In this chapter the Suzuki coupling with palladium complexes of the phosphinothiolate and –thioether ligands is discussed. The palladium phosphinothiolate complexes **1** and **2** and phosphinothioether complexes **4** and **5**, as shown in Figure 1, are excellent catalysts for Suzuki couplings. Various reagents have been explored along with a range of conditions.

1 : X = I
2 : X = Cl

4 : R = Me
5 : R = CH$_2$-3,5-xylene
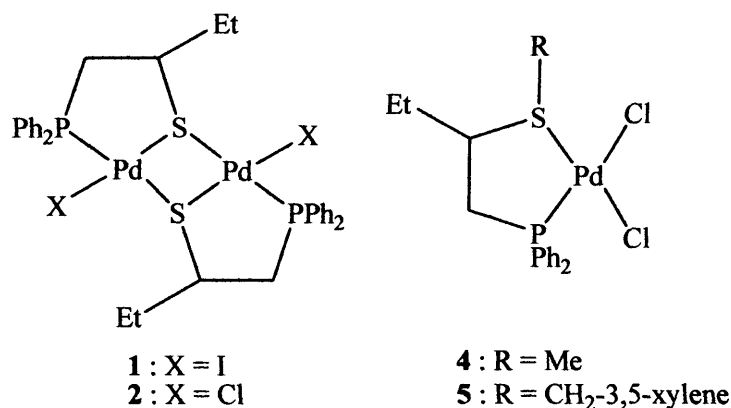
Fig 1. Pd (II) P, S complexes used in Suzuki coupling reactions

4.1.1 Background

The Suzuki reaction has been developed into a powerful method of C-C coupling in organic synthesis. The reaction can be defined as, 'the palladium catalysed cross-coupling of aryl halides and aryl triflates with arylboronic acids to form biaryls.'[1-6]
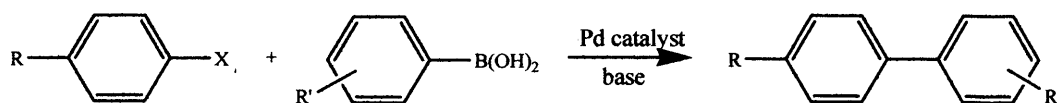
Scheme 1. The Suzuki reaction

Suzuki coupling was first published in 1979[7,8] and has since developed into one of the most important of the cross-coupling reactions, in particular, for the formation of unsymmetrical biaryls. It has emerged as an extremely powerful method for the reaction

of aryl bromides, iodides and triflates with aryl boronic acids, and holds the advantage that the boron-containing by-products are non-toxic and can be easily separated from the desired product.[9] The adaptability of the reaction stems from the easily obtainable reagents used and the mild reaction conditions employed. Today the Suzuki reaction accounts for a quarter of all palladium-catalysed cross coupling reactions, and has found use in the synthesis of natural products and pharmaceuticals.[10-14]

The general mechanism for the Suzuki reaction, and other Pd coupling reactions, has been proposed to involve a Pd(0)/(II) catalytic cycle[15] (Scheme 2).
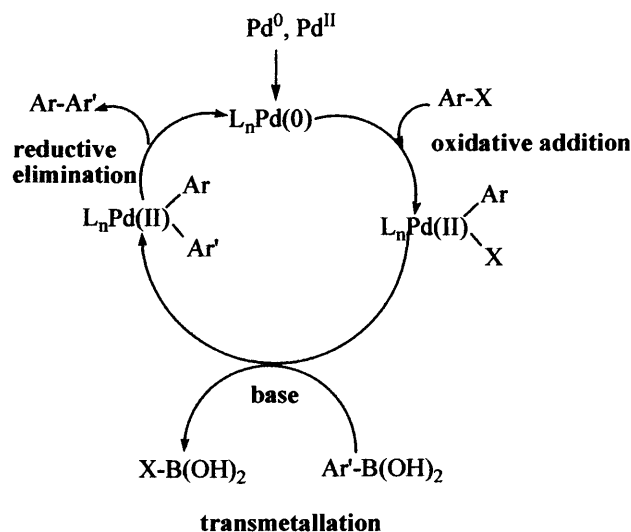
Scheme 2. Catalytic cycle of the Suzuki reaction

The catalytic cycle outlined (Scheme 2) is the widely accepted one. It is believed to begin with the oxidative addition step of an aryl or vinyl halide to a Pd(0) species. This is followed by transmetallation and formation of a Pd(II) intermediate. The reductive elimination step closes the cycle, producing the final cross-coupling product and regenerating the catalyst.

The main steps of the catalytic cycle i.e. oxidative addition, transmetallation and reductive elimination, can be related to a wide range of cross-coupling reactions, for example Heck,[2] Stille[2,16-20] and Sonogashira.[2] The cycle begins with the formation of a

catalytically active species. This is formed from the catalyst precursor, hence indicating how the palladium source can have an influence on the rate of the reaction. The three types of mechanism that describe ligand substitution are associative (A), dissociative (D) and interchange (I). In the associative pathway an intermediate is formed that possesses a higher coordination number than the original complex. Hence the new bond is formed before the old one is broken. This is typically seen for square-planar Pt(II) and Pd(II) complexes. The dissociative pathway has an intermediate species of reduced coordination number which is formed after the leaving group has departed. The final mechanism, interchange, is a one step reaction which can follow either an associative (I_a) or dissociative (I_d) reaction profile. The bulkier the phosphine group, the higher the activity, and therefore the rate.[1,9] The oxidative addition step has been found to be sensitive to the bulkiness of the phosphine. Bulky alkyl phosphines (such as P^tBu_3, PCy^tBu_2) undergo oxidative addition with aryl halides by the dissociative pathway,[21-23] whereas less bulky phosphines (such as $PCy_2{}^tBu$, PCy_3) follow the associative one.[24] Faster oxidation reactions are performed by electron rich metal complexes which are formed from electron donating ligands.[25]

The final product undergoes reductive elimination, closing the catalytic cycle. The intermediate during this step was deduced as a three coordinate palladium (II) species.[26,27] The process can be sped up when the palladium complex is bonded to electron withdrawing ligands which are also sterically demanding.[25] The electron withdrawing power of the ligands allows electron density to be taken from the metal centre generating a good environment for the reduction reaction to occur. Using bulky ligands makes this step scarcely the rate limiting one, and in these large ligands the steric constraints have been noted to govern over the electronic.[25] The understanding that has now been gained from these catalytic systems has enabled the design of catalysts for use in cross-coupling reactions.

Attractive features of the cross-coupling reaction include the low catalytic amounts of palladium catalyst needed and the reaction progressing regio- and stereoselectively. The use of a base is essential to enable the coupling to occur, in particular to accelerate the transmetallation step. The reaction has been found to be unaffected by water and can tolerate a variety of functional groups. Examples of known Suzuki catalysts include $Pd(PPh_3)_4$, $Pd(OAc)_2$ and $Pd(dba)_2$. These complexes have been reported to be good

catalysts for reactions involving porphyrins, halopyridines, aryl halides and phenanthrolines.[6]

On closer inspection of the formation of biaryls, the two catalysts Pd(OAc)$_2$ and Pd(PPh$_3$)$_4$ have been reported to be very useful. The first was used by Campi and co-workers[28] to produce mono-ortho substituted biaryls at 20 °C. The latter has found use in the coupling of iodobenzene with mesitylboronic acid. Following attempts by Suzuki[29] at temperatures of 80-100 °C, more favourable conditions were found by Anderson and Namli[30] using 10% aqueous TlOH, DMA and a temperature of only 20 °C.

The coupling of porphyrins with β-arylsubstituted arylboronic acids was investigated by Chan in 1995, who reported excellent yields of Suzuki product (>65%) using Pd(PPh$_3$)$_4$ as the catalyst.[31] This versatile catalyst has also been used for the synthesis of pyrroles (95% yield) and halo-pyridines. Pd(dba)$_2$ has been employed for the coupling of aryl fluoroalkanesulfonates, [ArOSO$_2$(CF$_2$)$_n$CF$_3$] (an alternative to triflates), with boronic acids giving good yields.[32] This phosphine-free catalyst has also been reported in the synthesis of 1,3-diarylpropenes.[33]

The use of N-heterocyclic carbene (NHC) ligands in Suzuki coupling was first reported in 1998 by Hermann and his group.[34] Subsequent investigations centred on the coupling of unactivated aryl chlorides with boronic acids, using bulky ligands with two large groups such as iMes and iPr.[15,35,36] These reactions were found to be successful and encouraged others to concentrate on this type of work. In 2003 NHC palladacycle complexes were synthesised which have shown good potential as catalyst precursors for cross-coupling reactions.[37-39]

4.1.2 Catalyst preparation and testing

The field concerning the use of complexes in catalytic applications is constantly growing and advancing. Complexes that possess only one donor atom that is phosphorus can be used as bidentate systems. These systems are suitable candidates for catalytic precursors. Chemically P,O- P,N- and P,S- ligands hold steric and electronic advantages over di-phosphines such as DIOP and BINAP, due to their mixed donor atom nature. This

feature has implications on the electronic properties of the ligands which in turn influences the trans effect of the system.

A range of P, S ligands were synthesised by our group (Scheme 3) and complexed onto palladium, as discussed in Chapter 2. The catalytic performance of the resulting P,S-palladium complexes has been tested in Suzuki reactions.

$$\text{KL}^1$$

$$\text{L}^1\text{Me} \quad (R = Me)$$
$$\text{L}^1\text{Bn} \quad (R = benzyl)$$
$$\text{L}^1\text{Xyl} \quad (R = CH_2\text{-}3,5\text{-xylene})$$
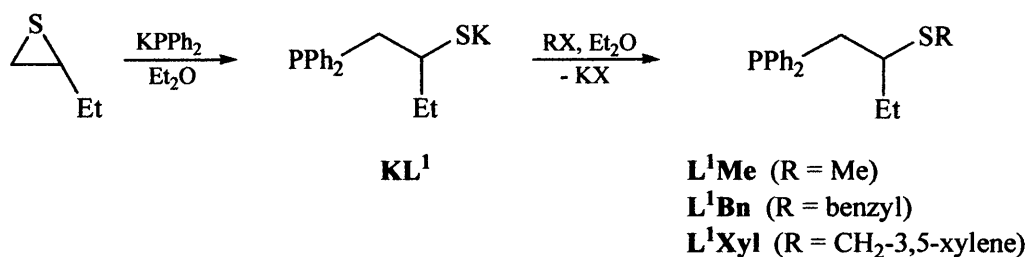
Scheme 3. Ligands synthesis.

The phosphino-thioether complexes **4** and **5,** and -thiolate complexes **1** and **2** (Fig 1) are air, water and thermally stable, enabling reactions to be carried out aerobically and at temperatures of up to 150 °C. The reagents and solvents used in the cross-coupling reactions were undistilled.

We have studied the Suzuki coupling of bromobenzene, 4-bromotolune, 2-bromotoluene, 4-bromoacetophenone and 4-chloroacetophenone with benzene boronic acid, using complexes **1, 2, 4** and **5** as catalyst precursors. Herein we report our progress in utilising these complexes for the Suzuki-Miyaura reaction.

4.2 Results and Discussion

4.2.1 C-C coupling of bromobenzene with benzene boronic acid

The cross-coupling reactions of bromobenzene were found to proceed best in dioxane with TONs of up to 1.98×10^{10} and yields of up to 100% (Table 1, Run 12). The reactions reported in Table 1 were performed in varying media and conditions (base, temperature and catalyst) and demonstrate the efficiency of the coupling reaction.[40]

Table 1. Suzuki couplings[a] of bromobenzene with phenylboronic acid.

Run	Base	Catalyst[d] (mol %)	T (°C)	TON[e]	TON[f]	Yield[g] (%)	Yield[h] (%)	TOF[i] (h⁻¹)
1[b]	K_2CO_3	4 (0.01)	110	0	1200	0	12	0
2[b]	K_2CO_3	1 (0.01)	110	2100	2400	21	24	3.5
3	K_2CO_3	4 (0.005)	110	1600	4600	8	23	1.3
4	K_2CO_3	1 (0.005)	110	0	12600	0	63	0
5	K_2CO_3	4 (0.01)	140	9400	9700	94	97	15.7
6	K_2CO_3	1 (0.01)	140	9900	10000	>99	100	3290
7[c]	K_2CO_3	4 (0.005)	140	20000	-	100	-	16.7
8[c]	K_2CO_3	1 (0.005)	140	20000	-	100	-	16.7
9	Cs_2CO3	1 (0.01)	110	-	1800	-	18	-
10	Cs_2CO_3	1 (0.01)	140	-	10000	-	100	-
11[j]	K_2CO_3	1 (5×10^{-7})	140	1.96×10^8	-	>98	-	1.96×10^8
12[k]	K_2CO_3	1 (5×10^{-9})	140	1.98×10^{10}	-	>99	-	3.96×10^{10}

[a]Determined by GC. Reaction conditions: ArBr (5mmol), $PhB(OH)_2$ (7mmol), base (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL); [b]ArBr (7 mmol), base (5 mmol); [c]Reaction stopped after 6 hours; [d][Pd(Ph₂PCH₂CH(Et)S)I]₂ (1), Pd(Ph₂PCH₂CH(Et)SMe)Cl₂ (4); [e]TON at 6 hours = turnover number (mol product. mol⁻¹ catalyst); [f]TON at 24 hours = turnover number (mol product. mol⁻¹ catalyst); [g]Yield at 6 hours; [h]Yield at 24 hours; [i]TOF at 3 hours = turnover frequency (mol product. mol⁻¹ catalyst. h⁻¹); [j]Reaction complete in 1 hour; [k]Reaction complete in ½ hour.

In our search for optimal reaction conditions, we examined, amongst other parameters, the effect of temperature. As can be seen from Table 1, in some cases reactions had run

to completion within 1 hour at 140 °C (Runs 11 and 12). Hence using only 5 x 10⁻⁹ mol % Pd catalyst **2** (Run 12) our best result can be reported.

4.2.1.1 Temperature effect

Investigations concerning the cross-coupling of bromobenzene with benzene boronic acid were initially carried out at a temperature of 110 °C. At this temperature catalysts **1** and **4** were seen to be active but coupling reactions were rather slow (Table 1, Runs 3 and 4 reached 23% and 63% conversion respectively at 24 hours). However, the increase of temperature to 140 °C caused a dramatic change in the rate of reaction. As can be seen from Figure 2 the reactions performed at 140 °C finished in less than 6 hours, a much more impressive result than at 110 °C.
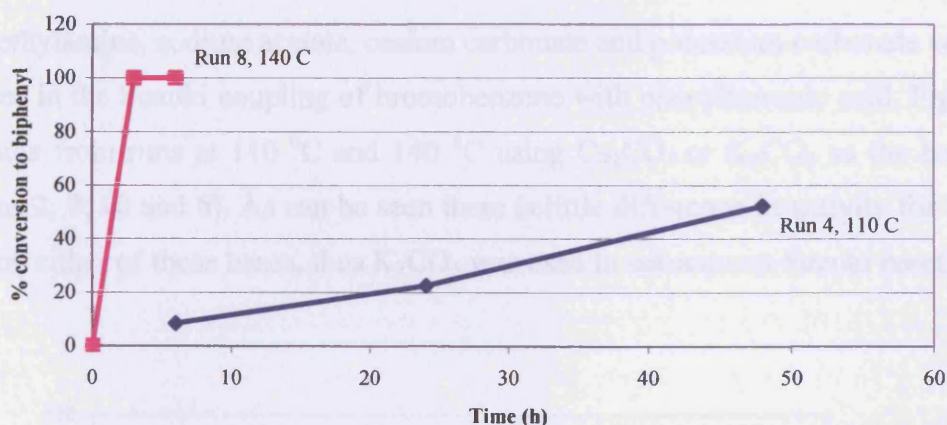
Fig 2. Comparison of temperatures (110 °C and 140 °C) for catalyst **1** (0.005 mol %). [a]Determined by GC. Reaction conditions: PhBr (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

Closer comparison of the two temperatures studied further outlines the difference in coupling observed between 110 °C (Table 1, Run 4, 63% yield after 24 hours) and 140 °C (Table 1, Run 8, 100% yield in less than 6 hours). The increase of 30 °C radically enhances the reaction rate. An increase of around 100% is noticeable at t = 6 hours, where the coupling reaction has reached completion for 140 °C (approximately 100%) but is considerably slower for 110 °C (negligible percentage of product formation). Reports have recently commented on the formation of soluble colloidal palladium at temperatures above 130 °C.[41,42] The colloidal palladium particles have shown activity in

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Suzuki reactions, hence suggesting that a different catalytic system may be involved for our runs between the two temperatures tested, 110 °C and 140 °C.

4.2.1.2 Base effect

The effect of base on cross-coupling reactions has been well documented. Strong bases, such as potassium t-butoxide, attain high yields of product, whereas other bases, such as sodium hydroxide, have proved not so desirable. Previous studies by Zhang and Chan revealed that rates were increased by use of a strong base (potassium t-butoxide, KOt-Bu, gave 86% yield in 4h). This result was reported for the Suzuki coupling of a range of halo-pyridines with a sterically bulky arylboronic acid.[43] Zhang later investigated the cross-coupling of bromobenzene with benzene boronic acid, testing a variety of bases (again reporting KOt-Bu to be the best) and finding that 3 equivalents of base were needed, as with only 1.5 equivalents the recorded yield was low (15%).[44]

Triethylamine, sodium acetate, cesium carbonate and potassium carbonate were tested as bases in the Suzuki coupling of bromobenzene with phenylboronic acid. Figure 3 shows results from runs at 110 °C and 140 °C using Cs_2CO_3 or K_2CO_3 as the base (Table 1, Runs 2, 9, 10 and 6). As can be seen there is little difference in activity for the reactions using either of these bases, thus K_2CO_3 was used in subsequent Suzuki reactions.
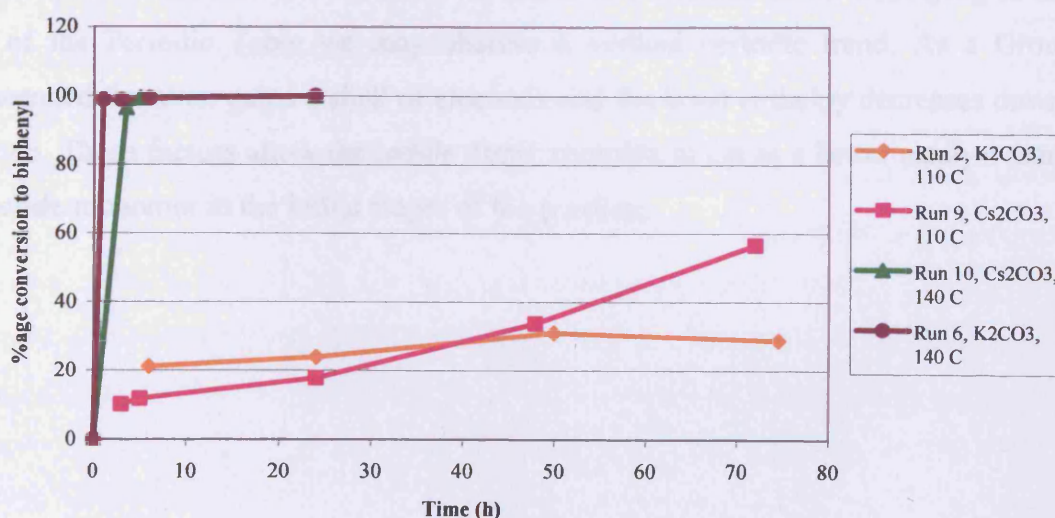
Fig 3. Comparison of base for catalyst **1** (0.01 mol %). Determined by GC. Reaction conditions: ArBr (5mmol), PhB(OH)$_2$ (7mmol), base (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

Inorganic bases, such as Cs_2CO_3 and K_2CO_3, are usually preferred over organic ones, such as NEt_3 and NaOAc, since they are thought not to interact with the benzene boronic acid. The activity of Cs_2CO_3 has been previously reported to be high.[1,45,46] This has acted to prove that base is an important entity in the reaction cycle (β-hydride elimination step), with its presence believed to be essential for the transmetallation step. It acts as a nucleophilic species, hence increasing the nucleophilicity of the borane group.[47] The base plays the role of a negatively charged nucleophile which can react with an organic halide or triflate, and undergo a Suzuki reaction.

In the transmetallation step, the action of the base is believed to involve the attack of the B-C bond, making the carbon atom nucleophilic. If the halide group (X) is I then the rate-limiting step is transmetallation, but if X = Br or Cl then the rate-limiting step is oxidative addition.[48]

4.2.1.3 Catalyst investigation

On a preliminary survey of the cross-coupling of bromobenzene with benzene boronic acid we found that both pre-catalyst **1** (iodide dimer) and pre-catalyst **4** (chloride monomer) reach similar yields after 72 hours, as shown in Figure 4 at 110 °C (Table 1, Runs 1 and 2). However, initial reaction rates with the catalyst system based on complex **1** are much faster than with complex **2**. This is probably due to the iodide being a more labile species than the chloride. With the iodine and chlorine atoms both lying in Group 17 of the Periodic Table we may observe a vertical periodic trend. As a Group is descended the atom gains a shell of electrons and the bond enthalpy decreases down the Group. These factors allow the iodide dimer complex to act as a better catalyst than the chloride monomer in the initial stages of the reaction.
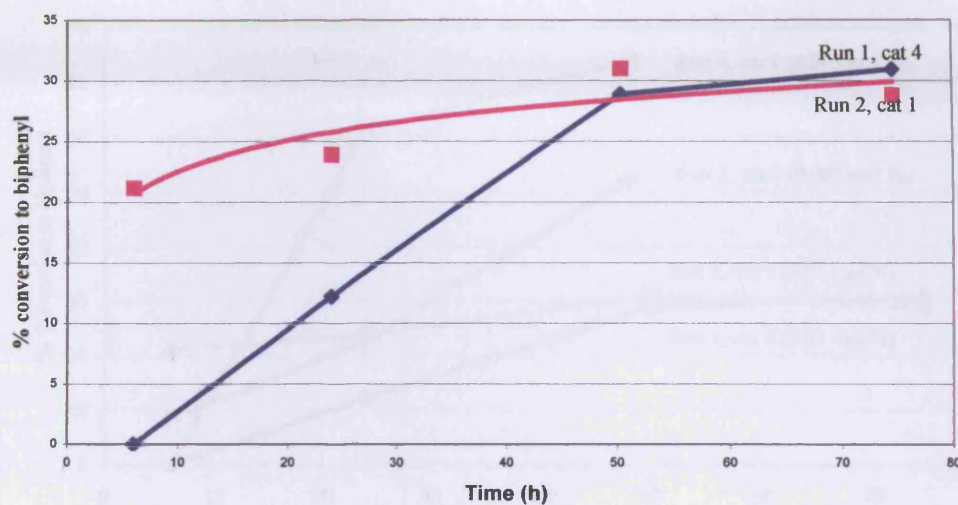
Fig 4. Comparison of catalyst **1** and **4** (0.01 mol %) at 110 °C. [a]Determined by GC. Reaction conditions: PhBr (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

These two pre-catalysts were also compared at 140°C and it was noted that pre-catalyst **1** was again slightly more active than pre-catalyst **4**. For the coupling of bromobenzene using the catalysts at 0.01 mol % (Table 1, Runs 5 and 6), after 6 hours the percentage conversions were 94% and 100% respectively.

Interestingly, the rate of conversion to biphenyl is faster as the catalyst percentage is lowered (from 0.01 mol % to 0.005 mol %) as shown in Figure 5 at 110 °C. Hence, by halving the Pd mol % a pronounced increase in catalytic activity can be observed. Essentially, this decrease in catalyst concentration more than doubles the yield of biphenyl formed, at any given time (for pre-catalyst **1**, when t = 48 hours the yield increases from 30% to 74%). A notable increase in the percentage conversion to the biphenyl product is also seen for catalyst **4**. This could be due to the optimum catalyst percentage being at 0.005 mol %, and above this percentage the extra catalyst present can not speed up the reaction further, and catalyst deactivation may slowly start to occur.
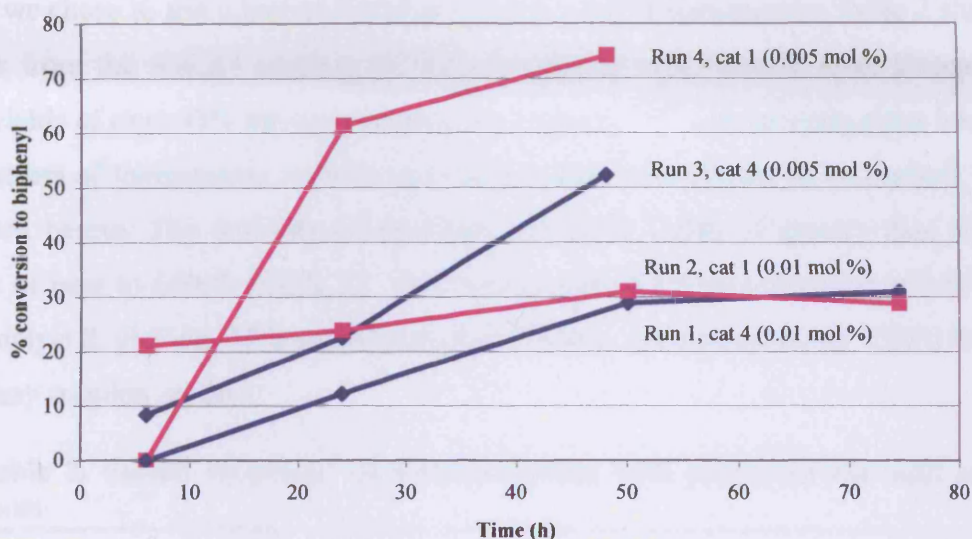
Fig 5. Comparison of catalyst percentages for **1** and **4** at 110 °C. [a]Determined by GC. Reaction conditions: ArBr (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

The analogous experiment was performed at 140 °C for pre-catalysts **1** and **4** (Table 1, Runs 5-8). On examining the catalytic activity of pre-catalysts **1** and **4** it becomes evident that the percentage dependence is normal. Hence, the lower the catalyst percent used the lower the rate of generation of coupling product. However due to the accelerated rates at this higher temperature the comparison of yields is difficult (Run 6, **1** (0.01 mol %) the yield after 1 hour = 98.7%; Run 11, **1** (5 x 10^{-7} mol %) the yield after 1 hour = 98.3%).

Catalyst levels as low as 5 x 10^{-9} mol % Pd have been achieved in the Suzuki coupling of bromobenzene at 140 °C. In this case 100% conversion had been reached in 30 minutes. Catalysts **1, 2, 4** and **5** show excellent catalytic activities at 140 °C. Complexes were tested for the cross-coupling of 4-bromotoluene with catalyst loadings of 0.0025 mol %. After 3 hours in all but one case (that of catalyst **2**, the chloride thiolate) the percentage conversion of 4-bromotoluene was above 80%. Previous research indicated low-coordinate phosphine complexes showed the optimum activity for Suzuki coupling of chlorides.[46]

4.2.2 C-C coupling of 4-bromotoluene with benzene boronic acid

Next, we chose to test a less activated aryl halide than bromobenzene. Table 2 shows our results from the Suzuki coupling of 4-bromotoluene with boronic acid. Exceptionally high yields of over 95% have previously been quoted. [45,49] Our investigations lead to the parameters of temperature, solvent and catalyst type and percent to be studied, and are reported herein. The majority of reactions produced yields of greater than 65% and TONs of near to 60000 (Table 2). Our lowest mol % Pd was recorded at 0.00125 for pre-catalyst **2**, yielding 73% conversion after 6 hours. An attempt using 0.0001% did not form any coupled product.

Table 2. Suzuki couplings[a] of 4-bromotoluene with phenylboronic acid at 6 hours

Me—⟨ ⟩—Br + ⟨ ⟩—B(OH)₂ ⟶ Me—⟨ ⟩—⟨ ⟩

Run	Base	Catalyst[b] (mol %)	Solvent	T (°C)	TON[c]	TOF[d] (h⁻¹)	Yield (%)
13	K_2CO_3	1 (0.0025)	Dioxane	110	35500	1100	71
14	K_2CO_3	1 (0.0025)	Dioxane	120	50000	14417	96
15	K_2CO_3	1 (0.0025)	Dioxane	130	50000	15900	100
16	K_2CO_3	1 (0.0025)	Dioxane	140	50000	16467	100
17	K_2CO_3	1 (0.0025)	Dioxane	150	50000	16333	100
16	K_2CO_3	1 (0.0025)	Dioxane	140	50000	16467	100
18	K_2CO_3	1 (0.0025)	DME	140	33500	10450	67
19	K_2CO_3	1 (0.0025)	DMA	140	8500	2817	17
20	K_2CO_3	1 (0.0025)	Glycol[e]	140	47500	13817	95
21	K_2CO_3	4 (0.0025)	Dioxane	140	45500	14217	91
16	K_2CO_3	1 (0.0025)	Dioxane	140	50000	16467	100
22	K_2CO_3	2 (0.0025)	Dioxane	140	42000	8367	84
23	K_2CO_3	5 (0.0025)	Dioxane	140	49500	13850	99
24	K_2CO_3	5 (0.0025)[g]	Dioxane	140	49500	11813	>99
25	K_2CO_3	1 (0.00125)	Dioxane	140	58400	7273[f]	73
26	K_2CO_3	1 (0.002)	Dioxane	140	30000	9167	60
27	K_2CO_3	1 (0.001)	Dioxane	110	96000	21667	96
28	K_2CO_3	4 (0.001)	Dioxane	110	94000	27333	94

[a]Determined by GC. Reaction conditions: 4-bromotoluene (5mmol), $PhB(OH)_2$ (7mmol), K_2CO_3 (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL); [b] $[Pd(Ph_2PCH_2CH(Et)S)I]_2$ (**1**), $[Pd(Ph_2PCH_2CH(Et)S)Cl]_2$ (**2**), $Pd(Ph_2PCH_2CH(Et)SMe)Cl_2$ (**4**), $Pd(Ph_2PCH_2CHEtSCH_2C_8H_9)Cl_2$ (**5**); [c]TON = turnover number (mol product. mol⁻¹ catalyst); [d]TOF at 3 hours = turnover frequency (mol product. mol⁻¹ catalyst. h⁻¹); [e]Glycol = di(ethylene glycol)diethyl ether; [f]Result at 3.3 hours; [g]KI (5mmol).

4.2.2.1 Temperature effect

Investigations of the temperature effect in 4-bromotoluene cross-couplings prompted runs between 110 and 150 °C (at 10 °C intervals; Table 2, Runs 13-17). On analysing the data from the runs at 110 to 140 °C, the effect on the rate of conversion was seen to increase as the temperature increased, as shown in Figure 6; When the 150 °C run was carried out, although 100 % conversion was reached in less than 6 hours, the activity was not faster than 140 °C. This indicates that the optimum temperature for runs with catalyst **2** was at 140 °C and above this temperature no further increase in catalytic activity occurs. A previous study of the Suzuki coupling of chloroarenes by Indolese revealed high conversions (67%) at 95 °C but low conversions (2%) at 130 °C, indicating fast catalyst decomposition at the higher temperature. The reaction rate was also noted to be slow at room temperature (2% conversion).[50]
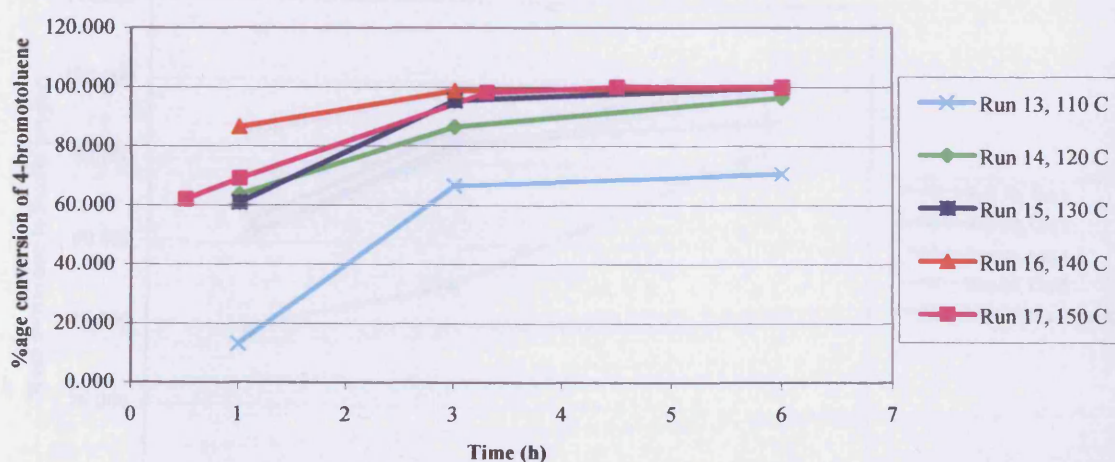
Fig 6. Comparison of temperatures using catalyst **1** (0.0025 mol %). Determined by GC. Reaction conditions: 4-bromotoluene (5mmol), PhB(OH)$_2$ (7mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

Previous investigations involving the effect of temperature on Suzuki cross-coupling reactions has shown a desire for high temperatures, typically around 80-100 °C, to promote the reaction.[30,50-52] However the continual demand for more favourable reaction conditions has called for the use of lower temperatures. Zhang and Shi have utilised a P,S-heterodonor ligand along with Pd(dba)$_2$ in the coupling of aryl bromides and iodides with benzene boronic acids, at temperatures of 60-80 °C. Using 1 mol % Pd(dba)$_2$

excellent yields of up to 90% were attained and reactions ran to completion in 4-6 hours.[44]

4.2.2.2 Catalyst investigation

Pre-catalysts **1** and **4** were extremely efficient catalysts in the coupling of 4-bromotoluene with benzene boronic acid, with reactions reaching >99% conversion in 3 hours (0.0025 mol % catalyst; Table 2, Runs 16 and 21) as shown in Figure 7. Following this, pre-catalysts **2** and **5** (Table 2, Runs 22 and 23) were tested and both showed excellent catalytic activity at 140 °C. KI was added to an arylation of 4-bromotoluene using pre-catalyst **5** (Table 2, Run 24), to observe whether this would result in a more active catalyst. The pre-catalyst was noted to be slightly more active than when used on its own, however pre-catalyst **1** was the most active catalyst tested.
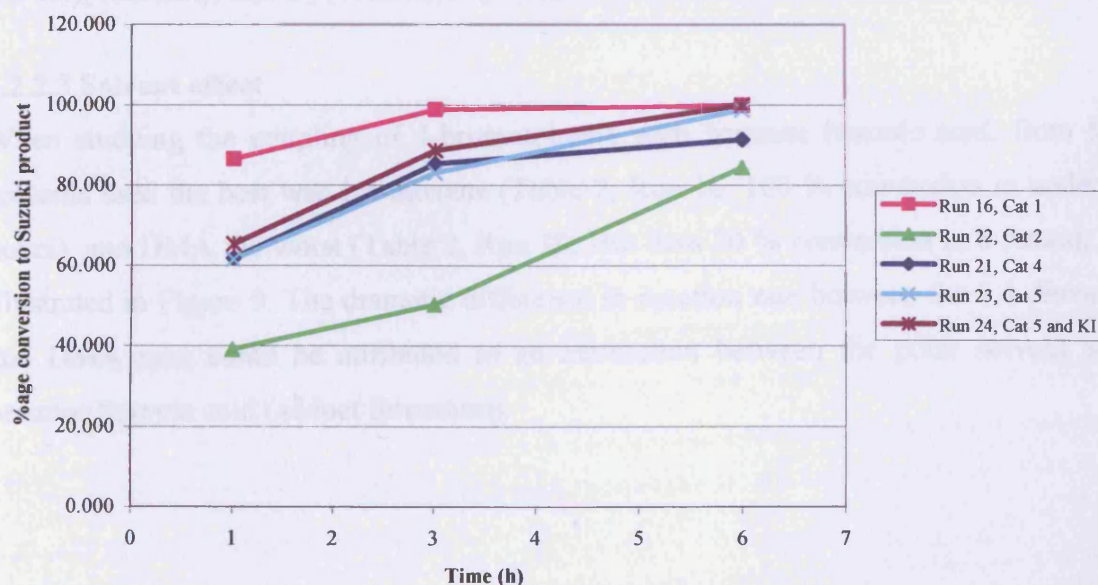
Fig 7. Comparison of catalysts (0.0025 mol %) at 140 °C. Determined by GC. Reaction conditions: 4-bromotoluene (5mmol), PhB(OH)₂ (7mmol), K₂CO₃ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL). For Run 24 KI (5mmol).

Comparison of pre-catalysts **1** and **4** at 110 °C revealed the iodide dimer **1** to be a more active catalyst than the chloride monomer **4**. This was attributed to the iodide **1** being more labile than the chloride **4** (as previously mentioned for the bromobenzene couplings) due to the relative positions of iodine and chlorine. Figure 8 illustrates this

for the coupling of 4-bromotoluene with benzene boronic acid at 110 °C (Table 2, Runs 27 and 28).
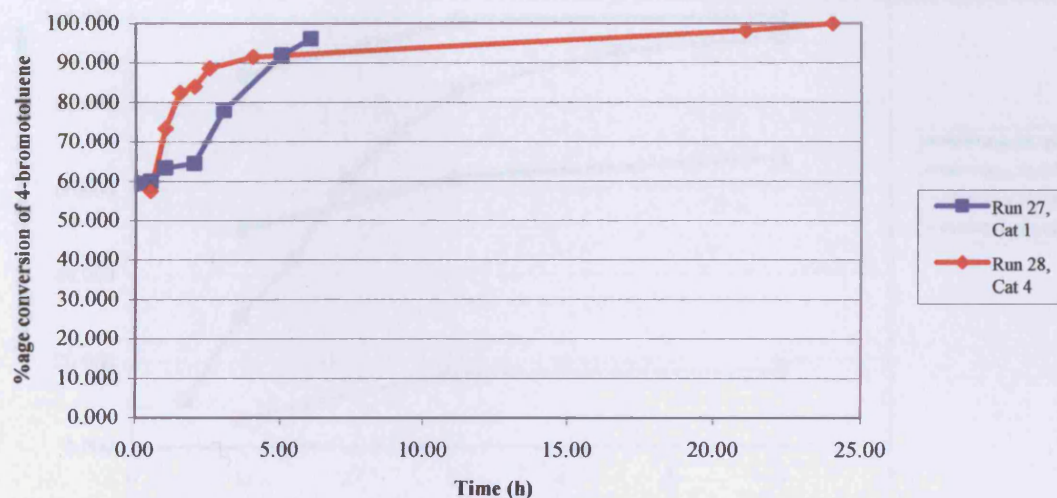
Fig 8. Comparison of catalysts **1** and **4** (0.001 mol %) at 110 °C. for the coupling of 4-bromotoluene Determined by GC. Reaction conditions: 4-bromotoluene (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

4.2.2.3 Solvent effect

When studying the coupling of 4-bromotoluene with benzene boronic acid, from the solvents used the best was 1,4-dioxane (Table 2, Run 16, 100 % conversion in under 6 hours), and DMA the worst (Table 2, Run 19, less than 20 % conversion in 6 hours), as illustrated in Figure 9. The dramatic difference in reaction rate between the 1,4-dioxane and DMA runs could be attributed to an interaction between the polar solvent and benzene boronic acid (adduct formation).
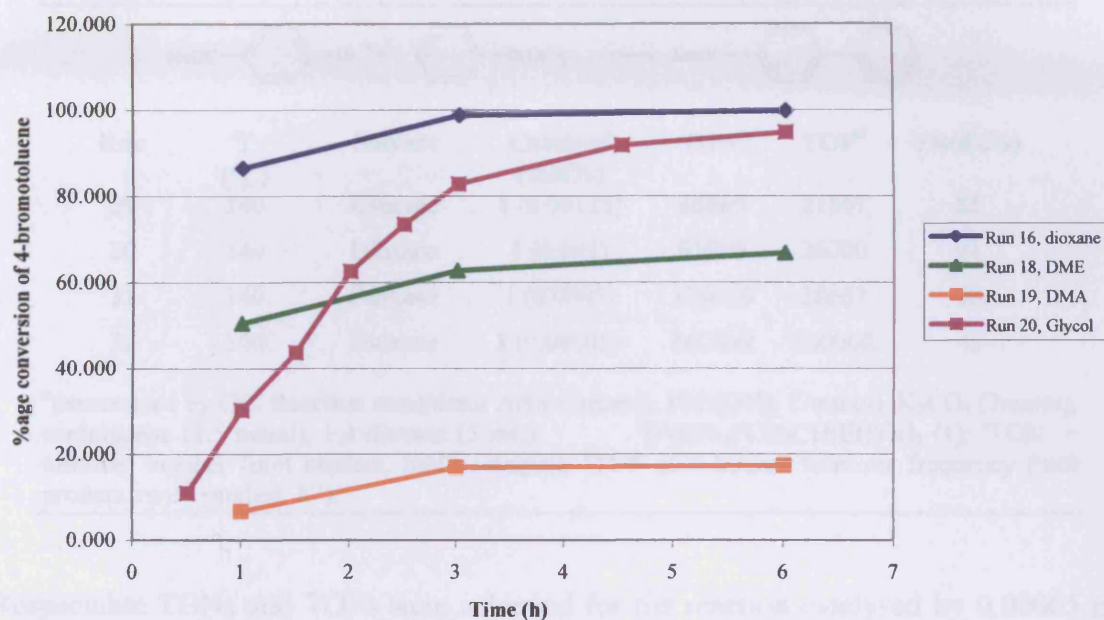
Fig 9. Comparison of solvents using catalyst **1** (0.0025 mol %) at 140 °C. Determined by GC. Reaction conditions: 4-bromotoluene (5mmol), PhB(OH)$_2$ (7mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), solvent (5 mL); DMA = dimethylacetamide, glycol = di(ethylene

Other researchers have previously shown that coupling reactions were optimised by using dioxane as the solvent.[1,45,46,50,53,54] Bedford and co-workers reported that changing the base to cesium carbonate (instead of potassium phosphate) and the solvent to dioxane (instead of toluene) yielded a much more desirable catalyst system. The new system was especially efficient at lower catalyst loadings.[46] However, Anderson and Namli tested the coupling reaction of iodobenzene with mesitylboronic acid using a range of solvents. Of those assessed, DMA was noted to give the best yield of product (92%), followed by DMF (68%). 1,4-dioxane gave a poor yield of product, at only 48%. The difference in performance of the two best solvents could not be explained.[30]

4.2.3 C-C coupling of 4-bromoacetophenone with benzene boronic acid

A number of coupling reactions were performed with 4-bromoacetophenone. It was anticipated that reactions with this substrate would progress with good catalytic efficiency, as couplings to date have shown.[49,52,55-58] Yields of 75% with 0.001 mol % catalyst[6] have been reported previously for this substrate. In the case of our P, S catalysts, reactions proceeded successfully with complex **1**,[40] as is shown in Table 3.

Table 3. Suzuki couplings[a] of 4-bromoacetophenone with phenylboronic acid at 6 hours.
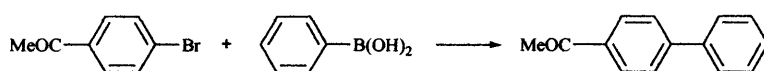
Run	T (°C)	Solvent	Catalyst[b] (mol%)	TON[c]	TOF[d]	Yield (%)
29	140	Dioxane	1 (0.00125)	68000	21867	85
30	140	Dioxane	1 (0.001)	91000	26000	91
31	140	Dioxane	1 (0.0005)	116000	28667	58
32	140	Dioxane	1 (0.00005)	860000	260000	43

[a]Determined by GC. Reaction conditions: ArBr (5mmol), $PhB(OH)_2$ (7mmol), K_2CO_3 (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL); [b]$[Pd(Ph_2PCH_2CH(Et)S)I]_2$ (1); [c]TON = turnover number (mol product. mol^{-1} catalyst); [d]TOF at 3 hours= turnover frequency (mol product. mol^{-1} catalyst. h^{-1}).

Respectable TONs and TOFs were achieved for the reaction catalysed by 0.00005 mol % pre-catalyst 1 (Table 3, Run 32). The yield after 6 hours however was less than 50%. The highest yield achieved from the four runs was recorded as 91%, obtained using 0.001 mol % pre-catalyst 1 (Table 3, Run 30). This is a noteworthy result when comparing it to previous literature.

4.2.3.1 Catalyst effect

At 140 °C the results from our catalyst investigations indicate that reactions with 4-bromoacetophenone afford the desired product in respectable times (6 hours using 0.001 mol % catalyst). The performance of pre-catalyst 1 at varying percentages was monitored for the first 6 hours and the results are presented in Figure 10 (Table 3, Runs 29-32). The results followed the expected correlation, with the minor exception that the highest mol % of pre-catalyst (0.00125 mol %) did not reveal the highest yield of product. Instead, the best yield was obtained by using 0.001 mol % of catalyst 1, indicating that this may be the optimum catalyst percent (for pre-catalyst 1) for the coupling of 4-bromoacetophenone with benzene boronic acid.
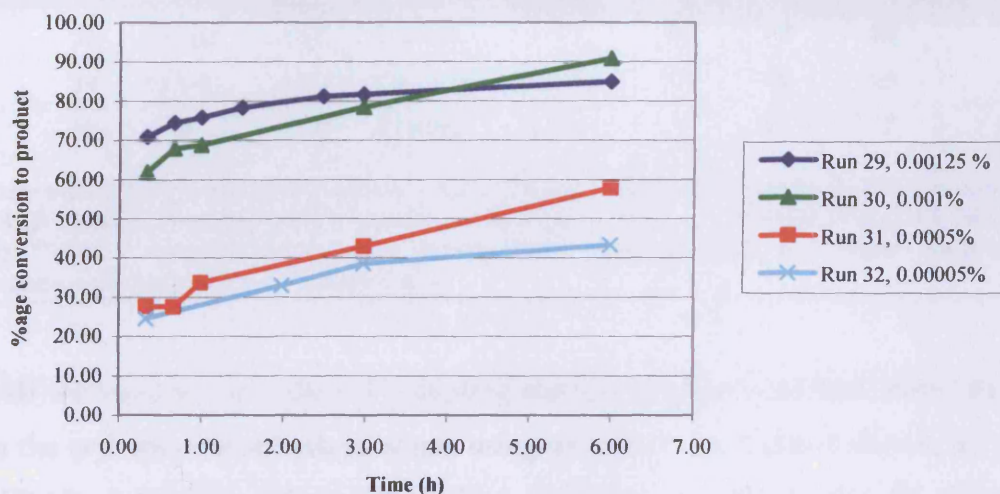
Fig 10. Comparison of catalyst percentages for catalyst **1** at 140 °C. Determined by GC. Reaction conditions: 4-bromoacetophenone (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

4.2.4 C-C coupling of aryl chlorides with benzene boronic acid

Coupling reactions with widely available aryl chlorides offer a cheaper and hence more attractive option for the synthesis of biaryls, than with their bromide counterparts. Aryl chlorides are less reactive than the analogous iodides and bromides, and a substantial amount of energy is needed to promote the oxidative insertion of the palladium catalysts in to the C-Cl bond.[59] The reaction can be inefficient if the aryl halide does not possess electron withdrawing substituents. The position of the electron withdrawing group also plays an important role in the coupling reaction. The group being in the meta position proved to make the aryl chloride less reactive, whereas an electron withdrawing group in the ortho or para positions was far more favourable.[59] There have been limited reports on the room temperature Suzuki cross-coupling reactions of aryl chlorides. Our investigations centred on the two substrates chlorobenzene and 4-chloroacteophenone.[40] Table 4 presents the results acquired using 1 equivalent of TBAB in the reaction.

Table 4. Suzuki couplings[a] of aryl chlorides with phenylboronic acid at 6 hours

Run	R	T (°C)	Solvent	Catalyst[b] (mol%)	TON[c]	TOF[d]	Yield (%)
33	COMe	140	Dioxane	1 (1)	86	1.9	86
34	COMe	140	Dioxane	1 (0.5)	32	40	16
35	H	140	Dioxane	1 (1)	2	0.7	2

[a]Determined by GC. Reaction conditions: ArCl (5mmol), PhB(OH)$_2$ (7mmol), K$_2$CO$_3$ (7mmol), TBAB (5mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL); [b][Pd(Ph$_2$PCH$_2$CH(Et)S)I]$_2$ (1); [c]TON = turnover number (mol product. mol^{-1} catalyst); [d]TOF at 3 hours= turnover frequency (mol product. mol^{-1} catalyst. h^{-1}).

TBAB was used to aid in the C-C coupling reaction as prior work had shown no product with the aryl chloride substrates alone, using catalyst 1. As Table 4 shows, the addition of TBAB drastically influenced product formation. In effect, the Br from TBAB replaced the Cl atom on the aryl chloride hence offering a more favourable path for the coupling reaction to take. Another possibility is that colloidal Pd could form stable TBAB-Pd and couple aryl chlorides.

Reports have also discussed the reactivity of nickel catalysts, which have shown good catalytic activity for the C-C coupling of unactivated aryl chlorides.[53,60] Their reactivity was at first only shown when they were combined with a reducing agent[61,62] but since then a method has been found that allows the coupling of chloroarenes with arylboronic acids, without the need of a reducing agent.[50]

4.2.5 C-C coupling of 4-chloroacetophenone with benzene boronic acid

The C-C coupling of 4-chloroacetophenone with benzene boronic acid was attempted at both 110 and 140 °C with catalyst 1. Loadings of Pd of up to 1 mol % were used however no catalytic activity was seen. Aryl chlorides are desirable reagents, however accounts of their use as coupling reagents remains limited in comparison to aryl bromides. The lower reactivity of alkyl chlorides in comparison to bromides and iodides can be accredited to the decreased leaving-group ability of the chloride ion and/or the increased strength of the C-Cl bond (C-Cl : ≈ 79; C-Br : ≈ 66; C-I : ≈ 52 kcal mol^{-1}).[54]

Previous reports show the coupling of 4-chloroacetophenone with benzene boronic acid to be successful.[9,50,52,53,59] Other reports uncovered a method whereby utilisation of tetra-

n-butylammonium bromide (TBAB) along with the aryl chloride reagent for the Suzuki coupling, recovered a higher yield of product than with the aryl chloride alone.[5,52,63-66] Using TBAB and 1% of catalyst loading 86% yield was obtained for 4-chloroacetophenone (Table 4, Run 33). From the coupling of substituted aryl halides, biphenyl as a by-product was also produced. At the beginning of the reaction with 4-chloroacetophenone this was the dominant product, but after 3 hours the phenone biphenyl was the main product.

Prior work on the Heck coupling of 4-chloroacetophenone[67] has shown that the percentage conversion was improved with the addition of TBAB, from no conversion to 65%. Researchers have postulated that the addition of TBAB may have hindered palladium agglomerisation together with substitution of the chloride ligand with bromide.

4.2.6 Comparison of the different substrates in Suzuki reactions

Substrates that were tested by us in Suzuki coupling reactions at 110 °C included 2-bromotoluene, 4-bromotoluene and 4-chlorotoluene. The results obtained are presented in Table 5.

Table 5. Suzuki couplings[a] of various substrates with phenylboronic acid at 24 hours.

Run	X	Base	Catalyst[b] (mol%)	TON[c]	TOF[d]	Yield (%)
36	2-Br	K_2CO_3	4 (0.001)	81000	3375	81
37	2-Br	K_2CO_3	1 (0.001)	89000	3708	89
38	4-Br	K_2CO_3	1 (0.001)	100000	4167	100
39	4-Br	K_2CO_3	4 (0.001)	98000	4083	98
40	2-Br	K_2CO_3	4 (0.001)	81000	3375	81
41	4-Cl	K_2CO_3	1 (0.001)	39000	1625	39

[a]Determined by GC. Reaction conditions: ArX (5mmol), $PhB(OH)_2$ (7mmol), K_2CO_3 (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL); [b]$[Pd(Ph_2PCH_2CH(Et)S)I]_2$ (1), $Pd(Ph_2PCH_2CH(Et)SMe)Cl_2$ (4); [c]TON = turnover number (mol product. mol^{-1} catalyst); [d]TOF at 24 hours= turnover frequency (mol product. mol^{-1} catalyst. h^{-1}).

The coupling of 2-bromotoluene with benzene boronic acid has been investigated by other researchers.[44,57] Our investigations using pre-catalyst **1** indicated that the reaction was complete in less than 50 hours (Figure 11; Table 5, Runs 36 and 37). The data indicates the coupling of 4-bromotoluene is about 10 times faster than 2-bromotoluene (Figure 13; Table 5, Runs 39 and 40).
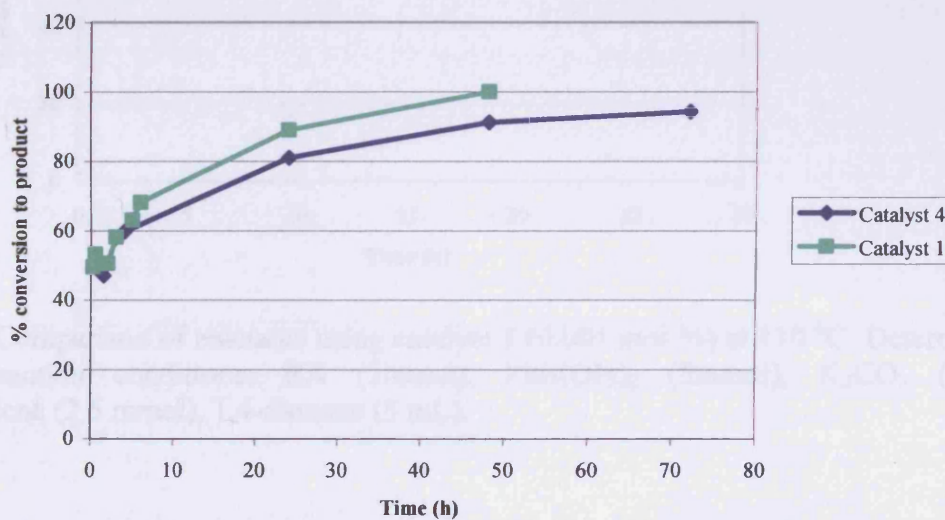
Fig 11. Comparison of catalysts **1** and **4** (0.001 mol %) at 110 °C for the coupling of 2-bromotoluene. Determined by GC. Reaction conditions: 2-bromotoluene (7mmol), $PhB(OH)_2$ (5mmol), K_2CO_3 (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

When comparing the two reagents 2-bromotoluene and 4-bromotoluene, it was found that 4-bromotoluene was consumed the quickest, as depicted in Figure 12 (Table 5, Runs 37 and 38), using catalyst **1**. This was the expected result due to the methyl and bromide being para to each other in the 4- substituent and hence a coupling reaction is more energetically favourable in this case. The analogous results are shown for catalyst **4** in Figure 13 (Table 5, Runs 39 and 40).
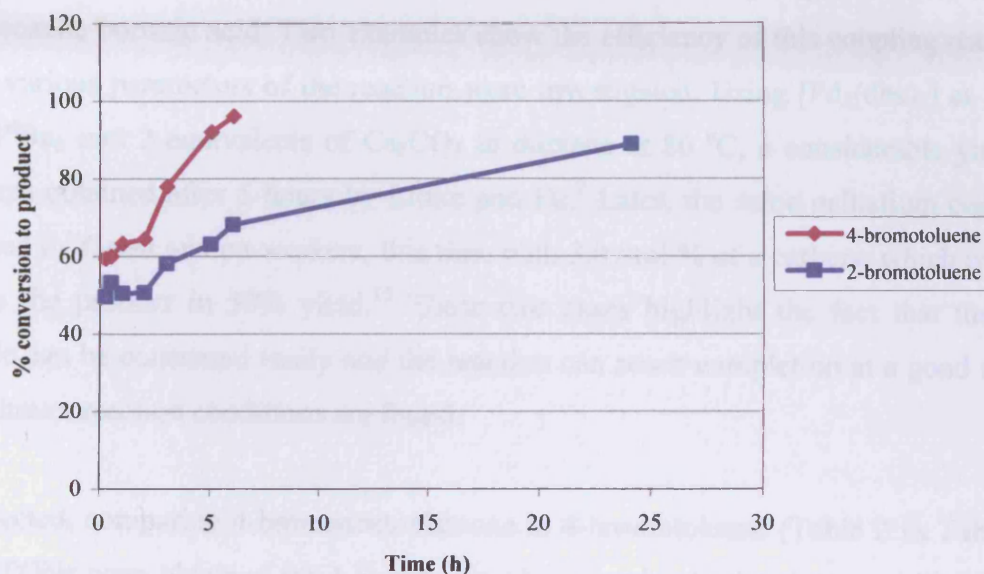
Fig 12. Comparison of reactants using catalyst **1** (0.001 mol %) at 110 °C. Determined by GC. Reaction conditions: RX (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).
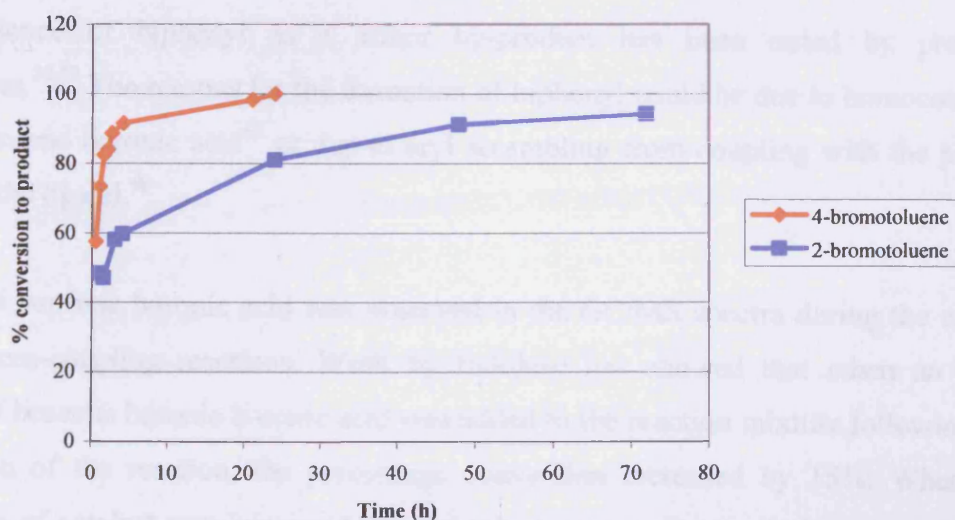
Fig 13. Comparison of reactants using catalyst **4** (0.001 mol %) at 110 °C. Determined by GC. Reaction conditions: RX (7mmol), PhB(OH)$_2$ (5mmol), K$_2$CO$_3$ (7mmol), naphthalene (2.5 mmol), 1,4-dioxane (5 mL).

4-bromotoluene and 2-bromotoluene were efficiently coupled in the presence of pre-catalyst **1** or **4**. However, when 4-chlorotoluene was used (Tabel 5, Run 41) little

coupling was observed. After 100 hours, 60% of the reactant still remained when catalysed with **1**. Previous research has shown the effective coupling of 4-chlorotoluene with benzene boronic acid. Two examples show the efficiency of this coupling reaction, where various parameters of the reaction were investigated. Using [Pd$_2$(dba)$_3$] at 1.5%, 3.6% P^{t}Bu$_3$ and 2 equivalents of Cs$_2$CO$_3$ in dioxane at 80 °C, a considerable yield of 86% was obtained after 5 hours by Littke and Fu.[9] Later, the same palladium complex was used by Grasa and co-workers, this time with 3.0 mol % of a carbene which reacted to give the product in 59% yield.[15] These two cases highlight the fact that the aryl chloride can be consumed easily and the reaction can reach completion at a good rate if the optimum reaction conditions are found.

As expected, comparing 4-bromoacetophenone to 4-bromotoluene (Table 2 vs Table 3), higher TONs were obtained for 4-bromoacetophenone, due to the electron-withdrawing effect of the R substituent (Table 3, Runs 29-32). Given the high reactivity of the catalyst we explored the possibility of lower catalyst at 0.00005 mol % Pd. Excellent results were obtained in this case (Table 3, Run 32).

4.2.7 GC comments

The presence of biphenyl as a minor by-product has been noted by previous researchers.[50,52] The reasons for the formation of biphenyl could be due to homocoupling of the benzene boronic acid[68] or due to aryl scrambling from coupling with the phenyl group of the ligand.[69]

Unreacted benzene boronic acid was observed in the GC/MS spectra during the course of the cross-coupling reactions. Work by Indolese has showed that when an extra amount of benzene boronic boronic acid was added to the reaction mixture following the completion of the reaction, the percentage conversion increased by 15%. When the percentage of catalyst was increased the percentage conversion again increased, but to not to such a large extent. These findings suggested the benzene boronic acid was being decomposed during the reaction.[50]

4.3 Conclusion

In conclusion, we have shown that the Suzuki cross-couplings of aryl halides with benzene boronic acid proceeds smoothly with P, S catalysts. Our catalyst systems yield the desired biphenyl product at high temperatures with K_2CO_3 as the base.

The reactions were noted to be clean with the expected product for the couplings identified by GC-MS. However a small amount of the homocoupled product, biphenyl, was also recorded during the runs with substituted aryl halides (<10%), formed by the homocoupling of benzene boronic acid.

Our investigations have reported the successful coupling of chlorobenzene and 4-chloroacetophenone with benzene boronic acid using 1 equivalent of TBAB. TBAB is believed to substitute one Br with a Cl from the aryl chloride, offering an energetically more favourable route for the C-C bond formation to take place. TBAB is also known to stabilise nano-sized transition metal colloids, which may be involved in the catalytic system.

Future work will involve the continuing investigation of novel active catalysts in Suzuki couplings, with particular attention being paid to chlorides. This will expand the scope of suitable substrates, and hence develop additional coupling processes.

4.4 Experimental

4.4.1 General procedure of coupling experiments

Reactions were performed in sealed pressure tubes. Reagents and solvents were used as received unless otherwise stated. A stock solution of Pd catalyst in DCM was prepared and the appropriate volume was added to the pressure tube. The DCM was evaporated. A solvent solution containing aryl halide, benzene boronic acid, base and standard were charged into the same pressure tube (quantities as stated for particular experiments). The pressure tube was sealed, heated and stirred at the stated temperature for the stated time. Samples (approximately 0.1 mL) were taken at set intervals during the reaction, filtered and extracted with water/DCM. Reagents and products were identified by GC/MS. Conversions and yields were quantified by GLC using naphthalene as internal standard.[67] Naphthalene was used as the internal standard.

4.4.2 Typical reaction conditions for Suzuki reactions with bromobenzene

Bromobenzene (0.53 mL, 5 mmol), benzene boronic acid (0.854 g, 7 mmol), base (7 mmol), naphthalene (0.320 g, 2.5 mmol), solvent (5 mL), Pd catalyst (5 x 10^{-9} – 0.01 mol% Pd), T = 110/140 °C, ½ - 24 h.

4.4.3 Typical reaction conditions for Suzuki reactions with 4-bromotoluene

4-bromotoluene (0.62 mL, 5 mmol), benzene boronic acid (0.854 g, 7 mmol), base (7 mmol), naphthalene (0.320 g, 2.5 mmol), solvent (5 mL), Pd catalyst (0.0025 – 0.01 mol% Pd), T = 110-140 °C, 3 - 24 h.

4.4.4 Typical reaction conditions for Suzuki reactions with 4-bromoacetophenone

4-bromoacetophenone (0.995 g, 5 mmol), benzene boronic acid (0.854 g, 7 mmol), K_2CO_3 (0.967 g, 7 mmol), naphthalene (0.320 g, 2.5 mmol), solvent (5 mL), Pd catalyst (0.00005 – 0.0125 mol% Pd), T = 140 °C, 6 h.

4.4.5 Typical reaction conditions for Suzuki reactions with 4-chloroacetophenone

4-chloroacetophenone (0.65 mL, 5 mmol), benzene boronic acid (0.854 g, 7 mmol), TBAB (g, 5 mmol), K_2CO_3 (0.967 g, 7 mmol), naphthalene (0.320 g, 2.5 mmol), solvent (5 mL), Pd catalyst (5 x 10^{-9} – 0.01 mol% Pd), T = 110/140 °C, ½ - 24 h.

4.4.6 Description of GC/MS analysis used for Suzuki reactions

Yields and substrate identities were determined by GC-MS analysis of reaction mixtures using an Agilent Technologies 6890N GC system with an Agilent Technologies 5973 inert MS detector with MSD. Column : Agilent 190915-433 capillary, 0.25 mm x 30 m x 0.25 µm. Capillary : 30 m x 250 µm x 0.25 µm nominal. Initial temperature at 50 °C, held for 4 minutes, ramp 5 °C/minute next 100 °C, ramp 10 °C/minute next 240 °C hold for 12 minutes. The temperature of the injector and the detector were held at 240 °C.

The retention times for analytes (in minutes), bromobenzene 8.1, 4-bromotoluene 11.2, naphthalene 15.85, 4-chloroacetophenone 17.2, 4-bromoacetophenone 18.3, biphenyl 19.5, stilbene 23.9, phenylboronic acid 30.9. Quantitative calculations of the reactant and product yields were made after GC calibration.

The instrument was used to monitor the formation of product / consumption of reactant during the course of the reaction. The method followed a slowed down version of the default Suzuki reaction method to enable analysis of low boiling analytes. 1 microlitre spitless injections of dilute samples (in dichloromethane) were passed into the column.

A number of samples of reactant and standard (naphthalene) in dichloromethane were run. The samples were made-up to recreate the conditions seen during the reaction i.e. the mass of the standard was kept constant throughout (0.320 g, 2.5 mmol) and the mass of reactant was varied (from 7 mmol to 2.5 mmol).

A calibration curve was plotted for the reactant (area of reactant / area of naphthalene vs moles of reactant) in order to determine the detector response factor (D_{RF}). D_{RF} = gradient of the graph.

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Appendix

Appendix

1. Data for complex 3, [PdPh₂PCH₂CHEtSI]₂

Table 1. Crystal data and structure refinement for ad0302.

Identification code	ad0302
Empirical formula	C32 H36 I2 P2 Pd2 S2
Formula weight	1013.27
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P bca
Unit cell dimensions	a = 14.50820(10) Å α = 90°.
	b = 16.0768(2) Å β = 90°.
	c = 29.9895(2) Å γ = 90°.
Volume	6994.91(11) Å³
Z	8
Density (calculated)	1.924 Mg/m³
Absorption coefficient	3.026 mm⁻¹
F(000)	3904
Crystal size	0.35 x 0.28 x 0.13 mm³
Theta range for data collection	2.98 to 30.06°.
Index ranges	-20<=h<=20, -22<=k<=22, -42<=l<=42
Reflections collected	76617
Independent reflections	10173 [R(int) = 0.1120]
Completeness to theta = 30.06°	99.1 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.576 and 0.436
Refinement method	Full-matrix least-squares on F²
Data / restraints / parameters	10173 / 0 / 379
Goodness-of-fit on F²	1.032
Final R indices [I>2sigma(I)]	R1 = 0.0367, wR2 = 0.0776
R indices (all data)	R1 = 0.0595, wR2 = 0.0860
Largest diff. peak and hole	0.991 and -1.256 e.Å⁻³

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2x 10^3) for ad0302. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7263(2)	-551(2)	5422(1)	20(1)
C(2)	7522(3)	228(2)	5573(1)	24(1)
C(3)	8273(3)	633(3)	5381(1)	31(1)
C(4)	8757(3)	266(3)	5038(1)	33(1)
C(5)	8505(3)	-512(3)	4886(1)	34(1)
C(6)	7759(3)	-924(3)	5076(1)	29(1)
C(7)	6484(3)	-1919(2)	5967(1)	22(1)
C(8)	7375(3)	-2217(2)	6001(1)	24(1)
C(9)	7551(3)	-2928(3)	6252(1)	29(1)
C(10)	6844(3)	-3332(3)	6466(1)	32(1)
C(11)	5951(3)	-3038(3)	6430(2)	39(1)
C(12)	5769(3)	-2325(3)	6186(1)	35(1)
C(13)	5706(2)	-1500(2)	5114(1)	20(1)
C(14)	4666(2)	-1611(2)	5152(1)	19(1)
C(15)	4232(2)	-1810(2)	4700(1)	24(1)
C(16)	4652(3)	-2573(3)	4479(2)	36(1)
C(17)	2743(3)	-1206(3)	7009(1)	35(1)
C(18A)	3473(12)	-1709(12)	6921(5)	28(3)
C(19A)	3807(13)	-2240(14)	7245(5)	81(9)
C(20)	3439(4)	-2274(5)	7657(2)	69(2)
C(21)	2717(5)	-1786(4)	7745(2)	69(2)
C(22)	2351(4)	-1263(4)	7422(2)	63(2)
C(23)	1062(3)	-510(3)	6581(1)	33(1)
C(24)	555(4)	-264(6)	6954(2)	82(3)
C(25)	-402(4)	-242(6)	6939(2)	83(3)
C(26)	-864(3)	-424(3)	6548(2)	47(1)
C(27)	-368(3)	-602(3)	6178(2)	40(1)
C(28)	585(3)	-655(3)	6195(1)	35(1)
C(29)	2597(3)	544(3)	6792(1)	35(1)
C(30)	3612(3)	735(3)	6696(1)	29(1)
C(31)	3909(3)	1622(3)	6815(2)	42(1)

C(32)	3993(4)	1737(5)	7316(2)	73(2)
I(1)	6065(1)	81(1)	6655(1)	27(1)
I(2)	2491(1)	-2177(1)	5769(1)	33(1)
P(1)	6198(1)	-1026(1)	5620(1)	18(1)
P(2)	2315(1)	-504(1)	6579(1)	28(1)
Pd(1)	5118(1)	-199(1)	5921(1)	17(1)
Pd(2)	3099(1)	-676(1)	5935(1)	20(1)
S(1)	3778(1)	585(1)	6090(1)	23(1)
S(2)	4179(1)	-604(1)	5345(1)	18(1)
C(19B)	4050(20)	-1847(17)	7304(9)	47(7)
C(18C)	3340(13)	-1991(10)	6905(6)	25(4)
C(18B)	3648(12)	-1375(11)	6962(6)	37(5)
C(19C)	3730(20)	-2535(18)	7211(11)	35(6)

Table 3. Bond lengths [Å] and angles [°] for ad0302.

C(1)-C(2)	1.383(5)	C(25)-C(26)	1.380(8)
C(1)-C(6)	1.399(5)	C(26)-C(27)	1.355(7)
C(1)-P(1)	1.823(4)	C(27)-C(28)	1.386(6)
C(2)-C(3)	1.395(5)	C(29)-C(30)	1.533(6)
C(3)-C(4)	1.377(6)	C(29)-P(2)	1.847(5)
C(4)-C(5)	1.382(6)	C(30)-C(31)	1.532(6)
C(5)-C(6)	1.391(6)	C(30)-S(1)	1.847(4)
C(7)-C(8)	1.382(5)	C(31)-C(32)	1.520(7)
C(7)-C(12)	1.391(5)	I(1)-Pd(1)	2.6349(4)
C(7)-P(1)	1.822(4)	I(2)-Pd(2)	2.6179(4)
C(8)-C(9)	1.391(5)	P(1)-Pd(1)	2.2436(9)
C(9)-C(10)	1.374(6)	P(2)-Pd(2)	2.2570(10)
C(10)-C(11)	1.383(6)	Pd(1)-S(2)	2.2947(9)
C(11)-C(12)	1.386(6)	Pd(1)-S(1)	2.3719(9)
C(13)-C(14)	1.524(5)	Pd(1)-Pd(2)	3.0273(4)
C(13)-P(1)	1.842(3)	Pd(2)-S(1)	2.3016(10)
C(14)-C(15)	1.528(5)	Pd(2)-S(2)	2.3679(9)
C(14)-S(2)	1.859(4)	C(19B)-C(18B)	1.40(3)
C(15)-C(16)	1.521(5)	C(18C)-C(19C)	1.39(4)
C(17)-C(18B)	1.348(19)		
C(17)-C(18A)	1.358(15)	C(2)-C(1)-C(6)	119.5(3)
C(17)-C(22)	1.366(6)	C(2)-C(1)-P(1)	120.2(3)
C(17)-C(18C)	1.562(18)	C(6)-C(1)-P(1)	119.9(3)
C(17)-P(2)	1.824(5)	C(1)-C(2)-C(3)	119.9(4)
C(18A)-C(19A)	1.38(2)	C(4)-C(3)-C(2)	120.5(4)
C(19A)-C(20)	1.345(17)	C(3)-C(4)-C(5)	120.0(4)
C(20)-C(21)	1.336(8)	C(4)-C(5)-C(6)	120.1(4)
C(20)-C(19C)	1.46(3)	C(5)-C(6)-C(1)	120.1(4)
C(20)-C(19B)	1.54(3)	C(8)-C(7)-C(12)	120.0(4)
C(21)-C(22)	1.387(8)	C(8)-C(7)-P(1)	122.0(3)
C(23)-C(28)	1.368(6)	C(12)-C(7)-P(1)	118.0(3)
C(23)-C(24)	1.397(7)	C(7)-C(8)-C(9)	119.8(4)
C(23)-P(2)	1.817(4)	C(10)-C(9)-C(8)	120.3(4)
C(24)-C(25)	1.390(8)	C(9)-C(10)-C(11)	120.1(4)

C(10)-C(11)-C(12)	120.1(4)	C(31)-C(30)-C(29)	114.4(4)
C(11)-C(12)-C(7)	119.7(4)	C(31)-C(30)-S(1)	108.3(3)
C(14)-C(13)-P(1)	111.8(2)	C(29)-C(30)-S(1)	106.5(3)
C(13)-C(14)-C(15)	111.5(3)	C(32)-C(31)-C(30)	111.5(5)
C(13)-C(14)-S(2)	107.3(2)	C(7)-P(1)-C(1)	108.81(17)
C(15)-C(14)-S(2)	107.6(2)	C(7)-P(1)-C(13)	103.41(16)
C(16)-C(15)-C(14)	112.9(3)	C(1)-P(1)-C(13)	103.53(16)
C(18B)-C(17)-C(18A)	25.9(9)	C(7)-P(1)-Pd(1)	113.38(12)
C(18B)-C(17)-C(22)	119.1(9)	C(1)-P(1)-Pd(1)	118.35(13)
C(18A)-C(17)-C(22)	117.4(7)	C(13)-P(1)-Pd(1)	107.82(11)
C(18B)-C(17)-C(18C)	43.7(9)	C(23)-P(2)-C(17)	109.6(2)
C(18A)-C(17)-C(18C)	17.8(10)	C(23)-P(2)-C(29)	103.0(2)
C(22)-C(17)-C(18C)	111.0(8)	C(17)-P(2)-C(29)	104.1(2)
C(18B)-C(17)-P(2)	112.5(8)	C(23)-P(2)-Pd(2)	120.44(13)
C(18A)-C(17)-P(2)	119.8(7)	C(17)-P(2)-Pd(2)	110.92(14)
C(22)-C(17)-P(2)	122.8(4)	C(29)-P(2)-Pd(2)	107.20(14)
C(18C)-C(17)-P(2)	123.2(7)	P(1)-Pd(1)-S(2)	86.76(3)
C(17)-C(18A)-C(19A)	120.3(13)	P(1)-Pd(1)-S(1)	166.71(3)
C(20)-C(19A)-C(18A)	122.1(13)	S(2)-Pd(1)-S(1)	79.98(3)
C(21)-C(20)-C(19A)	117.9(8)	P(1)-Pd(1)-I(1)	94.20(2)
C(21)-C(20)-C(19C)	125.3(15)	S(2)-Pd(1)-I(1)	170.96(3)
C(19A)-C(20)-C(19C)	19.7(16)	S(1)-Pd(1)-I(1)	99.04(2)
C(21)-C(20)-C(19B)	108.9(13)	P(1)-Pd(1)-Pd(2)	122.09(3)
C(19A)-C(20)-C(19B)	28.9(11)	S(2)-Pd(1)-Pd(2)	50.57(2)
C(19C)-C(20)-C(19B)	48.2(15)	S(1)-Pd(1)-Pd(2)	48.62(2)
C(20)-C(21)-C(22)	121.3(5)	I(1)-Pd(1)-Pd(2)	122.378(12)
C(17)-C(22)-C(21)	120.9(5)	P(2)-Pd(2)-S(1)	86.28(4)
C(28)-C(23)-C(24)	117.3(4)	P(2)-Pd(2)-S(2)	165.31(4)
C(28)-C(23)-P(2)	120.3(3)	S(1)-Pd(2)-S(2)	79.92(3)
C(24)-C(23)-P(2)	121.9(4)	P(2)-Pd(2)-I(2)	96.05(3)
C(25)-C(24)-C(23)	120.4(5)	S(1)-Pd(2)-I(2)	174.24(3)
C(26)-C(25)-C(24)	120.5(5)	S(2)-Pd(2)-I(2)	97.23(2)
C(27)-C(26)-C(25)	118.9(5)	P(2)-Pd(2)-Pd(1)	117.98(3)
C(26)-C(27)-C(28)	120.8(4)	S(1)-Pd(2)-Pd(1)	50.65(2)
C(23)-C(28)-C(27)	121.8(4)	S(2)-Pd(2)-Pd(1)	48.47(2)
C(30)-C(29)-P(2)	109.3(3)	I(2)-Pd(2)-Pd(1)	123.834(13)

C(30)-S(1)-Pd(2)	104.93(14)	Pd(1)-S(2)-Pd(2)	80.96(3)
C(30)-S(1)-Pd(1)	112.76(14)	C(18B)-C(19B)-C(20)	120(2)
Pd(2)-S(1)-Pd(1)	80.73(3)	C(19C)-C(18C)-C(17)	127.1(19)
C(14)-S(2)-Pd(1)	104.84(11)	C(17)-C(18B)-C(19B)	115.9(18)
C(14)-S(2)-Pd(2)	116.19(12)	C(18C)-C(19C)-C(20)	108(2)

Table 4. Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for ad0302. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\,h^2a^{*2}U^{11} + ... + 2\,h\,k\,a^*\,b^*\,U^{12}\,]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(2)	23(2)	21(2)	3(1)	0(1)	0(1)
C(2)	23(2)	24(2)	25(2)	-2(1)	0(1)	-2(2)
C(3)	27(2)	30(2)	36(2)	-3(2)	2(2)	-7(2)
C(4)	26(2)	37(2)	35(2)	8(2)	5(2)	-5(2)
C(5)	26(2)	46(3)	30(2)	-4(2)	11(2)	-3(2)
C(6)	24(2)	31(2)	30(2)	-4(2)	1(2)	-4(2)
C(7)	27(2)	18(2)	20(2)	-2(1)	-1(1)	2(1)
C(8)	22(2)	23(2)	29(2)	-1(2)	-1(1)	3(2)
C(9)	33(2)	25(2)	28(2)	-4(2)	-5(2)	9(2)
C(10)	46(3)	22(2)	29(2)	3(2)	4(2)	10(2)
C(11)	40(3)	36(2)	40(3)	13(2)	12(2)	5(2)
C(12)	25(2)	38(2)	41(2)	15(2)	7(2)	7(2)
C(13)	20(2)	18(2)	22(2)	-3(1)	-1(1)	3(1)
C(14)	22(2)	16(2)	20(2)	-1(1)	2(1)	1(1)
C(15)	16(2)	28(2)	28(2)	-9(2)	-1(1)	-2(2)
C(16)	25(2)	42(3)	41(2)	-22(2)	-3(2)	3(2)
C(17)	30(2)	53(3)	21(2)	-5(2)	1(2)	1(2)
C(18A)	33(9)	29(11)	21(7)	2(8)	3(6)	9(9)
C(19A)	83(14)	130(20)	31(7)	-16(12)	-13(7)	80(16)
C(20)	68(4)	100(5)	38(3)	16(3)	-10(3)	28(4)
C(21)	99(5)	64(4)	42(3)	16(3)	22(3)	22(4)
C(22)	84(4)	62(4)	42(3)	18(3)	29(3)	33(3)
C(23)	24(2)	51(3)	23(2)	-2(2)	3(2)	-2(2)
C(24)	27(3)	185(9)	35(3)	-16(4)	2(2)	9(4)
C(25)	25(3)	174(9)	50(4)	-15(4)	10(2)	6(4)
C(26)	26(2)	56(3)	60(3)	1(2)	-1(2)	2(2)
C(27)	31(2)	41(3)	46(3)	-10(2)	-9(2)	11(2)
C(28)	32(2)	41(3)	31(2)	-5(2)	-3(2)	9(2)
C(29)	27(2)	51(3)	26(2)	-16(2)	2(2)	7(2)
C(30)	29(2)	34(2)	24(2)	-10(2)	0(2)	3(2)
C(31)	42(3)	46(3)	37(2)	-19(2)	-6(2)	2(2)

C(32)	57(4)	103(6)	60(4)	-43(4)	0(3)	-13(4)
I(1)	23(1)	35(1)	22(1)	-1(1)	-3(1)	-2(1)
I(2)	29(1)	28(1)	43(1)	-6(1)	9(1)	-8(1)
P(1)	16(1)	19(1)	19(1)	0(1)	0(1)	1(1)
P(2)	20(1)	44(1)	20(1)	-6(1)	2(1)	-2(1)
Pd(1)	16(1)	17(1)	18(1)	-1(1)	0(1)	0(1)
Pd(2)	17(1)	24(1)	18(1)	-4(1)	1(1)	-1(1)
S(1)	22(1)	23(1)	23(1)	-5(1)	-1(1)	3(1)
S(2)	17(1)	20(1)	18(1)	0(1)	0(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2x 10^3)
for ad0302.

	x	y	z	U(eq)
H(2)	7188	486	5808	29
H(3)	8452	1166	5486	37
H(4)	9264	548	4907	40
H(5)	8841	-767	4650	41
H(6)	7586	-1459	4971	34
H(8)	7865	-1938	5854	29
H(9)	8163	-3134	6274	35
H(10)	6969	-3813	6640	39
H(11)	5462	-3327	6573	46
H(12)	5159	-2113	6169	41
H(13A)	5846	-1144	4854	24
H(13B)	5997	-2049	5064	24
H(14)	4519	-2061	5371	23
H(15A)	3563	-1903	4741	29
H(15B)	4309	-1326	4500	29
H(16A)	5317	-2490	4443	54
H(16B)	4368	-2657	4186	54
H(16C)	4542	-3063	4666	54
H(18A)	3755	-1696	6636	33
H(19A)	4313	-2592	7176	97
H(20)	3686	-2634	7878	83
H(21)	2449	-1797	8034	82
H(22)	1820	-941	7489	75
H(24)	867	-110	7220	99
H(25)	-741	-100	7199	100
H(26)	-1519	-424	6540	57
H(27)	-676	-693	5902	47
H(28)	916	-795	5932	42
H(29A)	2200	963	6645	42
H(29B)	2482	568	7117	42

H(30)	4008	330	6861	34
H(31A)	4511	1743	6673	50
H(31B)	3452	2021	6696	50
H(32A)	3390	1646	7456	110
H(32B)	4204	2303	7381	110
H(32C)	4438	1336	7436	110
H(19B)	4700	-1904	7319	56
H(18C)	3445	-2110	6599	30
H(18B)	3993	-1185	6713	44
H(19C)	4125	-2992	7143	42

2. Data for complex 8, Pd(Ph₂PCH₂CHEtSCH₂Ph)Cl₂

Table 1. Crystal data and structure refinement for ad0404.

Identification code	ad0404
Empirical formula	C24 H26 Cl5 P Pd S
Formula weight	661.13
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 14.7145(2) Å $\alpha = 90°$.
	b = 13.2355(2) Å $\beta = 112.7700(10)°$.
	c = 14.8381(2) Å $\gamma = 90°$.
Volume	2664.56(6) Å³
Z	4
Density (calculated)	1.648 Mg/m³
Absorption coefficient	1.349 mm⁻¹
F(000)	1328
Crystal size	0.23 x 0.20 x 0.20 mm³
Theta range for data collection	2.93 to 30.05°.
Index ranges	-20<=h<=20, -18<=k<=18, -20<=l<=20
Reflections collected	39701
Independent reflections	7770 [R(int) = 0.0873]
Completeness to theta = 30.05°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7742 and 0.7467
Refinement method	Full-matrix least-squares on F²
Data / restraints / parameters	7770 / 0 / 290
Goodness-of-fit on F²	1.020
Final R indices [I>2sigma(I)]	R1 = 0.0350, wR2 = 0.0761
R indices (all data)	R1 = 0.0497, wR2 = 0.0817
Largest diff. peak and hole	0.851 and -1.046 e.Å⁻³

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($\text{\AA}^2$x 10^3) for ad0404. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	2687(2)	10376(2)	-247(2)	17(1)
C(2)	1941(2)	10867(2)	-1010(2)	21(1)
C(3)	2184(2)	11549(2)	-1601(2)	27(1)
C(4)	3166(2)	11737(2)	-1420(2)	28(1)
C(5)	3906(2)	11257(2)	-663(2)	28(1)
C(6)	3672(2)	10577(2)	-69(2)	22(1)
C(7)	3445(2)	8819(2)	1254(2)	18(1)
C(8)	4089(2)	9325(2)	2086(2)	25(1)
C(9)	4946(2)	8847(2)	2699(2)	31(1)
C(10)	5150(2)	7868(2)	2506(2)	31(1)
C(11)	4518(2)	7369(2)	1689(2)	30(1)
C(12)	3668(2)	7844(2)	1055(2)	24(1)
C(13)	1575(2)	8552(2)	-445(2)	17(1)
C(14)	1043(2)	7815(2)	-25(2)	16(1)
C(15)	280(2)	7199(2)	-844(2)	23(1)
C(16)	-281(2)	6416(2)	-515(2)	36(1)
C(17)	566(2)	7751(2)	1701(2)	23(1)
C(18)	1582(2)	7353(2)	2268(2)	22(1)
C(19)	1806(2)	6345(2)	2176(2)	30(1)
C(20)	2751(2)	5973(2)	2698(2)	37(1)
C(21)	3471(2)	6602(3)	3321(2)	39(1)
C(22)	3258(2)	7601(2)	3426(2)	33(1)
C(23)	2319(2)	7976(2)	2899(2)	26(1)
C(24)	2685(2)	4335(2)	-459(2)	33(1)
Cl(1)	569(1)	10299(1)	2332(1)	22(1)
Cl(2)	2388(1)	11400(1)	1763(1)	24(1)
Cl(3)	2670(1)	3281(1)	251(1)	38(1)
Cl(4)	3846(1)	4486(1)	-524(1)	55(1)
Cl(5)	2390(1)	5422(1)	54(1)	66(1)
P(1)	2331(1)	9458(1)	458(1)	15(1)
Pd(1)	1443(1)	9948(1)	1290(1)	15(1)

S(1)	459(1)	8570(1)	658(1)	17(1)

Table 3. Bond lengths [Å] and angles [°] for ad0404.

C(1)-C(6)	1.394(3)	C(16)-H(16A)	0.9800
C(1)-C(2)	1.395(3)	C(16)-H(16B)	0.9800
C(1)-P(1)	1.809(2)	C(16)-H(16C)	0.9800
C(2)-C(3)	1.397(3)	C(17)-C(18)	1.499(3)
C(2)-H(2)	0.9500	C(17)-S(1)	1.846(2)
C(3)-C(4)	1.387(4)	C(17)-H(17A)	0.9900
C(3)-H(3)	0.9500	C(17)-H(17B)	0.9900
C(4)-C(5)	1.380(4)	C(18)-C(19)	1.394(4)
C(4)-H(4)	0.9500	C(18)-C(23)	1.396(4)
C(5)-C(6)	1.393(3)	C(19)-C(20)	1.393(4)
C(5)-H(5)	0.9500	C(19)-H(19)	0.9500
C(6)-H(6)	0.9500	C(20)-C(21)	1.383(5)
C(7)-C(12)	1.391(3)	C(20)-H(20)	0.9500
C(7)-C(8)	1.402(3)	C(21)-C(22)	1.381(4)
C(7)-P(1)	1.817(2)	C(21)-H(21)	0.9500
C(8)-C(9)	1.389(3)	C(22)-C(23)	1.389(4)
C(8)-H(8)	0.9500	C(22)-H(22)	0.9500
C(9)-C(10)	1.385(4)	C(23)-H(23)	0.9500
C(9)-H(9)	0.9500	C(24)-Cl(3)	1.753(3)
C(10)-C(11)	1.378(4)	C(24)-Cl(5)	1.759(3)
C(10)-H(10)	0.9500	C(24)-Cl(4)	1.759(3)
C(11)-C(12)	1.391(3)	C(24)-H(24)	1.0000
C(11)-H(11)	0.9500	Cl(1)-Pd(1)	2.4082(6)
C(12)-H(12)	0.9500	Cl(2)-Pd(1)	2.3163(6)
C(13)-C(14)	1.526(3)	P(1)-Pd(1)	2.2141(6)
C(13)-P(1)	1.820(2)	Pd(1)-S(1)	2.2916(6)
C(13)-H(13A)	0.9900		
C(13)-H(13B)	0.9900	C(6)-C(1)-C(2)	119.9(2)
C(14)-C(15)	1.532(3)	C(6)-C(1)-P(1)	122.13(17)
C(14)-S(1)	1.854(2)	C(2)-C(1)-P(1)	117.94(17)
C(14)-H(14)	1.0000	C(1)-C(2)-C(3)	119.9(2)
C(15)-C(16)	1.518(4)	C(1)-C(2)-H(2)	120.1
C(15)-H(15A)	0.9900	C(3)-C(2)-H(2)	120.1
C(15)-H(15B)	0.9900	C(4)-C(3)-C(2)	119.7(2)

C(4)-C(3)-H(3)	120.2	C(13)-C(14)-S(1)	107.34(15)
C(2)-C(3)-H(3)	120.2	C(15)-C(14)-S(1)	111.57(16)
C(5)-C(4)-C(3)	120.6(2)	C(13)-C(14)-H(14)	109.1
C(5)-C(4)-H(4)	119.7	C(15)-C(14)-H(14)	109.1
C(3)-C(4)-H(4)	119.7	S(1)-C(14)-H(14)	109.1
C(4)-C(5)-C(6)	120.1(2)	C(16)-C(15)-C(14)	115.5(2)
C(4)-C(5)-H(5)	119.9	C(16)-C(15)-H(15A)	108.4
C(6)-C(5)-H(5)	119.9	C(14)-C(15)-H(15A)	108.4
C(5)-C(6)-C(1)	119.8(2)	C(16)-C(15)-H(15B)	108.4
C(5)-C(6)-H(6)	120.1	C(14)-C(15)-H(15B)	108.4
C(1)-C(6)-H(6)	120.1	H(15A)-C(15)-H(15B)	107.5
C(12)-C(7)-C(8)	119.7(2)	C(15)-C(16)-H(16A)	109.5
C(12)-C(7)-P(1)	121.38(18)	C(15)-C(16)-H(16B)	109.5
C(8)-C(7)-P(1)	118.88(18)	H(16A)-C(16)-H(16B)	109.5
C(9)-C(8)-C(7)	119.5(2)	C(15)-C(16)-H(16C)	109.5
C(9)-C(8)-H(8)	120.3	H(16A)-C(16)-H(16C)	109.5
C(7)-C(8)-H(8)	120.3	H(16B)-C(16)-H(16C)	109.5
C(10)-C(9)-C(8)	120.3(3)	C(18)-C(17)-S(1)	114.78(16)
C(10)-C(9)-H(9)	119.8	C(18)-C(17)-H(17A)	108.6
C(8)-C(9)-H(9)	119.8	S(1)-C(17)-H(17A)	108.6
C(11)-C(10)-C(9)	120.2(2)	C(18)-C(17)-H(17B)	108.6
C(11)-C(10)-H(10)	119.9	S(1)-C(17)-H(17B)	108.6
C(9)-C(10)-H(10)	119.9	H(17A)-C(17)-H(17B)	107.5
C(10)-C(11)-C(12)	120.2(3)	C(19)-C(18)-C(23)	118.7(2)
C(10)-C(11)-H(11)	119.9	C(19)-C(18)-C(17)	120.2(2)
C(12)-C(11)-H(11)	119.9	C(23)-C(18)-C(17)	121.1(2)
C(11)-C(12)-C(7)	119.9(2)	C(20)-C(19)-C(18)	120.4(3)
C(11)-C(12)-H(12)	120.0	C(20)-C(19)-H(19)	119.8
C(7)-C(12)-H(12)	120.0	C(18)-C(19)-H(19)	119.8
C(14)-C(13)-P(1)	112.61(15)	C(21)-C(20)-C(19)	120.0(3)
C(14)-C(13)-H(13A)	109.1	C(21)-C(20)-H(20)	120.0
P(1)-C(13)-H(13A)	109.1	C(19)-C(20)-H(20)	120.0
C(14)-C(13)-H(13B)	109.1	C(22)-C(21)-C(20)	120.2(3)
P(1)-C(13)-H(13B)	109.1	C(22)-C(21)-H(21)	119.9
H(13A)-C(13)-H(13B)	107.8	C(20)-C(21)-H(21)	119.9
C(13)-C(14)-C(15)	110.58(18)	C(21)-C(22)-C(23)	119.9(3)

C(21)-C(22)-H(22)	120.1	C(7)-P(1)-C(13)	108.24(11)
C(23)-C(22)-H(22)	120.1	C(1)-P(1)-Pd(1)	119.45(8)
C(22)-C(23)-C(18)	120.8(3)	C(7)-P(1)-Pd(1)	110.62(7)
C(22)-C(23)-H(23)	119.6	C(13)-P(1)-Pd(1)	106.21(7)
C(18)-C(23)-H(23)	119.6	P(1)-Pd(1)-S(1)	87.36(2)
Cl(3)-C(24)-Cl(5)	109.19(16)	P(1)-Pd(1)-Cl(2)	89.86(2)
Cl(3)-C(24)-Cl(4)	111.18(15)	S(1)-Pd(1)-Cl(2)	174.01(2)
Cl(5)-C(24)-Cl(4)	109.75(16)	P(1)-Pd(1)-Cl(1)	172.61(2)
Cl(3)-C(24)-H(24)	108.9	S(1)-Pd(1)-Cl(1)	90.40(2)
Cl(5)-C(24)-H(24)	108.9	Cl(2)-Pd(1)-Cl(1)	93.00(2)
Cl(4)-C(24)-H(24)	108.9	C(17)-S(1)-C(14)	103.59(11)
C(1)-P(1)-C(7)	107.33(10)	C(17)-S(1)-Pd(1)	106.76(8)
C(1)-P(1)-C(13)	104.38(10)	C(14)-S(1)-Pd(1)	107.42(7)

Table 4. Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for ad0404. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	18(1)	19(1)	15(1)	2(1)	7(1)	-1(1)
C(2)	17(1)	24(1)	23(1)	3(1)	7(1)	1(1)
C(3)	26(1)	28(1)	25(1)	10(1)	8(1)	5(1)
C(4)	29(1)	28(1)	29(1)	9(1)	15(1)	1(1)
C(5)	21(1)	31(1)	34(1)	9(1)	13(1)	-3(1)
C(6)	17(1)	24(1)	22(1)	6(1)	4(1)	0(1)
C(7)	17(1)	23(1)	15(1)	4(1)	7(1)	0(1)
C(8)	23(1)	29(1)	18(1)	1(1)	3(1)	1(1)
C(9)	22(1)	46(2)	21(1)	4(1)	2(1)	3(1)
C(10)	21(1)	45(2)	28(1)	15(1)	10(1)	10(1)
C(11)	30(1)	30(1)	33(1)	10(1)	16(1)	10(1)
C(12)	25(1)	25(1)	23(1)	4(1)	11(1)	2(1)
C(13)	18(1)	20(1)	14(1)	-1(1)	7(1)	-2(1)
C(14)	18(1)	16(1)	15(1)	-1(1)	5(1)	-1(1)
C(15)	25(1)	20(1)	19(1)	-3(1)	5(1)	-5(1)
C(16)	40(2)	32(2)	32(2)	-3(1)	10(1)	-19(1)
C(17)	25(1)	26(1)	20(1)	5(1)	13(1)	-3(1)
C(18)	28(1)	26(1)	16(1)	8(1)	12(1)	2(1)
C(19)	41(2)	28(1)	22(1)	6(1)	14(1)	2(1)
C(20)	51(2)	34(2)	36(2)	14(1)	25(1)	17(1)
C(21)	32(2)	56(2)	30(2)	21(1)	15(1)	13(1)
C(22)	28(1)	48(2)	23(1)	12(1)	10(1)	-2(1)
C(23)	28(1)	31(1)	20(1)	7(1)	10(1)	-1(1)
C(24)	29(1)	33(2)	27(1)	1(1)	1(1)	-2(1)
Cl(1)	20(1)	30(1)	18(1)	-2(1)	8(1)	4(1)
Cl(2)	27(1)	19(1)	26(1)	-9(1)	9(1)	-7(1)
Cl(3)	36(1)	30(1)	44(1)	2(1)	12(1)	-1(1)
Cl(4)	42(1)	84(1)	42(1)	-1(1)	19(1)	-18(1)
Cl(5)	98(1)	33(1)	74(1)	1(1)	42(1)	13(1)
P(1)	14(1)	17(1)	13(1)	1(1)	5(1)	-1(1)
Pd(1)	15(1)	16(1)	13(1)	-1(1)	5(1)	0(1)
S(1)	16(1)	19(1)	16(1)	1(1)	6(1)	-1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($\mathring{A}^2$x 10^3)
for ad0404.

	x	y	z	U(eq)
H(2)	1270	10738	-1128	26
H(3)	1678	11882	-2123	32
H(4)	3331	12200	-1822	33
H(5)	4577	11391	-546	34
H(6)	4182	10252	456	27
H(8)	3940	9989	2230	30
H(9)	5395	9194	3253	38
H(10)	5728	7539	2939	37
H(11)	4663	6699	1559	36
H(12)	3239	7503	485	29
H(13A)	1081	8923	-997	20
H(13B)	1999	8166	-702	20
H(14)	1536	7345	437	20
H(15A)	-202	7672	-1299	27
H(15B)	621	6850	-1214	27
H(16A)	187	5964	-35	54
H(16B)	-706	6022	-1080	54
H(16C)	-687	6757	-216	54
H(17A)	346	8138	2152	27
H(17B)	112	7171	1454	27
H(19)	1311	5908	1754	36
H(20)	2900	5287	2627	45
H(21)	4114	6347	3678	46
H(22)	3752	8031	3859	40
H(23)	2177	8665	2968	31
H(24)	2177	4240	-1135	39

3. Data for complex 9, Pd(Ph₂PCH₂CHEtSCH₂C₈H₉)Cl₂

Table 1. Crystal data and structure refinement for ad0408.

Identification code	ad0408
Empirical formula	C25 H29 Cl2 P Pd S
Formula weight	569.81
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/n
Unit cell dimensions	a = 14.0290(2) Å α = 90.0000(10)°.
	b = 12.6000(2) Å β = 109.8350(10)°.
	c = 14.8700(3) Å γ = 90.0000(10)°.
Volume	2472.56(7) Å³
Z	4
Density (calculated)	1.531 Mg/m³
Absorption coefficient	1.127 mm⁻¹
F(000)	1160
Crystal size	0.35 x 0.25 x 0.25 mm³
Theta range for data collection	2.91 to 27.40°.
Index ranges	-18<=h<=16, -16<=k<=15, -19<=l<=19
Reflections collected	40943
Independent reflections	5613 [R(int) = 0.0784]
Completeness to theta = 27.40°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7660 and 0.6939
Refinement method	Full-matrix least-squares on F²
Data / restraints / parameters	5613 / 0 / 274
Goodness-of-fit on F²	1.034
Final R indices [I>2sigma(I)]	R1 = 0.0355, wR2 = 0.0802
R indices (all data)	R1 = 0.0490, wR2 = 0.0856
Largest diff. peak and hole	0.724 and -0.939 e.Å⁻³

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2x 10^3) for ad0408. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	3009(2)	4048(2)	4087(2)	23(1)
C(2)	3649(2)	3143(2)	3928(2)	23(1)
C(3)	3763(3)	3227(3)	2942(2)	30(1)
C(4)	4347(3)	2332(3)	2675(3)	41(1)
C(5)	5243(2)	1799(3)	5149(2)	28(1)
C(6)	4499(2)	1155(2)	5444(2)	23(1)
C(7)	3706(2)	626(2)	4771(2)	24(1)
C(8)	2988(2)	64(2)	5039(2)	25(1)
C(9)	3093(2)	34(2)	6002(2)	25(1)
C(10)	3892(2)	534(3)	6694(2)	27(1)
C(11)	4589(2)	1102(2)	6409(2)	25(1)
C(12)	2121(3)	-485(3)	4296(2)	35(1)
C(13)	3990(3)	476(3)	7734(3)	43(1)
C(14)	2173(2)	3019(2)	5436(2)	21(1)
C(15)	2154(2)	2775(3)	6347(2)	27(1)
C(16)	1512(2)	1990(3)	6460(2)	30(1)
C(17)	891(2)	1443(3)	5680(3)	31(1)
C(18)	905(2)	1676(3)	4777(2)	28(1)
C(19)	1545(2)	2456(2)	4648(2)	24(1)
C(20)	2396(2)	5304(2)	5401(2)	21(1)
C(21)	2974(2)	6180(2)	5845(2)	27(1)
C(22)	2503(2)	7142(3)	5856(3)	31(1)
C(23)	1464(3)	7239(3)	5429(2)	31(1)
C(24)	889(2)	6376(3)	4973(2)	29(1)
C(25)	1355(2)	5407(3)	4963(2)	25(1)
Pd(1)	4609(1)	3814(1)	6236(1)	19(1)
P(1)	3010(1)	4063(1)	5316(1)	19(1)
S(1)	4888(1)	3209(1)	4900(1)	22(1)
Cl(1)	4273(1)	4486(1)	7558(1)	26(1)
Cl(2)	6360(1)	3462(1)	7114(1)	26(1)

Table 3.   Bond lengths [Å] and angles [°] for ad0408.

C(1)-C(2)	1.519(4)
C(1)-P(1)	1.827(3)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.532(4)
C(2)-S(1)	1.847(3)
C(2)-H(2)	1.0000
C(3)-C(4)	1.524(5)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(4)-H(4C)	0.9800
C(5)-C(6)	1.501(4)
C(5)-S(1)	1.848(3)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-C(7)	1.388(4)
C(6)-C(11)	1.398(4)
C(7)-C(8)	1.395(5)
C(7)-H(7)	0.9500
C(8)-C(9)	1.390(4)
C(8)-C(12)	1.506(4)
C(9)-C(10)	1.389(4)
C(9)-H(9)	0.9500
C(10)-C(11)	1.389(5)
C(10)-C(13)	1.508(5)
C(11)-H(11)	0.9500
C(12)-H(12A)	0.9800
C(12)-H(12B)	0.9800
C(12)-H(12C)	0.9800
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-C(19)	1.397(4)

C(14)-C(15)	1.397(4)
C(14)-P(1)	1.812(3)
C(15)-C(16)	1.386(5)
C(15)-H(15)	0.9500
C(16)-C(17)	1.376(5)
C(16)-H(16)	0.9500
C(17)-C(18)	1.381(5)
C(17)-H(17)	0.9500
C(18)-C(19)	1.388(4)
C(18)-H(18)	0.9500
C(19)-H(19)	0.9500
C(20)-C(25)	1.389(4)
C(20)-C(21)	1.395(4)
C(20)-P(1)	1.811(3)
C(21)-C(22)	1.383(4)
C(21)-H(21)	0.9500
C(22)-C(23)	1.384(5)
C(22)-H(22)	0.9500
C(23)-C(24)	1.385(5)
C(23)-H(23)	0.9500
C(24)-C(25)	1.388(4)
C(24)-H(24)	0.9500
C(25)-H(25)	0.9500
Pd(1)-P(1)	2.2185(8)
Pd(1)-S(1)	2.2825(8)
Pd(1)-Cl(1)	2.3304(7)
Pd(1)-Cl(2)	2.3991(7)
C(2)-C(1)-P(1)	111.4(2)
C(2)-C(1)-H(1A)	109.4
P(1)-C(1)-H(1A)	109.4
C(2)-C(1)-H(1B)	109.4
P(1)-C(1)-H(1B)	109.4
H(1A)-C(1)-H(1B)	108.0
C(1)-C(2)-C(3)	110.9(3)
C(1)-C(2)-S(1)	107.1(2)
C(3)-C(2)-S(1)	111.7(2)

C(1)-C(2)-H(2)	109.0
C(3)-C(2)-H(2)	109.0
S(1)-C(2)-H(2)	109.0
C(4)-C(3)-C(2)	116.0(3)
C(4)-C(3)-H(3A)	108.3
C(2)-C(3)-H(3A)	108.3
C(4)-C(3)-H(3B)	108.3
C(2)-C(3)-H(3B)	108.3
H(3A)-C(3)-H(3B)	107.4
C(3)-C(4)-H(4A)	109.5
C(3)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	109.5
C(3)-C(4)-H(4C)	109.5
H(4A)-C(4)-H(4C)	109.5
H(4B)-C(4)-H(4C)	109.5
C(6)-C(5)-S(1)	114.3(2)
C(6)-C(5)-H(5A)	108.7
S(1)-C(5)-H(5A)	108.7
C(6)-C(5)-H(5B)	108.7
S(1)-C(5)-H(5B)	108.7
H(5A)-C(5)-H(5B)	107.6
C(7)-C(6)-C(11)	119.2(3)
C(7)-C(6)-C(5)	121.0(3)
C(11)-C(6)-C(5)	119.8(3)
C(6)-C(7)-C(8)	121.2(3)
C(6)-C(7)-H(7)	119.4
C(8)-C(7)-H(7)	119.4
C(9)-C(8)-C(7)	118.2(3)
C(9)-C(8)-C(12)	121.4(3)
C(7)-C(8)-C(12)	120.4(3)
C(10)-C(9)-C(8)	121.9(3)
C(10)-C(9)-H(9)	119.0
C(8)-C(9)-H(9)	119.0
C(9)-C(10)-C(11)	118.8(3)
C(9)-C(10)-C(13)	120.5(3)
C(11)-C(10)-C(13)	120.7(3)
C(10)-C(11)-C(6)	120.6(3)

C(10)-C(11)-H(11)	119.7
C(6)-C(11)-H(11)	119.7
C(8)-C(12)-H(12A)	109.5
C(8)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(8)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
C(10)-C(13)-H(13A)	109.5
C(10)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(10)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(19)-C(14)-C(15)	119.2(3)
C(19)-C(14)-P(1)	122.1(2)
C(15)-C(14)-P(1)	118.7(2)
C(16)-C(15)-C(14)	120.0(3)
C(16)-C(15)-H(15)	120.0
C(14)-C(15)-H(15)	120.0
C(17)-C(16)-C(15)	120.5(3)
C(17)-C(16)-H(16)	119.7
C(15)-C(16)-H(16)	119.7
C(16)-C(17)-C(18)	119.9(3)
C(16)-C(17)-H(17)	120.0
C(18)-C(17)-H(17)	120.0
C(17)-C(18)-C(19)	120.5(3)
C(17)-C(18)-H(18)	119.7
C(19)-C(18)-H(18)	119.7
C(18)-C(19)-C(14)	119.8(3)
C(18)-C(19)-H(19)	120.1
C(14)-C(19)-H(19)	120.1
C(25)-C(20)-C(21)	119.9(3)
C(25)-C(20)-P(1)	119.8(2)
C(21)-C(20)-P(1)	120.2(2)
C(22)-C(21)-C(20)	119.7(3)
C(22)-C(21)-H(21)	120.1

C(20)-C(21)-H(21)	120.1
C(21)-C(22)-C(23)	120.3(3)
C(21)-C(22)-H(22)	119.9
C(23)-C(22)-H(22)	119.9
C(22)-C(23)-C(24)	120.2(3)
C(22)-C(23)-H(23)	119.9
C(24)-C(23)-H(23)	119.9
C(23)-C(24)-C(25)	119.9(3)
C(23)-C(24)-H(24)	120.1
C(25)-C(24)-H(24)	120.1
C(24)-C(25)-C(20)	120.1(3)
C(24)-C(25)-H(25)	120.0
C(20)-C(25)-H(25)	120.0
P(1)-Pd(1)-S(1)	86.95(3)
P(1)-Pd(1)-Cl(1)	90.99(3)
S(1)-Pd(1)-Cl(1)	177.47(3)
P(1)-Pd(1)-Cl(2)	174.88(3)
S(1)-Pd(1)-Cl(2)	88.00(3)
Cl(1)-Pd(1)-Cl(2)	94.08(3)
C(20)-P(1)-C(14)	106.32(13)
C(20)-P(1)-C(1)	103.90(14)
C(14)-P(1)-C(1)	108.09(14)
C(20)-P(1)-Pd(1)	118.98(10)
C(14)-P(1)-Pd(1)	112.96(10)
C(1)-P(1)-Pd(1)	105.81(10)
C(2)-S(1)-C(5)	103.38(15)
C(2)-S(1)-Pd(1)	107.60(10)
C(5)-S(1)-Pd(1)	105.16(11)

Table 4. Anisotropic displacement parameters ($\text{Å}^2 \times 10^3$) for ad0408. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\, h^2a^{*2}U^{11} + ... + 2\,h\,k\,a^*\,b^*\,U^{12}\,]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	23(2)	24(2)	20(2)	4(1)	8(1)	2(1)
C(2)	24(2)	24(2)	22(2)	1(1)	9(1)	-1(1)
C(3)	35(2)	34(2)	24(2)	0(1)	14(1)	-2(2)
C(4)	50(2)	49(2)	32(2)	-7(2)	24(2)	1(2)
C(5)	28(2)	23(2)	35(2)	1(1)	16(1)	8(1)
C(6)	26(2)	17(1)	27(2)	0(1)	10(1)	7(1)
C(7)	33(2)	19(2)	22(2)	1(1)	10(1)	8(1)
C(8)	29(2)	15(2)	27(2)	2(1)	4(1)	5(1)
C(9)	26(2)	18(2)	34(2)	6(1)	13(1)	5(1)
C(10)	34(2)	25(2)	23(2)	3(1)	11(1)	9(1)
C(11)	27(2)	20(2)	25(2)	0(1)	6(1)	4(1)
C(12)	41(2)	21(2)	35(2)	0(1)	4(2)	-1(2)
C(13)	53(2)	47(2)	29(2)	3(2)	15(2)	-1(2)
C(14)	20(2)	19(2)	25(2)	2(1)	8(1)	6(1)
C(15)	26(2)	28(2)	25(2)	2(1)	8(1)	1(1)
C(16)	28(2)	34(2)	31(2)	12(2)	14(1)	6(2)
C(17)	20(2)	24(2)	47(2)	7(2)	11(1)	0(1)
C(18)	20(2)	22(2)	40(2)	-6(1)	7(1)	2(1)
C(19)	22(2)	26(2)	24(2)	0(1)	7(1)	4(1)
C(20)	23(2)	20(2)	23(2)	4(1)	11(1)	1(1)
C(21)	21(2)	24(2)	37(2)	4(1)	12(1)	3(1)
C(22)	27(2)	19(2)	48(2)	4(1)	14(2)	0(1)
C(23)	35(2)	20(2)	43(2)	10(1)	18(2)	11(1)
C(24)	22(2)	32(2)	32(2)	8(1)	9(1)	6(1)
C(25)	23(2)	26(2)	27(2)	2(1)	7(1)	2(1)
Pd(1)	18(1)	18(1)	21(1)	0(1)	5(1)	2(1)
P(1)	19(1)	19(1)	20(1)	2(1)	7(1)	3(1)
S(1)	21(1)	22(1)	26(1)	1(1)	11(1)	1(1)
Cl(1)	29(1)	28(1)	18(1)	-5(1)	4(1)	7(1)
Cl(2)	18(1)	26(1)	29(1)	0(1)	1(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2x 10^3) for ad0408.

	x	y	z	U(eq)
H(1A)	2305	3971	3642	27
H(1B)	3278	4730	3947	27
H(2)	3314	2453	3972	27
H(3A)	3078	3259	2453	36
H(3B)	4108	3905	2912	36
H(4A)	5054	2343	3104	62
H(4B)	4325	2427	2014	62
H(4C)	4039	1649	2735	62
H(5A)	5315	1476	4568	33
H(5B)	5913	1761	5662	33
H(7)	3652	646	4117	29
H(9)	2605	-339	6192	31
H(11)	5132	1458	6874	30
H(12A)	2332	-1199	4180	52
H(12B)	1922	-77	3700	52
H(12C)	1544	-538	4524	52
H(13A)	4322	-191	8008	64
H(13B)	3315	505	7792	64
H(13C)	4396	1075	8079	64
H(15)	2582	3148	6889	32
H(16)	1501	1828	7080	36
H(17)	452	906	5763	37
H(18)	473	1298	4240	34
H(19)	1555	2608	4026	29
H(21)	3687	6115	6140	32
H(22)	2895	7740	6157	37
H(23)	1143	7899	5448	37
H(24)	178	6448	4669	35
H(25)	962	4813	4656	31

4. Data for complex 10, Pd(Ph₂PCH₂CHEtSCH₂C₁₀H₇)Cl₂

Table 1. Crystal data and structure refinement for 2005src1625

Identification code	**2005src1625**	
Empirical formula	C₂₇H₂₇Cl₂PPdS	
Formula weight	591.82	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	$P-1$	
Unit cell dimensions	a = 9.9134(3) Å	α = 102.154(2)°
	b = 11.6302(5) Å	β = 99.477(2)°
	c = 11.7817(4) Å	γ = 103.735(2)°
Volume	1256.57(8) Å³	
Z	2	
Density (calculated)	1.564 Mg / m³	
Absorption coefficient	1.112 mm⁻¹	
$F(000)$	600	
Crystal	Slab; Light Orange	
Crystal size	0.18 × 0.16 × 0.05 mm³	
θ range for data collection	3.03 – 27.48°	
Index ranges	$-12 \le h \le 12, -15 \le k \le 15, -15 \le l \le 15$	
Reflections collected	24762	
Independent reflections	5748 [R_{int} = 0.0408]	
Completeness to θ = 27.48°	99.7 %	
Absorption correction	Semi–empirical from equivalents	
Max. and min. transmission	0.9465 and 0.8250	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5748 / 625 / 420	
Goodness-of-fit on F^2	1.056	
Final R indices [$F^2 > 2\sigma(F^2)$]	$R1$ = 0.0341, $wR2$ = 0.0745	
R indices (all data)	$R1$ = 0.0437, $wR2$ = 0.0785	
Extinction coefficient	0.0047(6)	
Largest diff. peak and hole	0.515 and –0.633 e Å⁻³	

Diffractometer: *Nonius KappaCCD* area detector (φ scans and ω scans to fill *asymmetric unit* sphere). **Cell determination:** DirAx (Duisenberg, A.J.M.(1992). J. Appl. Cryst. 25, 92-96.) **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction and cell refinement:** *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. 276: *Macromolecular Crystallography*, part A, pp. 307-326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). **Absorption correction:** *SADABS Version 2.10.* (G. M. Sheldrick (2003)) Bruker AXS Inc., Madison, Wisconsin, USA. **Structure solution:** *SHELXS97* (G. M. Sheldrick, Acta Cryst. (1990) A46 467-473). **Structure refinement:** *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** *ORTEP3 for Windows* (L. J. Farrugia, J. Appl. Crystallogr. 1997, 30, 565).

Special details:

The ligand is disordered in the naphthyl and ethyl groups.

Table 2. Atomic coordinates [$\times\ 10^4$], equivalent isotropic displacement parameters [$\text{Å}^2 \times 10^3$] and site occupancy factors. U_{eq} is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U_{eq}	S.o.f.
C1	10381(3)	2486(3)	5889(2)	45(1)	1
C2	9306(3)	2452(3)	4777(3)	61(1)	1
C3	9946(9)	3187(9)	3999(8)	50(2)	0.515(9)
C4	10916(8)	2530(7)	3443(5)	54(2)	0.515(9)
C5	8662(3)	3075(3)	7536(2)	42(1)	1
C6	7210(3)	2895(3)	7277(3)	67(1)	1
C7	6642(4)	3843(3)	7683(4)	86(1)	1
C8	7516(4)	4959(3)	8351(3)	71(1)	1
C9	8964(4)	5143(3)	8623(3)	68(1)	1
C10	9532(3)	4208(3)	8220(3)	57(1)	1
C11	10764(3)	1851(2)	8162(2)	35(1)	1
C12	10368(3)	1640(3)	9192(2)	42(1)	1
C13	11379(3)	1655(3)	10162(2)	44(1)	1
C14	12790(3)	1902(3)	10118(2)	48(1)	1
C15	13192(3)	2120(3)	9103(3)	58(1)	1
C16	12185(3)	2083(3)	8118(3)	48(1)	1
C17	6462(5)	799(5)	3423(4)	41(1)	0.658(5)
C18	6551(4)	1521(4)	2504(3)	34(1)	0.658(5)
C19	6756(15)	966(8)	1442(8)	47(2)	0.658(5)
C20	6938(19)	1672(9)	554(9)	64(2)	0.658(5)
C21	6865(6)	2825(7)	797(6)	70(2)	0.658(5)
C22	6640(30)	3353(15)	1830(17)	63(2)	0.658(5)
C23	6560(15)	4617(10)	2075(11)	98(3)	0.658(5)
C24	6369(9)	5142(9)	3146(12)	114(3)	0.658(5)
C25	6190(11)	4528(8)	4057(10)	99(3)	0.658(5)
C26	6154(18)	3354(11)	3788(9)	77(3)	0.658(5)
C27	6463(6)	2732(5)	2740(5)	44(1)	0.658(5)
P1	9424(1)	1881(1)	6928(1)	34(1)	1
S1	8238(2)	713(2)	4145(2)	35(1)	0.658(5)
Cl1	6193(1)	−1631(1)	4500(1)	48(1)	1
Cl2	7268(1)	−387(1)	7484(1)	48(1)	1
Pd1	7801(1)	179(1)	5818(1)	33(1)	1
C33	10138(10)	2661(9)	3720(8)	49(2)	0.485(9)
C34	10709(12)	4052(9)	3992(8)	108(4)	0.485(9)
C37	6346(8)	1414(10)	3883(9)	44(2)	0.342(5)
C38	6360(9)	2492(8)	3342(8)	42(2)	0.342(5)
C39	6250(30)	3530(16)	4029(12)	45(3)	0.342(5)
C40	6154(19)	4579(15)	3484(11)	56(3)	0.342(5)
C41	6370(20)	4528(13)	2399(11)	44(3)	0.342(5)
C42	6590(50)	3510(20)	1770(20)	39(3)	0.342(5)
C43	6801(9)	3417(10)	541(8)	52(2)	0.342(5)
C44	6966(9)	2376(10)	−101(9)	58(2)	0.342(5)
C45	6880(40)	1297(15)	334(15)	50(3)	0.342(5)
C46	6730(30)	1355(13)	1442(14)	40(3)	0.342(5)
C47	6563(11)	2435(9)	2189(8)	39(2)	0.342(5)
S37	8113(4)	1142(4)	4287(4)	31(1)	0.342(5)

Table 3. Bond lengths [Å] and angles [°].

C1–C2	1.534(4)	C21–C22	1.323(19)
C1–P1	1.823(3)	C22–C27	1.425(10)
C2–C3	1.495(9)	C22–C23	1.461(17)
C2–C33	1.631(10)	C23–C24	1.345(12)
C2–S37	1.613(6)	C24–C25	1.421(13)
C2–S1	1.963(4)	C25–C26	1.326(13)
C3–C4	1.512(10)	C26–C27	1.412(10)
C5–C6	1.377(4)	P1–Pd1	2.2187(7)
C5–C10	1.383(4)	S1–Pd1	2.265(2)
C5–P1	1.808(3)	Cl1–Pd1	2.3660(7)
C6–C7	1.386(5)	Cl2–Pd1	2.2986(7)
C7–C8	1.366(5)	Pd1–S37	2.339(4)
C8–C9	1.372(5)	C33–C34	1.525(13)
C9–C10	1.374(5)	C37–C38	1.520(11)
C11–C16	1.382(4)	C37–S37	1.857(8)
C11–C12	1.387(4)	C38–C39	1.345(15)
C11–P1	1.813(2)	C38–C47	1.396(10)
C12–C13	1.385(4)	C39–C40	1.507(17)
C13–C14	1.371(4)	C40–C41	1.322(13)
C14–C15	1.375(4)	C41–C42	1.34(2)
C15–C16	1.386(4)	C42–C47	1.433(13)
C17–C18	1.506(5)	C42–C43	1.48(2)
C17–S1	1.859(5)	C43–C44	1.347(13)
C18–C19	1.353(8)	C44–C45	1.442(17)
C18–C27	1.403(6)	C45–C46	1.327(19)
C19–C20	1.467(12)	C46–C47	1.435(14)
C20–C21	1.333(11)		

C2–C1–P1	109.33(19)	C13–C14–C15	119.8(3)
C3–C2–C1	113.6(4)	C14–C15–C16	120.7(3)
C1–C2–C33	109.3(4)	C11–C16–C15	119.9(3)
C3–C2–S37	124.4(5)	C18–C17–S1	112.5(3)
C1–C2–S37	111.3(3)	C19–C18–C27	120.9(5)
C33–C2–S37	107.6(4)	C19–C18–C17	117.2(5)
C3–C2–S1	121.6(5)	C27–C18–C17	121.8(4)
C1–C2–S1	104.2(2)	C18–C19–C20	118.6(6)
C33–C2–S1	100.6(4)	C21–C20–C19	119.7(8)
C2–C3–C4	107.0(6)	C22–C21–C20	121.2(7)
C6–C5–C10	118.8(3)	C21–C22–C27	122.3(11)
C6–C5–P1	120.6(2)	C21–C22–C23	120.3(9)
C10–C5–P1	120.6(2)	C27–C22–C23	117.4(14)
C5–C6–C7	120.2(3)	C24–C23–C22	119.0(11)
C8–C7–C6	120.4(3)	C23–C24–C25	123.9(9)
C7–C8–C9	119.8(3)	C26–C25–C24	116.4(10)
C8–C9–C10	120.0(3)	C25–C26–C27	124.7(11)
C9–C10–C5	120.8(3)	C18–C27–C22	117.1(9)
C16–C11–C12	119.1(2)	C18–C27–C26	124.8(7)
C16–C11–P1	121.4(2)	C22–C27–C26	118.0(10)
C12–C11–P1	119.5(2)	C5–P1–C11	105.03(12)
C13–C12–C11	120.6(3)	C5–P1–C1	104.33(14)
C14–C13–C12	120.0(3)	C11–P1–C1	106.55(12)

C5–P1–Pd1	113.32(9)	C39–C38–C37	118.1(10)
C11–P1–Pd1	121.32(9)	C47–C38–C37	121.2(8)
C1–P1–Pd1	104.91(10)	C38–C39–C40	118.8(11)
C17–S1–C2	102.1(2)	C41–C40–C39	119.7(13)
C17–S1–Pd1	101.85(17)	C42–C41–C40	119.5(12)
C2–S1–Pd1	101.87(13)	C41–C42–C47	123.8(15)
P1–Pd1–S1	90.14(6)	C41–C42–C43	120.5(10)
P1–Pd1–Cl2	91.45(2)	C47–C42–C43	115.7(17)
S1–Pd1–Cl2	177.85(6)	C44–C43–C42	120.1(11)
P1–Pd1–S37	82.95(11)	C43–C44–C45	122.6(11)
S1–Pd1–S37	13.37(8)	C46–C45–C44	118.9(13)
Cl2–Pd1–S37	166.13(11)	C45–C46–C47	121.7(12)
P1–Pd1–Cl1	174.78(3)	C38–C47–C42	117.0(12)
S1–Pd1–Cl1	85.31(6)	C38–C47–C46	122.2(9)
Cl2–Pd1–Cl1	93.16(3)	C42–C47–C46	120.8(12)
S37–Pd1–Cl1	93.08(11)	C2–S37–C37	108.4(4)
C34–C33–C2	103.8(8)	C2–S37–Pd1	111.3(2)
C38–C37–S37	114.8(6)	C37–S37–Pd1	101.3(3)
C39–C38–C47	120.7(9)		

Table 4. Anisotropic displacement parameters [$\text{Å}^2 \times 10^3$]. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + \cdots + 2\,h\,k\,a^*\,b^*\,U^{12}]$.

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C1	32(1)	57(2)	46(2)	28(1)	1(1)	5(1)
C2	34(2)	90(2)	61(2)	53(2)	−1(1)	3(2)
C3	31(4)	77(6)	57(5)	42(5)	9(3)	24(4)
C4	43(4)	86(5)	43(3)	32(3)	10(3)	25(3)
C5	38(1)	39(2)	46(2)	14(1)	−5(1)	13(1)
C6	43(2)	43(2)	95(3)	−6(2)	−15(2)	18(1)
C7	48(2)	55(2)	130(4)	−11(2)	−17(2)	28(2)
C8	65(2)	49(2)	86(3)	−2(2)	−11(2)	29(2)
C9	62(2)	41(2)	80(2)	−5(2)	−13(2)	14(2)
C10	42(2)	48(2)	66(2)	3(2)	−7(1)	9(1)
C11	35(1)	35(1)	32(1)	11(1)	−2(1)	9(1)
C12	37(1)	49(2)	37(1)	15(1)	1(1)	7(1)
C13	50(2)	46(2)	32(1)	15(1)	−3(1)	8(1)
C14	46(2)	52(2)	39(2)	13(1)	−11(1)	12(1)
C15	35(2)	86(3)	52(2)	28(2)	−2(1)	18(2)
C16	37(2)	69(2)	40(2)	21(1)	2(1)	17(1)
C17	37(2)	48(3)	36(2)	16(2)	−1(2)	11(2)
C18	28(2)	42(2)	31(2)	12(2)	0(2)	9(2)
C19	49(3)	54(4)	38(3)	9(3)	6(2)	21(4)
C20	42(4)	106(7)	32(4)	20(5)	1(4)	3(7)
C21	36(3)	101(5)	72(4)	64(4)	−10(3)	−4(3)
C22	28(4)	63(5)	98(5)	48(4)	−6(4)	6(4)
C23	40(4)	71(5)	175(9)	59(5)	−4(7)	−2(3)
C24	49(4)	68(5)	222(10)	37(5)	17(6)	19(4)
C25	65(4)	59(4)	156(8)	−9(5)	32(7)	13(4)
C26	60(6)	57(4)	98(6)	−10(4)	26(6)	10(4)
C27	28(2)	44(3)	55(4)	10(3)	4(3)	9(2)
P1	30(1)	39(1)	33(1)	14(1)	−1(1)	9(1)
S1	35(1)	42(1)	28(1)	12(1)	3(1)	11(1)
Cl1	35(1)	59(1)	37(1)	2(1)	2(1)	2(1)
Cl2	49(1)	56(1)	31(1)	19(1)	0(1)	−2(1)
Pd1	30(1)	42(1)	26(1)	12(1)	1(1)	9(1)
C33	34(5)	74(6)	49(5)	41(5)	6(3)	13(4)
C34	132(9)	81(6)	79(6)	49(5)	−3(6)	−37(6)
C37	25(4)	60(6)	50(5)	30(5)	2(4)	10(4)
C38	29(4)	56(5)	44(5)	21(4)	9(4)	12(4)
C39	40(6)	58(7)	32(4)	16(5)	2(4)	6(7)
C40	47(6)	69(7)	65(6)	28(6)	24(6)	24(6)
C41	48(8)	55(6)	38(5)	20(4)	12(4)	24(6)
C42	23(7)	41(6)	56(6)	26(4)	1(5)	6(6)
C43	20(4)	84(6)	50(5)	24(4)	5(4)	8(4)
C44	38(5)	93(7)	48(5)	30(4)	10(4)	16(5)
C45	42(7)	67(7)	28(6)	6(5)	−6(6)	4(8)
C46	31(5)	48(7)	41(5)	21(5)	−5(4)	13(7)
C47	27(4)	59(5)	37(5)	21(4)	8(4)	15(4)
S37	28(1)	43(2)	25(1)	13(1)	5(1)	12(1)

Table 5. Hydrogen coordinates [$\times 10^4$] and isotropic displacement parameters [$\mathring{A}^2 \times 10^3$].

Atom	x	y	z	U_{eq}	S.o.f.
H1A	10969	3340	6274	54	1
H1B	11023	1987	5660	54	1
H2	8615	2868	5083	73	1
H3A	10496	4025	4478	60	0.515(9)
H3B	9188	3250	3373	60	0.515(9)
H4A	11725	2563	4064	81	0.515(9)
H4B	11266	2927	2851	81	0.515(9)
H4C	10385	1672	3054	81	0.515(9)
H6	6595	2120	6819	80	1
H7	5639	3715	7495	103	1
H8	7122	5606	8626	85	1
H9	9573	5917	9090	81	1
H10	10536	4341	8413	68	1
H12	9394	1483	9232	50	1
H13	11095	1495	10858	53	1
H14	13486	1922	10786	57	1
H15	14171	2298	9076	69	1
H16	12471	2217	7415	58	1
H17A	5836	−42	3038	49	0.658(5)
H17B	6025	1185	4042	49	0.658(5)
H19	6783	138	1275	56	0.658(5)
H20	7107	1308	−190	77	0.658(5)
H21	6978	3276	217	84	0.658(5)
H23	6643	5062	1487	117	0.658(5)
H24	6353	5974	3302	137	0.658(5)
H25	6102	4937	4817	119	0.658(5)
H26	5903	2898	4340	92	0.658(5)
H33A	10926	2273	3745	59	0.485(9)
H33B	9477	2319	2927	59	0.485(9)
H34A	9923	4398	3775	162	0.485(9)
H34B	11426	4261	3531	162	0.485(9)
H34C	11144	4390	4845	162	0.485(9)
H37A	5689	665	3308	53	0.342(5)
H37B	5961	1553	4608	53	0.342(5)
H39	6222	3601	4843	54	0.342(5)
H40	5941	5274	3918	67	0.342(5)
H41	6374	5205	2068	53	0.342(5)
H43	6822	4095	206	63	0.342(5)
H44	7147	2352	−872	70	0.342(5)
H45	6924	557	−164	60	0.342(5)
H46	6731	662	1749	48	0.342(5)